諸外国のパテントリンケージ制度に関する調査
報告書

令和４年１１月

一般財団法人知的財産研究教育財団
知的財産研究所

本報告書は、一般財団法人知的財産研究教育財団の小林徹常務理事、同財団　知的財産研究所の大屋静男研究部長、安立幸司主任研究員、井手李咲主任研究員が担当した。

目次

第 1 章　はじめに

パテントリンケージ制度とは、薬事当局における後発医薬品の製造販売承認にあたり、先発特許権への侵害有無を確認することであり、先発医薬品会社と後発医薬品会社との競争を調整する仕組みである。

医療用医薬品の薬事当局による規制は国際的であり、パテントリンケージ制度も、米国をはじめとする先進諸国を中心に導入され、各国独自の制度によって運用されている。特に米国では、世界に先駆けて 1984 年に先発医薬品会社・後発医薬品会社のバランスを考慮した法律（ハッチ・ワックスマン法）が整備され、透明性かつ専門性の高い実務が行われている。

また、11 か国により署名され、中国、及び台湾が加入申請をしており、韓国が加入を検討している環太平洋パートナーシップに関する包括的及び先進的な協定（CPTPP 協定）第 18・53 条には、パテントリンケージ制度が規定されている。

本調査において、米国、カナダ、中国、韓国、及び台湾のパテントリンケージ制度と CPTPP 協定第 18・53 条との関係についてまとめた。

第 2 章　経済連携協定におけるパテントリンケージ制度

いくつかの経済連携協定においてパテントリンケージ制度を規定されている。以下、本調査における調査国のパテントリンケージ制度と関連する経済連携協定について、加入国の多い順に I. 環太平洋パートナーシップに関する包括的及び先進的な協定（Comprehensive and Progressive Agreement for Trans-Pacific Partnership (CPTPP)）、II. カナダ・米国・メキシコ協定（Canada-United States-Mexico Agreement (CUSMA)（新 NAFTA（North America Free Trade Agreement（北米自由協定））））、III. 米中経済貿易協定、IV. 米韓自由貿易協定におけるパテントリンケージ制度の規定を紹介する。

I. CPTPP

1. 加入国[1]

環太平洋パートナーシップ（TPP）協定とは、オーストラリア、ブルネイ、カナダ、チリ、日本、マレーシア、メキシコ、ニュージーランド、ペルー、シンガポール、米国及びベトナムの合計 12 カ国で高い水準の、野心的で、包括的な、バランスの取れた協定を目指し交渉が進められてきた経済連携協定である。2015 年 10 月のアトランタ閣僚会合において、大筋合意に至り、2016 年 2 月、ニュージーランドで署名された。日本は 2017 年 1 月に国内手続の完了を寄託国であるニュージーランドに通報し、TPP 協定を締結した。その後、2017 年 1 月に米国が離脱を表明したことを受けて、米国以外の 11 カ国の間で協定の早期発効を目指して協議を行い、2017 年 11 月のダナンでの閣僚会合で 11 カ国による TPP につき大筋合意に至り、2018 年 3 月、チリで「環太平洋パートナーシップに関する包括的及び先進的な協定（TPP11 協定：CPTPP）」が署名された。メキシコ、日本、シンガポール、ニュージーランド、カナダ、オーストラリア、ベトナムの 7 カ国が国内手続を完了した旨の通報を寄託国ニュージーランドに行っており、2018 年 12 月 30 日に発効した。2021 年 7 月、ペルーが国内手続を完了した旨を寄託国ニュージーランドに通報し、2021 年 9 月 19 日に発効した。

CPTPP 協定署名国：

オーストラリア、ブルネイ、カナダ、チリ、日本、マレーシア、メキシコ、ニュージーランド、ペルー、シンガポール、ベトナム

CPTPP 協定発効国（2022 年 8 月現在 8 か国）：

オーストラリア、カナダ、日本、メキシコ、ニュージーランド、ペルー、シンガポール、ベトナム

本報告書の調査対象国の CPTPP への加入状況は以下のとおりである。

米国：未加入（2017 年 1 月に TPP 離脱の大統領覚書を発出）

カナダ：加入（2018 年 12 月発効）

中国：未加入（2021 年 9 月加入申請）

[1] 環太平洋パートナーシップに関する包括的及び先進的な協定（TPP11 協定）（令和 4 年 10 月 外務省経済局）（外務省ウェブサイト）（最終アクセス日：2022 年 11 月 8 日、以後特記しない限り同じ）
https://www.mofa.go.jp/mofaj/files/000022863.pdf

韓国[2]：未加入（2022 年 4 月、韓国企画財政部が「CPTPP 加入推進計画」を議決）
台湾：未加入（2021 年 9 月加入申請）

第 18・53 条にパテントリンケージ制度が規定されている。

2. CPTPP 協定第 18・53 条

第18・53条　特定の医薬品の販売に関する措置[3]
１　締約国は、医薬の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。
(a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度
注　この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会
注　この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。
(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）
２　締約国は、１の規定の実施に代えて、特許権者若しくは販売承認の申請者により販売承認を行う当局に提出された特許に関連する情報に基づき又は販売承認を行う当局と特許官庁との間の直接の調整に基づき、当該特許権者の承諾又は黙認を得ない限り、請求の範囲に記載されている特許の対象である医薬品を販売しようとする第三者に販売承認を与えない司法上の手続以外の制度を採用し、又は維持する。

パテントリンケージ制度について、第 18・53 条第 1 項で、後発医薬品の販売前に特許権者に通知する制度、及び侵害救済措置が規定されている。また、第 18・53 条第 2 項で、第 1 項の代替として司法上の手続き以外の制度の採用・維持が規定されている。

[2] CPTPP 加入推進計画を対外経済長官会議で議決（ビジネス短信 2022 年 4 月 19 日）ジェトロウェブサイト
https://www.jetro.go.jp/biznews/2022/04/3d2e3a7da9e9b304.html
[3] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf

II. CUSMA

1. 加入国

NAFTA (North America Free Trade Agreement：北米自由貿易協定)は、米国、カナダ、メキシコの 3 か国で結ばれた経済連携協定である。1992 年 12 月 17 日に署名され、1994 年に発効した。2017 年 8 月 20 日の再交渉開始後、2018 年 9 月 30 日に CUSMA (Canada-United States-Mexico Agreement：カナダ・米国・メキシコ協定)として 3 か国間の枠組みを維持した貿易協定交渉が妥結した。カナダが 2020 年 4 月 2 日、メキシコが 2020 年 4 月 4 日、米国が 2020 年 4 月 24 日に国内手続き完了を通知した[4]。

第 20.50 条にパテントリンケージ制度が規定されている。

2. CUSMA Article 20.50[5]

Article 20.50: Measures Relating to the Marketing of Certain Pharmaceutical Products

1. If a Party permits, as a condition of approving the marketing of a pharmaceutical product, persons, other than the person originally submitting the safety and efficacy information, to rely on evidence or information concerning the safety and efficacy of a product that was previously approved, such as evidence of prior marketing approval by the Party or in another territory, that Party shall provide:

(a) a system to provide notice to a patent holder or to allow for a patent holder to be notified prior to the marketing of such a pharmaceutical product, that such other person is seeking to market that product during the term of an applicable patent claiming the approved product or its approved method of use;

(b) adequate time and sufficient opportunity for such a patent holder to seek, prior to the marketing of an allegedly infringing product, available remedies in subparagraph (c); and

(c) procedures, such as judicial or administrative proceedings, and expeditious remedies, such as preliminary injunctions or equivalent effective provisional measures, for the timely resolution of disputes concerning the validity or infringement of an applicable patent claiming an approved pharmaceutical product or its approved method of use.

2. Further to paragraph 1, that Party may also provide:

(a) effective rewards for a successful assertion of the invalidity or non-infringement of the applicable patent; and

[4] カナダ WTO・他協定加盟状況（ジェトロウェブサイト）
https://www.jetro.go.jp/world/n_america/ca/trade_01.html

[5] Canada-United States-Mexico Agreement (CUSMA) – Chapter 20 – Intellectual Property Rights（Government of Canada ウェブサイト）
https://www.international.gc.ca/trade-commerce/trade-agreements-accords-commerciaux/agr-acc/cusma-aceum/text-texte/20.aspx?lang=eng

(b) procedures, consistent with its obligations under this Chapter, to promote transparency by providing information regarding applicable patents and relevant periods of exclusivity for pharmaceutical products that have been approved in that Party.

3. CPTPP との比較

パテントリンケージ条項に関する CPTPP と CUSMA との比較を表 1 に示す。

表 1 パテントリンケージ条項に関する CPTPP と CUSMA との比較

CPTPP[6]	CUSMA[7]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	Article 20.50: Measures Relating to the Marketing of Certain Pharmaceutical Products 1. If a Party permits, as a condition of approving the marketing of a pharmaceutical product, persons, other than the person originally submitting the safety and efficacy information, to rely on evidence or information concerning the safety and efficacy of a product that was previously approved, such as evidence of prior marketing approval by the Party or in another territory, that Party shall provide: (a) a system to provide notice to a patent holder or to allow for a patent holder to be notified prior to the marketing of such a pharmaceutical product, that such other person is seeking to market that product during the term of an applicable patent claiming the approved product or its approved method of use;
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	(b) adequate time and sufficient opportunity for such a patent holder to seek, prior to the marketing of an allegedly infringing product, available remedies in subparagraph (c); and

[6] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf
[7] Canada-United States-Mexico Agreement (CUSMA) – Chapter 20 – Intellectual Property Rights（Government of Canada ウェブサイト）
https://www.international.gc.ca/trade-commerce/trade-agreements-accords-commerciaux/agr-acc/cusma-aceum/text-texte/20.aspx?lang=eng

(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	(c) procedures, such as judicial or administrative proceedings, and expeditious remedies, such as preliminary injunctions or equivalent effective provisional measures, for the timely resolution of disputes concerning the validity or infringement of an applicable patent claiming an approved pharmaceutical product or its approved method of use.
	2. Further to paragraph 1, that Party may also provide: (a) effective rewards for a successful assertion of the invalidity or non-infringement of the applicable patent; and (b) procedures, consistent with its obligations under this Chapter, to promote transparency by providing information regarding applicable patents and relevant periods of exclusivity for pharmaceutical products that have been approved in that Party.
２ 締約国は、１の規定の実施に代えて、特許権者若しくは販売承認の申請者により販売承認を行う当局に提出された特許に関連する情報に基づき又は販売承認を行う当局と特許官庁との間の直接の調整に基づき、当該特許権者の承諾又は黙認を得ない限り、請求の範囲に記載されている特許の対象である医薬品を販売しようとする第三者に販売承認を与えない司法上の手続以外の制度を採用し、又は維持する。	

III. 米中経済貿易協定

1. 加入国

2020 年 1 月 15 日、米国と中国は、米中経済貿易協定（Economic and Trade Agreement between the Government of the United States of America and the Government of the People's Republic of China）の第 1 弾（Phase 1）[8]に署名を行い、2020 年 2 月 14 日に発効した。当該経済貿易協定は、(1) 知的財産権、(2) 技術移転、(3) 食品・農産品の貿易、(4) 金融サービス、(5) マクロ経済政策、為替レート関連および透明性、(6) 貿易の拡大、(7) 2 国間の評価と紛争解決、(8) 最終規定の 8 章から構成される。米国が中国に求めていた知的財産の保護と貿易赤字の削減に応える構成となっている[9]。

当該経済貿易協定第 1.11 条に、特許権者等に後発医薬品会社の販売承認申請について通知し、仮差止を含む救済を求め、侵害・有効性の紛争を解決するための時間と機会を特許権者等に提供することなどが規定されている。

2. 米中経済貿易協定 Article 1.11[10]

Article 1.11: Effective Mechanism for Early Resolution of Patent Disputes

1. If China permits, as a condition of approving the marketing of a pharmaceutical product, including a biologic, persons, other than the person originally submitting the safety and efficacy information, to rely on evidence or information concerning the safety and efficacy of a product that was previously approved, such as evidence of prior marketing approval by China or in another territory, China shall provide:

(a) a system to provide notice to a patent holder, licensee, or holder of marketing approval, that such other person is seeking to market that product during the term of an applicable patent claiming the approved product or its approved method of use;

(b) adequate time and opportunity for such a patent holder to seek, prior to the marketing of an allegedly infringing product, available remedies in subparagraph (c); and

(c) procedures for judicial or administrative proceedings and expeditious remedies, such as preliminary injunctions or equivalent effective provisional measures, for the timely resolution of disputes concerning the validity or infringement of an applicable patent claiming an approved pharmaceutical product or its approved method of use.

2. China shall establish a nationwide system for pharmaceutical products consistent with paragraph 1,

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[8] Economic and Trade Agreement between the Government of the United States of America and the Government of the People's Republic of China （Office of the United States Trade Representative ウェブサイト）
https://ustr.gov/sites/default/files/files/agreements/phase%20one%20agreement/Economic_And_Trade_Agreement_Between_The_United_States_And_China_Text.pdf

[9] 米中が第 1 段階の経済・貿易協定に署名、対中追加関税の大部分を据え置き（ビジネス短信 2020 年 1 月 16 日）（ジェトロウェブサイト）
https://www.jetro.go.jp/biznews/2020/01/64d4f6d398b53d5f.html

[10] Economic and Trade Agreement between the Government of the United States of America and the Government of the People’s Republic of China（Office of the United States Trade Representative ウェブサイト）
https://ustr.gov/sites/default/files/files/agreements/phase%20one%20agreement/Economic_And_Trade_Agreement_Between_The_United_States_And_China_Text.pdf

including by providing a cause of action to allow the patent holder, licensee, or holder of marketing approval to seek, prior to the marketing approval of an allegedly infringing product, civil judicial proceedings and expeditious remedies for the resolution of disputes concerning the validity or infringement of an applicable patent. China may also provide for administrative proceedings for the resolution of such disputes.

3. The United States affirms that existing U.S. measures afford treatment equivalent to that provided for in this Article.

パテントリンケージ制度について、第1項で、後発医薬品の販売前に特許権者に通知する制度、及び侵害救済措置が規定されている。

3. CPTPP との比較

パテントリンケージ条項に関する CPTPP と米中経済協定との比較を表 2 に示す。

表 2 パテントリンケージ条項に関する CPTPP と米中経済協定との比較

CPTPP[11]	米中経済貿易協定[12]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	**Article 1.11: Effective Mechanism for Early Resolution of Patent Disputes** 1. If China permits, as a condition of approving the marketing of a pharmaceutical product, including a biologic, persons, other than the person originally submitting the safety and efficacy information, to rely on evidence or information concerning the safety and efficacy of a product that was previously approved, such as evidence of prior marketing approval by China or in another territory, China shall provide: (a) a system to provide notice to a patent holder, licensee, or holder of marketing approval, that such other person is seeking to market that product during the term of an applicable patent claiming the approved product or its approved method of use;
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	(b) adequate time and opportunity for such a patent holder to seek, prior to the marketing of an allegedly infringing product, available remedies in subparagraph (c); and

[11] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf
[12] Economic and Trade Agreement between the Government of the United States of America and the Government of the People's Republic of China（Office of the United States Trade Representative ウェブサイト）
https://ustr.gov/sites/default/files/files/agreements/phase%20one%20agreement/Economic_And_Trade_Agreement_Between_The_United_States_And_China_Text.pdf

(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	(c) procedures for judicial or administrative proceedings and expeditious remedies, such as preliminary injunctions or equivalent effective provisional measures, for the timely resolution of disputes concerning the validity or infringement of an applicable patent claiming an approved pharmaceutical product or its approved method of use.
	2. China shall establish a nationwide system for pharmaceutical products consistent with paragraph 1, including by providing a cause of action to allow the patent holder, licensee, or holder of marketing approval to seek, prior to the marketing approval of an allegedly infringing product, civil judicial proceedings and expeditious remedies for the resolution of disputes concerning the validity or infringement of an applicable patent. China may also provide for administrative proceedings for the resolution of such disputes. 3. The United States affirms that existing U.S. measures afford treatment equivalent to that provided for in this Article.
２ 締約国は、１の規定の実施に代えて、特許権者若しくは販売承認の申請者により販売承認を行う当局に提出された特許に関連する情報に基づき又は販売承認を行う当局と特許官庁との間の直接の調整に基づき、当該特許権者の承諾又は黙認を得ない限り、請求の範囲に記載されている特許の対象である医薬品を販売しようとする第三者に販売承認を与えない司法上の手続以外の制度を採用し、又は維持する。	

IV. 米韓自由貿易協定

1. 加入国

2006 年 2 月、米国・韓国両政府が交渉開始を発表し、2007 年 3 月までに全 8 回の交渉を行った後に、2007 年 4 月に交渉妥結し、2007 年 6 月に署名が行われ、2012 年 3 月に発効した[13]。

第 18.9 条にパテントリンケージ制度が規定されている。

2. 米韓自由貿易協定 Article 18.9[14]

ARTICLE 18.9: MEASURES RELATED TO CERTAIN REGULATED PRODUCTS 5. Where a Party permits, as a condition of approving the marketing of a pharmaceutical product, persons, other than the person originally submitting safety or efficacy information, to rely on that information or on evidence of safety or efficacy information of a product that was previously approved, such as evidence of prior marketing approval in the territory of the Party or in another territory, that Party shall: (a) provide that the patent owner shall be notified of the identity of any such other person that requests marketing approval to enter the market during the term of a patent notified to the approving authority as covering that product or its approved method of use; and (b) implement measures in its marketing approval process to prevent such other persons from marketing a product without the consent or acquiescence of the patent owner during the term of a patent notified to the approving authority as covering that product or its approved method of use.

パテントリンケージ制度について、第 5 項で、後発医薬品の販売前に特許権者に通知する制度、及び侵害救済措置が規定されている。

3. CPTPP との比較

パテントリンケージ条項に関する CPTPP と米韓自由貿易協定（FTA）との比較を表 3 に示す。

[13] 米韓 FTA の概要（平成 24 年 3 月 外務省）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/tpp/pdfs/tpp20120327_10.pdf
[14] KRUS FTA Final Text (as of January 1, 2019)（Office of the United States Trade Representative ウェブサイト）
https://ustr.gov/trade-agreements/free-trade-agreements/korus-fta/final-text

表 3 パテントリンケージ条項に関する CPTPP と米韓自由貿易協定（FTA）との比較

CPTPP[15]	米韓自由貿易協定（FTA）[16]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	ARTICLE 18.9: MEASURES RELATED TO CERTAIN REGULATED PRODUCTS 5. Where a Party permits, as a condition of approving the marketing of a pharmaceutical product, persons, other than the person originally submitting safety or efficacy information, to rely on that information or on evidence of safety or efficacy information of a product that was previously approved, such as evidence of prior marketing approval in the territory of the Party or in another territory, that Party shall: (a) provide that the patent owner shall be notified of the identity of any such other person that requests marketing approval to enter the market during the term of a patent notified to the approving authority as covering that product or its approved method of use; and
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	(b) implement measures in its marketing approval process to prevent such other persons from marketing a product without the consent or acquiescence of the patent owner during the term of a patent notified to the approving authority as covering that product or its approved method of use.

[15] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf
[16] KRUS FTA Final Text (as of January 1, 2019) Chapter Eighteen Intellectual Property Rights（Office of the United States Trade Representative ウェブサイト）
https://ustr.gov/sites/default/files/uploads/agreements/fta/korus/asset_upload_file273_12717.pdf

(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	
２ 締約国は、１の規定の実施に代えて、特許権者若しくは販売承認の申請者により販売承認を行う当局に提出された特許に関連する情報に基づき又は販売承認を行う当局と特許官庁との間の直接の調整に基づき、当該特許権者の承諾又は黙認を得ない限り、請求の範囲に記載されている特許の対象である医薬品を販売しようとする第三者に販売承認を与えない司法上の手続以外の制度を採用し、又は維持する。	

V. まとめ

パテントリンケージ制度は、1984 年に米国でハッチ・ワックスマン法が制定されたことを皮切りに、経済連携協定においては、1994 年に発効した NAFTA（2020 年 4 月に CUSMA に衣替えして発効）、2012 年に発効した米韓自由貿易協定、2018 年に発効した CPTPP、2020 年に第 1 弾が発効した米中経済貿易協定（Economic and Trade Agreement between the United States of America and the People's Republic of China）で導入されている。

パテントリンケージ制度について、CPTPP においては、「後発医薬品の販売前に特許権者に通知する制度、及び侵害救済措置」が規定（第 18・53 条第 1 項）されているとともに、代替として司法上の手続き以外の制度の採用・維持が規定（第 18・53 条第 2 項）されている。一方で、CUSMA、米中経済貿易協定、米韓自由貿易協定においては、CPTPP の第 18・53 条第 1 項相当が規定されており、CPTPP の第 18・53 条第 2 項相当の代替は規定されていない。

第 3 章　各国制度

I. 米国

1. 低分子医薬品

(1) 経緯

1984 年：Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act)（Hatch-Waxman 法）[17]

1962 年に食品医薬品局（Food and Drug Administration (FDA)）における新薬承認に安全性の証明に加えて有効性の証明も必要となって以降、新薬承認までに費やされる期間が長期化し、新薬会社の特許期間が侵食されることとなった。1963 年には FDA 規則により、臨床試験開始前に治験届を提出することが義務付けられた。本規則により、非臨床試験、第 1 相試験、第 2 相試験、第 3 相試験が規定され、新薬申請時に薬剤の有効性、安全性を証明する第 3 相試験の成功したデータを FDA に提出することになった。また、FDA は後発医薬品承認にも新薬と同様に有効性・安全性の証明を要求しており、1970 年代まで、米国において、後発医薬品はほとんど商用化されていなかった。また、新薬の特許期間満了前に後発医薬品の試験を行うことは特許侵害と解されていたため、後発医薬品が市場に浸透せず、医療費抑制の観点から好ましくない状況であった。こうした状況を打破するため、ハッチ・ワックスマン法が制定され、特許存続期間延長制度、ボーラー条項、パテントリンケージ制度の導入が行われた[18][19]。

2003 年：Medicare Prescription Drug Improvement and Modernized Act[20]

後発医薬品の 30 か月自動承認停止の回数が 1 回に限定され、また、オレンジブックに登載する特許権の種別が明確化された。

2021 年 1 月 5 日：Orange Book Transparency Act[21]

FDAが発行する医薬品に関するデータベースの正確性と透明性を高めることによって、後続医薬品会社による後続薬の市場投入を促進し、高騰化が進む処方薬の価格を下げることを目的として、Orange Book Transparency Actが成立した。本法により、医薬品承認申請を行う者がFDAに情報提供

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[17] Drug Price Competition and Patent Term Restoration Act of 1984（U.S. Government Publishing Office ウェブサイト）
https://www.govinfo.gov/content/pkg/STATUTE-98/pdf/STATUTE-98-Pg1585.pdf

[18] 米国 ANDA（簡略新薬申請）関連の制度及び訴訟における現状と留意点（知財管理 2004 年 8 月）

[19] The South Korean Patent Linkage System: A Model for Reforming the United States Hatch-Waxman Act (Kimberlee Thompson Raley, Emory International Law Review, Vol. 33(3), 459-492, 2019)
https://scholarlycommons.law.emory.edu/cgi/viewcontent.cgi?article=1215&context=eilr

[20] Medicare Prescription Drug Improvement and Modernized Act of 2003（アメリカ合衆国議会ウェブサイト）
https://www.congress.gov/108/plaws/publ173/PLAW-108publ173.pdf

[21] Orange Book Transparency Act of 2020（アメリカ合衆国議会ウェブサイト）
https://www.congress.gov/116/bills/hr1503/BILLS-116hr1503enr.pdf

しなければならない特許の種類は、薬の有効成分、製剤に関する特許、及びその薬の使用方法に関するものであることが明確化された。また、オレンジブックに掲載された特許について、米国特許商標庁特許審判部又は裁判所においてクレームのキャンセル又は無効が確定した場合は、14日以内に、その特許に関する医薬品の承認を受けた者はFDAにその旨を通知しなければならず、通知を受けたFDAは、速やかにオレンジブックの特許情報を修正又は削除しなければならないなどが規定された。

(2) パテントリンケージ制度の概要

米国のパテントリンケージ制度（低分子医薬品）の概要を表 4 にまとめる。

表 4 米国のパテントリンケージ制度（低分子医薬品）の概要

先発医薬品	
特許リスト	Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations[22] FDA は新薬承認申請（New Drug Application (NDA)）承認後速やかに提出された特許情報を掲載・公開する。NDA 承認後に特許情報が提出された場合は、当該提出後速やかに FDA は特許情報を掲載・公開する（21CFR314.53(e)）
対象特許	物質特許、結晶多形特許、製剤特許、医薬用途特許（21CFR314.53(b)(1)）
特許情報	特許番号、特許存続期間、（21USC355(b)(2), 21CFR314.53, Form FDA 3542, 3542a） パラグラフ IV の訴訟で簡略新薬承認申請（Abbreviated New Drug Application (ANDA)）申請者が反訴として無関係の特許のオレンジブックからの削除命令を裁判所に請求することができる（21USC355(j)(5)(c)(ii)）。
リスト登録者	NDA 申請者
リスト登録時期	NDA 承認前： NDA 申請時、及び NDA 提出後 NDA 承認前に特許登録された場合は当該登録から 30 日以内（21CFR314.53(d)(1)） NDA 承認後： NDA 承認から 30 日以内（21CFR314.53(c)(2)(ii)）、及び NDA 承認後に特許登録された場合には当該登録から 30 日以内（21CFR314.53(d)(3)）

[22] U.S. Food & Drug Administration ウェブサイト
https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm

後発医薬品申請後の提訴期間	特許権者は後述のパラグラフ IV の通知（Notice Letter）を受領した後、45 日以内に ANDA 申請者に対して特許権侵害訴訟を提起することができる（21USC355(j)(5)(B)(iii)）。
後発医薬品	
申請時期制限	対象薬が新規化学物質（New Chemical Entity (NCE)）である場合、当該新規化学物質の承認から 5 年間、後発医薬品申請は受理されない。ただし、後述のパラグラフ IV の通知に基づく後発医薬品申請は、当該新規化学物質の承認から 4 年経過後 NCE Exclusivity 満了の 1 年前以後）であれば、後発医薬品申請を行うことができる（21CFR314.108(b)(2)）。
申請手続	ANDA 申請者は、申請にあたり、先発医薬品との同一性の証明、及びオレンジブック掲載の先発特許との関係について、パラグラフ I～IV のいずれかの証明書を提出する。 パラグラフ I：オレンジブックに特許は掲載されていない パラグラフ II：特許満了または失効している パラグラフ III：特許満了後に発売予定である パラグラフ IV：掲載された特許は無効・権利行使不能、または非侵害である（21USC355(j)(2)(A)(vii), 21CFR314.94(a)(12)(i)） ANDA 申請者が承認を求めている適応症をクレームしない使用方法の特許に対しては、「セクション viii ステートメント」を提出することができ、この場合、通知は要求されない（21USC355(j)(2)(A)(viii)）。
承認の自動停止	30 ヶ月（21USC355(j)(5)(B)(iii)(I)-(III), 21CFR314.107(b)(3)(i)(A)）
後発医薬品申請情報の開示	パラグラフ IV 証明書の場合は、ANDA 申請者は提出から 20 日以内に NDA 保持者及び特許権者に通知（Notice Letter）をする必要がある（21CFR314.95(a), 21USC355(j)(2)(B)）。 ANDA 申請者は、訴訟が提起された場合、提訴日から 14 日以内に FDA にその旨を書面にて通知しなければならない。 Notice Letter による通知後 45 日間、特許権者が訴訟を提起しない場合、ANDA 申請者は、特許権者に対して、オレンジブックに掲載された特許が無効である、または ANDA 申請対象の医薬品がオレンジブックに掲載された特許を侵害しないことについて確認訴訟を提起することができる。なお、ANDA 申請者には、申請書に含まれる秘密情報へのアクセスを提供する書面を提出することが求められており、当該アクセスの提供は確認訴訟提起の要件となっている（21USC355(j)(5)(c)(i)）。

第 1 申請承認後発医薬品に与えられる独占期間	180 日（21USC355(j)(5)(B)(iv)(I), (II)） ただし、以下の場合には 180 日の独占期間は喪失される（21USC355(j)(5)(D)）。 (1) 市販の失敗、最初の後発医薬品許可申請人が次のいずれか遅い日までに後発医薬品を市販していない場合 - 最初の後発医薬品許可を受けた日から 75 日、又は最初の後発医薬品許可申請から 30 か月が経過した日から 75 日 - 特許無効又は非侵害の控訴審判決から 75 日、又は特許無効又は非侵害確認を含む合意の最終的な決定がなされたから 75 日､又は新薬の特許がオレンジブックから削除されたときから 75 日 (2) 最初の後発医薬品の許可申請が取り下げられた場合 (3) 特許の関係（パラグラフ IV）を変更、撤回した場合 (4) 後発医薬品許可申請から 30 か月以内に、一時的な許可（tentative approval）を確保することに失敗した場合 (5) 登録新薬承認権者又は特許権者と後発医薬品会社との間の反トラスト法違反という裁判所の最終判決を受けた談合があった場合 (6) パラグラフ IV を提出したすべての登録特許の存続期間が満了した場合

(3) 手続等、詳細事項

① 先発の特許登録

特許情報開示のタイミング：

NDA 承認前（Form FDA 3542）：

NDA 申請時、及び NDA 提出後 NDA 承認前に特許登録された場合は当該登録から 30 日以内（21CFR314.53(d)(1)）

NDA 承認後（Form FDA 3542a）：

NDA 承認から 30 日以内（21CFR314.53(c)(2)(ii)）、及び NDA 承認後に特許登録された場合には当該登録から 30 日以内（21CFR314.53(d)(3)）

特許情報開示は義務であり､NDA 承認前に付与された特許権に関する情報を提出しない場合は、申請の承認拒否事由となる（21USC355(d)(6)）。また、NDA 承認後に付与された特許権について 30 日以内に特許情報を届け出ない場合、NDA 承認の取消事由になる（21USC355(e)(4)）。さらに、特許情報が期限内に提出された場合でも、提出の様式と内容が FDA 規則を遵守しない場合、FDA は当該特許権をオレンジブックに掲載しない（21CFR314.53(c)(2)(ii)）。

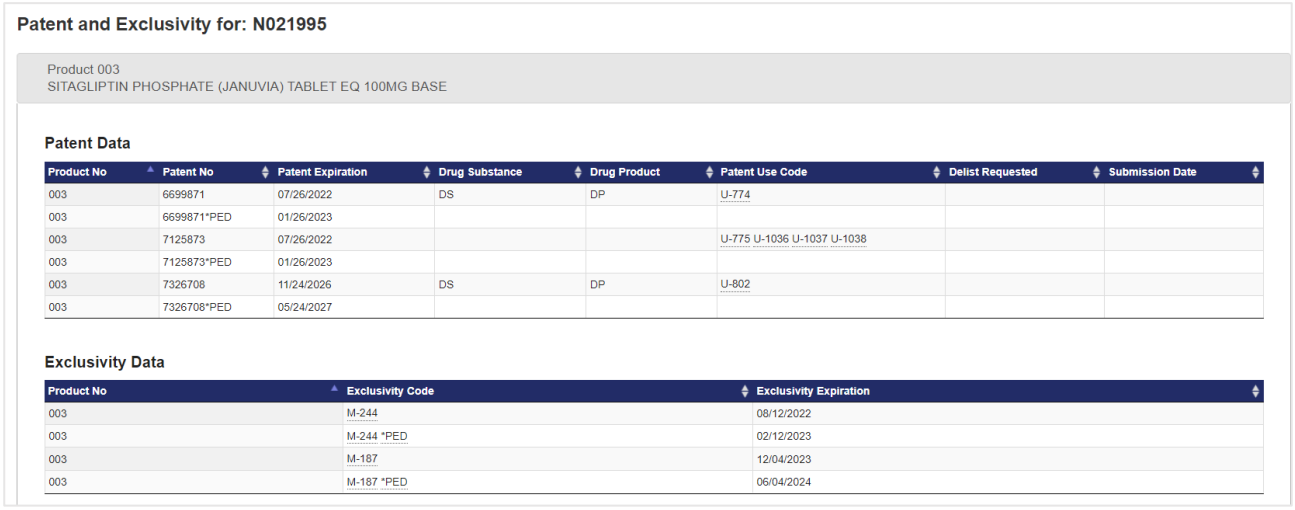
特許情報の開示内容：

FDA は NDA 承認後速やかに提出された特許情報（特許番号、特許存続期間）をオレンジブック[23]に掲載・公開する。また、用途特許については、21CFR314.53(c)(2)(ii)(P)(3)に規定される当該用途特許でクレームされる用途についても掲載・公開される。NDA 承認後に特許情報が提出された場合は、当該提出後速やかに FDA は特許情報を掲載・公開する（21CFR314.53(e)）。

FDA は、NDA 保持者に対して、用途特許権がクレームしている用途のうち、承認された用途のみを具体的に特定するように要求する（21CFR314.53(b)(1)）。これは、NDA 保持者が提出した特許情報のうちの用途特許権における用途が、FDA により承認された製品ラベルのいずれのセクション及びサブセクションに記載されているかを明確にすることを目的にしている（21CFR314.53(b)(1), 21CFR314.53(c)(2)(O)）。また、NDA 保持者には用途特許権の特許請求の範囲に影響する情報とともに特許ユースコードの更新を行う義務がある。例えば、NDA 保持者は、承認された用途で特許権により保護されているものについて、当該特許請求の範囲の解釈を変更するような米国特許商標庁（United States Patent and Trademark Office (USPTO)）、連邦地方裁判所、連邦巡回区控訴裁判所（Court of Appeal for the Federal Circuit (CAFC)）、または最高裁判所による判断がなされた場合、その後 30 日以内に特許ユースコードを更新しなければならない（21CFR314.50(i)(4)(i), 21CFR314.94(a)(12)(vi)(A)(3)）。FDA 規則により、NDA 保持者にはオレンジブックに公開された特許情報、およびオレンジブックへの掲載要件を満たさない「リストから削除すべき」特許権の更新を要求している（21CFR314.53(f)(2)(iii)）。

[23] Orange Book: Approved Drug Products with Therapeutic Equivalent Evaluations（U.S. Food and Drug Administration ウェブサイト）
https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm

図 1 オレンジブックでの特許情報の公開例（Merck 社 JANUVIA (sitagliptin)）[24]



Patent and Exclusivity for: N021995

Product 003
SITAGLIPTIN PHOSPHATE (JANUVIA) TABLET EQ 100MG BASE

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
003	6699871	07/26/2022	DS	DP	U-774		
003	6699871*PED	01/26/2023					
003	7125873	07/26/2022			U-775 U-1036 U-1037 U-1038		
003	7125873*PED	01/26/2023					
003	7326708	11/24/2026	DS	DP	U-802		
003	7326708*PED	05/24/2027					

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
003	M-244	08/12/2022
003	M-244 *PED	02/12/2023
003	M-187	12/04/2023
003	M-187 *PED	06/04/2024

21USC355(j)(7)(A)(i)(I)-(III)に基づき、FDA は、過去に 21USC355(c)により安全性と有効性について承認された医薬品のアルファベット順のリストを定期的に更新し、オレンジブックとして公表する。これには、承認日、医薬品の正式名称、商標名、及び in vitro もしくは in vivo 生物学的同等性試験、またはその双方が ANDA において必要であるかどうかに関する情報が含まれる。

登録情報への異議：

パラグラフ IV の訴訟で、ANDA 申請者が反訴として無関係の特許のオレンジブックからの削除命令を裁判所に請求することができる（21USC355(j)(5)(c)(ii)）。

② 後発医薬品申請＋先発医薬品会社への通知

後発医薬品申請者による宣言と告知：

ANDA 申請者は、申請にあたり、先発医薬品との同一性の証明、及びオレンジブック掲載の先発特許との関係について、パラグラフ I～IV のいずれかの証明書を提出する。

パラグラフ I：オレンジブックに特許は掲載されていない

パラグラフ II：特許満了または失効している

パラグラフ III：特許満了後に発売予定である

パラグラフ IV：掲載された特許は無効・権利行使不能、または非侵害である（21USC355(j)(2)(A)(vii), 21CFR314.94(a)(12)(i)）

パラグラフ IV 証明書の場合は、ANDA 申請者は提出から 20 日以内に NDA 保持者及び特許権者に通知（Notice Letter）をする必要がある（21CFR314.95(a), 21USC355(j)(2)(B)）。当該通知は、バイオアベイラビリティまたは生物学的同等性試験のデータとともに、特許の無効性・非侵害に関する

[24] Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluation – Patent and Exclusivity for: N021995 Sitagliptin Phosphate (JANUVIA)（U.S. Food & Drug Administration ウェブサイト）（2022 年 6 月 22 日アクセス時）
https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=003&Appl_No=021995&Appl_type=N

ANDA 申請者の見解の根拠の詳細な陳述（detailed statement of the factual and legal basis）を含まなければならない（21USC355(j)(2)(B)(iv)(II)）。また、特許非侵害を主張する場合、及び将来的に35USC505(j)(5)(C)に基づく確認訴訟を提起するオプションを確保する場合には、ANDA 申請者は特許権者等に対して、35USC271(e)(2)に基づく訴訟を提起するか否かを判断するために、ANDA 申請書への機密アクセス（アクセスされた情報の使用及び処分についての制限付）の機会を与えなければならない（21CFR314.95(c)(8)）。

対象薬が新規化学物質である場合、当該新規化学物質の承認から 5 年間、後発医薬品申請は受理されない。ただし、パラグラフ IV の通知に基づく後発医薬品申請は、当該新規化学物質の承認から 4 年経過後（NCE Exclusivity 満了の 1 年前以後）であれば、後発医薬品申請を行うことができる（21CFR314.108(b)(2)）。

パラグラフ IV 証明書のリストは FDA ウェブサイトで公開されている[25]。

[25] Patent Certifications and Suitability Petitions（FDA ウェブサイト）
https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions#List

図 2 パラグラフ IV 証明書のリスト公開例[26]

Paragraph IV Certifications

- Paragraph IV Patent Certifications (PPIV) as of June 13, 2022 (PDF - 2.5 MB)

Drug Name	Dosage Form	Strength	RLD/NDA	Date of Submission
Aprepitant	Intravenous Emulsion	130 mg/18 mL	Cinvanti 209296	4/29/2022
Azilsartan Medoxomil and Chlorthalidone	Tablets	40 mg/12.5 mg and 40 mg/25 mg	Edarbyclor 202331	4/19/2022
Bupivacaine Liposome	Injectable Suspension	133 mg/10 mL	Exparel 22496	12/28/2021
Cladribine	Tablets	10 mg	Mavenclad 22561	4/7/2022
Elrombopag Olamine	For Oral Suspension	12. mg/packet and 25 mg/packet	Promacta Kit 207027	4/22/2022
Fosnetupitant Chloride Hydrochloride and Palonosetron Hydrochloride	Solution in SDV	235 mg/0.25 mg per 20 mL	Akynzeo 210493	4/19/2022
Fostamatinib Disodium	Tablets	100 mg and 150 mg	Tavalisse 209299	4/18/2022
Ivacaftor	Oral Granules	25 mg, 50 mg and 75 mg	Kalydeco 207925	4/13/2022
Sodium Thiosulfate	Intravenous Injection	12.5 g/50 mL	Sodium Thiosulfate 203923	4/29/2022

パラグラフ IV 証明の通知を受けた特許権者が、ANDA 申請者に対して、35USC271(e)(2)に基づく訴訟を提起するか否かを判断するために、ANDA 申請書への機密アクセス（アクセスされた情報の使用及び処分についての制限付）を要求することができる。ANDA 申請者は、特許侵害と関連性のない情報を削除編集することができる（21USC355(j)(5)(C)(i)(III)）。

ANDA 申請者は、訴訟が提起された場合、提訴日から 14 日以内に FDA にその旨を書面にて通知なければならない。

Notice Letter による通知後 45 日以内に特許権者が訴訟を提起しない場合、ANDA 申請者は、特許権者に対して、オレンジブックに掲載された特許が無効である、または ANDA 申請対象の医薬品がオレンジブックに掲載された特許を侵害しないことについて確認訴訟を提起することができ

[26] Patent Certifications and Suitability Petitions（FDA ウェブサイト）（2022 年 6 月 22 日アクセス時）
https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions#List

る。なお、ANDA 申請者には、申請書に含まれる秘密情報へのアクセスを提供する書面を提出することが求められており、当該アクセスの提供は確認訴訟提起の要件となっている（21USC355(j)(5)(C)(i)(I)(cc)）。

ANDA 申請者が承認を求めている適応症をクレームしない使用方法の特許に対しては、「セクション viii ステートメント」を提出することができ、この場合、通知は要求されない（21USC355(j)(2)(A)(viii)）。

安全性および有効性の情報公開（21USC355(l)(1)）

新薬申請者により提出され、公衆に利用可能になっていない安全性及び有効性に関する情報は、特段の事情がない限り、請求により、以下の場合に公開される。

(a) 新薬申請者が承認手続きを進めなかった場合
(b) FDA が承認を行わなかった場合
(c) 新薬申請が取り下げられた場合
(d) FDA が、申請薬が新薬ではないと判断した場合
(e) 最初の ANDA 申請に基づく後発医薬品が承認された場合、または、新たに取得したデータに基づき後発医薬品が承認された場合

③ 後発医薬品の自動承認停止

パラグラフ IV 証明の通知を受けた特許権者は、ANDA 申請者に対して、35USC271(e)(2)に基づく訴訟を提起することができる。特許権者が通知受領後 45 日以内に訴訟を提起した場合、FDA はパラグラフ IV 証明の通知を NDA 保持者及び特許権者が受領した日から 30 か月は ANDA を承認しない（21USC355(j)(5)(B)(iii), 21CFR314.107(b)(3)(i)(A)）。

④ 後発医薬品会社へのインセンティブ

最初に医薬品許可証を取得した後発医薬品会社は、180 日間の独占販売期間を取得することができる（21USC355(j)(5)(B)(iv)(I), (II)）。ただし、以下の場合には 180 日の独占期間は喪失される（21USC355(j)(5)(D)）。

(1) 市販の失敗、最初の後発医薬品許可申請人が次のいずれか遅い日までに後発医薬品を市販していない場合
- 最初の後発医薬品許可を受けた日から 75 日、又は最初の後発医薬品許可申請から 30 か月が経過した日から 75 日
- 特許無効又は非侵害の控訴審判決から 75 日、又は特許無効又は非侵害確認を含む合意の最終的な決定がなされてから 75 日、又は新薬の特許がオレンジブックから削除されたときから 75 日

(2) 最初の後発医薬品の許可申請が取り下げられた場合
(3) 特許の関係（パラグラフ IV）を変更、撤回した場合
(4) 後発医薬品許可申請から 30 か月以内に、一時的な許可（tentative approval）を確保することに失敗した場合

(5) 登録新薬承認権者又は特許権者と後発医薬品会社との間の反トラスト法違反との裁判所の最終判決を受けた談合があった場合
(6) パラグラフ IV を提出したすべての登録特許の存続期間が満了した場合

(4) パテントリンケージ条項に関する CPTPP との比較

パテントリンケージ条項に関する CPTPP と米国法との比較を表 5 に示す。

表 5 パテントリンケージ条項に関する CPTPP と米国法との比較

CPTPP[27]	米国法[28]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	21USC355(j)(2)(B) (B) Notice of opinion that patent is invalid or will not be infringed.— (i) Agreement to give notice.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph. (ii) Timing of notice.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph— (I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or (II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

[27] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf
[28] 21USC355 - New Drugs（U.S. Government Publishing Office ウェブサイト）
https://www.govinfo.gov/content/pkg/USCODE-2010-title21/pdf/USCODE-2010-title21-chap9-subchapV-partA-sec355.pdf

	(iii) Recipients of notice.—An applicant required under this subparagraph to give notice shall give notice to— (I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and (II) the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice). (iv) Contents of notice.—A notice required under this subparagraph shall— (I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and (II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	21USC355(j)(5)(B)(iii) (5)(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii): (i) …（略）… (iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that

	is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) of this section before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. …（略）…
(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	21USC355(j)(5)(B)(iii) (B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii): (i) …（略）… (iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) of this section before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

	(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on— (aa) the date on which the court enters judgment reflecting the decision; or (bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed; (II) if before the expiration of such period the district court decides that the patent has been infringed— (aa) if the judgment of the district court is appealed, the approval shall be made effective on— (AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or (BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or (bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35; (III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the

	commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or (IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II). …（略）…

2. 生物学的製剤

(1) 経緯

2010 年：Biologics Price Competition and Innovation Act[29]

生物学的製剤治療の継続的な技術革新に対するインセンティブ、及び生物学的製剤治療の価格を下げることを目的とした 42USC262 Regulation of biological products の改正である。先行品に 12 年の Data Exclusivity を認めるとともに、簡略化された生物製剤認可申請で FDA から後続品の承認を得ることが可能になった。

2021 年：Consolidated Appropriations Act, 2021[30]

Public Health Service Act (42USC262(k))が改正され、FDAが発行するバイオ医薬品のリスト（パープルブック）に、同医薬品に関連する全ての特許とその有効期間の情報が掲載されるようになった。

(2) パテントリンケージ制度の概要

米国のパテントリンケージ制度（生物学的製剤）の概要を表 6 にまとめる。

[29] The Patient Protection and Affordable Care Act (Title VII – Improving Access to Innovative Medical Therapies, Subtitle Biologics Price Competition and Innovation Act of 2009)（U.S. Government Publishing Office ウェブサイト）
https://www.govinfo.gov/content/pkg/PLAW-111publ148/html/PLAW-111publ148.htm

[30] Consolidated Appropriations Act, 2021（アメリカ合衆国議会ウェブサイト）
https://www.congress.gov/116/bills/hr133/BILLS-116hr133enr.pdf

表 6 米国のパテントリンケージ制度（生物学的製剤）の概要

先発医薬品	
特許リスト	Purple Book: Database of Licensed Biological Products[31]
対象特許	先行品のスポンサーが、バイオ後続品申請者により侵害されたと考える特許（42USC262(l)(3)(A)または 42USC262(l)(7)）
リスト登録者	生物学的製剤承認取得者
リスト登録時期	42USC262(l)(3)(A)または 42USC262(l)(7)の特許リストから 30 日以内に、生物学的製剤承認取得者は長官に対して特許リスト及びそれらの満了日について提出しなければならない（42USC262(k)(9)(iii)）。
後発医薬品申請後の提訴期間	ラウンド 1 訴訟段階（Round 1 Litigation Phase）（42USC262(l)(4)-(6)） 特許侵害訴訟の対象となる特許が存在する場合には、当事者は、最長で 15 日間誠実に交渉を行って特許リストを作成する。当事者がリスト作成につき交渉の上、合意に至れば、先行品のスポンサーは、上記リスト作成から 30 日以内に、特許侵害訴訟を提起しなければならない。 ラウンド 2 訴訟段階（Round 2 Litigation Phase）（42USC262(l)(8)） バイオ後続品申請者は、当該バイオ後続品を最初に市場に出す 180 日前に先行品のスポンサーに対して通知を行わなければならない（42USC262(l)(8)(A)）。先行品のスポンサーは、上記通知を受けた後、上市をする前に、前記一次リストに含まれ、前記第 1 の訴訟の対象に含まれない特許に関し、裁判所がその有効性や侵害等の問題について決定を下すまで、バイオ後続品申請者が該当するバイオ後続品を製造・販売することを禁じる仮差止命令を請求することができる（42USC262(l)(8)(B)）。
Biosimilar/Interchangeable	
申請時期制限	先行品の承認から 4 年経過後でなければ、Biosimilar/Interchangeable を申請することはできない（42USC262(k)(7)(B)）。 先発品の承認から 12 年経過後でなければ、Biosimilar/Interchangeable は承認取得できない（42USC262(k)(7)(A)）。

[31] U.S. Food & Drug Administration ウェブサイト
https://purplebooksearch.fda.gov/patent-list

申請手続	Biosimilar/Interchangeable が参照製品と非常に類似することを実証する分析研究、毒性評価を含む動物実験結果、安全性、純度、効果を示す臨床試験結果等とともに申請（42USC262(k)(2)(A)）
承認の自動停止	なし 先行品のスポンサーは、後続品が発売される潜在的な危険を防ぐため、仮差止による救済（42USC262(l)(8)(B)）を積極的に求めていく必要がある。
後発医薬品申請情報の開示	1. 情報段階（Information Phase）（42USC262(l)(2)） ・バイオ後続品申請者は、FDA が略式承認申請を受け付けてから 20 日以内に、先行品のスポンサーに対して、バイオ後続品の申請及び関連する製造情報への、守秘義務を課した上でのアクセスを認めなければならない。 2. 包括リスト段階（Comprehensive List Phase）（42USC262(l)(3)） ・先行品のスポンサーは、上記資料を受領してから 60 日以内に、バイオ後続品申請者に対して、(1)侵害されたと考える特許リストを提出し、また、(2)上記リスト記載の特許の中で後続品申請者に対してライセンスしても構わないと考えるものが存在すれば特定する。 ・バイオ後続品申請者は、上記特許リスト受領から 60 日以内に、先行品のスポンサーに対して、各特許がなぜ無効であるか、なぜ執行することができないか、なぜ侵害されていないかという点について、事実上及び法律上の根拠をクレームごとに記載して提出しなければならない。バイオ後続品申請者は、この期間内に、先行品のスポンサーに対して、逆にバイオ後続品申請者側で特許訴訟の対象となると考える特許リストを提出して反論することもできる。 ・先行品のスポンサーは、上記資料を受領してから 60 日以内に、上記各特許侵害についての事実上及び法律上の根拠及び特許の有効性及び執行力の点に関する反論を、クレームごとに記載して提出しなければならない。 3. ラウンド 1 訴訟段階（Round 1 Litigation Phase）（42USC262(l)(4)-(6)） ・特許侵害訴訟の対象となる特許が存在する場合には、当事者は、最長で 15 日間誠実に交渉を行って当該特許リストを作成する。

	- 当事者がリスト作成につき交渉の上、合意に至れば、先行品のスポンサーは、上記リスト作成から 30 日以内に、特許侵害訴訟を提起しなければならない。 - 当事者がリスト作成につき交渉の上、合意に至らない場合、バイオ後続品申請者は、先行品のスポンサーに対して、上記やり取りを踏まえた上で改訂された第二次リストにおいて、提供する特許の数を通知しなければならない。そして、当事者は、上記通知から 5 日以内に、各当事者が侵害訴訟の対象となるべきと考える特許のリストを同時に交換しなければならない。先行品のスポンサーは、当該リストの交換から 30 日以内に、同時に交換したリストに記載されたすべての特許について、特許侵害訴訟を提起しなければならない。 4. ラウンド 2 訴訟段階（Round 2 Litigation Phase）（42USC262(l)(8)） バイオ後続品申請者は、当該バイオ後続品を最初に市場に出す 180 日前に先行品のスポンサーに対して通知を行わなければならない（42USC262(l)(8)(A)）。
第 1 申請承認後発医薬品に与えられる独占期間	代替可能医薬品（interchangeable）のみ、1 年（42USC262(k)(6)）

(3) 手続等、詳細事項

① 先発の特許登録

42USC262(l)(3)(A)または 42USC262(l)(7)の特許リストから 30 日以内に、生物学的製剤承認取得者は FDA に対して特許リスト及びそれらの満了日について提出しなければならない（42USC262(k)(9)(iii)）。FDA は、生物学的製剤承認取得者から特許リストが提供された日から 30 日以内にウェブサイトで公開する[32]。

[32] Purple Book – Database of Licensed Biological Products （U.S. Food & Drug Administration ウェブサイト）https://purplebooksearch.fda.gov/patent-list

図 3 Purple Book での公開例[33]

Showing 1 to 50 of 131 rows 50 rows per page

BLA Number	Applicant Name	Proprietary Name	Proper Name	Patent Number	Patent Expiration Date
125031	Amgen, Inc.	Neulasta	pegfilgrastim	9,856,287	06/21/2030
125156	Genentech, Inc.	Lucentis	ranibizumab	6,716,602	11/01/2021
125156	Genentech, Inc.	Lucentis	ranibizumab	6,828,121	07/08/2022
125156	Genentech, Inc.	Lucentis	ranibizumab	6,921,659	10/17/2023
125156	Genentech, Inc.	Lucentis	ranibizumab	8,574,869	07/08/2028
125156	Genentech, Inc.	Lucentis	ranibizumab	9,765,379	03/10/2034
125156	Genentech, Inc.	Lucentis	ranibizumab	10,017,732	03/14/2034
125156	Genentech, Inc.	Lucentis	ranibizumab	10,112,994	11/05/2035
125156	Genentech, Inc.	Lucentis	ranibizumab	10,421,984	09/19/2033
125156	Genentech, Inc.	Lucentis	ranibizumab	10,829,732	03/14/2034
125156	Genentech, Inc.	Lucentis	ranibizumab	8,383,773	12/13/2023
125156	Genentech, Inc.	Lucentis	ranibizumab	9,688,775	12/31/2022

低分子医薬品承認申請である新薬承認申請（New Drug Application (NDA)）については必要な情報の種類と程度が詳細に法定されているが、生物製剤承認申請（Biologic License Application (BLA)）については申請に必要な広範な情報について以下の書類を提出することが義務付けられていることが大まかに規定されている。すなわち、BLA では NDA で義務付けられている特許情報の提出の必要はない（21CFR601.2(a)）。

(1) 生物製剤評価研究センター（Center for Biologics Evaluation and Research (CBER)）または医薬品評価研究センター（Center for Drug Evaluation and Research (CDER)）に提出する定められた様式による申請書

(2) 医薬品が安全性、純度、及び力価に関する所定の要件を満たしていることを示す非臨床試験及び治験のデータ

(3) 各非臨床試験に関して、当該試験が医薬品安全性試験実施基準（Good Laboratory Practice (GLP)）の要件を遵守して行われたことに関する説明、または当該試験が GLP を遵守して行われなかった場合、不遵守の理由についての簡単な説明

(4) 各治験に関して、当該治験が治験審査委員会の定める要件を遵守した行われたこと、または当該要件の適用がなく、インフォームドコンセントの要件を遵守して行われたことに関する説明

(5) 製造方法に関する詳細な説明

(6) 医薬品の有効期間中の安定性を立証するデータ

(7) 米国国内に流通させる医薬品、または米国国内に流通させるために引き渡される医薬品の代表サンプル

[33] Purple Book – Database of Licensed Biological Products （U.S. Food & Drug Administration ウェブサイト）（2022 年 6 月 22 日アクセス）
https://purplebooksearch.fda.gov/patent-list

(8) 提出した医薬品サンプルに代表されるロットを対象として行った試験結果の要約
(9) ラベル、同封物、及び容器の見本
(10) メディケーションガイド

② 後発医薬品申請＋先発医薬品会社への通知

初めて承認された新規生物学的製剤(参照製品)に対しては､12 年間の独占排他権が与えられる。これは、参照製品の承認から 12 年間は当該参照製品の Biosimilar/Interchangeable は承認されないことを意味している（42USC262(k)(7)(A)）。また、FDA は参照製品の承認から 4 年間は Biosimilar/Interchangeable の申請を受理しない（42USC262(k)(7)(B)）。

バイオ後続品申請者は､Biosimilar/Interchangeable が参照製品と非常に類似することを実証する分析研究、毒性評価を含む動物実験結果、安全性、純度、効果を示す臨床試験結果等とともに申請（42USC262(k)(2)(A)）する。

1. 情報段階（Information Phase）（42USC262(l)(2)）

・バイオ後続品申請者は、FDA が略式承認申請を受け付けてから 20 日以内に、先行品のスポンサーに対して、バイオ後続品の申請及び関連する製造情報への、守秘義務を課した上でのアクセスを認めなければならない。

・バイオ後続品の申請及び関連する製造情報の開示は、先行医薬品の特許出願に公式／非公式に関与していない 1 人以上の外部弁護士（42USC262(l)(1)(B)(ii)(I)）、及び先行医薬品会社組織内の 1 人の弁護士（42USC262(l)(1)(B)(ii)(II)）に限定される。

2. 包括リスト段階（Comprehensive List Phase）（42USC262(l)(3)）

・先行品のスポンサーは、上記資料を受領してから 60 日以内に、バイオ後続品申請者に対して、(1)侵害されたと考える特許リスト（一次リスト）を提出し、また、(2)上記リスト記載の特許の中で後続品申請者に対してライセンスしても構わないと考えるものが存在すれば特定する。

・バイオ後続品申請者は、上記特許リスト受領から 60 日以内に、先行品のスポンサーに対して、各特許がなぜ無効であるか、なぜ執行することができないか、なぜ侵害されていないかという点について、事実上及び法律上の根拠をクレームごとに記載して提出しなければならない。バイオ後続品申請者は、この期間内に、先行品のスポンサーに対して、逆にバイオ後続品申請者側で特許訴訟の対象となると考える特許リストを提出して反論することもできる。

・先行品のスポンサーは、上記資料を受領してから 60 日以内に、上記各特許侵害についての事実上及び法律上の根拠及び特許の有効性及び執行力の点に関する反論を、クレームごとに記載して提出しなければならない。

3. ラウンド 1 訴訟段階（Round 1 Litigation Phase）（42USC262(l)(4)-(6)）

・特許侵害訴訟の対象となる特許が存在する場合には、当事者は、最長で 15 日間誠実に交渉を行って当該特許リスト（二次リスト）を作成する。

- 当事者がリスト作成につき交渉の上、合意に至れば、先行品のスポンサーは、上記リスト作成から 30 日以内に、特許侵害訴訟を提起しなければならない。
- 当事者がリスト作成につき交渉の上、合意に至らない場合、バイオ後続品申請者は、先行品のスポンサーに対して、上記やり取りを踏まえた上で改訂された第二次リストにおいて、提供する特許の数を通知しなければならない。そして、当事者は、上記通知から 5 日以内に、各当事者が侵害訴訟の対象となるべきと考える特許のリストを同時に交換しなければならない。先行品のスポンサーは、当該リストの交換から 30 日以内に、同時に交換したリストに記載されたすべての特許について、特許侵害訴訟を提起しなければならない。

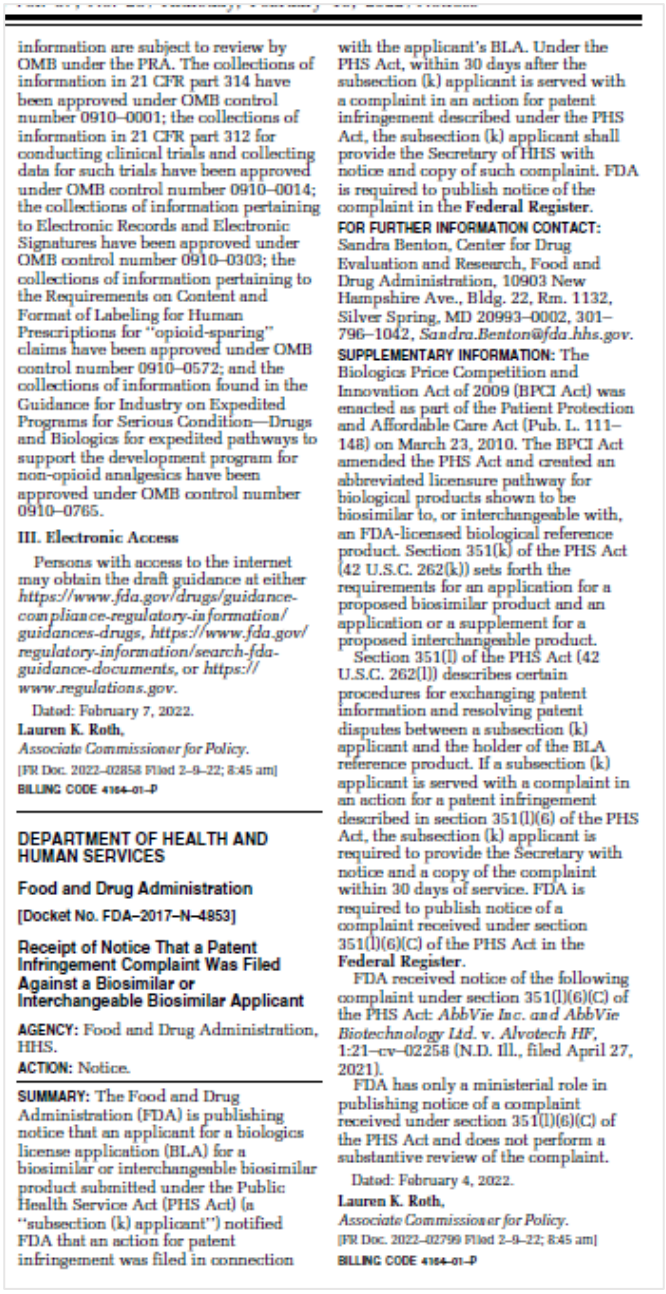
4. ラウンド 2 訴訟段階（Round 2 Litigation Phase）（42USC262(l)(8)）

・バイオ後続品申請者は、当該バイオ後続品を最初に市場に出す 180 日前に先行品のスポンサーに対して通知を行わなければならない（42USC262(l)(8)(A)）。

・先行品のスポンサーは、上記通知を受けた後、上市をする前に、前記一次リストに含まれ、前記第 1 の訴訟の対象に含まれない特許に関し、裁判所がその有効性や侵害等の問題について決定を下すまで、バイオ後続品申請者が該当するバイオ後続品を製造・販売することを禁じる仮差止命令を請求することができる（42USC262(l)(8)(B)）。

バイオ後続品申請者に訴状が送達後 30 日以内に、バイオ後続品申請者は FDA 長官に訴状とともに通知しなければならない（42USC262(l)(6)(C)(i)）。FDA 長官は当該通知を官報（Federal Register）で公開する（42USC262(l)(6)(C)(ii)）。

図 4 官報（Federal Register）で公開された訴訟事件例[34]



information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 314 have been approved under OMB control number 0910–0001; the collections of information in 21 CFR part 312 for conducting clinical trials and collecting data for such trials have been approved under OMB control number 0910–0014; the collections of information pertaining to Electronic Records and Electronic Signatures have been approved under OMB control number 0910–0303; the collections of information pertaining to the Requirements on Content and Format of Labeling for Human Prescriptions for "opioid-sparing" claims have been approved under OMB control number 0910–0572; and the collections of information found in the Guidance for Industry on Expedited Programs for Serious Condition—Drugs and Biologics for expedited pathways to support the development program for non-opioid analgesics have been approved under OMB control number 0910–0765.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either *https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs*, *https://www.fda.gov/regulatory-information/search-fda-guidance-documents*, or *https://www.regulations.gov*.

Dated: February 7, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–02858 Filed 2–9–22; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2017–N–4853]

Receipt of Notice That a Patent Infringement Complaint Was Filed Against a Biosimilar or Interchangeable Biosimilar Applicant

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is publishing notice that an applicant for a biologics license application (BLA) for a biosimilar or interchangeable biosimilar product submitted under the Public Health Service Act (PHS Act) (a "subsection (k) applicant") notified FDA that an action for patent infringement was filed in connection with the applicant's BLA. Under the PHS Act, within 30 days after the subsection (k) applicant is served with a complaint in an action for patent infringement described under the PHS Act, the subsection (k) applicant shall provide the Secretary of HHS with notice and copy of such complaint. FDA is required to publish notice of the complaint in the **Federal Register**.

FOR FURTHER INFORMATION CONTACT: Sandra Benton, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 1132, Silver Spring, MD 20993–0002, 301–796–1042, *Sandra.Benton@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION: The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) was enacted as part of the Patient Protection and Affordable Care Act (Pub. L. 111–148) on March 23, 2010. The BPCI Act amended the PHS Act and created an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product. Section 351(k) of the PHS Act (42 U.S.C. 262(k)) sets forth the requirements for an application for a proposed biosimilar product and an application or a supplement for a proposed interchangeable product.

Section 351(l) of the PHS Act (42 U.S.C. 262(l)) describes certain procedures for exchanging patent information and resolving patent disputes between a subsection (k) applicant and the holder of the BLA reference product. If a subsection (k) applicant is served with a complaint in an action for a patent infringement described in section 351(l)(6) of the PHS Act, the subsection (k) applicant is required to provide the Secretary with notice and a copy of the complaint within 30 days of service. FDA is required to publish notice of a complaint received under section 351(l)(6)(C) of the PHS Act in the **Federal Register**.

FDA received notice of the following complaint under section 351(l)(6)(C) of the PHS Act: *AbbVie Inc. and AbbVie Biotechnology Ltd.* v. *Alvotech HF*, 1:21–cv–02258 (N.D. Ill., filed April 27, 2021).

FDA has only a ministerial role in publishing notice of a complaint received under section 351(l)(6)(C) of the PHS Act and does not perform a substantive review of the complaint.

Dated: February 4, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2022–02799 Filed 2–9–22; 8:45 am]

BILLING CODE 4164–01–P

なお、バイオ後続品申請者が 42USC262(l)(2)(A)に基づき、先行品スポンサーに対して、申請及び関連する製造情報を提供する、いわゆる「パテントダンス」手続きは任意であるが、42USC262(l)(8)(A)に基づく上市通知は義務的であり、FDA によるバイオシミラーの承認後にのみ提出することができる[35]。バイオ後続品申請者が 42USC262(l)(2)(A)に基づき、先行品スポンサーに対して、申請及び関連する製造情報を提供する、いわゆる「パテントダンス」手続きを実施していた

[34] Federal Register 87(28), 7844 (February 10, 2022)
https://www.govinfo.gov/content/pkg/FR-2022-02-10/pdf/2022-02799.pdf

[35] Amgen Inc. v. Sandoz Inc. (Fed. Cir. 2015-1499, July 21, 2015)（CAFC ウェブサイト）
https://cafc.uscourts.gov/opinions-orders/s15-1499.pdf

場合であっても、42USC262(l)(8)(A)に基づく上市通知は義務的であり、かつ差止命令により同通知の提出を強制することができる[36]。

③ 後発医薬品の自動承認停止

なし

先行品のスポンサーは、後続品が発売される潜在的な危険を防ぐため、仮差止による救済（42USC262(l)(8)(B)）を積極的に求めていく必要がある。

④ 後発医薬品会社へのインセンティブ

バイオ後続品（バイオシミラー）というだけでは、先行品を代替できるわけではない。バイオ後続品は、先行品と同一ではなく、高度に類似しているに過ぎない。参照品と代替可能な程度に同一または極めて類似する代替可能医薬品（interchangeable）[37]のみ、以下の(A)-(C)のいずれか早い日まで独占販売権が与えられる（42USC262(k)(6)）。

(A) 最初の代替可能医薬品（interchangeable）の上市から 1 年後

(B) 以下の(i)または(ii)から 18 か月後

(i) 42USC262(l)(6)の特許侵害訴訟において係争中の特許権に関する最終判決なされた日

(ii) 42USC262(l)(6)の特許侵害訴訟の請求棄却（確定力の有無は問わない）

(C) (i)最初の代替可能医薬品（interchangeable）の承認から 42 か月後（42USC262(l)(6)の特許侵害訴訟が提起されており、当該訴訟が上記 42 か月間に依然として係属している場合）

(ii) 最初の代替可能医薬品（interchangeable）の承認から 18 か月後（42USC262(l)(6)の特許侵害訴訟が提起されていない場合）

以下、表 7 に米国の生物学的製剤の承認の流れをまとめる。

表 7 米国の生物物学的製剤（先発、biosimilar）の承認の流れ

Step		
1	先発（Reference Product Sponsor (RPS)）による先発品試験	安全性、有効性の試験が必要である。
2	RPS による特許出願、権利化	医薬組成物、製造方法、用途等の特許出願、権利化を行う。
3	RPS による申請（42USC262(a) Biologics License Application (BLA)）	RPS は、安全性、有効性等を示す臨床／非臨床試験データとともに 42USC262(a)および 21CFR601.2 に基づく BLA を申請する。
4	FDA による 42USC262(a) BLA 承認	FDA により 42USC262(a) BLA が承認されると、当該新薬には 12 年の market exclusivity が付与され、この期間

[36] Amgen Inc. v. Apotex Inc. (Fed. Cir. 2016-1308, July 5, 2016)（CAFC ウェブサイト）
https://cafc.uscourts.gov/opinions-orders/16-1308.opinion.6-30-2016.1.pdf

[37] Biosimilar and Interchangeable Products(U.S. Food & Drug Administration ウェブサイト)
https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products

		内に FDA が当該新薬の biosimilar（42USC262(k)(7)(A)）を承認しない。また、当該新薬承認日後 4 年間は後発（Biosimilar Applicant (BA)）による申請（42USC262(k) BLA）はできない。
5	BA による biosimilar 試験	上記 12 年の独占期間満了前に BA は biosimilar の試験を行うことができる（35USC271(e)(1)）。しかしながら、承認後のための製造備蓄は免責されない[38]。
6	BA による申請（42USC262(k) BLA）	新薬承認 4 年以降、BA は RPS の安全性／有効性のデータを基に biosimilar の申請を行うことができる（42USC262(k)(7)(B)）。 Biologics Price Competition and Innovation Act (BPCIA)において、BA は biosimilar が先行品に対して高度に類似（highly similar）し、臨床的に意味のある相違点がないことを示さなければならない（42USC262(i)(2), 42USC262(k)(2)(A)(i)(I)）。 BA は、後発品が、先発品を患者に投与した際と同じ臨床結果をもたらすことが期待され、複数回投与された際にも先発品の安全性リスクを増大させず、有効性を現象させない場合には interchangeable として申請することもできる（42USC262(k)(4)）。
7	パテントダンス	RPS の特許が存在する場合、BA による biosimilar の FDA への申請（42USC262(k)）は、特許侵害を形成する（35USC271(e)(2)(C)）。この時点で RPS は特許訴訟を提起できず、BA がパテントダンスと呼ばれる工程を開始するか否かを確認しなければならない。 パテントダンスはラウンド 1 の特許訴訟の対象となる特許リストを確定するための RPS と BA との訴訟前の情報交換であり、BA が当該パテントダンスを開始するか否かを決定できる。 パテントダンス： (1) BA がパテントダンスを開始することを決定すると、BA の 42USC262(k)の BLA が FDA に受理されてから 20 日以内に、BA は RPS に 42USC262(k)の BLA のコピーを送付しなければならない。 (2) RPS は 60 日以内に BA に対してライセンス可能な特許リストを提示する（42USC262(l)(3)(C)）。

[38] Amgen Inc. v. Hospira, Inc. (Fed. Cir. 2019-1067, 2019-1102, December 16, 2019)
https://cafc.uscourts.gov/opinions-orders/19-1067.opinion.12-16-2019.pdf

		(3) BA は、60 日以内にライセンスを希望する特許（及び、あれば、無効、権利行使不能、非侵害の訴訟対象とすべき特許）のリストを RPS に提示する（42USC262(l)(3)(B)(i), 42USC262(l)(3)(B)(iii)）。BA は、無効、権利行使不能、非侵害に関する事実／法的根拠を詳細な説明とともに、または、RPS の特許満了まで biosimilar を上市しない旨の文書を RPS に提示しなければならない（42USC262(l)(3)(B)(ii)）。 (4) BA が(3)の無効、権利行使不能、非侵害に関する事実／法的根拠を詳細な説明とともに RPS に提示した場合、60 日以内に RPS は有効性、権利行使可能性、侵害性について詳細に説明しなければならない（42USC262(l)(3)(C)）。 (5) 上記(1)-(4)の情報交換後、両当事者は訴訟対象とすべき特許の最終リストを作成する（42USC262(l)(4)-(6)）。15 日以内に当該最終リストに合意した場合、RPS は当該合意から 30 日以内に特許訴訟を提起しなければならない（42USC262(l)(4), 42USC262(l)(6)）。 (6) 上記(1)-(4)の情報交換後、作成された最終リストに 15 日以内に合意しない場合、両当事者は別の特許リストを作成する。BA が先にリストすべき特許の数を開示し、当該開示から 5 日以内に両当事者で特許リストを交換する（42USC262(l)(5)(A), 42USC262(l)(5)(B)(i)）。RPS は BA がリストする以上の特許をリストすることはできない（42USC262(l)(5)(B)(ii)）。RPS は 30 日以内に特許訴訟を提起しなければならない（42USC262(l)(6)(B)）。 (7) (5)または(6)において RPS が 30 日以内に訴訟提起しない場合、損害賠償は適正ロイヤルティに限定されることになる（42USC262(l)(6)(B)）。
8	BPCIA 訴訟（ラウンド 1）	BA がパテントダンスを開始した場合、RPS はパテントダンス終了後 30 日以内に交渉対象特許について特許侵害訴訟を行うことができる（35USC271(e)(2)(C)(i), 42USC262(l)）。BA がパテントダンスを開始した場合、BA が biosimilar 上市 180 日以上前の通知を行うまでは、BA, RPS ともに、リストに掲載されていない特許に関する確認訴訟を提起することはできない（42USC262(l)(9)(A)）。

9	FDA による 42USC262(k) BLA 承認	先発品の独占期間が満了し、biosimilar が BPCIA および FDA の要件を充足する場合、FDA は当該 biosimilar の承認を行う（42USC262(a)(1)）。
10	BA による上市 180 日前の通知	BA は biosimilar の最初の上市を行う 180 日前までに、RPS にその旨の通知を行わなければならない（42USC262(l)(8)(A)）。当該通知を行うために、BA は FDA からの承認を待つ必要はない。BA が早期に RPS に通知を行うことにより、BA は FDA による承認後、早期に biosimilar を上市することができる[39]。
11	BPCIA 訴訟（ラウンド 2）	上市 180 日前の通知を RPS が受領すると、RPS はラウンド 2 を開始し、biosimilar の製造販売を禁止するための仮差止請求を行うことができる。
12	RPS の特許満了	RPS の特許は訴訟の解決前後で満了するが、BA が特許満了後に biosimilar を上市するとしても、特許期間存続期間内に、将来の販売のために biosimilar を製造備蓄する行為は特許侵害を形成すると考えられている[40]。
13	訴訟終結	ラウンド 1 およびラウンド 2 の訴訟が終結すれば、BA は biosimilar を上市すべきか否かを判断できる。和解が行われる場合もあり、例えば Humira の biosimilar の上市を 2023 年以降とする AbbVie 社と複数の BA との和解契約があるとされている。

(4) パテントリンケージ条項に関する CPTPP との比較

パテントリンケージ条項に関する CPTPP と米国法との比較を表 8 に示す。

[39] Amgen Inc. v. Sandoz Inc. (Fed. Cir. 2015-1499, December 14, 2017)（CAFC ウェブサイト）
https://cafc.uscourts.gov/opinions-orders/15-1499.opinion.12-13-2017.1.pdf
[40] Amgen Inc. v. Hospira, Inc. (Fed. Cir. 2019-1067, 2019-1102, December 16, 2019)（CAFC ウェブサイト）
https://cafc.uscourts.gov/opinions-orders/19-1067.opinion.12-16-2019.pdf

表 8 パテントリンケージ条項に関する CPTPP と米国法との比較

CPTPP[41]	米国法[42]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	42USC262(l)(2) (l) Patents (1) …（略）… (2) Subsection (k) application information Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k) applicant— (A) shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application; and (B) may provide to the reference product sponsor additional information requested by or on behalf of the reference product sponsor.
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	42USC262(l)(4)-(6) (4) Patent resolution negotiations (A) In general After receipt by the subsection (k) applicant of the statement under paragraph (3)(C), the reference product sponsor and the subsection (k) applicant shall engage in good faith negotiations to agree on which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6).

[41] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf
[42] 42USC262 – Regulation of biological product（U.S. Government Publishing Office ウェブサイト）
https://www.govinfo.gov/content/pkg/USCODE-2010-title42/pdf/USCODE-2010-title42-chap6A-subchapII-partF-subpart1-sec262.pdf

	(B) Failure to reach agreement If, within 15 days of beginning negotiations under subparagraph (A), the subsection (k) applicant and the reference product sponsor fail to agree on a final and complete list of which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6), the provisions of paragraph (5) shall apply to the parties. (5) Patent resolution if no agreement (A) Number of patents The subsection (k) applicant shall notify the reference product sponsor of the number of patents that such applicant will provide to the reference product sponsor under subparagraph (B)(i)(I). (B) Exchange of patent lists (i) In general On a date agreed to by the subsection (k) applicant and the reference product sponsor, but in no case later than 5 days after the subsection (k) applicant notifies the reference product sponsor under subparagraph (A), the subsection (k) applicant and the reference product sponsor shall simultaneously exchange— (I) the list of patents that the subsection (k) applicant believes should be the subject of an action for patent infringement under paragraph (6); and (II) the list of patents, in accordance with clause (ii), that the reference product sponsor believes should be the subject of an action for patent infringement under paragraph (6). (ii) Number of patents listed by reference product sponsor (I) In general Subject to subclause (II), the number of patents listed by the reference product sponsor under clause (i)(II) may not exceed the number of patents listed by the subsection (k) applicant under clause (i)(I).

	(II) Exception If a subsection (k) applicant does not list any patent under clause (i)(I), the reference product sponsor may list 1 patent under clause (i)(II). (6) Immediate patent infringement action (A) Action if agreement on patent list If the subsection (k) applicant and the reference product sponsor agree on patents as described in paragraph (4), not later than 30 days after such agreement, the reference product sponsor shall bring an action for patent infringement with respect to each such patent. (B) Action if no agreement on patent list If the provisions of paragraph (5) apply to the parties as described in paragraph (4)(B), not later than 30 days after the exchange of lists under paragraph (5)(B), the reference product sponsor shall bring an action for patent infringement with respect to each patent that is included on such lists. (C) Notification and publication of complaint (i)Notification to Secretary Not later than 30 days after a complaint is served to a subsection (k) applicant in an action for patent infringement described under this paragraph, the subsection (k) applicant shall provide the Secretary with notice and a copy of such complaint. (ii) Publication by Secretary The Secretary shall publish in the Federal Register notice of a complaint received under clause (i).
(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	42USC262(l)(8) (8) Notice of commercial marketing and preliminary injunction (A) Notice of commercial marketing The subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k). (B) Preliminary injunction

	After receiving the notice under subparagraph (A) and before such date of the first commercial marketing of such biological product, the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale of such biological product until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent that is— (i) included in the list provided by the reference product sponsor under paragraph (3)(A) or in the list provided by the subsection (k) applicant under paragraph (3)(B); and (ii) not included, as applicable, on— (I) the list of patents described in paragraph (4); or (II) the lists of patents described in paragraph (5)(B). (C) Reasonable cooperation If the reference product sponsor has sought a preliminary injunction under subparagraph (B), the reference product sponsor and the subsection (k) applicant shall reasonably cooperate to expedite such further discovery as is needed in connection with the preliminary injunction motion.

II. カナダ

(1) 経緯

1993 年：

北米自由貿易協定（North America Free Trade Agreement (NAFTA)）を通してパテントリンケージ制度を特許法の下位法令である Patented Medicine (Notice of Compliance)（PMNOC）が導入された。

1998 年：

PMNOC の改正により、特許リストに登録可能な特許要件（新薬の効能効果、含量、投与方法等に関連するものに限定、許可当局に特許リストから不適格特許の削除・拒絶する権限を付与）を設定、販売禁止期間が 30 か月から 24 か月に縮小された。

2006 年：

PMNOC の改正により、特許リスト登載関連の規定（パテントリンケージ制度で保護する特許は特許リストに登録された特許に限定、登載対象特許を 4 種（物質特許、製剤特許、組成物特許、用途特許）に限定）を整備、24 か月の販売禁止申請は 1 回に限定された。

2017 年：

カナダ-欧州連合包括的経済貿易協定（EU-Canada Comprehensive Economic and Trade Agreement (CETA)）の実施のため PMNOC が改正された[43]。従来は先発医薬品会社が後発医薬品会社に PMNOC 訴訟において連邦裁判所で敗訴した場合には、Health Canada は後発医薬品会社に承認を与え販売開始を許可し、先発医薬品会社には当該判決について控訴することはできなかった[44]。しかしながら、CETA 実施のために改正が行われた。

CETA Article 20.28[45]

Patent linkage mechanisms relating to pharmaceutical products

If a Party relies on 'patent linkage' mechanisms whereby the granting of marketing authorisations (or notices of compliance or similar concepts) for generic pharmaceutical products is linked to the existence of patent protection, it shall ensure that all litigants are afforded equivalent and effective rights of appeal.

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[43] Regulations Amending the Patented Medicines (Notice of Compliance) Regulations, 2017（Canada Gasette ウェブサイト）
https://gazette.gc.ca/rp-pr/p2/2017/2017-09-07-x1/html/sor-dors166-eng.html

[44] Henry Bian et al., Canada's Patented Medicines (Notice of Compliance) Proceedings and Intellectual Property (Cold Spring Harbor Perspectives in Medicine, 2015; 5:a020842)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4448703/pdf/cshperspectmed-IPM-a020842.pdf

[45] Text of the Comprehensive Economic and Trade Agreement – Chapter twenty: Intellectual Property（Government of Canada ウェブサイト）
https://www.international.gc.ca/trade-commerce/trade-agreements-accords-commerciaux/agr-acc/ceta-aecg/text-texte/20.aspx?lang=eng

2020 年：

新 NAFTA（Canada-United States-Mexico Agreement (CUSMA)）が発効した[46]。

(2) パテントリンケージ制度の概要

カナダのパテントリンケージ制度の概要を表 9 にまとめる。

[46] Statement by the Deputy Prime Minister on the entry-into-force of the new NAFTA（Prime Minister of Canada ウェブサイト）
https://pm.gc.ca/en/news/statements/2020/06/30/statement-deputy-prime-minister-entry-force-new-nafta

表 9 カナダのパテントリンケージ制度の概要

先発医薬品	
特許リスト	Patent register[47]
対象特許	物質特許、製剤特許、用量特許、医薬用途特許（NOC4(2)）
リスト登録者	新薬承認の申請者
リスト登録時期	新薬許可申請時又は変更許可申請時に登録を希望する特許を提出しなければならず（NOC4(5)）、許可申請の後に特許が登録された場合には、登録後 30 日以内に登録の申請をしなければならない（NOC4(6)）
後発医薬品申請後の提訴期間	新薬申請者は通知を日から 45 日以内に、裁判所に対し、保健省が特許権存続期間満了するまで後発医薬品の承認を与えることを禁止するように訴えることができる（Judicial review application）（NOC6(1)）。
後発医薬品	
申請時期制限	先発医薬品に新規化学物質の Data Protection が認められれば、後発医薬品は先発医薬品承認から 6 年間は申請できない（NOC5(5), C.08.004.1(3)(a) of the Food and Drug Regulations）。なお、先発医薬品承認から 8 年間（小児承認が得られた場合は 8.5 年間）は、後発医薬品は承認されない（C.08.004.1(3)(b) and C.08.004.1(4) of the Food and Drug Regulations）。
申請手続	特許リストに登載された新薬の資料を引用する後発医薬品の許可申請者は、市販許可の申請時に、新薬に関連して登録された特許の存続期間が満了した、又は特許の存続期間満了後に販売する陳述をするか、あるいは特許の無効又は当該医薬品の製造・使用・販売が特許を侵害していないとの主張を根拠とともに陳述する必要がある（NOC5(1)）。
承認の自動停止	24 か月（NOC7(1)）
後発医薬品申請情報の開示	NOC5(2.1)(c)（先発特許の非侵害、無効を主張）を引用する後発医薬品申請者は、後発医薬品申請日後に新薬承認申請者等に通知しなければならない。通知には、(i)有効成分、製剤、投与量、投与経路、医薬用途、(ii)申立を行う法的・事実的基礎に関し詳細に記述する（NOC5(3)(a)(b)）。 Health Canada で後発医薬品申請が受理された後発医薬品（2018 年 10 月 1 日以降）、バイオシミラー（2016 年 5 月 1 日以降）についてはカナダ政府のウェブサイトで Generic submissions under

[47] Patent register（Government of Canada ウェブサイト）
https://pr-rdb.hc-sc.gc.ca/pr-rdb/index-eng.jsp

	review (GSUR)[48]及び Drug and Health Product Submissions Under Review (SUR)[49]として公開される。
第 1 申請承認後発医薬品に与えられる独占期間	なし 新薬特許権者等による”judicial review application”が取下げ、中止、もしくは裁判所による中止、裁判所による保健省への NOC 中止命令が後で覆った場合、新薬特許権者等は、所定の期間に生じた後発医薬品申請者等のいかなる損失も補填する責を負う（NOC8(1)-(6)）。

(3) 手続等、詳細事項

① 先発の特許登録

特許情報開示のタイミング：

新規医薬品申請時、又は変更許可申請時に登録を希望する特許を提出しなければならず（NOC4(5)）、許可申請の後に特許が登録された場合には、登録後 30 日以内に登録の申請をしなければならない（NOC4(6)）。最高裁判決により、特許情報の提出期限については厳格に適用される[50]。

特許情報の開示内容：

Health Canada ウェブサイトから入手できる Form IV[51]により、物質特許、製剤特許、用量特許、医薬用途特許の特許情報を提出する（NOC4(2)）。特許情報は Patent List として Health Canada ウェブサイト[52]で公開される。Patent List は 1993 年 3 月 12 日以降、毎晩更新されている。

[48] Generic submissions under review（Government of Canada ウェブサイト）
https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/generic-submissions-under-review.html

[49] Drug and Health Product Submissions Under Review (SUR)（Government of Canada ウェブサイト）
https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/submissions-under-review.html

[50] Merck Canada Inc. v. Minister of Health (40043, May 13, 2022, Supreme Court of Canada)（カナダ最高裁ウェブサイト）
https://scc-csc.lexum.com/scc-csc/scc-l-csc-a/en/item/19387/index.do

[51] Form IV（カナダ政府ウェブサイト）
https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/doc/prodpharma/applic-demande/form/priv_briv-eng.doc

[52] Patent register（Government of Canada ウェブサイト）
https://pr-rdb.hc-sc.gc.ca/pr-rdb/index-eng.jsp

図 5 Patent List での公開例（Merck 社 JANUVIA (sitagliptin)）[53]

Medicinal ingredient search results

Medicinal ingredient	Brand name	Strength	Dosage	DIN [1]	Patent	CSP [2]
sitagliptin phosphate monohydrate	JANUVIA	100mg	tablet	02303922	2450740 2529400 2536251	
sitagliptin phosphate monohydrate	JANUVIA	25 mg	tablets	02388839	2450740 2529400 2536251	
sitagliptin phosphate monohydrate	JANUVIA	50 mg	tablets	02388847	2450740 2529400 2536251	

② 後発医薬品申請＋先発医薬品会社への通知

先発医薬品に新規化学物質の Data Protection が認められれば、後発医薬品は先発医薬品承認から 6 年間は申請できない（NOC5(5), C.08.004.1(3)(a) of the Food and Drug Regulations）。なお、先発医薬品承認から 8 年間（小児承認が得られた場合は 8.5 年間）は、後発医薬品は承認されない（C.08.004.1(3)(b) and C.08.004.1(4) of the Food and Drug Regulations）。

特許リストに登載された新薬の資料を引用する後発医薬品の許可申請者は、市販許可の申請時に、新薬に関連して登録された特許の存続期間が満了した、又は特許の存続期間満了後に販売する陳述をするか、あるいは特許の無効又は当該医薬品の製造・使用・販売が特許を侵害していないとの主張を根拠とともに陳述する必要がある（NOC5(1)）。

NOC5(2.1)(c)（先発特許の非侵害、無効を主張）を引用する後発医薬品申請者は、後発医薬品申請日後に新薬承認申請者等に通知しなければならない。通知には、(i)有効成分、製剤、投与量、投与経路、医薬用途、(ii)申立を行う法的・事実的基礎に関し詳細に記述する（NOC5(3)(a)(b)）。

Health Canada で後発医薬品申請が受理された後発医薬品（2018 年 10 月 1 日以降）、バイオシミラー（2016 年 5 月 1 日以降）についてはカナダ政府のウェブサイトで Generic submissions under review (GSUR)[54]（図 6）及び Drug and Health Product Submissions Under Review (SUR)[55]（図 7）として公開される。

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[53] Patent register（Government of Canada ウェブサイト）（Brand Name = Januvia で検索）（2022 年 6 月 22 日アクセス）
https://pr-rdb.hc-sc.gc.ca/pr-rdb/index-eng.jsp

[54] Generic submissions under review（Government of Canada ウェブサイト）
https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/generic-submissions-under-review.html

[55] Drug and Health Product Submissions Under Review (SUR): New drug submissions under review（Government of Canada ウェブサイト）
https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/submissions-under-review/new-drug-submissions-under-review.html

図 6 Generic submissions under review (GSUR)での公開例[56]

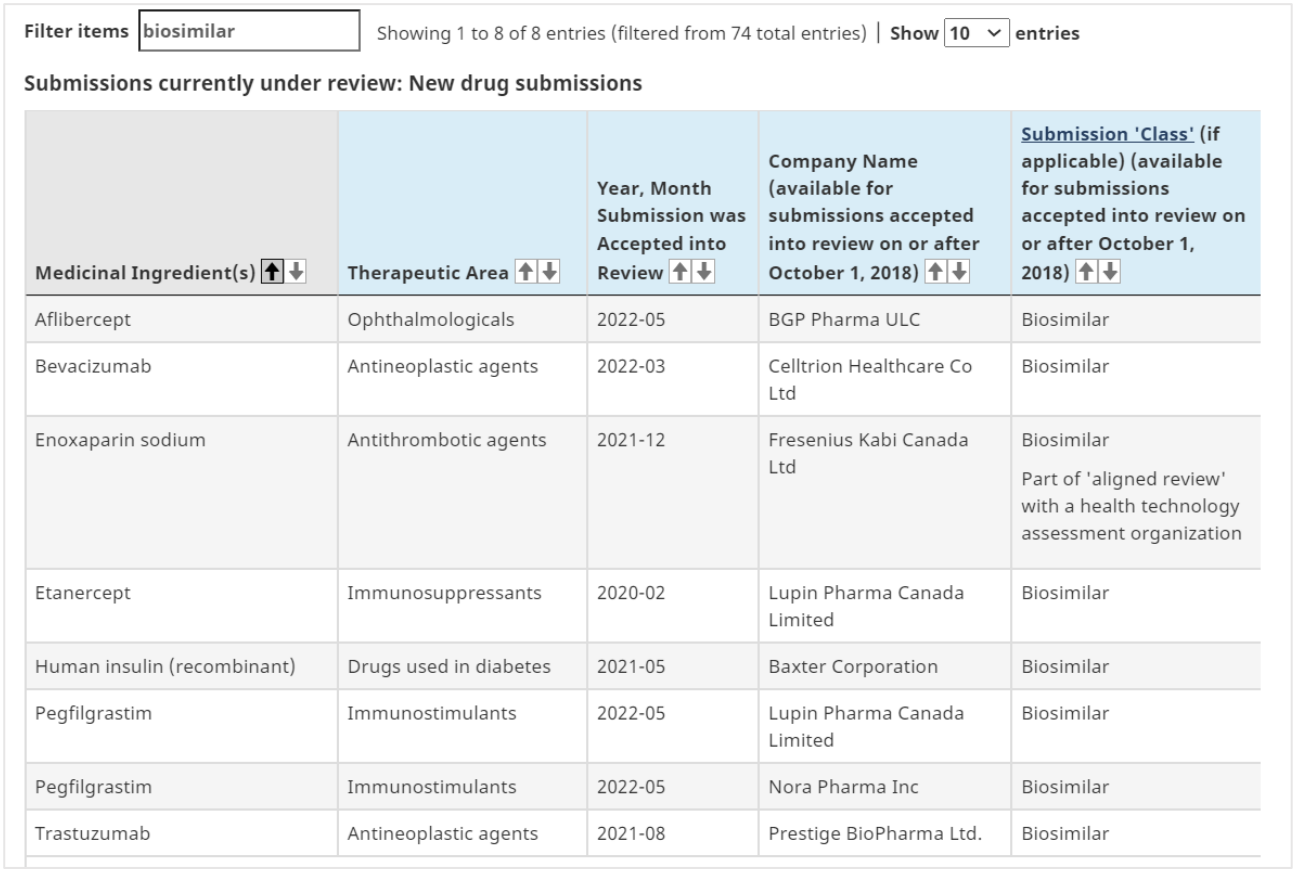
Generic submissions currently under review: Abbreviated new drug submissions

Medicinal Ingredient(s)	Therapeutic Area	Number of submissions under review
Abacavir sulfate, dolutegravir sodium, lamivudine	Antivirals for systemic use	1
Abiraterone acetate	Endocrine therapy	2
Acetylcysteine	Cough and cold preparations	1
Acyclovir	Antivirals for systemic use	1
Acyclovir sodium	Antivirals for systemic use	1
Afatinib	Antineoplastic agents	1
Afatinib dimaleate	Antineoplastic agents	3
Amantadine hydrochloride	Anti-Parkinson drugs	1
Ambrisentan	Antihypertensives	1
Amikacin sulfate	Antibacterials for systemic use	1

1 2 3 4 5 21 Next →

[56] Generic submissions under review（Government of Canada ウェブサイト）（2022 年 6 月 22 日アクセス）https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/generic-submissions-under-review.html

図 7 Drug and Health Product Submissions Under Review (SUR)での公開例[57]



Filter items: biosimilar　Showing 1 to 8 of 8 entries (filtered from 74 total entries) | Show 10 entries

Submissions currently under review: New drug submissions

Medicinal Ingredient(s)	Therapeutic Area	Year, Month Submission was Accepted into Review	Company Name (available for submissions accepted into review on or after October 1, 2018)	Submission 'Class' (if applicable) (available for submissions accepted into review on or after October 1, 2018)
Aflibercept	Ophthalmologicals	2022-05	BGP Pharma ULC	Biosimilar
Bevacizumab	Antineoplastic agents	2022-03	Celltrion Healthcare Co Ltd	Biosimilar
Enoxaparin sodium	Antithrombotic agents	2021-12	Fresenius Kabi Canada Ltd	Biosimilar Part of 'aligned review' with a health technology assessment organization
Etanercept	Immunosuppressants	2020-02	Lupin Pharma Canada Limited	Biosimilar
Human insulin (recombinant)	Drugs used in diabetes	2021-05	Baxter Corporation	Biosimilar
Pegfilgrastim	Immunostimulants	2022-05	Lupin Pharma Canada Limited	Biosimilar
Pegfilgrastim	Immunostimulants	2022-05	Nora Pharma Inc	Biosimilar
Trastuzumab	Antineoplastic agents	2021-08	Prestige BioPharma Ltd.	Biosimilar

機密情報

後発医薬品申請者は、先発医薬品承認取得者に、先発医薬品特許が侵害されているか否かを判断の根拠となる後発医薬品申請者所有の提出物の電子コピーを送付しなければならない（NOC5(3)(c)(iii)）。NOC5(3)(c)(iii)で言及される送付物について、後発医薬品申請者は、機密性を維持するための合理的な取り決め（rule）を課すことができる（NOC5(3.5)）。

また、先発医薬品特許が無効であることを主張する場合には、その主張の根拠となる文書を電子ファイルとともに先発医薬品承認取得者に送付しなければならない（NOC5(3)(c)(iv)）。

後発医薬品申請者が、先発医薬品特許が無効であることを主張する場合には、先発医薬品承認者に通知する際に、特許発明者の名前、連絡先、ラボノート、研究報告書等を要求することができる（NOC5(3.1)(a), 5(3.1)(b)）。先発医薬品承認取得者は、NOC5(3.1)(a), 5(3.1)(b)で言及される送付物について、後発医薬品申請者は、機密性を維持するための合理的な取り決め（rule）を課すことができる（NOC6.03(2)）。

[57] Drug and Health Product Submissions Under Review (SUR): New drug submissions under review （Government of Canada ウェブサイト）（Filter Item = biosimilar で検索）（2022 年 6 月 22 日アクセス）
https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/submissions-under-review/new-drug-submissions-under-review.html

③ 後発医薬品の自動承認停止

新薬申請者は通知を日から 45 日以内に、裁判所に対し、特許侵害訴訟を提起することができる（Judicial review application）（NOC6(1)）。当該訴えが提起された場合、当局は後発医薬品承認を 24 か月停止する（NOC7(1)）。

なお、先発医薬品会社は、上記の特許侵害訴訟の結果にもかかわらず、後発医薬品会社がその特許権を侵害していると考える場合、「通常の」特許侵害訴訟を開始することができると解されている[58]。

④ 後発医薬品会社へのインセンティブ

カナダでは後発医薬品の独占販売期間の制度はない。

新薬特許権者等による”judicial review application”が取下げ、中止、もしくは裁判所による中止、裁判所による保健省への NOC 中止命令が後で覆った場合、新薬特許権者等は、所定の期間に生じた後発医薬品申請者等のいかなる損失も補填する責を負う（NOC8(1)-(6)）。

(4) パテントリンケージ条項に関する CPTPP との比較

パテントリンケージ条項に関する CPTPP とカナダ法との比較を表 10 に示す。

表 10 パテントリンケージ条項に関する CPTPP とカナダ法との比較

CPTPP[59]	カナダ法[60]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許	PMNOC 5(3) A second person who makes an allegation referred to in paragraph (2.1)(c) shall (a) serve on the first person a notice of allegation relating to the submission or supplement filed under subsection (1) or (2) on or after its date of filing; (b) include in the notice of allegation (i) a description of the medicinal ingredient, dosage form, strength, route of administration and use of the drug in respect of

[58] Canada’s Patented Medicines (Notice of Compliance) Proceedings and Intellectual Property (Henry Bian and Conor McCourt, Cold Spring Harb Perspect Med, 2015 Jun; 5(6): a020842)

[59] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf

[60] Patented Medicines (Notice of Compliance) Regulations（Government of Canada ウェブサイト）
https://laws-lois.justice.gc.ca/PDF/SOR-93-133.pdf

の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	which the submission or supplement has been filed, and (ii) a statement of the legal and factual basis for the allegation, which statement must be detailed in the case of an allegation that the patent or certificate of supplementary protection is invalid or void;
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	PMNOC 6(1) The first person or an owner of a patent who receives a notice of allegation referred to in paragraph 5(3)(a) may, within 45 days after the day on which the first person is served with the notice, bring an action against the second person in the Federal Court for a declaration that the making, constructing, using or selling of a drug in accordance with the submission or supplement referred to in subsection 5(1) or (2) would infringe any patent or certificate of supplementary protection that is the subject of an allegation set out in that notice.
(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	PMNOC 7(1) The Minister shall not issue a notice of compliance to a second person before the latest of (a) the day after the expiry of all of the patents and certificates of supplementary protection in respect of which the second person is required to make a statement or allegation under subsection 5(1) or (2) and that are not the subject of an allegation; (b) the day on which the second person complies with paragraph 5(3)(e); (c) the 46th day after the day on which a notice of allegation under paragraph 5(3)(a) is served; (d) the day after the expiry of the 24-month period that begins on the day on which an action is brought under subsection 6(1);

	(e) the day after the expiry of all of the patents and certificates of supplementary protection in respect of which a declaration of infringement has been made in an action brought under subsection 6(1); and (f) the day after the expiry of all of the certificates of supplementary protection, other than any that were held not to be infringed in an action referred to in paragraph (e), that (i) set out a patent referred to in paragraph (a) or (e), (ii) are not the subject of a statement or allegation made under subsection 5(1) or (2), and (iii) are included on the register in respect of the same submission or supplement as the patent.

III. 中国

(1) 経緯

2002 年に制定された医薬品登録管理方法（2005 年、2007 年、及び 2020 年改正を経て現在に至る）第 11 条で、「申請者は登録を申請する医薬品または仕様処方、工程等について中国特許及びその権利帰属状態について説明し、他人の特許に対して侵害を構成しないという保証書を提出しなければならず、発生可能な侵害結果に対して責任を負わなければならない」と規定している。2005 年の改正時に、特許宣言の範囲を医薬品または仕様処方、工程だけでなく、医薬用途まで拡大した。また、2007 年の改正時に、後発医薬品申請期限条項、情報開示時条項等が追加された。

2007 年に、医薬登録規則第 18 条（2007 年施行）においてパテントリンケージ制度が導入された[61]。医薬品を申請する者は、新薬・後発医薬品を問わず、自己の有する特許権について、中国における特許状況を説明する書類を提出しなければならない。規制当局（国家食品薬品監督管理局、China Food and Drug Administration (CFDA)）は、ウェブサイト上にこれらの特許状況を掲載した。医薬品申請者は、第三者が中国における当該医薬品に関する特許権を有する場合、その特許権を侵害していないことを明言しなければならない。医薬品申請・承認手続きにおいて、特許紛争が起きた場合には、特許関連法、規則に従って解決されなければならない[62]。また、第 19 条（2007 年施行）において、後発医薬品製造会社は、オリジナル医薬品の特許期間が満了する 2 年以内に登録申請することができるが、行政省庁は当該医薬品について審査して規定に準拠しても、特許期間の切れた後にのみ、医薬品批准文書番号、輸入医薬品登録証または医薬製品登録証を発行できるように規定している。つまり、申請は、特許期間が満了する 2 年以内に行うことができるが、行政許可は特許期間が満了して初めて行うことができるとしていた[63]。しかし、この「2 年」という期間制限は 2020 年改正（2020 年 7 月 1 日施行）で削除された[64]。

2017 年に国家薬品監督管理局（NMPA）は、パブリックレビューのための一般的なパテントリンケージ手順の草案「医薬品医療機器の革新者権益保護に関する政策」（2017 年 5 月）、「医薬品および医療機器革新を奨励するための審査承認制度改革強化に関する意見」（2017 年 5 月）を公開した[65]が、進展はなかった。

2020 年 1 月 15 日、米国と中国は、米中経済貿易協定（Economic and Trade Agreement between the

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61 パテントリンケージ：医薬品の安定供給と特許制度に関する一考察 -ジェネリック医薬品申請・承認手続きにおける新薬関連特許権の侵害性判断の交際動向- （桝田祥子 AIPPI Vol. 59(11), 818-834, 2014）

62 平成 29 年度バイオ医薬品分野における知的財産戦略及び活用の最適化に関する調査研究報告書（平成 30 年 3 月 一般財団法人 知的財産研究教育財団 知的財産研究所）
https://www.amed.go.jp/content/000032002.pdf

63 中国医薬品登録管理弁法局令 28 号（2007 年 7 月 10 日公布）（ジェトロ大連事務所）（ジェトロウェブサイト）
https://www.jetro.go.jp/ext_images/world/asia/cn/law/pdf/invest_053.pdf

64 「医薬品登録管理規則」が公布（2020 年 4 月 7 日 中国食品医薬品国際交流センターウェブサイト）
http://www.cjpi.org.cn/zryyxxwjp/flfg/ypflfg/webinfo/2020/04/1573214815047592.htm

65 食品药品监管总局就鼓励药品医疗器械创新保护创新者权益征求意见（中华人民共和国中央人民政府ウェブサイト）
http://www.gov.cn/xinwen/2017-05/12/content_5193269.htm

United States of America and the People's Republic of China）の第 1 弾（Phase 1）[66]に署名を行い、2020 年 2 月 14 日に発効した。当該経済貿易協定第 1.11 条に、特許権者等に後発医薬品会社の販売承認申請について通知し、仮差止を含む救済を求め、侵害・有効性の紛争を解決するための時間と機会を特許権者等に提供することなどが規定されている。本規定に基づき、2021 年 6 月 1 日に施行された第 4 次改正専利法[67]（10 年以上の意見収束の結果によるもの）、及び医薬品特許紛争早期解決制実施方法により、パテントリンケージ制度の法制化が行われた。

2020 年 9 月 11 日、中国国家医薬品監督管理局と国家知識財産権局が連合して「医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）」を設け、公衆の意見を求め[68]、若干の修正を経て 2021 年 7 月に施行された[69]。本実施弁法は、その目的が「医薬品特許権者の合法的な権益を保護し、新薬研究と水準の高い後発医薬品の発展促進を奨励し、医薬品特許紛争の早期解決するためのもの」であることを第 1 条で明らかにしている。

2021 年 7 月 5 日に国家知識産権局が「医薬品特許紛争の早期解決メカニズムの行政裁定規定」[70]を、最高人民法院が「登録申請医薬品に関連する特許紛争民事事件の審理における法律適用の若干問題に関する規定」[71]を設けている。

2022 年 4 月 15 日、北京知的財産裁判所により、パテントリンケージ制度に基づく特許係争の最初の判決が下された[72]。その後、最高人民法院に上告されたが、2022 年 8 月、最高人民法院は北京知的財産裁判所判決（後発医薬品会社非侵害）を認容した[73]。

2022 年 4 月 25 日、国家知識産権局により、パテントリンケージ制度に基づく特許係争の最初の行政裁定が行われた[74]。

2022 年 5 月 9 日に医薬品登録管理方法施行規則の草案が公開され、第 38 条にパテントリンケー

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[66] Economic and Trade Agreement between the Government of the United States of America and the Government of the People's Republic of China（Office of the United States Trade Representative ウェブサイト）
https://ustr.gov/sites/default/files/files/agreements/phase%20one%20agreement/Economic_And_Trade_Agreement_Between_The_United_States_And_China_Text.pdf

[67] 中华人民共和国专利法（2020 年修正）（ジェトロウェブサイト）
https://www.jetro.go.jp/ext_images/world/asia/cn/ip/law/pdf/regulation/regulation20210601.pdf

[68] 国家药监局综合司 国家知识产权局办公室公开征求《药专利纠纷早期解决机制实施办法（试行）（征求意见稿）》意见（国家药品监督管理局ウェブサイト）
https://www.nmpa.gov.cn/xxgk/ggtg/qtggtg/20200911175627186.html

[69] 国家药监局 国家知识产权局关于发布《药品专利纠纷早期解决机制实施办法（试行）》的公告 2021 年第 89 号（中华人民共和国中央人民政府ウェブサイト）
https://www.gov.cn/zhengce/zhengceku/2021-07/04/content_5622330.htm

[70] 国家知识产权局 公告 国家知识产权局发布《药品专利纠纷早期解决机制行政裁决办法》的公告（第 435 号）（国家知识产权局ウェブサイト）
https://www.cnipa.gov.cn/art/2021/7/5/art_74_160566.html

[71] 最高人民法院关于审理申请注册的药品相关的专利权纠纷民事案件适用法律若干问题的规定（中华人民共和国最高人民法院ウェブサイト）
https://www.court.gov.cn/fabu-xiangqing-311791.html

[72] パテントリンケージ関連で最初の人民法院判断 Chugai Pharmaceutical v. Wenzhou Haihe（北京市知識産権法院 SNS）
https://mp.weixin.qq.com/s/-9SocP2TLE20Xw7me3OxNw

[73] Roche Loses Appeal Against Generic Co. At China's Top Court (LAW360, August 29, 2022)

[74] パテントリンケージ関連で最初の行政裁決 Humanwell v. Purdue Pharma（国家知識産権局ウェブサイト）
https://www.cnipa.gov.cn/art/2022/4/25/art_53_175126.html

ジ、第 39 条に最初の化学後発医薬品の市場独占期間が規定されている。2022 年 6 月 9 日までコメントが募集された[75]。

(2) パテントリンケージ制度の概要

中国のパテントリンケージ制度の概要を表 11 にまとめる。

[75] 药品管理法实施条例修订草案征求意见（国家市场监督管理总局ウェブサイト）
https://www.samr.gov.cn/xw/mtjj/202205/t20220513_344838.html

表 11 中国のパテントリンケージ制度の概要

先発医薬品	
特許リスト	中国上市药品专利信息登记平台[76]
対象特許	化学医薬品：物質特許、医薬用途特許、製剤特許（実施弁法第 5 条） 漢方薬：漢方薬組成物特許、漢方薬抽出物特許、医薬用途特許（実施弁法第 12 条） バイオ医薬品： 活性成分の配列構造特許、医薬用途特許（実施弁法第 12 条）
登録情報	医薬品の名称、剤形、規格、医薬品の製造販売承認を得た者、関連する特許番号、特許権の名称（発明の名称）、特許権者、特許権のライセンスを受けた者、特許権の付与日及び保護期間の満了日、特許権の状態、特許権の種類、医薬品と関連する特許権の請求項との対応関係、宛先住所、連絡者（担当者氏名）、連絡先（電話番号、E メールアドレスなど）（実施弁法第 4 条）
リスト登録者	医薬品販売承認取得者（実施弁法第 4 条）
リスト登録時期	医薬品登録証明書取得後 30 日以内 登録した特許情報に変更が生じた場合は、30 日以内に更新 登録しない場合はパテントリンケージ制度の対象外となる （実施弁法第 4 条）
後発医薬品申請後の提訴期間	化学医薬品： 特許権者／利害関係人は、不服ある場合は、後発医薬品承認申請の 45 日以内に、人民法院[77]に訴訟を提起するか、国務院特許行政部門（特許庁）[78]に行政裁決を請求することができる。 （特許権者／利害関係人が訴訟提起／行政裁決請求した場合） 1. 裁判所または特許庁は、訴訟の手続開始または行政裁決の請求を受理から 15 営業日以内に、医薬品審査機関および後発医薬品申請者に通知する（実施弁法第 7 条）。 2. 通知書を受けた場合、医薬品監督部門は、後発医薬品の申請に対して 9 ヶ月の待機期間を設定する。ただし、医薬品審査機関における審査は継続される（実施弁法第 8 条）。

[76] 中国上市药品专利信息登记平台ウェブサイト
https://zldj.cde.org.cn/home
[77] 北京市知識産権法院 SNS（パテントリンケージ関連で最初の人民法院判断 Chugai Pharmaceutical v. Wenzhou Haihe）
https://mp.weixin.qq.com/s/-9SocP2TLE20Xw7me3OxNw
[78] 国家知識産権局ウェブサイト（パテントリンケージ関連で最初の行政裁決 Humanwell v. Purdue Pharma）
https://www.cnipa.gov.cn/art/2022/4/25/art_53_175126.html

	3. 特許権者または利害関係者、後発医薬品申請者は、判決書または決定書を受けてから 10 営業日以内に、結果を医薬品審査機関に知らせる（実施弁法第 9 条）。 4. 技術評価を通過した後発医薬品承認申請について、医薬品審査機関、医薬品監督部門は、確定判決、調停合意または行政裁決の結果に応じて処理する。 （特許権者／利害関係人が訴訟提起／行政裁決請求しない場合） 医薬品監督部門は、技術審査評価の結論及び後発薬申請者が提出した宣言の状況に応じて、販売承認可否の決定を直接行う（実施弁法第 8 条）。 後発医薬品の製造販売承認申請者は、後発医薬品が関連特許権の保護範囲に包含されないことを確認するため、裁判所への訴訟提起または特許庁への行政裁決の請求が可能である（実施弁法第 8 条、CNIPA の規定第 4 条、最高裁の規定第 4 条）。 漢方薬、バイオ医薬品： 医薬品監督部門は、技術審査評価の結論及び後発薬申請者が提出した宣言に応じて、販売承認可否の決定を直接行う（9 ヶ月の待機期間は設定されない）（実施弁法第 12 条、第 13 条）。
後発医薬品	
申請時期制限	規定なし
申請手続	後発医薬品（化学医薬品、漢方薬、生物学的製剤）の製造販売承認申請者は、その申請をする際に、特許情報登録プラットフォームに登録されている、関連する先発医薬品の特許権ごとに声明を提出する必要がある（実施弁法第 6 条、第 12 条）。 声明 1： 対象となる先発医薬品について、いかなる特許情報も特許情報登録プラットフォームに掲載されていない。 声明 2： 特許情報登録プラットフォームに登録されている、対象となる先発医薬品の特許はすでに失効し、もしくは無効が確定している。または、後発医薬品の製造販売承認申請者が対象となる特許権の実施許諾を受けている。 声明 3：

	対象となる先発医薬品の特許権が特許情報登録プラットフォームに登録されているが、当該特許権の存続期間が満了するまで後発医薬品を製造販売しないことを承諾する。 声明 4： 特許情報登録プラットフォームに登録されている、対象となる先発医薬品の特許は無効と認められるべきであり、または申請する後発医薬品は当該特許権の保護範囲には包含されない（実施弁法第 6 条、第 12 条）。
承認の自動停止	9 ヶ月（化学医薬品のみ）（実施弁法第 8 条）
後発医薬品申請情報の開示	後発医薬品承認申請から 10 営業日以内に、国家医薬品審査評価機関は、プラットフォームで、後発医薬品承認申請の情報および宣言を公開する。 後発医薬品承認申請から 10 営業日以内に、後発医薬品申請者は、宣言とその根拠となるものを、先発医薬品承認保持者に知らせる（実施弁法第 6 条）。
第 1 申請承認後発医薬品に与えられる独占期間	12 ヶ月（化学医薬品のみ）（実施弁法第 11 条、医薬品管理法の施行に関する規則（案）第 39 条[79]）

(3) 手続等、詳細事項

① 先発の特許登録

医薬品販売承認取得者は、医薬品登録証明書取得後 30 日以内に、登録した特許情報に変更が生じた場合はその 30 日以内に、国家薬品監督管理局医薬品承認審査センターに対象特許（化学医薬品：物質特許、医薬用途特許、製剤特許（実施弁法第 5 条）、漢方薬：漢方薬組成物特許、漢方薬抽出物特許、医薬用途特許（実施弁法 12 条）、バイオ製薬：活性成分の配列構造特許、医薬用途特許（実施弁法第 12 条））について、特許情報（医薬品の名称、剤形、規格、医薬品の製造販売承認を得た者、関連する特許番号、特許権の名称（発明の名称）、特許権者、特許権のライセンスを受けた者、特許権の付与日及び保護期間の満了日、特許権の状態、特許権の種類、医薬品と関連する特許権の請求項との対応関係、宛先住所、連絡者（担当者氏名）、連絡先（電話番号、E メールアドレスなど））を届け出る必要がある。登録しない場合はパテントリンケージ制度の対象外となる（実施弁法第 4 条）。

特許情報は、ウェブサイトで公開される[80]（図 8、図 9）。

「医薬品販売承認取得者は、登録された関連情報の信憑性、正確性、完全性に責任を負い、受け取った関連する異議を迅速に検証して処理し、記録するものとする。」（実施弁法第 4 条）とあり、国家薬品監督管理局医薬品承認審査センターは登録内容については審査しないものとみられる。

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[79] 国家药监局综合司公开征求《中华人民共和国药品管理法实施条例（修订草案征求意见稿）》意见（国家药品监督管理局ウェブサイト）
https://www.nmpa.gov.cn/xxgk/zhqyj/zhqyjyp/20220509222233134.html

[80] 中国上市药品专利信息登记平台ウェブサイト
https://zldj.cde.org.cn/home

図 8 中国上市药品专利信息登记平台ウェブサイトでの公開例 1（低分子医薬品）（AstraZeneca 社安达唐（达格列净）（FORXIGA (dapagliflozin)））[81]

[81] 中国上市药品专利信息登记平台ウェブサイト（「化药专利信息公示」タブを選択し、「药品名称＝达格列净」で検索）（2022 年 6 月 22 日アクセス）
https://zldj.cde.org.cn/list?listType=PublicInfoList

図 9 中国上市药品专利信息登记平台ウェブサイトでの公開例 2（生物学的製剤）（Roche 社 雅美罗（托珠单抗）（ACTEMRA (tocilizumab)））[82]

② 後発医薬品申請＋先発医薬品会社への通知

後発医薬品（化学医薬品、漢方薬、生物学的製剤）の製造販売承認申請者は、その申請をする際に、特許情報登録プラットフォームに登録されている、関連する先発医薬品の特許権ごとに声明を提出する必要がある（実施弁法第 6 条、第 12 条）。

声明 1：

対象となる先発医薬品について、いかなる特許情報も特許情報登録プラットフォームに掲載されていない。

[82] 中国上市药品专利信息登记平台ウェブサイト（「生物制品专利信息公示」タブを選択し、「药品名称＝托珠单抗注射液（皮下注射）」で検索）（2022 年 6 月 22 日アクセス）
https://zldj.cde.org.cn/list?listType=PublicInfoList

声明 2：
特許情報登録プラットフォームに登録されている、対象となる先発医薬品の特許はすでに失効し、もしくは無効が確定している。または、後発医薬品の製造販売承認申請者が対象となる特許権の実施許諾を受けている。
声明 3：
対象となる先発医薬品の特許権が特許情報登録プラットフォームに登録されているが、当該特許権の存続期間が満了するまで後発医薬品を製造販売しないことを承諾する。
声明 4：
特許情報登録プラットフォームに登録されている、対象となる先発医薬品の特許は無効と認められるべきであり、または申請する後発医薬品は当該特許権の保護範囲には包含されない（実施弁法第 6 条、第 12 条）。

国家医薬品審査評価機構は、後発医薬品申請が受け付けられた後、10 営業日以内に、情報プラットフォーム[83]にパテントリンケージ制度に従って宣言をした後発医薬品許可申請情報と関連宣言を社会に公開する（図 10～図 12）。また、後発医薬品申請者は、対応する申請と根拠を先発医薬品承認保持者に通知する（実施弁法第 6 条、第 12 条）。なお、後発医薬品申請者から先発医薬品承認保持者への通知は義務ではないとの解釈[84]もあり、先発医薬品承認保持者は情報プラットフォームを適宜モニターしておく必要もある。

[83] 中国上市药品专利信息登记平台ウェブサイト
https://zldj.cde.org.cn/home
[84] Comparative Overview of Drug Patent Linkage Systems in China and the United States (Thomson Reuters Westlaw, May 4, 2021)（Westlaw ウェブサイト）
https://today.westlaw.com/Document/If268b0c5ad0911ebbea4f0dc9fb69570/View/FullText.html?contextData=(sc.Default)&transitionType=Default&firstPage=true

図 10 中国上市药品专利信息登记平台ウェブサイトでの公開例（後発医薬品：声明 2）（AstraZeneca 社 安达唐（达格列净）（FORXIGA (dapagliflozin)））[85]

[85] 中国上市药品专利信息登记平台ウェブサイト（「药品名称＝达格列净」で検索）（2022 年 6 月 22 日アクセス）
https://zldj.cde.org.cn/list?listType=PatentStatementList

図 11 中国上市药品专利信息登记平台ウェブサイトでの公開例（後発医薬品：声明 3）（Merck 社捷诺维（磷酸西格列汀片）（JANUVIA (sitagliptin)））[86]

[86] 中国上市药品专利信息登记平台ウェブサイト（「药品名称＝磷酸西格列汀片」で検索）（2022 年 6 月 22 日アクセス）
https://zldj.cde.org.cn/list?listType=PatentStatementList

図 12 中国上市药品专利信息登记平台ウェブサイトでの公開例（後発医薬品：声明 4.1）（Purdue 社 奥施康定（盐酸羟考酮）（OXYCONTIN (oxycodone hydrochloride)））[87]

国家知識産権局は、上場医薬品技術プログラムの申請が関連する特許権の保護範囲に該当するか否かを判断した場合、政府情報公開規則及び関連規定に従って公表しなければならないが、企業秘密に関する情報は削除する（医薬品特許紛争の早期解決メカニズムの行政裁定規定第 18 条）。当事者は行政裁定手続において企業秘密を秘密にしておく義務があり、無断で開示等した場合には適切な法的責任を負う（医薬品特許紛争の早期解決メカニズムの行政裁定規定第 20 条）。医薬品特許紛争に関する行政判断の処理者及びその職員による企業秘密の漏洩は、犯罪に該当しない場合には、法律に従って行政処分を受けるものとする（医薬品特許紛争の早期解決メカニズムの行政裁定規定第 21 条）。

当事者は、訴訟で取得した企業秘密その他の機密保持を必要とするその他の商業情報を秘密にしておく義務を負い、その訴訟活動以外で、無断で開示または使用または許可した場合、法律に従って民事責任を負うものとする。民事訴訟法第 111 条に規定する状況を構成する場合、人民裁判所は、法律に従って処理しなければならない（登録申請医薬品に関連する特許紛争民事事件の審理における法律適用の若干問題に関する規定第 8 条）。

[87] 中国上市药品专利信息登记平台ウェブサイト（「药品名称＝盐酸羟考酮」で検索）（2022 年 6 月 22 日アクセス）
https://zldj.cde.org.cn/list?listType=PatentStatementList

③ 後発医薬品の自動承認停止

化学医薬品：

特許権者／利害関係人は、不服ある場合は、後発医薬品承認申請の 45 日以内に、人民法院[88][89]に訴訟を提起するか、国務院特許行政部門（特許庁）[90]に行政裁決を請求することができる。

（特許権者／利害関係人が訴訟提起／行政裁決請求した場合）

1. 裁判所または特許庁は、訴訟の手続開始または行政裁決の請求を受理から 15 営業日以内に、医薬品審査機関および後発医薬品申請者に通知する（実施弁法第 7 条）。

2. 通知書を受けた場合、医薬品監督部門は、後発医薬品の申請に対して 9 ヶ月の待機期間を設定する。ただし、医薬品審査機関における審査は継続される（実施弁法第 8 条）。

3. 特許権者または利害関係者、後発医薬品申請者は、判決書または決定書を受けてから 10 営業日以内に、結果を医薬品審査機関に知らせる（実施弁法第 9 条）。

4. 技術評価を通過した後発医薬品承認申請について、医薬品審査機関、医薬品監督部門は、確定判決、調停合意または行政裁決の結果に応じて処理する。

（特許権者／利害関係人が訴訟提起／行政裁決請求しない場合）

医薬品監督部門は、技術審査評価の結論及び後発薬申請者が提出した宣言の状況に応じて、販売承認可否の決定を直接行う（実施弁法第 8 条）。

後発医薬品の製造販売承認申請者は、後発医薬品が関連特許権の保護範囲に包含されないことを確認するため、裁判所への訴訟提起または特許庁への行政裁決の請求が可能である（実施弁法第 8 条、CNIPA の規定第 4 条、最高裁の規定第 4 条）。

漢方薬、バイオ医薬品：

医薬品監督部門は、技術審査評価の結論及び後発薬申請者が提出した宣言に応じて、販売承認可否の決定を直接行う（9 ヶ月の待機期間は設定されない）（実施弁法第 12 条、第 13 条）。

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[88] 北京市知識産権法院 SNS（パテントリンケージ関連で最初の人民法院判断 Chugai Pharmaceutical v. Wenzhou Haihe）
https://mp.weixin.qq.com/s/-9SocP2TLE20Xw7me3OxNw

[89] 【案例报告】首例药品专利链接案：捐献规则和禁止反悔规则构成适用等同原则的限制（知识产权那点事 SNS）
https://mp.weixin.qq.com/s?__biz=MzA3NTI0NzYxNw==&mid=2651566677&idx=1&sn=43f3246df99e4372f37f0db888cd43b4&chksm=848c6b3bb3fbe22d34ca9e74f9d6960945dc1cb03d6a9239d1ce3b28b0e80b07d048726a005a&scene=90&subscene=93&sessionid=1661728732&clicktime=1661728741&enterid=1661728741#rd

[90] 国家知識産権局ウェブサイト（パテントリンケージ関連で最初の行政裁決 Humanwell v. Purdue Pharma）
https://www.cnipa.gov.cn/art/2022/4/25/art_53_175126.html

④ 後発医薬品会社へのインセンティブ

化学後発医薬品については、最初の特許挑戦に成功し、最初に販売許可を取得した後発医薬品会社に 12 ヶ月の優先販売品目許可が与えられる（実施弁法第 11 条、医薬品管理法の施行に関する規則（案）第 39 条[91]）。漢方薬、バイオ医薬品については、優先販売品目許可制度はない。

(4) パテントリンケージ条項に関する CPTPP との比較

パテントリンケージ条項に関する CPTPP と中国法との比較を表 12 に示す。

表 12 パテントリンケージ条項に関する CPTPP と中国法との比較

CPTPP[92]	中国法[93]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）第6条 化学後発医薬品の申請者は、医薬品販売承認の申請を行う場合、中国上場医薬品特許情報登録に公開されている特許情報と比較して、後発医薬品の関連医薬品特許ごとに陳述するものとする。・・・（略） ・・・後発医薬品の申請が受理されてから 10 営業日以内に、国内の医薬品審査機関は、情報プラットフォーム上で申請情報と対応する声明を一般に開示するものとする・・・（略）・・・後発医薬品の申請者は、対応する声明と根拠を販売承認取得者に通知するものとする。・・・（略）・・・。 医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）第 12 条 漢方薬および生物学的製剤の販売許可の保有者は、これらの措置の第 2 条、第 3 条、第 4 条、

[91] 国家药监局综合司公开征求《中华人民共和国药品管理法实施条例（修订草案征求意见稿）》意见（国家药品监督管理局ウェブサイト）
https://www.nmpa.gov.cn/xxgk/zhqyj/zhqyjyp/20220509222233134.html

[92] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf

[93] 药品专利纠纷早期解决机制实施办法（试行）（中華人民共和国中央人民政府ウェブサイト）
https://view.officeapps.live.com/op/view.aspx?src=http%3A%2F%2Fwww.gov.cn%2Fzhengce%2Fzhengceku%2F2021-07%2F04%2F5622330%2Ffiles%2F4d1b47cd16164643844c3f75c93a5dd5.doc&wdOrigin=BROWSELINK

	および第7条に従って関連する特許情報を登録するものとする。・・・（略）・・・。 漢方薬および生物学的製剤の申請者は、これらの措置の第6条に従って関連する特許宣言を行うものとする。
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）第7条 特許権者または利害関係者が4つのカテゴリーの特許宣言に異議を唱える場合、国の医薬品評価機関が医薬品販売承認の申請書を発行した日から45日以内に、関連するかどうかを判断することができる。・・・（略）・・・人民法院で訴訟を起こすか、省議会の下の特許管理部門に行政裁定を要求できる。・・・（略）・・・。 医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）第12条 漢方薬および生物学的製剤の販売許可の保有者は、これらの措置の第2条、第3条、第4条、および第7条に従って関連する特許情報を登録するものとする。・・・（略）・・・。
(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）第8条 人民法院による訴訟の写しまたは国務省の特許管理部門による受理の通知を受け取った後、国務省の薬物規制部門は、化学後発医薬品の登録の申請を9ヶ月の待機期間に設定するものとする。・・・（略）・・・。 特許権者または利害関係者が所定の期限内に訴訟を提起または行政裁定を要求しなかった場合、省議会の医薬品規制部門は、技術的レビューに基づいて後発医薬品の販売を承認するかどうかを直接決定するものとする。・・・（略）・・・。

	医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）第 13 条 漢方薬および生物学的製剤の登録申請については、国務省の医薬品規制部門が、技術審査の結論に基づいて販売を承認するかどうかを直接決定するものとする。人民法院または国務省の特許管理部門が、関連する技術的解決策が関連する特許権の保護の範囲内にあることを確認した場合、関連する医薬品は、対応する特許権の満了まで販売されない場合がある。

IV. 韓国[9495]

(1) 経緯

2007 年に締結された米韓自由貿易協定（FTA）が 2012 年 3 月 15 日に発効し、その協定文第 18.9 条第 5 項にパテントリンケージ制度が規定されている[96]。

2012 年 3 月 15 日にパテントリンケージ制度（特許リストへの登載、特許権者への通知）（薬事法第 50 条の 2～4）が施行された。

2015 年 3 月 15 日に後発医薬品の自動承認延長、後発医薬品独占期間（薬事法第 50 条の 5～10）が施行された。

(2) パテントリンケージ制度の概要

韓国のパテントリンケージ制度の概要を表 13 にまとめる。

94 医薬品許可特許連携制度の解説書 2018 年 11 月 食品医薬品安全処（和訳）（ジェトロウェブサイト）
https://www.jetro.go.jp/ext_images/world/asia/kr/ip/gov/movement/201811.pdf

95 医薬品許可特許連携制度 質疑応答集 2020 年 12 月 食品医薬品安全処 医薬知識財産政策 T/F（和訳）（ジェトロウェブサイト）
https://www.jetro.go.jp/ext_images/world/asia/kr/ip/gov/movement/202012.pdf

96 KRUS FTA Final Text (as of January 1, 2019)（Office of the United States Trade Representative ウェブサイト）
https://ustr.gov/trade-agreements/free-trade-agreements/korus-fta/final-text

表 13 韓国のパテントリンケージ制度の概要

先発医薬品	
特許リスト	K-オレンジブック（K-오렌지북）[97]
対象特許	物質特許、製剤特許、組成物特許、医薬用途特許（薬事法第 50 条の 2④）
特許情報	1. 医薬品の名称 2. 登載申請者の個人情報 3. 特許権者などの個人情報（国内に住所又は営業所を持たない場合、国内に住所又は営業所を持つ代理人の個人情報） 4. 特許番号 5. 特許権の存続期間満了日 6. 特許として保護を受けようとする事項（以下「特許請求項」という） 7. その他総理令で定める事項（薬事法第 50 条の 2②）
リスト登録者	新薬申請承認許可又は新薬申請承認変更許可を受けた者（薬事法第50条の2①）
リスト登録時期	当該医薬品の品目許可若しくは変更許可を受けた日又は「特許法」第 87 条によって特許権の設定登録があった日から 30 日以内（薬事法第 50 条の 2②）。
後発医薬品申請後の提訴期間	後発医薬品申請者による特許権登載者と登載特許権者などへの通知から 45 日以内（薬事法第 50 条の 5）。
後発医薬品	
申請時期制限	新薬の市販後調査期間（新医薬品等：6 年、薬事法第 32 条）満了後
申請手続	登載医薬品の安全性・有効性に関する資料を根拠に、第 31 条第 2 項又は第 3 項に基づいて医薬品の品目許可を申請し、又は同条第 9 項に基づいて効能・効果に関する変更許可を申請する。薬事法第 50 条の 4 に基づき通知しなければならない者は、無効審判・権利範囲確認審判を請求した上で、優先販売品目許可を申請することができる（薬事法第 50 条の 7）。
承認の自動停止	申請を行うことにより 9 ヶ月（薬事法第 50 条の 5、第 50 条の 6）。
後発医薬品申請情報の開示	登録医薬品の安全性・有効性に関する資料を根拠に医薬品の品目許可を申請、又は効能・効果に関する変更許可を申請した者

[97] 韓国 食品医薬品安全省ウェブサイト
https://nedrug.mfds.go.kr/searchBioeq

	は、許可を申請した事実、許可申請日など、総理令で定める事項を、品目許可申請日又は申請日から 20 日以内に、変更許可特許権登載者と登載特許権者などに通知しなければならない（薬事法第 50 条の 4①、④）。
第 1 申請承認後発医薬品に与えられる独占期間	9 ヶ月（薬事法第 50 条の 7～第 50 条の 10）

(3) 手続等、詳細事項

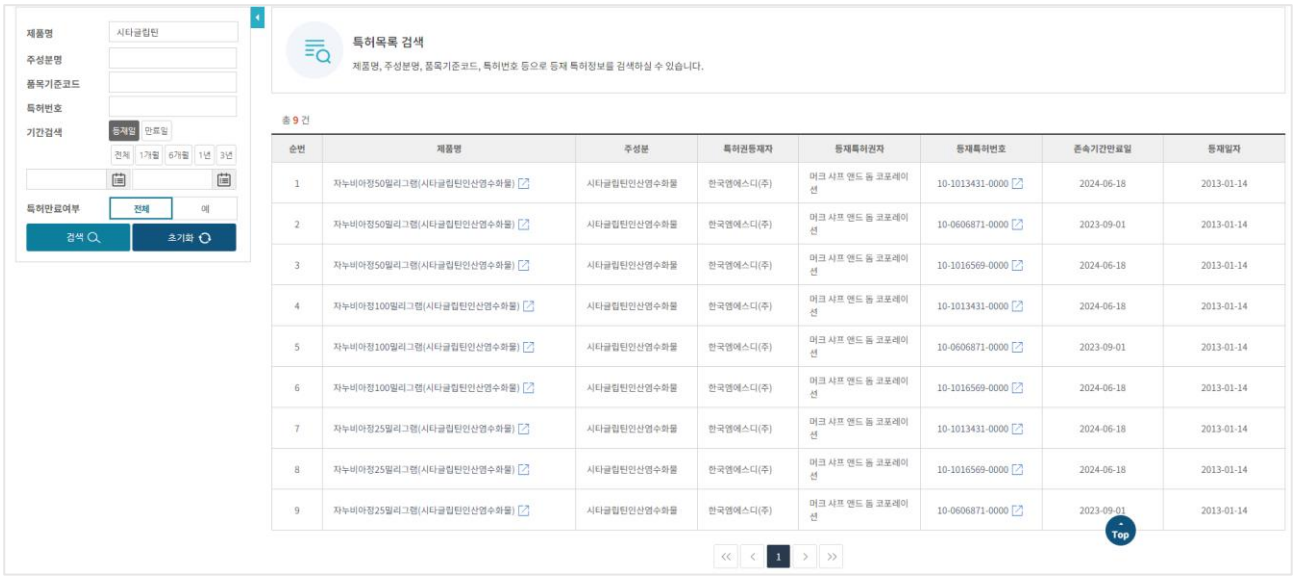
① 先発の特許登録

医薬品の製造・販売又は輸入の品目許可又は変更許可を受けた者が、当該医薬品に関する特許権について特許目録への登載を受けようとする場合、特許権者又は専用実施権者の同意を受けて品目許可又は変更許可を受けた日から 30 日以内に食薬処に特許目録の登載を申請しなければならない。品目許可を受けた日以降特許権が登録された場合は、その特許登録日から 30 日以内に申請することができる（薬事法第 50 条の 2）。

食薬処長は、登載申請された医薬品特許権が登載対象及び要件を満たす場合、医薬品の名称、特許権者などの個人情報、特許番号、特許存続期間等を特許目録に登載し、インターネット[98]で公開する（薬事法第 50 条の 2 第 4 項）（図 13）。なお、食薬処長は登載申請された医薬品特許権の登載対象及び要件を検討し（薬事法第 50 条の 2 第 5 項）、職権により登録事項を変更又は削除することができる（薬事法第 50 条の 3 第 4 項）。

[98] 韓国 食品医薬品安全省ウェブサイト
https://nedrug.mfds.go.kr/searchBioeq

図 13 インターネットでの公開例（Merck 社 JANUVIA (sitagliptin)）[99]



② 後発医薬品申請＋先発医薬品会社への通知

薬事法第 50 条の 2 によって特許目録に搭載された医薬品の安全性・有効性に関する資料を根拠に品目許可を申請し、又は効能・効果に関する変更許可を申請した後発製薬会社は、品目許可などを申請した日から 20 日以内に特許権登載者（登載医薬品の品目許可を受けた者）と特許権者又は専用実施権者に品目許可申請日、品目許可申請事実、登載特許の無効又は非侵害判断の根拠を通知しなければならない（薬事法第 50 条の 4）。ただし、登載特許権の存続期間満了、登載特許権の存続期間満了後の販売のための品目許可申請、特許権者などが通知しないことに同意した場合などは、申請事実を通知しなくても良い（薬事法第 50 条の 4 第 1 項、薬事法施行令第 32 条の 5）。通知をした者は、通知した事実を証明できる書類を遅滞なく食薬処庁に提出しなければならない。食薬処庁は、通知された後発医薬品の許可申請日、主成分及びその含量、製剤、用法用量、効能効果、登録医薬品の名称をインターネットホームページ[100]に公開する（薬事法第 50 条の 4 第 5 項、医薬品等の安全に関する規則第 62 条の 4 第 2 項）（図 14、図 15）。申請事実の通知を怠った場合には、その品目許可又は変更許可はしないように定められている（薬事法第 50 条の 4 第 6 項）。

[99] 특허목록 검색（韓国 食品医薬品安全省ウェブサイト）（「성분명＝시타글립틴」で検索）（2022 年 6 月 22 日アクセス）
https://nedrug.mfds.go.kr/searchPatent?page=1&searchYn=true&itemName=%EC%8B%9C%ED%83%80%EA%B8%80%EB%A6%BD%ED%8B%B4&mainIngr=&itemSeq=&patentNo=&dtStart=&dtEnd=&deleteYn=
[100] K-오렌지북（韓国 食品医薬品安全省ウェブサイト）
https://nedrug.mfds.go.kr/searchBioeq

図 14 インターネットでの公開例（sitagliptin）[101]

[101] K-오렌지북（韓国 食品医薬品安全省ウェブサイト）（「성분명＝시타글립틴」で検索）（2022 年 6 月 22 日アクセス）
https://nedrug.mfds.go.kr/searchBioeq?page=1&sort=&sortOrder=&searchYn=true&ExcelRowdata=&ingrName=%EC%8B%9C%ED%83%80%EA%B8%80%EB%A6%BD%ED%8B%B4&itemName=&entpName=&compDrugYn=&genericYn=&itemPermitDateStart=&itemPermitDateEnd=&patentYn=

図 15 医薬品特許一覧のウェブサイト[102]

図 15 中の左カラムの「의약품특허목록」（日本語訳：医薬品特許一覧）を展開することにより、以下の項目を検索することができる。

- 「의약품 특허목록」（日本語訳：医薬品特許一覧）
- 「우선판매품목허가의약품」（日本語訳：優先販売品目ライセンス）
- 「통지의약품」（日本語訳：通知薬）
- 「심판 청구 현황」（日本語訳：判決請求状況）

③ 後発医薬品の自動承認停止

後発製薬会社が特許目録に登載された医薬品の安全性・有効性資料に基づいて品目許可を申請した場合、登載医薬品の特許権者などは、通知を受けた日から 45 日以内に特許訴訟などを提起し、

102 통지의약품（韓国 食品医薬品安全省ウェブサイト）（「성분명＝시타글립틴」で検索）（2022 年 6 月 22 日アクセス）
https://nedrug.mfds.go.kr/pbp/CCBAM01

食薬処長に後発医薬品に対する販売禁止を申請することができる。販売禁止申請を受けた食薬処長は、登載特許権の無効又は通知医薬品が登載特許権の権利範囲に属しないという審決又は判決などがある場合などを除いては、通知を受けた日から 9 か月間、当該医薬品の販売を禁止させる。その他に、通知された同一医薬品の一部に対してのみ販売禁止請求をした場合、既に品目許可を受け販売が可能な同一医薬品がある場合などにも販売禁止されない（薬事法第 50 条の 5、第 50 条の 6）。なお、特許訴訟の頻度は米国と比較すると限定的であり、特に注射剤、生物学製剤に関する特許訴訟は稀であるとの指摘もある[103]。

④ 後発医薬品会社へのインセンティブ

登載特許に対して最も早く特許審判を請求した後、最も早い日に登載医薬品の安全性・有効性資料に基づいて品目許可を申請し、特許挑戦に成功するなど、①品目許可申請に関する要件、②特許審判請求に関する要件、③特許審判における認容審決獲得の要件などを満足する者は、優先販売品目許可を受けることができる。このとき、他の後発製薬会社の優先販売品目許可医薬品と同一の医薬品は 9 か月間販売禁止される可能性がある（薬事法第 50 条の 7～第 50 条の 10）。優先品目許可医薬品は、インターネットホームページ[104]に公開される。薬事法第 50 条の 10 で、「同一医薬品などに対する販売禁止効力の消滅など」が規定されており、本規定は First Filer が後発医薬品販売を遅延させた場合に優先販売許可を破棄することが規定されているため、米国と比較して、Pay for Delay 和解によるインセンティブは低いと指摘されている[105]。しかしながら、この「他の後発製薬会社の優先販売品目許可医薬品と同一の医薬品は 9 か月間販売禁止」は、韓国内後発医薬品会社にとっては十分なインセンティブにはなっていないとの指摘もある[106]。

(4) パテントリンケージ条項に関する CPTPP との比較

パテントリンケージ条項に関する CPTPP と韓国法との比較を表 14 に示す。

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[103] Patent challenges and factors associated with successful patent challengers under the patent linkage system: recent evidence from South Korea after the Korea United States free trade agreement (Son et al. Globalization and Health (2021) 17:116)
https://globalizationandhealth.biomedcentral.com/articles/10.1186/s12992-021-00765-6

[104] 韓国 食品医薬品安全省ウェブサイト
https://nedrug.mfds.go.kr/searchBioeq

[105] The South Korean Patent Linkage System: A Model for Reforming the United States Hatch-Waxman Act (Kimberlee Thompson Raley, Emory International Law Review, Vol. 33(3), 459-492, 2019)
https://scholarlycommons.law.emory.edu/cgi/viewcontent.cgi?article=1215&context=eilr

[106] Perceived impact of the patent linkage system on pharmaceutical market from the viewpoint of the domestic manufacturers in South Korea (Choi et al. Globalization and Health (2022) 18:34
https://globalizationandhealth.biomedcentral.com/articles/10.1186/s12992-022-00829-1

表 14 パテントリンケージ条項に関する CPTPP と韓国法との比較

CPTPP[107]	韓国法[108]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	薬事法第50条の4（品目許可などの申請事実の通知）（仮訳） ① 登載医薬品の安全性・有効性に関する資料を根拠に、第31条第2項又は第3項に基づいて医薬品の品目許可を申請し、又は同条第9項に基づいて効能・効果に関する変更許可を申請した者は、許可を申請した事実、許可申請日など、総理令で定める事項を特許権登載者と登載特許権者などに通知しなければならない。・・・（略）・・・。 ④ 第 1 項又は第 2 項による通知は、品目許可又は変更許可の申請日から 20 日以内にしなければならない。・・・（略）・・・。
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	薬事法第50条の5（販売禁止の申請）（仮訳） ① 登載特許権者などは、第 50 条の 4 による通知を受けた日から 45 日以内に食品医薬品安全処長に次の各号の事項が記載された陳述書を添付して通知医薬品の販売禁止を申請することができる。・・・（略）・・・。
(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用さ	薬事法第50条の5（販売禁止の申請）（仮訳） ① 登載特許権者などは、第50条の4による通知

[107] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf
[108] 医薬品許可特許連携制度の解説書 2018 年 11 月 食品医薬品安全処（和訳）（ジェトロウェブサイト）
https://www.jetro.go.jp/ext_images/world/asia/kr/ip/gov/movement/201811.pdf

れる特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	を受けた日から45日以内に食品医薬品安全処長に次の各号の事項が記載された陳述書を添付して通知医薬品の販売禁止を申請することができる。・・・（略）・・・。 薬事法第50条の6（販売禁止など）（仮訳） ① 第 50 条の 5 第 1 項に基づいて販売禁止申請を受けた食品医薬品安全処長は、販売禁止が申請された医薬品に対する品目許可又は変更許可をする際、次の各号のいずれかに該当する場合を除いては、第 50 条の 4 によって登載特許権者などが通知を受けた日(以下「通知を受けた日」という)から 9 カ月間販売を禁止しなければならない。・・・（略）・・・。

V. 台湾[109]

(1) 経緯

TPPへの加入を見据え、2017年に薬事法が改正され、新薬に関する特許情報の開示と登録、後発医薬品の申請者による宣言と告知、特許権に対するチャレンジ、後発医薬品の許可証発行の一時停止、最初に医薬品許可証を取得した後発医薬品会社の市場独占権などについて規定され、2019年8月20日に施行されている（第48条の3～第48条の22）[110]。

2020年12月31日、台湾初のパテントリンケージ訴訟判決が下された[111]。

制度導入時における議論[112][113]：

（学識経験者、専門家）

・国民全体の健康に影響を与える。

高齢者人口の割合が10年以内に20%を超えると考えられており、2030年の国民健康保険の費用は1兆1,000億台湾ドルになると推測される。後発医薬品が奨励されない場合、健康保険を維持することが困難になる。

・台湾国内製薬産業の発展に深刻な影響を与える

台湾の製薬産業は後発医薬品会社が多く、台湾国内の医薬品承認を取得できない場合、市場開拓のための中国・東南アジア進出が困難となる。パテントリンケージ制度は後発医薬品の開発を制限し、台湾国内における手頃な価格での医薬品供給を厳しく制限する。さらに、発展途上国における後発医薬品の普及が遅れる。

・パテントリンケージ制度の導入が十分に評価されていない

パテントリンケージ制度が及ぼす医薬品革新、産業開発、医薬品利用者の権利と利益、健康保険または医薬品価格の影響について、経済分析、影響評価を衛生福利部が行っていない。支援策の提案が必要である。

・戦略的思考が欠如している

TPP参加を前提とした法改正という理由は十分ではない。草案はTPPの基準よりも厳格であり、この点で譲歩すると、TPPの他の部分で交渉したいときの交渉カードが少なくなる。

（台湾製薬業界）

・パテントリンケージ制度の改定停止を求める

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109 中国及び台湾のパテントリンケージ制度の最新動向について（知財管理 Vol. 70, No. 6, 767-780, 2020）

110 台湾薬事法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=L0030001

111 智慧財產法院 109 年民專訴字第 46 號

112 專利連結藥事法修正立法過程觀察（全國律師月刊 2019 年 5 月號 14-36）
http://www.twba.org.tw/Manage/magz/UploadFile/5830_014-036%E5%B0%88%E5%88%A9%E9%80%A3%E7%B5%90%E8%97%A5%E4%BA%8B%E6%B3%95%E4%BF%AE%E6%AD%A3%E7%AB%8B%E6%B3%95%E9%81%8E%E7%A8%8B%E8%A7%80%E5%AF%9F-%E7%BF%81%E9%9B%85%E6%AC%A3.pdf

113 生物相似藥不可納入專利連結 台灣製藥工業同業公會 中華民國製藥發展協會 中華民國學名藥協會（2019 年 3 月 12 日）（中華民國製藥發展協會ウェブサイト）
https://www.cpmda.org.tw/file/Laws/1080416v10.pdf

・生物学製剤についてはパテントリンケージ制度の対象外とすべき。

医薬品独自の販売承認手順を使用して、医薬品のみに特許権者に別の保護を追加することは適切ではなく、公正な競争の下の句に悪影響を及ぼす。

台湾知的財産裁判所で審理された事件において、ほとんどの事例において、特許権者である製薬会社が敗訴している。パテントリンケージ制度により特許侵害が推定され後発医薬品の承認が一時停止されることは明らかに公正と正義に反する。

制度導入後の議論：

（専門家）

・登録特許情報の正確性が100%保証されるものではない[114]。

特許情報の登録や更新は新薬許可証所有者の自主性及び第三者からの訂正通知に依頼しており、登録情報の正確性や条件合致性がどこまで担保されるかについては不明である。薬事法第92条の1では、新薬許可証所有者が第三者からの通知の受領日翌日から45日以内に回答しなかった場合、3万元以上50万元以下の罰金に処すると規定されており、さらに薬事法第100条の1では、詐欺又は虚偽不実の方法で特許情報を登録・変更した場合の刑事罰も規定されている。しかしこうした罰金や刑事罰の規定が存在するとしても、新薬許可証所有者に対する強制性はないことから、登録情報の正確性が100%保証されるとは限らない。

・生物学製剤については製造法特許もパテントリンケージの掲載対象とすべきであり、また、衛生福利部は西洋薬パテントリンケージ登録システムに特許を掲載するだけでなく、実質的に特許庁と協働すべきである[115]。

上記改訂により、不適切な特許の西洋薬パテントリンケージ登録システムへの登載、新薬のエバーグリーニングを回避することができ、かつ、不適切な販売禁止期間の設定を防ぐことができる。また、新薬開発会社への報酬とバイオシミラー産業開発の促進の微妙なバランスがより達成可能な目標となりうる。

（台湾法律事務所コメント[116]）

パテントリンケージ制度の改正について、現在進行中の計画はない。一方、特許法第 60 条の 1 が成立する前に、パテントリンケージ訴訟についていくつかの判決が言い渡されている。智慧財産及商業法院（Intellectual Property and Commercial Court (IPC Court)）は、特許法第 96 条第 1 項はこのようなパテントリンケージ訴訟の法的根拠を提供するのに十分であると考えている。

(i) 特許登録の対象特許：

パテントリンケージ制度は、基本的に米国のオレンジブックの仕組みを採用している。記載された特許のクレーム番号を特定すべきか否か、及び結晶多形に関する特許を記載できるか否かについ

114 台湾 パテントリンケージ制度の紹介（2019 年 8 月実施）（維新國際専利法律事務所ウェブサイト）
http://www.wisdomlaw.com.tw/m/404-1596-88038.php?Lang=zh-cn

115 An Analysis of the Patent Linkage System and Development of the Biosimilar Industry in Taiwan (Brooklyn Journal of International Law, Vol 46(2), 479 2021)
https://brooklynworks.brooklaw.edu/cgi/viewcontent.cgi?article=1974&context=bjil

116 附属資料１（附属資料２）

ては論争がある。最終的に衛生福利部 台湾食品医薬品局（Taiwan Food and Drug Administrations (TFDA)）は、医療用途の特許についてのみクレーム番号を特定する必要があり、また結晶多形特許はリストに掲載できると判断した。ただし、特許の結晶多形が新薬の有効成分の結晶多形と異なる場合には、当該多形を含む製剤が同等の効果を発揮することを示す試験データを登録の際に提供しなければならない（西薬専利連結施行辦法第 3 条第 2 項参照）。なお、製造工程に関する特許はリストに掲載できないが、プロダクト・バイ・プロセス・クレームは製品そのもの（物質や組成物）をクレームしているものとみなされ、リスト可能である。

(ii) 後発医薬品の自動承認停止期間：

当初提案された承認停止期間は、第一審裁判所が特許訴訟事件を終結させるのに必要な平均期間に基づいた 15 か月であったが、議会によって 12 か月に短縮された。

(iii) 第一後発医薬品承認取得者へのインセンティブ：

当初提案された後発品販売の独占期間は 6 か月であったが、薬事法改正を進めるために、後発医薬品会社からの抵抗を減らすため、後発医薬品販売独占期間は 12 か月に延長された。

(iv) 生物学的製剤をパテントリンケージ制度の対象とすること：

現在の実務では、生物学的製剤は、薬事法第 7 条に従って、新しい化学物質(NCE)と同様に新しい分子物質として扱われる。さらに、薬事法には生物学的製剤とバイオシミラーの定義はない。従って、先発医薬品会社は、生物製剤は NCE のようにパテントリンケージ制度の対象とすべきであると考えている。米国でのパープルブックやパテントダンスと同様のメカニズムを使用するか否かについての議論があった。最終的に、TFDA はパテントダンスメカニズムが複雑すぎると判断し、パテントリンケージ制度に生物学的製剤を含めることを決定した。妥協案として、西薬専利連結施行辦法第 16 条第 3 項が追加され、すでに臨床試験中のバイオシミラーはパテントリンケージ制度から除外された。

TFDA は、パテントリンケージ制度の対象となる新薬は、薬事法第 7 条で定義されたものを指していると考えている。これは、新しい分子の実体、新しい適応症、新しい組み合わせ、および新しい投与経路に関連する薬のみを対象としている。新剤形（新製剤）、新投与量、新単位強度に関する医薬品は、薬事法第 7 条の新医薬品の定義に該当しない、いわゆる「2 型新薬」である。しかし、薬事法には「2 型新薬」の定義がなく、藥品查驗登記審查準則[117]（Regulations for Registration of Medicinal Products[118]）第 39 条第 2 項によると、第 2 章に定める新薬規制は、新剤型、新投与量、新単位強度の医薬品にも適用される。

パテントリンケージ制度の薬事法改正案の公聴会での議論では、米国の 505(b)2 新薬と同様に、2 型新薬もパテントリンケージ制度の対象になるとの認識が参加者全員にあった。しかし、既存の新薬の特許情報を掲載するためのパテントリンケージ制度制定法が制定されてから最初の 3 か月が

[117] 藥品查驗登記審查準則（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030057

[118] Regulations for Registration of Medicinal Products（Laws & Regulations Database of The Republic of China (Taiwan)ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030057

経過した後、TFDA は、2020 年 4 月から 7 月にかけて特許リストを見直し、2 型新薬許可の保有者に「2 型新薬許可証の特許情報を記載することは認められない」との書簡を送付した。先発医薬品会社が、TFDA が新薬に対してこれほど異なる見方をしていることに気付いたのはこれが初めてであった。新薬許可保有者の主張にもかかわらず、TFDA は関連する特許リストを削除する決定を下した。

MSD 社、Allergan 社はそれぞれ、2 型新薬の特許リストを拒否する TFDA の決定に対して行政訴訟を臺北高等行政法院に提起した[119][120]。裁判所は原告に有利な判決を下さず、2 件の訴状を却下した。判決書によれば、裁判所は、衛生福利部の主張を認めた。一方で、原告の主張（本システムから特許情報を取り消す（削除する）という衛生福利部の権限を支持する法的根拠は見いだせず、原告は、問題の市場承認（すなわち、2 型新薬）が「新薬」であると判断されたという衛生福利部の慣行と決定、主張に依存している）を無視した。これら 2 件の判決は最終的なものではなく、上訴裁判所（最高行政裁判所）で係争中である。

(2) パテントリンケージ制度の概要

台湾のパテントリンケージ制度の概要を表 15 にまとめる。

表 15 台湾のパテントリンケージ制度の概要

先発医薬品	
特許リスト	西洋薬パテントリンケージ登録システム[121]（薬事法第 40 条の 2）
対象特許	物質特許、医薬用途特許、製剤特許 （薬事法第 48 条の 3、西洋薬パテントリンケージ施行指針第 3 条）
特許情報	特許登録証書番号（特許の種類が医薬用途である場合、その請求項の番号）、特許権の存続期間、特許権者（薬事法第 48 条の 4）
リスト登録者	新薬許可証所有者 （薬事法第 48 条の 3、第 48 条の 5）
リスト登録時期	薬品許可証取得日の翌日から 45 日以内（薬事法第 48 条の 3）、または特許公告の翌日から 45 日以内（薬事法第 48 条の 5） 中央衛生主務官庁は新薬許可証所有者からの登録、変更申請について実質内容の審査は行わない。
後発医薬品申請後の提訴期間	薬事法第 48 条の 12 第 1 項の通知を受けてから 45 日以内（薬事法第 48 条の 13）

[119] 臺北高等行政法院 110 年度訴字第 824 號判決（2022 年 4 月 7 日辯論終結）
https://law.judicial.gov.tw/FILES/TPBA/110%2c%E8%A8%B4%2c824%2c20220512%2c1.pdf
[120] 臺北高等行政法院 110 年度訴字第 1048 號判決（2022 年 4 月 7 日辯論終結）
https://law.judicial.gov.tw/FILES/TPBA/110%2c%E8%A8%B4%2c1048%2c20220512%2c1.pdf
[121] 衛生福利部食品薬物管理署ウェブサイト
https://plls.fda.gov.tw/patentList

後発医薬品	
申請時期制限	新成分新薬許可証の発行日から 3 年以内に他の薬商は許可証所有者の同意なしに、その申請資料を引用し承認審査を申請することはできない（薬事法第 40 条の 2 第 2 項）。ただし、外国において承認取得してから 3 年以内に申請した場合に限る（薬事法第 40 条の 2 第 4 項）。 中央衛生主務官庁は、新成分新薬許可証の発行日から 5 年後の翌日から薬品許可証を発行することができる（薬事法第 40 条の 2 第 3 項）。 新規または変更適応症については、当該新規・変更適応症が追加されてから 2 年以内に他の薬商は許可証所有者の同意なしに、その申請資料を引用し承認審査を申請することはできない（薬事法第 40 条の 3 第 1 項）。ただし、外国において承認取得してから 2 年以内に申請した場合に限る（薬事法第 40 条の 3 第 3 項）。 中央衛生主務官庁は、当該新規・変更適応症の許可証の発行日から 5 年後の翌日から薬品許可証を発行することができる（薬事法第 40 条の 3 第 2 項）。
申請手続	後発医薬品許可証申請者は、中央衛生主務官庁に下記のいずれかの声明をしなければならない。 1. 当該新薬には特許情報が何ら掲載されていない 2. 当該新薬に対応する特許権が消滅した 3. 当該新薬に対応する特許権が消滅してから初めて中央衛生主務官庁は薬品許可証を発行する 4. 新薬に対応する特許権は取消されるべきであり、または薬品許可証を申請した後発医薬品は当該新薬に対応する特許権を侵害していない（薬事法第 48 条の 9）
承認の自動停止	12 ヶ月（薬事法第 48 条の 13）
後発医薬品申請情報の開示	薬事法第 48 条の 9 第 4 号（新薬に対応する特許権は取消されるべきであり、または薬品許可証を申請した後発医薬品は当該新薬に対応する特許権を侵害していない）の声明である場合、申請人は薬品許可証申請資料完備通知の送達日から 20 日以内に、書面で新薬薬品許可証所有者（及び特許権者、専用実施権被許諾者）及び中央衛生主務官庁に通知すべきである（薬事法第 48 条の 12）。
第 1 申請承認後発医薬品に与えられる独占期間	12 ヶ月（薬事法第 48 条の 16）

(3) 手続等、詳細事項

① 先発の特許登録

医薬品に係わる物質特許、組成物又は製剤特許、医薬用途特許について、新薬の医薬品許可証の所持者が許可証を取得した日の翌日から 45 日以内に特許情報を開示すべきとされている（改正薬事法第 48 条の 3）。

新たに特許を取得した場合、新薬の医薬品許可証が発行された後に、初めて登録された特許権について、査定公告日から 45 日以内に特許情報を開示すべきとされている（改正薬事法第 48 条の 5）。

特許情報には特許証書番号、特許権の存続期間、特許権者、及び実施権者がいれば当該実施権者の名前などの情報が含まれる。医薬用途特許の場合、承認された用途を保護している請求項番号も明記する必要がある。なお、新薬の医薬品許可証の所持者と特許権者が異なる場合、特許情報の開示には特許権者の同意が必要とされている（改正薬事法第 48 条の 3、第 48 条の 4）。

新薬の特許情報が登録された後、新薬会社はパテントリンケージ制度を利用できる。登録されれば、パテントリンケージ制度による効果、後発医薬品会社の宣言の通知や特許侵害訴訟による後発医薬品の許可証の承認留保の手続きがとられることになる。

登録された特許情報が法定要件を満たさない場合、または、過誤により登録された場合、何人も理由及び証拠を記載し TFDA に異議を行うことができる。TFDA は審査を行わず、異議に関する情報を新薬の医薬品許可証の所持者に通知する。新薬の医薬品許可証の所持者は、通知された日の翌日から 45 日以内に応答する義務がある。期限内に応答しない場合、3 万台湾元～50 万台湾元の罰金が課される（改正薬事法第 48 条の 7、第 48 条の 8）。

パテントリンケージ制度は新薬に関する特許情報がより早く公衆に公開されることにより、他の医薬品会社が当該特許の権利範囲に入らないように設けられた制度である（図 16）。しかし、新薬の医薬品許可証の所持者に対しては、特許情報の開示は義務付けられておらず、あくまでも自発行為であるため、特許情報の開示を行わない場合でも、権利侵害の疑いのある後発医薬品会社に対して依然として権利侵害を主張することは可能である。

図 16 インターネットでの公開例（Merck 社 JANUVIA (sitagliptin)）[122]

新藥專利資訊 (新藥)

案件編號：0960027　　領取日：096/07/13

許可證字號：衛署藥輸字第024668號　　藥商名稱：美商默沙東藥廠股份有限公司台灣分公司

藥品名稱：佳糖維100 毫克 膜衣錠
JANUVIA 100 mg F.C. Tablets

處方標示：Each tablet contains：

有效成分及含量：SITAGLIPTIN (AS MONOHYDRATE PHOSPHATE SALT) 128.5000MG

適應症：第二型糖尿病。

劑型：膜衣錠

(一) 專利

專利證書號	發明專利名稱	專利權期間
I226331	用於治療或預防糖尿病之貝塔-胺基雜環二肽基肽酶抑制劑 物質發明 組合物或配方發明 醫藥用途發明	自094/01/11 至 114/01/09 止
I347185	二肽基肽酶-IV抑制劑之磷酸鹽 物質發明 組合物或配方發明 醫藥用途發明 > 請求項筆數(1)	自100/08/21 至 113/06/15 止

(二) 事由

事由	專利資訊(證書號、專利名稱)、第三人檢視通知回覆資訊	公告時間
本公司（藥品許可證所有人）依藥事法第四十八條之二十一提報專利資訊 施行日起三個月內	I226331 用於治療或預防糖尿病之貝塔-胺基雜環二肽基肽酶抑制劑 094/01/11 ~ 114/01/09 I347185 二肽基肽酶-IV抑制劑之磷酸鹽 100/08/21 ~ 113/06/15	108/08/23 06:00

(三) 刪除所登載之專利資訊

查無資料

關閉視窗

医薬品パテントリンケージ施行弁法第 16 条第 3 項に規定するように、生物学的製剤の申請手続きも同様に扱われる。

（台湾法律事務所コメント[123]）

先発医薬品の安全性/有効性データは、一般または後発医薬品会社に開示されない。後発医薬品会社は、先発医薬品について言及し、バイオアベイラビリティ（BA）および/または生物学的同等性（BE）の研究報告書を提出するか、容認できる場合には BE 研究報告書を溶出プロファイル比較報告書に置き換えるだけで済む。

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[122] 専利資訊查詢（此資訊係為業者自行提報）（衛生福利部食品藥物管理署ウェブサイト）（薬品名稱（中、英文）＝Januvia で検索）（2022 年 6 月 22 日アクセス）
https://plls.fda.gov.tw/PatentSearch?r=2145630217

[123] 附属資料１（附属資料２）

後発医薬品会社は先発医薬品を独自に入手し、比較実験を行って生物学的同等性を証明することができる。後発医薬品申請者が in vitro および/または in vivo の生物学的同等実験結果を提供する必要があるかどうかは、藥品生體可用率及生體相等性試驗作業準則[124]（Regulations of Bioavailability and Bioequivalence Studies[125]）に従って決定される。規則の第 6 条と第 7 条は、BA または BE 研究を実施する必要があるか否かを決定するための特定の基準を提供している。後発医薬品会社が後発医薬品申請で BA/BE レポートを提出し、それに基づいて後発医薬品が承認された場合、TFDA は後発医薬品が BA/BE 研究に基づいて承認されたことを医薬品許可の公開ウェブサイトに表示する。ただし、BA/BE データは公開されない。

② 後発医薬品申請＋先発医薬品会社への通知

後発医薬品許可証の申請者は、次の各号の何れかについて宣言しなければならない。改正薬事法第 48 条の 9）。

(1) 当該新薬について、いかなる特許情報も登録されていない。
(2) 当該新薬に係わる特許権はすでに消滅した。
(3) 当該新薬に係わる特許権が消滅した後、初めて TFDA が医薬品許可証を発行する。
(4) 当該新薬に係わる特許権は取消すべきものである、又は許可証を申請する後発医薬品が当該新薬に係わる特許権を侵害していない。

販売が許可された後発医薬品は、いったん特許権に基づく紛争に巻き込まれると患者への医薬品の安定供給ができなくなるというリスクを低減するために、後発医薬品許可証の申請者が既に公開されている新薬に係る特許権について、これらの特許権を侵害しているか否かを自ら申告する必要がある。上記宣言(1)と宣言(2)の場合に権利侵害の恐れがないため、TFDA により薬事法に基づく審査が終了した後に許可証が発行される。上記宣言(3)の場合、一つの新薬に係わる特許権が複数ある可能性もあるため、存続期間が満了していない特許権が一つでもあれば、後発医薬品の製造販売は特許権を侵害する可能性がある。従って、全ての特許権が消滅した後に、医薬品許可証が発行されると説明されている。上記宣言(4)の場合、後発医薬品許可証の申請者が証拠と理由を付けて書面にて新薬の許可証所持者及び TFDA に告知しなければならない。

新薬の許可証所持者と、掲載された特許権者、専用実施権者が異なる場合、後発医薬品許可証の申請者が上記宣言(4)を併せて告知しなければならない。もし告知が行わなければ、TFDA が後発医薬品の申請を却下する。

上記宣言(4)の場合、申請情報についてウェブサイトで公開される[126]（図 17）。

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[124] 藥品生體可用率及生體相等性試驗作業準則（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030065

[125] Regulations of Bioavailability and Bioequivalence Studies（Laws & Regulations Database of The Republic of China (Taiwan)ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030065

[126] 資料齊備日及銷售專屬期（衛生福利部食品藥物管理署ウェブサイト）
https://plls.fda.gov.tw/DataStatement

図 17 公開される宣言(4)の申請情報[127]

衛生福利部食品藥物管理署 Food and Drug Administration

首頁 最新消息 專利資訊查詢 資料齊備日及銷售專屬期 FAQ | 登入

年度： 所有年度 排序： 依資料齊備日排序

對照新藥藥品之藥品許可證字號	有效成分及含量	劑型	P4專利聲明藥商	資料齊備日	銷售專屬期間狀態	銷售專屬期間	備註
衛署藥輸字第024727號	SORAFENIB TOSYLATE, MICRONIZED 274.0000MG	膜衣錠	美時化學製藥股份有限公司	111/04/12	尚在審查中		
衛署藥輸字第024929號	AMLODIPINE BESYLATE 6.9440MG ; OLMESARTAN MEDOXOMIL 20.0000MG	膜衣錠	台灣諾華股份有限公司	111/03/22	尚在審查中		
衛部藥輸字第027426號	Midostaurin 25.0000MG	軟膠囊劑	美時化學製藥股份有限公司	110/11/25	尚在審查中		
衛署藥輸字第024603號	DEFERASIROX 125.0000MG	可溶錠	瑩碩生技醫藥股份有限公司	110/11/23	未符合藥事法第48條之16或17		
衛署菌疫輸字第000928號	Rituximab 10.0000MG	注射劑	台灣賽特瑞恩有限公司	110/11/08	尚在審查中		

（台湾法律事務所コメント[128]）

薬事法第 48 条の 9 第 1 項第 4 号の陳述書（記載特許の無効又は非侵害：以下「P4 陳述書」という。）が提出された後発医薬品申請について、TFDA はまず、後発医薬品申請に必要なすべての書類が提出されているかどうかを確認するために形式的な審査を行う。その場合、TFDA は後発医薬品の申請者に「資料齊備通知」を発行し、オンラインで情報を公開する。

薬事法第 48 条の 12 第 1 項によると、後発医薬品の申請者は、TFDA が正式に準備された申請通知を受領した翌日から 20 日以内に、証拠と理由を記載した通知を先発医薬品会社と TFDA に送付しなければならない。また、西薬専利連結施行辦法[129]（Regulations for the Patent Linkage of Drugs[130]）の第 11 条によると、後発医薬品申請者は、後発医薬品の通知を、郵便局経由の往復受取書付二重署名郵便を使用して送信する必要がある。また、後発医薬品の申請者は、領収書または配達が成功したことを証明するその他の書類を、通知のサービスの翌日から 20 日以内に TFDA に提出する必要がある。後発医薬品通知義務は、TFDA がそのような送達の証拠を受け取った場合にのみ履行されたとみなされる。

実際には、宣言(4)に関する証拠は公開されない。図 17 中の「P4 専利聲明藥商」は、P4 陳述書を作成した後発医薬品申請者の名前を指す。P4 陳述書で提出された後発医薬品申請のみが公開され

127 資料齊備日及銷售專屬期（衛生福利部食品藥物管理署ウェブサイト）（2022 年 6 月 22 日アクセス）
https://plls.fda.gov.tw/DataStatement
128 附属資料１（附属資料２）
129 西薬専利連結施行辦法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030103
130 Regulations for the Patent Linkage of Drugs（Laws & Regulations Database of The Republic of China (Taiwan) ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030103

る。宣言(1)～(3)のいずれかの陳述書を提出した後発医薬品申請は公開されず、パテントリンケージウェブサイトにも表示されない。

薬事法第 48 条の 12 は、後発医薬品会社からの通知には、リストされた特許の無効化または非侵害の主張に関する理由および証拠を提供することを規定しているが、そのような理由、証拠に関する形式、内容、または能力に関する明確な要件はない。台湾法律事務所の弁護士の経験によると、後発医薬品会社はいずれも後発医薬品の通知で企業秘密に関する情報や証拠を提供していない。場合によっては、後発医薬品会社が提供する情報や証拠だけでは、後発医薬品がリストされた特許を侵害するかどうかを評価するには不十分ですらある。そのような場合、先発医薬品会社（つまり、パテントリンケージ訴訟の原告）は、特許侵害を証明するために、法廷に証拠保全の申し立てを行うか、訴訟中の証拠調査に頼って、後発医薬品会社および/または TFDA から証拠を入手する必要がある。後発医薬品会社または TFDA から取得した証拠に営業秘密が含まれている場合、原告は、智慧財產案件審理法[131]（Intellectual Property Case Adjudication Act[132]）第 11 条に従って裁判所が「秘密保持命令」を下さない限り、証拠を検討することはできない。公判が企業秘密に関係する証拠の議論に関するものである場合、審問は、当事者の動議と裁判所の承認に基づいて非公開で開催される。

③ 後発医薬品の自動承認停止

特許権者又は専用実施権者は、後発医薬品許可証の申請者により、上記宣言(4)の告知を受けた後に、当該告知書を受け取った日の翌日から 45 日以内に特許権侵害訴訟を提起し、且つ起訴日の翌日から 20 日以内に裁判所の受領印が付された起訴状の写しを TFDA に送達する必要がある（改正薬事法第 48 条の 13、施行弁法第 12 条）。

TFDA は、提訴する旨の通知を受け取った日の翌日から最長で 12 月間、後発医薬品の許可証の発行を一時的に停止しなければならない。ただし、特許権者又は専用実施権者が後発医薬品申請者からの告知書を受け取った日の翌日から 45 日以内に特許権侵害訴訟を提起しなかった場合、後発医薬品許可証の申請者が特許権を侵害していない旨の判決があった場合、台湾経済部知的財産局（TIPO）により特許権が無効にされた場合、当事者間での和解が成立した場合、あるいは、特許権が消滅した場合において、TFDA は後発医薬品の許可証を発行することができる。一方、特許権者又は専用実施権者が不正に特許権を行使することによって、医薬品許可証発行を一時的に停止させ、後発医薬品会社に損害を与えたと認められた場合には、特許権者又は専用実施権者はその損害賠償責任を負うことになる（改正薬事法第 48 条の 13）。

承認留保期間においても TFDA は後発医薬品の審査を中止することはない。審査が完了した後、TFDA は後発医薬品会社にその旨を通知する。後発医薬品会社は衛生福利部中央健康保険署に保険収載と価格算定を申請できる（改正薬事法第 48 条の 15）。

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131 智慧財產案件審理法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=A0030215

132 Intellectual Property Case Adjudication Act（Laws & Regulations Database of The Republic of China (Taiwan) ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=A0030215

（台湾法律事務所コメント[133]）

パテントリンケージ制度が制定される前は、医薬品関連の民事訴訟は通常、第一審で 15 か月から 2 年で終結していた。智慧財産及商業法院（IPC Court）は、12 か月足らずでパテントリンケージ訴訟の判決を下した。ただし、被告（後発医薬品会社）が第二審裁判所に控訴した場合、そのような判決は最終的な拘束力のある判決ではない。従って、過去のケースでは、TFDA は 12 か月の承認遅延期間満了後に後発医薬品の許可を発行している。第一審の判決が原告に有利な場合、後発医薬品会社は後発医薬品許可を取得しないことを選択できる。そのような場合、後発医薬品の販売独占権は取得できない。これまで、P4 陳述書で後発薬品申請を提出し、後発医薬品の販売独占権を確保することに成功した後発医薬品会社は 1 社だけである。

④ 後発医薬品会社へのインセンティブ

上記宣言(4)を提出した後発医薬品申請者のうち、その申請資料を最初に完備した後発医薬品会社は、12 か月の独占販売期間を取得できる。TFDA はその 12 か月内に他の後発医薬品許可証の申請者に医薬品許可証を発行してはならない（改正薬事法第 48 条の 16）。

なお、同じ日に二社以上の後発医薬品会社がともに最初に申請資料を完備した場合、二社共に独占期間を取得することができる。

後発医薬品会社は許可証を取得した日の翌日から 6 か月以内に販売を行い、且つ最初の販売日の翌日から 20 日以内に実販売日の証拠を添付し TFDA に通知する必要がある。TFDA は独占販売期間及びその起算日、終了日を決定する。仮に、最初の後発医薬品会社が期間内に後発医薬品の許可証を受領しない場合、または許可証受領後 6 か月以内に販売しても期間内に TFDA に通知しない場合、又は関連特許権が消滅した場合、該独占販売期間を取得できないとされている（改正薬事法第 48 条の 17、第 48 条の 18）。

TFDA は上記独占販売期間、その起算日、終了日を決定する際に、その決定内容を医薬品パテントリンケージ情報登載プラットフォーム[134]に搭載する。

（台湾法律事務所コメント[135]）

後発医薬品販売独占権が、上記ウェブサイトで公開される[136]。後発医薬品販売独占期間は、図 17 のヘッダー「銷售專屬期間」のカラムに示される。

(4) パテントリンケージ条項に関する CPTPP との比較

パテントリンケージ条項に関する CPTPP と台湾法との比較を表 16 に示す。

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133 附属資料１（附属資料２）

134 衛生福利部食品薬物管理署ウェブサイト
https://plls.fda.gov.tw/

135 附属資料１（附属資料２）

136 資料齊備日及銷售專屬期（衛生福利部食品藥物管理署ウェブサイト）
https://plls.fda.gov.tw/DataStatement

表 16 パテントリンケージ条項に関する CPTPP と台湾法との比較

CPTPP[137]	台湾法[138]
第 18・53 条 特定の医薬品の販売に関する措置 1 締約国は、医薬品の販売を承認する条件として、安全性及び有効性に関する情報を最初に提出した者以外の者が、以前に承認された製品の安全性又は有効性に関する証拠又は情報（例えば、先行する販売承認であって、当該締約国によるもの又は他の国若しくは地域の領域におけるもの）に依拠することを認める場合には、次のものを定める。 (a) 当該最初に提出した者以外の者が当該承認された製品又はその承認された使用の方法が請求の範囲に記載されている適用される特許の期間中に当該医薬品を販売しようとしていることについて、当該医薬品が販売される前に、特許権者（注）に通知し、又は特許権者が通知を受けられるようにする制度 注 この条の規定の適用上、締約国は、「特許権者」に特許の実施許諾を得た者又は正当に販売承認を与えられた者を含むことを定めることができる。	薬事法第 48 条の 12（仮訳） 後発医薬品許可証の申請案が第 48 条の 9 第 4 号に関わる声明である場合、申請人は中央衛生主務官庁より発行された薬品許可証申請資料完備通知の送達日の翌日から 20 日以内に、書面にて新薬薬品許可証所有者及び中央衛生主務官庁に通知すべきである。新薬薬品許可証所有者が登録された特許権者、専用実施権被許諾者と異なった場合は、併せて通知しなければならない。 ・・・（略）・・・。
(b) 特許権者が、侵害しているとされる製品の販売（注）前に、(c)に規定する利用可能な救済手段を求めるための十分な期間及び機会 注 この(b)の規定の適用上、締約国は、「販売」を、締約国が運用し、かつ、附属書二十六-A（医薬品及び医療機器に関する透明性及び手続の公正な実施）の付録に記載する国の保健医療制度に基づく償還のために医薬品が一覧に掲載された時に開始するものとして扱うことができる。	薬事法第 48 条の 13（仮訳） 特許権者または専用実施権被許諾者は、前条第 1 項の通知を受けてから、掲載された特許権について侵害訴訟を提起しようとする場合、通知を受けた日の翌日から 45 日以内に訴えを提起し、かつそれを中央衛生主務官庁に通知しなければならない。 ・・・（略）・・・。
(c) 承認された医薬品又はその承認された使用の方法が請求の範囲に記載されている適用さ	薬事法第 48 条の 13（仮訳）

[137] TPP 協定（和文）第 18 章（知的財産）（外務省ウェブサイト）
https://www.mofa.go.jp/mofaj/gaiko/treaty/pdfs/tpp/jp/tpp_jp_18.pdf
[138] 台湾薬事法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=L0030001

れる特許の有効性又は侵害に関する紛争を適時に解決するための手続（司法上又は行政上の手続等）及び迅速な救済措置（予備的差止命令又はこれと同等の効果的な暫定措置等）	特許権者または専用実施権被許諾者は、前条第 1 項の通知を受けてから、掲載された特許権について侵害訴訟を提起しようとする場合、通知を受けた日の翌日から 45 日以内に訴えを提起し、かつそれを中央衛生主務官庁に通知しなければならない。 中央衛生主務官庁は、新薬薬品許可証所有者が前条第 1 項の通知を受けた日の翌日から 12 ヶ月以内に、薬品許可証の発行を停止すべきである。・・・（略）・・・。

第 4 章　まとめ

I. 各国のパテントリンケージ制度の比較

以下、各国のパテントリンケージ制度の比較を表 17 にまとめる。

表 17 各国のパテントリンケージ制度の比較

分類	米国		カナダ	中国	韓国	台湾
	低分子医薬	生物製剤				
導入時期	1984/2003	2010	1993/2017	2021	2012/2015	2019
特許リスト	○	○	○	○	○	○
特許リスト審査	×	×	○	×	○	×
特許リスト公開	○	○	○	○	○	○
通知制度の運営	○	○	○	○	○	○
販売禁止制度運営	○	×	○	○	○	○
販売禁止申請に関する実体審査	×	×	×	×	○	×
販売禁止期間	30 か月	なし	24 か月	9 か月（化学医薬品のみ）	9 か月	12 か月
後発医薬品会社独占制度運営可否	○	○ Inter-changeable のみ	×	○（化学医薬品のみ）	○	○
後発医薬品会社独占期間	180 日	1 年 Inter changeable のみ	×	12 か月（化学医薬品のみ）	9 か月	12 か月

パテントリンケージ制度は、米国でハッチ・ワックスマン法として 1984 年に導入されたのを皮切りに、NAFTA（北米自由貿易協定）に基づいて 1993 年にカナダで、米韓 FTA に基づき 2012 年に韓国で、CPTPP 加入を目的として 2019 年に台湾で、米中米中経済貿易協定（Economic and Trade

Agreement between the United States of America and the People's Republic of China）の第 1 弾署名に基づき 2019 年に中国で導入された。

パテントリンケージ制度について、CPTPP においては、「後発医薬品の販売前に特許権者に通知する制度、及び侵害救済措置」が規定（第 18・53 条第 1 項）されているとともに、代替として司法上の手続き以外の制度の採用・維持が規定（第 18・53 条第 2 項）されている。一方で、CUSMA（新 NAFTA）、米中経済貿易協定、米韓自由貿易協定においては、CPTPP の第 18・53 条第 1 項相当が規定されており、CPTPP の第 18・53 条第 2 項相当の代替は規定されていない。それに従い、カナダ、中国、韓国、台湾のパテントリンケージ制度には CPTPP の第 18・53 条第 1 項相当が規定され、CPTPP の第 18・53 条第 2 項相当は規定されていない。

米国では、低分子医薬品と生物学的製剤と別の法律・規則で規定されているが、カナダ、中国、韓国、台湾では同一の法律・規則で規定されている。

特許リストへの掲載について、米国、中国、台湾では当局は審査を行わず申請者による申請に基づき掲載するが、カナダ、韓国では当局は掲載可否の審査を行う。

後発医薬品の自動承認停止は、米国における生物学的製剤、中国における生物学的製剤・漢方薬を除き、米国（30 か月）、カナダ（24 か月）、中国（9 か月）、韓国（9 か月）、台湾（12 か月）で認められているが、それぞれの自動承認停止期間は異なる。

後発医薬品について最初に承認を受けた後発医薬品会社に与えられる独占期間は、米国（低分子医薬品：180 日、interchangeable：1 年）、中国（低分子医薬品のみ：12 か月）、韓国（9 か月）、台湾（12 か月）で認められているが、カナダでは認められていない。

第 5 章　その他の参考資料

I. 総論（複数国）

（英語）

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（日本語）

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II. 米国

（日本語）

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III. カナダ

（英語）

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IV. 中国

（日本語）

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V. 台湾

（台湾語）

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http://www.twba.org.tw/Manage/magz/UploadFile/5829_004-013%E5%B0%88%E5%88%A9%E9%80%A3%E7%B5%90%E5%B0%8D%E6%96%BC%E7%94%A2%E6%A5%AD%E4%B9%8B%E5%BD%B1%E9%9F%BF-%E8%8E%8A%E9%83%81%E6%B2%81%20%E6%9C%B1%E6%B7%91%E5%B0%B9.pdf
專利連結藥事法修正立法過程觀察： 失落的台灣全民健康福祉 與本土製藥產業利益（翁雅欣 全國律師 2019 年 5 月號 14-36）
http://www.twba.org.tw/Manage/magz/UploadFile/5830_014-036%E5%B0%88%E5%88%A9%E9%80%A3%E7%B5%90%E8%97%A5%E4%BA%8B%E6%B3%95%E4%BF%AE%E6%AD%A3%E7%AB%8B%E6%B3%95%E9%81%8E%E7%A8%8B%E8%A7%80%E5%AF%9F-%E7%BF%81%E9%9B%85%E6%AC%A3.pdf
政策舞蹈 —生物藥與專利連結制度淺析（高詠文、彭德仁 全國律師 2019 年 5 月號 37-50）
http://www.twba.org.tw/Manage/magz/UploadFile/5831_037-050%E6%94%BF%E7%AD%96%E8%88%9E%E8%B9%88%20%E2%80%94%E7%94%9F%E7%89%A9%E8%97%A5%E8%88%87%E5%B0%88%E5%88%A9%E9%80%A3%E7%B5%90%E5%88%B6%E5%BA%A6%E6%B7%BA%E6%9E%90-%E9%AB%98%E8%A9%A0%E6%96%87%20%E5%BD%AD%E5%BE%B7%E4%BB%81.pdf
論生物藥品準用專利連結制度對我國 藥廠智慧財產權策略之影響（何娜瑩、林均郁 全國律師 2019 年 5 月號 51-59）
http://www.twba.org.tw/Manage/magz/UploadFile/5832_051-059%E8%AB%96%E7%94%9F%E7%89%A9%E8%97%A5%E5%93%81%E6%BA%96%E7%94%A8%E5%B0%88%E5%88%A9%E9%80%A3%E7%B5%90%E5%88%B6%E5%BA%A6-%E4%BD%95%E5%A8%9C%E7%91%A9%20%E6%9E%97%E5%9D%87%E9%83%81.pdf
（日本語）
中国及び台湾のパテントリンケージ制度の最新動向について（知財管理 2020 年 6 月）

附属資料

附属資料１：台湾法律事務所調査報告書（英語）
附属資料２：台湾法律事務所調査報告書（日本語訳）
附属資料３：米国関連条文（低分子医薬品）
附属資料４：米国関連条文（生物学的製剤）
附属資料５：カナダ関連条文
附属資料６：中国関連条文
附属資料７：韓国関連条文
附属資料８：台湾関連条文

附属資料１：台湾法律事務所調査報告書（英語）（質問事項：赤字、回答：青字）

We describe our understanding of patent linkage system in Taiwan dividing into four steps ((A) Patent Registration of Innovative Company (Patent List), (B) Generic Drug Application + Notification to the Innovative Company (the patentee or the exclusive licensee), (C) Automatic generic drug approval postponement and (D) Incentive to the generic company) and the background of the Patent Linkage System enactment. Could you let us know (1) whether our understanding is correct or not, (2) your comments on our inquiries and (3) your further usable comments on Patent Linkage System in Taiwan.

[(A) Patent Register of Innovative Company (Patent List)]

(Our Understanding and its related articles)

(I) Article 48-3 of Pharmaceutical Affairs Act defines that

1. If the holder of a new drug permit deems it necessary to submit the patent information regarding such drug, such holder shall submit relevant documents and information to the Central Competent Health Authority within 45 days after the next day to the receipt of the drug permit. If the holder fails to file such submission within the stipulated period, the regulations under this Chapter do not apply.

2. The drug patent stipulated under Paragraph 1 hereof shall be limited to the following:

(1) Substance.

(2) Composition or Formulation.

(3) Medical use.

(II) Article 48-5 of Pharmaceutical Affairs Act defines that

If the holder of a new drug permit obtains the approval of an application for an invention patent(s) from the Competent Patent Authority after the approval of said new drug permit from the Central Competent Health Authority, and such patent(s) is subject to the scope of drug patent set forth in Paragraph 2 of Article 48-3, the patent information thereof shall be submitted within 45 days after the next day to the patent issuance in accordance with Article 48-4. If the holder fails to file such submission within the stipulated period, the regulations under this Chapter do not apply.

(III) Article 48-4 of Pharmaceutical Affairs Act defines that

1. The "patent information" stipulated in Article 48-3 shall include the following items:

(1) Certification number of the invention patent(s); if the invention patent refers to medical use, the number of claims shall be concurrently provided.

(2) The expiration date of the patent(s).

(3) The patentee's name, nationality, place of domicile or business office; for a patentee having a legal representative, the name of the legal representative shall be listed. If said patent has been exclusively licensed and has been recorded in accordance with the Patent Act, the aforementioned information of the exclusive licensee shall be listed.

(4) If the patentee or the exclusive licensee in Item (3) hereunder does not have a domicile or a business office in the R.O.C., an agent thereof shall be appointed. The appointed agent's name, place of domicile or business office shall be submitted.

2. If the holder of a new drug permit is different from the patentee, the patentee's consent shall be obtained when submitting the patent information; if the patent has been exclusively licensed and has been recorded in accordance with the Patent Act, it is only required to obtain the exclusive licensee's consent.

(IV) The patentee or the exclusive licensee can utilize the Patent Linkage System (Effectiveness of Patent Linkage System: Notification from generic companies, and generic drug approval postponement based on the patent infringement litigation) after the Patent Register has been completed.

(V) Article 48-7 of Pharmaceutical Affairs Act defines that

1. Anyone may notify any of the following items to the Central Competent Health Authority with written explanations and evidence attached:

(1) The invention listed in the patent information is irrelevant to the approved drug.

(2) The invention listed in the patent information does not comply with Paragraph 2 of Article 48-3.

(3) The patent information listed is incorrect.

(4) No amendment or deletion has been made for any of the occurrences stipulated in Article 48-6.

2. The Central Competent Health Authority shall, within 20 days after the next day to its receipt of the notification under Paragraph 1 hereof, forward said notification to the holder of the new drug permit.

3. The holder of a new drug permit shall, within 45 days of the next day to its receipt of said notification, respond to the Central Competent Health Authority with written explanations, and may amend or delete the patent information as the case may be.

(VI) Article 48-8 of Pharmaceutical Affairs Act defines that

1. The Central Competent Health Authority shall establish a Registration System for Patent Linkage of Drugs to list and publish the patent information submitted by the holder of a new drug permit. The aforementioned shall also apply to the amendment and deletion of the patent information.

2. Upon the occurrence of the matters stipulated in Article 48-7 for the listed patent information, the Central Competent Health Authority shall publish the third party's allegations and the written responses made by the holder of the new drug permit.

(VII) Patent Register is not duty for the patentee or the exclusive licensee, but a voluntary activity. Therefore, even though the patentee or the exclusive licensee does not complete the Patent Register, the patentee or the exclusive licensee can allege the patent infringement towards the suspectable infringer.

(Inquiries)

(I) Could you let us know whether our understanding above is correct or not? If you have any further information, please let me know.

(Lee and Li's comments)

Your understanding above is correct. For your information, the day of receipt of the drug permit mentioned in Article 48-3, Paragraph 1of the Pharmaceutical Affairs Act (PAA) refers to the day on which the drug permit

is physically collected from the Central Competent Health Authority, i.e., Taiwan Food and Drug Administration (TFDA), rather than the issue date of the drug permit.

(II) The generic company file an application by showing the biological equivalence and utilizing the safety/efficacy data of the innovative drug. Could you let us know how the safety/efficacy data of the innovative drug is disclosed to the generic company with the related evidence (article) in Taiwan?
For your reference, in the United States, Food and Drug Administration (FDA) updates the alphabetical list of drugs approved for the safety/efficacy in line with 21USC355(c) and publishes the list as the Orange Book. The Orange Book includes approval date, official drug name, trademark, and the information whether the Abbreviated New Drug Application (ANDA) needs in vitro and/or in vivo biological equivalent experiment (21USC355(j)(7)(A)(i)(I)-(III)).

(Lee and Li's comments)
The safety/efficacy data of the innovative drug will not be disclosed to the public or the generic company. The generic company only needs to refer to the innovative drug and submit a bioavailability (BA) and/or bioequivalence (BE) study report, or even substitute the BE study report with a dissolution profile comparison report where acceptable.

The generic company can acquire the innovative drug by itself and conduct comparison experiments to prove bioequivalence. Whether an ANDA needs to provide in vitro and/or in vivo biological equivalent experiment results should be determined according to the Regulations of Bioavailability and Bioequivalence Studies. A link to the regulations is provided below:

https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030065

Articles 6 and 7 of the regulations provide certain criteria for the determination of whether BA or BE studies need to be conducted. If a generic company submitted a BA/BE report in an ANDA and the generic drug is approved based thereon, the TFDA will indicate on the public website of drug permits that the generic drug is approved based on BA/BE studies. However, the BA/BE data will not be published.

[(B) Generic Drug Application + Notification to the Innovative Company (the patentee or the exclusive licensee)]

(Our Understanding and its related articles)

(I) Article 48-9 of Pharmaceutical Affairs Act defines that

> The applicant for a generic drug permit shall, with respect to the patent(s) of the approved new drug listed by the holder of said new drug permit, declare one of the following item(s) when applying for a generic drug permit:
> (1) No patent information of said new drug has been listed.
> (2) The patent(s) corresponding to said new drug has extinguished.

(3) The Central Competent Health Authority will issue the generic drug permit after the patent(s) corresponding to said new drug extinguishes.

(4) The patent(s) corresponding to said new drugs shall be revoked, or the patent(s) corresponding to said new drugs will not be infringed by the generic drug subject to the application for drug permit.

(II) In case of the item (1) and item (2), TFDA issues the approval certification after the examination according to the Pharmaceutical Affairs Act since there is no infringement possibility. In case of the item (3), TFDA issues the approval certification after all the registered patents expires. In case of the item (4), the generic drug applicant shall send the innovative company and TFDA a notification with the evidence and reasons. If the innovative company and the registered patentee/exclusive licensee are different, the generic company shall send the notification to the registered patentee/exclusive licensee. Without the notification, TFDA shall reject the generic company's application.

(III) In case of the item (4), the application information shall be published on the website（資料齊備日及銷售專屬期 (衛生福利部食品藥物管理署 website https://plls.fda.gov.tw/DataStatement).

衛生福利部食品藥物管理署 Food and Drug Administration

首頁 最新消息 專利資訊查詢 資料齊備日及銷售專屬期 FAQ | 登入

年度： 所有年度 排序： 依資料齊備日排序

對照新藥藥品之藥品許可證字號	有效成分及含量	劑型	P4專利聲明藥商	資料齊備日	銷售專屬期間狀態	銷售專屬期間	備註
衛署藥輸字第024727號	SORAFENIB TOSYLATE, MICRONIZED 274.0000MG	膜衣錠	美時化學製藥股份有限公司	111/04/12	尚在審查中		
衛署藥輸字第024929號	AMLODIPINE BESYLATE 6.9440MG；OLMESARTAN MEDOXOMIL 20.0000MG	膜衣錠	台灣諾華股份有限公司	111/03/22	尚在審查中		
衛部藥輸字第027426號	Midostaurin 25.0000MG	軟膠囊劑	美時化學製藥股份有限公司	110/11/25	尚在審查中		
衛署藥輸字第024603號	DEFERASIROX 125.0000MG	可溶錠	瑩碩生技醫藥股份有限公司	110/11/23	未符合藥事法第48條之16或17		
衛署菌疫輸字第000928號	Rituximab 10.0000MG	注射劑	台灣賽特瑞恩有限公司	110/11/08	尚在審查中		

(Inquiries)

(I) Could you let us know whether our understanding above is correct or not? If you have any further information, please let me know.

(Lee and Li's comments)

Your understanding above is basically correct. We would like to clarify the procedure of generic notification.

For an ANDA filed with statement according to Article 48-9, Paragraph 1, Item (4) (i.e., invalidity of the listed patent(s) or non-infringement; hereinafter refers to as the "P4 statement"), the TFDA will first perform a formality review to see whether all the required documents for the ANDA are submitted. If so, the TFDA

will issue a "notice of application duly prepared (資料齊備通知)" to the generic drug applicant and publish the information on the online patent linkage system.

According to Article 48-12, Paragraph 1 of the PAA, the generic drug applicant must send the innovative company and the TFDA a notification with the evidence and reasons within 20 days after the next day to its receipt of the TFDA notice of application duly prepared. In addition, according to Article 11 of the Regulations for the Patent Linkage of Drugs (https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030103), the generic notification should be sent using double-signed mail with a return receipt, and the receipt or any other document proving successful delivery must be submitted to the TFDA within 20 days after the next day to the service of the notification. The duty of generic notification is considered fulfilled only when the TFDA receive such evidence of delivery.

(II) Actually, the evidence of item (4) is published on the website. Which article is the reason of the item (4) publication? In addition, there is “P4 專利聲明藥商” column in the table above. Does it mean that only the generic application information based on item (4) is published among the items (1)-(4)?

(Lee and Li's comments)
Actually, the evidence regarding item (4) will NOT be published. "P4 專利聲明藥商" refers to the name of the generic drug applicant making the P4 statement. Only the ANDA filed with a P4 statement will be published. The ANDA filed with a statement according to any one of items (1) to (3) will not be published and will not be shown on the patent linkage website.

(III) We understand that even the fact of the generic drug application was subject to the trade secret prior to the enactment of the Patent Linkage System unless the applicant voluntarily disclosed it. Was there discussion on losing the trade secret status of the generic drug application by publishing the item (4) on the website (and notifying of the patent owner the item (4)) when the Patent Linkage System was enacted? If so, please let us know the discussion in detail.

(Lee and Li's comments)
As mentioned above, the generic drug application or the generic notification with respect to a statement will not be published. Therefore, there is no relevant discussion in this regard.

(IV) The patentee or exclusive licensee shall confirm the detailed information of the generic drug in order to consider whether it files a patent litigation within 45 days. For the generic company, the detailed information shall be treated as confidential information. Under the situation, how is the detailed information treated as a legal matter (Law, Regulation/Rule, Guideline, Operation, etc.)? Which article is adapted for the confidentiality?
For example, following articles are adapted in the United States, Canada and China.

The United States:

For the small molecules, Federal Rule (21CFR314.95(c)(8)) defines that

> If the applicant alleges that the patent will not be infringed and the applicant seeks to preserve the option to later file a civil action for declaratory judgment in accordance with section 505(j)(5)(C) of the Federal Food, Drug, and Cosmetic Act, then the notice must be accompanied by an offer of confidential access to the ANDA for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the paragraph IV certification.

For the biologics, Federal Law (42USC262(l)(2)) defines that

> Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k) applicant—
>
> (A) shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application; and
>
> (B) may provide to the reference product sponsor additional information requested by or on behalf of the reference product sponsor.

Canada:

Patented Medicines (Notice of Compliance) Regulations 5(3)(c)(iii) defines that

> A second person who makes an allegation referred to in paragraph (2.1)(c) shall
>
> (a) …;
>
> (b) …;
>
> (c) serve the following documents with the notice:
>
> (i) a certification by the Minister of the date of filing of the submission or supplement,
>
> (ii) a document setting out the second person's address for service for the purpose of any action that may be brought against them under subsection 6(1), along with the names of and contact information for their anticipated solicitors of record if that action is brought,
>
> (iii) a searchable electronic copy of the portions of the submission or supplement that are under the control of the second person and relevant to determine if any patent or certificate of supplementary protection referred to in the allegation would be infringed, and
>
> (iv) if the second person is alleging that the patent or certificate of supplementary protection is invalid or void, an electronic copy of any document — along with an electronic copy of it in English or French if available — on which the person is relying in support of the allegation;
>
> (d) …; and
>
> (e) ….

And, Patented Medicines (Notice of Compliance) Regulations 5(3.5) defines that

> The second person may impose on the first person referred to in paragraph (3)(a) and any owner of a patent to whom a document is forwarded under subsection (3.3) any reasonable rules for maintaining the confidentiality of any portion of a submission or supplement referred to in subparagraph (3)(c)(iii).

China: (For your understanding, the articles are the original wording)

药品专利纠纷早期解决机制行政裁决办法 第十八条 defines that

国家知识产权局作出行政裁决的，应当就申请上市药品技术方案是否落入相关专利权保护范围作出认定，并说明理由和依据。行政裁决作出后，应当送达当事人并抄送国家药品监督管理部门，同时按照《政府信息公开条例》及有关规定向社会公开。行政裁决公开时，应当删除涉及商业秘密的信息。

药品专利纠纷早期解决机制行政裁决办法 第二十条 defines that

当事人对其提供的证据或者证明材料的真实性负责。

当事人对其在行政裁决程序中知悉的商业秘密负有保密义务，擅自披露、使用或者允许他人使用该商业秘密的，应当承担相应法律责任。

药品专利纠纷早期解决机制行政裁决办法 第二十一条 defines that

药品专利纠纷行政裁决案件办理人员以及其他工作人员滥用职权、玩忽职守、徇私舞弊或者泄露办理过程中知悉的商业秘密，尚不构成犯罪的，依法给予政务处分；涉嫌犯罪的，移送司法机关处理。

最高人民法院关于审理申请注册的药品相关的专利权纠纷民事案件适用法律若干问题的规定 第八条 defines that

当事人对其在诉讼中获取的商业秘密或者其他需要保密的商业信息负有保密义务，擅自披露或者在该诉讼活动之外使用、允许他人使用的，应当依法承担民事责任。构成民事诉讼法第一百一十一条规定情形的，人民法院应当依法处理。

(Lee and Li's comments)

Although Article 48-12 of the PAA stipulates that the generic notification be provided with reasons and evidence regarding the invalidation of listed patent(s) or non-infringement allegation, there are no clear requirements for the format, content or competency of such reasons or evidence. I, Joyce Liou, personally participated in six patent linkage litigations since the enactment of the Patent Linkage System. According to my experience, none of the generic company provides information or evidence involving trade secret in the generic notification. In some case, the information or evidence provided by the generic companies is even insufficient to evaluate whether the generic drug will infringe on the listed patent(s). In such case, the innovative company (i.e., the plaintiff of the patent linkage litigation) will have to file a motion for evidence preservation with the court or rely on evidence investigation during litigation to obtain evidence from the generic company and/or the TFDA to prove infringement. If the evidence obtained from the generic company or the TFDA involves trade secret, the plaintiff will not be allowed to review the evidence unless a "confidentiality preservation order" is rendered by the court according to Article 11 of the Intellectual Property Case Adjudication Act (https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=A0030215). If a trial concerns the discussion of evidence involving trade secret, the hearing will be held in private upon motion of the party and approval of the court.

[(C) Automatic generic drug approval postponement]

(Our Understanding and its related articles)

(I) Article 48-13 of Pharmaceutical Affairs Act defines that

1. If the patentee or the exclusive licensee intends to file a patent infringement complaint on the basis of the listed patent(s) after its receipt of the notification stipulated by Paragraph 1 of Article 48-12, it shall file the complaint within 45 days after the next day to its receipt of said notification and notify the Central Competent Health Authority.

2. The Central Competent Health Authority shall stay the issuance of the drug permit for twelve (12) months as of the next day to the new drug permit holder's receipt of the notification stipulated in Paragraph 1 of Article 48-12. However, if there is any of the following matters, the Central Competent Health Authority may issue the drug permit if [said application is] is examined to be in compliance with the regulations under this Act:

(1) The patentee or the exclusive licensee, after its receipt of the notification stipulated by Paragraphs 1 of Article 48-12, fails to file an infringement complaint within the 45-day period.

(2) The patentee or the exclusive license files an infringement complaint based on the patents which are not those listed before the date of the application for the generic drug permit.

(3) The patent infringement complaint filed by the patentee or the exclusive licensee pursuant to Paragraph 1 hereof is overruled by the court according to Paragraph 1 or 2 of Article 249 of the Coded of Civil Procedure.

(4) The court has determined that all of the patents pending in the infringement lawsuit shall be revoked, or a non-infringement judgment is obtained by the applicant for the generic drug permit.

(5) All the patents under the declaration stipulated in Item 4 of Article 48-9 made by the applicant for the generic drug permit are determined as invalid by the Competent Patent Authority in a cancellation action.

(6) A settlement or a mediation has been reached by the parties.

(7) All the patents under the declaration stipulated in Item 4 of Article 48-9 made by the applicant for the generic drug permit have become extinguished.

3. The period [for notification] stipulated in Item 1, Paragraph 2 hereof shall be commenced upon the receipt of the notification by the patentee(s) or the exclusive licensee(s), whichever is later.

4. If the patentee or the exclusive licensee obtains a final and binding judgment confirming infringement of the listed patent(s) within the 12-month period stipulated in Paragraph 2 hereof, the Central Competent Health Authority shall issue the generic drug permit after said patent(s) extinguishes.

5. Where the patent infringement complaint filed by the patentee or the exclusive licensee pursuant to Paragraph 1 hereof, if by reason of being improper exercise of patent right ab initio, the stay of drug permit issuance has caused damages to the applicant of a generic drug permit, [such patentee or the exclusive licensee] shall be held liable for compensation.

Article 12 of Regulations for the Patent Linkage defines that

If the patentee or the exclusive licensee files a patent infringement in accordance with Article 48-13 stipulated in the Act, the holder of the new drug permit license shall send photocopy of the complaint document with the court's stamp applied to it to the Central Competent Health Authority within 20 days after the next day of prosecution.

The holder of the new drug permit license who asserts to obtain a final and binding judgment confirming infringement, stipulated by Paragraph 4 in Article 48- 13 of the Act, shall submit the copy along with the evidence of the final and binding judgment, to the Central Competent Health Authority.

(II) Article 48-15 of Pharmaceutical Affairs Act defines that

1. During the period of stay of drug permit issuance stipulated in Paragraph 2 of Article 48-13, if the examination for the application for a generic drug permit has been completed, the Central Competent Health Authority shall inform the same to the applicant for said generic drug permit.

2. The applicant for a generic drug permit may apply for drug listing and reimbursement price with the National Health Insurance Administration after receiving the notification stipulated in Paragraph 1 hereof. However, no manufacture or importation [of the generic drug] is permitted before the Central Competent Health Authority's issuance of the generic drug permit.

(Inquiries)

(I) Could you let us know whether our understanding above is correct or not? If you have any further information, please let me know.

(Lee and Li's comments)

Your understanding is correct. Before the enactment of the Patent Linkage System, a pharmaceutical-related civil litigation usually concluded in 15 months to 2 years at the first instance court. The Intellectual Property and Commercial Court (IPC Court) has done a good job to render judgements of patent linkage litigations in less than 12 months. However, such a judgement is not a final and binding judgment if the defendant (the generic company) files an appeal to the second instance court. Therefore, for the past cases, the TFDA has issued the generic drug permits after the expiry of the 12-month stay period. If the first instance judgement is in favor of the plaintiff, the generic company may choose not to collect the generic drug permit. In such case, no generic marketing exclusivity can be obtained. Up to now, only one generic company filing an ANDA with a P4 statement successfully secure a generic marketing exclusivity.

[(D) Incentive to the generic company]

(Our Understanding and its related articles)

(I) Article 48-16 of Pharmaceutical Affairs Act defines that

1. The application for a generic drug permit in accordance with Item 4 of Article 48-9 with application documents duly prepared at the earliest shall be granted a 12-month period of marketing exclusivity; the Central Competent Health Authority shall not issue other drug permits to other applicants for a generic drug permit before the expiration of the aforementioned period.

2. For the aforementioned application for a generic drug permit with documents duly prepared under

Item 4 of Article 48-9, upon occurrence of [vacancy due to] any of the following matters, the vacancy will be fulfilled by the subsequent applicant with application documents duly prepared:

(1) During the period of drug permit examination, the declaration under Item 4 of Article 48-9 is amended.

(2) The earliest applicant fails to obtain from the Central Competent Health Authority the notification that the examination of the application for generic drug permit has completed within 12 months after the next day to the date that all the application documents are duly prepared.

(3) Any matter as stipulated in Paragraph 4 of Article 48-13

occurs.

3. If more than one application for a generic drug permit in compliance with the requirements regarding the earliest duly prepared application documents is filed on the same date, such applications are jointly subject to the 12-month period of marketing exclusivity.

And, if more than two generic companies complete the first generic applications on the same day, the more than two generic companies share the 12-month period of marketing exclusivity.

(II) Article 48-17 of Pharmaceutical Affairs Act defines that

1. The holder of a generic drug permit shall market the drug within 6 months after the next day to such holder's obtaining of said drug permit, and shall, within 20 days after the next day to the earliest marketing date, provide the evidence of the actual marketing date to the Central Competent Health Authority for its determination of the marketing exclusivity period granted and the commencement date and end date thereof.

2. The marketing exclusivity period stipulated in Paragraph 1 hereof starts from the date of the actual marketing of the drug.

3. If more than one application for the generic drug permit is jointly subject to the marketing exclusivity period, the commencement date thereof shall be the date on which any of such drugs are actually first marketed.

Article 48-18 of Pharmaceutical Affairs Act defines that

If any of the following matters occur to the applicant for generic drug permit subject to the marketing exclusivity period, the Central Competent Health Authority may issue generic drug permits to other applicants without being restricted by Paragraph 1 of Article 48-16:

(1) Failure to collect the drug permit within the period prescribed by the Central Competent Health Authority.

(2) Failure to abide by Paragraph 1 of Article 48-17.

(3) All the patents declared under Item 4 of Article 48-9 have become extinguished.

(III) TFDA publishes the exclusivity term, its starting date and its expiration date on the website.

(Inquiries)

(I) Could you let us know whether our understanding above is correct or not? If you have any further information, please let me know.

(Lee and Li's comments)

Your understanding is correct. However, as stated above, currently, only one generic company filing an ANDA with a P4 statement successfully secure a generic marketing exclusivity.

(II) In Our Understanding and its related articles (III) above, we assume that the website (underlined) is 資料齊備日及銷售專屬期(衛生福利部食品藥物管理署 website) https://plls.fda.gov.tw/DataStatement. Is our assumption correct?

You are correct that the generic marketing exclusivity will be published on the website shown below. The exclusivity period will be indicated in the column with the header "銷售專屬期間".

衛生福利部食品藥物管理署 Food and Drug Administration

首頁 最新消息 專利資訊查詢 資料齊備日及銷售專屬期 FAQ | 登入

年度： 所有年度 排序： 依資料齊備日排序

對照新藥藥品之藥品許可證字號	有效成分及含量	劑型	P4專利聲明藥商	資料齊備日	銷售專屬期間狀態	銷售專屬期間	備註
衛署藥輸字第024727號	SORAFENIB TOSYLATE, MICRONIZED 274.0000MG	膜衣錠	美時化學製藥股份有限公司	111/04/12	尚在審查中		
衛署藥輸字第024929號	AMLODIPINE BESYLATE 6.9440MG；OLMESARTAN MEDOXOMIL 20.0000MG	膜衣錠	台灣諾華股份有限公司	111/03/22	尚在審查中		
衛部藥輸字第027426號	Midostaurin 25.0000MG	軟膠囊劑	美時化學製藥股份有限公司	110/11/25	尚在審查中		
衛署藥輸字第024603號	DEFERASIROX 125.0000MG	可溶錠	瑩碩生技醫藥股份有限公司	110/11/23	未符合藥事法第48條之16或17		
衛署菌疫輸字第000928號	Rituximab 10.0000MG	注射劑	台灣賽特瑞恩有限公司	110/11/08	尚在審查中		

[Background of the Patent Linkage System enactment]

(Our Understanding and its related articles)

Considering the joining to Trans-Pacific Partnership agreement (TPP), Taiwan amended Pharmaceutical Affairs Act in 2017 to include (i) Registration and Publication of the patent information for the innovative drug, (ii) Declaration of the generic company and Notification to the innovative company, (iii) Challenge to the patent of the innovative company, (iv) automatic approval postponement of the generic drug and (v) generic drug exclusivity for the first approval of the generic drug. And the amendment was enacted on August 20, 2019 as Articles 48-3 to 48-22 of Pharmaceutical Affairs Act.

(Inquiries)

(I) Is our understanding correct? If you have any further information, please let me know.

(Lee and Li's comments)

Your understanding is correct. However, after the US withdrawn from the TPP, the driving force of the implementation of the Patent Linkage System is in the hope of having a Trade and Investment Framework Agreement (TIFA) with the US.

(II) We caught patent law amendment (Article 60-1), which passed the Congress on February 24, 2022, and enacted on July 1, 2022 relating to the Patent Linkage System enactment. If there is further legal update after the enactment of the Patent Linkage System of August 2019, please let us know.

(Lee and Li's comments)
There is no ongoing plan for the amendment to the Patent Linkage System. We will keep you updated of any developments.

On the other hand, several judgements for patent linkage litigations have been rendered before Article 60-1 of the Patent Act is passed. The IPC court considers that Article 96, Paragraph 1 of the Patent Act is sufficient to provide legal basis for such patent linkage litigations.

(III) Prior to the enactment of the Patent Linkage System, there would be various discussion regarding (i) subject patent to the Patent Register, (ii) the term of the automatic generic drug approval postponement, (iii) incentives to the first generic company obtaining the generic approval, (iv) inclusion of the biologics into the Patent Linkage System, and so on. Could you let us know the summary of them?

(Lee and Li's comments)

(i) The Patent Linkage System basically adopts the US Orange Book mechanism. There is disputes over whether the claim number of a listed patent should be identified and whether patents relating to polymorphs can be listed. At the end, the TFDA decided that the claim number only needs to be identified for medical use patent, and polymorph patents are eligible for listing. However, if the patented polymorph is different from the polymorph of the active ingredient of a new drug preparation, the test data demonstrated that a drug preparation containing the polymorph perform the equal effectiveness shall be provided when registration (*see* Article 3, Paragraph 2 of the Regulations for the Patent Linkage of Drugs). For your information, although patent covering manufacturing process is not eligible for listing, product-by-process claims are deemed to claim the product *per se* (i.e., a substance or a composition), and thus can be listed.

(ii) The originally proposed stay period is 15 months based on the average time required for the first instance court to conclude a patent litigation case. It was shorten to 12 months by the Congress.

(iii) The originally proposed generic marketing exclusivity period is six months. However, in order to move the amendment to the PAA forward, the generic marketing exclusivity period was extended to 12 months to reduce the resistance from the generic companies.

(iv) Under current practice, biologics are treated as new molecular entities similar to new chemical entities (NCEs) according to Article 7 of the PAA. Furthermore, there is no definitions of biologics and

biosimilars in the PAA. Therefore, the innovative companies consider that biologics should be subjected to the Patent Linkage System like NCEs. There were discussion on whether to use a mechanism similar to the Purple Book and patent dance in the US. At the end, the TFDA considers that the patent dance mechanism is too complicated and decided to include biologics in the Patent Linkage System. As a compromise, Article 16, Paragraph 3 of the Regulations for the Patent Linkage of Drugs was added to exempt the biosimilars already under clinical trials from the Patent Linkage System.

[ADDITIONAL INQUIRIES 1]

(I) Are new formulation drugs, new dosage drugs and new administration drugs subject to the Patent Linkage System?

(Lee and Li's comments)

The TFDA considers that the new drugs subjected the Patent Linkage Systems refer to those defined in Article 7 of the PAA, which only cover drugs relating to new molecular entities, new indications, new combinations and new routes of administration. Drugs relating to new dosage forms (new formulations), new administration doses and new unit strengths are so-called "Type 2 New Drugs" not falling within the definitions of new drugs in Article 7 of the PAA.

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(II) If (I) is **no**, could you let us know why these new drugs are not subject to the Patent Linkage System based on the discussion prior to the enactment of the Patent Linkage System?

(Lee and Li's comments)

Please see the explanation above for (I) above. We disagree with the TFDA's interpretation of the new drugs covered by the Patent Linkage System. There is no definition of "Type 2 New Drugs" in the PAA, and according to Article 39, Paragraph 2 of the Regulations for Registration of Medicinal Products (https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030057), regulations for new drugs stipulated in Chapter 2 are also applicable to pharmaceutical preparations with new dosage forms, new administration doses and new unit strengths. Some of our pharma clients have filed administrative suits against the TFDA's decisions to reject the patent listings of such Type 2 new drugs. The cases are still pending before the Taipei High Administrative Court or the Supreme Administrative Court.

(III) If (I) is **yes**, could you let us know the legal basis of it?

[Background of the ADDITIONAL INQUIRIES]

There was difference of the understanding on the Patent Linkage System in our internal team ((a) v. (b)).

(a) The reason why new formulation drugs, new dosage drugs and new administration drugs are subject to the Patent Linkage System:

- In Taiwan IP seminar, he heard that (i) new ingredient new drugs, new formulation new drugs, new use new drugs and new administration new drugs are subject to the Patent Linkage System, but (ii) generic drugs, biosimilars, skinny labeled drugs are not subject to the Patent Linkage System.
- He assumes that Articles 7 and 48-3 of Pharmaceutical Affairs Act are the basis of it.

(b) The reason why new formulation drugs, new dosage drugs and new administration drugs are **not** subject to the Patent Linkage System:

- This is because new formulation drugs, new dosage drugs and new administration drugs are so-called "Type 2 New Drug".

(Lee and Li's notes)

During the discussion at the public hearings for the draft amendment to the PAA for Patent Linkage System, the participants all think that Type 2 New Drug is subject to the Patent Linkage System, like the 505(b)2 new drugs in the US system. However, after the initial three months from the enactment of the Patent Linkage System enactment for listing patent information for existing new drugs, the TFDA reviewed the patent listings and sent letters to the holders of such Type 2 new drug permits in April to July 2020 stating that it is not allowable to list patent information for Type 2 new drug permits. This was the first time that the innovative companies were aware that the TFDA takes such a different view of new drugs. Despite the new drug permit holders' arguments, the TFDA issued decisions deleting the related patent listings. We represent several "brave" innovative companies to file appeals and administrative suits against the TFDA' delisting decisions.

[ADDITIONAL INQUIRIES 2]

(I) We understand that you represent some companies to file appeals and administration suits against TFDA's delisting decision for Type 2 New Drug. If you have any publicly available updates on the matter during our agreement term (by October 31, 2022), please let me know.

(Lee and Li's notes)

For the "Type 2 new drug" cases we are handling, two of them received judgments rendered by the first-instance administrative court, and the judgments were published. We hereby share some information of them with you.

To challenge the determinations of revoking the patent information, which corresponds to the Type 2 new drugs (new dosage forms, new administration doses and new unit strengths), from the Patent Linkage System rendered by the Ministry of Health and Welfare ("MOHW"; the MOHW is the competent authority of pharmaceutical affairs at the central level, and the Food and Drug Administration is under it), the two cases were respectively initiated by MERCK SHARP & DOHME (I.A.) LLC. TAIWAN BRANCH (U.S.A.) and Allergan Pharmaceuticals Taiwan Co., Ltd. (collectively referred to as "plaintiffs") with the Taipei High Administrative Court ("Court").

It is regretful that the Court does not find in the plaintiffs' favor but dismissed the two complaints. According to the written judgments, the Court accepted the MOHW's arguments but disregarded the plaintiffs' claim that no legal bases can be found to support the MOHW's authority to revoke (delete) patent information from the System, and that the plaintiffs have reliance on the MOHW's practice and decisions that the market approvals at issue (i.e., Type 2 new drugs) were determined to be "new drugs."

The Court's reasoning is summarized as follows:

1. Said "new drugs" prescribed in Articles 48-3 and 48-21 of the Pharmaceutical Affairs Act (i.e., the legal bases supporting the listing of the patents by the holders of new drug market approval; hereinafter "PAA") shall be confined by Article 7 of the same Act; that is, only the drugs for new molecular entities, new therapeutic combinations or new methods of administration (i.e., Type 1 new drugs) are "new drugs." The market approvals involving the delisting by the MOHW cover the drugs for new unit strength and/or new dosage form, so they are not new drugs qualified to have patent information listed in the Patent Linkage System ("System") with the patent information.

2. The MOHW has the authority to establish the System as well as list and publicize the patent information submitted by the holders of new drug market approvals in the System. As such, the MOHW has the authority to render an administrative disposition regarding whether listing patent information is allowed or not. When the MOHW found the former administrative disposition illegal (i.e., the market approvals covering new unit strengths and/or new dosage forms were listed and publicized in the System), it of course has the authority to revoke it.

3. The plaintiffs argued that the MOHW determined that the market approvals at issue cover "new drugs" when granting the market approvals, and that the two plaintiffs' reliance on the new-drug decisions shall be protected. Nonetheless, the two plaintiffs are fully aware of the fact that the market approvals at issue (which cover the drugs having new unit strength and/or new dosage form) are not new drugs defined in Article 7 of the PAA. Accordingly, the MOHW's decision to delist the patent information of such market approvals in the System based on the fact that they are not a new drug defined by Article 7 of the PAA does not impair the Plaintiff's reliance.

The judgments for the two cases are not final, and the cases are pending before the appellate court (i.e., the Supreme Administrative Court).

End of Document

附属資料２：台湾法律事務所調査報告書（日本語訳）（質問事項：赤字、回答：青字）

パテントリンケージ制度の 4 つのステップ（①先発の特許登録、②後発医薬品申請＋先発医薬品会社への通知、③後発医薬品の自動承認停止、④後発医薬品会社へのインセンティブ）、および、制度導入の背景について、当方の理解の確認、及び質問へのご回答をお願いいたします。また、パテントリンケージ制度に関する有益な情報がありましたらご教示いただけましたら幸甚です。

【①先発の特許登録】

（当方の理解）

(1) 医薬品に係わる物質特許、組成物又は製剤特許、医薬用途特許について、新薬の医薬品許可証の所持者が許可証を取得した日の翌日から 45 日以内に特許情報を開示すべきとされている（改正薬事法第 48 条の 3）。

(2) 新たに特許を取得した場合、新薬の医薬品許可証が発行された後に、初めて登録された特許権について、査定公告日から 45 日以内に特許情報を開示すべきとされている（改正薬事法第 48 条の 5）。

(3) 特許情報には特許証書番号、特許権の存続期間、特許権者、及び実施権者がいれば当該実施権者の名前などの情報が含まれる。医薬用途特許の場合、承認された用途を保護している請求項番号も明記する必要がある。なお、新薬の医薬品許可証の所持者と特許権者が異なる場合、特許情報の開示には特許権者の同意が必要とされている（改正薬事法第 48 条の 3、第 48 条の 4）。

(4) 新薬の特許情報が登録された後、新薬会社はパテントリンケージ制度を利用できる。登録されれば、パテントリンケージ制度による効果、後発医薬品会社の宣言の通知や特許侵害訴訟による後発医薬品の許可証の承認留保の手続きがとられることになる.

(5) 登録された特許情報が法定要件を満たさない場合、または、過誤により登録された場合、何人も理由及び証拠を記載し TFDA に異議を行うことができる。TFDA は審査を行わず、異議に関する情報を新薬の医薬品許可証の所持者に通知する。新薬の医薬品許可証の所持者は、通知された日の翌日から 45 日以内に応答する義務がある。期限内に応答しない場合、台湾元 3 万元～50 万元の罰金が課される（改正薬事法第 48 条の 7、第 48 条の 8）。

(6) 新薬の医薬品許可証の所持者に対しては、特許情報の開示は義務付けられておらず、あくまでも自発行為であるため、特許情報の開示を行わない場合でも、権利侵害の疑いのある後発医薬品会社に対して依然として権利侵害を主張することは可能である。

（質問）

(Q1-1) 上記の理解で正しいか否か。

(A1-1) 上記の理解は正しい。なお、薬事法第 48 条の 3 第 1 項に規定されている薬事許可証の受領日とは、薬事許可証を中央主務衛生機関（食品医薬品局 (TFDA)）が物理的に回収した日を指し、医薬品許可の発行日ではない。

(Q1-2) 後発医薬品会社は「先発医薬品会社の安全性／有効性のデータ」を利用し、先発医薬品との生物学的同等性を示すことで後発医薬品の承認申請手続きを進める。その参照とする先発医薬品のデータはどのように公開されているのか？
例えば、米国では「21USC355(j)(7)(A)(i)(I)-(III)に基づき、FDA は、過去に 21USC355(c)により安全性と有効性について承認された医薬品のアルファベット順のリストを定期的に更新し、オレンジブックとして公表する。これには、承認日、医薬品の正式名称、商標名、及び in vitro もしくは in vivo 生物学的同等性試験、またはその双方が ANDA において必要であるかどうかに関する情報が含まれる。」とされている。
台湾での現状、及びその根拠を教えて欲しい。
(A1-2) 先発医薬品の安全性/有効性データは、一般または後発医薬品会社に開示されない。後発医薬品会社は、先発医薬品について言及し、バイオアベイラビリティ（BA）および/または生物学的同等性（BE）の研究報告書を提出するか、容認できる場合には BE 研究報告書を溶出プロファイル比較報告書に置き換えるだけで済む。

後発医薬品会社は先発医薬品を独自に入手し、比較実験を行って生物学的同等性を証明することができる。後発医薬品申請者が in vitro および/または in vivo の生物学的同等実験結果を提供する必要があるかどうかは、藥品生體可用率及生體相等性試験作業準則[1]（Regulations of Bioavailability and Bioequivalence Studies[2]）に従って決定される。

規則の第 6 条と第 7 条は、BA または BE 研究を実施する必要があるか否かを決定するための特定の基準を提供している。後発医薬品会社が ANDA で BA/BE レポートを提出し、それに基づいて後発医薬品が承認された場合、TFDA は後発医薬品が BA/BE 研究に基づいて承認されたことを医薬品許可の公開ウェブサイトに表示する。ただし、BA/BE データは公開されない。

【②後発医薬品申請＋先発医薬品会社への通知】

（当方の理解）

(1) 後発医薬品許可証の申請者は、次の各号の何れかについて宣言しなければならない（改正薬事法第 48 条の 9）。

(i) 当該新薬について、いかなる特許情報も登録されていない。
(ii) 当該新薬に係わる特許権はすでに消滅した。
(iii) 当該新薬に係わる特許権が消滅した後、初めて TFDA が医薬品許可証を発行する。
(iv) 当該新薬に係わる特許権は取消すべきものである、又は許可証を申請する後発医薬品が当該新薬に係わる特許権を侵害していない。

[1] 藥品生體可用率及生體相等性試験作業準則（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030065
[2] Regulations of Bioavailability and Bioequivalence Studies（Laws & Regulations Database of The Republic of China (Taiwan)ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030065

(2) 上記宣言(i)と宣言(ii)の場合に権利侵害の恐れがないため、TFDA により薬事法に基づく審査が終了した後に許可証が発行される。上記宣言(iii)の場合、全ての特許権が消滅した後に医薬品許可証が発行される。上記宣言(iv)の場合、後発医薬品許可証の申請者が証拠と理由を付けて書面にて新薬の許可証所持者及び TFDA に告知しなければならない。新薬の許可証所持者と、掲載された特許権者、専用実施権者が異なる場合、後発医薬品許可証の申請者が特許権者、及び専用実施権者に上記宣言(iv)を併せて告知しなければならない。もし告知が行わなければ、TFDA が後発医薬品の申請を却下する。

(3) 上記宣言(iv)の場合、申請情報についてウェブサイト[3]で公開される。

衛生福利部食品藥物管理署 Food and Drug Administration

首頁　最新消息　專利資訊查詢　資料齊備日及銷售專屬期　FAQ　|　登入

年度：所有年度　排序：依資料齊備日排序

對照新藥藥品之藥品許可證字號	有效成分及含量	劑型	P4專利聲明藥商	資料齊備日	銷售專屬期間狀態	銷售專屬期間	備註
衛署藥輸字第024727號	SORAFENIB TOSYLATE, MICRONIZED 274.0000MG	膜衣錠	美時化學製藥股份有限公司	111/04/12	尚在審查中		
衛署藥輸字第024929號	AMLODIPINE BESYLATE 6.9440MG；OLMESARTAN MEDOXOMIL 20.0000MG	膜衣錠	台灣諾華股份有限公司	111/03/22	尚在審查中		
衛部藥輸字第027426號	Midostaurin 25.0000MG	軟膠囊劑	美時化學製藥股份有限公司	110/11/25	尚在審查中		
衛署藥輸字第024603號	DEFERASIROX 125.0000MG	可溶錠	瑩碩生技醫藥股份有限公司	110/11/23	未符合藥事法第48條之16或17		
衛署菌疫輸字第000928號	Rituximab 10.0000MG	注射劑	台灣賽特瑞恩有限公司	110/11/08	尚在審查中		

（質問）

(Q2-1) 上記の理解で正しいか否か。

(A2-1) 上記の理解は基本的に正しい。以下、後発医薬品申請の手続きを明確化する。

薬事法第 48 条の 9 第 1 項第 4 号の陳述書（記載特許の無効又は非侵害：以下「P4 陳述書」という。）が提出された ANDA について、TFDA はまず、ANDA に必要なすべての書類が提出されているかどうかを確認するために形式的な審査を行う。その場合、TFDA は後発医薬品の申請者に「資料齊備通知」を発行し、オンラインで情報を公開する。

薬事法第 48 条の 12 第 1 項によると、後発医薬品の申請者は、TFDA が正式に準備された申請通知を受領した翌日から 20 日以内に、証拠と理由を記載した通知を先発医薬品会社と TFDA に送付し

[3] 資料齊備日及銷售專屬期（衛生福利部食品藥物管理署ウェブサイト）
https://plls.fda.gov.tw/DataStatement

なければならない。また、西薬専利連結施行辦法[4]（Regulations for the Patent Linkage of Drugs[5]）の第11条によると、後発医薬品申請者は、後発医薬品の通知を、郵便局経由の往復受取書付二重署名郵便を使用して送信する必要がある。また、後発医薬品の申請者は、領収書または配達が成功したことを証明するその他の書類を、通知のサービスの翌日から20日以内にTFDAに提出する必要がある。後発医薬品通知の義務は、TFDAがそのような送達の証拠を受け取った場合にのみ履行されたとみなされる。

(Q2-2) 宣言(iv)の場合は事実としてウェブサイトで公開されているが、公開されることの根拠条文はどこにあるのか？また、ウェブサイト上のカラムには「P4専利聲明藥商」とあるため、「公開は宣言(iv)の後発申請に限定されている（すなわち、宣言(i)～(iii)に基づく後発医薬品申請は公開されない）」との理解でよいか？

(A2-2) 実際には、宣言(iv)に関する証拠は公開されない。「P4専利聲明藥商」は、P4陳述書を作成した後発医薬品申請者の名前を指す。P4陳述書で提出された後発医薬品申請のみが公開される。宣言(i)～(iii)のいずれかの陳述書を提出した後発医薬品申請は公開されず、パテントリンケージウェブサイトにも表示されない。

(Q2-3) パテントリンケージ制度が導入される以前は、後発医薬品許可証の申請の事実ですら（申請者が自ら開示しない限り）営業秘密に該当するものであったところ、パテントリンケージ制度の導入後は宣言(iv)の場合には上記ウェブサイトへの公開（および新薬の許可証保持者への告知）によって営業秘密性が損なわれることについて、パテントリンケージ制度の導入に際して何らかの議論はあったか？

(A2-3) 上記のとおり、ステートメントに関する後発医薬品申請またはジェネリック通知は公開されない。従って、この点に関連する議論はない。

(Q2-4) 特許権者又は専用実施権者が45日以内に訴訟提起するか否かを判断するためには、後発医薬品の詳細情報を確認する必要がある。後発医薬品の詳細情報を特許権者又は専用実施権者に開示するためには秘密保持の取り扱いが必要であると考えられるが、何（法律、規則などの下位の法令、ガイドライン、運用等）で規定されているのか？根拠条文はどこにあるのか？
例えば、米国、カナダ、中国には以下のように規定されているが、台湾法の同様の規定はどこにあるのか？

米国：
低分子医薬品では、連邦規則（21CFR314.95(c)(8)）で「ANDA申請者は特許権者等に対して、35USC271(e)(2)に基づく訴訟を提起するか否かを判断するために、ANDA申請書への

[4] 西薬専利連結施行辦法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030103
[5] Regulations for the Patent Linkage of Drugs（Laws & Regulations Database of The Republic of China (Taiwan) ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030103

機密アクセス（アクセスされた情報の使用及び処分についての制限付）の機会を与えなければならない」と規定されている。

生物学的製剤では、合衆国法典（42USC262(l)(2)）で、「バイオ後続品申請者は、FDA が略式承認申請を受け付けてから 20 日以内に、先行品のスポンサーに対して、バイオ後続品の申請及び関連する製造情報への、守秘義務を課した上でのアクセスを認めなければならない。」と規定されている。

カナダ：

規則（NOC5(3)(c)(iii)）で、「後発医薬品申請者は、先発医薬品承認取得者に、先発医薬品特許が侵害されているか否かを判断の根拠となる後発医薬品申請者所有の提出物の電子コピーを送付しなければならない。」と規定され、さらに、NOC5(3.5)で、「NOC5(3)(c)(iii)で言及される送付物について、後発医薬品申請者は、機密性を維持するための合理的な取り決め（rule）を課すことができる。」と規定されている。

中国：

規則（医薬品特許紛争の早期解決メカニズムの行政裁定規定第 18 条）において、「国家知識産権局は、上場医薬品技術プログラムの申請が関連する特許権の保護範囲に該当するか否かを判断した場合、政府情報公開規則及び関連規定に従って公表しなければならないが、企業秘密に関する情報は削除する」、第 20 条において、「当事者は行政裁定手続において企業秘密を秘密にしておく義務があり、無断で開示等した場合には適切な法的責任を負う」、第 21 条において、「医薬品特許紛争に関する行政判断の処理者及びその職員による企業秘密の漏洩は、犯罪に該当しない場合には、法律に従って行政処分を受けるものとする」と規定されている。

規則（登録申請医薬品に関連する特許紛争民事事件の審理における法律適用の若干問題に関する規定第 8 条）において、「当事者は、訴訟で取得した企業秘密その他の機密保持を必要とするその他の商業情報を秘密にしておく義務を負い、その訴訟活動以外で、無断で開示または使用または許可した場合、法律に従って民事責任を負うものとする。民事訴訟法第 111 条に規定する状況を構成する場合、人民裁判所は、法律に従って処理しなければならない」と規定されている。

(A2-4) 薬事法第 48 条の 12 は、後発医薬品会社からの通知には、リストされた特許の無効化または非侵害の主張に関する理由および証拠を提供することを規定しているが、そのような理由、証拠に関する形式、内容、または能力に関する明確な要件はない。理律法律事務所の弁護士 Joyce Liou は、パテントリンケージ制度の制定以来、6 件のパテントリンケージ訴訟に個人的に参加した。Joyce Liou の経験によると、後発医薬品会社はいずれも後発医薬品通知で企業秘密に関する情報や証拠を提供していない。場合によっては、後発医薬品会社が提供する情報や証拠だけでは、後発医薬品がリストされた特許を侵害するかどうかを評価するには不十分ですらある。そのような場合、先発医薬品会社（つまり、パテントリンケージ訴訟の原告）は、特許侵害を証明するために、法廷に証拠保全の申し立てを行うか、訴訟中の証拠調査に頼って、後発医薬品会社および/または TFDA から証拠を入手する必要がある。後発医薬品会社または TFDA から取得した証拠に営業秘密が含まれて

いる場合、原告は、智慧財産案件審理法[6]（Intellectual Property Case Adjudication Act[7]）第 11 条に従って裁判所が「秘密保持命令」を下さない限り、証拠を検討することはできない。公判が企業秘密に関係する証拠の議論に関するものである場合、審問は、当事者の動議と裁判所の承認に基づいて非公開で開催される。

【③後発医薬品の自動承認停止】

（当方の理解）

(1) 特許権者又は専用実施権者は、後発医薬品許可証の申請者により、上記宣言(iv)の告知を受けた後に、当該告知書を受け取った日の翌日から 45 日以内に特許権侵害訴訟を提起し、且つ起訴日の翌日から 20 日以内に裁判所の受領印が付された起訴状の写しを TFDA に送達する必要がある（改正薬事法第 48 条の 13、施行弁法第 12 条）。

(2) TFDA は、提訴する旨の通知を受け取った日の翌日から最長で 12 月間、後発医薬品の許可証の発行を一時的に停止しなければならない。ただし、特許権者又は専用実施権者が後発医薬品申請者からの告知書を受け取った日の翌日から 45 日以内に特許権侵害訴訟を提起しなかった場合、後発医薬品許可証の申請者が特許権を侵害していない旨の判決があった場合、台湾経済部知的財産局（TIPO）により特許権が無効にされた場合、当事者間での和解が成立した場合、あるいは、特許権が消滅した場合において、TFDA は後発医薬品の許可証を発行することができる。一方、特許権者又は専用実施権者が不正に特許権を行使することによって、医薬品許可証発行を一時的に停止させ、後発医薬品会社に損害を与えたと認められた場合には、特許権者又は専用実施権者はその損害賠償責任を負うことになる（改正薬事法第 48 条の 13）。

(3) 承認留保期間においても TFDA は後発医薬品の審査を中止することはない。審査が完了した後、TFDA は後発医薬品会社にその旨を通知する。後発医薬品会社は衛生福利部中央健康保険署に保険収載と価格算定を申請できる（改正薬事法第 48 条の 15）。

（質問）

(Q3-1) 上記の理解で正しいか否か。

(Q3-1) 上記の理解は正しい。パテントリンケージ制度が制定される前は、医薬品関連の民事訴訟は通常、第一審で 15 か月から 2 年で終結していた。智慧財産及商業法院（IPC Court）は、12 か月足らずでパテントリンケージ訴訟の判決を下した。ただし、被告（後発医薬品会社）が第二審裁判所に控訴した場合、そのような判決は最終的な拘束力のある判決ではない。従って、過去のケースでは、TFDA は 12 か月の承認遅延期間満了後に後発医薬品の許可を発行している。第一審の判決が原告に有利な場合、後発医薬品会社は後発医薬品許可を取得しないことを選択できる。そのような場合、後発医薬品の販売独占権は取得できない。これまで、P4 陳述書で後発医薬品申請を提出し、後発医薬品の販売独占権を確保することに成功した後発医薬品会社は 1 社だけである。

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[6] 智慧財産案件審理法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=A0030215

[7] Intellectual Property Case Adjudication Act（Laws & Regulations Database of The Republic of China (Taiwan) ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=A0030215

【④後発医薬品会社へのインセンティブ】

（当方の理解）

(1) 上記宣言(iv)を提出した後発医薬品申請者のうち、その申請資料を最初に完備した後発医薬品会社は、12 か月の独占販売期間を取得できる。TFDA はその 12 か月内に他の後発医薬品許可証の申請者に医薬品許可証を発行してはならない（改正薬事法第 48 条の 16）。なお、同じ日に二社以上の後発医薬品会社がともに最初に申請資料を完備した場合、共に独占期間を取得することができる。

(2) 後発医薬品会社は許可証を取得した日の翌日から 6 か月以内に販売を行い、且つ最初の販売日の翌日から 20 日以内に実販売日の証拠を添付し TFDA に通知する必要がある。TFDA は独占販売期間及びその起算日、終了日を決定する。仮に、最初の後発医薬品会社が期間内に後発医薬品の許可証を受領しない場合、または許可証受領後 6 か月以内に販売しても期間内に TFDA に通知しない場合、又は関連特許権が消滅した場合、該独占販売期間を取得できないとされている（改正薬事法第 48 条の 17、第 48 条の 18）。

(3) TFDA は上記独占販売期間、その起算日、終了日を決定する際に、その決定内容を医薬品パテントリンケージ情報登載プラットフォームに搭載する。

（質問）

(Q4-1) 上記の理解で正しいか否か。

(A4-1) 上記の理解は正しい。ただし、前述のように、これまで、P4 陳述書で後発医薬品申請を提出し、後発医薬品の販売独占権を確保することに成功した後発医薬品会社は 1 社だけである。

(Q4-2) 上記の理解(3)の登載される「医薬品パテントリンケージ情報登載プラットフォーム」とは、**【②後発医薬品申請＋先発医薬品会社への通知】**に記載のウェブサイト[8]であるとの理解でよいか？

[8] 資料齊備日及銷售專屬期（衛生福利部食品藥物管理署ウェブサイト）
https://plls.fda.gov.tw/DataStatement

對照新藥藥品之藥品許可證字號	有效成分及含量	劑型	P4專利聲明藥商	資料齊備日	銷售專屬期間 狀態	銷售專屬期間	備註
衛署藥輸字第024727號	SORAFENIB TOSYLATE, MICRONIZED 274.0000MG	膜衣錠	美時化學製藥股份有限公司	111/04/12	尚在審查中		
衛署藥輸字第024929號	AMLODIPINE BESYLATE 6.9440MG ; OLMESARTAN MEDOXOMIL 20.0000MG	膜衣錠	台灣諾華股份有限公司	111/03/22	尚在審查中		
衛部藥輸字第027426號	Midostaurin 25.0000MG	軟膠囊劑	美時化學製藥股份有限公司	110/11/25	尚在審查中		
衛署藥輸字第024603號	DEFERASIROX 125.0000MG	可溶錠	瑩碩生技醫藥股份有限公司	110/11/23	未符合藥事法第48條之16或17		
衛署菌疫輸字第000928號	Rituximab 10.0000MG	注射劑	台灣賽特瑞恩有限公司	110/11/08	尚在審查中		

(A4-2) 後発医薬品販売独占権が、上記ウェブサイトで公開されることは正しい。後発医薬品販売独占期間は、ヘッダー「銷售專屬期間」のカラムに示される。

【制度導入の背景】

（当方の理解）

TPP への加入を見据え、2017 年に薬事法が改正され、新薬に関する特許情報の開示と登録、後発医薬品の申請者による宣言と告知、特許権に対するチャレンジ、後発医薬品の許可証発行の一時停止、最初に医薬品許可証を取得した後発医薬品会社の市場独占権などについて規定され、2019 年 8 月 20 日に施行された（第 48 条の 3～第 48 条の 22）。

（質問）

(Q5-1) 制度導入の背景は上記の理解で正しいのか？

(A5-1) 上記の理解は正しい。しかし、米国の TPP から離脱後、パテントリンケージ制度の実施の原動力は、米国との貿易投資枠組協定(TIFA)に期待されている。

(Q5-2) 制度導入（2019 年 8 月）後の法改正として、例えば、専利法第 60 条の 1 の導入（2022 年 2 月 24 日に行政院により改正案を可決、2022 年 7 月 1 日施行）があると理解しているが、その他にはどのようなものがあるのか？

(A5-2) パテントリンケージ制度の改正について、現在進行中の計画はない。

一方、特許法第 60 条の 1 が成立する前に、パテントリンケージ訴訟についていくつかの判決が言い渡されている。裁判所智慧財産及商業法院（IPC Court）は、特許法第 96 条第 1 項はこのようなパテントリンケージ訴訟の法的根拠を提供するのに十分であると考えている。

(Q5-3) パテントリンケージ制度導入前に、(i) 特許登録の対象特許、(ii) 後発医薬品の自動承認停止期間、(iii) 第一後発医薬品承認取得者へのインセンティブ、(iv) 生物学的製剤をパテントリンケー

ジ制度の対象とすること等について様々な議論があったのではないかと考えるが、議論の概略について教えて欲しい。

(A5-3) (i) 特許登録の対象特許：

パテントリンケージ制度は、基本的に米国のオレンジブックの仕組みを採用している。記載された特許のクレーム番号を特定すべきか否か、及び結晶多形に関する特許を記載できるか否かについては論争がある。最終的に TFDA は、医療用途の特許についてのみクレーム番号を特定する必要があり、また結晶多形特許はリストに掲載できると判断した。ただし、特許の結晶多形が新薬の有効成分の結晶多形と異なる場合には、当該多形を含む製剤が同等の効果を発揮することを示す試験データを登録の際に提供しなければならない（西薬専利連結施行辦法第 3 条第 2 項参照）。なお、製造工程に関する特許はリストに掲載できないが、プロダクト・バイ・プロセス・クレームは製品そのもの（物質や組成物）をクレームしているものとみなされ、リスト可能である。

(ii) 後発医薬品の自動承認停止期間：

当初提案された承認停止期間は、第一審裁判所が特許訴訟事件を終結させるのに必要な平均期間に基づいた 15 か月であったが、議会によって 12 か月に短縮された。

(iii) 第一後発医薬品承認取得者へのインセンティブ：

当初提案された後発品販売の独占期間は 6 か月であったが、薬事法改正を進めるために、後発医薬品会社からの抵抗を減らすため、後発医薬品販売独占期間は 12 か月に延長された。

(iv) 生物学的製剤をパテントリンケージ制度の対象とすること：

現在の実務では、生物学的製剤は、薬事法第 7 条に従って、新しい化学物質(NCE)と同様に新しい分子物質として扱われる。さらに、薬事法には生物学的製剤とバイオシミラーの定義はない。従って、先発医薬品会社は、生物製剤は NCE のようにパテントリンケージ制度の対象とすべきであると考えている。米国でのパープルブックやパテントダンスと同様のメカニズムを使用するか否かについての議論があった。最終的に、TFDA はパテント ダンス メカニズムが複雑すぎると判断し、パテントリンケージ制度に生物学的製剤を含めることを決定した。妥協案として、西薬専利連結施行辦法第 16 条第 3 項が追加され、すでに臨床試験中のバイオシミラーはパテントリンケージ制度から除外された。

【追加質問１】

(Q6-1) 新剤形、新用量、新規格の医薬品はパテントリンケージの対象となるか否か？

(A6-1) TFDA は、パテントリンケージ制度の対象となる新薬は、薬事法第 7 条で定義されたものを指していると考えている。これは、新しい分子の実体、新しい適応症、新しい組み合わせ、および新しい投与経路に関連する薬のみを対象としている。新剤形（新製剤）、新投与量、新単位強度に関する医薬品は、薬事法第 7 条の新医薬品の定義に該当しない、いわゆる「2 型新薬」である。

(Q6-2) (Q6-1)でパテントリンケージの対象とならないのであれば、なぜ対象とならなかったのかの議論について教えて欲しい。

(Q6-3) (Q6-1)でパテントリンケージの対象となるのであれば、その根拠条文はどこか？

(A6-2, -3) 上記(A6-1)の説明を参照のこと。当事務所は、パテントリンケージ制度の対象となる新薬に関する TFDA の解釈に同意しない。薬事法には「2 型新薬」の定義がなく、薬品査驗登記審査準則[9]（Regulations for Registration of Medicinal Products[10]）第 39 条第 2 項によると、第 2 章に定める新薬規制は、新剤型、新投与量、新単位強度の医薬品にも適用される。当事務所の製薬会社クライアントの一部は、2 型新薬の特許リストを拒否する TFDA の決定に対して行政訴訟を提起した。当該訴訟は、台北高等行政裁判所または最高行政裁判所で係争中である。

(その他コメント)
パテントリンケージ制度の薬事法改正案の公聴会での議論では、米国の 505(b)2 新薬と同様に、2 型新薬もパテントリンケージ制度の対象になるとの認識が参加者全員にあった。しかし、既存の新薬の特許情報を掲載するためのパテントリンケージ制度制定法が制定されてから最初の 3 か月が経過した後、TFDA は、2020 年 4 月から 7 月にかけて特許リストを見直し、2 型新薬許可の保有者に「2 型新薬許可証の特許情報を記載することは認められない」との書簡を送付した。先発医薬品会社が、TFDA が新薬に対してこれほど異なる見方をしていることに気付いたのはこれが初めてであった。新薬許可保有者の主張にもかかわらず、TFDA は関連する特許リストを削除する決定を下した。当事務所は、TFDA の特許リスト削除決定に対して控訴や行政訴訟を起こすいくつかの「勇敢な」先発医薬品会社の代理をしている。

（追加質問の背景）
弊所内ディスカッションで、理解の相違があった。
(a) 新剤形、新用量、新規格の医薬品はパテントリンケージの対象となると考える理由：
・台湾特許セミナーで、「新成分新薬、新製剤新薬、新用途新薬、新投与経路はパテントリンケージの対象であり、後発医薬品、バイオシミラー、効能の除外（skinny label）はパテントリンケージの対象外となる」と聞いた。
・根拠条文は、薬事法第 7 条、及び第 48 条の 3 と推測している。
(b) 新剤形、新用量、新規格の医薬品はパテントリンケージの対象とならないと考える理由：
・新剤形、新用量、新規格の医薬品はいわゆる 2 型新薬（Type II New Drug）であるため。

【追加質問２】
(Q7-1) 貴所が TFDA の特許リスト削除決定に対する控訴や行政訴訟の代理をしているとのことだが、当該控訴や行政訴訟の進展の公開情報があれば教えて欲しい。

[9] 薬品查驗登記審查準則（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030057
[10] Regulations for Registration of Medicinal Products（Laws & Regulations Database of The Republic of China (Taiwan)ウェブサイト）
https://law.moj.gov.tw/ENG/LawClass/LawAll.aspx?pcode=L0030057

(A7-1) 当事務所が取り扱う「2 型新薬」事件のうち 2 件について一審行政裁判所の判決が下され、公表された[11][12]。ここにそれらの情報を共有する。

2 型新薬（新剤形、新投与量、新単位力価）に相当する特許情報を厚生省（MOHW：中央レベルの薬事の権限のある当局であり、食品医薬品局はその下にある）がパテントリンケージ制度から抹消する決定に異議を唱えることを目的として、MERCK SHARP & DOHME (I.A.) LLC TAIWAN BRANCH (U.S.A.)、及び Allergan Pharmaceuticals Taiwan Co., Ltd.（以下、「原告」）によって台北高等行政裁判所（以下、「裁判所」)で 2 つの裁判が開始された。

残念なことに、裁判所は原告に有利な判決を下さず、2 件の訴状を却下した。判決書によれば、裁判所は、衛生福利部の主張を認めた。一方で、原告の主張（本システムから特許情報を取り消す（削除する）という衛生福利部の権限を支持する法的根拠は見いだせず、原告は、問題の市場承認（すなわち、2 型新薬）が「新薬」であると判断されたという衛生福利部の慣行と決定。主張に依存している）を無視した。

裁判所の判断は以下のように要約される。
1　薬事法（新薬承認取得者が特許を収載することを裏付ける法的根拠。以下「薬事法」という。）第 48 条の 3 及び第 48 条の 21 に規定する「新薬」とは、同法第 7 条の規定によるものである。すなわち、新しい分子の実体、新しい治療の組み合わせ、または新しい投与方法（すなわち、1 型新薬）のための薬のみが「新薬」である。衛生福利部によりリストから削除された医薬に関する販売承認は、新単位力価および/または新剤形の医薬品を対象としているため、特許情報と一緒にパテントリンケージシステム（以下、「システム」）に特許情報を掲載する資格のある新薬ではない。

2. 衛生福利部は、本システムを構築し、新薬上市承認取得者から提出された特許情報を本システムに掲載し、公表する権限を有する。このように、衛生福利部は、特許情報の掲載の可否に関する行政処分を行う権限を有している。衛生福利部は、以前の行政処分が違法であると判断した場合（つまり、新しい単位強度および/または新しい剤形を対象とする市場承認がシステムにリストされ、公表された場合）、もちろんそれを取り消す権限を有する。

3. 原告は、衛生福利部が、問題となっている市場承認は、市場承認を付与する際に「新薬」を対象としていると判断し、原告 2 社の新薬決定への依存は保護されるべきであると主張した。それにもかかわらず、原告 2 社は、問題となっている市場承認（新しい単位強度および/または新しい剤形を有する医薬品を対象とする）が、薬事法第 7 条で定義された新薬ではないという事実を十分に認識

[11] 臺北高等行政法院 110 年度訴字第 824 號判決（2022 年 4 月 7 日辯論終結）
https://law.judicial.gov.tw/FILES/TPBA/110%2c%E8%A8%B4%2c824%2c20220512%2c1.pdf
[12] 臺北高等行政法院 110 年度訴字第 1048 號判決（2022 年 4 月 7 日辯論終結）
https://law.judicial.gov.tw/FILES/TPBA/110%2c%E8%A8%B4%2c1048%2c20220512%2c1.pdf

している。従って、衛生福利部が薬事法第 7 条に規定する新薬ではないことを理由に、当該販売承認の特許情報をシステムから除外する決定を下したことは、原告の信頼を損なうものではない。

上記 2 件の判決は最終的なものではなく、上訴裁判所（最高行政裁判所）で係争中である。

以上

附属資料３：米国関連条文（低分子医薬品）

① 35USC271 Infringement of patent[13]

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States, or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination, or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

(d) No patent owner otherwise entitled to relief for infringement or contributory infringement of a patent shall be denied relief or deemed guilty of misuse or illegal extension of the patent right by reason of his having done one or more of the following: (1) derived revenue from acts which if performed by another without his consent would constitute contributory infringement of the patent; (2) licensed or authorized another to perform acts which if performed without his consent would constitute contributory infringement of the patent; (3) sought to enforce his patent rights against infringement or contributory infringement; (4) refused to license or use any rights to the patent; or (5) conditioned the license of any rights to the patentor the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

(e)(1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

(2) It shall be an act of infringement to submit —

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent,

(B) an application under section 512 of such Actor under the Act of March 4, 1913 (21 U.S.C. 151 - 158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patentor the use of which is claimed in a patent, or

[13] 35USC271（Discover U.S. Government Information ウェブサイト）
https://www.govinfo.gov/content/pkg/USCODE-2011-title35/pdf/USCODE-2011-title35-partIII-chap28-sec271.pdf

(C)
(i) with respect to a patent that is identified in the list of patents described in section 351(l)(3) of the Public Health Service Act (including as provided under section351(l)(7) of such Act), an application seeking approval of a biological product, or
(ii) if the applicant for the application fails to provide the application and information required under section351(l)(2)(A) of such Act, an application seeking approval of a biological product for a patent that could be identified pursuant to section 351(l)(3)(A)(i) of such Act, if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug, veterinary biological product, or biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.
(3) In any action for patent infringement brought under this section, no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under paragraph (1).
(4) For an act of infringement described in paragraph(2)—
(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,
(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product,
(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product, and
(D) the court shall order a permanent injunction prohibiting any infringement of the patent by the biological product involved in the infringement until a date which is not earlier than the date of the expiration of the patent that has been infringed under paragraph (2)(C), provided the patent is the subject of a final court decision, as defined in section 351(k)(6)of the Public Health Service Act, in an action for infringement of the patent under section 351(l)(6) of such Act, and the biological product has not yet been approved because of section351(k)(7) of such Act.

The remedies prescribed by subparagraphs (A), (B), (C), and(D) are the only remedies which may be granted by a court foran act of infringement described in paragraph (2), except that acourt may award attorney fees under section 285.
(5) Where a person has filed an application described in paragraph (2) that includes a certification under subsection(b)(2)(A)(iv) or (j) (2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), and neither the owner of the patent that is the subject of the certification nor the holder of the approved application under subsection (b) of such section for the drug that is claimed by the patent or a use of which is claimed by the patent brought an action for infringement of such patent before the expiration of 45 days after the date on which the notice given under subsection (b)(3)or (j) (2)(B) of such section was received,

the courts of the United States shall, to the extent consistent with the Constitution, have subject matter jurisdiction in any action brought by such person under section 2201 of title 28 for a declaratory judgment that such patent is invalid or not infringed.

(6)(A) Subparagraph (B) applies, in lieu of paragraph (4), in the case of a patent-

(i) that is identified, as applicable, in the list of patents described in section 351(l)(4) of the Public Health Service Act or the lists of patents described in section351(l)(5)(B) of such Act with respect to a biological product; and

(ii) for which an action for infringement of the pate¥nt with respect to the biological product—

(I) was brought after the expiration of the30-day period described in subparagraph (A) or (B), as applicable, of section 351(l)(6) of such Act; or

(II) was brought before the expiration of the 30-day period described in subclause (I), but which was dismissed without prejudice or was not prosecuted to judgment in good faith.

(B) In an action for infringement of a patent described in subparagraph (A), the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty.

(C) The owner of a patent that should have been included in the list described in section 351(l)(3)(A) of the Public Health Service Act, including as provided under section 351(l)(7) of such Act for a biological product, but was not timely included in such list, may not bring an action under this section for infringement of the patent with respect to the biological product.

(f)(1) Whoever without authority supplies or causes to be supplied in or from the United States all or a substantial portion of the components of a patented invention, where such components are uncombined in whole or in part, in such manner as to actively induce the combination of such components outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(2) Whoever without authority supplies or causes to be supplied in or from the United States any component of a patented invention that is especially made or especially adapted for use in the invention and not a staple article or commodity of commerce suitable for substantial noninfringing use, where such component is uncombined in whole or in part, knowing that such component is so made or adapted and intending that such component will be combined outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent. In an action for infringement of a process patent, no remedy may be granted for infringement on account of the noncommercial use or retail sale of a product unless there is no adequate remedy under this title for infringement on account of the importation or other use, offer to sell, or sale of that product. A product which is made by a patented process will, for purposes of this title, not be considered to be so made after —

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and nonessential component of another product.
(h) As used in this section, the term “whoever” includes any State, any instrumentality of a State, any officer or employee of a State or instrumentality of a State acting in his official capacity. Any State, and any such instrumentality, officer, or
employee, shall be subject to the provisions of this title in the same manner and to the same extent as any nongovernmental entity.
(i) As used in this section, an “offer for sale” or an “offer to sell” by a person other than the patentee or any assignee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.

② 21USC355 New drug[14]

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

(b) Filing application; contents

(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, and (G) any assessments required under section 355c of this title. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences. The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).

[14] 21USC355（Discover U.S. Government Information ウェブサイト）
https://www.govinfo.gov/content/pkg/USCODE-2010-title21/pdf/USCODE-2010-title21-chap9-subchapV-partA-sec355.pdf

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3) Notice of opinion that patent is invalid or will not be infringed.—

(A) Agreement to give notice.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give notice as required by this paragraph.

(B) Timing of notice.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph—

(i) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(ii) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(C) Recipients of notice.—An applicant required under this paragraph to give notice shall give notice to—

(i) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(ii) the holder of the approved application under this subsection for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(D) Contents of notice.—A notice required under this paragraph shall—

(i) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain

approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(ii) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(4)(A) An applicant may not amend or supplement an application referred to in paragraph (2) to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary.

(B) With respect to the drug for which such an application is submitted, nothing in this subsection or subsection (c)(3) of this section prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(5)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under section 262 of title 42, which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 262 of title 42 if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of clinical trials intended to form the primary basis of an effectiveness claim or, with respect to an applicant for approval of a biological product under section 262(k) of title 42, any necessary clinical study or studies. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

(C) Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or section 262 of title 42 (including all scientific and medical matters, chemistry, manufacturing, and controls).

(6) An application submitted under this subsection shall be accompanied by the certification required under section 282(j)(5)(B) of title 42. Such certification shall not be considered an element of such application.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b) of this section, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

(B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined by applying the following to each certification made under subsection (b)(2)(A) of this section:

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) of this section or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A) of this section, the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) of this section is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) of this section before the date on which the application (excluding an amendment or supplement to the application) was submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) of this section or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(i) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(I) the date on which the court enters judgment reflecting the decision; or

(II) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(ii) if before the expiration of such period the district court decides that the patent has been infringed—

(I) if the judgment of the district court is appealed, the approval shall be made effective on—

(aa) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(bb) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(II) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35;

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in clause (i); or

(iv) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues

of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in clause (ii).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(D) Civil action to obtain patent certainty.—

(i) Declaratory judgment absent infringement action.—

(I) In general.—No action may be brought under section 2201 of title 28 by an applicant referred to in subsection (b)(2) of this section for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (C) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) Offer of confidential access to application.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) of this section for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) of this section and for no other purpose, and may not

disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) Counterclaim to infringement action.—

(I) In general.—If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) of this section or this subsection on the ground that the patent does not claim either—

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(E)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the

one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailabilty studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(d) Grounds for refusing application; approval of application; “substantial evidence” defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b) of this section; or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term “substantial evidence” means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or

(3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) of this section was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided*, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based. The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 355–1(g)(2)(D) of this title.

(f) Revocation of order refusing, withdrawing or suspending approval of application

Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Service of orders

Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

(h) Appeal from order

An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

(i) Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

(B) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of

investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings;

(C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b) of this section; and

(D) the submission to the Secretary by the manufacturer or the sponsor of the investigation of a new drug of a statement of intent regarding whether the manufacturer or sponsor has plans for assessing pediatric safety and efficacy.

(2) Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including—

(A) information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a "clinical hold") if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that—

(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before November 21, 1997).

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational

purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible or it is contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. The Secretary shall update such regulations to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 282 of title 42.

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c) of this section—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B) Notice of opinion that patent is invalid or will not be infringed.—

(i) Agreement to give notice.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph.

(ii) Timing of notice.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph—

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(iii) Recipients of notice.—An applicant required under this subparagraph to give notice shall give notice to—

(I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(II) the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(iv) Contents of notice.—A notice required under this subparagraph shall—

(I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(D)(i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.

(ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(iii) Within 60 days after December 8, 2003, the Secretary shall issue guidance defining the term “listed drug” for purposes of this subparagraph.

(3)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such application. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of such studies. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

(C) Any agreement regarding the parameters of design and size of bioavailability and bioequivalence studies of a drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection (including scientific matters, chemistry, manufacturing, and controls).

(4) Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds—

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show—

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title,

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of this section of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section, the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) of this section for grounds described in the first sentence of subsection (e) of this section, the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (6), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) of this section before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(II) if before the expiration of such period the district court decides that the patent has been infringed—

(aa) if the judgment of the district court is appealed, the approval shall be made effective on—

(AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35;

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or

(IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(iv) 180-day exclusivity period.—

(I) Effectiveness of application.—Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) Definitions.—In this paragraph:

(aa) 180-day exclusivity period.—The term "180-day exclusivity period" means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) First applicant.—As used in this subsection, the term "first applicant" means an applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.

(cc) Substantially complete application.—As used in this subsection, the term "substantially complete application" means an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A).

(dd) Tentative approval.—

(AA) In general.—The term "tentative approval" means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the requirements of this subparagraph, there is a period of exclusivity for the listed drug under subparagraph (F) or section 355a of this title, or there is a 7-year period of exclusivity for the listed drug under section 360cc of this title.

(BB) Limitation.—A drug that is granted tentative approval by the Secretary is not an approved drug and shall not have an effective approval until the Secretary issues an approval after any necessary additional review of the application.

(C) Civil action to obtain patent certainty.—

(i) Declaratory judgment absent infringement action.—

(I) In general.—No action may be brought under section 2201 of title 28 by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) Filing of civil action.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) Offer of confidential access to application.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) Counterclaim to infringement action.—

(I) In general.—If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) of this section on the ground that the patent does not claim either—

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) No independent cause of action.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) No damages.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(D) Forfeiture of 180-day exclusivity period.—

(i) Definition of forfeiture event.—In this subparagraph, the term "forfeiture event", with respect to an application under this subsection, means the occurrence of any of the following:

(I) Failure to market.—The first applicant fails to market the drug by the later of—

(aa) the earlier of the date that is—

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) of this section is withdrawn by the holder of the application approved under subsection (b) of this section.

(II) Withdrawal of application.—The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) Amendment of certification.—The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) Failure to obtain tentative approval.—The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) Agreement with another applicant, the listed drug application holder, or a patent owner.—The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint

from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 12 of title 15, except that the term includes section 45 of title 15 to the extent that that section applies to unfair methods of competition).

(VI) Expiration of all patents.—All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) Forfeiture.—The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) Subsequent applicant.—If all first applicants forfeit the 180-day exclusivity period under clause (ii)—

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(F)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of

time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section for such drug.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from September 24, 1984.

(6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) for the same period as the withdrawal or suspension under subsection (e) of this section or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public—

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) of this section before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) of this section or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (b) or (c) of this section respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) of this section or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under paragraph (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) of this section or paragraph (6), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(8) For purposes of this subsection:

(A)(i) The term “bioavailability” means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if—

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is

not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

(9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(10)(A) If the proposed labeling of a drug that is the subject of an application under this subsection differs from the listed drug due to a labeling revision described under clause (i), the drug that is the subject of such application shall, notwithstanding any other provision of this chapter, be eligible for approval and shall not be considered misbranded under section 352 of this title if—

(i) the application is otherwise eligible for approval under this subsection but for expiration of patent, an exclusivity period, or of a delay in approval described in paragraph (5)(B)(iii), and a revision to the labeling of the listed drug has been approved by the Secretary within 60 days of such expiration;

(ii) the labeling revision described under clause (i) does not include a change to the “Warnings” section of the labeling;

(iii) the sponsor of the application under this subsection agrees to submit revised labeling of the drug that is the subject of such application not later than 60 days after the notification of any changes to such labeling required by the Secretary; and

(iv) such application otherwise meets the applicable requirements for approval under this subsection.

(B) If, after a labeling revision described in subparagraph (A)(i), the Secretary determines that the continued presence in interstate commerce of the labeling of the listed drug (as in effect before the revision described in subparagraph (A)(i)) adversely impacts the safe use of the drug, no application under this subsection shall be eligible for approval with such labeling.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained

by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(3) Active postmarket risk identification.—

(A) Definition.—In this paragraph, the term "data" refers to information with respect to a drug approved under this section or under section 262 of title 42, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

(B) Development of postmarket risk identification and analysis methods.—The Secretary shall, not later than 2 years after September 27, 2007, in collaboration with public, academic, and private entities—

(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

(I) at least 25,000,000 patients by July 1, 2010; and

(II) at least 100,000,000 patients by July 1, 2012; and

(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

(C) Establishment of the postmarket risk identification and analysis system.—

(i) In general.—The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures—

(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 355–1(b) of this title) submitted to the Secretary under paragraph (1), and those adverse events submitted by patients, providers, and drug sponsors, when appropriate;

(III) to provide for active adverse event surveillance using the following data sources, as available:

(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

(IV) to identify certain trends and patterns with respect to data accessed by the system;

(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

(VI) to enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

(ii) Timeliness of reporting.—The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

(iii) Private sector resources.—To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(iv) Complementary approaches.—To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including—

(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

(v) Authority for contracts.—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

(4) Advanced analysis of drug safety data.—

(A) Purpose.—The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 299b–1 of title

42, to provide for advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to—

(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

(B) Privacy.—Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

(C) Public process for priority questions.—At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on—

(i) priority drug safety questions; and

(ii) mechanisms for answering such questions, including through—

(I) active risk identification under paragraph (3); and

(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (*o*)(3).

(D) Procedures for the development of drug safety collaborations.—

(i) In general.—Not later than 180 days after the date of the establishment of the active postmarket risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to—

(I) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

(II) allow for prompt investigation of priority drug safety questions, including—

(aa) unresolved safety questions for drugs or classes of drugs; and

(bb) for a newly-approved drugs,[2] safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

(III) perform advanced research and analysis on identified drug safety risks;

(IV) focus postapproval studies and clinical trials under subsection (*o*)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

(ii) Request for specific methodology.—The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

(E) Use of analyses.—The Secretary shall provide the analyses described in this paragraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

(F) Qualified entities.—

(i) In general.—The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

(ii) Qualification.—The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

(II) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

(G) Contract requirements.—Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

(i) Ensuring privacy.—The qualified entity shall ensure that the entity will not use data under this subsection in a manner that—

(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

(II) violates sections 552 or 552a of title 5 with regard to the privacy of individually-identifiable beneficiary health information; or

(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends.

Nothing in this clause prohibits lawful disclosure for other purposes.

(ii) Component of another organization.—If a qualified entity is a component of another organization—

(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

(iii) Termination or nonrenewal.—If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

(I) Confidentiality and privacy protections.—The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

(II) Disposition of data.—The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

(H) Competitive procedures.—The Secretary shall use competitive procedures (as defined in section 132 of title 41) to enter into contracts under subparagraph (G).

(I) Review of contract in the event of a merger or acquisition.—The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this paragraph will continue to be met.

(J) Coordination.—In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.

(5) The Secretary shall—

(A) conduct regular, bi-weekly screening of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse [3] Event Reporting System within the last quarter;

(B) report to Congress not later than 2 year [4] after September 27, 2007, on procedures and processes of the Food and Drug Administration for addressing ongoing post market safety issues identified by the Office of Surveillance and Epidemiology and how recommendations of the Office of Surveillance and Epidemiology are handled within the agency; and

(C) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments.

(l) Public disclosure of safety and effectiveness data and action package

(1) Safety and effectiveness data and information which has been submitted in an application under subsection (b) of this section for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this section which refers to such drug could be made effective if such an application had been submitted.

(2) Action Package for Approval.—

(A) Action package.—The Secretary shall publish the action package for approval of an application under subsection (b) or section 262 of title 42 on the Internet Web site of the Food and Drug Administration—

(i) not later than 30 days after the date of approval of such application for a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42; and

(ii) not later than 30 days after the third request for such action package for approval received under section 552 of title 5 for any other drug.

(B) Immediate publication of summary review.—Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug, except where such materials require redaction by the Secretary.

(C) Contents.—An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

(i) Documents generated by the Food and Drug Administration related to review of the application.

(ii) Documents pertaining to the format and content of the application generated during drug development.

(iii) Labeling submitted by the applicant.

(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

(v) The Division Director and Office Director's decision document which includes—

(I) a brief statement of concurrence with the summary review;

(II) a separate review or addendum to the review if disagreeing with the summary review; and

(III) a separate review or addendum to the review to add further analysis.

(vi) Identification by name of each officer or employee of the Food and Drug Administration who—

(I) participated in the decision to approve the application; and

(II) consents to have his or her name included in the package.

(D) Review.—A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

(E) Confidential information.—This paragraph does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of title 5.

(m) “Patent” defined

For purposes of this section, the term “patent” means a patent issued by the United States Patent and Trademark Office.

(n) Scientific advisory panels

(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under this section or section 262 of title 42, the Secretary shall establish panels of experts or use panels of experts established before November 21, 1997, or both.

(2) The Secretary may delegate the appointment and oversight authority granted under section 394 of this title to a director of a center or successor entity within the Food and Drug Administration.

(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of—

(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related professions;

(C) a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this chapter and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

(5) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS–15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per

diem in lieu of subsistence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

(6) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

(7) Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(o) Postmarket studies and clinical trials; labeling

(1) In general

A responsible person may not introduce or deliver for introduction into interstate commerce the new drug involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

(2) Definitions

For purposes of this subsection:

(A) Responsible person

The term “responsible person” means a person who—

(i) has submitted to the Secretary a covered application that is pending; or

(ii) is the holder of an approved covered application.

(B) Covered application

The term “covered application” means—

(i) an application under subsection (b) for a drug that is subject to section 353(b) of this title; and

(ii) an application under section 262 of title 42.

(C) New safety information; serious risk

The terms “new safety information”, “serious risk”, and “signal of a serious risk” have the meanings given such terms in section 355–1(b) of this title.

(3) Studies and clinical trials

(A) In general

For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed

appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

(B) Purposes of study or clinical trial

The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

(i) To assess a known serious risk related to the use of the drug involved.

(ii) To assess signals of serious risk related to the use of the drug.

(iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

(C) Establishment of requirement after approval of covered application

The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

(D) Determination by Secretary

(i) Postapproval studies

The Secretary may not require the responsible person to conduct a study under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

(ii) Postapproval clinical trials

The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

(E) Notification; timetables; periodic reports

(i) Notification

The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person regarding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(ii) Timetable; periodic reports

For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the responsible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary

on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 282(j) of title 42. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

(F) Dispute resolution

The responsible person may appeal a requirement to conduct a study or clinical trial under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

(4) Safety labeling changes requested by Secretary

(A) New safety information

If the Secretary becomes aware of new safety information that the Secretary believes should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under subsection (b) is not currently marketed, the holder of an approved application under subsection (j).

(B) Response to notification

Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under subsection (j) shall within 30 days—

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions; or

(ii) notify the Secretary that the responsible person or the holder of the approved application under subsection (j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

(C) Review

Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety information, and if so, the contents of such labeling changes.

(D) Discussions

Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

(E) Order

Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under subsection (j) to make such a labeling change as the Secretary deems appropriate to address the new safety information.

Within 15 days of such an order, the responsible person or the holder of the approved application under subsection (j) shall submit a supplement containing the labeling change.

(F) Dispute resolution

Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under subsection (j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

(G) Violation

If the responsible person or the holder of the approved application under subsection (j) has not submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

(H) Public health threat

Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

(I) Rule of construction

This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under subsection (j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

(5) Non-delegation

Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(p) Risk evaluation and mitigation strategy

(1) In general

A person may not introduce or deliver for introduction into interstate commerce a new drug if—

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 353(b) of this title; or

(ii) the application for such drug is approved under section 262 of title 42; and

(B) a risk evaluation and mitigation strategy is required under section 355–1 of this title with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 355–1 of this title, including requirements regarding assessments of approved strategies.

(2) Certain postmarket studies

The failure to conduct a postmarket study under section 356 of this title, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).

(q) Petitions and civil actions regarding approval of certain applications

(1) In general

(A) Determination

The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) because of any request to take any form of action relating to the application, either before or during consideration of the request, unless—

(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.

(B) Notification

If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall provide to the applicant, not later than 30 days after making such determination, the following information:

(i) Notification of the fact that a determination under subparagraph (A) has been made.

(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

(C) Format

The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary—

(i) a document; or

(ii) a meeting with the applicant involved.

(D) Public disclosure

Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

(E) Denial based on intent to delay

If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe the factors that will be used to determine

under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

(F) Final agency action

The Secretary shall take final agency action on a petition not later than 180 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including—

(i) any determination made under subparagraph (A);

(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

(iii) the consent of the petitioner.

(G) Extension of 30-month period

If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

(H) Certification

The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the following certification: "I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(I) Verification

The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: "I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from

the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(2) Exhaustion of administrative remedies

(A) Final agency action within 180 days

The Secretary shall be considered to have taken final agency action on a petition if—

(i) during the 180-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or

(ii) such period expires without the Secretary having made such a final decision.

(B) Dismissal of certain civil actions

If a civil action is filed against the Secretary with respect to any issue raised in the petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

(C) Administrative record

For purposes of judicial review related to the approval of an application for which a petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include—

(i) the petition filed under paragraph (1) and any supplements and comments thereto;

(ii) the Secretary's response to such petition, if issued; and

(iii) other information, as designated by the Secretary, related to the Secretary's determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

(3) Annual report on delays in approvals per petitions

The Secretary shall annually submit to the Congress a report that specifies—

(A) the number of applications that were approved during the preceding 12-month period;

(B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;

(C) the number of days by which such applications were so delayed; and

(D) the number of such petitions that were submitted during such period.

(4) Exceptions

This subsection does not apply to—

(A) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or

(B) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

(5) Definitions

(A) Application

For purposes of this subsection, the term "application" means an application submitted under subsection (b)(2) or (j).

(B) Petition

For purposes of this subsection, other than paragraph (1)(A)(i), the term "petition" means a request described in paragraph (1)(A)(i).

(r) Postmarket drug safety information for patients and providers

(1) Establishment

Not later than 1 year after September 27, 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that—

(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 262 of title 42; and

(B) improves communication of drug safety information to patients and providers.

(2) Internet Web site

The Secretary shall carry out paragraph (1) by—

(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine's Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate—

(i) patient labeling and patient packaging inserts;

(ii) a link to a list of each drug, whether approved under this section or licensed under such section 262, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 282 of title 42;

(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (*o*);

(vi) guidance documents and regulations related to drug safety; and

(vii) other material determined appropriate by the Secretary;

(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 262;

(D) preparing, by 18 months after approval of a drug or after use of the drug by 10,000 individuals, whichever is later, a summary analysis of the adverse drug reaction reports received for the drug, including identification of any new risks not previously identified, potential new risks, or known risks reported in unusual number;

(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

(3) Posting of drug labeling

The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 262 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

(4) Private sector resources

To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(5) Authority for contracts

The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

(6) Review

The Advisory Committee on Risk Communication under section 360bbb–6 of this title shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to

work with outside entities to help facilitate the dispensing of risk communication information to patients and providers.

(s) Referral to advisory committee

Prior to the approval of a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 262 of title 42, the Secretary shall—

(1) refer such drug to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee; or

(2) if the Secretary does not refer such a drug to a Food and Drug Administration advisory committee prior to the approval of the drug, provide in the action letter on the application for the drug a summary of the reasons why the Secretary did not refer the drug to an advisory committee prior to approval.

(t) Database for authorized generic drugs

(1) In general

(A) Publication

The Commissioner shall—

(i) not later than 9 months after September 27, 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

(B) Notification

The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

(2) Inclusion

The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

(3) Authorized generic drug

In this section, the term “authorized generic drug” means a listed drug (as that term is used in subsection (j)) that—

(A) has been approved under subsection (c); and

(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar

packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.

(u) Certain drugs containing single enantiomers

(1) In general

For purposes of subsections (c)(3)(E)(ii) and (j)(5)(F)(ii), if an application is submitted under subsection (b) for a non-racemic drug containing as an active ingredient (including any ester or salt of the active ingredient) a single enantiomer that is contained in a racemic drug approved in another application under subsection (b), the applicant may, in the application for such non-racemic drug, elect to have the single enantiomer not be considered the same active ingredient as that contained in the approved racemic drug, if—

(A)(i) the single enantiomer has not been previously approved except in the approved racemic drug; and

(ii) the application submitted under subsection (b) for such non-racemic drug—

(I) includes full reports of new clinical investigations (other than bioavailability studies)—

(aa) necessary for the approval of the application under subsections (c) and (d); and

(bb) conducted or sponsored by the applicant; and

(II) does not rely on any investigations that are part of an application submitted under subsection (b) for approval of the approved racemic drug; and

(B) the application submitted under subsection (b) for such non-racemic drug is not submitted for approval of a condition of use—

(i) in a therapeutic category in which the approved racemic drug has been approved; or

(ii) for which any other enantiomer of the racemic drug has been approved.

(2) Limitation

(A) No approval in certain therapeutic categories

Until the date that is 10 years after the date of approval of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph, the Secretary shall not approve such non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved.

(B) Labeling

If applicable, the labeling of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph shall include a statement that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug.

(3) Definition

(A) In general

For purposes of this subsection, the term "therapeutic category" means a therapeutic category identified in the list developed by the United States Pharmacopeia pursuant to section 1395w–104(b)(3)(C)(ii) of title 42 and as in effect on September 27, 2007.

(B) Publication by Secretary

The Secretary shall publish the list described in subparagraph (A) and may amend such list by regulation.

(4) Availability

The election referred to in paragraph (1) may be made only in an application that is submitted to the Secretary after September 27, 2007, and before October 1, 2012.

(v) Antibiotic drugs submitted before November 21, 1997

(1) Antibiotic drugs approved before November 21, 1997

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) shall be eligible for, with respect to the drug, the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of an application approved by the Secretary under section 357 of this title (as in effect before November 21, 1997).

(2) Antibiotic drugs submitted before November 21, 1997, but not approved

(A) In general

Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) may elect to be eligible for, with respect to the drug—

(i)(I) the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; and

(II) the 5-year exclusivity period referred to under clause (ii) of subsection (c)(3)(E) and under clause (ii) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; or

(ii) a patent term extension under section 156 of title 35, subject to the requirements of such section.

(B) Application; antibiotic drug described

(i) Application

An application described in this clause is an application for marketing submitted under this section after October 8, 2008, in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) Antibiotic drug

An antibiotic drug described in this clause is an antibiotic drug that was the subject of 1 or more applications received by the Secretary under section 357 of this title (as in effect before November 21, 1997), none of which was approved by the Secretary under such section.

(3) Limitations

(A) Exclusivities and extensions

Paragraphs (1)(A) and (2)(A) shall not be construed to entitle a drug that is the subject of an approved application described in subparagraphs [5] (1)(B)(i) or (2)(B)(i), as applicable, to any market exclusivities or patent extensions other than those exclusivities or extensions described in paragraph (1)(A) or (2)(A).

(B) Conditions of use

Paragraphs (1)(A) and (2)(A)(i) shall not apply to any condition of use for which the drug referred to in subparagraph (1)(B)(i) or (2)(B)(i), as applicable, was approved before October 8, 2008.

(4) Application of certain provisions

Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in paragraphs (1), (2), and (3), the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

③ 21CFR314[15]

Subpart A—General Provisions

§ 314.1 Scope of this part.

(a) This part sets forth procedures and requirements for the submission to, and the review by, the Food and Drug Administration of applications and abbreviated applications to market a new drug under section 505 of the Federal Food, Drug, and Cosmetic Act, as well as amendments, supplements, and postmarketing reports to them.

(b) This part does not apply to drug products subject to licensing by FDA under the Public Health Service Act (58 Stat. 632 as amended (42 U.S.C. 201 *et seq.*)) and subchapter F of chapter I of title 21 of the Code of Federal Regulations.

(c) References in this part to regulations in the Code of Federal Regulations are to chapter I of title 21, unless otherwise noted.

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[15] Food and Drug Administration, HHS Part 314 – Applications for FDA Approval to Market a New Drug（Discover U.S. Government Information ウェブサイト）
https://www.govinfo.gov/content/pkg/CFR-2021-title21-vol5/pdf/CFR-2021-title21-vol5-part314.pdf

§ 314.2 Purpose.

The purpose of this part is to establish an efficient and thorough drug review process in order to: (a) Facilitate the approval of drugs shown to be safe and effective; and (b) ensure the disapproval of drugs not shown to be safe and effective. These regulations are also intended to establish an effective system for FDA's surveillance of marketed drugs. These regulations shall be construed in light of these objectives.

§ 314.3 Definitions.

(a) The definitions and interpretations contained in section 201 of the Federal Food, Drug, and Cosmetic Act apply to those terms when used in this part and part 320 of this chapter.

(b) The following definitions of terms apply to this part and part 320 of this chapter:

180-day exclusivity period is the 180-day period beginning on the date of the first commercial marketing of the drug (including the commercial marketing of the reference listed drug) by any first applicant. The 180-day period ends on the day before the date on which an ANDA submitted by an applicant other than a first applicant could be approved.

505(b)(2) application is an NDA submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for a drug for which at least some of the investigations described in section 505(b)(1)(A) of the Federal Food, Drug, and Cosmetic Act and relied upon by the applicant for approval of the NDA were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

Abbreviated application, abbreviated new drug application, or ANDA is the application described under § 314.94, including all amendments and supplements to the application.

Acknowledgment letter is a written, postmarked communication from FDA to an applicant stating that the Agency has determined that an ANDA is sufficiently complete to permit a substantive review. An acknowledgment letter indicates that the ANDA is regarded as received.

Act is the Federal Food, Drug, and Cosmetic Act (section 201 *et seq.* (21 U.S.C. 301 *et seq.*)).

Active ingredient is any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.

Active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

ANDA holder is the applicant that owns an approved ANDA.*Applicant* is any person who submits an NDA (including a 505(b)(2) application) or ANDA or an amendment or supplement to an NDA or ANDA under this part to obtain FDA approval of a new drug and any person who owns an approved NDA (including a 505(b)(2) application) or ANDA.

Application, new drug application, or NDA is the application described under § 314.50, including all amendments and supplements to the application. An NDA refers to "stand-alone" applications submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act and to 505(b)(2) applications.

Approval letter is a written communication to an applicant from FDA approving an NDA or an ANDA.

Assess the effects of the change is to evaluate the effects of a manufacturing change on the identity, strength, quality, purity, and potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

Authorized generic drug is a listed drug, as defined in this section, that has been approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and is marketed, sold, or distributed directly or indirectly to the retail class of trade with labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trademark that differs from that of the listed drug.

Bioavailability is the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of drug action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of drug action.

Bioequivalence is the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. Where there is an intentional difference in rate (e.g., in certain extended-release dosage forms), certain pharmaceutical equivalents or alternatives may be considered bioequivalent if there is no significant difference in the extent to which the active ingredient or moiety from each product becomes available at the site of drug action. This applies only if the difference in the rate at which the active ingredient or moiety becomes available at the site of drug action is intentional and is reflected in the proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug. For drug products that are not intended to be absorbed into the bloodstream, bioequivalence may be assessed by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of drug action.

Bioequivalence requirement is a requirement imposed by FDA for in vitro and/or in vivo testing of specified drug products that must be satisfied as a condition of marketing.

Class 1 resubmission is the resubmission of an NDA or efficacy supplement, following receipt of a complete response letter, that contains one or more of the following: Final printed labeling, draft labeling, certain safety updates, stability updates to support provisional or final dating periods, commitments to perform postmarketing studies (including proposals for such studies), assay validation data, final release testing on the last lots used to support approval, minor reanalyses of previously submitted data, and other comparatively minor information.

Class 2 resubmission is the resubmission of an NDA or efficacy supplement, following receipt of a complete response letter, that includes any item not specified in the definition of "Class 1 resubmission," including any item that would require presentation to an advisory committee.

Commercial marketing is the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant, except that the term does not include transfer of the drug product for investigational use under part 312 of this chapter or transfer of the drug product to parties identified in the ANDA for reasons other than sale. Commercial marketing includes the introduction or delivery for introduction into interstate commerce of the reference listed drug by the ANDA applicant.

Complete response letter is a written communication to an applicant from FDA usually describing all of the deficiencies that the Agency has identified in an NDA or ANDA that must be satisfactorily addressed before it can be approved.

Component is any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug product.

Date of approval is the date on the approval letter from FDA stating that the NDA or ANDA is approved, except that the date of approval for an NDA described in section 505(x)(1) of the Federal Food, Drug, and Cosmetic Act is determined as described in section 505(x)(2) of the Federal Food, Drug, and Cosmetic Act. "Date of approval" refers only to a final approval and not to a tentative approval.

Dosage form is the physical manifestation containing the active and inactive ingredients that delivers a dose of the drug product. This includes such factors as:

(1) The physical appearance of the drug product;

(2) The physical form of the drug product prior to dispensing to the patient;

(3) The way the product is administered; and

(4) The design features that affect frequency of dosing.

Drug product is a finished dosage form, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.

Drug substance is an active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body, but does not include intermediates used in the synthesis of such ingredient.

Efficacy supplement is a supplement to an approved NDA proposing to make one or more related changes from among the following changes to product labeling:

(1) Add or modify an indication or claim;

(2) Revise the dose or dose regimen;

(3) Provide for a new route of administration;

(4) Make a comparative efficacy claim naming another drug product;

(5) Significantly alter the intended patient population;

(6) Change the marketing status from prescription to over-the-counter use;

(7) Provide for, or provide evidence of effectiveness necessary for, the traditional approval of a product originally approved under subpart H of this part; or

(8) Incorporate other information based on at least one adequate and well-controlled clinical study.

FDA or Agency is the Food and Drug Administration.

First applicant is an ANDA applicant that, on the first day on which a substantially complete application containing a paragraph IV certification is submitted for approval of a drug, submits a substantially complete application that contains, and for which the applicant lawfully maintains, a paragraph IV certification for the drug.

Inactive ingredient is any component other than an active ingredient.

Listed drug is a new drug product that has been approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act for safety and effectiveness or under section 505(j) of the Federal Food, Drug, and Cosmetic Act, which has not been withdrawn or suspended under section 505(e)(1) through (5) or section 505(j)(6) of the Federal Food, Drug, and Cosmetic Act, and which has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness. Listed drug status is evidenced by the drug product's identification in the current edition of FDA's "Approved Drug Products With Therapeutic Equivalence Evaluations" (the list) as an approved drug. A drug product is deemed to be a listed drug on the date of approval for the NDA or ANDA for that drug product.

NDA holder is the applicant that owns an approved NDA.

Newly acquired information is data, analyses, or other information not previously submitted to the Agency, which may include (but is not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

Original application or original NDA is a pending NDA for which FDA has never issued a complete response letter or approval letter, or an NDA that was submitted again after FDA had refused to file it or after it was withdrawn without being approved.

Paragraph IV acknowledgment letter is a written, postmarked communication from FDA to an applicant stating that the Agency has determined that a 505(b)(2) application or ANDA containing a paragraph IV certification is sufficiently complete to permit a substantive review. A paragraph IV acknowledgment letter indicates that the 505(b)(2) application is regarded as filed or the ANDA is regarded as received.

Paragraph IV certification is a patent certification of invalidity, unenforceability, or noninfringement described in § 314.50(i)(1)(i)(A)(*4*) or § 314.94(a)(12)(i)(A)(*4*).

Patent owner is the owner of the patent for which information is submitted for an NDA.

Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates.

Pharmaceutical equivalents are drug products in identical dosage forms and route(s) of administration that contain identical amounts of the identical active drug ingredient, *i.e.*, the same salt or ester of the same therapeutic moiety, or, in the case of modified-release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; do not necessarily contain the same inactive ingredients; and meet

the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates.

Postmark is an independently verifiable evidentiary record of the date on which a document is transmitted, in an unmodifiable format, to another party. For postmarks made by the U.S. Postal Service or a designated delivery service, the date of transmission is the date on which the document is received by the domestic mail service of the U.S. Postal Service or by a designated delivery service. For postmarks documenting an electronic event, the date of transmission is the date (in a particular time zone) that FDA sends the electronic transmission on its host system as evidenced by a verifiable record. If the sender and the intended recipient are located in different time zones, it is the sender's time zone that provides the controlling date of electronic transmission.

Reference listed drug is the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its ANDA.

Reference standard is the drug product selected by FDA that an applicant seeking approval of an ANDA must use in conducting an in vivo bioequivalence study required for approval.

Resubmission, in the context of a complete response letter, is submission by the applicant of all materials needed to fully address all deficiencies identified in the complete response letter. An NDA or ANDA for which FDA issued a complete response letter, but which was withdrawn before approval and later submitted again, is not a resubmission.

Right of reference or use is the authority to rely upon, and otherwise use, an investigation for the purpose of obtaining approval of an NDA, including the ability to make available the underlying raw data from the investigation for FDA audit, if necessary.

Same drug product formulation is the formulation of the drug product submitted for approval and any formulations that have minor differences in composition or method of manufacture from the formulation submitted for approval, but are similar enough to be relevant to the Agency's determination of bioequivalence.

Specification is the quality standard (*i.e.,* tests, analytical procedures, and acceptance criteria) provided in an approved NDA or ANDA to confirm the quality of drug substances, drug products, intermediates, raw materials, reagents, components, in-process materials, container closure systems, and other materials used in the production of a drug substance or drug product. For the purpose of this definition, acceptance criteria means numerical limits, ranges, or other criteria for the tests described.

Strength is the amount of drug substance contained in, delivered, or deliverable from a drug product, which includes:

(1)(i) The total quantity of drug substance in mass or units of activity in a dosage unit or container closure (e.g., weight/unit dose, weight/volume or weight/weight in a container closure, or units/volume or units/weight in a container closure); and/or, as applicable.

(ii) The concentration of the drug substance in mass or units of activity per unit volume or mass (e.g., weight/weight, weight/volume, or units/volume); or

(2) Such other criteria the Agency establishes for determining the amount of drug substance contained in, delivered, or deliverable from a drug product if the weights and measures described in paragraph (i) of this definition do not apply (e.g., certain drug-device combination products for which the amount of drug substance is emitted per use or unit time).

Substantially complete application is an ANDA that on its face is sufficiently complete to permit a substantive review. Sufficiently complete means that the ANDA contains all the information required under section 505(j)(2)(A) of the Federal Food, Drug, and Cosmetic Act and does not contain a deficiency described in § 314.101(d) and (e).

Tentative approval is notification that an NDA or ANDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved because there is a 7-year period of orphan exclusivity for a listed drug under section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter, or that a 505(b)(2) application or ANDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved until the conditions in § 314.107(b)(1)(iii), (b)(3), or (c) are met; because there is a period of exclusivity for the listed drug under § 314.108; because there is a period of pediatric exclusivity for the listed drug under section 505A of the Federal Food, Drug, and Cosmetic Act; because there is a period of exclusivity for the listed drug under section 505E of the Federal Food, Drug, and Cosmetic Act; or because a court order pursuant to 35 U.S.C. 271(e)(4)(A) orders that the NDA or ANDA may be approved no earlier than the date specified. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval letter after any necessary additional review of the NDA or ANDA.

The list is the list of approved drug products published in FDA's current "Approved Drug Products With Therapeutic Equivalence Evaluations," available electronically on FDA's Web site at *http://www.fda.gov/cder*.

Therapeutic equivalents are approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.

Subpart B—Applications

§ 314.50 Content and format of an NDA.

NDAs and supplements to approved NDAs are required to be submitted in the form and contain the information, as appropriate for the particular submission, required under this section. Three copies of the NDA are required: An archival copy, a review copy, and a field copy. An NDA for a new chemical entity will generally contain an application form, an index, a summary, five or six technical sections, case report tabulations of patient data, case report forms, drug samples, and labeling, including, if applicable, any Medication Guide required under part 208 of this chapter. Other NDAs will generally contain only some of those items, and information will be limited to that needed to support the particular submission. These include an NDA of the type described in section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, an amendment, and a supplement. The NDA is required to contain reports of all investigations of the drug product sponsored by the applicant, and all other information about the drug pertinent to an evaluation of the NDA that is received or otherwise obtained by the applicant from any source. FDA will maintain guidance documents on the format and content of NDAs to assist applicants in their preparation.

(a) *Application form.* The applicant must submit a completed and signed application form that contains the following:

(1) The name and address of the applicant; the date of the NDA; the NDA number if previously issued (for example, if the NDA is a resubmission or an amendment or supplement); the name of the drug product, including its established, proprietary, code, and chemical names; the dosage form and strength; the route of administration; the identification numbers of all INDs (as defined in § 312.3(b) of this chapter) that are referenced in the NDA; the identification numbers of all drug master files and other applications under this part that are referenced in the NDA; and the drug product's proposed indications for use.

(2) A statement whether the submission is an original submission, a 505(b)(2) application, a resubmission, or a supplement to an application under § 314.70.

(3) A statement whether the applicant proposes to market the drug product as a prescription or an over-the-counter product.

(4) A check-list identifying what enclosures required under this section the applicant is submitting.

(5) The applicant, or the applicant's attorney, agent, or other authorized official must sign the NDA. If the person signing the NDA does not reside or have a place of business within the United States, the NDA is required to contain the name and address of, and be countersigned by, an attorney, agent, or other authorized official who resides or maintains a place of business within the United States.

(b) *Index.* The archival copy of the NDA is required to contain a comprehensive index by volume number and page number to the summary under paragraph (c) of this section, the technical sections under paragraph (d) of this section, and the supporting information under paragraph (f) of this section.

(c) *Summary.* (1) An NDA is required to contain a summary of the NDA in enough detail that the reader may gain a good general understanding of the data and information in the NDA, including an understanding of the quantitative aspects of the data. The summary is not required for supplements under § 314.70. Resubmissions of an NDA should contain an updated summary, as appropriate. The summary should discuss all aspects of the NDA, and synthesize the information into a well-structured and unified document. The summary should be written at approximately the level of detail required for publication in, and meet the editorial standards generally applied by, refereed scientific and medical journals. In addition to the agency personnel reviewing the summary in the context of their review of the NDA, FDA may furnish the summary to FDA advisory committee members and agency officials whose duties require an understanding of the NDA. To the extent possible, data in the summary should be presented in tabular and graphic forms. FDA has prepared a guideline under § 10.90(b) that provides information about how to prepare a summary. The summary required under this paragraph may be used by FDA or the applicant to prepare the Summary Basis of Approval document for public disclosure (under § 314.430(e)(2)(ii)) when the NDA is approved.

(2) The summary is required to contain the following information:

(i) The proposed text of the labeling, including, if applicable, any Medication Guide required under part 208 of this chapter, for the drug, with annotations to the information in the summary and technical sections of the NDA that support the inclusion of each statement in the labeling, and, if the NDA is for a prescription drug, statements describing the reasons for omitting a section or subsection of the labeling format in § 201.57 of this chapter.

(ii) A statement identifying the pharmacologic class of the drug and a discussion of the scientific rationale for the drug, its intended use, and the potential clinical benefits of the drug product.

(iii) A brief description of the marketing history, if any, of the drug outside the United States, including a list of the countries in which the drug has been marketed, a list of any countries in which the drug has been withdrawn from marketing for any reason related to safety or effectiveness, and a list of countries in which applications for marketing are pending. The description is required to describe both marketing by the applicant and, if known, the marketing history of other persons.

(iv) A summary of the chemistry, manufacturing, and controls section of the NDA.

(v) A summary of the nonclinical pharmacology and toxicology section of the NDA.

(vi) A summary of the human pharmacokinetics and bioavailability section of the NDA.

(vii) A summary of the microbiology section of the NDA (for anti-infective drugs only).

(viii) A summary of the clinical data section of the NDA, including the results of statistical analyses of the clinical trials.

(ix) A concluding discussion that presents the benefit and risk considerations related to the drug, including a discussion of any proposed additional studies or surveillance the applicant intends to conduct postmarketing.

(d) *Technical sections.* The NDA is required to contain the technical sections described below. Each technical section is required to contain data and information in sufficient detail to permit the agency to make a knowledgeable judgment about whether to approve the NDA or whether grounds exist under section 505(d) of the Federal Food, Drug, and Cosmetic Act to refuse to approve the NDA. The required technical sections are as follows:

(1) *Chemistry, manufacturing, and controls section.* A section describing the composition, manufacture, and specification of the drug substance and the drug product, including the following:

(i) *Drug substance.* A full description of the drug substance including its physical and chemical characteristics and stability; the name and address of its manufacturer; the method of synthesis (or isolation) and purification of the drug substance; the process controls used during manufacture and packaging; and the specifications necessary to ensure the identity, strength, quality, and purity of the drug substance and the bioavailability of the drug products made from the substance, including, for example, tests, analytical procedures, and acceptance criteria relating to stability, sterility, particle size, and crystalline form. The NDA may provide additionally for the use of alternatives to meet any of these requirements, including alternative sources, process controls, and analytical procedures. Reference to the current edition of the U.S. Pharmacopeia and the National Formulary may satisfy relevant requirements in this paragraph.

(ii)(*(a)*) *Drug product.* A list of all components used in the manufacture of the drug product (regardless of whether they appear in the drug product) and a statement of the composition of the drug product; the specifications for each component; the name and address of each manufacturer of the drug product; a description of the manufacturing and packaging procedures and in-process controls for the drug product; the specifications necessary to ensure the identity, strength, quality, purity, potency, and bioavailability of the drug product, including, for example, tests, analytical procedures, and acceptance criteria relating to sterility, dissolution rate, container closure systems; and stability data with proposed expiration dating. The NDA may provide additionally for the use of alternatives to meet any of these requirements, including alternative components, manufacturing and packaging procedures, in-process controls, and analytical procedures.

Reference to the current edition of the U.S. Pharmacopeia and the National Formulary may satisfy relevant requirements in this paragraph.

(*b*) Unless provided by paragraph (d)(1)(ii)(*a*) of this section, for each batch of the drug product used to conduct a bioavailability or bioequivalence study described in § 320.38 or § 320.63 of this chapter or used to conduct a primary stability study: The batch production record; the specification for each component and for the drug product; the names and addresses of the sources of the active and noncompendial inactive components and of the container and closure system for the drug product; the name and address of each contract facility involved in the manufacture, processing, packaging, or testing of the drug product and identification of the operation performed by each contract facility; and the results of any test performed on the components used in the manufacture of the drug product as required by § 211.84(d) of this chapter and on the drug product as required by § 211.165 of this chapter.

(*c*) The proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product or a comparably detailed description of the production process for a representative batch of the drug product.

(iii) *Environmental impact.* The NDA is required to contain either a claim for categorical exclusion under § 25.30 or 25.31 of this chapter or an environmental assessment under § 25.40 of this chapter.

(iv) The applicant may, at its option, submit a complete chemistry, manufacturing, and controls section 90 to 120 days before the anticipated submission of the remainder of the NDA. FDA will review such early submissions as resources permit.

(v) The applicant must include a statement certifying that the field copy of the NDA has been provided to the applicant's home FDA district office.

(2) *Nonclinical pharmacology and toxicology section.* A section describing, with the aid of graphs and tables, animal and in vitro studies with drug, including the following:

(i) Studies of the pharmacological actions of the drug in relation to its proposed therapeutic indication and studies that otherwise define the pharmacologic properties of the drug or are pertinent to possible adverse effects.

(ii) Studies of the toxicological effects of the drug as they relate to the drug's intended clinical uses, including, as appropriate, studies assessing the drug's acute, subacute, and chronic toxicity; carcinogenicity; and studies of toxicities related to the drug's particular mode of administration or conditions of use.

(iii) Studies, as appropriate, of the effects of the drug on reproduction and on the developing fetus.

(iv) Any studies of the absorption, distribution, metabolism, and excretion of the drug in animals.

(v) For each nonclinical laboratory study subject to the good laboratory practice regulations under part 58 a statement that it was conducted in compliance with the good laboratory practice regulations in part 58, or, if the study was not conducted in compliance with those regulations, a brief statement of the reason for the noncompliance.

(3) *Human pharmacokinetics and bioavailability section.* A section describing the human pharmacokinetic data and human bioavailability data, or information supporting a waiver of the submission of in vivo bioavailability data under subpart B of part 320, including the following:

(i) A description of each of the bioavailability and pharmacokinetic studies of the drug in humans performed by or on behalf of the applicant that includes a description of the analytical procedures and statistical methods used in each study and a statement with respect to each study that it either was conducted in compliance with the institutional review board regulations in part 56, or was not subject to the regulations under § 56.104 or § 56.105, and that it was conducted in compliance with the informed consent regulations in part 50.

(ii) If the NDA describes in the chemistry, manufacturing, and controls section tests, analytical procedures, and acceptance criteria needed to assure the bioavailability of the drug product or drug substance, or both, a statement in this section of the rationale for establishing the tests, analytical procedures, and acceptance criteria, including data and information supporting the rationale.

(iii) A summarizing discussion and analysis of the pharmacokinetics and metabolism of the active ingredients and the bioavailability or bioequivalence, or both, of the drug product.

(4) *Microbiology section.* If the drug is an anti-infective drug, a section describing the microbiology data, including the following:

(i) A description of the biochemical basis of the drug's action on microbial physiology.

(ii) A description of the antimicrobial spectra of the drug, including results of in vitro preclinical studies to demonstrate concentrations of the drug required for effective use.

(iii) A description of any known mechanisms of resistance to the drug, including results of any known epidemiologic studies to demonstrate prevalence of resistance factors.

(iv) A description of clinical microbiology laboratory procedures (for example, in vitro sensitivity discs) needed for effective use of the drug.

(5) *Clinical data section.* A section describing the clinical investigations of the drug, including the following:

(i) A description and analysis of each clinical pharmacology study of the drug, including a brief comparison of the results of the human studies with the animal pharmacology and toxicology data.

(ii) A description and analysis of each controlled clinical study pertinent to a proposed use of the drug, including the protocol and a description of the statistical analyses used to evaluate the study. If the study report is an interim analysis, this is to be noted and a projected completion date provided. Controlled clinical studies that have not been analyzed in detail for any reason (e.g., because they have been discontinued or are incomplete) are to be included in this section, including a copy of the protocol and a brief description of the results and status of the study.

(iii) A description of each uncontrolled clinical study, a summary of the results, and a brief statement explaining why the study is classified as uncontrolled.

(iv) A description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from clinical investigations, including controlled and uncontrolled studies of uses of the drug other than those proposed in the NDA, commercial marketing experience, reports in the scientific literature, and unpublished scientific papers.

(v) An integrated summary of the data demonstrating substantial evidence of effectiveness for the claimed indications. Evidence is also required to support the dosage and administration section of the labeling,

including support for the dosage and dose interval recommended. The effectiveness data must be presented by gender, age, and racial subgroups and must identify any modifications of dose or dose interval needed for specific subgroups. Effectiveness data from other subgroups of the population of patients treated, when appropriate, such as patients with renal failure or patients with different levels of severity of the disease, also must be presented.

(vi) A summary and updates of safety information, as follows:

(*a*) The applicant must submit an integrated summary of all available information about the safety of the drug product, including pertinent animal data, demonstrated or potential adverse effects of the drug, clinically significant drug/drug interactions, and other safety considerations, such as data from epidemiological studies of related drugs. The safety data must be presented by gender, age, and racial subgroups. When appropriate, safety data from other subgroups of the population of patients treated also must be presented, such as for patients with renal failure or patients with different levels of severity of the disease. A description of any statistical analyses performed in analyzing safety data should also be included, unless already included under paragraph (d)(5)(ii) of this section.

(*b*) The applicant must, under section 505(i) of the Federal Food, Drug, and Cosmetic Act, update periodically its pending NDA with new safety information learned about the drug that may reasonably affect the statement of contraindications, warnings, precautions, and adverse reactions in the draft labeling and, if applicable, any Medication Guide required under part 208 of this chapter. These “safety update reports” must include the same kinds of information (from clinical studies, animal studies, and other sources) and must be submitted in the same format as the integrated summary in paragraph (d)(5)(vi)(*a*) of this section. In addition, the reports must include the case report forms for each patient who died during a clinical study or who did not complete the study because of an adverse event (unless this requirement is waived). The applicant must submit these reports (*1*) 4 months after the initial submission; (*2*) in a resubmission following receipt of a complete response letter; and (*3*) at other times as requested by FDA. Before submitting the first such report, applicants are encouraged to consult with FDA regarding further details on its form and content.

(vii) If the drug has a potential for abuse, a description and analysis of studies or information related to abuse of the drug, including a proposal for scheduling under the Controlled Substances Act. A description of any studies related to overdosage is also required, including information on dialysis, antidotes, or other treatments, if known.

(viii) An integrated summary of the benefits and risks of the drug, including a discussion of why the benefits exceed the risks under the conditions stated in the labeling.

(ix) A statement with respect to each clinical study involving human subjects that it either was conducted in compliance with the institutional review board regulations in part 56, or was not subject to the regulations under § 56.104 or § 56.105, and that it was conducted in compliance with the informed consent regulations in part 50.

(x) If a sponsor has transferred any obligations for the conduct of any clinical study to a contract research organization, a statement containing the name and address of the contract research organization, identification of the clinical study, and a listing of the obligations transferred. If all obligations governing the conduct of the

study have been transferred, a general statement of this transfer—in lieu of a listing of the specific obligations transferred—may be submitted.

(xi) If original subject records were audited or reviewed by the sponsor in the course of monitoring any clinical study to verify the accuracy of the case reports submitted to the sponsor, a list identifying each clinical study so audited or reviewed.

(6) *Statistical section.* A section describing the statistical evaluation of clinical data, including the following:

(i) A copy of the information submitted under paragraph (d)(5)(ii) of this section concerning the description and analysis of each controlled clinical study, and the documentation and supporting statistical analyses used in evaluating the controlled clinical studies.

(ii) A copy of the information submitted under paragraph (d)(5)(vi)(*a*) of this section concerning a summary of information about the safety of the drug product, and the documentation and supporting statistical analyses used in evaluating the safety information.

(7) *Pediatric use section.* A section describing the investigation of the drug for use in pediatric populations, including an integrated summary of the information (the clinical pharmacology studies, controlled clinical studies, or uncontrolled clinical studies, or other data or information) that is relevant to the safety and effectiveness and benefits and risks of the drug in pediatric populations for the claimed indications, a reference to the full descriptions of such studies provided under paragraphs (d)(3) and (d)(5) of this section, and information required to be submitted under § 314.55.

(e) *Samples and labeling.* (1) Upon request from FDA, the applicant must submit the samples described below to the places identified in the Agency's request. FDA generally will ask applicants to submit samples directly to two or more Agency laboratories that will perform all necessary tests on the samples and validate the applicant's analytical procedures.

(i) Four representative samples of the following, each sample in sufficient quantity to permit FDA to perform three times each test described in the NDA to determine whether the drug substance and the drug product meet the specifications given in the NDA:

(*a*) The drug product proposed for marketing;

(*b*) The drug substance used in the drug product from which the samples of the drug product were taken; and

(*c*) Reference standards and blanks (except that reference standards recognized in an official compendium need not be submitted).

(ii) Samples of the finished market package, if requested by FDA.

(2) The applicant must submit the following in the archival copy of the NDA:

(i) Three copies of the analytical procedures and related descriptive information contained in the chemistry, manufacturing, and controls section under paragraph (d)(1) of this section for the drug substance and the drug product that are necessary for FDA's laboratories to perform all necessary tests on the samples and to validate the applicant's analytical procedures. The related descriptive information includes a description of each sample; the proposed regulatory specifications for the drug; a detailed description of the methods of analysis; supporting data for accuracy, specificity, precision and ruggedness; and complete results of the applicant's tests on each sample.

(ii) Copies of the label and all labeling for the drug product (including, if applicable, any Medication Guide required under part 208 of this chapter) for the drug product (4 copies of draft labeling or 12 copies of final printed labeling).

(f) *Case report forms and tabulations.* The archival copy of the NDA is required to contain the following case report tabulations and case report forms:

(1) *Case report tabulations.* The NDA is required to contain tabulations of the data from each adequate and well-controlled study under § 314.126 (Phase 2 and Phase 3 studies as described in §§ 312.21 (b) and (c) of this chapter), tabulations of the data from the earliest clinical pharmacology studies (Phase 1 studies as described in § 312.21(a) of this chapter), and tabulations of the safety data from other clinical studies. Routine submission of other patient data from uncontrolled studies is not required. The tabulations are required to include the data on each patient in each study, except that the applicant may delete those tabulations which the agency agrees, in advance, are not pertinent to a review of the drug's safety or effectiveness. Upon request, FDA will discuss with the applicant in a "pre-NDA" conference those tabulations that may be appropriate for such deletion. Barring unforeseen circumstances, tabulations agreed to be deleted at such a conference will not be requested during the conduct of FDA's review of the NDA. If such unforeseen circumstances do occur, any request for deleted tabulations will be made by the director of the FDA division responsible for reviewing the NDA, in accordance with paragraph (f)(3) of this section.

(2) *Case report forms.* The NDA is required to contain copies of individual case report forms for each patient who died during a clinical study or who did not complete the study because of an adverse event, whether believed to be drug related or not, including patients receiving reference drugs or placebo. This requirement may be waived by FDA for specific studies if the case report forms are unnecessary for a proper review of the study.

(3) *Additional data.* The applicant must submit to FDA additional case report forms and tabulations needed to conduct a proper review of the NDA, as requested by the director of the FDA division responsible for reviewing the NDA. The applicant's failure to submit information requested by FDA within 30 days after receipt of the request may result in the agency viewing any eventual submission as a major amendment under § 314.60 and extending the review period as necessary. If desired by the applicant, the FDA division director will verify in writing any request for additional data that was made orally.

(4) *Presentation and format.* Applicants are invited to meet with FDA before submitting an NDA to discuss the presentation and format of supporting information. If the applicant and FDA agree, the applicant may submit tabulations of patient data and case report forms in an alternate form.

(g) *Other.* The following general requirements apply to the submission of information within the summary under paragraph (c) of this section and within the technical sections under paragraph (d) of this section.

(1) The applicant ordinarily is not required to resubmit information previously submitted, but may incorporate the information by reference. A reference to information submitted previously is required to identify the file by name, reference number, volume, and page number in the agency's records where the information can be found. A reference to information submitted to the agency by a person other than the applicant is required to contain a written statement that authorizes the reference and that is signed by the person who submitted the information.

(2) The applicant must submit an accurate and complete English translation of each part of the NDA that is not in English. The applicant must submit a copy of each original literature publication for which an English translation is submitted.

(3) If an applicant who submits an NDA under section 505(b) of the Federal Food, Drug, and Cosmetic Act obtains a "right of reference or use," as defined under § 314.3(b), to an investigation described in clause (A) of section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, the applicant must include in its NDA a written statement signed by the owner of the data from each such investigation that the applicant may rely on in support of the approval of its NDA, and provide FDA access to, the underlying raw data that provide the basis for the report of the investigation submitted in its NDA.

(h) *Patent information.* The NDA is required to contain the patent information described under § 314.53.

(i) *Patent certification* —(1) *Contents.* A 505(b)(2) application is required to contain the following:

(i) *Patents claiming drug substance, drug product, or method of use.* (A) An appropriate patent certification or statement with respect to each patent issued by the U.S. Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims the drug substance or drug product on which investigations that are relied upon by the applicant for approval of its 505(b)(2) application were conducted or that claims an approved use for such drug and for which information is required to be filed under section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53. For each such patent, the applicant must provide the patent number and certify, in its opinion and to the best of its knowledge, one of the following circumstances:

(*1*) That the patent information has not been submitted to FDA. The applicant must entitle such a certification "Paragraph I Certification";

(*2*) That the patent has expired. The applicant must entitle such a certification "Paragraph II Certification";

(*3*) The date on which the patent will expire. The applicant must entitle such a certification "Paragraph III Certification"; or

(*4*)(*I*) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the 505(b)(2) application is submitted. The applicant must entitle such a certification "Paragraph IV Certification". This certification must be submitted in the following form:

I, (*NAME OF APPLICANT*), CERTIFY THAT PATENT NO. ____ (*IS INVALID, UNENFORCEABLE, OR WILL NOT BE INFRINGED BY THE MANUFACTURE, USE, OR SALE OF*) (*NAME OF PROPOSED DRUG PRODUCT*) FOR WHICH THIS 505(B)(2) APPLICATION IS SUBMITTED.

(*ii*) The certification must be accompanied by a statement that the applicant will comply with the requirements under § 314.52(a) with respect to providing a notice to each owner of the patent or its representative and to the NDA holder (or, if the NDA holder does not reside or maintain a place of business within the United States, its attorney, agent, or other authorized official) for the drug product that is claimed by the patent or a use of which is claimed by the patent and with the requirements under § 314.52(b) with respect to sending the notice and under § 314.52(c) with respect to the content of the notice.

(B) If the drug on which investigations that are relied upon by the applicant were conducted is itself a licensed generic drug of a patented drug first approved under section 505(b) of the Federal Food, Drug, and

Cosmetic Act, an appropriate patent certification or statement under this section with respect to each patent that claims the first-approved patented drug or that claims an approved use for such a drug.

(C) If, before the date of submission of an original 505(b)(2) application, there is a drug product approved in an NDA that is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application is submitted, an appropriate patent certification or statement under this section with respect to each patent that claims the drug substance or drug product or that claims an approved use for one such drug product.

(ii) *No relevant patents.* If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (i)(1)(i) of this section, a certification in the following form:

IN THE OPINION AND TO THE BEST KNOWLEDGE OF (*NAME OF APPLICANT*), THERE ARE NO PATENTS THAT CLAIM THE DRUG OR DRUGS ON WHICH INVESTIGATIONS THAT ARE RELIED UPON IN THIS 505(B)(2) APPLICATION WERE CONDUCTED OR THAT CLAIM A USE OF SUCH DRUG OR DRUGS.

(iii) *Method-of-use patent.* (A) If information that is submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53 is for a method-of-use patent, and the labeling for the drug product for which the applicant is seeking approval does not include an indication or other condition of use that is covered by the method-of-use patent, a statement explaining that the method-of-use patent does not claim a proposed indication or other condition of use.

(B) If the labeling of the drug product for which the applicant is seeking approval includes an indication or other condition of use that, according to the patent information submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53 or in the opinion of the applicant, is claimed by a method-of-use patent, the applicant must submit an applicable certification under paragraph (i)(1)(i) of this section.

(2) [Reserved]

(3) *Licensing agreements.* If a 505(b)(2) application is submitted for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, the applicant must submit a paragraph IV certification as to that patent and a statement that the applicant has been granted a patent license. If the patent owner consents to approval of the 505(b)(2) application (if otherwise eligible for approval) as of a specific date, the 505(b)(2) application must contain a written statement from the patent owner that it has a licensing agreement with the applicant and that it consents to approval of the 505(b)(2) application as of a specific date.

(4) *Untimely filing of patent information.* (i) If a patent described in paragraph (i)(1)(i)(A) of this section is issued and the holder of the approved NDA for the patented drug does not file with FDA the required information on the patent within 30 days of issuance of the patent, an applicant who submitted a 505(b)(2) application that, before the submission of the patent information, contained an appropriate patent certification or statement is not required to submit a patent certification or statement to address the patent or patent information that is late-listed with respect to the pending 505(b)(2) application. Except as provided in § 314.53(f)(1), an NDA holder's amendment to the description of the approved method(s) of use claimed by the patent will be considered untimely filing of patent information unless:

(A) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of patent issuance;

(B) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of approval of a corresponding change to product labeling; or

(C) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision.

(ii) An applicant whose 505(b)(2) application is submitted after the NDA holder's untimely filing of patent information or whose 505(b)(2) application was previously filed but did not contain an appropriate patent certification or statement at the time of the patent submission must submit a certification under paragraph (i)(1)(i) of this section and/or a statement under paragraph (i)(1)(iii) of this section as to that patent.

(5) *Disputed patent information.* If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn, the applicant must submit an appropriate certification or statement for each listed patent.

(6) *Amended certifications.* A patent certification or statement submitted under paragraphs (i)(1)(i) through (iii) of this section may be amended at any time before the approval of the 505(b)(2) application. An applicant must submit an amended certification as an amendment to a pending 505(b)(2) application. If an applicant with a pending 505(b)(2) application voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. Once an amendment is submitted to change the certification, the 505(b)(2) application will no longer be considered to contain the prior certification.

(i) *After finding of infringement.* An applicant who has submitted a paragraph IV certification and is sued for patent infringement must submit an amendment to change its certification if a court enters a final decision from which no appeal has been or can be taken, or signs and enters a settlement order or consent decree in the action that includes a finding that the patent is infringed, unless the final decision, settlement order, or consent decree also finds the patent to be invalid. In its amendment, the applicant must certify under paragraph (i)(1)(i)(A)(*3*) of this section that the patent will expire on a specific date or, with respect to a patent claiming a method of use, the applicant may instead provide a statement under paragraph (i)(1)(iii) of this section if the applicant amends its 505(b)(2) application such that the applicant is no longer seeking approval for a method of use claimed by the patent. Once an amendment for the change has been submitted, the 505(b)(2) application will no longer be considered to contain a paragraph IV certification to the patent. If a final decision finds the patent to be invalid and infringed, an amended certification is not required.

(ii) *After request to remove a patent or patent information from the list.* If the list reflects that an NDA holder has requested that a patent or patent information be removed from the list and no ANDA applicant is eligible for 180-day exclusivity based on a paragraph IV certification to that patent, the patent or patent information will be removed and any applicant with a pending 505(b)(2) application (including a tentatively approved 505(b)(2) application) who has made a certification with respect to such patent must submit an amendment to withdraw its certification. In the amendment, the applicant must state the reason for withdrawing the certification or statement (that the patent has been removed from the list). If the list reflects that an NDA

holder has requested that a patent or patent information be removed from the list and one or more first applicants are eligible for 180-day exclusivity based on a paragraph IV certification to that patent, the patent will remain listed until any 180-day exclusivity based on that patent has expired or has been extinguished. A 505(b)(2) applicant is not required to provide or maintain a certification to a patent or patent information that remains listed only for purposes of a first applicant's 180-day exclusivity for its ANDA. Once an amendment to withdraw the certification has been submitted, the 505(b)(2) application will no longer be considered to contain a paragraph IV certification to the patent. If removal of a patent from the list results in there being no patents listed for the listed drug(s) identified in the 505(b)(2) application, the applicant must submit an amended certification reflecting that there are no listed patents.

(iii) *Other amendments.* (A) Except as provided in paragraphs (i)(4) and (i)(6)(iii)(B) of this section:

(*1*) An applicant must amend a submitted certification or statement if, at any time before the approval of the 505(b)(2) application, the applicant learns that the submitted certification or statement is no longer accurate; and

(*2*) An applicant must submit an appropriate patent certification or statement under paragraph (i)(1) of this section if, after submission of the 505(b)(2) application, a new patent is issued by the U.S. Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims a listed drug relied upon or that claims an approved use for such listed drug for which information is required to be filed under section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53.

(B) An applicant is not required to submit a supplement to change a submitted certification when information on an otherwise applicable patent is submitted after the approval of the 505(b)(2) application.

(j) *Claimed exclusivity.* A new drug product, upon approval, may be entitled to a period of marketing exclusivity under the provisions of § 314.108. If an applicant believes its drug product is entitled to a period of exclusivity, it must submit with the NDA prior to approval the following information:

(1) A statement that the applicant is claiming exclusivity.

(2) A reference to the appropriate paragraph under § 314.108 that supports its claim.

(3) If the applicant claims exclusivity under § 314.108(b)(2), information to show that, to the best of its knowledge or belief, a drug has not previously been approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act containing any active moiety in the drug for which the applicant is seeking approval.

(4) If the applicant claims exclusivity under § 314.108(b)(4) or (b)(5), the following information to show that the NDA contains “new clinical investigations” that are “essential to approval of the NDA or supplement” and were “conducted or sponsored by the applicant:”

(i) *“New clinical investigations.* ” A certification that to the best of the applicant's knowledge each of the clinical investigations included in the NDA meets the definition of “new clinical investigation” set forth in § 314.108(a).

(ii) *“Essential to approval.”* A list of all published studies or publicly available reports of clinical investigations known to the applicant through a literature search that are relevant to the conditions for which the applicant is seeking approval, a certification that the applicant has thoroughly searched the scientific literature and, to the best of the applicant's knowledge, the list is complete and accurate and, in the applicant's opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval

of the conditions for which the applicant is seeking approval without reference to the new clinical investigation(s) in the NDA, and an explanation as to why the studies or reports are insufficient.

(iii) *"Conducted or sponsored by."* If the applicant was the sponsor named in the Form FDA 1571 for an IND under which the new clinical investigation(s) that is essential to the approval of its NDA was conducted, identification of the IND by number. If the applicant was not the sponsor of the IND under which the clinical investigation(s) was conducted, a certification that the applicant or its predecessor in interest provided substantial support for the clinical investigation(s) that is essential to the approval of its NDA, and information supporting the certification. To demonstrate "substantial support," an applicant must either provide a certified statement from a certified public accountant that the applicant provided 50 percent or more of the cost of conducting the study or provide an explanation of why FDA should consider the applicant to have conducted or sponsored the study if the applicant's financial contribution to the study is less than 50 percent or the applicant did not sponsor the investigational new drug. A predecessor in interest is an entity, e.g., a corporation, that the applicant has taken over, merged with, or purchased, or from which the applicant has purchased all rights to the drug. Purchase of nonexclusive rights to a clinical investigation after it is completed is not sufficient to satisfy this definition.

(k) *Financial certification or disclosure statement.* The NDA must contain a financial certification or disclosure statement or both as required by part 54 of this chapter.

(l) *Format of an original NDA* —(1) *Archival copy.* The applicant must submit a complete archival copy of the NDA that contains the information required under paragraphs (a) through (f) of this section. FDA will maintain the archival copy during the review of the NDA to permit individual reviewers to refer to information that is not contained in their particular technical sections of the NDA, to give other agency personnel access to the NDA for official business, and to maintain in one place a complete copy of the NDA. Except as required by paragraph (l)(1)(i) of this section, applicants may submit the archival copy on paper or in electronic format provided that electronic submissions are made in accordance with part 11 of this chapter.

(i) *Labeling.* The content of labeling required under § 201.100(d)(3) of this chapter (commonly referred to as the package insert or professional labeling), including all text, tables, and figures, must be submitted to the agency in electronic format as described in paragraph (l)(5) of this section. This requirement is in addition to the requirements of paragraph (e)(2)(ii) of this section that copies of the formatted label and all labeling be submitted. Submissions under this paragraph must be made in accordance with part 11 of this chapter, except for the requirements of § 11.10(a), (c) through (h), and (k), and the corresponding requirements of § 11.30.

(ii) [Reserved]

(2) *Review copy.* The applicant must submit a review copy of the NDA. Each of the technical sections, described in paragraphs (d)(1) through (6) of this section, in the review copy is required to be separately bound with a copy of the application form required under paragraph (a) of this section and a copy of the summary required under paragraph (c) of this section.

(3) *Field copy.* The applicant must submit a field copy of the NDA that contains the technical section described in paragraph (d)(1) of this section, a copy of the application form required under paragraph (a) of this section, a copy of the summary required under paragraph (c) of this section, and a certification that the

field copy is a true copy of the technical section described in paragraph (d)(1) of this section contained in the archival and review copies of the NDA.

(4) *Binding folders.* The applicant may obtain from FDA sufficient folders to bind the archival, the review, and the field copies of the NDA.

(5) *Electronic format submissions.* Electronic format submissions must be in a form that FDA can process, review, and archive. FDA will periodically issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files).

§ 314.52 Notice of certification of invalidity, unenforceability, or noninfringement of a patent.

(a) *Notice of certification.* For each patent that claims the listed drug or drugs relied upon or that claims a use for such listed drug or drugs and for which the 505(b)(2) applicant submits a paragraph IV certification, the applicant must send notice of such certification by registered or certified mail, return receipt requested, or by a designated delivery service, as defined in paragraph (g) of this section, to each of the following persons:

(1) Each owner of the patent that is the subject of the certification or the representative designated by the owner to receive the notice. The name and address of the patent owner or its representative may be obtained from the U.S. Patent and Trademark Office; and

(2) The holder of the approved NDA under section 505(b) of the Federal Food, Drug, and Cosmetic Act for each drug product which is claimed by the patent or a use of which is claimed by the patent and for which the applicant is seeking approval, or, if the NDA holder does not reside or maintain a place of business within the United States, the NDA holder's attorney, agent, or other authorized official. The name and address of the NDA holder or its attorney, agent, or authorized official may be obtained by sending a written or electronic communication to the Central Document Room, Attn: Orange Book Staff, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266, or to the Orange Book Staff at the email address listed on the Agency's Web site at *http://www.fda.gov*.

(3) This paragraph (a) does not apply to a method-of-use patent that does not claim a use for which the applicant is seeking approval.

(4) An applicant may send notice by an alternative method only if FDA has agreed in advance that the method will produce an acceptable form of documentation.

(b) *Sending the notice.* (1) Except as provided under paragraph (d) of this section, the applicant must send the notice required by paragraph (a) of this section on or after the date of filing described in § 314.101(a)(2) or (3), as applicable, but not later than 20 days after the date of the postmark on the paragraph IV acknowledgment letter. The 20-day clock described in this paragraph (b) begins on the day after the date of the postmark on the paragraph IV acknowledgment letter. When the 20th day falls on Saturday, Sunday, or a Federal holiday, the 20th day will be the next day that is not a Saturday, Sunday, or Federal holiday.

(2) Any notice required by paragraph (a) of this section is invalid if it is sent before the date of filing described in § 314.101(a)(2) or, if FDA notifies the applicant that FDA has refused to file the 505(b)(2) application, before the date described in § 314.101(a)(3) on which the 505(b)(2) application is filed. The applicant will not have complied with this paragraph (b) until it sends valid notice.

(3) The applicant must submit to FDA an amendment to its 505(b)(2) application that includes a statement certifying that the notice has been provided to each person identified under paragraph (a) of this section and that the notice met the content requirement under paragraph (c) of this section. A copy of the notice itself need not be submitted to the Agency.

(c) *Content of a notice.* In the notice, the applicant must cite section 505(b)(3)(D) of the Federal Food, Drug, and Cosmetic Act and the notice must include, but is not limited to, the following information:

(1) A statement that a 505(b)(2) application that contains any required bioavailability or bioequivalence studies has been submitted by the applicant and filed by FDA.

(2) The NDA number.

(3) The established name, if any, as defined in section 502(e)(3) of the Federal Food, Drug, and Cosmetic Act, of the proposed drug product.

(4) The active ingredient, strength, and dosage form of the proposed drug product.

(5) The patent number and expiration date of each patent on the list alleged to be invalid, unenforceable, or not infringed.

(6) A detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed. The applicant must include in the detailed statement:

(i) For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed.

(ii) For each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation.

(7) If the applicant alleges that the patent will not be infringed and the applicant seeks to preserve the option to later file a civil action for declaratory judgment in accordance with section 505(c)(3)(D) of the Federal Food, Drug, and Cosmetic Act, then the notice must be accompanied by an offer of confidential access to the 505(b)(2) application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the paragraph IV certification.

(8) If the applicant does not reside or have a place of business in the United States, the name and address of an agent in the United States authorized to accept service of process for the applicant.

(d) *Amendment or supplement to a 505(b)(2) application.* (1) If, after the date of filing described in § 314.101(a)(2) or (3), as applicable, an applicant submits an amendment or supplement to its 505(b)(2) application that includes a paragraph IV certification, the applicant must send the notice required by paragraph (a) of this section at the same time that the amendment or supplement to the 505(b)(2) application is submitted to FDA, regardless of whether the applicant has already given notice with respect to another such certification contained in the 505(b)(2) application or in an amendment or supplement to the 505(b)(2) application.

(2) If, before the date of filing described in § 314.101(a)(2) or (3), as applicable, an applicant submits a paragraph IV certification in an amendment, the applicant must send the notice required by paragraph (a) of this section in accordance with the procedures in paragraph (b) of this section.

(3) An applicant that submits an amendment or supplement to seek approval of a different strength must provide notice of any paragraph IV certification in accordance with paragraph (d)(1) or (2) of this section, as applicable.

(e) *Documentation of timely sending and receipt of notice.* The applicant must amend its 505(b)(2) application to provide documentation of the date of receipt of the notice required under paragraph (a) of this section by each person provided the notice. The amendment must be submitted to FDA within 30 days after the last date on which notice was received by a person described in paragraph (a) of this section. The applicant's amendment also must include documentation that its notice was sent on a date that complies with the timeframe required by paragraph (b) or (d) of this section, as applicable. FDA will accept, as adequate documentation of the date the notice was sent, a copy of the registered mail receipt, certified mail receipt, or receipt from a designated delivery service, as defined in paragraph (g) of this section. FDA will accept as adequate documentation of the date of receipt a return receipt, a signature proof of delivery by a designated delivery service, or a letter acknowledging receipt by the person provided the notice. An applicant may rely on another form of documentation only if FDA has agreed to such documentation in advance. A copy of the notice itself need not be submitted to the Agency.

(f) *Forty-five day period after receipt of notice.* If the requirements of this section are met, the Agency will presume the notice to be complete and sufficient and will count the day following the date of receipt of the notice by the patent owner or its representative and by the approved NDA holder or its attorney, agent, or other authorized official as the first day of the 45-day period provided for in section 505(c)(3)(C) of the Federal Food, Drug, and Cosmetic Act. FDA may, if the applicant amends its 505(b)(2) application with a written statement that a later date should be used, count from such later date.

(g) *Designated delivery services.* (1) For purposes of this section, the term “designated delivery service” is any delivery service provided by a trade or business that the Agency determines:(i) Is available to the general public throughout the United States;(ii) Records electronically to its database, kept in the regular course of its business, or marks on the cover in which any item referred to in this section is to be delivered, the date on which such item was given to such trade or business for delivery; and(iii) Provides overnight or 2-day delivery service throughout the United States.(2) FDA may periodically issue guidance regarding designated delivery services.

§ 314.53 Submission of patent information.

(a) *Who must submit patent information.* This section applies to any applicant who submits to FDA an NDA or an amendment to it under section 505(b) of the Federal Food, Drug, and Cosmetic Act and § 314.50 or a supplement to an approved NDA under § 314.70, except as provided in paragraph (d)(2) of this section.

(b) *Patents for which information must be submitted and patents for which information must not be submitted —*(1) *General requirements.* An applicant described in paragraph (a) of this section must submit to its NDA the required information, on the required FDA declaration form, set forth in paragraph (c) of this section for each patent that claims the drug or a method of using the drug that is the subject of the NDA or amendment or supplement to it and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. For purposes of this part, such patents consist of drug substance (active ingredient) patents, drug product (formulation and composition) patents, and method-of-use patents. For patents that claim the drug substance,

the applicant must submit information only on those patents that claim the drug substance that is the subject of the pending or approved NDA or that claim a drug substance that is the same as the active ingredient that is the subject of the approved or pending NDA. For patents that claim only a polymorph that is the same as the active ingredient described in the approved or pending NDA, the applicant must certify in the required FDA declaration form that the applicant has test data, as set forth in paragraph (b)(2) of this section, demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA. For patents that claim a drug product, the applicant must submit information only on those patents that claim the drug product, as is defined in § 314.3, that is described in the pending or approved NDA. For patents that claim a method of use, the applicant must submit information only on those patents that claim indications or other conditions of use for which approval is sought or has been granted in the NDA. The applicant must separately identify each pending or approved method of use and related patent claim(s). For approved NDAs, the NDA holder's description of the patented method of use required by paragraph (c)(2)(ii)(P)(*3*) of this section must describe only the approved method(s) of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. If the method(s) of use claimed by the patent does not cover an indication or other approved condition of use in its entirety, the applicant must describe only the specific approved method of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. For approved NDAs, the NDA holder submitting information on the method-of-use patent must identify with specificity the section(s) and subsection(s) of the approved labeling that describes the method(s) of use claimed by the patent submitted. Process patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates are not covered by this section, and information on these patents must not be submitted to FDA.

(2) *Test data for submission of patent information for patents that claim only a polymorph.* The test data, referenced in paragraph (b)(1) of this section, must include the following:

(i) A full description of the polymorphic form of the drug substance, including its physical and chemical characteristics and stability; the method of synthesis (or isolation) and purification of the drug substance; the process controls used during manufacture and packaging; and such specifications and analytical methods as are necessary to assure the identity, strength, quality, and purity of the polymorphic form of the drug substance;

(ii) The executed batch record for a drug product containing the polymorphic form of the drug substance and documentation that the batch was manufactured under current good manufacturing practice requirements;

(iii) Demonstration of bioequivalence between the executed batch of the drug product that contains the polymorphic form of the drug substance and the drug product as described in the NDA;

(iv) A list of all components used in the manufacture of the drug product containing the polymorphic form and a statement of the composition of the drug product; a statement of the specifications and analytical methods for each component; a description of the manufacturing and packaging procedures and in-process controls for the drug product; such specifications and analytical methods as are necessary to assure the identity, strength, quality, purity, and bioavailability of the drug product, including release and stability data complying with the

approved product specifications to demonstrate pharmaceutical equivalence and comparable product stability; and

(v) Comparative in vitro dissolution testing on 12 dosage units each of the executed test batch and the NDA product.

(c) *Reporting requirements* —(1) *General requirements.* An applicant described in paragraph (a) of this section must submit the required patent information described in paragraph (c)(2) of this section for each patent that meets the requirements described in paragraph (b) of this section. We will not accept the patent information unless it is submitted on the appropriate form, Form FDA 3542 or 3542a, and contains the information required in paragraph (c)(2) of this section. These forms may be obtained on the Internet at *http://www.fda.gov* by searching for "forms".

(2) *Drug substance (active ingredient), drug product (formulation or composition), and method-of-use patents* —(i) *Original declaration.* For each patent that claims a drug substance (active ingredient), drug product (formulation and composition), or method of use, the applicant must submit Form FDA 3542a. The following information and verification is required, subject to the exceptions listed in paragraph (c)(2)(i)(S) of this section:

(A) NDA number;

(B) The NDA applicant's name, full address, phone number and, if available, fax number and email address;

(C) Trade name (or proposed trade name) of new drug;

(D) Active ingredient(s) of new drug;

(E) Strength(s) of new drug;

(F) Dosage form(s) and route(s) of administration of new drug, and whether the applicant proposes to market the new drug for prescription use or over-the-counter use;

(G) U.S. patent number, issue date, and expiration date of patent submitted;

(H) The patent owner's name, full address, phone number and, if available, fax number and email address;

(I) The name, full address, phone number and, if available, fax number and email address of an agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and §§ 314.52 and 314.95 (if patent owner or NDA applicant or holder does not reside or have a place of business within the United States);

(J) Information on whether the patent has been submitted previously for the NDA or supplement;

(K) If the patent has been submitted previously for listing, identify all change(s) from the previously submitted patent information and specify whether the change is related to the patent or related to an FDA action or procedure;

(L) Information on whether the patent is a product-by-process patent in which the product claimed is novel;

(M) Information on the drug substance (active ingredient) patent, including the following:

(*1*) Whether the patent claims a drug substance that is an active ingredient in the drug product described in the NDA or supplement;

(*2*) Whether the patent claims only a polymorph that is the same active ingredient that is described in the pending NDA or supplement;

(*3*) Whether the applicant has test data, described in paragraph (b)(2) of this section, demonstrating that a drug product containing only the polymorph will perform the same as the drug product described in the NDA or supplement, and a description of the polymorphic form(s) claimed by the patent for which such test data exist;

(*4*) Whether the patent claims only a metabolite of the active ingredient; and

(*5*) Whether the patent claims only an intermediate;

(N) Information on the drug product (composition/formulation) patent, including the following:

(*1*) Whether the patent claims the drug product for which approval is being sought, as defined in § 314.3; and

(*2*) Whether the patent claims only an intermediate;

(O) Information on each method-of-use patent, including the following:

(*1*) Whether the patent claims one or more methods of using the drug product for which approval is being sought and a description of each pending method of use and related patent claim of the patent being submitted;

(*2*) Identification of the specific section(s) and subsection(s) of the proposed labeling for the drug product that describes the method of use claimed by the patent submitted; and

(*3*) An applicant that submits information for a patent that claims one or more methods of using the drug product must also submit information described in either paragraph (c)(2)(i)(M) or (N) of this section, regarding whether that patent also claims either the drug substance (active ingredient) or the drug product (composition/formulation).

(P) Whether there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition), or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product;

(Q) A signed verification that states:

THE UNDERSIGNED DECLARES THAT THIS IS AN ACCURATE AND COMPLETE SUBMISSION OF PATENT INFORMATION FOR THE NDA, AMENDMENT, OR SUPPLEMENT PENDING UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT. THIS TIME-SENSITIVE PATENT INFORMATION IS SUBMITTED PURSUANT TO 21 CFR 314.53. I ATTEST THAT I AM FAMILIAR WITH 21 CFR 314.53 AND THIS SUBMISSION COMPLIES WITH THE REQUIREMENTS OF THE REGULATION. I VERIFY UNDER PENALTY OF PERJURY THAT THE FOREGOING IS TRUE AND CORRECT.

(R) Information on whether the applicant, patent owner or attorney, agent, representative, or other authorized official signed the form; the name of the person; and the full address, phone number and, if available, the fax number and email address; and

(S) Exceptions to required submission of patent information:

(*1*) If an applicant submits the information described in paragraph (c)(2)(i)(M) of this section for a patent that claims the drug substance (active ingredient) and meets the requirements for listing on that basis, then the

applicant is not required to provide the information described in paragraph (c)(2)(i)(N) of this section on whether that patent also claims the drug product (composition/formulation);

(*2*) If an applicant submits the information described in paragraph (c)(2)(i)(N) of this section for a patent that claims the drug product (composition/formulation) and meets the requirements for listing on that basis, then the applicant is not required to provide the information described in paragraph (c)(2)(i)(M) of this section on whether that patent also claims the drug substance (active ingredient);

(*3*) If the applicant submits a supplement for a change other than one of the changes listed under paragraph (d)(2)(i) of this section, then the patent information submission requirements of paragraph (d)(2)(ii) of this section apply.

(ii) *Submission of patent information upon and after approval.* Within 30 days after the date of approval of its NDA or supplement, the applicant must submit Form FDA 3542 for each patent that claims the drug substance (active ingredient), drug product (formulation and composition), or approved method of use. FDA will not list or publish patent information if it is not provided on this form or if the patent declaration does not contain the required information or indicates the patent is not eligible for listing. Patent information must also be submitted for patents issued after the date of approval of the NDA as required in paragraph (c)(2)(ii) of this section. As described in paragraph (d)(3) of this section, to be timely filed, patent information for patents issued after the date of approval of the NDA must be submitted to FDA within 30 days of the date of issuance of the patent. If the applicant submits the required patent information within the 30 days, but we notify an applicant that a declaration form is incomplete or shows that the patent is not eligible for listing, the applicant must submit an acceptable declaration form within 15 days of FDA notification to be considered timely filed. The following information and verification statement is required, subject to the exceptions listed in paragraph (c)(2)(ii)(T) of this section:

(A) NDA number;

(B) The NDA holder's name, full address, phone number and, if available, fax number and email address;

(C) Trade name of new drug;

(D) Active ingredient(s) of new drug;

(E) Strength(s) of new drug;

(F) Dosage form(s) and route(s) of administration of new drug, and whether the new drug is approved for prescription use or over-the-counter use;

(G) Approval date of NDA or supplement;

(H) U.S. patent number, issue date, and expiration date of patent submitted;

(I) The patent owner's name, full address, phone number and, if available, fax number and email address;

(J) The name, full address, phone number and, if available, fax number and email address of an agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and §§ 314.52 and 314.95 (if patent owner or NDA applicant or holder does not reside or have a place of business within the United States);

(K) Information on whether the patent has been submitted previously for the NDA or supplement;

(L) If the patent has been submitted previously for listing, identify all change(s) from the previously submitted patent information and specify whether the change is related to the patent or related to an FDA action or procedure;

(M) Information on whether the patent is a product-by-process patent in which the product claimed is novel;

(N) Information on the drug substance (active ingredient) patent, including the following:

(*1*) Whether the patent claims a drug substance that is an active ingredient in the drug product described in the approved NDA;

(*2*) Whether the patent claims only a polymorph that is the same as the active ingredient that is described in the approved NDA;

(*3*) Whether the applicant has test data, described in paragraph (b)(2) of this section, demonstrating that a drug product containing only the polymorph will perform the same as the drug product described in the approved NDA and a description of the polymorphic form(s) claimed by the patent for which such test data exist;

(*4*) Whether the patent claims only a metabolite of the active ingredient; and

(*5*) Whether the patent claims only an intermediate;

(O) Information on the drug product (composition/formulation) patent, including the following:

(*1*) Whether the patent claims the approved drug product as defined in § 314.3; and

(*2*) Whether the patent claims only an intermediate;

(P) Information on each method-of-use patent, including the following:

(*1*) Whether the patent claims one or more approved methods of using the approved drug product and a description of each approved method of use and related patent claim of the patent being submitted;

(*2*) Identification of the specific section(s) and subsection(s) of the approved labeling for the drug product that describes the method of use claimed by the patent submitted;

(*3*) The description of the patented method of use as required for publication, which must contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method-of-use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval (for example, if the method(s) of use claimed by the patent does not cover an indication or other approved condition of use in its entirety, then the applicant must describe only the specific approved method of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product); and

(*4*) An applicant that submits information for a patent that claims one or more methods of using the drug product must also submit information described in either paragraph (c)(2)(ii)(N) or (O) of this section, regarding whether that patent also claims either the drug substance (active ingredient) or the drug product (composition/formulation).

(Q) Whether there are no relevant patents that claim the approved drug substance (active ingredient), the approved drug product (formulation or composition), or approved method(s) of use and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product;

(R) A signed verification that states:

THE UNDERSIGNED DECLARES THAT THIS IS AN ACCURATE AND COMPLETE SUBMISSION OF PATENT INFORMATION FOR THE NDA, AMENDMENT, OR SUPPLEMENT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT. THIS TIME-SENSITIVE PATENT INFORMATION OR RESPONSE TO A REQUEST UNDER 21 CFR 314.53(F)(1) IS SUBMITTED PURSUANT TO 21 CFR 314.53. I ATTEST THAT I AM FAMILIAR WITH 21 CFR 314.53 AND THIS SUBMISSION COMPLIES WITH THE REQUIREMENTS OF THE REGULATION. I VERIFY UNDER PENALTY OF PERJURY THAT THE FOREGOING IS TRUE AND CORRECT.

(S) Information on whether the applicant, patent owner or attorney, agent, representative, or other authorized official signed the form; the name of the person; and the full address, phone number and, if available, the fax number and email address; and

(T) Exceptions to required submission of patent information:

(*1*) If an applicant submits the information described in paragraph (c)(2)(ii)(N) of this section for a patent that claims the drug substance (active ingredient) and meets the requirements for listing on that basis, then the applicant is not required to provide the information described in paragraph (c)(2)(ii)(O) of this section on whether that patent also claims the drug product (composition/formulation).

(*2*) If an applicant submits the information described in paragraph (c)(2)(ii)(O) of this section for a patent that claims the drug product (composition/formulation) and meets the requirements for listing on that basis, then the applicant is not required to provide the information described in paragraph (c)(2)(ii)(N) of this section on whether that patent also claims the drug substance (active ingredient).

(*3*) If the applicant submits a supplement for a change other than one of the changes listed under paragraph (d)(2)(i) of this section, then the patent information submission requirements of paragraph (d)(2)(ii) of this section apply.

(3) *No relevant patents.* If the applicant believes that there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition), or the method(s) of use for which the applicant has received approval, and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product, the applicant will verify this information in the appropriate form, Form FDA 3542 or 3542a.

(4) *Authorized signature.* The declarations required by this section must be signed by the applicant or patent owner, or the applicant's or patent owner's attorney, agent (representative), or other authorized official.

(d) *When and where to submit patent information* —(1) *Original NDA.* An applicant must submit with its original NDA submitted under this part, the information described in paragraph (c) of this section on each drug substance (active ingredient), drug product (formulation and composition), and method-of-use patent issued before the NDA is filed with FDA and for which patent information is required to be submitted under this section. If a patent is issued after the NDA is filed with FDA but before the NDA is approved, the applicant must, within 30 days of the date of issuance of the patent, submit the required patent information in an amendment to the NDA under § 314.60.

(2) *Supplements.* (i) An applicant must submit patent information required under paragraph (c) of this section for a patent that claims the drug substance, drug product, or method of use for which approval is sought in any of the following supplements:

(A) To add or change the dosage form or route of administration;

(B) To add or change the strength; or

(C) To change the drug product from prescription use to over-the-counter use.

(ii) If the applicant submits a supplement for a change other than one of the changes listed under paragraph (d)(2)(i) of this section (for example, to change the formulation, to add a new indication or other condition of use, or to make any other patented change regarding the drug substance, drug product, or any method of use), the following patent information submission requirements apply:

(A) If existing patents for which information required by paragraph (c) of this section has already been submitted to FDA for the product approved in the original NDA claim the changed product, the applicant is not required to resubmit this patent information pursuant to paragraph (c) of this section unless the published description of the patented method of use would change upon approval of the supplement, and FDA will continue to list this patent information for the product;

(B) If one or more existing patents for which information has already been submitted to FDA no longer claim the changed product, the applicant must submit a request under paragraph (f)(2)(iv) of this section to remove that patent information from the list at the time of approval of the supplement;

(C) If one or more existing drug substance (active ingredient), drug product (formulation and composition), or method-of-use patents claim the changed product for which approval is sought in the supplement and such patent information has not been submitted to FDA, the applicant must submit the patent information required under paragraph (c) of this section.

(3) *Newly issued patents.* If a patent is issued for a drug substance, drug product, or method of use after an NDA is approved, the applicant must submit to FDA, as described in paragraph (d)(4) of this section, the required patent information within 30 days of the date of issuance of the patent. If the required patent information is not submitted within 30 days of the issuance of the patent, FDA will list the patent, but patent certifications or statements will be governed by the provisions regarding untimely filed patent information at §§ 314.50(i)(4) and (6) and 314.94(a)(12)(vi) and (viii).

(4) *Submission of Forms FDA 3542a and 3542 —*(i) *Patent information submitted with the filing of an NDA, amendment, or supplement.* The applicant must submit patent information required by paragraphs (c)(1) and (c)(2)(i) of this section and § 314.50(h) or § 314.70(f) on Form FDA 3542a to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266, or to FDA in an electronic format submission that complies with § 314.50(l)(5). Form FDA 3542a should not be submitted to the Orange Book Staff in the Office of Generic Drugs.

(ii) *Patent information submitted upon and after approval of an NDA or supplement.* The applicant must submit patent information required by paragraphs (c)(1) and (c)(2)(ii) of this section on Form FDA 3542 to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266, or to FDA in an electronic format submission that complies

with § 314.50(l)(5). Form FDA 3542 should not be submitted to the Orange Book Staff in the Office of Generic Drugs.

(5) *Submission date.* Patent information will be considered to be submitted to FDA for purposes of paragraph (d)(3) of this section as of the earlier of the date the information submitted on Form FDA 3542 is date-stamped by the Central Document Room, or officially received by FDA in an electronic format submission that complies with § 314.50(l)(5).

(6) *Identification.* Each submission of patent information, except information submitted with an original NDA, must bear prominent identification as to its contents, *i.e.* "Patent Information," or, if submitted after approval of an NDA, "Time Sensitive Patent Information."

(e) *Public disclosure of patent information.* FDA will publish in the list the patent number and expiration date of each patent that is required to be, and is, submitted to FDA by an applicant, and for each method-of-use patent, the description of the method of use claimed by the patent as required by § 314.53(c)(2)(ii)(P)(*3*). FDA will publish such patent information upon approval of the NDA, or, if the patent information is submitted by the applicant after approval of an NDA as provided under paragraph (d)(2) of this section, as soon as possible after the submission to the Agency of the patent information. A request for copies of the submitted patent information must be sent in writing to the Freedom of Information Staff at the address listed on the Agency's Web site at *http://www.fda.gov* . The submitted patent information, and requests to remove a patent or patent information from the list, may be subject to public disclosure.

(f) *Correction of patent information errors* —(1) *Requests by persons other than the NDA holder.* If any person disputes the accuracy or relevance of patent information submitted to the Agency under this section and published by FDA in the list, or believes that an NDA holder has failed to submit required patent information, that person must first notify the Agency in a written or electronic communication titled "314.53(f) Patent Listing Dispute." The patent listing dispute communication must include a statement of dispute that describes the specific grounds for disagreement regarding the accuracy or relevance of patent information for FDA to send to the applicable NDA holder. For a dispute regarding the accuracy or relevance of patent information regarding an approved method of using the drug product, this statement of dispute must be only a narrative description (no more than 250 words) of the person's interpretation of the scope of the patent. This statement of dispute must only contain information for which the person consents to disclosure because FDA will send the text of the statement to the applicable NDA holder without review or redaction. The patent listing dispute communication should be directed to the Central Document Room, Attn: Orange Book Staff, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266, or to the Orange Book Staff at the email address listed on the Agency's Web site at *http://www.fda.gov* .

(i) *Communication with the NDA holder* —(A) *Drug substance or drug product claim.* For requests submitted under this paragraph (f)(1) that are directed to the accuracy or relevance of submitted patent information regarding a drug substance or drug product claim, the Agency will send the statement of dispute to the applicable NDA holder. The NDA holder must confirm the correctness of the patent information and include

the signed verification required by paragraph (c)(2)(ii)(R) of this section or withdraw or amend the patent information in accordance with paragraph (f)(2) of this section within 30 days of the date on which the Agency sends the statement of dispute. Unless the NDA holder withdraws or amends its patent information in response to the patent listing dispute, the Agency will not change the patent information in the Orange Book.

(B) *Method-of-use claim.* For requests submitted under this paragraph (f)(1) that are directed to the accuracy or relevance of submitted patent information regarding an approved method of using the drug product, FDA will send the statement of dispute to the NDA holder. The NDA holder must confirm the correctness of its description of the approved method of use claimed by the patent that has been included as the "Use Code" in the Orange Book, or withdraw or amend the patent information in accordance with paragraph (f)(2) of this section, provide a narrative description (no more than 250 words) of the NDA holder's interpretation of the scope of the patent that explains why the existing or amended "Use Code" describes only the specific approved method of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product, and include the signed verification required by paragraph (c)(2)(ii)(R) of this section within 30 days of the date on which the Agency sends the statement of dispute. The narrative description must only contain information for which the NDA holder consents to disclosure because FDA will send the text of the statement to the person who submitted the patent listing dispute without review or redaction.

(*1*) If the NDA holder confirms the correctness of the patent information, provides the narrative description required by paragraph (f)(1)(i)(B) of this section, and includes the signed verification required by paragraph (c)(2)(ii)(R) of this section within 30 days of the date on which the Agency sends the statement of dispute, the Agency will not change the patent information in the Orange Book.

(*2*) If the NDA holder responds to the patent listing dispute with amended patent information in accordance with paragraph (f)(2) of this section, provides the narrative description required by paragraph (f)(1)(i)(B) of this section, and includes the signed verification required by paragraph (c)(2)(ii)(R) of this section within 30 days of the date on which the Agency sends the statement of dispute, FDA will update the Orange Book to reflect the amended patent information.

(ii) *Patent certification or statement during and after patent listing dispute.* A 505(b)(2) application or ANDA must contain an appropriate certification or statement for each listed patent, including the disputed patent, during and after the patent listing dispute.

(iii) *Information on patent listing disputes.* FDA will promptly post information on its Web site regarding whether a patent listing dispute has been submitted for a published description of a patented method of use for a drug product and whether the NDA holder has timely responded to the patent listing dispute.

(2) *Requests by the NDA holder —*(i) *Patents or patent claims that no longer meet the statutory requirements for listing.* If the NDA holder determines that a patent or patent claim no longer meets the requirements for listing in section 505(b)(1) or (c)(2) of the Federal Food, Drug, and Cosmetic Act (including if there has been a judicial finding of invalidity for a listed patent, from which no appeal has been or can be taken), the NDA holder is required to promptly notify FDA to amend the patent information or withdraw the patent or patent information and request that the patent or patent information be removed from the list. If the NDA holder is required by court order to amend patent information or withdraw a patent from the list, it must submit an

amendment to its NDA that includes a copy of the order, within 14 days of the date the order was entered, to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266. The amendment to the NDA must bear the identification described in paragraph (d)(6) of this section. FDA will remove a patent or patent information from the list if there is no first applicant eligible for 180-day exclusivity based on a paragraph IV certification to that patent or after the 180-day exclusivity period of a first applicant based on that patent has expired or has been extinguished.

(ii) *Patent term restoration.* If the term of a listed patent is extended pursuant to 35 U.S.C. 156(e), the NDA holder must submit on Form FDA 3542 a correction to the expiration date of the patent. This correction must be submitted within 30 days of receipt of a certificate of extension as described in 35 U.S.C. 156(e)(1) or documentation of an extension of the term of the patent as described in 35 U.S.C. 156(e)(2).

(iii) *Submission of corrections or changes to patent information.* Corrections or changes to previously submitted patent information, other than withdrawal of a patent and requests to remove a patent from the list, must be submitted on Form FDA 3542 or 3542a, as appropriate, in an amendment or supplement to the NDA. The amendment or supplement to the NDA must bear the identification described in paragraph (d)(6) of this section. We will not accept the corrections or changes unless they are submitted on the appropriate forms.

(iv) *Submission of patent withdrawals and requests to remove a patent from the list.* Withdrawal of a patent and requests to remove a patent from the list must be submitted to the same addresses described in paragraph (d)(4)(ii) of this section, except that the withdrawal or request to remove a patent from the list is not required to be submitted on Form FDA 3542 and may be submitted by letter. Withdrawal of a patent and a request to remove a patent from the list must contain the following information:

(A) The NDA number to which the request applies;

(B) Each product(s) approved in the NDA to which the request applies; and

(C) The patent number.

§ 314.54 Procedure for submission of a 505(b)(2) application requiring investigations for approval of a new indication for, or other change from, a listed drug.

(a) The Federal Food, Drug, and Cosmetic Act does not permit approval of an ANDA for a new indication, nor does it permit approval of other changes in a listed drug if investigations, other than bioavailability or bioequivalence studies, are essential to the approval of the change. Any person seeking approval of a drug product that represents a modification of a listed drug (e.g., a new indication or new dosage form) and for which investigations, other than bioavailability or bioequivalence studies, are essential to the approval of the changes may, except as provided in paragraph (b) of this section, submit a 505(b)(2) application. This 505(b)(2) application need contain only that information needed to support the modification(s) of the listed drug.

(1) The applicant must submit a complete archival copy of the application that contains the following:(i) The information required under § 314.50(a), (b), (c), (d)(1), (d)(3), (e), and (g), except that § 314.50(d)(1)(ii)(*c*) must contain the proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product.

(ii) The information required under § 314.50 (d)(2), (d)(4) (if an anti-infective drug), (d)(5), (d)(6), and (f) as needed to support the safety and effectiveness of the drug product.

(iii) Identification of each listed drug for which FDA has made a finding of safety and effectiveness and on which finding the applicant relies in seeking approval of its proposed drug product by established name, if any, proprietary name, dosage form, strength, route of administration, name of listed drug's application holder, and listed drug's approved NDA number. The listed drug(s) identified as relied upon must include a drug product approved in an NDA that:

(A) Is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application is submitted; and

(B) Was approved before the original 505(b)(2) application was submitted.

(iv) If the applicant is seeking approval only for a new indication and not for the indications approved for the listed drug on which the applicant relies, a certification so stating.

(v) Any patent information required under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act with respect to any patent which claims the drug for which approval is sought or a method of using such drug and to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

(vi) Any patent certification or statement required under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act with respect to any relevant patents that claim the listed drug(s) on which investigations relied on by the applicant for approval of the application were conducted, or that claim a use for the listed drug(s). A 505(b)(2) applicant seeking approval of a drug that is pharmaceutically equivalent to a listed drug approved in an NDA implicitly relies upon one such pharmaceutically equivalent listed drug.

(vii) If the applicant believes the change for which it is seeking approval is entitled to a period of exclusivity, the information required under § 314.50(j).

(2) The applicant must submit a review copy that contains the technical sections described in § 314.50(d)(1), except that the section described in § 314.50(d)(1)(ii)(*c*) must contain the proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product, and § 314.50(d)(3), and the technical sections described in § 314.50(d)(2), (d)(4) through (6), and (f) when needed to support the modification. Each of the technical sections in the review copy is required to be separately bound with a copy of the information required under § 314.50(a), (b), and (c) and a copy of the proposed labeling.

(3) The information required by § 314.50 (d)(2), (d)(4) (if an anti-infective drug), (d)(5), (d)(6), and (f) for the listed drug on which the applicant relies must be satisfied by reference to the listed drug under paragraph (a)(1)(iii) of this section.

(4) The applicant must submit a field copy of the 505(b)(2) application that contains the technical section described in § 314.50(d)(1), a copy of the information required under § 314.50(a) and (c), and certification that the field copy is a true copy of the technical section described in § 314.50(d)(1) contained in the archival and review copies of the 505(b)(2) application.

(b) A 505(b)(2) application may not be submitted under this section for a drug product whose only difference from a listed drug is that:

(1) The extent to which its active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the listed drug; or

(2) The rate at which its active ingredient(s) is absorbed or otherwise made available to the site of action is unintentionally less than that of the listed drug.

§ 314.55 Pediatric use information.

(a) *Required assessment.* Except as provided in paragraphs (b), (c), and (d) of this section, each application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration shall contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. Where the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, FDA may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies. Studies may not be needed in each pediatric age group, if data from one age group can be extrapolated to another. Assessments of safety and effectiveness required under this section for a drug product that represents a meaningful therapeutic benefit over existing treatments for pediatric patients must be carried out using appropriate formulations for each age group(s) for which the assessment is required.

(b) *Deferred submission.* (1) FDA may, on its own initiative or at the request of an applicant, defer submission of some or all assessments of safety and effectiveness described in paragraph (a) of this section until after approval of the drug product for use in adults. Deferral may be granted if, among other reasons, the drug is ready for approval in adults before studies in pediatric patients are complete, or pediatric studies should be delayed until additional safety or effectiveness data have been collected. If an applicant requests deferred submission, the request must provide a certification from the applicant of the grounds for delaying pediatric studies, a description of the planned or ongoing studies, and evidence that the studies are being or will be conducted with due diligence and at the earliest possible time.

(2) If FDA determines that there is an adequate justification for temporarily delaying the submission of assessments of pediatric safety and effectiveness, the drug product may be approved for use in adults subject to the requirement that the applicant submit the required assessments within a specified time.

(c) *Waivers* —(1) *General.* FDA may grant a full or partial waiver of the requirements of paragraph (a) of this section on its own initiative or at the request of an applicant. A request for a waiver must provide an adequate justification.

(2) *Full waiver.* An applicant may request a waiver of the requirements of paragraph (a) of this section if the applicant certifies that:

(i) The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and is not likely to be used in a substantial number of pediatric patients;

(ii) Necessary studies are impossible or highly impractical because, e.g., the number of such patients is so small or geographically dispersed; or

(iii) There is evidence strongly suggesting that the drug product would be ineffective or unsafe in all pediatric age groups.

(3) *Partial waiver.* An applicant may request a waiver of the requirements of paragraph (a) of this section with respect to a specified pediatric age group, if the applicant certifies that:

(i) The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients in that age group, and is not likely to be used in a substantial number of patients in that age group;

(ii) Necessary studies are impossible or highly impractical because, e.g., the number of patients in that age group is so small or geographically dispersed;

(iii) There is evidence strongly suggesting that the drug product would be ineffective or unsafe in that age group; or

(iv) The applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(4) *FDA action on waiver.* FDA shall grant a full or partial waiver, as appropriate, if the agency finds that there is a reasonable basis on which to conclude that one or more of the grounds for waiver specified in paragraphs (c)(2) or (c)(3) of this section have been met. If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver will cover only those pediatric age groups requiring that formulation. If a waiver is granted because there is evidence that the product would be ineffective or unsafe in pediatric populations, this information will be included in the product's labeling.

(5) *Definition of "meaningful therapeutic benefit".* For purposes of this section and § 201.23 of this chapter, a drug will be considered to offer a meaningful therapeutic benefit over existing therapies if FDA estimates that:

(i) If approved, the drug would represent a significant improvement in the treatment, diagnosis, or prevention of a disease, compared to marketed products adequately labeled for that use in the relevant pediatric population. Examples of how improvement might be demonstrated include, for example, evidence of increased effectiveness in treatment, prevention, or diagnosis of disease, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of compliance, or evidence of safety and effectiveness in a new subpopulation; or

(ii) The drug is in a class of drugs or for an indication for which there is a need for additional therapeutic options.

(d) *Exemption for orphan drugs.* This section does not apply to any drug for an indication or indications for which orphan designation has been granted under part 316, subpart C, of this chapter.

§ 314.60 Amendments to an unapproved NDA, supplement, or resubmission.

(a) *Submission of NDA.* FDA generally assumes that when an original NDA, supplement to an approved NDA, or resubmission of an NDA or supplement is submitted to the Agency for review, the applicant believes that the Agency can approve the NDA, supplement, or resubmission as submitted. However, the applicant may submit an amendment to an NDA, supplement, or resubmission that has been filed under § 314.101 but is not yet approved.

(b) *Submission of major amendment.* (1) Submission of a major amendment to an original NDA, efficacy supplement, or resubmission of an NDA or efficacy supplement within 3 months of the end of the initial review cycle constitutes an agreement by the applicant under section 505(c) of the Federal Food, Drug, and Cosmetic Act to extend the initial review cycle by 3 months. (For references to a resubmission of an NDA or efficacy supplement in paragraph (b) of this section, the timeframe for reviewing the resubmission is the "review cycle" rather than the "initial review cycle.") FDA may instead defer review of the amendment until the subsequent review cycle. If the agency extends the initial review cycle for an original NDA, efficacy supplement, or resubmission under this paragraph, the division responsible for reviewing the NDA, supplement, or resubmission will notify the applicant of the extension. The initial review cycle for an original NDA, efficacy supplement, or resubmission of an NDA or efficacy supplement may be extended only once due to submission of a major amendment. FDA may, at its discretion, review any subsequent major amendment during the initial review cycle (as extended) or defer review until the subsequent review cycle.

(2) Submission of a major amendment to an original NDA, efficacy supplement, or resubmission of an NDA or efficacy supplement more than 3 months before the end of the initial review cycle will not extend the cycle. FDA may, at its discretion, review such an amendment during the initial review cycle or defer review until the subsequent review cycle.

(3) Submission of an amendment to an original NDA, efficacy supplement, or resubmission of an NDA or efficacy supplement that is not a major amendment will not extend the initial review cycle. FDA may, at its discretion, review such an amendment during the initial review cycle or defer review until the subsequent review cycle.

(4) Submission of a major amendment to a manufacturing supplement within 2 months of the end of the initial review cycle constitutes an agreement by the applicant under section 505(c) of the Federal Food, Drug, and Cosmetic Act to extend the initial review cycle by 2 months. FDA may instead defer review of the amendment until the subsequent review cycle. If the agency extends the initial review cycle for a manufacturing supplement under this paragraph, the division responsible for reviewing the supplement will notify the applicant of the extension. The initial review cycle for a manufacturing supplement may be extended only once due to submission of a major amendment. FDA may, at its discretion, review any subsequent major amendment during the initial review cycle (as extended) or defer review until the subsequent review cycle.

(5) Submission of an amendment to a supplement other than an efficacy or manufacturing supplement will not extend the initial review cycle. FDA may, at its discretion, review such an amendment during the initial review cycle or defer review until the subsequent review cycle.

(6) A major amendment may not include data to support an indication or claim that was not included in the original NDA, supplement, or resubmission, but it may include data to support a minor modification of an indication or claim that was included in the original NDA, supplement, or resubmission.

(7) When FDA defers review of an amendment until the subsequent review cycle, the agency will notify the applicant of the deferral in the complete response letter sent to the applicant under § 314.110 of this part.

(c) *Limitation on certain amendments.* (1) An unapproved NDA may not be amended if all of the following conditions apply:

(i) The unapproved NDA is for a drug for which a previous NDA has been approved and granted a period of exclusivity in accordance with section 505(c)(3)(E)(ii) of the Federal Food, Drug, and Cosmetic Act that has not expired;

(ii) The applicant seeks to amend the unapproved NDA to include a published report of an investigation that was conducted or sponsored by the applicant entitled to exclusivity for the drug;

(iii) The applicant has not obtained a right of reference or use to the investigation described in paragraph (c)(1)(ii) of this section; and

(iv) The report of the investigation described in paragraph (c)(1)(ii) of this section would be essential to the approval of the unapproved NDA.

(2) The submission of an amendment described in paragraph (c)(1) of this section will cause the unapproved NDA to be deemed to be withdrawn by the applicant under § 314.65 on the date of receipt by FDA of the amendment. The amendment will be considered a resubmission of the NDA, which may not be accepted except as provided in accordance with section 505(c)(3)(E)(ii) of the Federal Food, Drug, and Cosmetic Act.

(d) *Field copy.* The applicant must submit a field copy of each amendment to a section of the NDA described in § 314.50(d)(1). The applicant must include in its submission of each such amendment to FDA a statement certifying that a field copy of the amendment has been sent to the applicant's home FDA district office.

(e) *Different drug.* An applicant may not amend a 505(b)(2) application to seek approval of a drug that is a different drug from the drug in the original submission of the 505(b)(2) application. For purposes of this paragraph (e), a drug is a different drug if it has been modified to have a different active ingredient, different route of administration, different dosage form, or difference in excipients that requires either a separate clinical study to establish safety or effectiveness or, for topical products, that requires a separate in vivo demonstration of bioequivalence. However, notwithstanding the limitation described in this paragraph (e), an applicant may amend the 505(b)(2) application to seek approval of a different strength.

(f) *Patent certification requirements.* (1) An amendment to a 505(b)(2) application is required to contain an appropriate patent certification or statement described in § 314.50(i) or a recertification for a previously submitted paragraph IV certification if approval is sought for any of the following types of amendments:

(i) To add a new indication or other condition of use;

(ii) To add a new strength;

(iii) To make other than minor changes in product formulation; or

(iv) To change the physical form or crystalline structure of the active ingredient.

(2) If the amendment to the 505(b)(2) application does not contain a patent certification or statement, the applicant must verify that the proposed change described in the amendment is not one of the types of amendments described in paragraph (f)(1) of this section.

§ 314.65 Withdrawal by the applicant of an unapproved application.

An applicant may at any time withdraw an application that is not yet approved by notifying the Food and Drug Administration in writing. If, by the time it receives such notice, the agency has identified any deficiencies in the application, we will list such deficiencies in the letter we send the applicant acknowledging the withdrawal. A decision to withdraw the application is without prejudice to refiling. The agency will retain the application

and will provide a copy to the applicant on request under the fee schedule in § 20.45 of FDA's public information regulations.

§ 314.70 Supplements and other changes to an approved NDA.

(a) *Changes to an approved NDA.* (1)(i) Except as provided in paragraph (a)(1)(ii) of this section, the applicant must notify FDA about each change in each condition established in an approved NDA beyond the variations already provided for in the NDA. The notice is required to describe the change fully. Depending on the type of change, the applicant must notify FDA about the change in a supplement under paragraph (b) or (c) of this section or by inclusion of the information in the annual report to the NDA under paragraph (d) of this section.

(ii) The submission and grant of a written request for an exception or alternative under § 201.26 of this chapter satisfies the applicable requirements in paragraphs (a) through (c) of this section. However, any grant of a request for an exception or alternative under § 201.26 of this chapter must be reported as part of the annual report to the NDA under paragraph (d) of this section.

(2) The NDA holder must assess the effects of the change before distributing a drug product made with a manufacturing change.

(3) Notwithstanding the requirements of paragraphs (b) and (c) of this section, an applicant must make a change provided for in those paragraphs in accordance with a regulation or guidance that provides for a less burdensome notification of the change (for example, by submission of a supplement that does not require approval prior to distribution of the product or in an annual report).

(4) The applicant must promptly revise all promotional labeling and advertising to make it consistent with any labeling change implemented in accordance with paragraphs (b) and (c) of this section.

(5) Except for a supplement providing for a change in the labeling, the applicant must include in each supplement and amendment to a supplement providing for a change under paragraph (b) or (c) of this section a statement certifying that a field copy has been provided in accordance with § 314.440(a)(4).

(6) A supplement or annual report must include a list of all changes contained in the supplement or annual report. For supplements, this list must be provided in the submission.

(b) *Changes requiring supplement submission and approval prior to distribution of the product made using the change (major changes).* (1) A supplement must be submitted for any change in the drug substance, drug product, production process, quality controls, equipment, or facilities that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product.

(2) These changes include, but are not limited to:

(i) Except those described in paragraphs (c) and (d) of this section, changes in the qualitative or quantitative formulation of the drug product, including inactive ingredients, or in the specifications provided in the approved NDA;

(ii) Changes requiring completion of studies in accordance with part 320 of this chapter to demonstrate the equivalence of the drug product to the drug product as manufactured without the change or to the reference listed drug;

(iii) Changes that may affect drug substance or drug product sterility assurance, such as changes in drug substance, drug product, or component sterilization method(s) or an addition, deletion, or substitution of steps in an aseptic processing operation;

(iv) Changes in the synthesis or manufacture of the drug substance that may affect the impurity profile and/or the physical, chemical, or biological properties of the drug substance;

(v) The following labeling changes:

(A) Changes in labeling, except those described in paragraphs (c)(6)(iii), (d)(2)(ix), or (d)(2)(x) of this section;

(B) If applicable, any change to a Medication Guide required under part 208 of this chapter, except for changes in the information specified in § 208.20(b)(8)(iii) and (b)(8)(iv) of this chapter; and

(C) Any change to the information required by § 201.57(a) of this chapter, with the following exceptions that may be reported in an annual report under paragraph (d)(2)(x) of this section:

(*1*) Removal of a listed section(s) specified in § 201.57(a)(5) of this chapter; and

(*2*) Changes to the most recent revision date of the labeling as specified in § 201.57(a)(15) of this chapter.

(vi) Changes in a drug product container closure system that controls the drug product delivered to a patient or changes in the type (e.g., glass to high density polyethylene (HDPE), HDPE to polyvinyl chloride, vial to syringe) or composition (e.g., one HDPE resin to another HDPE resin) of a packaging component that may affect the impurity profile of the drug product.

(vii) Changes solely affecting a natural product, a recombinant DNA-derived protein/polypeptide, or a complex or conjugate of a drug substance with a monoclonal antibody for the following:

(A) Changes in the virus or adventitious agent removal or inactivation method(s);

(B) Changes in the source material or cell line; and

(C) Establishment of a new master cell bank or seed.

(viii) Changes to a drug product under an NDA that is subject to a validity assessment because of significant questions regarding the integrity of the data supporting that NDA.

(3) The applicant must obtain approval of a supplement from FDA prior to distribution of a drug product made using a change under paragraph (b) of this section. Except for submissions under paragraph (e) of this section, the following information must be contained in the supplement:

(i) A detailed description of the proposed change;

(ii) The drug product(s) involved;

(iii) The manufacturing site(s) or area(s) affected;

(iv) A description of the methods used and studies performed to assess the effects of the change;

(v) The data derived from such studies;

(vi) For a natural product, a recombinant DNA-derived protein/polypeptide, or a complex or conjugate of a drug substance with a monoclonal antibody, relevant validation protocols and a list of relevant standard operating procedures must be provided in addition to the requirements in paragraphs (b)(3)(iv) and (b)(3)(v) of this section; and

(vii) For sterilization process and test methodologies related to sterilization process validation, relevant validation protocols and a list of relevant standard operating procedures must be provided in addition to the requirements in paragraphs (b)(3)(iv) and (b)(3)(v) of this section.

(4) An applicant may ask FDA to expedite its review of a supplement for public health reasons or if a delay in making the change described in it would impose an extraordinary hardship on the applicant. Such a supplement should be plainly marked: "Prior Approval Supplement-Expedited Review Requested."

(c) *Changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change (moderate changes).* (1) A supplement must be submitted for any change in the drug substance, drug product, production process, quality controls, equipment, or facilities that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. If the supplement provides for a labeling change under paragraph (c)(6)(iii) of this section, 12 copies of the final printed labeling must be included.

(2) These changes include, but are not limited to:

(i) A change in the container closure system that does not affect the quality of the drug product, except those described in paragraphs (b) and (d) of this section; and

(ii) Changes solely affecting a natural protein, a recombinant DNA-derived protein/polypeptide or a complex or conjugate of a drug substance with a monoclonal antibody, including:

(A) An increase or decrease in production scale during finishing steps that involves different equipment; and

(B) Replacement of equipment with that of a different design that does not affect the process methodology or process operating parameters.

(iii) Relaxation of an acceptance criterion or deletion of a test to comply with an official compendium that is consistent with FDA statutory and regulatory requirements.

(3) A supplement submitted under paragraph (c)(1) of this section is required to give a full explanation of the basis for the change and identify the date on which the change is to be made. The supplement must be labeled "Supplement—Changes Being Effected in 30 Days" or, if applicable under paragraph (c)(6) of this section, "Supplement—Changes Being Effected."

(4) Pending approval of the supplement by FDA, except as provided in paragraph (c)(6) of this section, distribution of the drug product made using the change may begin not less than 30 days after receipt of the supplement by FDA. The information listed in paragraphs (b)(3)(i) through (b)(3)(vii) of this section must be contained in the supplement.

(5) The applicant must not distribute the drug product made using the change if within 30 days following FDA's receipt of the supplement, FDA informs the applicant that either:

(i) The change requires approval prior to distribution of the drug product in accordance with paragraph (b) of this section; or

(ii) Any of the information required under paragraph (c)(4) of this section is missing; the applicant must not distribute the drug product made using the change until the supplement has been amended to provide the missing information.

(6) The agency may designate a category of changes for the purpose of providing that, in the case of a change in such category, the holder of an approved NDA may commence distribution of the drug product involved upon receipt by the agency of a supplement for the change. These changes include, but are not limited to:

(i) Addition to a specification or changes in the methods or controls to provide increased assurance that the drug substance or drug product will have the characteristics of identity, strength, quality, purity, or potency that it purports or is represented to possess;

(ii) A change in the size and/or shape of a container for a nonsterile drug product, except for solid dosage forms, without a change in the labeled amount of drug product or from one container closure system to another;

(iii) Changes in the labeling to reflect newly acquired information, except for changes to the information required in § 201.57(a) of this chapter (which must be made under paragraph (b)(2)(v)(C) of this section), to accomplish any of the following:

(A) To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter;

(B) To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage;

(C) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product;

(D) To delete false, misleading, or unsupported indications for use or claims for effectiveness; or

(E) Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision.

(7) If the agency disapproves the supplemental NDA, it may order the manufacturer to cease distribution of the drug product(s) made with the manufacturing change.

(d) *Changes to be described in an annual report (minor changes).* (1) Changes in the drug substance, drug product, production process, quality controls, equipment, or facilities that have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product must be documented by the applicant in the next annual report in accordance with § 314.81(b)(2).

(2) These changes include, but are not limited to:

(i) Any change made to comply with a change to an official compendium, except a change described in paragraph (c)(2)(iii) of this section, that is consistent with FDA statutory and regulatory requirements.

(ii) The deletion or reduction of an ingredient intended to affect only the color of the drug product;

(iii) Replacement of equipment with that of the same design and operating principles except those equipment changes described in paragraph (c) of this section;

(iv) A change in the size and/or shape of a container containing the same number of dosage units for a nonsterile solid dosage form drug product, without a change from one container closure system to another;

(v) A change within the container closure system for a nonsterile drug product, based upon a showing of equivalency to the approved system under a protocol approved in the NDA or published in an official compendium;

(vi) An extension of an expiration dating period based upon full shelf life data on production batches obtained from a protocol approved in the NDA;

(vii) The addition or revision of an alternative analytical procedure that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved NDA, or deletion of an alternative analytical procedure;

(viii) The addition by embossing, debossing, or engraving of a code imprint to a solid oral dosage form drug product other than a modified release dosage form, or a minor change in an existing code imprint;

(ix) A change in the labeling concerning the description of the drug product or in the information about how the drug product is supplied, that does not involve a change in the dosage strength or dosage form; and

(x) An editorial or similar minor change in labeling, including a change to the information allowed by paragraphs (b)(2)(v)(C)(*1*) and (*2*) of this section.

(3) For changes under this category, the applicant is required to submit in the annual report:

(i) A statement by the holder of the approved NDA that the effects of the change have been assessed;

(ii) A full description of the manufacturing and controls changes, including the manufacturing site(s) or area(s) involved;

(iii) The date each change was implemented;

(iv) Data from studies and tests performed to assess the effects of the change; and,

(v) For a natural product, recombinant DNA-derived protein/polypeptide, complex or conjugate of a drug substance with a monoclonal antibody, sterilization process or test methodology related to sterilization process validation, a cross-reference to relevant validation protocols and/or standard operating procedures.

(e) *Protocols.* An applicant may submit one or more protocols describing the specific tests and studies and acceptance criteria to be achieved to demonstrate the lack of adverse effect for specified types of manufacturing changes on the identity, strength, quality, purity, and potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. Any such protocols, if not included in the approved NDA, or changes to an approved protocol, must be submitted as a supplement requiring approval from FDA prior to distribution of a drug product produced with the manufacturing change. The supplement, if approved, may subsequently justify a reduced reporting category for the particular change because the use of the protocol for that type of change reduces the potential risk of an adverse effect.

(f) *Patent information.* The applicant must comply with the patent information requirements under section 505(c)(2) of the Federal Food, Drug, and Cosmetic Act and § 314.53.

(g) *Claimed exclusivity.* If an applicant claims exclusivity under § 314.108 upon approval of a supplement for change to its previously approved drug product, the applicant must include with its supplement the information required under § 314.50(j).

(h) *Different drug.* An applicant may not supplement a 505(b)(2) application to seek approval of a drug that is a different drug from the drug in the approved 505(b)(2) application. For purposes of this paragraph (h), a drug is a different drug if it has been modified to have a different active ingredient, different route of administration, different dosage form, or difference in excipients that requires either a separate clinical study to establish safety or effectiveness or, for topical products, that requires a separate in vivo demonstration of bioequivalence. However, notwithstanding the limitation described in this paragraph (h), an applicant may supplement the 505(b)(2) application to seek approval of a different strength.

§ 314.71 Procedures for submission of a supplement to an approved application.

(a) Only the applicant may submit a supplement to an application.

(b) All procedures and actions that apply to an application under § 314.50 also apply to supplements, except that the information required in the supplement is limited to that needed to support the change. A supplement is required to contain an archival copy and a review copy that include an application form and appropriate technical sections, samples, and labeling; except that a supplement for a change other than a change in labeling is required also to contain a field copy.

(c) All procedures and actions that apply to applications under this part, including actions by applicants and the Food and Drug Administration, also apply to supplements except as specified otherwise in this part.

§ 314.72 Change in ownership of an application.

(a) An applicant may transfer ownership of its application. At the time of transfer the new and former owners are required to submit information to the Food and Drug Administration as follows:

(1) The former owner shall submit a letter or other document that states that all rights to the application have been transferred to the new owner.

(2) The new owner shall submit an application form signed by the new owner and a letter or other document containing the following:

(i) The new owner's commitment to agreements, promises, and conditions made by the former owner and contained in the application;

(ii) The date that the change in ownership is effective; and

(iii) Either a statement that the new owner has a complete copy of the approved application, including supplements and records that are required to be kept under § 314.81, or a request for a copy of the application from FDA's files. FDA will provide a copy of the application to the new owner under the fee schedule in § 20.45 of FDA's public information regulations.

(b) The new owner shall advise FDA about any change in the conditions in the approved application under § 314.70, except the new owner may advise FDA in the next annual report about a change in the drug product's label or labeling to change the product's brand or the name of its manufacturer, packer, or distributor.

§ 314.80 Postmarketing reporting of adverse drug experiences.

(a) *Definitions.* The following definitions of terms apply to this section:

Adverse drug experience. Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: An adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action.

Individual case safety report (ICSR). A description of an adverse drug experience related to an individual patient or subject.

ICSR attachments. Documents related to the adverse drug experience described in an ICSR, such as medical records, hospital discharge summaries, or other documentation.

Disability. A substantial disruption of a person's ability to conduct normal life functions.

Life-threatening adverse drug experience. Any adverse drug experience that places the patient, in the view of the initial reporter, at *immediate* risk of death from the adverse drug experience as it occurred, *i.e.* , it does not include an adverse drug experience that, had it occurred in a more severe form, might have caused death.

Serious adverse drug experience. Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Unexpected adverse drug experience. Any adverse drug experience that is not listed in the current labeling for the drug product. This includes events that may be symptomatically and pathophysiologically related to an event listed in the labeling, but differ from the event because of greater severity or specificity. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the labeling only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the labeling only listed cerebral vascular accidents. "Unexpected," as used in this definition, refers to an adverse drug experience that has not been previously observed (*i.e.* , included in the labeling) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

(b) *Review of adverse drug experiences.* Each applicant having an approved application under § 314.50 or, in the case of a 505(b)(2) application, an effective approved application, must promptly review all adverse drug experience information obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers. Applicants are not required to resubmit to FDA adverse drug experience reports forwarded to the applicant by FDA; however, applicants must submit all followup information on such reports to FDA. Any person subject to the reporting requirements under paragraph (c) of this section must also develop written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences to FDA.

(c) *Reporting requirements.* The applicant must submit to FDA adverse drug experience information as described in this section. Except as provided in paragraph (g)(2) of this section, these reports must be submitted to the Agency in electronic format as described in paragraph (g)(1) of this section.

(1)(i) *Postmarketing 15-day "Alert reports".* The applicant must report each adverse drug experience that is both serious and unexpected, whether foreign or domestic, as soon as possible but no later than 15 calendar days from initial receipt of the information by the applicant.

(ii) *Postmarketing 15-day "Alert reports"—followup.* The applicant must promptly investigate all adverse drug experiences that are the subject of these postmarketing 15-day Alert reports and must submit followup reports within 15 calendar days of receipt of new information or as requested by FDA. If additional information is not obtainable, records should be maintained of the unsuccessful steps taken to seek additional information.

(iii) *Submission of reports.* The requirements of paragraphs (c)(1)(i) and (c)(1)(ii) of this section, concerning the submission of postmarketing 15-day Alert reports, also apply to any person other than the applicant whose name appears on the label of an approved drug product as a manufacturer, packer, or distributor (nonapplicant). To avoid unnecessary duplication in the submission to FDA of reports required by paragraphs (c)(1)(i) and (c)(1)(ii) of this section, obligations of a nonapplicant may be met by submission of all reports of serious adverse drug experiences to the applicant. If a nonapplicant elects to submit adverse drug experience reports to the applicant rather than to FDA, the nonapplicant must submit, by any appropriate means, each report to the applicant within 5 calendar days of initial receipt of the information by the nonapplicant, and the applicant must then comply with the requirements of this section. Under this circumstance, the nonapplicant must maintain a record of this action which must include:

(A) A copy of each adverse drug experience report;

(B) The date the report was received by the nonapplicant;

(C) The date the report was submitted to the applicant; and

(D) The name and address of the applicant.

(2) *Periodic adverse drug experience reports.* (i) The applicant must report each adverse drug experience not reported under paragraph (c)(1)(i) of this section at quarterly intervals, for 3 years from the date of approval of the application, and then at annual intervals. The applicant must submit each quarterly report within 30 days of the close of the quarter (the first quarter beginning on the date of approval of the application) and each annual report within 60 days of the anniversary date of approval of the application. Upon written notice, FDA may extend or reestablish the requirement that an applicant submit quarterly reports, or require that the applicant submit reports under this section at different times than those stated. For example, the agency may reestablish a quarterly reporting requirement following the approval of a major supplement. Followup information to adverse drug experiences submitted in a periodic report may be submitted in the next periodic report.

(ii) Each periodic report is required to contain:

(A) *Descriptive information.* (*1*) A narrative summary and analysis of the information in the report;

(*2*) An analysis of the 15-day Alert reports submitted during the reporting interval (all 15-day Alert reports being appropriately referenced by the applicant's patient identification code, adverse reaction term(s), and date of submission to FDA);

(*3*) A history of actions taken since the last report because of adverse drug experiences (for example, labeling changes or studies initiated); and

(*4*) An index consisting of a line listing of the applicant's patient identification code, and adverse reaction term(s) for all ICSRs submitted under paragraph (c)(2)(ii)(B) of this section.

(B) *ICSRs for serious, expected, and nonserious adverse drug experiences.* An ICSR for each adverse drug experience not reported under paragraph (c)(1)(i) of this section (all serious, expected and nonserious adverse

drug experiences). All such ICSRs must be submitted to FDA (either individually or in one or more batches) within the timeframe specified in paragraph (c)(2)(i) of this section. ICSRs must only be submitted to FDA once.

(iii) Periodic reporting, except for information regarding 15-day Alert reports, does not apply to adverse drug experience information obtained from postmarketing studies (whether or not conducted under an investigational new drug application), from reports in the scientific literature, and from foreign marketing experience.

(d) *Scientific literature.* A 15-day Alert report based on information in the scientific literature must be accompanied by a copy of the published article. The 15-day reporting requirements in paragraph (c)(1)(i) of this section (*i.e.* , serious, unexpected adverse drug experiences) apply only to reports found in scientific and medical journals either as case reports or as the result of a formal clinical trial.

(e) *Postmarketing studies.* An applicant is not required to submit a 15-day Alert report under paragraph (c) of this section for an adverse drug experience obtained from a postmarketing study (whether or not conducted under an investigational new drug application) unless the applicant concludes that there is a reasonable possibility that the drug caused the adverse experience.

(f) *Information reported on ICSRs.* ICSRs include the following information:

(1) *Patient information.*

(i) Patient identification code;

(ii) Patient age at the time of adverse drug experience, or date of birth;

(iii) Patient gender; and

(iv) Patient weight.

(2) *Adverse drug experience.*

(i) Outcome attributed to adverse drug experience;

(ii) Date of adverse drug experience;

(iii) Date of ICSR submission;

(iv) Description of adverse drug experience (including a concise medical narrative);

(v) Adverse drug experience term(s);

(vi) Description of relevant tests, including dates and laboratory data; and

(vii) Other relevant patient history, including preexisting medical conditions.

(3) *Suspect medical product(s).*

(i) Name;

(ii) Dose, frequency, and route of administration used;

(iii) Therapy dates;

(iv) Diagnosis for use (indication);

(v) Whether the product is a prescription or nonprescription product;

(vi) Whether the product is a combination product as defined in § 3.2(e) of this chapter;

(vii) Whether adverse drug experience abated after drug use stopped or dose reduced;

(viii) Whether adverse drug experience reappeared after reintroduction of drug;

(ix) Lot number;

(x) Expiration date;

(xi) National Drug Code (NDC) number; and

(xii) Concomitant medical products and therapy dates.

(4) *Initial reporter information.*

(i) Name, address, and telephone number;

(ii) Whether the initial reporter is a health care professional; and

(iii) Occupation, if a health care professional.

(5) *Applicant information.*

(i) Applicant name and contact office address;

(ii) Telephone number;

(iii) Report source, such as spontaneous, literature, or study;

(iv) Date the report was received by applicant;

(v) Application number and type;

(vi) Whether the ICSR is a 15-day "Alert report";

(vii) Whether the ICSR is an initial report or followup report; and

(viii) Unique case identification number, which must be the same in the initial report and any subsequent followup report(s).

(g) *Electronic format for submissions.*

(1) Safety report submissions, including ICSRs, ICSR attachments, and the descriptive information in periodic reports, must be in an electronic format that FDA can process, review, and archive. FDA will issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files).

(2) An applicant or nonapplicant may request, in writing, a temporary waiver of the requirements in paragraph (g)(1) of this section. These waivers will be granted on a limited basis for good cause shown. FDA will issue guidance on requesting a waiver of the requirements in paragraph (g)(1) of this section.

(h) *Multiple reports.* An applicant should not include in reports under this section any adverse drug experiences that occurred in clinical trials if they were previously submitted as part of the approved application. If a report applies to a drug for which an applicant holds more than one approved application, the applicant should submit the report to the application that was first approved. If a report refers to more than one drug marketed by an applicant, the applicant should submit the report to the application for the drug listed first in the report.

(i) *Patient privacy.* An applicant should not include in reports under this section the names and addresses of individual patients; instead, the applicant should assign a unique code for identification of the patient. The applicant should include the name of the reporter from whom the information was received as part of the initial reporter information, even when the reporter is the patient. The names of patients, health care professionals, hospitals, and geographical identifiers in adverse drug experience reports are not releasable to the public under FDA's public information regulations in part 20 of this chapter.

(j) *Recordkeeping.* The applicant must maintain for a period of 10 years records of all adverse drug experiences known to the applicant, including raw data and any correspondence relating to adverse drug experiences.

(k) *Withdrawal of approval.* If an applicant fails to establish and maintain records and make reports required under this section, FDA may withdraw approval of the application and, thus, prohibit continued marketing of the drug product that is the subject of the application.

(l) *Disclaimer.* A report or information submitted by an applicant under this section (and any release by FDA of that report or information) does not necessarily reflect a conclusion by the applicant or FDA that the report or information constitutes an admission that the drug caused or contributed to an adverse effect. An applicant need not admit, and may deny, that the report or information submitted under this section constitutes an admission that the drug caused or contributed to an adverse effect. For purposes of this provision, the term "applicant" also includes any person reporting under paragraph (c)(1)(iii) of this section.

§ 314.81 Other postmarketing reports.

(a) *Applicability.* Each applicant shall make the reports for each of its approved applications and abbreviated applications required under this section and section 505(k) of the act.

(b) *Reporting requirements.* The applicant shall submit to the Food and Drug Administration at the specified times two copies of the following reports:

(1) *NDA—Field alert report.* The applicant shall submit information of the following kinds about distributed drug products and articles to the FDA district office that is responsible for the facility involved within 3 working days of receipt by the applicant. The information may be provided by telephone or other rapid communication means, with prompt written followup. The report and its mailing cover should be plainly marked: "NDA—Field Alert Report."

(i) Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article.

(ii) Information concerning any bacteriological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug product, or any failure of one or more distributed batches of the drug product to meet the specification established for it in the application.

(2) *Annual report.* The applicant shall submit each year within 60 days of the anniversary date of U.S. approval of the application, two copies of the report to the FDA division responsible for reviewing the application. Each annual report is required to be accompanied by a completed transmittal Form FDA 2252 (Transmittal of Periodic Reports for Drugs for Human Use), and must include all the information required under this section that the applicant received or otherwise obtained during the annual reporting interval that ends on the U.S. anniversary date. The report is required to contain in the order listed:

(i) *Summary.* A brief summary of significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product. The report is also required to contain a brief description of actions the applicant has taken or intends to take as a result of this new information, for example, submit a labeling supplement, add a warning to the labeling, or initiate a new study. The summary shall briefly state whether labeling supplements for pediatric use have been submitted and whether new studies in the pediatric

population to support appropriate labeling for the pediatric population have been initiated. Where possible, an estimate of patient exposure to the drug product, with special reference to the pediatric population (neonates, infants, children, and adolescents) shall be provided, including dosage form.

(ii)(*a*) *Distribution data.* Information about the quantity of the drug product distributed under the approved application, including that distributed to distributors. The information is required to include the National Drug Code (NDC) number, the total number of dosage units of each strength or potency distributed (e.g., 100,000/5 milligram tablets, 50,000/10 milliliter vials), and the quantities distributed for domestic use and the quantities distributed for foreign use. Disclosure of financial or pricing data is not required.

(*b*) *Authorized generic drugs.* If applicable, the date each authorized generic drug (as defined in § 314.3) entered the market, the date each authorized generic drug ceased being distributed, and the corresponding trade or brand name. Each dosage form and/or strength is a different authorized generic drug and should be listed separately. The first annual report submitted on or after January 25, 2010 must include the information listed in this paragraph for any authorized generic drug that was marketed during the time period covered by an annual report submitted after January 1, 1999. If information is included in the annual report with respect to any authorized generic drug, a copy of that portion of the annual report must be sent to the Food and Drug Administration, Center for Drug Evaluation and Research, Office of New Drug Quality Assessment, Bldg. 21, rm. 2562, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, and marked "Authorized Generic Submission" or, by e-mail, to the Authorized Generics electronic mailbox at *AuthorizedGenerics@fda.hhs.gov* with "Authorized Generic Submission" indicated in the subject line. However, at such time that FDA has required that annual reports be submitted in an electronic format, the information required by this paragraph must be submitted as part of the annual report, in the electronic format specified for submission of annual reports at that time, and not as a separate submission under the preceding sentence in this paragraph.

(iii) *Labeling.* (*a*) Currently used professional labeling, patient brochures or package inserts (if any), and a representative sample of the package labels.

(*b*) The content of labeling required under § 201.100(d)(3) of this chapter (*i.e.* , the package insert or professional labeling), including all text, tables, and figures, must be submitted in electronic format. Electronic format submissions must be in a form that FDA can process, review, and archive. FDA will periodically issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files). Submissions under this paragraph must be made in accordance with part 11 of this chapter, except for the requirements of § 11.10(a), (c) through (h), and (k), and the corresponding requirements of § 11.30.

(*c*) A summary of any changes in labeling that have been made since the last report listed by date in the order in which they were implemented, or if no changes, a statement of that fact.

(iv) *Chemistry, manufacturing, and controls changes.* (*a*) Reports of experiences, investigations, studies, or tests involving chemical or physical properties, or any other properties of the drug (such as the drug's behavior or properties in relation to microorganisms, including both the effects of the drug on microorganisms and the effects of microorganisms on the drug). These reports are only required for new information that may affect FDA's previous conclusions about the safety or effectiveness of the drug product.

(*b*) A full description of the manufacturing and controls changes not requiring a supplemental application under § 314.70 (b) and (c), listed by date in the order in which they were implemented.

(v) *Nonclinical laboratory studies.* Copies of unpublished reports and summaries of published reports of new toxicological findings in animal studies and in vitro studies (e.g., mutagenicity) conducted by, or otherwise obtained by, the applicant concerning the ingredients in the drug product. The applicant shall submit a copy of a published report if requested by FDA.

(vi) *Clinical data.* (*a*) Published clinical trials of the drug (or abstracts of them), including clinical trials on safety and effectiveness; clinical trials on new uses; biopharmaceutic, pharmacokinetic, and clinical pharmacology studies; and reports of clinical experience pertinent to safety (for example, epidemiologic studies or analyses of experience in a monitored series of patients) conducted by or otherwise obtained by the applicant. Review articles, papers describing the use of the drug product in medical practice, papers and abstracts in which the drug is used as a research tool, promotional articles, press clippings, and papers that do not contain tabulations or summaries of original data should not be reported.

(*b*) Summaries of completed unpublished clinical trials, or prepublication manuscripts if available, conducted by, or otherwise obtained by, the applicant. Supporting information should not be reported. (A study is considered completed 1 year after it is concluded.)

(*c*) Analysis of available safety and efficacy data in the pediatric population and changes proposed in the labeling based on this information. An assessment of data needed to ensure appropriate labeling for the pediatric population shall be included.

(vii) *Status reports of postmarketing study commitments.* A status report of each postmarketing study of the drug product concerning clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology that is required by FDA (e.g., accelerated approval clinical benefit studies, pediatric studies) or that the applicant has committed, in writing, to conduct either at the time of approval of an application for the drug product or a supplement to an application, or after approval of the application or a supplement. For pediatric studies, the status report shall include a statement indicating whether postmarketing clinical studies in pediatric populations were required by FDA under § 201.23 of this chapter. The status of these postmarketing studies shall be reported annually until FDA notifies the applicant, in writing, that the agency concurs with the applicant's determination that the study commitment has been fulfilled or that the study is either no longer feasible or would no longer provide useful information.

(*a*) *Content of status report.* The following information must be provided for each postmarketing study reported under this paragraph:

(*1*) *Applicant's name.*

(*2*) *Product name.* Include the approved drug product's established name and proprietary name, if any.

(*3*) *NDA, ANDA, and supplement number.*

(*4*) *Date of U.S. approval of NDA or ANDA.*

(*5*) *Date of postmarketing study commitment.*

(*6*) *Description of postmarketing study commitment.* The description must include sufficient information to uniquely describe the study. This information may include the purpose of the study, the type of study, the patient population addressed by the study and the indication(s) and dosage(s) that are to be studied.

(*7*) *Schedule for completion and reporting of the postmarketing study commitment.* The schedule should include the actual or projected dates for submission of the study protocol to FDA, completion of patient accrual or initiation of an animal study, completion of the study, submission of the final study report to FDA, and any additional milestones or submissions for which projected dates were specified as part of the commitment. In addition, it should include a revised schedule, as appropriate. If the schedule has been previously revised, provide both the original schedule and the most recent, previously submitted revision.

(*8*) *Current status of the postmarketing study commitment.* The status of each postmarketing study should be categorized using one of the following terms that describes the study's status on the anniversary date of U.S. approval of the application or other agreed upon date:

(*I*) *Pending.* The study has not been initiated, but does not meet the criterion for delayed.

(*ii*) *Ongoing.* The study is proceeding according to or ahead of the original schedule described under paragraph (b)(2)(vii)(*a*)(*7*) of this section.

(*iii*) *Delayed.* The study is behind the original schedule described under paragraph (b)(2)(vii)(*a*)(*7*) of this section.

(*iv*) *Terminated.* The study was ended before completion but a final study report has not been submitted to FDA.

(*v*) *Submitted.* The study has been completed or terminated and a final study report has been submitted to FDA.

(*9*) *Explanation of the study's status.* Provide a brief description of the status of the study, including the patient accrual rate (expressed by providing the number of patients or subjects enrolled to date, and the total planned enrollment), and an explanation of the study's status identified under paragraph (b)(2)(vii)(*a*)(*8*) of this section. If the study has been completed, include the date the study was completed and the date the final study report was submitted to FDA, as applicable. Provide a revised schedule, as well as the reason(s) for the revision, if the schedule under paragraph (b)(2)(vii)(*a*)(*7*) of this section has changed since the last report.

(*b*) *Public disclosure of information.* Except for the information described in this paragraph, FDA may publicly disclose any information described in paragraph (b)(2)(vii) of this section, concerning a postmarketing study, if the agency determines that the information is necessary to identify the applicant or to establish the status of the study, including the reasons, if any, for failure to conduct, complete, and report the study. Under this section, FDA will not publicly disclose trade secrets, as defined in § 20.61 of this chapter, or information, described in § 20.63 of this chapter, the disclosure of which would constitute an unwarranted invasion of personal privacy.

(viii) *Status of other postmarketing studies.* A status report of any postmarketing study not included under paragraph (b)(2)(vii) of this section that is being performed by, or on behalf of, the applicant. A status report is to be included for any chemistry, manufacturing, and controls studies that the applicant has agreed to perform and for all product stability studies.

(ix) *Log of outstanding regulatory business.* To facilitate communications between FDA and the applicant, the report may, at the applicant's discretion, also contain a list of any open regulatory business with FDA concerning the drug product subject to the application (e.g., a list of the applicant's unanswered correspondence with the agency, a list of the agency's unanswered correspondence with the applicant).

(3) *Other reporting* —(i) *Advertisements and promotional labeling.* The applicant shall submit specimens of mailing pieces and any other labeling or advertising devised for promotion of the drug product at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product. Mailing pieces and labeling that are designed to contain samples of a drug product are required to be complete, except the sample of the drug product may be omitted. Each submission is required to be accompanied by a completed transmittal Form FDA-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) and is required to include a copy of the product's current professional labeling. Form FDA-2253 is available on the Internet at *http://www.fda.gov/opacom/morechoices/fdaforms/cder.html*.

(ii) *Special reports.* Upon written request the agency may require that the applicant submit the reports under this section at different times than those stated.

(iii) *Notification of a permanent discontinuance or an interruption in manufacturing.* (*a*) An applicant of a prescription drug product must notify FDA in writing of a permanent discontinuance of manufacture of the drug product or an interruption in manufacturing of the drug product that is likely to lead to a meaningful disruption in supply of that drug in the United States if:

(*1*) The drug product is life supporting, life sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition, including any such drug used in emergency medical care or during surgery; and

(*2*) The drug product is not a radiopharmaceutical drug product.

(*b*) Notifications required by paragraph (b)(3)(iii)(*a*) of this section must be submitted to FDA electronically in a format that FDA can process, review, and archive:

(*1*) At least 6 months prior to the date of the permanent discontinuance or interruption in manufacturing; or

(*2*) If 6 months' advance notice is not possible because the permanent discontinuance or interruption in manufacturing was not reasonably anticipated 6 months in advance, as soon as practicable thereafter, but in no case later than 5 business days after the permanent discontinuance or interruption in manufacturing occurs.

(*c*) Notifications required by paragraph (b)(3)(iii)(*a*) of this section must include the following information:

(*1*) The name of the drug subject to the notification, including the NDC for such drug;

(*2*) The name of the applicant;

(*3*) Whether the notification relates to a permanent discontinuance of the drug or an interruption in manufacturing of the drug;

(*4*) A description of the reason for the permanent discontinuance or interruption in manufacturing; and

(*5*) The estimated duration of the interruption in manufacturing.

(*d*)(*1*) FDA will maintain a publicly available list of drugs that are determined by FDA to be in shortage. This drug shortages list will include the following information:

(*I*) The names and NDC(s) for such drugs;

(*ii*) The name of each applicant for such drugs;

(*iii*) The reason for the shortage, as determined by FDA from the following categories: Requirements related to complying with good manufacturing practices; regulatory delay; shortage of an active ingredient; shortage of an inactive ingredient component; discontinuation of the manufacture of the drug; delay in shipping of the drug; demand increase for the drug; or other reason; and

(*iv*) The estimated duration of the shortage.

(*2*) FDA may choose not to make information collected to implement this paragraph available on the drug shortages list or available under section 506C(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356c(c)) if FDA determines that disclosure of such information would adversely affect the public health (such as by increasing the possibility of hoarding or other disruption of the availability of the drug to patients). FDA will also not provide information on the public drug shortages list or under section 506C(c) of the Federal Food, Drug, and Cosmetic Act that is protected by 18 U.S.C. 1905 or 5 U.S.C. 552(b)(4), including trade secrets and commercial or financial information that is considered confidential or privileged under § 20.61 of this chapter.

(*e*) If an applicant fails to submit a notification as required under paragraph (b)(3)(iii)(*a*) of this section and in accordance with paragraph (b)(3)(iii)(*b*) of this section, FDA will issue a letter to the applicant informing it of such failure.

(*1*) Not later than 30 calendar days after the issuance of such a letter, the applicant must submit to FDA a written response setting forth the basis for noncompliance and providing the required notification under paragraph (b)(3)(iii)(*a*) of this section and including the information required under paragraph (b)(3)(iii)(*c*) of this section; and

(*2*) Not later than 45 calendar days after the issuance of a letter under paragraph (b)(3)(iii)(*e*) of this section, FDA will make the letter and the applicant's response to the letter public, unless, after review of the applicant's response, FDA determines that the applicant had a reasonable basis for not notifying FDA as required under paragraph (b)(3)(iii)(*a*) of this section.

(*f*) The following definitions of terms apply to paragraph (b)(3)(iii) of this section:

Drug shortage or *shortage* means a period of time when the demand or projected demand for the drug within the United States exceeds the supply of the drug.

Intended for use in the prevention or treatment of a debilitating disease or condition means a drug product intended for use in the prevention or treatment of a disease or condition associated with mortality or morbidity that has a substantial impact on day-to-day functioning.

Life supporting or life sustaining means a drug product that is essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life.

Meaningful disruption means a change in production that is reasonably likely to lead to a reduction in the supply of a drug by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product, and does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time.

(iv) *Withdrawal of approved drug product from sale.* (*a*) Within 30 calendar days of the withdrawal of an approved drug from sale, applicants who are manufacturers, repackers, or relabelers subject to part 207 of this

chapter must submit the following information about the drug, in accordance with the applicable requirements described in §§ 207.61 and 207.65:

(*1*) The National Drug Code (NDC);

(*2*) The identity of the drug by established name and by proprietary name, if any;

(*3*) The new drug application number or abbreviated application number;

(*4*) The date on which the drug is expected to be no longer in commercial distribution. FDA requests that the reason for withdrawal of the drug from sale be included with the information.

(*b*) Within 30 calendar days of the withdrawal of an approved drug from sale, applicants who are not subject to part 207 of this chapter must submit the information listed in paragraphs (b)(3)(iv)(*a*)(*1*) through (*4*) of this section. The information must be submitted either electronically or in writing to the Drug Registration and Listing Office, Food and Drug Administration, Center for Drug Evaluation and Research.

(*c*) Reporting under paragraph (b)(3)(iv *)* (*a*) of this section constitutes compliance with the requirements of § 207.57 of this chapter to update drug listing information with respect to the withdrawal from sale.

(c) *General requirements* —(1) *Multiple applications.* For all reports required by this section, the applicant shall submit the information common to more than one application only to the application first approved, and shall not report separately on each application. The submission is required to identify all the applications to which the report applies.

(2) *Patient identification.* Applicants should not include in reports under this section the names and addresses of individual patients; instead, the applicant should code the patient names whenever possible and retain the code in the applicant's files. The applicant shall maintain sufficient patient identification information to permit FDA, by using that information alone or along with records maintained by the investigator of a study, to identify the name and address of individual patients; this will ordinarily occur only when the agency needs to investigate the reports further or when there is reason to believe that the reports do not represent actual results obtained.

(d) *Withdrawal of approval.* If an applicant fails to make reports required under this section, FDA may withdraw approval of the application and, thus, prohibit continued marketing of the drug product that is the subject of the application.

§ 314.90 Waivers.

(a) An applicant may ask the Food and Drug Administration to waive under this section any requirement that applies to the applicant under §§ 314.50 through 314.81. An applicant may ask FDA to waive under § 314.126(c) any criteria of an adequate and well-controlled study described in § 314.126(b). A waiver request under this section is required to be submitted with supporting documentation in an NDA, or in an amendment or supplement to an NDA. The waiver request is required to contain one of the following:

(1) An explanation why the applicant's compliance with the requirement is unnecessary or cannot be achieved;

(2) A description of an alternative submission that satisfies the purpose of the requirement; or

(3) Other information justifying a waiver.

(b) FDA may grant a waiver if it finds one of the following:

(1) The applicant's compliance with the requirement is unnecessary for the agency to evaluate the NDA or compliance cannot be achieved;

(2) The applicant's alternative submission satisfies the requirement; or

(3) The applicant's submission otherwise justifies a waiver.

(c) If FDA grants the applicant's waiver request with respect to a requirement under §§ 314.50 through 314.81, the waived requirement will not constitute a basis for refusal to approve an NDA under § 314.125.

Subpart C—Abbreviated Applications

§ 314.92Drug products for which abbreviated applications may be submitted.

(a) Abbreviated applications are suitable for the following drug products within the limits set forth under § 314.93:

(1) Drug products that are the same as a listed drug. A “listed drug” is defined in § 314.3. For determining the suitability of an abbreviated new drug application, the term “same as” means identical in active ingredient(s), dosage form, strength, route of administration, and conditions of use, except that conditions of use for which approval cannot be granted because of exclusivity or an existing patent may be omitted. If a listed drug has been voluntarily withdrawn from or not offered for sale by its manufacturer, a person who wishes to submit an abbreviated new drug application for the drug shall comply with § 314.122.

(2) [Reserved]

(3) Drug products that have been declared suitable for an abbreviated new drug application submission by FDA through the petition procedures set forth under § 10.30 of this chapter and § 314.93.

(b) FDA will publish in the list listed drugs for which abbreviated applications may be submitted. The list is available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402, 202-783-3238.

§ 314.93 Petition to request a change from a listed drug.

(a) The only changes from a listed drug for which the agency will accept a petition under this section are those changes described in paragraph (b) of this section. Petitions to submit ANDAs for other changes from a listed drug will not be approved.

(b) A person who wants to submit an ANDA for a drug product which is not identical to a listed drug in route of administration, dosage form, and strength, or in which one active ingredient is substituted for one of the active ingredients in a listed combination drug, must first obtain permission from FDA to submit such an ANDA.

(c) To obtain permission to submit an ANDA for a change described in paragraph (b) of this section, a person must submit and obtain approval of a petition requesting the change. A person seeking permission to request such a change from a reference listed drug shall submit a petition in accordance with § 10.20 of this chapter and in the format specified in § 10.30 of this chapter. The petition shall contain the information specified in § 10.30 of this chapter and any additional information required by this section. If any provision of § 10.20 or § 10.30 of this chapter is inconsistent with any provision of this section, the provisions of this section apply.

(d) The petitioner shall identify a listed drug and include a copy of the proposed labeling for the drug product that is the subject of the petition and a copy of the approved labeling for the listed drug. The petitioner may, under limited circumstances, identify more than one listed drug, for example, when the proposed drug product is a combination product that differs from the combination reference listed drug with regard to an active ingredient, and the different active ingredient is an active ingredient of a listed drug. The petitioner shall also include information to show that:

(1) The active ingredients of the proposed drug product are of the same pharmacological or therapeutic class as those of the reference listed drug.

(2) The drug product can be expected to have the same therapeutic effect as the reference listed drug when administered to patients for each condition of use in the reference listed drug's labeling for which the applicant seeks approval.

(3) If the proposed drug product is a combination product with one different active ingredient, including a different ester or salt, from the reference listed drug, that the different active ingredient has previously been approved in a listed drug or is a drug that does not meet the definition of “new drug” in section 201(p) of the Federal Food, Drug, and Cosmetic Act.

(e) No later than 90 days after the date a petition that is permitted under paragraph (a) of this section is submitted, FDA will approve or disapprove the petition.

(1) FDA will approve a petition properly submited under this section unless it finds that:

(i) Investigations must be conducted to show the safety and effectiveness of the drug product or of any of its active ingredients, its route of administration, dosage form, or strength which differs from the reference listed drug; or

(ii) For a petition that seeks to change an active ingredient, the drug product that is the subject of the petition is not a combination drug; or

(iii) For a combination drug product that is the subject of the petition and has an active ingredient different from the reference listed drug:

(A) The drug product may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted under § 314.94; or

(B) The petition does not contain information to show that the different active ingredient of the drug product is of the same pharmacological or therapeutic class as the ingredient of the reference listed drug that is to be changed and that the drug product can be expected to have the same therapeutic effect as the reference listed drug when administered to patients for each condition of use in the listed drug's labeling for which the applicant seeks approval; or

(C) The different active ingredient is not an active ingredient in a listed drug or a drug that meets the requirements of section 201(p) of the Federal Food, Drug, and Cosmetic Act; or

(D) The remaining active ingredients are not identical to those of the listed combination drug; or

(iv) Any of the proposed changes from the listed drug would jeopardize the safe or effective use of the product so as to necessitate significant labeling changes to address the newly introduced safety or effectiveness problem; or

(v) FDA has determined that the reference listed drug has been withdrawn from sale for safety or effectiveness reasons under § 314.161, or the reference listed drug has been voluntarily withdrawn from sale and the agency has not determined whether the withdrawal is for safety or effectiveness reasons; or

(vi) A drug product is approved in an NDA for the change described in the petition.

(2) For purposes of this paragraph, "investigations must be conducted" means that information derived from animal or clinical studies is necessary to show that the drug product is safe or effective. Such information may be contained in published or unpublished reports.

(3) If FDA approves a petition submitted under this section, the agency's response may describe what additional information, if any, will be required to support an ANDA for the drug product. FDA may, at any time during the course of its review of an ANDA, request additional information required to evaluate the change approved under the petition.

(f)(1) FDA may withdraw approval of a petition if the agency receives any information demonstrating that the petition no longer satisfies the conditions under paragraph (e) of this section.

(2) If, after approval of a petition and before approval of an ANDA submitted pursuant to the approved petition, a drug product is approved in an NDA for the change described in the petition, the petition and the listed drug identified in the petition can no longer be the basis for ANDA submission, irrespective of whether FDA has withdrawn approval of the petition. A person seeking approval for such drug product must submit a new ANDA that identifies the pharmaceutically equivalent reference listed drug as the basis for ANDA submission and comply with applicable regulatory requirements.

§ 314.94 Content and format of an ANDA.

ANDAs are required to be submitted in the form and contain the information required under this section. Three copies of the ANDA are required, an archival copy, a review copy, and a field copy. FDA will maintain guidance documents on the format and content of ANDAs to assist applicants in their preparation.

(a) *ANDAs.* Except as provided in paragraph (b) of this section, the applicant must submit a complete archival copy of the abbreviated new drug application that includes the following:

(1) *Application form.* The applicant must submit a completed and signed application form that contains the information described under § 314.50(a)(1), (a)(3), (a)(4), and (a)(5). The applicant must state whether the submission is an ANDA under this section or a supplement to an ANDA under § 314.97.

(2) *Table of contents.* The archival copy of the ANDA is required to contain a table of contents that shows the volume number and page number of the contents of the submission.

(3) *Basis for ANDA submission.* An ANDA must refer to a listed drug. Ordinarily, that listed drug will be the drug product selected by the Agency as the reference standard for conducting bioequivalence testing. The ANDA must contain:

(i) The name of the reference listed drug, including its dosage form and strength. For an ANDA based on an approved petition under § 10.30 of this chapter and § 314.93, the reference listed drug must be the same as the listed drug referenced in the approved petition.

(ii) A statement as to whether, according to the information published in the list, the reference listed drug is entitled to a period of marketing exclusivity under section 505(j)(5)(F) of the Federal Food, Drug, and Cosmetic Act.

(iii) For an ANDA based on an approved petition under § 10.30 of this chapter and § 314.93, a reference to the FDA-assigned docket number for the petition and a copy of FDA's correspondence approving the petition.

(4) *Conditions of use.* (i) A statement that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the drug product have been previously approved for the reference listed drug.

(ii) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(5) *Active ingredients.* (i) For a single-active-ingredient drug product, information to show that the active ingredient is the same as that of the reference single-active-ingredient listed drug, as follows:

(A) A statement that the active ingredient of the proposed drug product is the same as that of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(ii) For a combination drug product, information to show that the active ingredients are the same as those of the reference listed drug except for any different active ingredient that has been the subject of an approved petition, as follows:

(A) A statement that the active ingredients of the proposed drug product are the same as those of the reference listed drug, or if one of the active ingredients differs from one of the active ingredients of the reference listed drug and the ANDA is submitted under the approval of a petition under § 314.93 to vary such active ingredient, information to show that the other active ingredients of the drug product are the same as the other active ingredients of the reference listed drug, information to show that the different active ingredient is an active ingredient of another listed drug or of a drug that does not meet the definition of “new drug” in section 201(p) of the Federal Food, Drug, and Cosmetic Act, and such other information about the different active ingredient that FDA may require.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(6) *Route of administration, dosage form, and strength.* (i) Information to show that the route of administration, dosage form, and strength of the drug product are the same as those of the reference listed drug except for any differences that have been the subject of an approved petition, as follows:

(A) A statement that the route of administration, dosage form, and strength of the proposed drug product are the same as those of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(ii) If the route of administration, dosage form, or strength of the drug product differs from the reference listed drug and the ANDA is submitted under an approved petition under § 314.93, such information about the different route of administration, dosage form, or strength that FDA may require.

(7) *Bioequivalence.* (i) Information that shows that the drug product is bioequivalent to the reference listed drug upon which the applicant relies. A complete study report must be submitted for the bioequivalence study upon which the applicant relies for approval. For all other bioequivalence studies conducted on the same drug product formulation as defined in § 314.3(b), the applicant must submit either a complete or summary report. If a summary report of a bioequivalence study is submitted and FDA determines that there may be bioequivalence issues or concerns with the product, FDA may require that the applicant submit a complete report of the bioequivalence study to FDA; or

(ii) If the ANDA is submitted pursuant to a petition approved under § 314.93, the results of any bioavailability or bioequivalence testing required by the Agency, or any other information required by the Agency to show that the active ingredients of the proposed drug product are of the same pharmacological or therapeutic class as those in the reference listed drug and that the proposed drug product can be expected to have the same therapeutic effect as the reference listed drug. If the proposed drug product contains a different active ingredient than the reference listed drug, FDA will consider the proposed drug product to have the same therapeutic effect as the reference listed drug if the applicant provides information demonstrating that:(A) There is an adequate scientific basis for determining that substitution of the specific proposed dose of the different active ingredient for the dose of the member of the same pharmacological or therapeutic class in the reference listed drug will yield a resulting drug product whose safety and effectiveness have not been adversely affected.

(B) The unchanged active ingredients in the proposed drug product are bioequivalent to those in the reference listed drug.

(C) The different active ingredient in the proposed drug product is bioequivalent to an approved dosage form containing that ingredient and approved for the same indication as the proposed drug product or is bioequivalent to a drug product offered for that indication which does not meet the definition of “new drug” under section 201(p) of the Federal Food, Drug, and Cosmetic Act.

(iii) For each in vivo or in vitro bioequivalence study contained in the ANDA:

(A) A description of the analytical and statistical methods used in each study; and

(B) With respect to each study involving human subjects, a statement that the study either was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to the regulations under § 56.104 or § 56.105 of this chapter, and that it was conducted in compliance with the informed consent regulations in part 50 of this chapter.

(8) *Labeling* —(i) *Listed drug labeling.* A copy of the currently approved labeling (including, if applicable, any Medication Guide required under part 208 of this chapter) for the listed drug referred to in the ANDA, if the ANDA relies on a reference listed drug.

(ii) *Copies of proposed labeling.* Copies of the label and all labeling for the drug product including, if applicable, any Medication Guide required under part 208 of this chapter (4 copies of draft labeling or 12 copies of final printed labeling).

(iii) *Statement on proposed labeling.* A statement that the applicant's proposed labeling including, if applicable, any Medication Guide required under part 208 of this chapter is the same as the labeling of the reference listed drug except for differences annotated and explained under paragraph (a)(8)(iv) of this section.

(iv) *Comparison of approved and proposed labeling.* A side-by-side comparison of the applicant's proposed labeling including, if applicable, any Medication Guide required under part 208 of this chapter with the approved labeling for the reference listed drug with all differences annotated and explained. Labeling (including the container label, package insert, and, if applicable, Medication Guide) proposed for the drug product must be the same as the labeling approved for the reference listed drug, except for changes required because of differences approved under a petition filed under § 314.93 or because the drug product and the reference listed drug are produced or distributed by different manufacturers. Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(F) of the Federal Food, Drug, and Cosmetic Act.

(9) *Chemistry, manufacturing, and controls.* (i) The information required under § 314.50(d)(1), except that the information required under § 314.50(d)(1)(ii)(*c*) must contain the proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product.

(ii) *Inactive ingredients.* Unless otherwise stated in paragraphs (a)(9)(iii) through (a)(9)(v) of this section, an applicant must identify and characterize the inactive ingredients in the proposed drug product and provide information demonstrating that such inactive ingredients do not affect the safety or efficacy of the proposed drug product.

(iii) *Inactive ingredient changes permitted in drug products intended for parenteral use.* Generally, a drug product intended for parenteral use must contain the same inactive ingredients and in the same concentration as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.

(iv) *Inactive ingredient changes permitted in drug products intended for ophthalmic or otic use.* Generally, a drug product intended for ophthalmic or otic use must contain the same inactive ingredients and in the same concentration as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, substance to adjust tonicity, or thickening agent provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product, except that, in a product intended for ophthalmic use, an applicant may not change a buffer or substance to adjust tonicity for the purpose of claiming a therapeutic advantage over or difference from the listed drug, e.g., by using a balanced salt solution as a diluent as opposed to an isotonic saline solution, or by making a significant change in the pH or other change that may raise questions of irritability.

(v) *Inactive ingredient changes permitted in drug products intended for topical use.* Generally, a drug product intended for topical use, solutions for aerosolization or nebulization, and nasal solutions shall contain the same

inactive ingredients as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an ANDA may include different inactive ingredients provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.

(10) *Samples.* The information required under § 314.50(e)(1) and (e)(2)(i). Samples need not be submitted until requested by FDA.

(11) *Other.* The information required under § 314.50(g).

(12) *Patent certification —*(i) *Patents claiming drug substance, drug product, or method of use.* (A) An appropriate patent certification or statement with respect to each patent issued by the U.S. Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims the reference listed drug or that claims a use of such listed drug for which the applicant is seeking approval under section 505(j) of the Federal Food, Drug, and Cosmetic Act and for which information is required to be filed under section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53. For each such patent, the applicant must provide the patent number and certify, in its opinion and to the best of its knowledge, one of the following circumstances:

(*1*) That the patent information has not been submitted to FDA. The applicant must entitle such a certification "Paragraph I Certification";

(*2*) That the patent has expired. The applicant must entitle such a certification "Paragraph II Certification";

(*3*) The date on which the patent will expire. The applicant must entitle such a certification "Paragraph III Certification"; or

(*4*)(*I*) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted. The applicant must entitle such a certification "Paragraph IV Certification". This certification must be submitted in the following form:

I, (*NAME OF APPLICANT),* CERTIFY THAT PATENT NO. _____ (*IS INVALID, UNENFORCEABLE, OR WILL NOT BE INFRINGED BY THE MANUFACTURE, USE, OR SALE OF*) (*NAME OF PROPOSED DRUG PRODUCT*) FOR WHICH THIS ANDA IS SUBMITTED.

(*ii*) The certification must be accompanied by a statement that the applicant will comply with the requirements under § 314.95(a) with respect to providing a notice to each owner of the patent or its representative and to the NDA holder (or, if the NDA holder does not reside or maintain a place of business within the United States, its attorney, agent, or other authorized official) for the listed drug, with the requirements under § 314.95(b) with respect to sending the notice, and with the requirements under § 314.95(c) with respect to the content of the notice.

(B) If the ANDA refers to a listed drug that is itself a licensed generic product of a patented drug first approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act, an appropriate patent certification or statement under paragraph (a)(12)(i) and/or (iii) of this section with respect to each patent that claims the first-approved patented drug or that claims a use for such drug.

(ii) *No relevant patents.* If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (a)(12)(i) of this section, a certification in the following form:

IN THE OPINION AND TO THE BEST KNOWLEDGE OF (NAME OF APPLICANT), THERE ARE NO PATENTS THAT CLAIM THE LISTED DRUG REFERRED TO IN THIS ANDA OR THAT CLAIM A USE OF THE LISTED DRUG.

(iii) *Method-of-use patent.* (A) If patent information is submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53 for a patent claiming a method of using the listed drug, and the labeling for the drug product for which the applicant is seeking approval does not include an indication or other condition of use that is covered by the method-of-use patent, a statement explaining that the method-of-use patent does not claim a proposed indication or other condition of use.

(B) If the labeling of the drug product for which the applicant is seeking approval includes an indication or other condition of use that, according to the patent information submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53 or in the opinion of the applicant, is claimed by a method-of-use patent, an applicable certification under paragraph (a)(12)(i) of this section.

(iv) [Reserved]

(v) *Licensing agreements.* If the ANDA is for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, the applicant must submit a paragraph IV certification as to that patent and a statement that the applicant has been granted a patent license. If the patent owner consents to approval of the ANDA (if otherwise eligible for approval) as of a specific date, the ANDA must contain a written statement from the patent owner that it has a licensing agreement with the applicant and that it consents to approval of the ANDA as of a specific date.

(vi) *Untimely filing of patent information.* (A) If a patent on the listed drug is issued and the holder of the approved NDA for the listed drug does not file with FDA the required information on the patent within 30 days of issuance of the patent, an applicant who submitted an ANDA for that drug that contained an appropriate patent certification or statement before the submission of the patent information is not required to submit a patent certification or statement to address the patent or patent information that is late-listed with respect to the pending ANDA. Except as provided in § 314.53(f)(1), an NDA holder's amendment to the description of the approved method(s) of use claimed by the patent will be considered untimely filing of patent information unless:

(*1*) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of patent issuance;

(*2*) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of approval of a corresponding change to product labeling; or

(*3*) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision.

(B) An applicant whose ANDA is submitted after the NDA holder's untimely filing of patent information, or whose pending ANDA was previously submitted but did not contain an appropriate patent certification or statement at the time of the patent submission, must submit a certification under paragraph (a)(12)(i) of this section and/or a statement under paragraph (a)(12)(iii) of this section as to that patent.

(vii) *Disputed patent information.* If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn, the applicant must submit an appropriate certification or statement for each listed patent.

(viii) *Amended certifications.* A patent certification or statement submitted under paragraphs (a)(12)(i) through (iii) of this section may be amended at any time before the approval of the ANDA. If an applicant with a pending ANDA voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. An applicant must submit an amended certification as an amendment to a pending ANDA. Once an amendment is submitted to change a certification, the ANDA will no longer be considered to contain the prior certification.

(A) *After finding of infringement.* An applicant who has submitted a paragraph IV certification and is sued for patent infringement must submit an amendment to change its certification if a court enters a final decision from which no appeal has been or can be taken, or signs and enters a settlement order or consent decree in the action that includes a finding that the patent is infringed, unless the final decision, settlement order, or consent decree also finds the patent to be invalid. In its amendment, the applicant must certify under paragraph (a)(12)(i)(A)(*3*) of this section that the patent will expire on a specific date or, with respect to a patent claiming a method of use, the applicant may instead provide a statement under paragraph (a)(12)(iii) of this section if the applicant amends its ANDA such that the applicant is no longer seeking approval for a method of use claimed by the patent. Once an amendment for the change has been submitted, the ANDA will no longer be considered to contain a paragraph IV certification to the patent. If a final judgment finds the patent to be invalid and infringed, an amended certification is not required.

(B) *After request to remove a patent or patent information from the list.* If the list reflects that an NDA holder has requested that a patent or patent information be removed from the list and no ANDA applicant is eligible for 180-day exclusivity based on a paragraph IV certification to that patent, the patent or patent information will be removed and any applicant with a pending ANDA (including a tentatively approved ANDA) who has made a certification with respect to such patent must submit an amendment to withdraw its certification. In the amendment, the applicant must state the reason for withdrawing the certification or statement (that the patent has been removed from the list). If the list reflects that an NDA holder has requested that a patent or patent information be removed from the list and one or more first applicants are eligible for 180-day exclusivity based on a paragraph IV certification to that patent, the patent will remain listed until any 180-day exclusivity based on that patent has expired or has been extinguished. After any applicable 180-day exclusivity has expired or has been extinguished, the patent or patent information will be removed and any applicant with a pending ANDA (including a tentatively approved ANDA) who has made a certification with respect to such patent must submit an amendment to withdraw its certification. Once an amendment to withdraw the certification has been submitted, the ANDA will no longer be considered to contain a paragraph IV certification to the patent. If removal of a patent from the list results in there being no patents listed for the listed drug identified in the ANDA, the applicant must submit an amended certification reflecting that there are no relevant patents.

(C) *Other amendments.* (*1*) Except as provided in paragraphs (a)(12)(vi) and (a)(12)(viii)(C)(*2*) of this section:

(*I*) An applicant must amend a submitted certification or statement if, at any time before the date of approval of the ANDA, the applicant learns that the submitted certification or statement is no longer accurate; and

(*ii*) An applicant must submit an appropriate patent certification or statement under paragraph (a)(12)(i) and/or (iii) of this section if, after submission of the ANDA, a new patent is issued by the U.S. Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims the reference listed drug or that claims an approved use for such reference listed drug and for which information is required to be filed under section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53. For a paragraph IV certification, the certification must not be submitted earlier than the first working day after the day the patent is published in the list.

(*2*) An applicant is not required to submit a supplement to change a submitted certification when information on a patent on the listed drug is submitted after the approval of the ANDA.

(13) *Financial certification or disclosure statement.* An ANDA must contain a financial certification or disclosure statement as required by part 54 of this chapter.

(b) *Drug products subject to the Drug Efficacy Study Implementation (DESI) review.* If the ANDA is for a duplicate of a drug product that is subject to FDA's DESI review (a review of drug products approved as safe between 1938 and 1962) or other DESI-like review and the drug product evaluated in the review is a listed drug, the applicant must comply with the provisions of paragraph (a) of this section.

(c) [Reserved]

(d) *Format of an ANDA.* (1) The applicant must submit a complete archival copy of the ANDA as required under paragraphs (a) and (c) of this section. FDA will maintain the archival copy during the review of the ANDA to permit individual reviewers to refer to information that is not contained in their particular technical sections of the ANDA, to give other Agency personnel access to the ANDA for official business, and to maintain in one place a complete copy of the ANDA.

(i) *Format of submission.* An applicant may submit portions of the archival copy of the ANDA in any form that the applicant and FDA agree is acceptable, except as provided in paragraph (d)(1)(ii) of this section.

(ii) *Labeling.* The content of labeling required under § 201.100(d)(3) of this chapter (commonly referred to as the package insert or professional labeling), including all text, tables, and figures, must be submitted to the agency in electronic format as described in paragraph (d)(1)(iii) of this section. This requirement applies to the content of labeling for the proposed drug product only and is in addition to the requirements of paragraph (a)(8)(ii) of this section that copies of the formatted label and all proposed labeling be submitted. Submissions under this paragraph must be made in accordance with part 11 of this chapter, except for the requirements of § 11.10(a), (c) through (h), and (k), and the corresponding requirements of § 11.30.

(iii) *Electronic format submissions.* Electronic format submissions must be in a form that FDA can process, review, and archive. FDA will periodically issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files).

(2) For ANDAs, the applicant must submit a review copy of the ANDA that contains two separate sections. One section must contain the information described under paragraphs (a)(2) through (6) and (8) and (9) of this section and section 505(j)(2)(A)(vii) of the Federal Food, Drug, and Cosmetic Act and a copy of the analytical procedures and descriptive information needed by FDA's laboratories to perform tests on samples of the

proposed drug product and to validate the applicant's analytical procedures. The other section must contain the information described under paragraphs (a)(3), (7), and (8) of this section. Each of the sections in the review copy is required to contain a copy of the application form described under paragraph (a) of this section.

(3) [Reserved]

(4) The applicant may obtain from FDA sufficient folders to bind the archival, the review, and the field copies of the ANDA.

(5) The applicant must submit a field copy of the ANDA that contains the technical section described in paragraph (a)(9) of this section, a copy of the application form required under paragraph (a)(1) of this section, and a certification that the field copy is a true copy of the technical section described in paragraph (a)(9) of this section contained in the archival and review copies of the ANDA.

§ 314.95 Notice of certification of invalidity, unenforceability, or noninfringement of a patent.

(a) *Notice of certification.* For each patent that claims the listed drug or that claims a use for such listed drug for which the applicant is seeking approval and for which the applicant submits a paragraph IV certification, the applicant must send notice of such certification by registered or certified mail, return receipt requested, or by a designated delivery service, as defined in paragraph (g) of this section to each of the following persons:

(1) Each owner of the patent that is the subject of the certification or the representative designated by the owner to receive the notice. The name and address of the patent owner or its representative may be obtained from the U.S. Patent and Trademark Office; and

(2) The holder of the approved NDA under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the listed drug that is claimed by the patent and for which the applicant is seeking approval, or, if the NDA holder does not reside or maintain a place of business within the United States, the NDA holder's attorney, agent, or other authorized official. The name and address of the NDA holder or its attorney, agent, or authorized official may be obtained by sending a written or electronic communication to the Central Document Room, Attn: Orange Book Staff, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266 or to the Orange Book Staff at the email address listed on the Agency's Web site at *http://www.fda.gov* .

(3) This paragraph (a) does not apply to a method-of-use patent that does not claim a use for which the applicant is seeking approval.

(4) An applicant may send notice by an alternative method only if FDA has agreed in advance that the method will produce an acceptable form of documentation.

(b) *Sending the notice.* (1) Except as provided under paragraph (d) of this section, the applicant must send the notice required by paragraph (a) of this section on or after the date it receives a paragraph IV acknowledgment letter from FDA, but not later than 20 days after the date of the postmark on the paragraph IV acknowledgment letter. The 20-day clock described in this paragraph (b) begins on the day after the date of the postmark on the paragraph IV acknowledgment letter. When the 20th day falls on Saturday, Sunday, or a Federal holiday, the 20th day will be the next day that is not a Saturday, Sunday, or Federal holiday.

(2) Any notice required by paragraph (a) of this section is invalid if it is sent before the applicant's receipt of a paragraph IV acknowledgment letter, or before the first working day after the day the patent is published in the list. The applicant will not have complied with this paragraph (b) until it sends valid notice.

(3) The applicant must submit to FDA an amendment to its ANDA that includes a statement certifying that the notice has been provided to each person identified under paragraph (a) of this section and that the notice met the content requirements under paragraph (c) of this section. A copy of the notice itself need not be submitted to the Agency.

(c) *Contents of a notice.* In the notice, the applicant must cite section 505(j)(2)(B)(iv) of the Federal Food, Drug, and Cosmetic Act and the notice must include, but is not limited to, the following information:

(1) A statement that FDA has received an ANDA submitted by the applicant containing any required bioavailability or bioequivalence data or information.

(2) The ANDA number.

(3) A statement that the applicant has received the paragraph IV acknowledgment letter for the ANDA.

(4) The established name, if any, as defined in section 502(e)(3) of the Federal Food, Drug, and Cosmetic Act, of the proposed drug product.

(5) The active ingredient, strength, and dosage form of the proposed drug product.

(6) The patent number and expiration date of each listed patent for the reference listed drug alleged to be invalid, unenforceable, or not infringed.

(7) A detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed. The applicant must include in the detailed statement:

(i) For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed.

(ii) For each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation.

(8) If the applicant alleges that the patent will not be infringed and the applicant seeks to preserve the option to later file a civil action for declaratory judgment in accordance with section 505(j)(5)(C) of the Federal Food, Drug, and Cosmetic Act, then the notice must be accompanied by an offer of confidential access to the ANDA for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the paragraph IV certification.

(9) If the applicant does not reside or have a place of business in the United States, the name and address of an agent in the United States authorized to accept service of process for the applicant.

(d) *Amendment or supplement to an ANDA.* (1) If, after receipt of a paragraph IV acknowledgment letter or acknowledgment letter, an applicant submits an amendment or supplement to its ANDA that includes a paragraph IV certification, the applicant must send the notice required by paragraph (a) of this section at the same time that the amendment or supplement to the ANDA is submitted to FDA, regardless of whether the applicant has already given notice with respect to another such certification contained in the ANDA or in an amendment or supplement to the ANDA.

(2) If, before receipt of a paragraph IV acknowledgment letter, an applicant submits an amendment to its ANDA that includes a paragraph IV certification, the applicant must send the notice required by paragraph (a)

of this section in accordance with the procedures in paragraph (b) of this section. If an ANDA applicant's notice of its paragraph IV certification is timely provided in accordance with paragraph (b) of this section and the applicant has not submitted a previous paragraph IV certification, FDA will base its determination of whether the applicant is a first applicant on the date of submission of the amendment containing the paragraph IV certification.

(3) An applicant that submits an amendment or supplement to seek approval of a different strength must provide notice of any paragraph IV certification in accordance with paragraph (d)(1) or (2) of this section, as applicable.

(e) *Documentation of timely sending and receipt of notice.* The applicant must amend its ANDA to provide documentation of the date of receipt of the notice required under paragraph (a) of this section by each person provided the notice. The amendment must be submitted to FDA within 30 days after the last date on which notice was received by a person described in paragraph (a) of this section. The applicant's amendment also must include documentation that its notice was sent on a date that complies with the timeframe required by paragraph (b) or (d) of this section, as applicable, and a dated printout of the entry for the reference listed drug in FDA's "Approved Drug Products With Therapeutic Equivalence Evaluations" (the list) that includes the patent that is the subject of the paragraph IV certification. FDA will accept, as adequate documentation of the date the notice was sent, a copy of the registered mail receipt, certified mail receipt, or receipt from a designated delivery service as defined in paragraph (g) of this section. FDA will accept as adequate documentation of the date of receipt a return receipt, signature proof of delivery by a designated delivery service, or a letter acknowledging receipt by the person provided the notice. An applicant may rely on another form of documentation only if FDA has agreed to such documentation in advance. A copy of the notice itself need not be submitted to the Agency.

(f) *Forty-five day period after receipt of notice.* If the requirements of this section are met, FDA will presume the notice to be complete and sufficient, and it will count the day following the date of receipt of the notice by the patent owner or its representative and by the approved NDA holder or its attorney, agent, or other authorized official as the first day of the 45-day period provided for in section 505(j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act. FDA may, if the applicant provides a written statement to FDA that a later date should be used, count from such later date.

(g) *Designated delivery services.* (1) For purposes of this section, the term "designated delivery service" means any delivery service provided by a trade or business that the Agency determines:

(i) Is available to the general public throughout the United States;

(ii) Records electronically to its database, kept in the regular course of its business, or marks on the cover in which any item referred to in this section is to be delivered, the date on which such item was given to such trade or business for delivery; and

(iii) Provides overnight or 2-day delivery service throughout the United States.

(2) FDA may periodically issue guidance regarding designated delivery services.

§ 314.96 Amendments to an unapproved ANDA.

(a) *ANDA.* (1) An applicant may amend an ANDA that is submitted under § 314.94, but not yet approved, to revise existing information or provide additional information. Amendments containing bioequivalence studies must contain reports of all bioequivalence studies conducted by the applicant on the same drug product formulation, unless the information has previously been submitted to FDA in the ANDA. A complete study report must be submitted for any bioequivalence study upon which the applicant relies for approval. For all other bioequivalence studies conducted on the same drug product formulation as defined in § 314.3 of this chapter, the applicant must submit either a complete or summary report. If a summary report of a bioequivalence study is submitted and FDA determines that there may be bioequivalence issues or concerns with the product, FDA may require that the applicant submit a complete report of the bioequivalence study to FDA.

(2) Submission of an amendment containing significant data or information before the end of the initial review cycle constitutes an agreement between FDA and the applicant to extend the initial review cycle only for the time necessary to review the significant data or information and for no more than 180 days.

(b) *Field copy.* The applicant must submit a field copy of each amendment under § 314.94(a)(9). The applicant, other than a foreign applicant, must include in its submission of each such amendment to FDA a statement certifying that a field copy of the amendment has been sent to the applicant's home FDA district office.

(c) *Different listed drug.* An applicant may not amend an ANDA to seek approval of a drug referring to a listed drug that is different from the reference listed drug identified in the ANDA. This paragraph (c) applies if, at any time before the approval of the ANDA, a different listed drug is approved that is the pharmaceutical equivalent to the product in the ANDA and is designated as a reference listed drug. This paragraph (c) also applies if changes are proposed in an amendment to the ANDA such that the proposed product is a pharmaceutical equivalent to a different listed drug than the reference listed drug identified in the ANDA. A change of the reference listed drug must be submitted in a new ANDA. However, notwithstanding the limitation described in this paragraph (c), an applicant may amend the ANDA to seek approval of a different strength.

(d)(1) *Patent certification requirements.* An amendment to an ANDA is required to contain an appropriate patent certification or statement described in § 314.94(a)(12) or a recertification for a previously submitted paragraph IV certification if approval is sought for any of the following types of amendments:

(i) To add a new indication or other condition of use;

(ii) To add a new strength;

(iii) To make other than minor changes in product formulation; or

(iv) To change the physical form or crystalline structure of the active ingredient.

(2) If the amendment to the ANDA does not contain a patent certification or statement, the applicant must verify that the proposed change described in the amendment is not one of the types of amendments described in paragraph (d)(1) of this section.

§ 314.97 Supplements and other changes to an approved ANDA.

(a) *General requirements.* The applicant must comply with the requirements of §§ 314.70 and 314.71 regarding the submission of supplemental ANDAs and other changes to an approved ANDA.

(b) *Different listed drug.* An applicant may not supplement an ANDA to seek approval of a drug referring to a listed drug that is different from the current reference listed drug identified in the ANDA. This paragraph (b) applies if changes are proposed in a supplement to the ANDA such that the proposed product is a pharmaceutical equivalent to a different listed drug than the reference listed drug identified in the ANDA. A change of reference listed drug must be submitted in a new ANDA. However, notwithstanding the limitation described in this paragraph (b), an applicant may supplement the ANDA to seek approval of a different strength.

§ 314.98 Postmarketing reports.

(a) Each applicant having an approved abbreviated new drug application under § 314.94 that is effective must comply with the requirements of § 314.80 regarding the reporting and recordkeeping of adverse drug experiences.

(b) Each applicant must make the reports required under § 314.81 and section 505(k) of the Federal Food, Drug, and Cosmetic Act for each of its approved abbreviated applications.

§ 314.99 Other responsibilities of an applicant of an ANDA.

(a) An applicant must comply with the requirements of § 314.65 regarding withdrawal by the applicant of an unapproved ANDA and § 314.72 regarding a change in ownership of an ANDA.

(b) An applicant may ask FDA to waive under this section any requirement that applies to the applicant under §§ 314.92 through 314.99. The applicant must comply with the requirements for a waiver under § 314.90. If FDA grants the applicant's waiver request with respect to a requirement under §§ 314.92 through 314.99, the waived requirement will not constitute a basis for refusal to approve an ANDA under § 314.127.

Subpart D—FDA Action on Applications and Abbreviated ApplicationsSource:

§ 314.100 Timeframes for reviewing applications and abbreviated applications.

(a) Except as provided in paragraph (c) of this section, within 180 days of receipt of an application for a new drug under section 505(b) of the act or an abbreviated application for a new drug under section 505(j) of the act, FDA will review it and send the applicant either an approval letter under § 314.105 or a complete response letter under § 314.110. This 180-day period is called the “initial review cycle.”

(b) At any time before approval, an applicant may withdraw an application under § 314.65 or an abbreviated application under § 314.99 and later submit it again for consideration.

(c) The initial review cycle may be adjusted by mutual agreement between FDA and an applicant or as provided in §§ 314.60 and 314.96, as the result of a major amendment.

§ 314.101 Filing an NDA and receiving an ANDA.

(a) *Filing an NDA.* (1) Within 60 days after FDA receives an NDA, the Agency will determine whether the NDA may be filed. The filing of an NDA means that FDA has made a threshold determination that the NDA is sufficiently complete to permit a substantive review.

(2) If FDA finds that none of the reasons in paragraphs (d) and (e) of this section for refusing to file the NDA apply, the Agency will file the NDA and notify the applicant in writing. In the case of a 505(b)(2) application that contains a paragraph IV certification, the applicant will be notified via a paragraph IV acknowledgment letter. The date of filing will be the date 60 days after the date FDA received the NDA. The date of filing begins the 180-day period described in section 505(c) of the Federal Food, Drug, and Cosmetic Act. This 180-day period is called the "filing clock."

(3) If FDA refuses to file the NDA, the Agency will notify the applicant in writing and state the reason under paragraph (d) or (e) of this section for the refusal. If FDA refuses to file the NDA under paragraph (d) of this section, the applicant may request in writing within 30 days of the date of the Agency's notification an informal conference with the Agency about whether the Agency should file the NDA. If, following the informal conference, the applicant requests that FDA file the NDA (with or without amendments to correct the deficiencies), the Agency will file the NDA over protest under paragraph (a)(2) of this section, notify the applicant in writing, and review it as filed. If the NDA is filed over protest, the date of filing will be the date 60 days after the date the applicant requested the informal conference. The applicant need not resubmit a copy of an NDA that is filed over protest. If FDA refuses to file the NDA under paragraph (e) of this section, the applicant may amend the NDA and resubmit it, and the Agency will make a determination under this section whether it may be filed.

(b)(1) *Receiving an ANDA.* An ANDA will be evaluated after it is submitted to determine whether the ANDA may be received. Receipt of an ANDA means that FDA has made a threshold determination that the abbreviated application is substantially complete.

(2) If FDA finds that none of the reasons in paragraphs (d) and (e) of this section for considering the ANDA not to have been received applies, the ANDA is substantially complete and the Agency will receive the ANDA and notify the applicant in writing. If FDA determines, upon evaluation, that an ANDA was substantially complete as of the date it was submitted to FDA, FDA will consider the ANDA to have been received as of the date of submission. In the case of an ANDA that contains a paragraph IV certification, the applicant will be notified via a paragraph IV acknowledgment letter.

(3) If FDA considers the ANDA not to have been received under paragraph (d) or (e) of this section, FDA will notify the applicant of the refuse-to-receive decision. The applicant may then:

(i) Withdraw the ANDA under § 314.99; or

(ii) Correct the deficiencies and resubmit the ANDA; or

(iii) Take no action, in which case FDA may consider the ANDA withdrawn after 1 year.

(c) [Reserved]

(d) *NDA or ANDA deficiencies.* FDA may refuse to file an NDA or may not consider an ANDA to be received if any of the following applies:

(1) The NDA or ANDA does not contain a completed application form.

(2) The NDA or ANDA is not submitted in the form required under § 314.50 or § 314.94.

(3) The NDA or ANDA is incomplete because it does not on its face contain information required under section 505(b) or section 505(j) of the Federal Food, Drug, and Cosmetic Act and § 314.50 or § 314.94. In determining whether an ANDA is incomplete on its face, FDA will consider the nature (e.g., major or minor) of the deficiencies, including the number of deficiencies in the ANDA.

(4) The applicant fails to submit a complete environmental assessment, which addresses each of the items specified in the applicable format under § 25.40 of this chapter or fails to provide sufficient information to establish that the requested action is subject to categorical exclusion under § 25.30 or § 25.31 of this chapter.

(5) The NDA or ANDA does not contain an accurate and complete English translation of each part of the NDA or ANDA that is not in English.

(6) The NDA or ANDA does not contain a statement for each nonclinical laboratory study that the study was conducted in compliance with the requirements set forth in part 58 of this chapter, or, for each study not conducted in compliance with part 58 of this chapter, a brief statement of the reason for the noncompliance.

(7) The NDA or ANDA does not contain a statement for each clinical study that the study was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to those regulations, and that it was conducted in compliance with the informed consent regulations in part 50 of this chapter, or, if the study was subject to but was not conducted in compliance with those regulations, the NDA or ANDA does not contain a brief statement of the reason for the noncompliance.

(8) The drug product that is the subject of the submission is already covered by an approved NDA or ANDA and the applicant of the submission:(i) Has an approved NDA or ANDA for the same drug product; or

(ii) Is merely a distributor and/or repackager of the already approved drug product.

(9) The NDA is submitted as a 505(b)(2) application for a drug that is a duplicate of a listed drug and is eligible for approval under section 505(j) of the Federal Food, Drug, and Cosmetic Act.

(e) *Regulatory deficiencies.* The Agency will refuse to file an NDA or will consider an ANDA not to have been received if any of the following applies:

(1) The drug product is subject to licensing by FDA under the Public Health Service Act (42 U.S.C. 201 *et seq.*) and subchapter F of this chapter.

(2) Submission of a 505(b)(2) application or an ANDA is not permitted under section 505(c)(3)(E)(ii), 505(j)(5)(F)(ii), 505A(b)(1)(A)(i)(I), 505A(c)(1)(A)(i)(I), or 505E(a) of the Federal Food, Drug, and Cosmetic Act.

(f) *Outcome of FDA review.* (1) Within 180 days after the date of filing, plus the period of time the review period was extended (if any), FDA will either:

(i) Approve the NDA; or

(ii) Issue a notice of opportunity for a hearing if the applicant asked FDA to provide it an opportunity for a hearing on an NDA in response to a complete response letter.

(2) Within 180 days after the date of receipt, plus the period of time the review clock was extended (if any), FDA will either approve or disapprove the ANDA. If FDA disapproves the ANDA, FDA will issue a notice of opportunity for hearing if the applicant asked FDA to provide it an opportunity for a hearing on an ANDA in response to a complete response letter.

(3) This paragraph (f) does not apply to NDAs or ANDAs that have been withdrawn from FDA review by the applicant.

§ 314.102 Communications between FDA and applicants.

(a) *General principles.* During the course of reviewing an application or an abbreviated application, FDA shall communicate with applicants about scientific, medical, and procedural issues that arise during the review process. Such communication may take the form of telephone conversations, letters, or meetings, whichever is most appropriate to discuss the particular issue at hand. Communications shall be appropriately documented in the application in accordance with § 10.65 of this chapter. Further details on the procedures for communication between FDA and applicants are contained in a staff manual guide that is publicly available.

(b) *Notification of easily correctable deficiencies.* FDA reviewers shall make every reasonable effort to communicate promptly to applicants easily correctable deficiencies found in an application or an abbreviated application when those deficiencies are discovered, particularly deficiencies concerning chemistry, manufacturing, and controls issues. The agency will also inform applicants promptly of its need for more data or information or for technical changes in the application or the abbreviated application needed to facilitate the agency's review. This early communication is intended to permit applicants to correct such readily identified deficiencies relatively early in the review process and to submit an amendment before the review period has elapsed. Such early communication would not ordinarily apply to major scientific issues, which require consideration of the entire pending application or abbreviated application by agency managers as well as reviewing staff. Instead, major scientific issues will ordinarily be addressed in a complete response letter.

(c) *Ninety-day conference.* Approximately 90 days after the agency receives the application, FDA will provide applicants with an opportunity to meet with agency reviewing officials. The purpose of the meeting will be to inform applicants of the general progress and status of their applications, and to advise applicants of deficiencies that have been identified by that time and that have not already been communicated. This meeting will be available on applications for all new chemical entities and major new indications of marketed drugs. Such meetings will be held at the applicant's option, and may be held by telephone if mutually agreed upon. Such meetings would not ordinarily be held on abbreviated applications because they are not submitted for new chemical entities or new indications.

(d) *End-of-review conference.* At the conclusion of FDA's review of an NDA as designated by the issuance of a complete response letter, FDA will provide the applicant with an opportunity to meet with agency reviewing officials. The purpose of the meeting will be to discuss what further steps need to be taken by the applicant before the application can be approved. Requests for such meetings must be directed to the director of the division responsible for reviewing the application.

(e) *Other meetings.* Other meetings between FDA and applicants may be held, with advance notice, to discuss scientific, medical, and other issues that arise during the review process. Requests for meetings shall be directed to the director of the division responsible for reviewing the application or abbreviated application. FDA will make every attempt to grant requests for meetings that involve important issues and that can be scheduled at mutually convenient times. However, “drop-in” visits (*i.e.* , an unannounced and unscheduled

visit by a company representative) are discouraged except for urgent matters, such as to discuss an important new safety issue.

§ 314.103 Dispute resolution.

(a) *General.* FDA is committed to resolving differences between applicants and FDA reviewing divisions with respect to technical requirements for applications or abbreviated applications as quickly and amicably as possible through the cooperative exchange of information and views.

(b) *Administrative and procedural issues.* When administrative or procedural disputes arise, the applicant should first attempt to resolve the matter with the division responsible for reviewing the application or abbreviated application, beginning with the consumer safety officer assigned to the application or abbreviated application. If resolution is not achieved, the applicant may raise the matter with the person designated as ombudsman, whose function shall be to investigate what has happened and to facilitate a timely and equitable resolution. Appropriate issues to raise with the ombudsman include resolving difficulties in scheduling meetings, obtaining timely replies to inquiries, and obtaining timely completion of pending reviews. Further details on this procedure are contained in a staff manual guide that is publicly available under FDA's public information regulations in part 20.

(c) *Scientific and medical disputes.* (1) Because major scientific issues are ordinarily communicated to applicants in a complete response letter pursuant to § 314.110, the "end-of-review conference" described in § 314.102(d) will provide a timely forum for discussing and resolving, if possible, scientific and medical issues on which the applicant disagrees with the agency. In addition, the "ninety-day conference" described in § 314.102(c) will provide a timely forum for discussing and resolving, if possible, issues identified by that date.

(2) When scientific or medical disputes arise at other times during the review process, applicants should discuss the matter directly with the responsible reviewing officials. If necessary, applicants may request a meeting with the appropriate reviewing officials and management representatives in order to seek a resolution. Ordinarily, such meetings would be held first with the Division Director, then with the Office Director, and finally with the Center Director if the matter is still unresolved. Requests for such meetings shall be directed to the director of the division responsible for reviewing the application or abrreviated application. FDA will make every attempt to grant requests for meetings that involve important issues and that can be scheduled at mutually convenient times.

(3) In requesting a meeting designed to resolve a scientific or medical dispute, applicants may suggest that FDA seek the advice of outside experts, in which case FDA may, in its discretion, invite to the meeting one or more of its advisory committee members or other consultants, as designated by the agency. Applicants may also bring their own consultants. For major scientific and medical policy issues not resolved by informal meetings, FDA may refer the matter to one of its standing advisory committees for its consideration and recommendations.

§ 314.104 Drugs with potential for abuse.

The Food and Drug Administration will inform the Drug Enforcement Administration under section 201(f) of the Controlled Substances Act (21 U.S.C. 801) when an application or abbreviated application is submitted for a drug that appears to have an abuse potential.

§ 314.105 Approval of an NDA and an ANDA.

(a) FDA will approve an NDA and send the applicant an approval letter if none of the reasons in § 314.125 for refusing to approve the NDA applies. FDA will issue a tentative approval letter if an NDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved because there is a 7-year period of orphan exclusivity for the listed drug under section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter, or if a 505(b)(2) application otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved until the conditions in § 314.107(b)(3) are met; because there is a period of exclusivity for the listed drug under § 314.108; because there is a period of pediatric exclusivity for the listed drug under section 505A of the Federal Food, Drug, and Cosmetic Act; or because there is a period of exclusivity for the listed drug under section 505E of the Federal Food, Drug, and Cosmetic Act. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval after any necessary additional review of the NDA. FDA's tentative approval of a drug product is based on information available to FDA at the time of the tentative approval letter (*i.e.,* information in the 505(b)(2) application and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to FDA's attention. A new drug product may not be marketed until the date of approval.

(b) FDA will approve an NDA and issue the applicant an approval letter on the basis of draft labeling if the only deficiencies in the NDA concern editorial or similar minor deficiencies in the draft labeling. Such approval will be conditioned upon the applicant incorporating the specified labeling changes exactly as directed, and upon the applicant submitting to FDA a copy of the final printed labeling prior to marketing.

(c) FDA will approve an NDA after it determines that the drug meets the statutory standards for safety and effectiveness, manufacturing and controls, and labeling, and an ANDA after it determines that the drug meets the statutory standards for manufacturing and controls, labeling, and, where applicable, bioequivalence. While the statutory standards apply to all drugs, the many kinds of drugs that are subject to the statutory standards and the wide range of uses for those drugs demand flexibility in applying the standards. Thus FDA is required to exercise its scientific judgment to determine the kind and quantity of data and information an applicant is required to provide for a particular drug to meet the statutory standards. FDA makes its views on drug products and classes of drugs available through guidance documents, recommendations, and other statements of policy.

(d) FDA will approve an ANDA and send the applicant an approval letter if none of the reasons in § 314.127 for refusing to approve the ANDA applies. FDA will issue a tentative approval letter if an ANDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved because there is a 7-year period of orphan exclusivity for the listed drug under section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter, or cannot be approved until the conditions in § 314.107(b)(3) or (c) are met; because there is a period of exclusivity for the listed drug under § 314.108;

because there is a period of pediatric exclusivity for the listed drug under section 505A of the Federal Food, Drug, and Cosmetic Act; or because there is a period of exclusivity for the listed drug under section 505E of the Federal Food, Drug, and Cosmetic Act. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval after any necessary additional review of the ANDA. FDA's tentative approval of a drug product is based on information available to FDA at the time of the tentative approval letter (*i.e.,* information in the ANDA and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to FDA's attention. A new drug product may not be marketed until the date of approval.

§ 314.106 Foreign data.

(a) *General.* The acceptance of foreign data in an application generally is governed by § 312.120 of this chapter.

(b) *As sole basis for marketing approval.* An application based solely on foreign clinical data meeting U.S. criteria for marketing approval may be approved if: (1) The foreign data are applicable to the U.S. population and U.S. medical practice; (2) the studies have been performed by clinical investigators of recognized competence; and (3) the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or other appropriate means. Failure of an application to meet any of these criteria will result in the application not being approvable based on the foreign data alone. FDA will apply this policy in a flexible manner according to the nature of the drug and the data being considered.

(c) *Consultation between FDA and applicants.* Applicants are encouraged to meet with agency officials in a "presubmission" meeting when approval based solely on foreign data will be sought.

§ 314.107 Date of approval of a 505(b)(2) application or ANDA.

(a) *General.* A drug product may be introduced or delivered for introduction into interstate commerce when the 505(b)(2) application or ANDA for the drug product is approved. A 505(b)(2) application or ANDA for a drug product is approved on the date FDA issues an approval letter under § 314.105 for the 505(b)(2) application or ANDA.

(b) *Effect of patent(s) on the listed drug.* As described in paragraphs (b)(1) and (2) of this section, the status of patents listed for the listed drug(s) relied upon or reference listed drug, as applicable, must be considered in determining the first possible date on which a 505(b)(2) application or ANDA can be approved. The criteria in paragraphs (b)(1) and (2) of this section will be used to determine, for each relevant patent, the date that patent will no longer prevent approval. The first possible date on which the 505(b)(2) application or ANDA can be approved will be calculated for each patent, and the 505(b)(2) application or ANDA may be approved on the last applicable date.

(1) *Timing of approval based on patent certification or statement.* If none of the reasons in § 314.125 or § 314.127, as applicable, for refusing to approve the 505(b)(2) application or ANDA applies, and none of the

reasons in paragraph (d) of this section for delaying approval applies, the 505(b)(2) application or ANDA may be approved as follows:

(i) Immediately, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that:

(A) The applicant is aware of a relevant patent but the patent information required under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act has not been submitted to FDA; or

(B) The relevant patent has expired; or

(C) The relevant patent is invalid, unenforceable, or will not be infringed, except as provided in paragraphs (b)(3) and (c) of this section, and the 45-day period provided for in section 505(c)(3)(C) and (j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act has expired; or

(D) There are no relevant patents.

(ii) Immediately, if the applicant submits an appropriate statement under § 314.50(i) or § 314.94(a)(12) explaining that a method-of-use patent does not claim an indication or other condition of use for which the applicant is seeking approval, except that if the applicant also submits a paragraph IV certification to the patent, then the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(1)(i)(C) of this section.

(iii) On the date specified, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent will expire on a specified date.

(2) *Patent information filed after submission of 505(b)(2) application or ANDA.* If the holder of the approved NDA for the listed drug submits patent information required under § 314.53 after the date on which the 505(b)(2) application or ANDA was submitted to FDA, the 505(b)(2) applicant or ANDA applicant must comply with the requirements of § 314.50(i)(4) and (6) and § 314.94(a)(12)(vi) and (viii) regarding submission of an appropriate patent certification or statement. If the applicant submits an amendment certifying under § 314.50(i)(1)(i)(A)(*4*) or § 314.94(a)(12)(i)(A)(*4*) that the relevant patent is invalid, unenforceable, or will not be infringed, and complies with the requirements of § 314.52 or § 314.95, the 505(b)(2) application or ANDA may be approved immediately upon submission of documentation of receipt of notice of paragraph IV certification under § 314.52(e) or § 314.95(e). The 45-day period provided for in section 505(c)(3)(C) and (j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act does not apply in these circumstances.

(3) *Disposition of patent litigation —*(i) *Approval upon expiration of 30-month period or 7 1/2 years from date of listed drug approval.* (A) Except as provided in paragraphs (b)(3)(ii) through (viii) of this section, if, with respect to patents for which required information was submitted under § 314.53 before the date on which the 505(b)(2) application or ANDA was submitted to FDA (excluding an amendment or supplement to the 505(b)(2) application or ANDA), the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent is invalid, unenforceable, or will not be infringed, and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement within 45 days of receipt of the notice of crtification from the applicant under § 314.52 or § 314.95, the 505(b)(2) application or ANDA may be approved 30 months after the later of the date of the receipt of the notice of certification by any owner of the listed patent or by the NDA holder (or its representative(s)) unless the court has extended or reduced the period because of a failure of either the plaintiff or defendant to cooperate reasonably in expediting the action; or

(B) If the patented drug product qualifies for 5 years of exclusive marketing under § 314.108(b)(2) and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement during

the 1-year period beginning 4 years after the date of approval of the patented drug and within 45 days of receipt of the notice of certification from the applicant under § 314.52 or § 314.95, the 505(b)(2) application or ANDA may be approved at the expiration of the 7 1/2 years from the date of approval of the NDA for the patented drug product.

(ii) *Federal district court decision of invalidity, unenforceability, or non-infringement.* If before the expiration of the 30-month period, or 7 1/2 years where applicable, the district court decides that the patent is invalid, unenforceable, or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the 505(b)(2) application or ANDA may be approved on:

(A) The date on which the court enters judgment reflecting the decision; or

(B) The date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid, unenforceable, or not infringed.

(iii) *Appeal of Federal district court judgment of infringement.* If before the expiration of the 30-month period, or 7 1/2 years where applicable, the district court decides that the patent has been infringed, and if the judgment of the district court is appealed, the 505(b)(2) application or ANDA may be approved on:

(A) The date on which the mandate is issued by the court of appeals entering judgment that the patent is invalid, unenforceable, or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(B) The date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid, unenforceable, or not infringed.

(iv) *Affirmation or non-appeal of Federal district court judgment of infringement.* If before the expiration of the 30-month period, or 7 1/2 years where applicable, the district court decides that the patent has been infringed, and if the judgment of the district court is not appealed or is affirmed, the 505(b)(2) application or ANDA may be approved no earlier than the date specified by the district court in an order under 35 U.S.C. 271(e)(4)(A).

(v) *Grant of preliminary injunction by Federal district court.* If before the expiration of the 30-month period, or 7 1/2 years where applicable, the district court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug product until the court decides the issues of patent validity and infringement, and if the court later decides that:

(A) The patent is invalid, unenforceable, or not infringed, the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(3)(ii) of this section; or

(B) The patent is infringed, the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(3)(iii) or (iv) of this section, whichever is applicable.

(vi) *Written consent to approval by patent owner or exclusive patent licensee.* If before the expiration of the 30-month period, or 7 1/2 years where applicable, the patent owner or the exclusive patent licensee (or their representatives) agrees in writing that the 505(b)(2) application or ANDA may be approved any time on or after the date of the consent, approval may be granted on or after that date.

(vii) *Court order terminating 30-month or 7 1/2 -year period.* If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court enters an order requiring the 30-month or 7 1/2 -year period to be terminated, the 505(b)(2) application or ANDA may be approved in accordance with the court's order.

(viii) *Court order of dismissal without a finding of infringement.* If before the expiration of the 30-month period, or 7 1/2 years where applicable, the court(s) enter(s) an order of dismissal, with or without prejudice, without a finding of infringement in each pending suit for patent infringement brought within 45 days of receipt of the notice of paragraph IV certification sent by the 505(b)(2) or ANDA applicant, the 505(b)(2) application or ANDA may be approved on or after the date of the order.

(4) *Tentative approval.* FDA will issue a tentative approval letter when tentative approval is appropriate in accordance with this section. In order for a 505(b)(2) application or ANDA to be approved under paragraph (b)(3) of this section, the applicant must receive an approval letter from the Agency. Tentative approval of an NDA or ANDA does not constitute "approval" of an NDA or ANDA and cannot, absent an approval letter from the Agency, result in an approval under paragraph (b)(3) of this section.

(c) *Timing of approval of subsequent ANDA.* (1) If an ANDA contains a paragraph IV certification for a relevant patent and the ANDA is not that of a first applicant, the ANDA is regarded as the ANDA of a subsequent applicant. The ANDA of a subsequent applicant will not be approved during the period when any first applicant is eligible for 180-day exclusivity or during the 180-day exclusivity period of a first applicant. Any applicable 180-day exclusivity period cannot extend beyond the expiration of the patent upon which the 180-day exclusivity period was based.

(2) A first applicant must submit correspondence to its ANDA notifying FDA within 30 days of the date of its first commercial marketing of its drug product or the reference listed drug. If an applicant does not notify FDA, as required in this paragraph (c)(2), of this date, the date of first commercial marketing will be deemed to be the date of the drug product's approval.

(3) If FDA concludes that a first applicant is not actively pursuing approval of its ANDA, FDA may immediately approve an ANDA(s) of a subsequent applicant(s) if the ANDA(s) is otherwise eligible for approval.

(d) *Delay due to exclusivity.* The Agency will also delay the approval of a 505(b)(2) application or ANDA if delay is required by the exclusivity provisions in § 314.108; section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act; or section 505E of the Federal Food, Drug, and Cosmetic Act. When the approval of a 505(b)(2) application or ANDA is delayed under this section and § 314.108; section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act; or section 505E of the Federal Food, Drug, and Cosmetic Act, the 505(b)(2) application or ANDA will be approved on the latest of the days specified under this section and § 314.108; section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act; or section 505E of the Federal Food, Drug, and Cosmetic Act, as applicable.

(e) *Notification of court actions or written consent to approval.* (1) The applicant must submit the following information to FDA, as applicable:

(i) A copy of any judgment by the court (district court or mandate of the court of appeals) or settlement order or consent decree signed and entered by the court (district court or court of appeals) finding a patent described in paragraph (b)(3) of this section invalid, unenforceable, or not infringed, or finding the patent valid and infringed;

(ii) Written notification of whether or not any action by the court described in paragraph (e)(1)(i) of this section has been appealed within the time permitted for an appeal;

(iii) A copy of any order entered by the court terminating the 30-month or 7 1/2 -year period as described in paragraph (b)(3)(i), (ii), (vii), or (viii) of this section;

(iv) A copy of any written consent to approval by the patent owner or exclusive patent licensee described in paragraph (b)(3)(vi) of this section;

(v) A copy of any preliminary injunction described in paragraph (b)(3)(v) of this section, and a copy of any subsequent court order lifting the injunction; and

(vi) A copy of any court order pursuant to 35 U.S.C. 271(e)(4)(A) ordering that a 505(b)(2) application or ANDA may be approved no earlier than the date specified (irrespective of whether the injunction relates to a patent described in paragraph (b)(3) of this section).

(2) All information required by paragraph (e)(1) of this section must be sent to the applicant's NDA or ANDA, as appropriate, within 14 days of the date of entry by the court, the date of appeal or expiration of the time for appeal, or the date of written consent to approval, as applicable.

(f) *Forty-five day period after receipt of notice of paragraph IV certification* —(1) *Computation of 45-day time clock.* The 45-day clock described in paragraph (b)(3) of this section as to each recipient required to receive notice of paragraph IV certification under § 314.52 or § 314.95 begins on the day after the date of receipt of the applicant's notice of paragraph IV certification by the recipient. When the 45th day falls on Saturday, Sunday, or a Federal holiday, the 45th day will be the next day that is not a Saturday, Sunday, or a Federal holiday.

(2) *Notification of filing of legal action.* (i) The 505(b)(2) or ANDA applicant must notify FDA in writing within 14 days of the filing of any legal action filed within 45 days of receipt of the notice of paragraph IV certification by any recipient. A 505(b)(2) applicant must send the notification to its NDA. An ANDA applicant must send the notification to its ANDA. The notification to FDA of the legal action must include:

(A) The 505(b)(2) application or ANDA number.

(B) The name of the 505(b)(2) or ANDA applicant.

(C) The established name of the drug product or, if no established name exists, the name(s) of the active ingredient(s), the drug product's strength, and dosage form.

(D) A statement that an action for patent infringement, identified by court, case number, and the patent number(s) of the patent(s) at issue in the action, has been filed in an appropriate court on a specified date.

(ii) A patent owner or NDA holder (or its representative(s)) may also notify FDA of the filing of any legal action for patent infringement. The notice should contain the information and be sent to the offices or divisions described in paragraph (f)(2)(i) of this section.

(iii) If the 505(b)(2) or ANDA applicant, the patent owner(s), the NDA holder, or its representative(s) does not notify FDA in writing before the expiration of the 45-day time period or the completion of the Agency's review of the 505(b)(2) application or ANDA, whichever occurs later, that a legal action for patent infringement was filed within 45 days of receipt of the notice of paragraph IV certification, the 505(b)(2) application or ANDA may be approved upon expiration of the 45-day period (if the 505(b)(2) or ANDA

applicant confirms that a legal action for patent infringement has not been filed) or upon completion of the Agency's review of the 505(b)(2) application or ANDA, whichever is later.

(3) *Waiver.* If the patent owner or NDA holder who is an exclusive patent licensee (or its representative(s)) waives its opportunity to file a legal action for patent infringement within 45 days of a receipt of the notice of certification and the patent owner or NDA holder who is an exclusive patent licensee (or its representative(s)) submits to FDA a valid waiver before the 45 days elapse, the 505(b)(2) application or ANDA may be approved upon completion of the Agency's review of the NDA or ANDA. FDA will only accept a waiver in the following form:

(*NAME OF PATENT OWNER OR NDA HOLDER WHO IS AN EXCLUSIVE PATENT LICENSEE OR ITS REPRESENTATIVE(S)*) HAS RECEIVED NOTICE FROM (*NAME OF APPLICANT*) UNDER (*SECTION 505(B)(3) OR 505(J)(2)(B) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT*) AND DOES NOT INTEND TO FILE AN ACTION FOR PATENT INFRINGEMENT AGAINST (*NAME OF APPLICANT*) CONCERNING THE DRUG (*NAME OF DRUG*) BEFORE (*DATE ON WHICH 45 DAYS ELAPSE*). (*NAME OF PATENT OWNER OR NDA HOLDER WHO IS AN EXCLUSIVE PATENT LICENSEE*) WAIVES THE OPPORTUNITY PROVIDED BY (*SECTION 505(C)(3)(C) OR 505(J)(5)(B)(III) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT*) AND DOES NOT OBJECT TO FDA'S APPROVAL OF (*NAME OF APPLICANT*)'S (*505(B)(2) APPLICATION OR ANDA*) FOR (*NAME OF DRUG*) WITH AN APPROVAL DATE ON OR AFTER THE DATE OF THIS SUBMISSION.

(g) *Conversion of approval to tentative approval.* If FDA issues an approval letter in error or a court enters an order requiring, in the case of an already approved 505(b)(2) application or ANDA, that the date of approval be delayed, FDA will convert the approval to a tentative approval if appropriate.

§ 314.108 New drug product exclusivity.

(a) *Definitions.* The definitions in § 314.3 and the following definitions of terms apply to this section:

Approved under section 505(b) means an NDA submitted under section 505(b) and approved on or after October 10, 1962, or an application that was “deemed approved” under section 107(c)(2) of Public Law 87-781.

Bioavailability study means a study to determine the bioavailability or the pharmacokinetics of a drug.

Clinical investigation means any experiment other than a bioavailability study in which a drug is administered or dispensed to, or used on, human subjects.

Conducted or sponsored by the applicant with regard to an investigation means that before or during the investigation, the applicant was named in Form FDA-1571 filed with FDA as the sponsor of the investigational new drug application under which the investigation was conducted, or the applicant or the applicant's predecessor in interest, provided substantial support for the investigation. To demonstrate “substantial support,” an applicant must either provide a certified statement from a certified public accountant that the applicant provided 50 percent or more of the cost of conducting the study or provide an explanation why FDA should consider the applicant to have conducted or sponsored the study if the applicant's financial contribution to the study is less than 50 percent or the applicant did not sponsor the investigational new drug. A predecessor in interest is an entity, e.g., a corporation, that the applicant has taken over, merged with, or purchased, or from

which the applicant has purchased all rights to the drug. Purchase of nonexclusive rights to a clinical investigation after it is completed is not sufficient to satisfy this definition.

Essential to approval means, with regard to an investigation, that there are no other data available that could support approval of the NDA.

New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other NDA submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act.

New clinical investigation means an investigation in humans the results of which have not been relied on by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population and do not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness or safety in a new patient population of a previously approved drug product. For purposes of this section, data from a clinical investigation previously submitted for use in the comprehensive evaluation of the safety of a drug product but not to support the effectiveness of the drug product would be considered new.

(b) *Submission of and timing of approval of a 505(b)(2) application or ANDA.* (1) [Reserved]

(2) If a drug product that contains a new chemical entity was approved after September 24, 1984, in an NDA submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, no person may submit a 505(b)(2) application or ANDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act for a drug product that contains the same active moiety as in the new chemical entity for a period of 5 years from the date of approval of the first approved NDA, except that the 505(b)(2) application or ANDA may be submitted after 4 years if it contains a certification of patent invalidity or noninfringement described in § 314.50(i)(1)(i)(A)(*4*) or § 314.94(a)(12)(i)(A)(*4*).

(3) The approval of a 505(b)(2) application or ANDA described in paragraph (b)(2) of this section will occur as provided in § 314.107(b)(1) or (2), unless the owner of a patent that claims the drug, the patent owner's representative, or exclusive licensee brings suit for patent infringement against the applicant during the 1-year period beginning 48 months after the date of approval of the NDA for the new chemical entity and within 45 days after receipt of the notice described at § 314.52 or § 314.95, in which case, approval of the 505(b)(2) application or ANDA will occur as provided in § 314.107(b)(3).

(4) If an NDA:

(i) Was submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act;

(ii) Was approved after September 24, 1984;

(iii) Was for a drug product that contains an active moiety that has been previously approved in another NDA under section 505(b) of the Federal Food, Drug, and Cosmetic Act; and

(iv) Contained reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application, for a period of 3 years after the date of approval of the application, the Agency will not approve a 505(b)(2) application or an ANDA for the conditions of approval of the NDA, or an ANDA submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting the conditions of approval of an original NDA.

(5) If a supplemental NDA:

(i) Was approved after September 24, 1984; and

(ii) Contained reports of new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant that were essential to approval of the supplemental NDA, for a period of 3 years after the date of approval of the supplemental application, the Agency will not approve a 505(b)(2) application or an ANDA for a change, or an ANDA submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting a change approved in the supplemental NDA.

§ 314.110Complete response letter to the applicant.

(a) *Complete response letter.* FDA will send the applicant a complete response letter if the agency determines that we will not approve the application or abbreviated application in its present form for one or more of the reasons given in § 314.125 or § 314.127, respectively.

(1) *Description of specific deficiencies.* A complete response letter will describe all of the specific deficiencies that the agency has identified in an application or abbreviated application, except as stated in paragraph (a)(3) of this section.

(2) *Complete review of data.* A complete response letter reflects FDA's complete review of the data submitted in an original application or abbreviated application (or, where appropriate, a resubmission) and any amendments that the agency has reviewed. The complete response letter will identify any amendments that the agency has not yet reviewed.

(3) *Inadequate data.* If FDA determines, after an application is filed or an abbreviated application is received, that the data submitted are inadequate to support approval, the agency might issue a complete response letter without first conducting required inspections and/or reviewing proposed product labeling.

(4) *Recommendation of actions for approval.* When possible, a complete response letter will recommend actions that the applicant might take to place the application or abbreviated application in condition for approval.

(b) *Applicant actions.* After receiving a complete response letter, the applicant must take one of following actions:

(1) *Resubmission.* Resubmit the application or abbreviated application, addressing all deficiencies identified in the complete response letter.

(i) A resubmission of an application or efficacy supplement that FDA classifies as a Class 1 resubmission constitutes an agreement by the applicant to start a new 2-month review cycle beginning on the date FDA receives the resubmission.

(ii) A resubmission of an application or efficacy supplement that FDA classifies as a Class 2 resubmission constitutes an agreement by the applicant to start a new 6-month review cycle beginning on the date FDA receives the resubmission.

(iii) A resubmission of an NDA supplement other than an efficacy supplement constitutes an agreement by the applicant to start a new review cycle the same length as the initial review cycle for the supplement (excluding any extension due to a major amendment of the initial supplement), beginning on the date FDA receives the resubmission.

(iv) A major resubmission of an abbreviated application constitutes an agreement by the applicant to start a new 6-month review cycle beginning on the date FDA receives the resubmission.

(v) A minor resubmission of an abbreviated application constitutes an agreement by the applicant to start a new review cycle beginning on the date FDA receives the resubmission.

(2) *Withdrawal.* Withdraw the application or abbreviated application. A decision to withdraw an application or abbreviated application is without prejudice to a subsequent submission.

(3) *Request opportunity for hearing.* Ask the agency to provide the applicant an opportunity for a hearing on the question of whether there are grounds for denying approval of the application or abbreviated application under section 505(d) or (j)(4) of the act, respectively. The applicant must submit the request to the Associate Director for Policy, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993. Within 60 days of the date of the request for an opportunity for a hearing, or within a different time period to which FDA and the applicant agree, the agency will either approve the application or abbreviated application under § 314.105, or refuse to approve the application under § 314.125 or abbreviated application under § 314.127 and give the applicant written notice of an opportunity for a hearing under § 314.200 and section 505(c)(1)(B) or (j)(5)(c) of the act on the question of whether there are grounds for denying approval of the application or abbreviated application under section 505(d) or (j)(4) of the act, respectively.

(c) *Failure to take action.* (1) An applicant agrees to extend the review period under section 505(c)(1) or (j)(5)(A) of the act until it takes any of the actions listed in paragraph (b) of this section. For an application or abbreviated application, FDA may consider an applicant's failure to take any of such actions within 1 year after issuance of a complete response letter to be a request by the applicant to withdraw the application, unless the applicant has requested an extension of time in which to resubmit the application. FDA will grant any reasonable request for such an extension. FDA may consider an applicant's failure to resubmit the application within the extended time period or to request an additional extension to be a request by the applicant to withdraw the application.

(2) If FDA considers an applicant's failure to take action in accordance with paragraph (c)(1) of this section to be a request to withdraw the application, the agency will notify the applicant in writing. The applicant will have 30 days from the date of the notification to explain why the application should not be withdrawn and to request an extension of time in which to resubmit the application. FDA will grant any reasonable request for an extension. If the applicant does not respond to the notification within 30 days, the application will be deemed to be withdrawn.

§ 314.120 [Reserved]

§ 314.122 Submitting an abbreviated application for, or a 505(j)(2)(C) petition that relies on, a listed drug that is no longer marketed.

(a) An abbreviated new drug application that refers to, or a petition under section 505(j)(2)(C) of the act and § 314.93 that relies on, a listed drug that has been voluntarily withdrawn from sale in the United States must be accompanied by a petition seeking a determination whether the listed drug was withdrawn for safety or

effectiveness reasons. The petition must be submitted under §§ 10.25(a) and 10.30 of this chapter and must contain all evidence available to the petitioner concerning the reasons for the withdrawal from sale.

(b) When a petition described in paragraph (a) of this section is submitted, the agency will consider the evidence in the petition and any other evidence before the agency, and determine whether the listed drug is withdrawn from sale for safety or effectiveness reasons, in accordance with the procedures in § 314.161.

(c) An abbreviated new drug application described in paragraph (a) of this section will be disapproved, under § 314.127(a)(11), and a 505(j)(2)(C) petition described in paragraph (a) of this section will be disapproved, under § 314.93(e)(1)(iv), unless the agency determines that the withdrawal of the listed drug was not for safety or effectiveness reasons.

(d) Certain drug products approved for safety and effectiveness that were no longer marketed on September 24, 1984, are not included in the list. Any person who wishes to obtain marketing approval for such a drug product under an abbreviated new drug application must petition FDA for a determination whether the drug product was withdrawn from the market for safety or effectiveness reasons and request that the list be amended to include the drug product. A person seeking such a determination shall use the petition procedures established in § 10.30 of this chapter. The petitioner shall include in the petition information to show that the drug product was approved for safety and effectiveness and all evidence available to the petitioner concerning the reason that marketing of the drug product ceased.

§ 314.125 Refusal to approve an NDA.

(a) The Food and Drug Administration will refuse to approve the NDA and for a new drug give the applicant written notice of an opportunity for a hearing under § 314.200 on the question of whether there are grounds for denying approval of the NDA under section 505(d) of the Federal Food, Drug, and Cosmetic Act, if:

(1) FDA sends the applicant a complete response letter under § 314.110;

(2) The applicant requests an opportunity for hearing for a new drug on the question of whether the NDA is approvable; and

(3) FDA finds that any of the reasons given in paragraph (b) of this section apply.

(b) FDA may refuse to approve an NDA for any of the following reasons, unless the requirement has been waived under § 314.90:

(1) The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance or the drug product are inadequate to preserve its identity, strength, quality, purity, stability, and bioavailability.

(2) The investigations required under section 505(b) of the Federal Food, Drug, and Cosmetic Act do not include adequate tests by all methods reasonably applicable to show whether or not the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling.

(3) The results of the tests show that the drug is unsafe for use under the conditions prescribed, recommended, or suggested in its proposed labeling or the results do not show that the drug product is safe for use under those conditions.

(4) There is insufficient information about the drug to determine whether the product is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling.

(5) There is a lack of substantial evidence consisting of adequate and well-controlled investigations, as defined in § 314.126, that the drug product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in its proposed labeling.

(6) The proposed labeling is false or misleading in any particular.

(7) The NDA contains an untrue statement of a material fact.

(8) The drug product's proposed labeling does not comply with the requirements for labels and labeling in part 201.

(9) The NDA does not contain bioavailability or bioequivalence data required under part 320 of this chapter.

(10) A reason given in a letter refusing to file the NDA under § 314.101(d), if the deficiency is not corrected.

(11) The drug will be manufactured in whole or in part in an establishment that is not registered and not exempt from registration under section 510 of the Federal Food, Drug, and Cosmetic Act and part 207.

(12) The applicant does not permit a properly authorized officer or employee of the Department of Health and Human Services an adequate opportunity to inspect the facilities, controls, and any records relevant to the NDA.

(13) The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance or the drug product do not comply with the current good manufacturing practice regulations in parts 210 and 211.

(14) The NDA does not contain an explanation of the omission of a report of any investigation of the drug product sponsored by the applicant, or an explanation of the omission of other information about the drug pertinent to an evaluation of the NDA that is received or otherwise obtained by the applicant from any source.

(15) A nonclinical laboratory study that is described in the NDA and that is essential to show that the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling was not conducted in compliance with the good laboratory practice regulations in part 58 of this chapter and no reason for the noncompliance is provided or, if it is, the differences between the practices used in conducting the study and the good laboratory practice regulations do not support the validity of the study.

(16) Any clinical investigation involving human subjects described in the NDA, subject to the institutional review board regulations in part 56 of this chapter or informed consent regulations in part 50 of this chapter, was not conducted in compliance with those regulations such that the rights or safety of human subjects were not adequately protected.

(17) The applicant or contract research organization that conducted a bioavailability or bioequivalence study described in § 320.38 or § 320.63 of this chapter that is contained in the NDA refuses to permit an inspection of facilities or records relevant to the study by a properly authorized officer or employee of the Department of Health and Human Services or refuses to submit reserve samples of the drug products used in the study when requested by FDA.

(18) For a new drug, the NDA failed to contain the patent information required by section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act.

(19) The 505(b)(2) application failed to contain a patent certification or statement with respect to each listed patent for a drug product approved in an NDA that:

(i) Is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application is submitted; and

(ii) Was approved before the original 505(b)(2) application was submitted.

(c) For drugs intended to treat life-threatening or severely-debilitating illnesses that are developed in accordance with §§ 312.80 through 312.88 of this chapter, the criteria contained in paragraphs (b) (3), (4), and (5) of this section shall be applied according to the considerations contained in § 312.84 of this chapter.

§ 314.126 Adequate and well-controlled studies.

(a) The purpose of conducting clinical investigations of a drug is to distinguish the effect of a drug from other influences, such as spontaneous change in the course of the disease, placebo effect, or biased observation. The characteristics described in paragraph (b) of this section have been developed over a period of years and are recognized by the scientific community as the essentials of an adequate and well-controlled clinical investigation. The Food and Drug Administration considers these characteristics in determining whether an investigation is adequate and well-controlled for purposes of section 505 of the act. Reports of adequate and well-controlled investigations provide the primary basis for determining whether there is "substantial evidence" to support the claims of effectiveness for new drugs. Therefore, the study report should provide sufficient details of study design, conduct, and analysis to allow critical evaluation and a determination of whether the characteristics of an adequate and well-controlled study are present.

(b) An adequate and well-controlled study has the following characteristics:

(1) There is a clear statement of the objectives of the investigation and a summary of the proposed or actual methods of analysis in the protocol for the study and in the report of its results. In addition, the protocol should contain a description of the proposed methods of analysis, and the study report should contain a description of the methods of analysis ultimately used. If the protocol does not contain a description of the proposed methods of analysis, the study report should describe how the methods used were selected.

(2) The study uses a design that permits a valid comparison with a control to provide a quantitative assessment of drug effect. The protocol for the study and report of results should describe the study design precisely; for example, duration of treatment periods, whether treatments are parallel, sequential, or crossover, and whether the sample size is predetermined or based upon some interim analysis. Generally, the following types of control are recognized:

(i) *Placebo concurrent control.* The test drug is compared with an inactive preparation designed to resemble the test drug as far as possible. A placebo-controlled study may include additional treatment groups, such as an active treatment control or a dose-comparison control, and usually includes randomization and blinding of patients or investigators, or both.

(ii) *Dose-comparison concurrent control.* At least two doses of the drug are compared. A dose-comparison study may include additional treatment groups, such as placebo control or active control. Dose-comparison trials usually include randomization and blinding of patients or investigators, or both.

(iii) *No treatment concurrent control.* Where objective measurements of effectiveness are available and placebo effect is negligible, the test drug is compared with no treatment. No treatment concurrent control trials usually include randomization.

(iv) *Active treatment concurrent control.* The test drug is compared with known effective therapy; for example, where the condition treated is such that administration of placebo or no treatment would be contrary to the interest of the patient. An active treatment study may include additional treatment groups, however, such as a placebo control or a dose-comparison control. Active treatment trials usually include randomization and blinding of patients or investigators, or both. If the intent of the trial is to show similarity of the test and control drugs, the report of the study should assess the ability of the study to have detected a difference between treatments. Similarity of test drug and active control can mean either that both drugs were effective or that neither was effective. The analysis of the study should explain why the drugs should be considered effective in the study, for example, by reference to results in previous placebo-controlled studies of the active control drug.

(v) *Historical control.* The results of treatment with the test drug are compared with experience historically derived from the adequately documented natural history of the disease or condition, or from the results of active treatment, in comparable patients or populations. Because historical control populations usually cannot be as well assessed with respect to pertinent variables as can concurrent control populations, historical control designs are usually reserved for special circumstances. Examples include studies of diseases with high and predictable mortality (for example, certain malignancies) and studies in which the effect of the drug is self-evident (general anesthetics, drug metabolism).

(3) The method of selection of subjects provides adequate assurance that they have the disease or condition being studied, or evidence of susceptibility and exposure to the condition against which prophylaxis is directed.

(4) The method of assigning patients to treatment and control groups minimizes bias and is intended to assure comparability of the groups with respect to pertinent variables such as age, sex, severity of disease, duration of disease, and use of drugs or therapy other than the test drug. The protocol for the study and the report of its results should describe how subjects were assigned to groups. Ordinarily, in a concurrently controlled study, assignment is by randomization, with or without stratification.

(5) Adequate measures are taken to minimize bias on the part of the subjects, observers, and analysts of the data. The protocol and report of the study should describe the procedures used to accomplish this, such as blinding.

(6) The methods of assessment of subjects' response are well-defined and reliable. The protocol for the study and the report of results should explain the variables measured, the methods of observation, and criteria used to assess response.

(7) There is an analysis of the results of the study adequate to assess the effects of the drug. The report of the study should describe the results and the analytic methods used to evaluate them, including any appropriate statistical methods. The analysis should assess, among other things, the comparability of test and control groups with respect to pertinent variables, and the effects of any interim data analyses performed.

(c) The Director of the Center for Drug Evaluation and Research may, on the Director's own initiative or on the petition of an interested person, waive in whole or in part any of the criteria in paragraph (b) of this section with respect to a specific clinical investigation, either prior to the investigation or in the evaluation of a completed study. A petition for a waiver is required to set forth clearly and concisely the specific criteria from which waiver is sought, why the criteria are not reasonably applicable to the particular clinical investigation,

what alternative procedures, if any, are to be, or have been employed, and what results have been obtained. The petition is also required to state why the clinical investigations so conducted will yield, or have yielded, substantial evidence of effectiveness, notwithstanding nonconformance with the criteria for which waiver is requested.

(d) For an investigation to be considered adequate for approval of a new drug, it is required that the test drug be standardized as to identity, strength, quality, purity, and dosage form to give significance to the results of the investigation.

(e) Uncontrolled studies or partially controlled studies are not acceptable as the sole basis for the approval of claims of effectiveness. Such studies carefully conducted and documented, may provide corroborative support of well-controlled studies regarding efficacy and may yield valuable data regarding safety of the test drug. Such studies will be considered on their merits in the light of the principles listed here, with the exception of the requirement for the comparison of the treated subjects with controls. Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered.

§ 314.127 Refusal to approve an ANDA.

(a) FDA will refuse to approve an ANDA for a new drug under section 505(j) of the Federal Food, Drug, and Cosmetic Act for any of the following reasons, unless the requirement has been waived under § 314.99:

(1) The methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug product are inadequate to ensure and preserve its identity, strength, quality, and purity.

(2) Information submitted with the ANDA is insufficient to show that each of the proposed conditions of use has been previously approved for the listed drug referred to in the ANDA.

(3)(i) If the reference listed drug has only one active ingredient, information submitted with the ANDA is insufficient to show that the active ingredient is the same as that of the reference listed drug;

(ii) If the reference listed drug has more than one active ingredient, information submitted with the ANDA is insufficient to show that the active ingredients are the same as the active ingredients of the reference listed drug; or

(iii) If the reference listed drug has more than one active ingredient and if the ANDAis for a drug product that has an active ingredient different from the reference listed drug:

(A) Information submitted with the ANDA is insufficient to show:

(*1*) That the other active ingredients are the same as the active ingredients of the reference listed drug; or

(*2*) That the different active ingredient is an active ingredient of a listed drug or a drug that does not meet the requirements of section 201(p) of the Federal Food, Drug, and Cosmetic Act; or

(B) No petition to submit an ANDA for the drug product with the different active ingredient was approved under § 314.93.

(4)(i) If the ANDA is for a drug product whose route of administration, dosage form, or strength purports to be the same as that of the listed drug referred to in the ANDA, information submitted in the abbreviated new drug application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the reference listed drug; or

(ii) If the ANDA is for a drug product whose route of administration, dosage form, or strength is different from that of the listed drug referred to in the application, no petition to submit an ANDA for the drug product with the different route of administration, dosage form, or strength was approved under § 314.93.

(5) If the ANDA was submitted under the approval of a petition under § 314.93, the ANDA did not contain the information required by FDA with respect to the active ingredient, route of administration, dosage form, or strength that is not the same as that of the reference listed drug.

(6)(i) Information submitted in the ANDA is insufficient to show that the drug product is bioequivalent to the listed drug referred to in the ANDA; or

(ii) If the ANDA was submitted under a petition approved under § 314.93, information submitted in the ANDA is insufficient to show that the active ingredients of the drug product are of the same pharmacological or therapeutic class as those of the reference listed drug and that the drug product can be expected to have the same therapeutic effect as the reference listed drug when administered to patients for each condition of use approved for the reference listed drug.

(7) Information submitted in the ANDA is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the ANDA except for changes required because of differences approved in a petition under § 314.93 or because the drug product and the reference listed drug are produced or distributed by different manufacturers or because aspects of the listed drug's labeling are protected by patent, or by exclusivity, and such differences do not render the proposed drug product less safe or effective than the listed drug for all remaining, nonprotected conditions of use.

(8)(i) Information submitted in the ANDA or any other information available to FDA shows that:

(A) The inactive ingredients of the drug product are unsafe for use, as described in paragraph (a)(8)(ii) of this section, under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug product; or

(B) The composition of the drug product is unsafe, as described in paragraph (a)(8)(ii) of this section, under the conditions prescribed, recommended, or suggested in the proposed labeling because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included.

(ii)(A) FDA will consider the inactive ingredients or composition of a drug product unsafe and refuse to approve an ANDA under paragraph (a)(8)(i) of this section if, on the basis of information available to the agency, there is a reasonable basis to conclude that one or more of the inactive ingredients of the proposed drug or its composition raises serious questions of safety or efficacy. From its experience with reviewing inactive ingredients, and from other information available to it, FDA may identify changes in inactive ingredients or composition that may adversely affect a drug product's safety or efficacy. The inactive ingredients or composition of a proposed drug product will be considered to raise serious questions of safety or efficacy if the product incorporates one or more of these changes. Examples of the changes that may raise serious questions of safety or efficacy include, but are not limited to, the following:

(*1*) A change in an inactive ingredient so that the product does not comply with an official compendium.

(*2*) A change in composition to include an inactive ingredient that has not been previously approved in a drug product for human use by the same route of administration.

(*3*) A change in the composition of a parenteral drug product to include an inactive ingredient that has not been previously approved in a parenteral drug product.

(*4*) A change in composition of a drug product for ophthalmic use to include an inactive ingredient that has not been previously approved in a drug for ophthalmic use.

(*5*) The use of a delivery or a modified release mechanism never before approved for the drug.

(*6*) A change in composition to include a significantly greater content of one or more inactive ingredients than previously used in the drug product.

(*7*) If the drug product is intended for topical administration, a change in the properties of the vehicle or base that might increase absorption of certain potentially toxic active ingredients thereby affecting the safety of the drug product, or a change in the lipophilic properties of a vehicle or base, e.g., a change from an oleaginous to a water soluble vehicle or base.

(B) FDA will consider an inactive ingredient in, or the composition of, a drug product intended for parenteral use to be unsafe and will refuse to approve the ANDA unless it contains the same inactive ingredients, other than preservatives, buffers, and antioxidants, in the same concentration as the listed drug, and, if it differs from the listed drug in a preservative, buffer, or antioxidant, the ANDA contains sufficient information to demonstrate that the difference does not affect the safety or efficacy of the drug product.

(C) FDA will consider an inactive ingredient in, or the composition of, a drug product intended for ophthalmic or otic use unsafe and will refuse to approve the ANDA unless it contains the same inactive ingredients, other than preservatives, buffers, substances to adjust tonicity, or thickening agents, in the same concentration as the listed drug, and if it differs from the listed drug in a preservative, buffer, substance to adjust tonicity, or thickening agent, the ANDA contains sufficient information to demonstrate that the difference does not affect the safety or efficacy of the drug product and the labeling does not claim any therapeutic advantage over or difference from the listed drug.

(9) Approval of the listed drug referred to in the ANDA has been withdrawn or suspended for grounds described in § 314.150(a) or FDA has published a notice of opportunity for hearing to withdraw approval of the reference listed drug under § 314.150(a).

(10) Approval of the listed drug referred to in the ANDA has been withdrawn under § 314.151 or FDA has proposed to withdraw approval of the reference listed drug under § 314.151(a).

(11) FDA has determined that the reference listed drug has been withdrawn from sale for safety or effectiveness reasons under § 314.161, or the reference listed drug has been voluntarily withdrawn from sale and the agency has not determined whether the withdrawal is for safety or effectiveness reasons, or approval of the reference listed drug has been suspended under § 314.153, or the agency has issued an initial decision proposing to suspend the reference listed drug under § 314.153(a)(1).

(12) The abbreviated new drug application does not meet any other requirement under section 505(j)(2)(A) of the Federal Food, Drug, and Cosmetic Act.

(13) The abbreviated new drug application contains an untrue statement of material fact.

(14) For an ANDA submitted pursuant to an approved petition under § 10.30 of this chapter and § 314.93, an NDA subsequently has been approved for the change described in the approved petition.

(b) FDA may refuse to approve an ANDA for a new drug if the applicant or contract research organization that conducted a bioavailability or bioequivalence study described in § 320.63 of this chapter that is contained in the ANDA refuses to permit an inspection of facilities or records relevant to the study by a properly authorized officer or employee of the Department of Health and Human Services or refuses to submit reserve samples of the drug products used in the study when requested by FDA.

§ 314.150 Withdrawal of approval of an application or abbreviated application.

(a) The Food and Drug Administration will notify the applicant, and, if appropriate, all other persons who manufacture or distribute identical, related, or similar drug products as defined in §§ 310.6 and 314.151(a) of this chapter and for a new drug afford an opportunity for a hearing on a proposal to withdraw approval of the application or abbreviated new drug application under section 505(e) of the act and under the procedure in § 314.200, if any of the following apply:

(1) The Secretary of Health and Human Services has suspended the approval of the application or abbreviated application for a new drug on a finding that there is an imminent hazard to the public health. FDA will promptly afford the applicant an expedited hearing following summary suspension on a finding of imminent hazard to health.

(2) FDA finds:

(i) That clinical or other experience, tests, or other scientific data show that the drug is unsafe for use under the conditions of use upon the basis of which the application or abbreviated application was approved; or

(ii) That new evidence of clinical experience, not contained in the application or not available to FDA until after the application or abbreviated application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when the application or abbreviated application was approved, evaluated together with the evidence available when the application or abbreviated application was approved, reveal that the drug is not shown to be safe for use under the conditions of use upon the basis of which the application or abbreviated application was approved; or

(iii) Upon the basis of new information before FDA with respect to the drug, evaluated together with the evidence available when the application or abbreviated application was approved, that there is a lack of substantial evidence from adequate and well-controlled investigations as defined in § 314.126, that the drug will have the effect it is purported or represented to have under the conditions of use prescribed, recommended, or suggested in its labeling; or

(iv) That the application or abbreviated application contains any untrue statement of a material fact; or

(v) That the patent information prescribed by section 505(c) of the act was not submitted within 30 days after the receipt of written notice from FDA specifying the failure to submit such information; or

(b) FDA may notify the applicant, and, if appropriate, all other persons who manufacture or distribute identical, related, or similar drug products as defined in § 310.6, and for a new drug afford an opportunity for a hearing on a proposal to withdraw approval of the application or abbreviated new drug application under section 505(e) of the act and under the procedure in § 314.200, if the agency finds:

(1) That the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain required records or to make required reports under section 505(k) or 507(g) of

the act and § 314.80, § 314.81, or § 314.98, or that the applicant has refused to permit access to, or copying or verification of, its records.

(2) That on the basis of new information before FDA, evaluated together with the evidence available when the application or abbreviated application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to ensure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the agency.

(3) That on the basis of new information before FDA, evaluated together with the evidence available when the application or abbreviated application was approved, the labeling of the drug, based on a fair evaluation of all material facts, is false or misleading in any particular, and the labeling was not corrected by the applicant within a reasonable time after receipt of written notice from the agency.

(4) That the applicant has failed to comply with the notice requirements of section 510(j)(2) of the act.

(5) That the applicant has failed to submit bioavailability or bioequivalence data required under part 320 of this chapter.

(6) The application or abbreviated application does not contain an explanation of the omission of a report of any investigation of the drug product sponsored by the applicant, or an explanation of the omission of other information about the drug pertinent to an evaluation of the application or abbreviated application that is received or otherwise obtained by the applicant from any source.

(7) That any nonclinical laboratory study that is described in the application or abbreviated application and that is essential to show that the drug is safe for use under the conditions prescribed, recommended, or suggested in its labeling was not conducted in compliance with the good laboratory practice regulations in part 58 of this chapter and no reason for the noncompliance was provided or, if it was, the differences between the practices used in conducting the study and the good laboratory practice regulations do not support the validity of the study.

(8) Any clinical investigation involving human subjects described in the application or abbreviated application, subject to the institutional review board regulations in part 56 of this chapter or informed consent regulations in part 50 of this chapter, was not conducted in compliance with those regulations such that the rights or safety of human subjects were not adequately protected.

(9) That the applicant or contract research organization that conducted a bioavailability or bioequivalence study described in § 320.38 or § 320.63 of this chapter that is contained in the application or abbreviated application refuses to permit an inspection of facilities or records relevant to the study by a properly authorized officer or employee of the Department of Health and Human Services or refuses to submit reserve samples of the drug products used in the study when requested by FDA.

(10) That the labeling for the drug product that is the subject of the abbreviated new drug application is no longer consistent with that for the listed drug referred to in the abbreviated new drug application, except for differences approved in the abbreviated new drug application or those differences resulting from:

(i) A patent on the listed drug issued after approval of the abbreviated new drug application; or

(ii) Exclusivity accorded to the listed drug after approval of the abbreviated new drug application that do not render the drug product less safe or effective than the listed drug for any remaining, nonprotected condition(s) of use.

(c) FDA will withdraw approval of an application or abbreviated application if the applicant requests its withdrawal because the drug subject to the application or abbreviated application is no longer being marketed, provided none of the conditions listed in paragraphs (a) and (b) of this section applies to the drug. FDA will consider a written request for a withdrawal under this paragraph to be a waiver of an opportunity for hearing otherwise provided for in this section. Withdrawal of approval of an application or abbreviated application under this paragraph is without prejudice to refiling.

(d) FDA may notify an applicant that it believes a potential problem associated with a drug is sufficiently serious that the drug should be removed from the market and may ask the applicant to waive the opportunity for hearing otherwise provided for under this section, to permit FDA to withdraw approval of the application or abbreviated application for the product, and to remove voluntarily the product from the market. If the applicant agrees, the agency will not make a finding under paragraph (b) of this section, but will withdraw approval of the application or abbreviated application in a notice published in the **Federal Register** that contains a brief summary of the agency's and the applicant's views of the reasons for withdrawal.

§ 314.151 Withdrawal of approval of an abbreviated new drug application under section 505(j)(5) of the act.

(a) Approval of an abbreviated new drug application approved under § 314.105(d) may be withdrawn when the agency withdraws approval, under § 314.150(a) or under this section, of the approved drug referred to in the abbreviated new drug application. If the agency proposed to withdraw approval of a listed drug under § 314.150(a), the holder of an approved application for the listed drug has a right to notice and opportunity for hearing. The published notice of opportunity for hearing will identify all drug products approved under § 314.105(d) whose applications are subject to withdrawal under this section if the listed drug is withdrawn, and will propose to withdraw such drugs. Holders of approved applications for the identified drug products will be provided notice and an opportunity to respond to the proposed withdrawal of their applications as described in paragraphs (b) and (c) of this section.

(b)(1) The published notice of opportunity for hearing on the withdrawal of the listed drug will serve as notice to holders of identified abbreviated new drug applications of the grounds for the proposed withdrawal.

(2) Holders of applications for drug products identified in the notice of opportunity for hearing may submit written comments on the notice of opportunity for hearing issued on the proposed withdrawal of the listed drug. If an abbreviated new drug application holder submits comments on the notice of opportunity for hearing and a hearing is granted, the abbreviated new drug application holder may participate in the hearing as a nonparty participant as provided for in § 12.89 of this chapter.

(3) Except as provided in paragraphs (c) and (d) of this section, the approval of an abbreviated new drug application for a drug product identified in the notice of opportunity for hearing on the withdrawal of a listed drug will be withdrawn when the agency has completed the withdrawal of approval of the listed drug.

(c)(1) If the holder of an application for a drug identified in the notice of opportunity for hearing has submitted timely comments but does not have an opportunity to participate in a hearing because a hearing is not requested or is settled, the submitted comments will be considered by the agency, which will issue an initial decision. The initial decision will respond to the comments, and contain the agency's decision whether there are grounds to withdraw approval of the listed drug and of the abbreviated new drug applications on which timely comments were submitted. The initial decision will be sent to each abbreviated new drug application holder that has submitted comments.

(2) Abbreviated new drug application holders to whom the initial decision was sent may, within 30 days of the issuance of the initial decision, submit written objections.

(3) The agency may, at its discretion, hold a limited oral hearing to resolve dispositive factual issues that cannot be resolved on the basis of written submissions.

(4) If there are no timely objections to the initial decision, it will become final at the expiration of 30 days.

(5) If timely objections are submitted, they will be reviewed and responded to in a final decision.

(6) The written comments received, the initial decision, the evidence relied on in the comments and in the initial decision, the objections to the initial decision, and, if a limited oral hearing has been held, the transcript of that hearing and any documents submitted therein, shall form the record upon which the agency shall make a final decision.

(7) Except as provided in paragraph (d) of this section, any abbreviated new drug application whose holder submitted comments on the notice of opportunity for hearing shall be withdrawn upon the issuance of a final decision concluding that the listed drug should be withdrawn for grounds as described in § 314.150(a). The final decision shall be in writing and shall constitute final agency action, reviewable in a judicial proceeding.

(8) Documents in the record will be publicly available in accordance with § 10.20(j) of this chapter. Documents available for examination or copying will be placed on public display in the Division of Dockets Management (HFA-305), Food and Drug Administration, room. 1-23, 12420 Parklawn Dr., Rockville, MD 20857, promptly upon receipt in that office.

(d) If the agency determines, based upon information submitted by the holder of an abbreviated new drug application, that the grounds for withdrawal of the listed drug are not applicable to a drug identified in the notice of opportunity for hearing, the final decision will state that the approval of the abbreviated new drug application for such drug is not withdrawn.

§ 314.152 Notice of withdrawal of approval of an application or abbreviated application for a new drug.

If the Food and Drug Administration withdraws approval of an application or abbreviated application for a new drug, FDA will publish a notice in the **Federal Register** announcing the withdrawal of approval. If the application or abbreviated application was withdrawn for grounds described in § 314.150(a) or § 314.151, the notice will announce the removal of the drug from the list of approved drugs published under section 505(j)(6) of the act and shall satisfy the requirement of § 314.162(b).

§ 314.153 Suspension of approval of an abbreviated new drug application.

(a) *Suspension of approval.* The approval of an abbreviated new drug application approved under § 314.105(d) shall be suspended for the period stated when:

(1) The Secretary of the Department of Health and Human Services, under the imminent hazard authority of section 505(e) of the act or the authority of this paragraph, suspends approval of a listed drug referred to in the abbreviated new drug application, for the period of the suspension;

(2) The agency, in the notice described in paragraph (b) of this section, or in any subsequent written notice given an abbreviated new drug application holder by the agency, concludes that the risk of continued marketing and use of the drug is inappropriate, pending completion of proceedings to withdraw or suspend approval under § 314.151 or paragraph (b) of this section; or

(3) The agency, under the procedures set forth in paragraph (b) of this section, issues a final decision stating the determination that the abbreviated application is suspended because the listed drug on which the approval of the abbreviated new drug application depends has been withdrawn from sale for reasons of safety or effectiveness or has been suspended under paragraph (b) of this section. The suspension will take effect on the date stated in the decision and will remain in effect until the agency determines that the marketing of the drug has resumed or that the withdrawal is not for safety or effectiveness reasons.

(b) *Procedures for suspension of abbreviated new drug applications when a listed drug is voluntarily withdrawn for safety or effectiveness reasons.* (1) If a listed drug is voluntarily withdrawn from sale, and the agency determines that the withdrawal from sale was for reasons of safety or effectiveness, the agency will send each holder of an approved abbreviated new drug application that is subject to suspension as a result of this determination a copy of the agency's initial decision setting forth the reasons for the determination. The initial decision will also be placed on file with the Division of Dockets Management (HFA-305), Food and Drug Administration, room 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

(2) Each abbreviated new drug application holder will have 30 days from the issuance of the initial decision to present, in writing, comments and information bearing on the initial decision. If no comments or information is received, the initial decision will become final at the expiration of 30 days.

(3) Comments and information received within 30 days of the issuance of the initial decision will be considered by the agency and responded to in a final decision.

(4) The agency may, in its discretion, hold a limited oral hearing to resolve dispositive factual issues that cannot be resolved on the basis of written submissions.

(5) If the final decision affirms the agency's initial decision that the listed drug was withdrawn for reasons of safety or effectiveness, the decision will be published in the **Federal Register** in compliance with § 314.152, and will, except as provided in paragraph (b)(6) of this section, suspend approval of all abbreviated new drug applications identified under paragraph (b)(1) of this section and remove from the list the listed drug and any drug whose approval was suspended under this paragraph. The notice will satisfy the requirement of § 314.162(b). The agency's final decision and copies of materials on which it relies will also be filed with the Division of Dockets Management (address in paragraph (b)(1) of this section).

(6) If the agency determines in its final decision that the listed drug was withdrawn for reasons of safety or effectiveness but, based upon information submitted by the holder of an abbreviated new drug application, also determines that the reasons for the withdrawal of the listed drug are not relevant to the safety and

effectiveness of the drug subject to such abbreviated new drug application, the final decision will state that the approval of such abbreviated new drug application is not suspended.

(7) Documents in the record will be publicly available in accordance with § 10.20(j) of this chapter. Documents available for examination or copying will be placed on public display in the Division of Dockets Management (address in paragraph (b)(1) of this section) promptly upon receipt in that office.

§ 314.160 Approval of an application or abbreviated application for which approval was previously refused, suspended, or withdrawn.

Upon the Food and Drug Administration's own initiative or upon request of an applicant, FDA may, on the basis of new data, approve an application or abbreviated application which it had previously refused, suspended, or withdrawn approval. FDA will publish a notice in the **Federal Register** announcing the approval.

§ 314.161 Determination of reasons for voluntary withdrawal of a listed drug.

(a) A determination whether a listed drug that has been voluntarily withdrawn from sale was withdrawn for safety or effectiveness reasons may be made by the agency at any time after the drug has been voluntarily withdrawn from sale, but must be made:

(1) Prior to approving an abbreviated new drug application that refers to the listed drug;

(2) Whenever a listed drug is voluntarily withdrawn from sale and abbreviated new drug applications that referred to the listed drug have been approved; and

(3) When a person petitions for such a determination under §§ 10.25(a) and 10.30 of this chapter.

(b) Any person may petition under §§ 10.25(a) and 10.30 of this chapter for a determination whether a listed drug has been voluntarily withdrawn for safety or effectiveness reasons. Any such petition must contain all evidence available to the petitioner concerning the reason that the drug is withdrawn from sale.

(c) If the agency determines that a listed drug is withdrawn from sale for safety or effectiveness reasons, the agency will, except as provided in paragraph (d) of this section, publish a notice of the determination in the Federal Register.

(d) If the agency determines under paragraph (a) of this section that a listed drug is withdrawn from sale for safety and effectiveness reasons and there are approved abbreviated new drug applications that are subject to suspension under section 505(j)(5) of the act, FDA will initiate a proceeding in accordance with § 314.153(b).

(e) A drug that the agency determines is withdrawn for safety or effectiveness reasons will be removed from the list, under § 314.162. The drug may be relisted if the agency has evidence that marketing of the drug has resumed or that the withdrawal is not for safety or effectiveness reasons. A determination that the drug is not withdrawn for safety or effectiveness reasons may be made at any time after its removal from the list, upon the agency's initiative, or upon the submission of a petition under §§ 10.25(a) and 10.30 of this chapter. If the agency determines that the drug is not withdrawn for safety or effectiveness reasons, the agency shall publish a notice of this determination in the Federal Register. The notice will also announce that the drug is relisted, under § 314.162(c). The notice will also serve to reinstate approval of all suspended abbreviated new drug applications that referred to the listed drug.

§ 314.162 Removal of a drug product from the list.

(a) FDA will remove a previously approved new drug product from the list for the period stated when:

(1) The agency withdraws or suspends approval of a new drug application or an abbreviated new drug application under § 314.150(a) or § 314.151 or under the imminent hazard authority of section 505(e) of the act, for the same period as the withdrawal or suspension of the application; or

(2) The agency, in accordance with the procedures in § 314.153(b) or § 314.161, issues a final decision stating that the listed drug was withdrawn from sale for safety or effectiveness reasons, or suspended under § 314.153(b), until the agency determines that the withdrawal from the market has ceased or is not for safety or effectiveness reasons.

(b) FDA will publish in the **Federal Register** a notice announcing the removal of a drug from the list.

(c) At the end of the period specified in paragraph (a)(1) or (a)(2) of this section, FDA will relist a drug that has been removed from the list. The agency will publish in the **Federal Register** a notice announcing the relisting of the drug.

§ 314.170 Adulteration and misbranding of an approved drug.

All drugs, including those the Food and Drug Administration approves under section 505 of the act and this part, are subject to the adulteration and misbranding provisions in sections 501, 502, and 503 of the act. FDA is authorized to regulate approved new drugs by regulations issued through informal rulemaking under sections 501, 502, and 503 of the act.

Subpart E—Hearing Procedures for New DrugsSource:

§ 314.200 Notice of opportunity for hearing; notice of participation and request for hearing; grant or denial of hearing.

(a) *Notice of opportunity for hearing.* The Director of the Center for Drug Evaluation and Research, Food and Drug Administration, will give the applicant, and all other persons who manufacture or distribute identical, related, or similar drug products as defined in § 310.6 of this chapter, notice and an opportunity for a hearing on the Center's proposal to refuse to approve an application or to withdraw the approval of an application or abbreviated application under section 505(e) of the act. The notice will state the reasons for the action and the proposed grounds for the order.

(1) The notice may be general (that is, simply summarizing in a general way the information resulting in the notice) or specific (that is, either referring to specific requirements in the statute and regulations with which there is a lack of compliance, or providing a detailed description and analysis of the specific facts resulting in the notice).

(2) FDA will publish the notice in the **Federal Register** and will state that the applicant, and other persons subject to the notice under § 310.6, who wishes to participate in a hearing, has 30 days after the date of publication of the notice to file a written notice of participation and request for hearing. The applicant, or other persons subject to the notice under § 310.6, who fails to file a written notice of participation and request for hearing within 30 days, waives the opportunity for a hearing.

(3) It is the responsibility of every manufacturer and distributor of a drug product to review every notice of opportunity for a hearing published in the Federal Register to determine whether it covers any drug product that person manufactures or distributes. Any person may request an opinion of the applicability of a notice to a specific product that may be identical, related, or similar to a product listed in a notice by writing to the Division of New Drugs and Labeling Compliance, Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002. A person shall request an opinion within 30 days of the date of publication of the notice to be eligible for an opportunity for a hearing under the notice. If a person requests an opinion, that person's time for filing an appearance and request for a hearing and supporting studies and analyses begins on the date the person receives the opinion from FDA.

(b) FDA will provide the notice of opportunity for a hearing to applicants and to other persons subject to the notice under § 310.6, as follows:(1) To any person who has submitted an application or abbreviated application, by delivering the notice in person or by sending it by registered or certified mail to the last address shown in the application or abbreviated application.

(2) To any person who has not submitted an application or abbreviated application but who is subject to the notice under § 310.6 of this chapter, by publication of the notice in the Federal Register**.**

(c)(1) *Notice of participation and request for a hearing, and submission of studies and comments.* The applicant, or any other person subject to the notice under § 310.6, who wishes to participate in a hearing, shall file with the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, (i) within 30 days after the date of the publication of the notice (or of the date of receipt of an opinion requested under paragraph (a)(3) of this section) a written notice of participation and request for a hearing and (ii) within 60 days after the date of publication of the notice, unless a different period of time is specified in the notice of opportunity for a hearing, the studies on which the person relies to justify a hearing as specified in paragraph (d) of this section. The applicant, or other person, may incorporate by reference the raw data underlying a study if the data were previously submitted to FDA as part of an application, abbreviated application, or other report.

(2) FDA will not consider data or analyses submitted after 60 days in determining whether a hearing is warranted unless they are derived from well-controlled studies begun before the date of the notice of opportunity for hearing and the results of the studies were not available within 60 days after the date of publication of the notice. Nevertheless, FDA may consider other studies on the basis of a showing by the person requesting a hearing of inadvertent omission and hardship. The person requesting a hearing shall list in the request for hearing all studies in progress, the results of which the person intends later to submit in support of the request for a hearing. The person shall submit under paragraph (c)(1)(ii) of this section a copy of the complete protocol, a list of the participating investigators, and a brief status report of the studies.

(3) Any other interested person who is not subject to the notice of opportunity for a hearing may also submit comments on the proposal to withdraw approval of the application or abbreviated application. The comments are requested to be submitted within the time and under the conditions specified in this section.

(d) The person requesting a hearing is required to submit under paragraph (c)(1)(ii) of this section the studies (including all protocols and underlying raw data) on which the person relies to justify a hearing with respect

to the drug product. Except, a person who requests a hearing on the refusal to approve an application is not required to submit additional studies and analyses if the studies upon which the person relies have been submitted in the application and in the format and containing the summaries required under § 314.50.

(1) If the grounds for FDA's proposed action concern the effectiveness of the drug, each request for hearing is required to be supported only by adequate and well-controlled clinical studies meeting all of the precise requirements of § 314.126 and, for combination drug products, § 300.50, or by other studies not meeting those requirements for which a waiver has been previously granted by FDA under § 314.126. Each person requesting a hearing shall submit all adequate and well-controlled clinical studies on the drug product, including any unfavorable analyses, views, or judgments with respect to the studies. No other data, information, or studies may be submitted.

(2) The submission is required to include a factual analysis of all the studies submitted. If the grounds for FDA's proposed action concern the effectiveness of the drug, the analysis is required to specify how each study accords, on a point-by-point basis, with each criterion required for an adequate well-controlled clinical investigation established under § 314.126 and, if the product is a combination drug product, with each of the requirements for a combination drug established in § 300.50, or the study is required to be accompanied by an appropriate waiver previously granted by FDA. If a study concerns a drug or dosage form or condition of use or mode of administration other than the one in question, that fact is required to be clearly stated. Any study conducted on the final marketed form of the drug product is required to be clearly identified.

(3) Each person requesting a hearing shall submit an analysis of the data upon which the person relies, except that the required information relating either to safety or to effectiveness may be omitted if the notice of opportunity for hearing does not raise any issue with respect to that aspect of the drug; information on compliance with § 300.50 may be omitted if the drug product is not a combination drug product. A financial certification or disclosure statement or both as required by part 54 of this chapter must accompany all clinical data submitted. FDA can most efficiently consider submissions made in the following format.

I. SAFETY DATA.

A. ANIMAL SAFETY DATA.

1. INDIVIDUAL ACTIVE COMPONENTS.

A. CONTROLLED STUDIES.

B. PARTIALLY CONTROLLED OR UNCONTROLLED STUDIES.

2. COMBINATIONS OF THE INDIVIDUAL ACTIVE COMPONENTS.

A. CONTROLLED STUDIES.

B. PARTIALLY CONTROLLED OR UNCONTROLLED STUDIES.

B. HUMAN SAFETY DATA.

1. INDIVIDUAL ACTIVE COMPONENTS.

A. CONTROLLED STUDIES.

B. PARTIALLY CONTROLLED OR UNCONTROLLED STUDIES.

C. DOCUMENTED CASE REPORTS.

D. PERTINENT MARKETING EXPERIENCES THAT MAY INFLUENCE A DETERMINATION ABOUT THE SAFETY OF EACH INDIVIDUAL ACTIVE COMPONENT.

2. COMBINATIONS OF THE INDIVIDUAL ACTIVE COMPONENTS.

A. CONTROLLED STUDIES.

B. PARTIALLY CONTROLLED OR UNCONTROLLED STUDIES.

C. DOCUMENTED CASE REPORTS.

D. PERTINENT MARKETING EXPERIENCES THAT MAY INFLUENCE A DETERMINATION ABOUT THE SAFETY OF EACH INDIVIDUAL ACTIVE COMPONENT.

II. EFFECTIVENESS DATA.

A. INDIVIDUAL ACTIVE COMPONENTS: CONTROLLED STUDIES, WITH AN ANALYSIS SHOWING CLEARLY HOW EACH STUDY SATISFIES, ON A POINT-BY-POINT BASIS, EACH OF THE CRITERIA REQUIRED BY § 314.126.

B. COMBINATIONS OF INDIVIDUAL ACTIVE COMPONENTS.

1. CONTROLLED STUDIES WITH AN ANALYSIS SHOWING CLEARLY HOW EACH STUDY SATISFIES ON A POINT-BY-POINT BASIS, EACH OF THE CRITERIA REQUIRED BY § 314.126.

2. AN ANALYSIS SHOWING CLEARLY HOW EACH REQUIREMENT OF § 300.50 HAS BEEN SATISFIED.

III. A SUMMARY OF THE DATA AND VIEWS SETTING FORTH THE MEDICAL RATIONALE AND PURPOSE FOR THE DRUG AND ITS INGREDIENTS AND THE SCIENTIFIC BASIS FOR THE CONCLUSION THAT THE DRUG AND ITS INGREDIENTS HAVE BEEN PROVEN SAFE AND/OR EFFECTIVE FOR THE INTENDED USE. IF THERE IS AN ABSENCE OF CONTROLLED STUDIES IN THE MATERIAL SUBMITTED OR THE REQUIREMENTS OF ANY ELEMENT OF § 300.50 OR § 314.126 HAVE NOT BEEN FULLY MET, THAT FACT IS REQUIRED TO BE STATED CLEARLY AND A WAIVER OBTAINED UNDER § 314.126 IS REQUIRED TO BE SUBMITTED.

IV. A STATEMENT SIGNED BY THE PERSON RESPONSIBLE FOR SUCH SUBMISSION THAT IT INCLUDES IN FULL (OR INCORPORATES BY REFERENCE AS PERMITTED IN § 314.200(C)(2)) ALL STUDIES AND INFORMATION SPECIFIED IN § 314.200(D).(**WARNING:** A WILLFULLY FALSE STATEMENT IS A CRIMINAL OFFENSE, 18 U.S.C. 1001.)

(e) *Contentions that a drug product is not subject to the new drug requirements.* A notice of opportunity for a hearing encompasses all issues relating to the legal status of each drug product subject to it, including identical, related, and similar drug products as defined in § 310.6. A notice of appearance and request for a hearing under paragraph (c)(1)(i) of this section is required to contain any contention that the product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act, or because it is exempt from part or all of the new drug provisions of the act under the exemption for products marketed before June 25, 1938, contained in section 201(p) of the act or under section 107(c) of the Drug Amendments of 1962, or for any other reason. Each contention is required to be supported by a submission under paragraph (c)(1)(ii) of this section and the Commissioner of Food and Drugs will make an administrative determination on each contention. The failure of any person subject to a notice of opportunity for a hearing, including any person who manufactures or distributes an identical, related, or similar drug product as defined in § 310.6, to submit a notice of participation and request for hearing or to raise all such contentions constitutes a waiver of any contentions not raised.

(1) A contention that a drug product is generally recognized as safe and effective within the meaning of section 201(p) of the act is required to be supported by submission of the same quantity and quality of scientific evidence that is required to obtain approval of an application for the product, unless FDA has waived a requirement for effectiveness (under § 314.126) or safety, or both. The submission should be in the format and with the analyses required under paragraph (d) of this section. A person who fails to submit the required scientific evidence required under paragraph (d) waives the contention. General recognition of safety and effectiveness shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data and information.

(2) A contention that a drug product is exempt from part or all of the new drug provisions of the act under the exemption for products marketed before June 25, 1938, contained in section 201(p) of the act, or under section 107(c) of the Drug Amendments of 1962, is required to be supported by evidence of past and present quantitative formulas, labeling, and evidence of marketing. A person who makes such a contention should submit the formulas, labeling, and evidence of marketing in the following format.

I. FORMULATION.

A. A COPY OF EACH PERTINENT DOCUMENT OR RECORD TO ESTABLISH THE EXACT QUANTITATIVE FORMULATION OF THE DRUG (BOTH ACTIVE AND INACTIVE INGREDIENTS) ON THE DATE OF INITIAL MARKETING OF THE DRUG.

B. A STATEMENT WHETHER SUCH FORMULATION HAS AT ANY SUBSEQUENT TIME BEEN CHANGED IN ANY MANNER. IF ANY SUCH CHANGE HAS BEEN MADE, THE EXACT DATE, NATURE, AND RATIONALE FOR EACH CHANGE IN FORMULATION, INCLUDING ANY DELETION OR CHANGE IN THE CONCENTRATION OF ANY ACTIVE INGREDIENT AND/OR INACTIVE INGREDIENT, SHOULD BE STATED, TOGETHER WITH A COPY OF EACH PERTINENT DOCUMENT OR RECORD TO ESTABLISH THE DATE AND NATURE OF EACH SUCH CHANGE, INCLUDING, BUT NOT LIMITED TO, THE FORMULA WHICH RESULTED FROM EACH SUCH CHANGE. IF NO SUCH CHANGE HAS BEEN MADE, A COPY OF REPRESENTATIVE DOCUMENTS OR RECORDS SHOWING THE FORMULA AT REPRESENTATIVE POINTS IN TIME SHOULD BE SUBMITTED TO SUPPORT THE STATEMENT.

II. LABELING.

A. A COPY OF EACH PERTINENT DOCUMENT OR RECORD TO ESTABLISH THE IDENTITY OF EACH ITEM OF WRITTEN, PRINTED, OR GRAPHIC MATTER USED AS LABELING ON THE DATE THE DRUG WAS INITIALLY MARKETED.

B. A STATEMENT WHETHER SUCH LABELING HAS AT ANY SUBSEQUENT TIME BEEN DISCONTINUED OR CHANGED IN ANY MANNER. IF SUCH DISCONTINUANCE OR CHANGE HAS BEEN MADE, THE EXACT DATE, NATURE, AND RATIONALE FOR EACH DISCONTINUANCE OR CHANGE AND A COPY OF EACH PERTINENT DOCUMENT OR RECORD TO ESTABLISH EACH SUCH DISCONTINUANCE OR CHANGE SHOULD BE SUBMITTED, INCLUDING, BUT NOT LIMITED TO, THE LABELING WHICH RESULTED FROM EACH SUCH DISCONTINUANCE OR CHANGE. IF NO SUCH DISCONTINUANCE OR CHANGE HAS BEEN MADE, A COPY OF

REPRESENTATIVE DOCUMENTS OR RECORDS SHOWING LABELING AT REPRESENTATIVE POINTS IN TIME SHOULD BE SUBMITTED TO SUPPORT THE STATEMENT.

III. MARKETING.

A. A COPY OF EACH PERTINENT DOCUMENT OR RECORD TO ESTABLISH THE EXACT DATE THE DRUG WAS INITIALLY MARKETED.

B. A STATEMENT WHETHER SUCH MARKETING HAS AT ANY SUBSEQUENT TIME BEEN DISCONTINUED. IF SUCH MARKETING HAS BEEN DISCONTINUED, THE EXACT DATE OF EACH SUCH DISCONTINUANCE SHOULD BE SUBMITTED, TOGETHER WITH A COPY OF EACH PERTINENT DOCUMENT OR RECORD TO ESTABLISH EACH SUCH DATE.

IV. VERIFICATION.

A STATEMENT SIGNED BY THE PERSON RESPONSIBLE FOR SUCH SUBMISSION, THAT ALL APPROPRIATE RECORDS HAVE BEEN SEARCHED AND TO THE BEST OF THAT PERSON'S KNOWLEDGE AND BELIEF IT INCLUDES A TRUE AND ACCURATE PRESENTATION OF THE FACTS.**(WARNING:** A WILLFULLY FALSE STATEMENT IS A CRIMINAL OFFENSE, 18 U.S.C. 1001.)

(3) The Food and Drug Administration will not find a drug product, including any active ingredient, which is identical, related, or similar, as described in § 310.6, to a drug product, including any active ingredient for which an application is or at any time has been effective or deemed approved, or approved under section 505 of the act, to be exempt from part or all of the new drug provisions of the act.

(4) A contention that a drug product is not a new drug for any other reason is required to be supported by submission of the factual records, data, and information that are necessary and appropriate to support the contention.

(5) It is the responsibility of every person who manufactures or distributes a drug product in reliance upon a “grandfather” provision of the act to maintain files that contain the data and information necessary fully to document and support that status.

(f) *Separation of functions.* Separation of functions commences upon receipt of a request for hearing. The Director of the Center for Drug Evaluation and Research, Food and Drug Administration, will prepare an analysis of the request and a proposed order ruling on the matter. The analysis and proposed order, the request for hearing, and any proposed order denying a hearing and response under paragraph (g) (2) or (3) of this section will be submitted to the Office of the Commissioner of Food and Drugs for review and decision. When the Center for Drug Evaluation and Research recommends denial of a hearing on all issues on which a hearing is requested, no representative of the Center will participate or advise in the review and decision by the Commissioner. When the Center for Drug Evaluation and Research recommends that a hearing be granted on one or more issues on which a hearing is requested, separation of functions terminates as to those issues, and representatives of the Center may participate or advise in the review and decision by the Commissioner on those issues. The Commissioner may modify the text of the issues, but may not deny a hearing on those issues. Separation of functions continues with respect to issues on which the Center for Drug Evaluation and Research has recommended denial of a hearing. The Commissioner will neither evaluate nor rule on the Center's recommendation on such issues and such issues will not be included in the notice of hearing. Participants in

the hearing may make a motion to the presiding officer for the inclusion of any such issue in the hearing. The ruling on such a motion is subject to review in accordance with § 12.35(b). Failure to so move constitutes a waiver of the right to a hearing on such an issue. Separation of functions on all issues resumes upon issuance of a notice of hearing. The Office of the General Counsel, Department of Health and Human Services, will observe the same separation of functions.

(g) *Summary judgment.* A person who requests a hearing may not rely upon allegations or denials but is required to set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing with respect to a particular drug product specified in the request for hearing.

(1) Where a specific notice of opportunity for hearing (as defined in paragraph (a)(1) of this section) is used, the Commissioner will enter summary judgment against a person who requests a hearing, making findings and conclusions, denying a hearing, if it conclusively appears from the face of the data, information, and factual analyses in the request for the hearing that there is no genuine and substantial issue of fact which precludes the refusal to approve the application or abbreviated application or the withdrawal of approval of the application or abbreviated application; for example, no adequate and well-controlled clinical investigations meeting each of the precise elements of § 314.126 and, for a combination drug product, § 300.50 of this chapter, showing effectiveness have been identified. Any order entering summary judgment is required to set forth the Commissioner's findings and conclusions in detail and is required to specify why each study submitted fails to meet the requirements of the statute and regulations or why the request for hearing does not raise a genuine and substantial issue of fact.

(2) When following a general notice of opportunity for a hearing (as defined in paragraph (a)(1) of this section) the Director of the Center for Drug Evaluation and Research concludes that summary judgment against a person requesting a hearing should be considered, the Director will serve upon the person requesting a hearing by registered mail a proposed order denying a hearing. This person has 60 days after receipt of the proposed order to respond with sufficient data, information, and analyses to demonstrate that there is a genuine and substantial issue of fact which justifies a hearing.

(3) When following a general or specific notice of opportunity for a hearing a person requesting a hearing submits data or information of a type required by the statute and regulations, and the Director of the Center for Drug Evaluation and Research concludes that summary judgment against the person should be considered, the Director will serve upon the person by registered mail a proposed order denying a hearing. The person has 60 days after receipt of the proposed order to respond with sufficient data, information, and analyses to demonstrate that there is a genuine and substantial issue of fact which justifies a hearing.

(4) If review of the data, information, and analyses submitted show that the grounds cited in the notice are not valid, for example, that substantial evidence of effectiveness exists, the Commissioner will enter summary judgment for the person requesting the hearing, and rescind the notice of opportunity for hearing.

(5) If the Commissioner grants a hearing, it will begin within 90 days after the expiration of the time for requesting the hearing unless the parties otherwise agree in the case of denial of approval, and as soon as practicable in the case of withdrawal of approval.

(6) The Commissioner will grant a hearing if there exists a genuine and substantial issue of fact or if the Commissioner concludes that a hearing would otherwise be in the public interest.

(7) If the manufacturer or distributor of an identical, related, or similar drug product requests and is granted a hearing, the hearing may consider whether the product is in fact identical, related, or similar to the drug product named in the notice of opportunity for a hearing.

(8) A request for a hearing, and any subsequent grant or denial of a hearing, applies only to the drug products named in such documents.

(h) FDA will issue a notice withdrawing approval and declaring all products unlawful for drug products subject to a notice of opportunity for a hearing, including any identical, related, or similar drug product under § 310.6, for which an opportunity for a hearing is waived or for which a hearing is denied. The Commissioner may defer or stay the action pending a ruling on any related request for a hearing or pending any related hearing or other administrative or judicial proceeding.

§ 314.201 Procedure for hearings.

Parts 10 through 16 apply to hearings relating to new drugs under section 505 (d) and (e) of the act.

§ 314.235Judicial review.

(a) The Commissioner of Food and Drugs will certify the transcript and record. In any case in which the Commissioner enters an order without a hearing under § 314.200(g), the record certified by the Commissioner is required to include the requests for hearing together with the data and information submitted and the Commissioner's findings and conclusion.

(b) A manufacturer or distributor of an identical, related, or similar drug product under § 310.6 may seek judicial review of an order withdrawing approval of a new drug application, whether or not a hearing has been held, in a United States court of appeals under section 505(h) of the act.

Subpart F [Reserved]

Subpart G—Miscellaneous Provisions

§ 314.410 Imports and exports of new drugs.

(a) *Imports.* (1) A new drug may be imported into the United States if: (i) It is the subject of an approved application under this part; or (ii) it complies with the regulations pertaining to investigational new drugs under part 312; and it complies with the general regulations pertaining to imports under subpart E of part 1.

(2) A drug substance intended for use in the manufacture, processing, or repacking of a new drug may be imported into the United States if it complies with the labeling exemption in § 201.122 pertaining to shipments of drug substances in domestic commerce.

(b) *Exports.* (1) A new drug may be exported if it is the subject of an approved application under this part or it complies with the regulations pertaining to investigational new drugs under part 312.

(2) A new drug substance that is covered by an application approved under this part for use in the manufacture of an approved drug product may be exported by the applicant or any person listed as a supplier in the approved

application, provided the drug substance intended for export meets the specification of, and is shipped with a copy of the labeling required for, the approved drug product.

(3) Insulin or an antibiotic drug may be exported without regard to the requirements in section 802 of the act if the insulin or antibiotic drug meets the requirements of section 801(e)(1) of the act.

§ 314.420 Drug master files.

(a) A drug master file is a submission of information to the Food and Drug Administration by a person (the drug master file holder) who intends it to be used for one of the following purposes: To permit the holder to incorporate the information by reference when the holder submits an investigational new drug application under part 312 or submits an application or an abbreviated application or an amendment or supplement to them under this part, or to permit the holder to authorize other persons to rely on the information to support a submission to FDA without the holder having to disclose the information to the person. FDA ordinarily neither independently reviews drug master files nor approves or disapproves submissions to a drug master file. Instead, the agency customarily reviews the information only in the context of an application under part 312 or this part. A drug master file may contain information of the kind required for any submission to the agency, including information about the following:

(1) [Reserved]

(2) Drug substance, drug substance intermediate, and materials used in their preparation, or drug product;

(3) Packaging materials;

(4) Excipient, colorant, flavor, essence, or materials used in their preparation;

(5) FDA-accepted reference information. (A person wishing to submit information and supporting data in a drug master file (DMF) that is not covered by Types II through IV DMF's must first submit a letter of intent to the Drug Master File Staff, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266.) FDA will then contact the person to discuss the proposed submission.

(b) An investigational new drug application or an application, abbreviated application, amendment, or supplement may incorporate by reference all or part of the contents of any drug master file in support of the submission if the holder authorizes the incorporation in writing. Each incorporation by reference is required to describe the incorporated material by name, reference number, volume, and page number of the drug master file.

(c) A drug master file is required to be submitted in two copies. The agency has prepared guidance that provides information about how to prepare a well-organized drug master file. If the drug master file holder adds, changes, or deletes any information in the file, the holder shall notify in writing, each person authorized to reference that information. Any addition, change, or deletion of information in a drug master file (except the list required under paragraph (d) of this section) is required to be submitted in two copies and to describe by name, reference number, volume, and page number the information affected in the drug master file.

(d) The drug master file is required to contain a complete list of each person currently authorized to incorporate by reference any information in the file, identifying by name, reference number, volume, and page number the information that each person is authorized to incorporate. If the holder restricts the authorization

to particular drug products, the list is required to include the name of each drug product and the application number, if known, to which the authorization applies.

(e) The public availability of data and information in a drug master file, including the availability of data and information in the file to a person authorized to reference the file, is determined under part 20 and § 314.430.

§ 314.430 Availability for public disclosure of data and information in an application or abbreviated application.

(a) The Food and Drug Administration will determine the public availability of any part of an application or abbreviated application under this section and part 20 of this chapter. For purposes of this section, the application or abbreviated application includes all data and information submitted with or incorporated by reference in the application or abbreviated application, including investigational new drug applications, drug master files under § 314.420, supplements submitted under § 314.70 or § 314.97, reports under § 314.80 or § 314.98, and other submissions. For purposes of this section, safety and effectiveness data include all studies and tests of a drug on animals and humans and all studies and tests of the drug for identity, stability, purity, potency, and bioavailability.

(b) FDA will not publicly disclose the existence of an application or abbreviated application before an approval letter is sent to the applicant under § 314.105 or tentative approval letter is sent to the applicant under § 314.107, unless the existence of the application or abbreviated application has been previously publicly disclosed or acknowledged.

(c) If the existence of an unapproved application or abbreviated application has not been publicly disclosed or acknowledged, no data or information in the application or abbreviated application is available for public disclosure.

(d)(1) If the existence of an application or abbreviated application has been publicly disclosed or acknowledged before the agency sends an approval letter to the applicant, no data or information contained in the application or abbreviated application is available for public disclosure before the agency sends an approval letter, but the Commissioner may, in his or her discretion, disclose a summary of selected portions of the safety and effectiveness data that are appropriate for public consideration of a specific pending issue; for example, for consideration of an open session of an FDA advisory committee.

(2) Notwithstanding paragraph (d)(1) of this section, FDA will make available to the public upon request the information in the investigational new drug application that was required to be filed in Docket Number 95S-0158 in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, for investigations involving an exception from informed consent under § 50.24 of this chapter. Persons wishing to request this information shall submit a request under the Freedom of Information Act.

(e) After FDA sends an approval letter to the applicant, the following data and information in the application or abbreviated application are immediately available for public disclosure, unless the applicant shows that extraordinary circumstances exist. A list of approved applications and abbreviated applications, entitled "Approved Drug Products with Therapeutic Equivalence Evaluations," is available from the Government Printing Office, Washington, DC 20402. This list is updated monthly.

(1) [Reserved]

(2) If the application applies to a new drug, all safety and effectiveness data previously disclosed to the public as set forth in § 20.81 and a summary or summaries of the safety and effectiveness data and information submitted with or incorporated by reference in the application. The summaries do not constitute the full reports of investigations under section 505(b)(1) of the act (21 U.S.C. 355(b)(1)) on which the safety or effectiveness of the drug may be approved. The summaries consist of the following:

(i) For an application approved before July 1, 1975, internal agency records that describe safety and effectiveness data and information, for example, a summary of the basis for approval or internal reviews of the data and information, after deletion of the following:

(*a*) Names and any information that would identify patients or test subjects or investigators.

(*b*) Any inappropriate gratuitous comments unnecessary to an objective analysis of the data and information.

(ii) For an application approved on or after July 1, 1975, a Summary Basis of Approval (SBA) document that contains a summary of the safety and effectiveness data and information evaluated by FDA during the drug approval process. The SBA is prepared in one of the following ways:

(*a*) Before approval of the application, the applicant may prepare a draft SBA which the Center for Drug Evaluation and Research will review and may revise. The draft may be submitted with the application or as an amendment.

(*b*) The Center for Drug Evaluation and Research may prepare the SBA.

(3) A protocol for a test or study, unless it is shown to fall within the exemption established for trade secrets and confidential commercial information in § 20.61.

(4) Adverse reaction reports, product experience reports, consumer complaints, and other similar data and information after deletion of the following:

(i) Names and any information that would identify the person using the product.

(ii) Names and any information that would identify any third party involved with the report, such as a physician or hospital or other institution.

(5) A list of all active ingredients and any inactive ingredients previously disclosed to the public as set forth in § 20.81.

(6) An assay procedure or other analytical procedure, unless it serves no regulatory or compliance purpose and is shown to fall within the exemption established for trade secrets and confidential commercial information in § 20.61.

(7) All correspondence and written summaries of oral discussions between FDA and the applicant relating to the application, under the provisions of part 20.

(f) All safety and effectiveness data and information which have been submitted in an application and which have not previously been disclosed to the public are available to the public, upon request, at the time any one of the following events occurs unless extraordinary circumstances are shown:

(1) No work is being or will be undertaken to have the application approved.

(2) A final determination is made that the application is not approvable and all legal appeals have been exhausted.

(3) Approval of the application is withdrawn and all legal appeals have been exhausted.

(4) A final determination has been made that the drug is not a new drug.

(5) For applications submitted under section 505(b) of the act, the effective date of the approval of the first abbreviated application submitted under section 505(j) of the act which refers to such drug, or the date on which the approval of an abbreviated application under section 505(j) of the act which refers to such drug could be made effective if such an abbreviated application had been submitted.

(6) For abbreviated applications submitted under section 505(j) of the act, when FDA sends an approval letter to the applicant.

(g) The following data and information in an application or abbreviated application are not available for public disclosure unless they have been previously disclosed to the public as set forth in § 20.81 of this chapter or they relate to a product or ingredient that has been abandoned and they do not represent a trade secret or confidential commercial or financial information under § 20.61 of this chapter:

(1) Manufacturing methods or processes, including quality control procedures.

(2) Production, sales distribution, and similar data and information, except that any compilation of that data and information aggregated and prepared in a way that does not reveal data or information which is not available for public disclosure under this provision is available for public disclosure.

(3) Quantitative or semiquantitative formulas.

(h) The compilations of information specified in § 20.117 are available for public disclosure.

§ 314.440 Addresses for applications and abbreviated applications.

(a) Applicants shall send applications, abbreviated applications, and other correspondence relating to matters covered by this part, except for products listed in paragraph (b) of this section, to the appropriate office identified below:

(1) Except as provided in paragraph (a)(4) of this section, an application under § 314.50 or § 314.54 submitted for filing should be directed to the Central Document Room, 5901-B Ammendale Rd., Beltsville, MD 20705-1266. Applicants may obtain information about folders for binding applications on the Internet at *http://www.fda.gov/cder/ddms/binders.htm*. After FDA has filed the application, the agency will inform the applicant which division is responsible for the application. Amendments, supplements, resubmissions, requests for waivers, and other correspondence about an application that has been filed should be addressed to 5901-B Ammendale Rd., Beltsville, MD 20705-1266, to the attention of the appropriate division.

(2) Except as provided in paragraph (a)(4) of this section, an abbreviated application under § 314.94, and amendments, supplements, and resubmissions should be directed to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266. This includes items sent by parcel post or overnight courier service. Correspondence not associated with an abbreviated application also should be addressed to 5901-B Ammendale Rd., Beltsville, MD 20705-1266.

(3) A request for an opportunity for a hearing under § 314.110 on the question of whether there are grounds for denying approval of an application, except an application under paragraph (b) of this section, should be directed to the Associate Director for Policy (HFD-5).

(4) The field copy of an application, an abbreviated application, amendments, supplements, resubmissions, requests for waivers, and other correspondence about an application and an abbreviated application shall be sent to the applicant's home FDA district office, except that a foreign applicant shall send the field copy to the appropriate address identified in paragraphs (a)(1) and (a)(2) of this section.

(b) Applicants shall send applications and other correspondence relating to matters covered by this part for the drug products listed below to the Food and Drug Administration, Center for Biologics Evaluation and Research, Document Control Center, 10903 New Hampshire Ave., Bldg. 71, Rm. G112, Silver Spring, MD 20993-0002, except applicants shall send a request for an opportunity for a hearing under § 314.110 on the question of whether there are grounds for denying approval of an application to the Center for Biologics Evaluation and Research, ATTN: Director, at the same address.

(1) Ingredients packaged together with containers intended for the collection, processing, or storage of blood and blood components;

(2) Plasma volume expanders and hydroxyethyl starch for leukapheresis;

(3) Blood component processing solutions and shelf life extenders; and

(4) Oxygen carriers.

§ 314.445 Guidance documents.

(a) FDA has made available guidance documents under § 10.115 of this chapter to help you to comply with certain requirements of this part.

(b) The Center for Drug Evaluation and Research (CDER) maintains a list of guidance documents that apply to CDER's regulations. The list is maintained on the Internet and is published annually in the Federal Register**.** A request for a copy of the CDER list should be directed to the Office of Training and Communications, Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993-0002.

Subpart H—Accelerated Approval of New Drugs for Serious or Life-Threatening IllnessesSource:

§ 314.500 Scope.

This subpart applies to certain new drug products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments (e.g., ability to treat patients unresponsive to, or intolerant of, available therapy, or improved patient response over available therapy).

§ 314.510 Approval based on a surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity.

FDA may grant marketing approval for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. Approval under this

section will be subject to the requirement that the applicant study the drug further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome. Postmarketing studies would usually be studies already underway. When required to be conducted, such studies must also be adequate and well-controlled. The applicant shall carry out any such studies with due diligence.

§ 314.520 Approval with restrictions to assure safe use.

(a) If FDA concludes that a drug product shown to be effective can be safely used only if distribution or use is restricted, FDA will require such postmarketing restrictions as are needed to assure safe use of the drug product, such as:

(1) Distribution restricted to certain facilities or physicians with special training or experience; or

(2) Distribution conditioned on the performance of specified medical procedures.

(b) The limitations imposed will be commensurate with the specific safety concerns presented by the drug product.

§ 314.530 Withdrawal procedures.

(a) For new drugs approved under §§ 314.510 and 314.520, FDA may withdraw approval, following a hearing as provided in part 15 of this chapter, as modified by this section, if:

(1) A postmarketing clinical study fails to verify clinical benefit;

(2) The applicant fails to perform the required postmarketing study with due diligence;

(3) Use after marketing demonstrates that postmarketing restrictions are inadequate to assure safe use of the drug product;

(4) The applicant fails to adhere to the postmarketing restrictions agreed upon;

(5) The promotional materials are false or misleading; or

(6) Other evidence demonstrates that the drug product is not shown to be safe or effective under its conditions of use.

(b) *Notice of opportunity for a hearing.* The Director of the Center for Drug Evaluation and Research will give the applicant notice of an opportunity for a hearing on the Center's proposal to withdraw the approval of an application approved under § 314.510 or § 314.520. The notice, which will ordinarily be a letter, will state generally the reasons for the action and the proposed grounds for the order.

(c) *Submission of data and information.*

(1) If the applicant fails to file a written request for a hearing within 15 days of receipt of the notice, the applicant waives the opportunity for a hearing.

(2) If the applicant files a timely request for a hearing, the agency will publish a notice of hearing in the Federal Register in accordance with §§ 12.32(e) and 15.20 of this chapter.

(3) An applicant who requests a hearing under this section must, within 30 days of receipt of the notice of opportunity for a hearing, submit the data and information upon which the applicant intends to rely at the hearing.

(d) *Separation of functions.* Separation of functions (as specified in § 10.55 of this chapter) will not apply at any point in withdrawal proceedings under this section.

(e) *Procedures for hearings.* Hearings held under this section will be conducted in accordance with the provisions of part 15 of this chapter, with the following modifications:

(1) An advisory committee duly constituted under part 14 of this chapter will be present at the hearing. The committee will be asked to review the issues involved and to provide advice and recommendations to the Commissioner of Food and Drugs.

(2) The presiding officer, the advisory committee members, up to three representatives of the applicant, and up to three representatives of the Center may question any person during or at the conclusion of the person's presentation. No other person attending the hearing may question a person making a presentation. The presiding officer may, as a matter of discretion, permit questions to be submitted to the presiding officer for response by a person making a presentation.

(f) *Judicial review.* The Commissioner's decision constitutes final agency action from which the applicant may petition for judicial review. Before requesting an order from a court for a stay of action pending review, an applicant must first submit a petition for a stay of action under § 10.35 of this chapter.

§ 314.540 Postmarketing safety reporting.

Drug products approved under this program are subject to the postmarketing recordkeeping and safety reporting applicable to all approved drug products, as provided in §§ 314.80 and 314.81.

§ 314.550 Promotional materials.

For drug products being considered for approval under this subpart, unless otherwise informed by the agency, applicants must submit to the agency for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the agency, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

§ 314.560 Termination of requirements.

If FDA determines after approval that the requirements established in § 314.520, § 314.530, or § 314.550 are no longer necessary for the safe and effective use of a drug product, it will so notify the applicant. Ordinarily, for drug products approved under § 314.510, these requirements will no longer apply when FDA determines that the required postmarketing study verifies and describes the drug product's clinical benefit and the drug product would be appropriate for approval under traditional procedures. For drug products approved under § 314.520, the restrictions would no longer apply when FDA determines that safe use of the drug product can be assured through appropriate labeling. FDA also retains the discretion to remove specific postapproval requirements upon review of a petition submitted by the sponsor in accordance with § 10.30.

Subpart I—Approval of New Drugs When Human Efficacy Studies Are Not Ethical or FeasibleSource:

§ 314.600 Scope.

This subpart applies to certain new drug products that have been studied for their safety and efficacy in ameliorating or preventing serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substances. This subpart applies only to those new drug products for which: Definitive human efficacy studies cannot be conducted because it would be unethical to deliberately expose healthy human volunteers to a lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substance; and field trials to study the product's effectiveness after an accidental or hostile exposure have not been feasible. This subpart does not apply to products that can be approved based on efficacy standards described elsewhere in FDA's regulations (e.g., accelerated approval based on surrogate markers or clinical endpoints other than survival or irreversible morbidity), nor does it address the safety evaluation for the products to which it does apply.

§ 314.610 Approval based on evidence of effectiveness from studies in animals.

(a) FDA may grant marketing approval for a new drug product for which safety has been established and for which the requirements of § 314.600 are met based on adequate and well-controlled animal studies when the results of those animal studies establish that the drug product is reasonably likely to produce clinical benefit in humans. In assessing the sufficiency of animal data, the agency may take into account other data, including human data, available to the agency. FDA will rely on the evidence from studies in animals to provide substantial evidence of the effectiveness of these products only when:

(1) There is a reasonably well-understood pathophysiological mechanism of the toxicity of the substance and its prevention or substantial reduction by the product;

(2) The effect is demonstrated in more than one animal species expected to react with a response predictive for humans, unless the effect is demonstrated in a single animal species that represents a sufficiently well-characterized animal model for predicting the response in humans;

(3) The animal study endpoint is clearly related to the desired benefit in humans, generally the enhancement of survival or prevention of major morbidity; and

(4) The data or information on the kinetics and pharmacodynamics of the product or other relevant data or information, in animals and humans, allows selection of an effective dose in humans.

(b) Approval under this subpart will be subject to three requirements:

(1) *Postmarketing studies.* The applicant must conduct postmarketing studies, such as field studies, to verify and describe the drug's clinical benefit and to assess its safety when used as indicated when such studies are feasible and ethical. Such postmarketing studies would not be feasible until an exigency arises. When such studies are feasible, the applicant must conduct such studies with due diligence. Applicants must include as part of their application a plan or approach to postmarketing study commitments in the event such studies become ethical and feasible.

(2) *Approval with restrictions to ensure safe use.* If FDA concludes that a drug product shown to be effective under this subpart can be safely used only if distribution or use is restricted, FDA will require such

postmarketing restrictions as are needed to ensure safe use of the drug product, commensurate with the specific safety concerns presented by the drug product, such as:

(i) Distribution restricted to certain facilities or health care practitioners with special training or experience;

(ii) Distribution conditioned on the performance of specified medical procedures, including medical followup; and

(iii) Distribution conditioned on specified recordkeeping requirements.

(3) *Information to be provided to patient recipients.* For drug products or specific indications approved under this subpart, applicants must prepare, as part of their proposed labeling, labeling to be provided to patient recipients. The patient labeling must explain that, for ethical or feasibility reasons, the drug's approval was based on efficacy studies conducted in animals alone and must give the drug's indication(s), directions for use (dosage and administration), contraindications, a description of any reasonably foreseeable risks, adverse reactions, anticipated benefits, drug interactions, and any other relevant information required by FDA at the time of approval. The patient labeling must be available with the product to be provided to patients prior to administration or dispensing of the drug product for the use approved under this subpart, if possible.

§ 314.620 Withdrawal procedures.

(a) *Reasons to withdraw approval.* For new drugs approved under this subpart, FDA may withdraw approval, following a hearing as provided in part 15 of this chapter, as modified by this section, if:

(1) A postmarketing clinical study fails to verify clinical benefit;

(2) The applicant fails to perform the postmarketing study with due diligence;

(3) Use after marketing demonstrates that postmarketing restrictions are inadequate to ensure safe use of the drug product;

(4) The applicant fails to adhere to the postmarketing restrictions applied at the time of approval under this subpart;

(5) The promotional materials are false or misleading; or

(6) Other evidence demonstrates that the drug product is not shown to be safe or effective under its conditions of use.

(b) *Notice of opportunity for a hearing.* The Director of the Center for Drug Evaluation and Research (CDER) will give the applicant notice of an opportunity for a hearing on CDER's proposal to withdraw the approval of an application approved under this subpart. The notice, which will ordinarily be a letter, will state generally the reasons for the action and the proposed grounds for the order.

(c) *Submission of data and information.* (1) If the applicant fails to file a written request for a hearing within 15 days of receipt of the notice, the applicant waives the opportunity for a hearing.

(2) If the applicant files a timely request for a hearing, the agency will publish a notice of hearing in the Federal Register in accordance with §§ 12.32(e) and 15.20 of this chapter.

(3) An applicant who requests a hearing under this section must, within 30 days of receipt of the notice of opportunity for a hearing, submit the data and information upon which the applicant intends to rely at the hearing.

(d) *Separation of functions.* Separation of functions (as specified in § 10.55 of this chapter) will not apply at any point in withdrawal proceedings under this section.

(e) *Procedures for hearings.* Hearings held under this section will be conducted in accordance with the provisions of part 15 of this chapter, with the following modifications:

(1) An advisory committee duly constituted under part 14 of this chapter will be present at the hearing. The committee will be asked to review the issues involved and to provide advice and recommendations to the Commissioner of Food and Drugs.

(2) The presiding officer, the advisory committee members, up to three representatives of the applicant, and up to three representatives of CDER may question any person during or at the conclusion of the person's presentation. No other person attending the hearing may question a person making a presentation. The presiding officer may, as a matter of discretion, permit questions to be submitted to the presiding officer for response by a person making a presentation.

(f) *Judicial review.* The Commissioner of Food and Drugs' decision constitutes final agency action from which the applicant may petition for judicial review. Before requesting an order from a court for a stay of action pending review, an applicant must first submit a petition for a stay of action under § 10.35 of this chapter.

§ 314.630 Postmarketing safety reporting.

Drug products approved under this subpart are subject to the postmarketing recordkeeping and safety reporting requirements applicable to all approved drug products, as provided in §§ 314.80 and 314.81.

§ 314.640 Promotional materials.

For drug products being considered for approval under this subpart, unless otherwise informed by the agency, applicants must submit to the agency for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the agency, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

§ 314.650 Termination of requirements.

If FDA determines after approval under this subpart that the requirements established in §§ 314.610(b)(2), 314.620, and 314.630 are no longer necessary for the safe and effective use of a drug product, FDA will so notify the applicant. Ordinarily, for drug products approved under § 314.610, these requirements will no longer apply when FDA determines that the postmarketing study verifies and describes the drug product's clinical benefit. For drug products approved under § 314.610, the restrictions would no longer apply when FDA determines that safe use of the drug product can be ensured through appropriate labeling. FDA also retains the discretion to remove specific postapproval requirements upon review of a petition submitted by the sponsor in accordance with § 10.30 of this chapter.

附属資料４：米国関連条文（生物学的製剤）

① 35USC271 Infringement of patent.[16]

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States, or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination, or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

(d) No patent owner otherwise entitled to relief for infringement or contributory infringement of a patent shall be denied relief or deemed guilty of misuse or illegal extension of the patent right by reason of his having done one or more of the following: (1) derived revenue from acts which if performed by another without his consent would constitute contributory infringement of the patent; (2) licensed or authorized another to perform acts which if performed without his consent would constitute contributory infringement of the patent; (3) sought to enforce his patent rights against infringement or contributory infringement; (4) refused to license or use any rights to the patent; or (5) conditioned the license of any rights to the patentor the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

(e)(1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

(2) It shall be an act of infringement to submit —

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent,

(B) an application under section 512 of such Actor under the Act of March 4, 1913 (21 U.S.C. 151 - 158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation

[16] 35USC271（Discover U.S. Government Information ウェブサイト）
https://www.govinfo.gov/content/pkg/USCODE-2011-title35/pdf/USCODE-2011-title35-partIII-chap28-sec271.pdf

techniques and which is claimed in a patentor the use of which is claimed in a patent, or

(C)

(i) with respect to a patent that is identified in the list of patents described in section 351(l)(3) of the Public Health Service Act (including as provided under section351(l)(7) of such Act), an application seeking approval of a biological product, or

(ii) if the applicant for the application fails to provide the application and information required under section351(l)(2)(A) of such Act, an application seeking approval of a biological product for a patent that could be identified pursuant to section 351(l)(3)(A)(i) of such Act, if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug, veterinary biological product, or biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

(3) In any action for patent infringement brought under this section, no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under paragraph (1).

(4) For an act of infringement described in paragraph(2)—

(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product,

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product, and

(D) the court shall order a permanent injunction prohibiting any infringement of the patent by the biological product involved in the infringement until a date which is not earlier than the date of the expiration of the patent that has been infringed under paragraph (2)(C), provided the patent is the subject of a final court decision, as defined in section 351(k)(6)of the Public Health Service Act, in an action for infringement of the patent under section 351(l)(6) of such Act, and the biological product has not yet been approved because of section 351(k)(7) of such Act.

The remedies prescribed by subparagraphs (A), (B), (C), and(D) are the only remedies which may be granted by a court for an act of infringement described in paragraph (2), except that acourt may award attorney fees under section 285.

(5) Where a person has filed an application described in paragraph (2) that includes a certification under subsection(b)(2)(A)(iv) or (j) (2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), and neither the owner of the patent that is the subject of the certification nor the holder of the approved application under subsection (b) of such section for the drug that is claimed by the patent or a use of which is claimed by the patent brought an action for infringement of such patent before the expiration of 45 days after the date on which the notice given under subsection (b)(3)or (j) (2)(B) of such section was received,

the courts of the United States shall, to the extent consistent with the Constitution, have subject matter jurisdiction in any action brought by such person under section 2201 of title 28 for a declaratory judgment that such patent is invalid or not infringed.

(6)(A) Subparagraph (B) applies, in lieu of paragraph (4), in the case of a patent-

(i) that is identified, as applicable, in the list of patents described in section 351(l)(4) of the Public Health Service Act or the lists of patents described in section351(l)(5)(B) of such Act with respect to a biological product; and

(ii) for which an action for infringement of the pate¥nt with respect to the biological product—

(I) was brought after the expiration of the30-day period described in subparagraph (A) or (B), as applicable, of section 351(l)(6) of such Act; or

(II) was brought before the expiration of the 30-day period described in subclause (I), but which was dismissed without prejudice or was not prosecuted to judgment in good faith.

(B) In an action for infringement of a patent described in subparagraph (A), the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty.

(C) The owner of a patent that should have been included in the list described in section 351(l)(3)(A) of the Public Health Service Act, including as provided under section 351(l)(7) of such Act for a biological product, but was not timely included in such list, may not bring an action under this section for infringement of the patent with respect to the biological product.

(f)(1) Whoever without authority supplies or causes to be supplied in or from the United States all or a substantial portion of the components of a patented invention, where such components are uncombined in whole or in part, in such manner as to actively induce the combination of such components outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(2) Whoever without authority supplies or causes to be supplied in or from the United States any component of a patented invention that is especially made or especially adapted for use in the invention and not a staple article or commodity of commerce suitable for substantial noninfringing use, where such component is uncombined in whole or in part, knowing that such component is so made or adapted and intending that such component will be combined outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent. In an action for infringement of a process patent, no remedy may be granted for infringement on account of the noncommercial use or retail sale of a product unless there is no adequate remedy under this title for infringement on account of the importation or other use, offer to sell, or sale of that product. A product which is made by a patented process will, for purposes of this title, not be considered to be so made after —

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and nonessential component of another product.
(h) As used in this section, the term “whoever” includes any State, any instrumentality of a State, any officer or employee of a State or instrumentality of a State acting in his official capacity. Any State, and any such instrumentality, officer, or
employee, shall be subject to the provisions of this title in the same manner and to the same extent as any nongovernmental entity.
(i) As used in this section, an “offer for sale” or an “offer to sell” by a person other than the patentee or any assignee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.

② 42USC262 Regulation of biological products[17]

(a) Biologics license
(1) No person shall introduce or deliver for introduction into interstate commerce any biological product unless—
(A) a biologics license under this subsection or subsection (k) is in effect for the biological product; and
(B) each package of the biological product is plainly marked with—
(i) the proper name of the biological product contained in the package;
(ii) the name, address, and applicable license number of the manufacturer of the biological product; and
(iii) the expiration date of the biological product.
(2)
(A) The Secretary shall establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.
(B) Pediatric studies.—
A person that submits an application for a license under this paragraph shall submit to the Secretary as part of the application any assessments required under section 505B of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c].
(C) The Secretary shall approve a biologics license application—
(i) on the basis of a demonstration that—
(I) the biological product that is the subject of the application is safe, pure, and potent; and
(II) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and
(ii) if the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).
(D) Postmarket studies and clinical trials; labeling; risk evaluation and mitigation strategy.—
A person that submits an application for a license under this paragraph is subject to sections 505(o), 505(p), and 505–1 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(o), (p), 355–1].

[17] 42USC262 Regulation of biological products（Discover U.S. Government Information ウェブサイト）
https://www.govinfo.gov/content/pkg/USCODE-2010-title42/pdf/USCODE-2010-title42-chap6A-subchapII-partF-subpart1-sec262.pdf

(E)
(i) The Secretary may rely upon qualified data summaries to support the approval of a supplemental application, with respect to a qualified indication for a drug, submitted under this subsection, if such supplemental application complies with the requirements of subparagraph (B) of section 505(c)(5) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(c)(5)].
(ii) In this subparagraph, the terms "qualified indication" and "qualified data summary" have the meanings given such terms in section 505(c)(5) of the Federal Food, Drug, and Cosmetic Act.
(3) The Secretary shall prescribe requirements under which a biological product undergoing investigation shall be exempt from the requirements of paragraph (1).

(b) Falsely labeling or marking package or container; altering label or mark
No person shall falsely label or mark any package or container of any biological product or alter any label or mark on the package or container of the biological product so as to falsify the label or mark.

(c) Inspection of establishment for propagation and preparation
Any officer, agent, or employee of the Department of Health and Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any biological product.

(d) Recall of product presenting imminent hazard; violations
(1) Upon a determination that a batch, lot, or other quantity of a product licensed under this section presents an imminent or substantial hazard to the public health, the Secretary shall issue an order immediately ordering the recall of such batch, lot, or other quantity of such product. An order under this paragraph shall be issued in accordance with section 554 of title 5.
(2) Any violation of paragraph (1) shall subject the violator to a civil penalty of up to $100,000 per day of violation. The amount of a civil penalty under this paragraph shall, effective December 1 of each year beginning 1 year after the effective date of this paragraph, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest ⅒ of 1 percent. For purposes of this paragraph, the term "base quarter", as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.

(e) Interference with officers
No person shall interfere with any officer, agent, or employee of the Service in the performance of any duty imposed upon him by this section or by regulations made by authority thereof.

(f) Penalties for offenses

Any person who shall violate, or aid or abet in violating, any of the provisions of this section shall be punished upon conviction by a fine not exceeding $500 or by imprisonment not exceeding one year, or by both such fine and imprisonment, in the discretion of the court.

(g) Construction with other laws

Nothing contained in this chapter shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.].

(h) Exportation of partially processed biological products

A partially processed biological product which—

(1) is not in a form applicable to the prevention, treatment, or cure of diseases or injuries of man;

(2) is not intended for sale in the United States; and

(3) is intended for further manufacture into final dosage form outside the United States,

shall be subject to no restriction on the export of the product under this chapter or the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] if the product is manufactured, processed, packaged, and held in conformity with current good manufacturing practice requirements or meets international manufacturing standards as certified by an international standards organization recognized by the Secretary and meets the requirements of section 801(e)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381(e)).

(i) “Biological product” defined

In this section:

(1) The term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

(2) The term “biosimilar” or “biosimilarity”, in reference to a biological product that is the subject of an application under subsection (k), means—

(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and

(B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

(3) The term “interchangeable” or “interchangeability”, in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

(4) The term “reference product” means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k).

(j) Application of Federal Food, Drug, and Cosmetic Act

The Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.], including the requirements under sections 505(o), 505(p), and 505–1 of such Act [21 U.S.C. 355(o), (p), 355–1], applies to a biological product subject to regulation under this section, except that a product for which a license has been approved under subsection (a) shall not be required to have an approved application under section 505 of such Act.

(k) Licensure of biological products as biosimilar or interchangeable

(1) In general

Any person may submit an application for licensure of a biological product under this subsection.

(2) Content

(A) In general

(i) Required information An application submitted under this subsection shall include information demonstrating that—

(I) the biological product is biosimilar to a reference product based upon data derived from—

(aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;

(bb) animal studies (including the assessment of toxicity); and

(cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency in 1 or more appropriate conditions of use for which the reference product is licensed and intended to be used and for which licensure is sought for the biological product;

(II) the biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism or mechanisms of action are known for the reference product;

(III) the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product;

(IV) the route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product; and

(V) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

(ii) Determination by Secretary

The Secretary may determine, in the Secretary’s discretion, that an element described in clause (i)(I) is unnecessary in an application submitted under this subsection.

(iii) Additional information An application submitted under this subsection—

(I) shall include publicly-available information regarding the Secretary’s previous determination that the reference product is safe, pure, and potent;

(II) may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product; and

(III) may include information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product.

(B) Interchangeability

An application (or a supplement to an application) submitted under this subsection may include information demonstrating that the biological product meets the standards described in paragraph (4).

(3) Evaluation by Secretary

Upon review of an application (or a supplement to an application) submitted under this subsection, the Secretary shall license the biological product under this subsection if—

(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product—

(i) is biosimilar to the reference product; or

(ii) meets the standards described in paragraph (4), and therefore is interchangeable with the reference product; and

(B) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

(4) Safety standards for determining interchangeability Upon review of an application submitted under this subsection or any supplement to such application, the Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application (or a supplement to such application) is sufficient to show that—

(A) the biological product—

(i) is biosimilar to the reference product; and

(ii) can be expected to produce the same clinical result as the reference product in any given patient; and

(B) for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

(5) General rules

(A) One reference product per application

A biological product, in an application submitted under this subsection, may not be evaluated against more than 1 reference product.

(B) Review

An application submitted under this subsection shall be reviewed by the division within the Food and Drug Administration that is responsible for the review and approval of the application under which the reference product is licensed.

(C) Risk evaluation and mitigation strategies

The authority of the Secretary with respect to risk evaluation and mitigation strategies under the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] shall apply to biological products licensed under this subsection in the same manner as such authority applies to biological products licensed under subsection (a).

(6) Exclusivity for first interchangeable biological product Upon review of an application submitted under this subsection relying on the same reference product for which a prior biological product has received a determination of interchangeability for any condition of use, the Secretary shall not make a determination

under paragraph (4) that the second or subsequent biological product is interchangeable for any condition of use until the earlier of—

(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;

(B)18 months after—

(i) a final court decision on all patents in suit in an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(ii) the dismissal with or without prejudice of an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(C)

(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (l)(6) and such litigation is still ongoing within such 42-month period; or

(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (l)(6).

For purposes of this paragraph, the term "final court decision" means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken.

(7) Exclusivity for reference product

(A) Effective date of biosimilar application approval

Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

(B) Filing period

An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a).

(C) First licensure

Subparagraphs (A) and (B) shall not apply to a license for or approval of—

(i) a supplement for the biological product that is the reference product; or

(ii) a subsequent application filed by the same sponsor or manufacturer of the biological product that is the reference product (or a licensor, predecessor in interest, or other related entity) for—

(I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or

(II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

(D) Deemed licenses

(i) No additional exclusivity through deeming

An approved application that is deemed to be a license for a biological product under this section pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009 shall not be treated as having been first licensed under subsection (a) for purposes of subparagraphs (A) and (B).

(ii) Application of limitations on exclusivity

Subparagraph (C) shall apply with respect to a reference product referred to in such subparagraph that was the subject of an approved application that was deemed to be a license pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009.

(iii) Applicability

The exclusivity periods described in section 527, section 505A(b)(1)(A)(ii), and section 505A(c)(1)(A)(ii) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360cc and 355a(b)(1)(A)(ii), (c)(1)(A)(ii)] shall continue to apply to a biological product after an approved application for the biological product is deemed to be a license for the biological product under subsection (a) pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009.

(8) Guidance documents

(A) In general

The Secretary may, after opportunity for public comment, issue guidance in accordance, except as provided in subparagraph (B)(i), with section 701(h) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 371(h)] with respect to the licensure of a biological product under this subsection. Any such guidance may be general or specific.

(B) Public comment

(i) In general

The Secretary shall provide the public an opportunity to comment on any proposed guidance issued under subparagraph (A) before issuing final guidance.

(ii) Input regarding most valuable guidance

The Secretary shall establish a process through which the public may provide the Secretary with input regarding priorities for issuing guidance.

(C) No requirement for application consideration

The issuance (or non-issuance) of guidance under subparagraph (A) shall not preclude the review of, or action on, an application submitted under this subsection.

(D) Requirement for product class-specific guidance If the Secretary issues product class-specific guidance under subparagraph (A), such guidance shall include a description of—

(i) the criteria that the Secretary will use to determine whether a biological product is highly similar to a reference product in such product class; and

(ii) the criteria, if available, that the Secretary will use to determine whether a biological product meets the standards described in paragraph (4).

(E) Certain product classes

(i) Guidance

The Secretary may indicate in a guidance document that the science and experience, as of the date of such guidance, with respect to a product or product class (not including any recombinant protein) does not allow approval of an application for a license as provided under this subsection for such product or product class.

(ii) Modification or reversal

The Secretary may issue a subsequent guidance document under subparagraph (A) to modify or reverse a guidance document under clause (i).

(iii) No effect on ability to deny license

Clause (i) shall not be construed to require the Secretary to approve a product with respect to which the Secretary has not indicated in a guidance document that the science and experience, as described in clause (i), does not allow approval of such an application.

(9) Public listing

(A) In general

(i) Initial publication

Not later than 180 days after December 27, 2020, the Secretary shall publish and make available to the public in a searchable, electronic format—

(I) a list of each biological product, by nonproprietary name (proper name), for which, as of December 27, 2020, a biologics license under subsection (a) or this subsection is in effect, or that, as of such date of enactment, is deemed to be licensed under this section pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009;

(II) the date of licensure of the marketing application and the application number; and

(III) with respect to each biological product described in subclause (I), the licensure status, and, as available, the marketing status.

(ii) Revisions

Every 30 days after the publication of the first list under clause (i), the Secretary shall revise the list to include each biological product which has been licensed under subsection (a) or this subsection during the 30-day period or deemed licensed under this section pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009.

(iii) Patent information

Not later than 30 days after a list of patents under subsection (l)(3)(A), or a supplement to such list under subsection (l)(7), has been provided by the reference product sponsor to the subsection (k) applicant respecting a biological product included on the list published under this subparagraph, the reference product sponsor shall provide such list of patents (or supplement thereto) and their corresponding expiry dates to the Secretary, and the Secretary shall, in revisions made under clause (ii), include such information for such biological product. Within 30 days of providing any subsequent or supplemental list of patents to any subsequent subsection (k) applicant under subsection (l)(3)(A) or (l)(7), the reference product sponsor shall update the information provided to the Secretary under this clause with any additional patents from such subsequent or supplemental list and their corresponding expiry dates.

(iv) Listing of exclusivities

For each biological product included on the list published under this subparagraph, the Secretary shall specify each exclusivity period under paragraph (6) or paragraph (7) for which the Secretary has determined such biological product to be eligible and that has not concluded.

(B) Revocation or suspension of license If the license of a biological product is determined by the Secretary to have been revoked or suspended for safety, purity, or potency reasons, it may not be published in the list under subparagraph (A). If such revocation or suspension occurred after inclusion of such biological product in the list published under subparagraph (A), the reference product sponsor shall notify the Secretary that—

(i) the biological product shall be immediately removed from such list for the same period as the revocation or suspension; and

(ii) a notice of the removal shall be published in the Federal Register.

(l) Patents

(1) Confidential access to subsection (k) application

(A) Application of paragraph

Unless otherwise agreed to by a person that submits an application under subsection (k) (referred to in this subsection as the "subsection (k) applicant") and the sponsor of the application for the reference product (referred to in this subsection as the "reference product sponsor"), the provisions of this paragraph shall apply to the exchange of information described in this subsection.

(B) In general

(i) Provision of confidential information

When a subsection (k) applicant submits an application under subsection (k), such applicant shall provide to the persons described in clause (ii), subject to the terms of this paragraph, confidential access to the information required to be produced pursuant to paragraph (2) and any other information that the subsection (k) applicant determines, in its sole discretion, to be appropriate (referred to in this subsection as the "confidential information").

(ii) Recipients of information The persons described in this clause are the following:

(I) Outside counsel

One or more attorneys designated by the reference product sponsor who are employees of an entity other than the reference product sponsor (referred to in this paragraph as the "outside counsel"), provided that such attorneys do not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(II) In-house counsel

One attorney that represents the reference product sponsor who is an employee of the reference product sponsor, provided that such attorney does not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(iii) Patent owner access

A representative of the owner of a patent exclusively licensed to a reference product sponsor with respect to the reference product and who has retained a right to assert the patent or participate in litigation concerning the patent may be provided the confidential information, provided that the representative informs the reference

product sponsor and the subsection (k) applicant of his or her agreement to be subject to the confidentiality provisions set forth in this paragraph, including those under clause (ii).

(C) Limitation on disclosure

No person that receives confidential information pursuant to subparagraph (B) shall disclose any confidential information to any other person or entity, including the reference product sponsor employees, outside scientific consultants, or other outside counsel retained by the reference product sponsor, without the prior written consent of the subsection (k) applicant, which shall not be unreasonably withheld.

(D) Use of confidential information

Confidential information shall be used for the sole and exclusive purpose of determining, with respect to each patent assigned to or exclusively licensed by the reference product sponsor, whether a claim of patent infringement could reasonably be asserted if the subsection (k) applicant engaged in the manufacture, use, offering for sale, sale, or importation into the United States of the biological product that is the subject of the application under subsection (k).

(E) Ownership of confidential information

The confidential information disclosed under this paragraph is, and shall remain, the property of the subsection (k) applicant. By providing the confidential information pursuant to this paragraph, the subsection (k) applicant does not provide the reference product sponsor or the outside counsel any interest in or license to use the confidential information, for purposes other than those specified in subparagraph (D).

(F) Effect of infringement action

In the event that the reference product sponsor files a patent infringement suit, the use of confidential information shall continue to be governed by the terms of this paragraph until such time as a court enters a protective order regarding the information. Upon entry of such order, the subsection (k) applicant may redesignate confidential information in accordance with the terms of that order. No confidential information shall be included in any publicly-available complaint or other pleading. In the event that the reference product sponsor does not file an infringement action by the date specified in paragraph (6), the reference product sponsor shall return or destroy all confidential information received under this paragraph, provided that if the reference product sponsor opts to destroy such information, it will confirm destruction in writing to the subsection (k) applicant.

(G) Rule of construction Nothing in this paragraph shall be construed—

(i) as an admission by the subsection (k) applicant regarding the validity, enforceability, or infringement of any patent; or

(ii) as an agreement or admission by the subsection (k) applicant with respect to the competency, relevance, or materiality of any confidential information.

(H) Effect of violation

The disclosure of any confidential information in violation of this paragraph shall be deemed to cause the subsection (k) applicant to suffer irreparable harm for which there is no adequate legal remedy and the court shall consider immediate injunctive relief to be an appropriate and necessary remedy for any violation or threatened violation of this paragraph.

(2) Subsection (k) application information Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k) applicant—

(A) shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application; and

(B) may provide to the reference product sponsor additional information requested by or on behalf of the reference product sponsor.

(3) List and description of patents

(A) List by reference product sponsor Not later than 60 days after the receipt of the application and information under paragraph (2), the reference product sponsor shall provide to the subsection (k) applicant—

(i) a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted by the reference product sponsor, or by a patent owner that has granted an exclusive license to the reference product sponsor with respect to the reference product , if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application; and

(ii) an identification of the patents on such list that the reference product sponsor would be prepared to license to the subsection (k) applicant.

(B) List and description by subsection (k) applicant Not later than 60 days after receipt of the list under subparagraph (A), the subsection (k) applicant—

(i) may provide to the reference product sponsor a list of patents to which the subsection (k) applicant believes a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application;

(ii) shall provide to the reference product sponsor, with respect to each patent listed by the reference product sponsor under subparagraph (A) or listed by the subsection (k) applicant under clause (i)—

(I) a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of the subsection (k) applicant that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application; or

(II) a statement that the subsection (k) applicant does not intend to begin commercial marketing of the biological product before the date that such patent expires; and

(iii) shall provide to the reference product sponsor a response regarding each patent identified by the reference product sponsor under subparagraph (A)(ii).

(C) Description by reference product sponsor

Not later than 60 days after receipt of the list and statement under subparagraph (B), the reference product sponsor shall provide to the subsection (k) applicant a detailed statement that describes, with respect to each patent described in subparagraph (B)(ii)(I), on a claim by claim basis, the factual and legal basis of the opinion of the reference product sponsor that such patent will be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application and a response to the statement concerning validity and enforceability provided under subparagraph (B)(ii)(I).

(4) Patent resolution negotiations

(A) In general

After receipt by the subsection (k) applicant of the statement under paragraph (3)(C), the reference product sponsor and the subsection (k) applicant shall engage in good faith negotiations to agree on which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6).

(B) Failure to reach agreement

If, within 15 days of beginning negotiations under subparagraph (A), the subsection (k) applicant and the reference product sponsor fail to agree on a final and complete list of which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6), the provisions of paragraph (5) shall apply to the parties.

(5) Patent resolution if no agreement

(A) Number of patents

The subsection (k) applicant shall notify the reference product sponsor of the number of patents that such applicant will provide to the reference product sponsor under subparagraph (B)(i)(I).

(B) Exchange of patent lists

(i) In generalOn a date agreed to by the subsection (k) applicant and the reference product sponsor, but in no case later than 5 days after the subsection (k) applicant notifies the reference product sponsor under subparagraph (A), the subsection (k) applicant and the reference product sponsor shall simultaneously exchange—

(I) the list of patents that the subsection (k) applicant believes should be the subject of an action for patent infringement under paragraph (6); and

(II) the list of patents, in accordance with clause (ii), that the reference product sponsor believes should be the subject of an action for patent infringement under paragraph (6).

(ii) Number of patents listed by reference product sponsor

(I) In general

Subject to subclause (II), the number of patents listed by the reference product sponsor under clause (i)(II) may not exceed the number of patents listed by the subsection (k) applicant under clause (i)(I).

(II) Exception

If a subsection (k) applicant does not list any patent under clause (i)(I), the reference product sponsor may list 1 patent under clause (i)(II).

(6) Immediate patent infringement action

(A) Action if agreement on patent list

If the subsection (k) applicant and the reference product sponsor agree on patents as described in paragraph (4), not later than 30 days after such agreement, the reference product sponsor shall bring an action for patent infringement with respect to each such patent.

(B) Action if no agreement on patent list

If the provisions of paragraph (5) apply to the parties as described in paragraph (4)(B), not later than 30 days after the exchange of lists under paragraph (5)(B), the reference product sponsor shall bring an action for patent infringement with respect to each patent that is included on such lists.

(C) Notification and publication of complaint

(i)Notification to Secretary

Not later than 30 days after a complaint is served to a subsection (k) applicant in an action for patent infringement described under this paragraph, the subsection (k) applicant shall provide the Secretary with notice and a copy of such complaint.

(ii) Publication by Secretary

The Secretary shall publish in the Federal Register notice of a complaint received under clause (i).

(7)Newly issued or licensed patents In the case of a patent that—

(A) is issued to, or exclusively licensed by, the reference product sponsor after the date that the reference product sponsor provided the list to the subsection (k) applicant under paragraph (3)(A); and

(B) the reference product sponsor reasonably believes that, due to the issuance of such patent, a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application,

not later than 30 days after such issuance or licensing, the reference product sponsor shall provide to the subsection (k) applicant a supplement to the list provided by the reference product sponsor under paragraph (3)(A) that includes such patent, not later than 30 days after such supplement is provided, the subsection (k) applicant shall provide a statement to the reference product sponsor in accordance with paragraph (3)(B), and such patent shall be subject to paragraph (8).

(8) Notice of commercial marketing and preliminary injunction

(A) Notice of commercial marketing

The subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k).

(B) Preliminary injunction

After receiving the notice under subparagraph (A) and before such date of the first commercial marketing of such biological product, the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale of such biological product until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent that is—

(i) included in the list provided by the reference product sponsor under paragraph (3)(A) or in the list provided by the subsection (k) applicant under paragraph (3)(B); and

(ii) not included, as applicable, on—

(I) the list of patents described in paragraph (4); or

(II) the lists of patents described in paragraph (5)(B).

(C) Reasonable cooperation

If the reference product sponsor has sought a preliminary injunction under subparagraph (B), thereference product sponsor and the subsection (k) applicant shall reasonably cooperate to expedite such further discovery as is needed in connection with the preliminary injunction motion.

(9) Limitation on declaratory judgment action

(A) Subsection (k) application provided

If a subsection (k) applicant provides the application and information required under paragraph (2)(A), neither the reference product sponsor nor the subsection (k) applicant may, prior to the date notice is received under paragraph (8)(A), bring any action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent that is described in clauses (i) and (ii) of paragraph (8)(B).

(B) Subsequent failure to act by subsection (k) applicant

If a subsection (k) applicant fails to complete an action required of the subsection (k) applicant under paragraph (3)(B)(ii), paragraph (5), paragraph (6)(C)(i), paragraph (7), or paragraph (8)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent included in the list described in paragraph (3)(A), including as provided under paragraph (7).

(C) Subsection (k) application not provided

If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product.

(m) Pediatric studies

(1) Application of certain provisions

The provisions of subsections (a), (d), (e), (f), (h), (i), (j), (k), (l), (n), and (p) of section 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(a), (d), (e), (f), (h), (i), (j), (k), (l), (n), (p)] shall apply with respect to the extension of a period under paragraphs (2) and (3) to the same extent and in the same manner as such provisions apply with respect to the extension of a period under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(b), (c)].

(2) Market exclusivity for new biological products If, prior to approval of an application that is submitted under subsection (a), the Secretary determines that information relating to the use of a new biological product in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(4) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(d)(4)]—

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526 [1] [21 U.S.C. 360bb] for a rare disease or condition, the period for such biological product referred to in section 527(a) [1] [21 U.S.C. 360cc(a)] is deemed to be 7 years and 6 months rather than 7 years.

(3) Market exclusivity for already-marketed biological products

If the Secretary determines that information relating to the use of a licensed biological product in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under subsection (a) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(4) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(d)(4)]—

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526 1 [21 U.S.C. 360bb] for a rare disease or condition, the period for such biological product referred to in section 527(a) 1 [21 U.S.C. 360cc(a)] is deemed to be 7 years and 6 months rather than 7 years.

(4) Exception

The Secretary shall not extend a period referred to in paragraph (2)(A), (2)(B), (3)(A), or (3)(B) if the determination under section 505A(d)(4) 1 [21 U.S.C. 355a(d)(4)] is made later than 9 months prior to the expiration of such period.

(n) Date of approval in the case of recommended controls under the CSA

(1) In general

In the case of an application under subsection (a) with respect to a biological product for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act [21 U.S.C. 801 et seq.], approval of such application shall not take effect until the interim final rule controlling the biological product is issued in accordance with section 201(j) of the Controlled Substances Act [21 U.S.C. 811(j)].

(2) Date of approval For purposes of this section, with respect to an application described in paragraph (1), references to the date of approval of such application, or licensure of the product subject to such application, shall mean the later of—

(A) the date an application is approved under subsection (a); or

(B) the date of issuance of the interim final rule controlling the biological product.

(July 1, 1944, ch. 373, title III, § 351, 58 Stat. 702; 1953 Reorg. Plan No. 1, §§ 5, 8, eff. Apr. 11, 1953, 18 F.R. 2053, 67 Stat. 631; Pub. L. 85–881, § 2, Sept. 2, 1958, 72 Stat. 1704; Pub. L. 91–515, title II, § 291, Oct. 30, 1970, 84 Stat. 1308; Pub. L. 96–88, title V, § 509(b), Oct. 17, 1979, 93 Stat. 695; Pub. L. 99–660, title I, § 105(a), title III, § 315, Nov. 14, 1986, 100 Stat. 3751, 3783; Pub. L. 102–300, § 6(b)(1), June 16, 1992, 106 Stat. 240; Pub. L. 104–134, title II, §§ 2102(d)(2), 2104, Apr. 26, 1996, 110 Stat. 1321–319, 1321–320; Pub. L. 105–115, title I, § 123(a)–(d), (g), Nov. 21, 1997, 111 Stat. 2323, 2324; Pub. L. 108–155, § 2(b)(3), Dec. 3,

2003, 117 Stat. 1941; Pub. L. 110–85, title IX, § 901(c), Sept. 27, 2007, 121 Stat. 939; Pub. L. 111–148, title VII, § 7002(a), (b), (g)(1), Mar. 23, 2010, 124 Stat. 804, 814, 819; Pub. L. 112–144, title V, § 502(a)(2), July 9, 2012, 126 Stat. 1040; Pub. L. 114–89, § 2(a)(2), Nov. 25, 2015, 129 Stat. 698; Pub. L. 114–255, div. A, title III, § 3031(b), Dec. 13, 2016, 130 Stat. 1100; Pub. L. 115–52, title V, § 505(b)(2)(B), Aug. 18, 2017, 131 Stat. 1046; Pub. L. 116–94, div. N, title I, §§ 605, 606, Dec. 20, 2019, 133 Stat. 3127; Pub. L. 116–260, div. BB, title III, §§ 322, 325(a), Dec. 27, 2020, 134 Stat. 2933, 2936.)

③ 21CFR601 Licensing[18]

Subpart A - General Provisions

§ 601.2 Applications for biologics licenses; procedures for filing.

(a) ***General.*** To obtain a biologics license under section 351 of the Public Health Service Act for any biological product, the manufacturer shall submit an application to the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research (see mailing addresses in § 600.2(a) or (b) of this chapter), on forms prescribed for such purposes, and shall submit data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency; with respect to each nonclinical laboratory study, either a statement that the study was conducted in compliance with the requirements set forth in part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance; statements regarding each clinical investigation involving human subjects contained in the application, that it either was conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter; or was not subject to such requirements in accordance with § 56.104 or § 56.105, and was conducted in compliance with requirements for informed consent set forth in part 50 of this chapter. A full description of manufacturing methods; data establishing stability of the product through the dating period; sample(s) representative of the product for introduction or delivery for introduction into interstate commerce; summaries of results of tests performed on the lot(s) represented by the submitted sample(s); specimens of the labels, enclosures, and containers, and if applicable, any Medication Guide required under part 208 of this chapter proposed to be used for the product; and the address of each location involved in the manufacture of the biological product shall be listed in the biologics license application. The applicant shall also include a financial certification or disclosure statement(s) or both for clinical investigators as required by part 54 of this chapter. An application for a biologics license shall not be considered as filed until all pertinent information and data have been received by the Food and Drug Administration. The applicant shall also include either a claim for categorical exclusion under § 25.30 or § 25.31 of this chapter or an environmental assessment under § 25.40 of this chapter. The applicant, or the applicant's attorney, agent, or other authorized official shall sign the application. An application for any of

[18] 21CFR601 Licensing（Code of Federal Regulations ウェブサイト）
https://www.ecfr.gov/current/title-21/chapter-I/subchapter-F/part-601#

the following specified categories of biological products subject to licensure shall be handled as set forth in paragraph (c) of this section:

(1) Therapeutic DNA plasmid products;

(2) Therapeutic synthetic peptide products of 40 or fewer amino acids;

(3) Monoclonal antibody products for in vivo use; and

(4) Therapeutic recombinant DNA-derived products.

(b) [Reserved]

(c)

(1) To obtain marketing approval for a biological product subject to licensure which is a therapeutic DNA plasmid product, therapeutic synthetic peptide product of 40 or fewer amino acids, monoclonal antibody product for in vivo use, or therapeutic recombinant DNA-derived product, an applicant shall submit a biologics license application in accordance with paragraph (a) of this section except that the following sections in parts 600 through 680 of this chapter shall not be applicable to such products: §§ 600.10(b) and (c), 600.11, 600.12, 600.13, 610.53, and 610.62 of this chapter.

(2) To the extent that the requirements in this paragraph (c) conflict with other requirements in this subchapter, this paragraph (c) shall supersede other requirements.

(d) Approval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products. Applicable requirements for the maintenance of establishments for the manufacture of a product subject to this section shall include but not be limited to the good manufacturing practice requirements set forth in parts 210, 211, 600, 606, and 820 of this chapter.

(e) Any establishment and product license for a biological product issued under section 351 of the Public Health Service Act (42 U.S.C. 201 *et seq.*) that has not been revoked or suspended as of December 20, 1999, shall constitute an approved biologics license application in effect under the same terms and conditions set forth in such product license and such portions of the establishment license relating to such product.

(f) ***Withdrawal from sale of approved biological products.*** A holder of a biologics license application (BLA) must report to FDA, in accordance with the requirements of §§ 207.61 and 207.65, the withdrawal from sale of an approved biological product. The information must be submitted to FDA within 30 working days of the biological product's withdrawal from sale. The following information must be submitted: The holder's name; product name; BLA number; the National Drug Code; and the date on which the product is

expected to be no longer in commercial distribution. The reason for the withdrawal of the biological product is requested but not required to be submitted.

[64 FR 56450, Oct. 20, 1999, as amended at 70 FR 14983, Mar. 24, 2005; 80 FR 18092, Apr. 3, 2015; 80 FR 37974, July 2, 2015; 81 FR 60221, Aug. 31, 2016]

§ 601.3 Complete response letter to the applicant.

(a) ***Complete response letter.*** The Food and Drug Administration will send the biologics license applicant or supplement applicant a complete response letter if the agency determines that it will not approve the biologics license application or supplement in its present form.

(1) ***Description of specific deficiencies.*** A complete response letter will describe all of the deficiencies that the agency has identified in a biologics license application or supplement, except as stated in paragraph (a)(2) of this section.

(2) ***Inadequate data.*** If FDA determines, after a biologics license application or supplement is filed, that the data submitted are inadequate to support approval, the agency might issue a complete response letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed product labeling.

(3) ***Recommendation of actions for approval.*** When possible, a complete response letter will recommend actions that the applicant might take to place its biologics license application or supplement in condition for approval.

(b) ***Applicant actions.*** After receiving a complete response letter, the biologics license applicant or supplement applicant must take either of the following actions:

(1) ***Resubmission.*** Resubmit the application or supplement, addressing all deficiencies identified in the complete response letter.

(2) ***Withdrawal.*** Withdraw the application or supplement. A decision to withdraw the application or supplement is without prejudice to a subsequent submission.

(c) ***Failure to take action.***

(1) FDA may consider a biologics license applicant or supplement applicant's failure to either resubmit or withdraw the application or supplement within 1 year after issuance of a complete response letter to be a request by the applicant to withdraw the application or supplement, unless the applicant has requested an extension of time in which to resubmit the application or supplement. FDA will grant any reasonable request for such an extension. FDA may consider an applicant's failure to resubmit the application or

supplement within the extended time period or request an additional extension to be a request by the applicant to withdraw the application.

(2) If FDA considers an applicant's failure to take action in accordance with paragraph (c)(1) of this section to be a request to withdraw the application, the agency will notify the applicant in writing. The applicant will have 30 days from the date of the notification to explain why the application or supplement should not be withdrawn and to request an extension of time in which to resubmit the application or supplement. FDA will grant any reasonable request for an extension. If the applicant does not respond to the notification within 30 days, the application or supplement will be deemed to be withdrawn.

[73 FR 39611, July 10, 2008]

§ 601.4 Issuance and denial of license.

(a) A biologics license shall be issued upon a determination by the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research that the establishment(s) and the product meet the applicable requirements established in this chapter. A biologics license shall be valid until suspended or revoked.

(b) If the Commissioner determines that the establishment or product does not meet the requirements established in this chapter, the biologics license application shall be denied and the applicant shall be informed of the grounds for, and of an opportunity for a hearing on, the decision. If the applicant so requests, the Commissioner shall issue a notice of opportunity for hearing on the matter pursuant to § 12.21(b) of this chapter.

[42 FR 4718, Jan. 25, 1977, as amended at 42 FR 15676, Mar. 22, 1977; 42 FR 19142, Apr. 12, 1977; 64 FR 56450, Oct. 20, 1999; 70 FR 14983, Mar. 24, 2005]

§ 601.5 Revocation of license.

(a) A biologics license shall be revoked upon application of the manufacturer giving notice of intention to discontinue the manufacture of all products manufactured under such license or to discontinue the manufacture of a particular product for which a license is held and waiving an opportunity for a hearing on the matter.

(b)

(1) The Commissioner shall notify the licensed manufacturer of the intention to revoke the biologics license, setting forth the grounds for, and offering an opportunity for a hearing on the proposed revocation if the Commissioner finds any of the following:

(i) Authorized Food and Drug Administration employees after reasonable efforts have been unable to gain access to an establishment or a location for the purpose of carrying out the inspection required under § 600.21 of this chapter,

(ii) Manufacturing of products or of a product has been discontinued to an extent that a meaningful inspection or evaluation cannot be made,

(iii) The manufacturer has failed to report a change as required by § 601.12 of this chapter,

(iv) The establishment or any location thereof, or the product for which the license has been issued, fails to conform to the applicable standards established in the license and in this chapter designed to ensure the continued safety, purity, and potency of the manufactured product,

(v) The establishment or the manufacturing methods have been so changed as to require a new showing that the establishment or product meets the requirements established in this chapter in order to protect the public health, or

(vi) The licensed product is not safe and effective for all of its intended uses or is misbranded with respect to any such use.

(2) Except as provided in § 601.6 of this chapter, or in cases involving willfulness, the notification required in this paragraph shall provide a reasonable period for the licensed manufacturer to demonstrate or achieve compliance with the requirements of this chapter, before proceedings will be instituted for the revocation of the license. If compliance is not demonstrated or achieved and the licensed manufacturer does not waive the opportunity for a hearing, the Commissioner shall issue a notice of opportunity for hearing on the matter under § 12.21(b) of this chapter.

[64 FR 56451, Oct. 20, 1999]

§ 601.6 Suspension of license.

(a) Whenever the Commissioner has reasonable grounds to believe that any of the grounds for revocation of a license exist and that by reason thereof there is a danger to health, the Commissioner may notify the licensed manufacturer that the biologics license is suspended and require that the licensed manufacturer do the following:

(1) Notify the selling agents and distributors to whom such product or products have been delivered of such suspension, and

(2) Furnish to the Center for Biologics Evaluation and Research or the Center for Drug Evaluation and Research, complete records of such deliveries and notice of suspension.

(b) Upon suspension of a license, the Commissioner shall either:

(1) Proceed under the provisions of § 601.5(b) of this chapter to revoke the license, or

(2) If the licensed manufacturer agrees, hold revocation in abeyance pending resolution of the matters involved.

[64 FR 56451, Oct. 20, 1999, as amended at 70 FR 14983, Mar. 24, 2005]

§ 601.7 Procedure for hearings.

(a) A notice of opportunity for hearing, notice of appearance and request for hearing, and grant or denial of hearing for a biological drug pursuant to this part, for which the exemption from the Federal Food, Drug, and Cosmetic Act in § 310.4 of this chapter has been revoked, shall be subject to the provisions of § 314.200 of this chapter except to the extent that the notice of opportunity for hearing on the matter issued pursuant to § 12.21(b) of this chapter specifically provides otherwise.

(b) Hearings pursuant to §§ 601.4 through 601.6 shall be governed by part 12 of this chapter.

(c) When a license has been suspended pursuant to § 601.6 and a hearing request has been granted, the hearing shall proceed on an expedited basis.

[42 FR 4718, Jan. 25, 1977, as amended at 42 FR 15676, Mar. 22, 1977; 42 FR 19143, Apr. 12, 1977]

§ 601.8 Publication of revocation.

The Commissioner, following revocation of a biologics license under 21 CFR 601.5(b), will publish a notice in the Federal Register with a statement of the specific grounds for the revocation.

[74 FR 20585, May 5, 2009]

§ 601.9 Licenses; reissuance.

(a) ***Compliance with requirements.*** A biologics license, previously suspended or revoked, may be reissued or reinstated upon a showing of compliance with requirements and upon such inspection and examination as may be considered necessary by the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research.

(b) ***Exclusion of noncomplying location.*** A biologics license, excluding a location or locations that fail to comply with the requirements in this chapter, may be issued without further application and concurrently with the suspension or revocation of the license for noncompliance at the excluded location or locations.

(c) ***Exclusion of noncomplying product(s).*** In the case of multiple products included under a single biologics license application, a biologics license may be issued, excluding the noncompliant product(s), without further application and concurrently with the suspension or revocation of the biologics license for a noncompliant product(s).

[64 FR 56451, Oct. 20, 1999, as amended at 70 FR 14983, Mar. 24, 2005]

Subpart B [Reserved]

Subpart C - Biologics Licensing

§ 601.12 Changes to an approved application.

(a) ***General.***

(1) As provided by this section, an applicant must inform the Food and Drug Administration (FDA) (see mailing addresses in § 600.2 of this chapter) about each change in the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling established in the approved license application(s).

(2) Before distributing a product made using a change, an applicant must assess the effects of the change and demonstrate through appropriate validation and/or other clinical and/or nonclinical laboratory studies the lack of adverse effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(3) Notwithstanding the requirements of paragraphs (b), (c), and (f) of this section, an applicant must make a change provided for in those paragraphs in accordance with a regulation or guidance that provides for a less burdensome notification of the change (for example, by submission of a supplement that does not require approval prior to distribution of the product or in an annual report).

(4) The applicant must promptly revise all promotional labeling and advertising to make it consistent with any labeling change implemented in accordance with paragraphs (f)(1) and (f)(2) of this section.

(5) A supplement or annual report must include a list of all changes contained in the supplement or annual report. For supplements, this list must be provided in the cover letter.

(b) ***Changes requiring supplement submission and approval prior to distribution of the product made using the change (major changes).***

(1) A supplement shall be submitted for any change in the product, production process, quality controls, equipment, facilities, or responsible personnel that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(2) These changes include, but are not limited to:

(i) Except as provided in paragraphs (c) and (d) of this section, changes in the qualitative or quantitative formulation, including inactive ingredients, or in the specifications provided in the approved application;

(ii) Changes requiring completion of an appropriate human study to demonstrate the equivalence of the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(iii) Changes in the virus or adventitious agent removal or inactivation method(s);

(iv) Changes in the source material or cell line;

(v) Establishment of a new master cell bank or seed; and

(vi) Changes which may affect product sterility assurance, such as changes in product or component sterilization method(s), or an addition, deletion, or substitution of steps in an aseptic processing operation.

(3) The applicant must obtain approval of the supplement from FDA prior to distribution of the product made using the change. Except for submissions under paragraph (e) of this section, the following shall be contained in the supplement:

(i) A detailed description of the proposed change;

(ii) The product(s) involved;

(iii) The manufacturing site(s) or area(s) affected;

(iv) A description of the methods used and studies performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(v) The data derived from such studies;

(vi) Relevant validation protocols and data; and

(vii) A reference list of relevant standard operating procedures (SOP's).

(4) An applicant may ask FDA to expedite its review of a supplement for public health reasons or if a delay in making the change described in it would impose an extraordinary hardship on the applicant. Such a supplement and its mailing cover should be plainly marked: “Prior Approval Supplement-Expedited Review Requested.

(c) ***Changes requiring supplement submission at least 30 days prior to distribution of the product made using the change.***

(1) A supplement shall be submitted for any change in the product, production process, quality controls, equipment, facilities, or responsible personnel that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. The supplement shall be labeled "Supplement - Changes Being Effected in 30 Days" or, if applicable under paragraph (c)(5) of this section, "Supplement - Changes Being Effected."

(2) These changes include, but are not limited to:

(i) [Reserved]

(ii) An increase or decrease in production scale during finishing steps that involves different equipment; and

(iii) Replacement of equipment with that of similar, but not identical, design and operating principle that does not affect the process methodology or process operating parameters.

(iv) Relaxation of an acceptance criterion or deletion of a test to comply with an official compendium that is consistent with FDA statutory and regulatory requirements.

(3) Pending approval of the supplement by FDA, and except as provided in paragraph (c)(5) of this section, distribution of the product made using the change may begin not less than 30 days after receipt of the supplement by FDA. The information listed in paragraph (b)(3)(i) through (b)(3)(vii) of this section shall be contained in the supplement.

(4) If within 30 days following FDA's receipt of the supplement, FDA informs the applicant that either:

(i) The change requires approval prior to distribution of the product in accordance with paragraph (b) of this section; or

(ii) Any of the information required under paragraph (c)(3) of this section is missing; the applicant shall not distribute the product made using the change until FDA determines that compliance with this section is achieved.

(5) In certain circumstances, FDA may determine that, based on experience with a particular type of change, the supplement for such change is usually complete and provides the proper information, and on particular assurances that the proposed change has been appropriately submitted, the product made using the change may be distributed immediately upon receipt of the supplement by FDA. These circumstances may include substantial similarity with a type of change regularly involving a "Supplement - Changes

Being Effected" supplement or a situation in which the applicant presents evidence that the proposed change has been validated in accordance with an approved protocol for such change under paragraph (e) of this section.

(6) If the agency disapproves the supplemental application, it may order the manufacturer to cease distribution of the products made with the manufacturing change.

(d) ***Changes to be described in an annual report (minor changes).***

(1) Changes in the product, production process, quality controls, equipment, facilities, or responsible personnel that have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product shall be documented by the applicant in an annual report submitted each year within 60 days of the anniversary date of approval of the application. The Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research, may approve a written request for an alternative date to combine annual reports for multiple approved applications into a single annual report submission.

(2) These changes include, but are not limited to:

(i) Any change made to comply with a change to an official compendium, except a change described in paragraph (c)(2)(iv) of this section, that is consistent with FDA statutory and regulatory requirements.

(ii) The deletion or reduction of an ingredient intended only to affect the color of the product, except that a change intended only to affect Blood Grouping Reagents requires supplement submission and approval prior to distribution of the product made using the change in accordance with the requirements set forth in paragraph (b) of this section;

(iii) An extension of an expiration dating period based upon full shelf life data on production batches obtained from a protocol approved in the application;

(iv) A change within the container closure system for a nonsterile product, based upon a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium;

(v) A change in the size and/or shape of a container containing the same number of dosage units for a nonsterile solid dosage form product, without a change from one container closure system to another;

(vi) The addition by embossing, debossing, or engraving of a code imprint to a solid dosage form biological product other than a modified release dosage form, or a minor change in an existing code imprint; and

(vii) The addition or revision of an alternative analytical procedure that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application, or deletion of an alternative analytical procedure.

(3) The following information for each change shall be contained in the annual report:

(i) A list of all products involved; and

(ii) A full description of the manufacturing and controls changes including: the manufacturing site(s) or area(s) involved; the date the change was made; a cross-reference to relevant validation protocols and/or SOP's; and relevant data from studies and tests performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(iii) A statement by the holder of the approved application or license that the effects of the change have been assessed.

(4) The applicant shall submit the report to the FDA office responsible for reviewing the application. The report shall include all the information required under this paragraph for each change made during the annual reporting interval which ends on the anniversary date in the order in which they were implemented.

(e) An applicant may submit one or more protocols describing the specific tests and validation studies and acceptable limits to be achieved to demonstrate the lack of adverse effect for specified types of manufacturing changes on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. Any such protocols, or change to a protocol, shall be submitted as a supplement requiring approval from FDA prior to distribution of the product which, if approved, may justify a reduced reporting category for the particular change because the use of the protocol for that type of change reduces the potential risk of an adverse effect.

(f) ***Labeling changes.***

(1) Labeling changes requiring supplement submission - FDA approval must be obtained before distribution of the product with the labeling change. Except as described in paragraphs (f)(2) and (f)(3) of this section, an applicant shall submit a supplement describing a proposed change in the package insert, package label, container label, or, if applicable, a Medication Guide required under part 208 of this chapter, and include the information necessary to support the proposed change. An applicant cannot use paragraph (f)(2) of this section to make any change to the information required in § 201.57(a) of this chapter. An applicant may report the minor changes to the information specified in paragraph (f)(3)(i)(D) of this section in an annual report. The supplement shall clearly highlight the proposed change in the labeling. The applicant shall obtain approval from FDA prior to distribution of the product with the labeling change.

(2) ***Labeling changes requiring supplement submission - product with a labeling change that may be distributed before FDA approval.***

(i) An applicant shall submit, at the time such change is made, a supplement for any change in the package insert, package label, or container label to reflect newly acquired information, except for changes to the package insert required in § 201.57(a) of this chapter (which must be made under paragraph (f)(1) of this section), to accomplish any of the following:

(A) To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter;

(B) To add or strengthen a statement about abuse, dependence, psychological effect, or overdosage;

(C) To add or strengthen an instruction about dosage and administration that is intended to increase the safety of the use of the product; and

(D) To delete false, misleading, or unsupported indications for use or claims for effectiveness.

(E) Any labeling change normally requiring a supplement submission and approval prior to distribution of the product that FDA specifically requests be submitted under this provision.

(ii) Pending approval of the supplement by FDA, the applicant may distribute a product with a package insert, package label, or container label bearing such change at the time the supplement is submitted. The supplement shall clearly identify the change being made and include necessary supporting data. The supplement and its mailing cover shall be plainly marked: "Special Labeling Supplement - Changes Being Effected."

(3) ***Labeling changes requiring submission in an annual report.***

(i) An applicant shall submit any final printed package insert, package label, container label, or Medication Guide required under part 208 of this chapter incorporating the following changes in an annual report submitted to FDA each year as provided in paragraph (d)(1) of this section:

(A) Editorial or similar minor changes;

(B) A change in the information on how the product is supplied that does not involve a change in the dosage strength or dosage form;

(C) A change in the information specified in § 208.20(b)(8)(iii) and (b)(8)(iv) of this chapter for a Medication Guide; and

(D) A change to the information required in § 201.57(a) of this chapter as follows:

(*1*) Removal of a listed section(s) specified in § 201.57(a)(5) of this chapter; and

(*2*) Changes to the most recent revision date of the labeling as specified in § 201.57(a)(15) of this chapter.

(E) A change made pursuant to an exception or alternative granted under § 201.26 or § 610.68 of this chapter.

(ii) The applicant may distribute a product with a package insert, package label, or container label bearing such change at the time the change is made.

(4) ***Advertisements and promotional labeling.*** Advertisements and promotional labeling shall be submitted to the Center for Biologics Evaluation and Research or Center for Drug Evaluation and Research in accordance with the requirements set forth in § 314.81(b)(3)(i) of this chapter.

(5) The submission and grant of a written request for an exception or alternative under § 201.26 or § 610.68 of this chapter satisfies the requirements in paragraphs (f)(1) through (f)(2) of this section.

(6) For purposes of paragraph (f)(2) of this section, information will be considered newly acquired if it consists of data, analyses, or other information not previously submitted to the agency, which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

(g) ***Failure to comply.*** In addition to other remedies available in law and regulations, in the event of repeated failure of the applicant to comply with this section, FDA may require that the applicant submit a supplement for any proposed change and obtain approval of the supplement by FDA prior to distribution of the product made using the change.

(h) ***Administrative review.*** Under § 10.75 of this chapter, an applicant may request internal FDA review of FDA employee decisions under this section.

[62 FR 39901, July 24, 1997, as amended at 63 FR 66399, Dec. 1, 1998. Redesignated at 65 FR 59718, Oct. 6, 2000, and amended at 69 FR 18766, Apr. 8, 2004; 70 FR 14983, Mar. 24, 2005; 71 FR 3997, Jan. 24, 2006; 72 FR 73600, Dec. 28, 2007; 73 FR 49609, Aug. 22, 2008; 73 FR 68333, Nov. 18, 2008; 80 FR 18092, Apr. 3, 2015]

§ 601.14 Regulatory submissions in electronic format.

(a) ***General.*** Electronic format submissions must be in a form that FDA can process, review, and archive. FDA will periodically issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files.)

(b) ***Labeling.*** The content of labeling required under § 201.100(d)(3) of this chapter (commonly referred to as the package insert or professional labeling), including all text, tables, and figures, must be submitted to the agency in electronic format as described in paragraph (a) of this section. This requirement is in addition to the provisions of §§ 601.2(a) and 601.12(f) that require applicants to submit specimens of the labels, enclosures, and containers, or to submit other final printed labeling. Submissions under this paragraph must be made in accordance with part 11 of this chapter except for the requirements of § 11.10(a), (c) through (h), and (k), and the corresponding requirements of § 11.30.

[68 FR 69020, Dec. 11, 2003]

§ 601.15 Foreign establishments and products: samples for each importation.

Random samples of each importation, obtained by the District Director of Customs and forwarded to the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research (see mailing addresses in § 600.2(c) of this chapter) must be at least two final containers of each lot of product. A copy of the associated documents which describe and identify the shipment must accompany the shipment for forwarding with the samples to the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research (see mailing addresses in § 600.2(c)). For shipments of 20 or less final containers, samples need not be forwarded, provided a copy of an official release from the Center for Biologics Evaluation and Research or Center for Drug Evaluation and Research accompanies each shipment.

[70 FR 14983, Mar. 24, 2005, as amended at 80 FR 18092, Apr. 3, 2015]

§ 601.20 Biologics licenses; issuance and conditions.

(a) ***Examination - compliance with requirements.*** A biologics license application shall be approved only upon examination of the product and upon a determination that the product complies with the standards established in the biologics license application and the requirements prescribed in the regulations in this chapter including but not limited to the good manufacturing practice requirements set forth in parts 210, 211, 600, 606 and 820 of this chapter.

(b) ***Availability of product.*** No biologics license shall be issued unless:

(1) The product intended for introduction into interstate commerce is available for examination, and

(2) Such product is available for inspection during all phases of manufacture.

(c) ***Manufacturing process - impairment of assurances.*** No product shall be licensed if any part of the process of or relating to the manufacture of such product, in the judgment of the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research, would impair the assurances of continued safety, purity, and potency as provided by the regulations contained in this chapter.

(d) ***Inspection - compliance with requirements.*** A biologics license shall be issued or a biologics license application approved only after inspection of the establishment(s) listed in the biologics license application and upon a determination that the establishment(s) complies with the standards established in the biologics license application and the requirements prescribed in applicable regulations.

(e) ***One biologics license to cover all locations.*** One biologics license shall be issued to cover all locations meeting the establishment standards identified in the approved biologics license application and each location shall be subject to inspection by FDA officials.

[64 FR 56451, Oct. 20, 1999, as amended at 70 FR 14983, Mar. 24, 2005]

§ 601.21 Products under development

A biological product undergoing development, but not yet ready for a biologics license, may be shipped or otherwise delivered from one State or possession into another State or possession provided such shipment or delivery is not for introduction or delivery for introduction into interstate commerce, except as provided in sections 505(i) and 520(g) of the Federal Food, Drug, and Cosmetic Act, as amended, and the regulations thereunder (21 CFR parts 312 and 812).

[64 FR 56451, Oct. 20, 1999]

§ 601.22 Products in short supply; initial manufacturing at other than licensed location.

A biologics license issued to a manufacturer and covering all locations of manufacture shall authorize persons other than such manufacturer to conduct at places other than such locations the initial, and partial manufacturing of a product for shipment solely to such manufacturer only to the extent that the names of such persons and places are registered with the Commissioner of Food and Drugs and it is found upon application of such manufacturer, that the product is in short supply due either to the peculiar growth requirements of the organism involved or to the scarcity of the animal required for manufacturing purposes, and such manufacturer has established with respect to such persons and places such procedures, inspections, tests or other arrangements as will ensure full compliance with the applicable regulations of this subchapter related to continued safety, purity, and potency. Such persons and places shall be subject to all regulations of this subchapter except §§ 601.2 to 601.6, 601.9, 601.10, 601.20, 601.21 to 601.33, and 610.60 to 610.65 of this chapter.

For persons and places authorized under this section to conduct the initial and partial manufacturing of a product for shipment solely to a manufacturer of a product subject to licensure under § 601.2(c), the following additional regulations shall not be applicable: §§ 600.10(b) and (c), 600.11, 600.12, 600.13, and 610.53 of this chapter. Failure of such manufacturer to maintain such procedures, inspections, tests, or other arrangements, or failure of any person conducting such partial manufacturing to comply with applicable regulations shall constitute a ground for suspension or revocation of the authority conferred pursuant to this section on the same basis as provided in §§ 601.6 to 601.8 with respect to the suspension and the revocation of licenses.

[42 FR 4718, Jan. 25, 1977, as amended at 61 FR 24233, May 14, 1996; 64 FR 56452, Oct. 20, 1999; 80 FR 37974, July 2, 2015]

§ 601.27 Pediatric studies.

(a) ***Required assessment.*** Except as provided in paragraphs (b), (c), and (d) of this section, each application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration shall contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Where the course of the disease and the effects of the product are similar in adults and pediatric patients, FDA may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled effectiveness studies in adults, usually supplemented with other information in pediatric patients, such as pharmacokinetic studies. In addition, studies may not be needed in each pediatric age group, if data from one age group can be extrapolated to another. Assessments required under this section for a product that represents a meaningful therapeutic benefit over existing treatments must be carried out using appropriate formulations for the age group(s) for which the assessment is required.

(b) ***Deferred submission.***

(1) FDA may, on its own initiative or at the request of an applicant, defer submission of some or all assessments of safety and effectiveness described in paragraph (a) of this section until after licensing of the product for use in adults. Deferral may be granted if, among other reasons, the product is ready for approval in adults before studies in pediatric patients are complete, pediatric studies should be delayed until additional safety or effectiveness data have been collected. If an applicant requests deferred submission, the request must provide an adequate justification for delaying pediatric studies, a description of the planned or ongoing studies, and evidence that the studies are being or will be conducted with due diligence and at the earliest possible time.

(2) If FDA determines that there is an adequate justification for temporarily delaying the submission of assessments of pediatric safety and effectiveness, the product may be licensed for use in adults subject to the requirement that the applicant submit the required assessments within a specified time.

(c) ***Waivers*** -

(1) ***General.*** FDA may grant a full or partial waiver of the requirements of paragraph (a) of this section on its own initiative or at the request of an applicant. A request for a waiver must provide an adequate justification.

(2) ***Full waiver.*** An applicant may request a waiver of the requirements of paragraph (a) of this section if the applicant certifies that:

(i) The product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is not likely to be used in a substantial number of pediatric patients;

(ii) Necessary studies are impossible or highly impractical because, e.g., the number of such patients is so small or geographically dispersed; or

(iii) There is evidence strongly suggesting that the product would be ineffective or unsafe in all pediatric age groups.

(3) ***Partial waiver.*** An applicant may request a waiver of the requirements of paragraph (a) of this section with respect to a specified pediatric age group, if the applicant certifies that:

(i) The product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group, and is not likely to be used in a substantial number of patients in that age group;

(ii) Necessary studies are impossible or highly impractical because, e.g., the number of patients in that age group is so small or geographically dispersed;

(iii) There is evidence strongly suggesting that the product would be ineffective or unsafe in that age group; or

(iv) The applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(4) ***FDA action on waiver.*** FDA shall grant a full or partial waiver, as appropriate, if the agency finds that there is a reasonable basis on which to conclude that one or more of the grounds for waiver specified in paragraphs (c)(2) or (c)(3) of this section have been met. If a waiver is granted on the ground that it is

not possible to develop a pediatric formulation, the waiver will cover only those pediatric age groups requiring that formulation. If a waiver is granted because there is evidence that the product would be ineffective or unsafe in pediatric populations, this information will be included in the product's labeling.

(5) ***Definition of "meaningful therapeutic benefit".*** For purposes of this section, a product will be considered to offer a meaningful therapeutic benefit over existing therapies if FDA estimates that:

(i) If approved, the product would represent a significant improvement in the treatment, diagnosis, or prevention of a disease, compared to marketed products adequately labeled for that use in the relevant pediatric population. Examples of how improvement might be demonstrated include, e.g., evidence of increased effectiveness in treatment, prevention, or diagnosis of disease; elimination or substantial reduction of a treatment-limiting drug reaction; documented enhancement of compliance; or evidence of safety and effectiveness in a new subpopulation; or

(ii) The product is in a class of products or for an indication for which there is a need for additional therapeutic options.

(d) ***Exemption for orphan drugs.*** This section does not apply to any product for an indication or indications for which orphan designation has been granted under part 316, subpart C, of this chapter.

[63 FR 66671, Dec. 2, 1998]

§ 601.28 Annual reports of postmarketing pediatric studies.

Sponsors of licensed biological products shall submit the following information each year within 60 days of the anniversary date of approval of each product under the license to the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research (see mailing addresses in § 600.2(a) or (b) of this chapter):

(a) ***Summary.*** A brief summary stating whether labeling supplements for pediatric use have been submitted and whether new studies in the pediatric population to support appropriate labeling for the pediatric population have been initiated. Where possible, an estimate of patient exposure to the drug product, with special reference to the pediatric population (neonates, infants, children, and adolescents) shall be provided, including dosage form.

(b) ***Clinical data.*** Analysis of available safety and efficacy data in the pediatric population and changes proposed in the labeling based on this information. An assessment of data needed to ensure appropriate labeling for the pediatric population shall be included.

(c) ***Status reports.*** A statement on the current status of any postmarketing studies in the pediatric population performed by, or on behalf of, the applicant. The statement shall include whether postmarketing

clinical studies in pediatric populations were required or agreed to, and, if so, the status of these studies shall be reported to FDA in annual progress reports of postmarketing studies under § 601.70 rather than under this section.

[65 FR 59718, Oct. 6, 2000, as amended at 65 FR 64618, Oct. 30, 2000; 70 FR 14984, Mar. 24, 2005; 80 FR 18092, Apr. 3, 2015]

§ 601.29 Guidance documents.

(a) FDA has made available guidance documents under § 10.115 of this chapter to help you comply with certain requirements of this part.

(b) The Center for Biologics Evaluation and Research (CBER) maintains a list of guidance documents that apply to the center's regulations. The lists are maintained on the Internet and are published annually in the Federal Register. You may request a copy of the CBER list from the Food and Drug Administration, Center for Biologics Evaluation and Research, Office of Communication, Outreach and Development, 10903 New Hampshire Ave., Bldg. 71, Rm. 3103, Silver Spring, MD 20993-0002.

[65 FR 56480, Sept. 19, 2000, as amended at 70 FR 14984, Mar. 24, 2005; 80 FR 18092, Apr. 3, 2015]

Subpart D - Diagnostic Radiopharmaceuticals

Source: 64 FR 26668, May 17, 1999, unless otherwise noted.

§ 601.30 Scope.

This subpart applies to radiopharmaceuticals intended for in vivo administration for diagnostic and monitoring use. It does not apply to radiopharmaceuticals intended for therapeutic purposes. In situations where a particular radiopharmaceutical is proposed for both diagnostic and therapeutic uses, the radiopharmaceutical must be evaluated taking into account each intended use.

§ 601.31 Definition.

For purposes of this part,*diagnostic radiopharmaceutical* means:

(a) An article that is intended for use in the diagnosis or monitoring of a disease or a manifestation of a disease in humans and that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons; or

(b) Any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of such article as defined in paragraph (a) of this section.

§ 601.32 General factors relevant to safety and effectiveness.

FDA's determination of the safety and effectiveness of a diagnostic radiopharmaceutical includes consideration of the following:

(a) The proposed use of the diagnostic radiopharmaceutical in the practice of medicine;

(b) The pharmacological and toxicological activity of the diagnostic radiopharmaceutical (including any carrier or ligand component of the diagnostic radiopharmaceutical); and

(c) The estimated absorbed radiation dose of the diagnostic radiopharmaceutical.

§ 601.33 Indications.

(a) For diagnostic radiopharmaceuticals, the categories of proposed indications for use include, but are not limited to, the following:

(1) Structure delineation;

(2) Functional, physiological, or biochemical assessment;

(3) Disease or pathology detection or assessment; and

(4) Diagnostic or therapeutic patient management.

(b) Where a diagnostic radiopharmaceutical is not intended to provide disease-specific information, the proposed indications for use may refer to a biochemical, physiological, anatomical, or pathological process or to more than one disease or condition.

§ 601.34 Evaluation of effectiveness.

(a) The effectiveness of a diagnostic radiopharmaceutical is assessed by evaluating its ability to provide useful clinical information related to its proposed indications for use. The method of this evaluation varies depending upon the proposed indication(s) and may use one or more of the following criteria:

(1) The claim of structure delineation is established by demonstrating in a defined clinical setting the ability to locate anatomical structures and to characterize their anatomy.

(2) The claim of functional, physiological, or biochemical assessment is established by demonstrating in a defined clinical setting reliable measurement of function(s) or physiological, biochemical, or molecular process(es).

(3) The claim of disease or pathology detection or assessment is established by demonstrating in a defined clinical setting that the diagnostic radiopharmaceutical has sufficient accuracy in identifying or characterizing the disease or pathology.

(4) The claim of diagnostic or therapeutic patient management is established by demonstrating in a defined clinical setting that the test is useful in diagnostic or therapeutic patient management.

(5) For a claim that does not fall within the indication categories identified in § 601.33, the applicant or sponsor should consult FDA on how to establish the effectiveness of the diagnostic radiopharmaceutical for the claim.

(b) The accuracy and usefulness of the diagnostic information is determined by comparison with a reliable assessment of actual clinical status. A reliable assessment of actual clinical status may be provided by a diagnostic standard or standards of demonstrated accuracy. In the absence of such diagnostic standard(s), the actual clinical status must be established in another manner, e.g., patient followup.

§ 601.35 Evaluation of safety.

(a) Factors considered in the safety assessment of a diagnostic radiopharmaceutical include, among others, the following:

(1) The radiation dose;

(2) The pharmacology and toxicology of the radiopharmaceutical, including any radionuclide, carrier, or ligand;

(3) The risks of an incorrect diagnostic determination;

(4) The adverse reaction profile of the drug;

(5) Results of human experience with the radiopharmaceutical for other uses; and

(6) Results of any previous human experience with the carrier or ligand of the radiopharmaceutical when the same chemical entity as the carrier or ligand has been used in a previously studied product.

(b) The assessment of the adverse reaction profile includes, but is not limited to, an evaluation of the potential of the diagnostic radiopharmaceutical, including the carrier or ligand, to elicit the following:

(1) Allergic or hypersensitivity responses,

(2) Immunologic responses,

(3) Changes in the physiologic or biochemical function of the target and nontarget tissues, and

(4) Clinically detectable signs or symptoms.

(c)

(1) To establish the safety of a diagnostic radiopharmaceutical, FDA may require, among other information, the following types of data:

(A) Pharmacology data,

(B) Toxicology data,

(C) Clinical adverse event data, and

(D) Radiation safety assessment.

(2) The amount of new safety data required will depend on the characteristics of the product and available information regarding the safety of the diagnostic radiopharmaceutical, and its carrier or ligand, obtained from other studies and uses. Such information may include, but is not limited to, the dose, route of administration, frequency of use, half-life of the ligand or carrier, half-life of the radionuclide, and results of clinical and preclinical studies. FDA will establish categories of diagnostic radiopharmaceuticals based on defined characteristics relevant to risk and will specify the amount and type of safety data that are appropriate for each category (e.g., required safety data may be limited for diagnostic radiopharmaceuticals with a well established, low-risk profile). Upon reviewing the relevant product characteristics and safety information, FDA will place each diagnostic radiopharmaceutical into the appropriate safety risk category.

(d) ***Radiation safety assessment.*** The radiation safety assessment must establish the radiation dose of a diagnostic radiopharmaceutical by radiation dosimetry evaluations in humans and appropriate animal models. The maximum tolerated dose need not be established.

Subpart E - Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses

Source: 57 FR 58959, Dec. 11, 1992, unless otherwise noted.

§ 601.40 Scope.

This subpart applies to certain biological products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments (e.g., ability to treat patients unresponsive to, or intolerant of, available therapy, or improved patient response over available therapy).

§ 601.41 Approval based on a surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity.

FDA may grant marketing approval for a biological product on the basis of adequate and well-controlled clinical trials establishing that the biological product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. Approval under this section will be subject to the requirement that the applicant study the biological product further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome. Postmarketing studies would usually be studies already underway. When required to be conducted, such studies must also be adequate and well-controlled. The applicant shall carry out any such studies with due diligence.

§ 601.42 Approval with restrictions to assure safe use.

(a) If FDA concludes that a biological product shown to be effective can be safely used only if distribution or use is restricted, FDA will require such postmarketing restrictions as are needed to assure safe use of the biological product, such as:

(1) Distribution restricted to certain facilities or physicians with special training or experience; or

(2) Distribution conditioned on the performance of specified medical procedures.

(b) The limitations imposed will be commensurate with the specific safety concerns presented by the biological product.

§ 601.43 Withdrawal procedures.

(a) For biological products approved under § 601.41 or § 601.42, FDA may withdraw approval, following a hearing as provided in part 15 of this chapter, as modified by this section, if:

(1) A postmarketing clinical study fails to verify clinical benefit;

(2) The applicant fails to perform the required postmarketing study with due diligence;

(3) Use after marketing demonstrates that postmarketing restrictions are inadequate to ensure safe use of the biological product;

(4) The applicant fails to adhere to the postmarketing restrictions agreed upon;

(5) The promotional materials are false or misleading; or

(6) Other evidence demonstrates that the biological product is not shown to be safe or effective under its conditions of use.

(b) ***Notice of opportunity for a hearing.*** The Director of the Center for Biologics Evaluation and Research or the Director of the Center for Drug Evaluation and Research will give the applicant notice of an opportunity for a hearing on the Center's proposal to withdraw the approval of an application approved under § 601.41 or § 601.42. The notice, which will ordinarily be a letter, will state generally the reasons for the action and the proposed grounds for the order.

(c) ***Submission of data and information.***

(1) If the applicant fails to file a written request for a hearing within 15 days of receipt of the notice, the applicant waives the opportunity for a hearing.

(2) If the applicant files a timely request for a hearing, the agency will publish a notice of hearing in the Federal Register in accordance with §§ 12.32(e) and 15.20 of this chapter.

(3) An applicant who requests a hearing under this section must, within 30 days of receipt of the notice of opportunity for a hearing, submit the data and information upon which the applicant intends to rely at the hearing.

(d) ***Separation of functions.*** Separation of functions (as specified in § 10.55 of this chapter) will not apply at any point in withdrawal proceedings under this section.

(e) ***Procedures for hearings.*** Hearings held under this section will be conducted in accordance with the provisions of part 15 of this chapter, with the following modifications:

(1) An advisory committee duly constituted under part 14 of this chapter will be present at the hearing. The committee will be asked to review the issues involved and to provide advice and recommendations to the Commissioner of Food and Drugs.

(2) The presiding officer, the advisory committee members, up to three representatives of the applicant, and up to three representatives of the Center may question any person during or at the conclusion of the person's presentation. No other person attending the hearing may question a person making a presentation. The presiding officer may, as a matter of discretion, permit questions to be submitted to the presiding officer for response by a person making a presentation.

(f) ***Judicial review.*** The Commissioner's decision constitutes final agency action from which the applicant may petition for judicial review. Before requesting an order from a court for a stay of action pending review, an applicant must first submit a petition for a stay of action under § 10.35 of this chapter.

[57 FR 58959, Dec. 11, 1992, as amended at 68 FR 34797, June 11, 2003; 70 FR 14984, Mar. 24, 2005]

§ 601.44 Postmarketing safety reporting.

Biological products approved under this program are subject to the postmarketing recordkeeping and safety reporting applicable to all approved biological products.

§ 601.45 Promotional materials.

For biological products being considered for approval under this subpart, unless otherwise informed by the agency, applicants must submit to the agency for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the agency, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

§ 601.46 Termination of requirements.

If FDA determines after approval that the requirements established in § 601.42, § 601.43, or § 601.45 are no longer necessary for the safe and effective use of a biological product, it will so notify the applicant. Ordinarily, for biological products approved under § 601.41, these requirements will no longer apply when FDA determines that the required postmarketing study verifies and describes the biological product's clinical benefit and the biological product would be appropriate for approval under traditional procedures. For biological products approved under § 601.42, the restrictions would no longer apply when FDA determines that safe use of the biological product can be assured through appropriate labeling. FDA also retains the discretion to remove specific postapproval requirements upon review of a petition submitted by the sponsor in accordance with § 10.30.

Subpart F - Confidentiality of Information

§ 601.50 Confidentiality of data and information in an investigational new drug notice for a biological product.

(a) The existence of an IND notice for a biological product will not be disclosed by the Food and Drug Administration unless it has previously been publicly disclosed or acknowledged.

(b) The availability for public disclosure of all data and information in an IND file for a biological product shall be handled in accordance with the provisions established in § 601.51.

(c) Notwithstanding the provisions of § 601.51, the Food and Drug Administration shall disclose upon request to an individual on whom an investigational biological product has been used a copy of any adverse reaction report relating to such use.

[39 FR 44656, Dec. 24, 1974]

§ 601.51 Confidentiality of data and information in applications for biologics licenses.

(a) For purposes of this section the biological product file includes all data and information submitted with or incorporated by reference in any application for a biologics license, IND's incorporated into any such application, master files, and other related submissions. The availability for public disclosure of any record in the biological product file shall be handled in accordance with the provisions of this section.

(b) The existence of a biological product file will not be disclosed by the Food and Drug Administration before a biologics license application has been approved unless it has previously been publicly disclosed or acknowledged. The Food and Drug Administration will maintain a list available for public disclosure of biological products for which a license application has been approved.

(c) If the existence of a biological product file has not been publicly disclosed or acknowledged, no data or information in the biological product file is available for public disclosure.

(d)

(1) If the existence of a biological product file has been publicly disclosed or acknowledged before a license has been issued, no data or information contained in the file is available for public disclosure before such license is issued, but the Commissioner may, in his discretion, disclose a summary of such selected portions of the safety and effectiveness data as are appropriate for public consideration of a specific pending issue, e.g., at an open session of a Food and Drug Administration advisory committee or pursuant to an exchange of important regulatory information with a foreign government.

(2) Notwithstanding paragraph (d)(1) of this section, FDA will make available to the public upon request the information in the IND that was required to be filed in Docket Number 95S-0158 in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, for investigations involving an exception from informed consent under § 50.24 of this chapter. Persons wishing to request this information shall submit a request under the Freedom of Information Act.

(e) After a license has been issued, the following data and information in the biological product file are immediately available for public disclosure unless extraordinary circumstances are shown:

(1) All safety and effectiveness data and information.

(2) A protocol for a test or study, unless it is shown to fall within the exemption established for trade secrets and confidential commercial or financial information in § 20.61 of this chapter.

(3) Adverse reaction reports, product experience reports, consumer complaints, and other similar data and information, after deletion of:

(i) Names and any information that would identify the person using the product.

(ii) Names and any information that would identify any third party involved with the report, such as a physician or hospital or other institution.

(4) A list of all active ingredients and any inactive ingredients previously disclosed to the public, as defined in § 20.81 of this chapter.

(5) An assay method or other analytical method, unless it serves no regulatory or compliance purpose and it is shown to fall within the exemption established in § 20.61 of this chapter.

(6) All correspondence and written summaries of oral discussions relating to the biological product file, in accordance with the provisions of part 20 of this chapter.

(7) All records showing the manufacturer's testing of a particular lot, after deletion of data or information that would show the volume of the drug produced, manufacturing procedures and controls, yield from raw materials, costs, or other material falling within § 20.61 of this chapter.

(8) All records showing the testing of and action on a particular lot by the Food and Drug Administration.

(f) The following data and information in a biological product file are not available for public disclosure unless they have been previously disclosed to the public as defined in § 20.81 of this chapter or they relate to a product or ingredient that has been abandoned and they no longer represent a trade secret or confidential commercial or financial information as defined in § 20.61 of this chapter:

(1) Manufacturing methods or processes, including quality control procedures.

(2) Production, sales, distribution, and similar data and information, except that any compilation of such data and information aggregated and prepared in a way that does not reveal data or information which is not available for public disclosure under this provision is available for public disclosure.

(3) Quantitative or semiquantitative formulas.

(g) For purposes of this regulation, safety and effectiveness data include all studies and tests of a biological product on animals and humans and all studies and tests on the drug for identity, stability, purity, potency, and bioavailability.

[39 FR 44656, Dec. 24, 1974, as amended at 42 FR 15676, Mar. 22, 1977; 49 FR 23833, June 8, 1984; 55 FR 11013, Mar. 26, 1990; 61 FR 51530, Oct. 2, 1996; 64 FR 56452, Oct. 20, 1999; 68 FR 24879, May 9, 2003; 69 FR 13717, Mar. 24, 2004; 70 FR 14984, Mar. 24, 2005]

Subpart G - Postmarketing Studies

Source: 65 FR 64618, Oct. 30, 2000, unless otherwise noted.

§ 601.70 Annual progress reports of postmarketing studies.

(a) ***General requirements.*** This section applies to all required postmarketing studies (e.g., accelerated approval clinical benefit studies, pediatric studies) and postmarketing studies that an applicant has committed, in writing, to conduct either at the time of approval of an application or a supplement to an application, or after approval of an application or a supplement. Postmarketing studies within the meaning of this section are those that concern:

(1) Clinical safety;

(2) Clinical efficacy;

(3) Clinical pharmacology; and

(4) Nonclinical toxicology.

(b) ***What to report.*** Each applicant of a licensed biological product shall submit a report to FDA on the status of postmarketing studies for each approved product application. The status of these postmarketing studies shall be reported annually until FDA notifies the applicant, in writing, that the agency concurs with the applicant's determination that the study commitment has been fulfilled, or that the study is either no longer feasible or would no longer provide useful information. Each annual progress report shall be accompanied by a completed transmittal Form FDA-2252, and shall include all the information required under this section that the applicant received or otherwise obtained during the annual reporting interval which ends on the U.S. anniversary date. The report must provide the following information for each postmarketing study:

(1) ***Applicant's name.***

(2) ***Product name.*** Include the approved product's proper name and the proprietary name, if any.

(3) ***Biologics license application (BLA) and supplement number.***

(4) ***Date of U.S. approval of BLA.***

(5) ***Date of postmarketing study commitment.***

(6) ***Description of postmarketing study commitment.*** The description must include sufficient information to uniquely describe the study. This information may include the purpose of the study, the type of study, the patient population addressed by the study and the indication(s) and dosage(s) that are to be studied.

(7) ***Schedule for completion and reporting of the postmarketing study commitment.*** The schedule should include the actual or projected dates for submission of the study protocol to FDA, completion of patient accrual or initiation of an animal study, completion of the study, submission of the final study report to FDA, and any additional milestones or submissions for which projected dates were specified as part of the commitment. In addition, it should include a revised schedule, as appropriate. If the schedule has been previously revised, provide both the original schedule and the most recent, previously submitted revision.

(8) ***Current status of the postmarketing study commitment.*** The status of each postmarketing study should be categorized using one of the following terms that describes the study's status on the anniversary date of U.S. approval of the application or other agreed upon date:

(i) ***Pending.*** The study has not been initiated, but does not meet the criterion for delayed.

(ii) ***Ongoing.*** The study is proceeding according to or ahead of the original schedule described under paragraph (b)(7) of this section.

(iii) ***Delayed.*** The study is behind the original schedule described under paragraph (b)(7) of this section.

(iv) ***Terminated.*** The study was ended before completion but a final study report has not been submitted to FDA.

(v) ***Submitted.*** The study has been completed or terminated and a final study report has been submitted to FDA.

(9) ***Explanation of the study's status.*** Provide a brief description of the status of the study, including the patient accrual rate (expressed by providing the number of patients or subjects enrolled to date, and the total planned enrollment), and an explanation of the study's status identified under paragraph (b)(8) of this section. If the study has been completed, include the date the study was completed and the date the final study report was submitted to FDA, as applicable. Provide a revised schedule, as well as the reason(s) for the revision, if the schedule under paragraph (b)(7) of this section has changed since the previous report.

(c) ***When to report.*** Annual progress reports for postmarketing study commitments entered into by applicants shall be reported to FDA within 60 days of the anniversary date of the U.S. approval of the application for the product.

(d) ***Where to report.*** Submit two copies of the annual progress report of postmarketing studies to the Center for Biologics Evaluation and Research or Center for Drug Evaluation and Research (see mailing addresses in § 600.2(a) or (b) of this chapter).

(e) ***Public disclosure of information.*** Except for the information described in this paragraph, FDA may publicly disclose any information concerning a postmarketing study, within the meaning of this section, if the agency determines that the information is necessary to identify an applicant or to establish the status of the study including the reasons, if any, for failure to conduct, complete, and report the study. Under this section, FDA will not publicly disclose trade secrets, as defined in § 20.61 of this chapter, or information, described in § 20.63 of this chapter, the disclosure of which would constitute an unwarranted invasion of personal privacy.

[65 FR 64618, Oct. 30, 2000, as amended at 70 FR 14984, Mar. 24, 2005; 80 FR 18092, Apr. 3, 2015]

Subpart H - Approval of Biological Products When Human Efficacy Studies Are Not Ethical or Feasible

Source: 67 FR 37996, May 31, 2002, unless otherwise noted.

§ 601.90 Scope.

This subpart applies to certain biological products that have been studied for their safety and efficacy in ameliorating or preventing serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substances. This subpart applies only to those biological products for which: Definitive human efficacy studies cannot be conducted because it would be unethical to deliberately expose healthy human volunteers to a lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substance; and field trials to study the product's efficacy after an accidental or hostile exposure have not been feasible. This subpart does not apply to products that can be approved based on efficacy standards described elsewhere in FDA's regulations (e.g., accelerated approval based on surrogate markers or clinical endpoints other than survival or irreversible morbidity), nor does it address the safety evaluation for the products to which it does apply.

§ 601.91 Approval based on evidence of effectiveness from studies in animals.

(a) FDA may grant marketing approval for a biological product for which safety has been established and for which the requirements of § 601.90 are met based on adequate and well-controlled animal studies when the results of those animal studies establish that the biological product is reasonably likely to produce clinical benefit in humans. In assessing the sufficiency of animal data, the agency may take into account other data,

including human data, available to the agency. FDA will rely on the evidence from studies in animals to provide substantial evidence of the effectiveness of these products only when:

(1) There is a reasonably well-understood pathophysiological mechanism of the toxicity of the substance and its prevention or substantial reduction by the product;

(2) The effect is demonstrated in more than one animal species expected to react with a response predictive for humans, unless the effect is demonstrated in a single animal species that represents a sufficiently well-characterized animal model for predicting the response in humans;

(3) The animal study endpoint is clearly related to the desired benefit in humans, generally the enhancement of survival or prevention of major morbidity; and

(4) The data or information on the kinetics and pharmacodynamics of the product or other relevant data or information, in animals and humans, allows selection of an effective dose in humans.

(b) Approval under this subpart will be subject to three requirements:

(1) ***Postmarketing studies.*** The applicant must conduct postmarketing studies, such as field studies, to verify and describe the biological product's clinical benefit and to assess its safety when used as indicated when such studies are feasible and ethical. Such postmarketing studies would not be feasible until an exigency arises. When such studies are feasible, the applicant must conduct such studies with due diligence. Applicants must include as part of their application a plan or approach to postmarketing study commitments in the event such studies become ethical and feasible.

(2) ***Approval with restrictions to ensure safe use.*** If FDA concludes that a biological product shown to be effective under this subpart can be safely used only if distribution or use is restricted, FDA will require such postmarketing restrictions as are needed to ensure safe use of the biological product, commensurate with the specific safety concerns presented by the biological product, such as:

(i) Distribution restricted to certain facilities or health care practitioners with special training or experience;

(ii) Distribution conditioned on the performance of specified medical procedures, including medical followup; and

(iii) Distribution conditioned on specified recordkeeping requirements.

(3) ***Information to be provided to patient recipients.*** For biological products or specific indications approved under this subpart, applicants must prepare, as part of their proposed labeling, labeling to be provided to patient recipients. The patient labeling must explain that, for ethical or feasibility reasons, the

biological product's approval was based on efficacy studies conducted in animals alone and must give the biological product's indication(s), directions for use (dosage and administration), contraindications, a description of any reasonably foreseeable risks, adverse reactions, anticipated benefits, drug interactions, and any other relevant information required by FDA at the time of approval. The patient labeling must be available with the product to be provided to patients prior to administration or dispensing of the biological product for the use approved under this subpart, if possible.

§ 601.92 Withdrawal procedures.

(a) ***Reasons to withdraw approval.*** For biological products approved under this subpart, FDA may withdraw approval, following a hearing as provided in part 15 of this chapter, as modified by this section, if:

(1) A postmarketing clinical study fails to verify clinical benefit;

(2) The applicant fails to perform the postmarketing study with due diligence;

(3) Use after marketing demonstrates that postmarketing restrictions are inadequate to ensure safe use of the biological product;

(4) The applicant fails to adhere to the postmarketing restrictions applied at the time of approval under this subpart;

(5) The promotional materials are false or misleading; or

(6) Other evidence demonstrates that the biological product is not shown to be safe or effective under its conditions of use.

(b) ***Notice of opportunity for a hearing.*** The Director of the Center for Biologics Evaluation and Research or the Director of the Center for Drug Evaluation and Research will give the applicant notice of an opportunity for a hearing on the proposal to withdraw the approval of an application approved under this subpart. The notice, which will ordinarily be a letter, will state generally the reasons for the action and the proposed grounds for the order.

(c) ***Submission of data and information.***

(1) If the applicant fails to file a written request for a hearing within 15 days of receipt of the notice, the applicant waives the opportunity for a hearing.

(2) If the applicant files a timely request for a hearing, the agency will publish a notice of hearing in the Federal Register in accordance with §§ 12.32(e) and 15.20 of this chapter.

(3) An applicant who requests a hearing under this section must, within 30 days of receipt of the notice of opportunity for a hearing, submit the data and information upon which the applicant intends to rely at the hearing.

(d) ***Separation of functions.*** Separation of functions (as specified in § 10.55 of this chapter) will not apply at any point in withdrawal proceedings under this section.

(e) ***Procedures for hearings.*** Hearings held under this section will be conducted in accordance with the provisions of part 15 of this chapter, with the following modifications:

(1) An advisory committee duly constituted under part 14 of this chapter will be present at the hearing. The committee will be asked to review the issues involved and to provide advice and recommendations to the Commissioner of Food and Drugs.

(2) The presiding officer, the advisory committee members, up to three representatives of the applicant, and up to three representatives of CBER may question any person during or at the conclusion of the person's presentation. No other person attending the hearing may question a person making a presentation. The presiding officer may, as a matter of discretion, permit questions to be submitted to the presiding officer for response by a person making a presentation.

(f) ***Judicial review.*** The Commissioner of Food and Drugs' decision constitutes final agency action from which the applicant may petition for judicial review. Before requesting an order from a court for a stay of action pending review, an applicant must first submit a petition for a stay of action under § 10.35 of this chapter.

[67 FR 37996, May 31, 2002, as amended at 70 FR 14984, Mar. 24, 2005]

§ 601.93 Postmarketing safety reporting.

Biological products approved under this subpart are subject to the postmarketing recordkeeping and safety reporting applicable to all approved biological products.

§ 601.94 Promotional materials.

For biological products being considered for approval under this subpart, unless otherwise informed by the agency, applicants must submit to the agency for consideration during the preapproval review period copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the agency, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

§ 601.95 Termination of requirements.

If FDA determines after approval under this subpart that the requirements established in §§ 601.91(b)(2), 601.92, and 601.93 are no longer necessary for the safe and effective use of a biological product, FDA will so notify the applicant. Ordinarily, for biological products approved under § 601.91, these requirements will no longer apply when FDA determines that the postmarketing study verifies and describes the biological product's clinical benefit. For biological products approved under § 601.91, the restrictions would no longer apply when FDA determines that safe use of the biological product can be ensured through appropriate labeling. FDA also retains the discretion to remove specific postapproval requirements upon review of a petition submitted by the sponsor in accordance with § 10.30 of this chapter.

附属資料５：カナダ関連条文

① Patented Medicines (Notice of Compliance) Regulations[19]

Short Title

1 These Regulations may be cited as the *Patented Medicines (Notice of Compliance) Regulations*.

Interpretation

2(1) In these Regulations,

claim for the dosage form means a claim for a delivery system for administering a medicinal ingredient in a drug or a formulation of a drug that includes within its scope that medicinal ingredient or formulation; (*revendication de la forme posologique*)

claim for the formulation means a claim for a mixture that is composed of medicinal and non-medicinal ingredients, that is contained in a drug and that is administered to a patient in a particular dosage form; (*revendication de la formulation*)

claim for the medicinal ingredient includes a claim in the patent for the medicinal ingredient, whether chemical or biological in nature, when prepared or produced by the methods or processes of manufacture particularly described and claimed in the patent, or by their obvious chemical equivalents, and also includes a claim for different polymorphs of the medicinal ingredient, but does not include different chemical forms of the medicinal ingredient; (*revendication de l'ingrédient médicinal*)

claim for the medicine itself [Repealed]

claim for the use of the medicinal ingredient means a claim for the use of the medicinal ingredient for the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms; (*revendication de l'utilisation de l'ingrédient médicinal*)

claim for the use of the medicine [Repealed]

court [Repealed]

expire means

(a) in relation to a patent, expire, lapse or terminate by operation of law; and

(b) in relation to a certificate of supplementary protection, expire or terminate by operation of law; (*expiré*)

first person means the person referred to in subsection 4(1); (*première personne*)

medicine [Repealed]

Minister means the Minister of Health; (*ministre*)

notice of compliance means a notice issued under section C.08.004 or C.08.004.01 of the *Food and Drug Regulations*; (*avis de conformité*)

patent list means a list submitted under subsection 4(1); (*liste de brevets*)

register means the register maintained by the Minister in accordance with subsection 3(2); (*registre*)

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[19] Patented Medicines (Notice of Compliance) Regulations（Justice Laws Website）
https://laws-lois.justice.gc.ca/PDF/SOR-93-133.pdf

second person means the person referred to in subsection 5(1) or (2) who files a submission or supplement referred to in those subsections. (*seconde personne*)

(2) For the purposes of the definition *claim for the formulation* in subsection (1), the claim for the formulation need not specify the non-medicinal ingredients contained in the drug.

(3) In these Regulations, a reference to the owner of a patent includes the owner of a patent set out in a certificate of supplementary protection.

Register and Patent List

3(1) The following definitions apply in this section and in section 4.

identification number means a number, preceded by the letters "DIN", that is assigned for a drug in accordance with subsection C.01.014.2(1) of the *Food and Drug Regulations*. (*identification numérique*)

new drug submission means a new drug submission or an extraordinary use new drug submission as those terms are used in Division 8 of Part C of the *Food and Drug Regulations*, but excludes such a submission that is based solely on the change of name of the manufacturer. (*présentation de drogue nouvelle*)

supplement to a new drug submission means a supplement to a new drug submission or a supplement to an extraordinary use new drug submission as those terms are used in Division 8 of Part C of the *Food and Drug Regulations*, but excludes such a supplement that is based solely on one or more of the matters mentioned in any of paragraphs C.08.003(2)(b) and (d) to (g) and subparagraphs C.08.003(2)(h)(iv) and (v) of those Regulations. (*supplément à une présentation de drogue nouvelle*)

(2) The Minister shall maintain a register of patents that have been submitted for addition to the register and certificates of supplementary protection in which any of those patents are set out

(a) by adding any patent on a patent list or certificate of supplementary protection that meets the requirements for addition to the register;

(b) by refusing to add any patent or certificate of supplementary protection that does not meet the requirements for addition to the register;

(c) by deleting any patent or certificate of supplementary protection

(i) that was added to the register due to an administrative error,

(ii) that has, under subsection 60(1) or 125(1) of the *Patent Act*, been declared to be invalid or void,

(iii) that has, under subsection 6.07(1), been declared to be ineligible for inclusion on the register, or

(iv) the deletion of which was requested by the first person in respect of the patent list that includes that patent;

(d) by deleting, in respect of a new drug submission or a supplement to a new drug submission, any patent that has expired, unless a certificate of supplementary protection in which the patent is set out is included on the register in respect of that submission or supplement; and

(e) by deleting any certificate of supplementary protection that has expired.

(2.1) The Minister is not permitted to make a deletion referred to in subparagraph (2)(c)(iii) based on a decision by the Federal Court before the later of the day on which the period for appealing that decision to the Federal Court of Appeal ends and the day on which any appeal of that decision to the Federal Court of Appeal is discontinued or dismissed.

(2.2) The Minister shall add any patent or certificate of supplementary protection to the register that has been deleted under subparagraph (2)(c)(ii) or (iii) based on a decision that subsequently is reversed or set aside on appeal.

(2.3) The Minister may review the register to determine whether any patents or certificates of supplementary protection do not meet the requirements for inclusion on the register and, if the Minister conducts that review, shall delete any patent or certificate of supplementary protection that is determined not to meet those requirements.

(3) If a patent is listed on the register in respect of a new drug submission or supplement to a new drug submission for a drug for which the identification number has been cancelled under paragraph C.01.014.6(1)(a) of the *Food and Drug Regulations*, the Minister shall delete the patent from the register 90 days after the date of cancellation.

(4) Subsection (3) does not apply if the identification number is cancelled under paragraph C.01.014.6(1)(a) of the *Food and Drug Regulations* because of a change in manufacturer.

(5) If, after an identification number is cancelled under paragraph C.01.014.6(1)(a) of the *Food and Drug Regulations*, an identification number is assigned for the same drug, the Minister shall add to the register the patent that was deleted under subsection (3) when the Minister receives the document required by section C.01.014.3 of the *Food and Drug Regulations* in respect of the drug.

(6) The register shall be open to public inspection during business hours.

(7) No patent on a patent list or certificate of supplementary protection shall be added to the register until after the Minister has issued a notice of compliance in respect of the new drug submission or the supplement to a new drug submission, as the case may be, to which the patent or certificate of supplementary protection relates.

(8) For the purpose of determining whether a patent or certificate of supplementary protection is to be added to or deleted from the register, the Minister may consult with officers or employees of the Patent Office.

3.1(1) The Minister shall not delete from the register a patent on a patent list that was submitted before June 17, 2006, unless

(a) the patent has expired;

(b) a court has, under subsection 60(1) of the *Patent Act*, declared that the patent is invalid or void;

(c) the identification number assigned to the drug in respect of which the patent is listed is cancelled under paragraph C.01.014.6(1)(a) of the *Food and Drug Regulations*; or

(d) the first person in respect of that patent list requests the Minister to delete the patent.

(2) The Minister shall not refuse to add to the register a patent on a patent list that was submitted before June 17, 2006 solely on the basis that the patent is not relevant to the submission for a notice of compliance to which the patent list relates.

3.2 [Repealed]

4(1) A first person who files or who has filed a new drug submission or a supplement to a new drug submission may submit to the Minister a patent list in relation to the submission or supplement for addition to the register.

(1.1) The patent list may include a patent whose term under section 44 of the *Patent Act*, without taking into account section 46 of that Act, has expired and that is set out in a certificate of supplementary protection that has taken effect.

(2) A patent on a patent list in relation to a new drug submission is eligible to be added to the register if the patent contains

(a) a claim for the medicinal ingredient and the medicinal ingredient has been approved through the issuance of a notice of compliance in respect of the submission;

(b) a claim for the formulation that contains the medicinal ingredient and the formulation has been approved through the issuance of a notice of compliance in respect of the submission;

(c) a claim for the dosage form and the dosage form has been approved through the issuance of a notice of compliance in respect of the submission; or

(d) a claim for the use of the medicinal ingredient, and the use has been approved through the issuance of a notice of compliance in respect of the submission.

(2.1) The following rules apply when determining the eligibility of a patent to be added to the register under subsection (2):

(a) for the purposes of paragraph (2)(a), a patent that contains a claim for the medicinal ingredient is eligible even if the submission includes, in addition to the medicinal ingredient claimed in the patent, other medicinal ingredients;

(b) for the purposes of paragraph (2)(b), a patent that contains a claim for the formulation is eligible if the submission includes the non-medicinal ingredients specified in the claim, if any are specified, even if the submission contains any additional non-medicinal ingredients; and

(c) for the purposes of paragraph (2)(d), a patent that contains a claim for the use of the medicinal ingredient is eligible if the submission includes the use claimed in the patent, even if

(i) the submission includes additional medicinal ingredients,

(ii) the submission includes other additional uses of the medicinal ingredient, or

(iii) the use that is included in the submission requires the use of the medicinal ingredient in combination with another drug.

(3) A patent on a patent list in relation to a supplement to a new drug submission is eligible to be added to the register if the supplement is for a change in formulation, a change in dosage form or a change in use of the medicinal ingredient, and

(a) in the case of a change in formulation, the patent contains a claim for the changed formulation that has been approved through the issuance of a notice of compliance in respect of the supplement;

(b) in the case of a change in dosage form, the patent contains a claim for the changed dosage form that has been approved through the issuance of a notice of compliance in respect of the supplement; or

(c) in the case of a change in use of the medicinal ingredient, the patent contains a claim for the changed use of the medicinal ingredient that has been approved through the issuance of a notice of compliance in respect of the supplement.

(3.1) A certificate of supplementary protection is eligible to be added to the register in respect of a new drug submission or a supplement to a new drug submission if

(a) the patent that is set out in the certificate of supplementary protection is included on the register in respect of that submission or supplement; and

(b) the submission or supplement relates to a drug with respect to which the certificate of supplementary protection grants rights, privileges and liberties referred to in section 115 of the *Patent Act*.

(4) A patent list shall contain the following:

(a) an identification of the new drug submission or the supplement to a new drug submission to which the list relates;

(b) the medicinal ingredient, brand name, dosage form, strength, route of administration and use set out in the new drug submission or the supplement to a new drug submission to which the list relates;

(c) for each patent on the list, the patent number, the filing date of the patent application in Canada, the date of grant of the patent and the date on which the term limited for the duration of the patent will expire under section 44 or 45 of the Patent Act;

(d) for each patent on the list, a statement that the first person who filed the new drug submission or the supplement to a new drug submission to which the list relates

(i) is the owner of the patent,

(ii) has an exclusive licence to the patent or to a certificate of supplementary protection in which that patent is set out, or

(iii) has obtained the consent of the owner of the patent to its inclusion on the list;

(e) the address in Canada for service, on the first person, of a notice of allegation referred to in paragraph 5(3)(a) or the name and address in Canada of another person on whom service may be made with the same effect as if service were made on the first person; and

(f) a certification by the first person that the information submitted under this subsection is accurate and that each patent on the list meets the eligibility requirements of subsection (2) or (3).

(5) Subject to subsection (6), a first person who submits a patent list must do so at the time the person files the new drug submission or the supplement to a new drug submission to which the patent list relates.

(6) A first person may, after the date of filing of a new drug submission or a supplement to a new drug submission, and within 30 days after the issuance of a patent that was issued on the basis of an application that has a filing date in Canada that precedes the date of filing of the submission or supplement, submit a patent list, including the information referred to in subsection (4), in relation to the submission or supplement.

(7) A first person who has submitted a patent list must keep the information on the list up to date but, in so doing, may not add a patent to the list.

(8) The Minister shall insert on the patent list the date of filing and submission number of the new drug submission or the supplement to a new drug submission in relation to which the list was submitted.

4.1(1) In this section, ***supplement to the new drug submission*** means a supplement to a new drug submission or a supplement to an extraordinary use new drug submission as those terms are used in Division 8 of Part C of the *Food and Drug Regulations*.

(2) A first person who submits a patent list in relation to a new drug submission referred to in subsection 4(2) may, if the list is added to the register, resubmit the same list in relation to a supplement to the new drug submission, but may not submit a new patent list in relation to a supplement except in accordance with subsection 4(3).

5(1) If a second person files a submission for a notice of compliance in respect of a drug and the submission directly or indirectly compares the drug with, or makes reference to, another drug marketed in Canada under a notice of compliance issued to a first person and in respect of which a patent list has been submitted, the second person shall include in the submission the required statements or allegations set out in subsection (2.1).

(2) If a second person files a supplement to a submission referred to in subsection (1) seeking a notice of compliance for a change in formulation, a change in dosage form or a change in use of the medicinal ingredient and the supplement directly or indirectly compares the drug for which the supplement is filed with, or makes reference to, another drug that has been marketed in Canada under a notice of compliance issued to a first

person and in respect of which a patent list has been submitted, the second person shall include in the supplement the required statements or allegations set out in subsection (2.1).

(2.1) The statements or allegations required for the submission or the supplement, as the case may be, are — with respect to each patent included on the register in respect of the other drug and with respect to each certificate of supplementary protection in which the patent is set out and that is included on the register in respect of the other drug — the following:

(a) a statement that the owner of that patent has consented to the making, constructing, using or selling in Canada of the drug for which the submission or supplement is filed by the second person;

(b) a statement that the second person accepts that the notice of compliance will not issue until that patent or certificate of supplementary protection, as the case may be, expires; or

(c) an allegation that

(i) the statement made by the first person under paragraph 4(4)(d) is false,

(ii) that patent or certificate of supplementary protection is invalid or void,

(iii) that patent or certificate of supplementary protection is ineligible for inclusion on the register,

(iv) that patent or certificate of supplementary protection would not be infringed by the second person making, constructing, using or selling the drug for which the submission or the supplement is filed,

(v) that patent or certificate of supplementary protection has expired, or

(vi) in the case of a certificate of supplementary protection, that certificate of supplementary protection cannot take effect.

(3) A second person who makes an allegation referred to in paragraph (2.1)(c) shall

(a) serve on the first person a notice of allegation relating to the submission or supplement filed under subsection (1) or (2) on or after its date of filing;

(b) include in the notice of allegation

(i) a description of the medicinal ingredient, dosage form, strength, route of administration and use of the drug in respect of which the submission or supplement has been filed, and

(ii) a statement of the legal and factual basis for the allegation, which statement must be detailed in the case of an allegation that the patent or certificate of supplementary protection is invalid or void;

(c) serve the following documents with the notice:

(i) a certification by the Minister of the date of filing of the submission or supplement,

(ii) a document setting out the second person’s address for service for the purpose of any action that may be brought against them under subsection 6(1), along with the names of and contact information for their anticipated solicitors of record if that action is brought,

(iii) a searchable electronic copy of the portions of the submission or supplement that are under the control of the second person and relevant to determine if any patent or certificate of supplementary protection referred to in the allegation would be infringed, and

(iv) if the second person is alleging that the patent or certificate of supplementary protection is invalid or void, an electronic copy of any document — along with an electronic copy of it in English or French if available — on which the person is relying in support of the allegation;

(d) provide, without delay, to the first person any portion of a submission or supplement referred to in subparagraph (c)(iii) that is changed on or before the later of the 45th day after the day on which the notice of allegation is served and the day of the disposition of any action that has been brought under subsection 6(1); and

(e) provide to the Minister proof of service of the documents referred to in paragraphs (a) and (b), along with a copy of the notice of allegation.

(3.1) A second person who makes an allegation that the patent or certificate of supplementary protection is invalid or void may, when the notice of allegation is served, request

(a) the name of and contact information for any inventor who might have information relevant to the allegation, along with an indication as to whether that inventor is an employee of the first person or of the patent owner; and

(b) any laboratory notebook, research report or other document that may be relevant to determine whether a particular property, advantage, or use asserted by the second person to be part of the invention was established as of the filing date of the application for the patent, if the second person identifies the specific allegation in the notice of allegation that is relevant to the request and the portion of the patent in which that property, advantage or use is set out.

(3.2) A document referred to in paragraph (3.1)(b) must be provided in a searchable electronic format but, if it is not available in that format, in an electronic format. In addition, if the document provided is not already in English or French, it must also be provided, if available, in English or French and be in a searchable electronic format but, if it is not available in that format, in an electronic format.

(3.3) Within five days after the day on which the first person is served with any notice or document under subsection (3), they shall forward a copy of it, along with any request made under subsection (3.1) when the notice was served and an indication of the date of the service,

(a) to the owner of each patent in respect of which an allegation is made in that notice; and

(b) to the owner of a patent that is set out in each certificate of supplementary protection in respect of which an allegation is made in that notice.

(3.4) The first person shall, without delay, notify the second person that they forwarded the copy under subsection (3.3) and, if they are owner of any patent referred to in that subsection, that they are its owner.

(3.5) The second person may impose on the first person referred to in paragraph (3)(a) and any owner of a patent to whom a document is forwarded under subsection (3.3) any reasonable rules for maintaining the confidentiality of any portion of a submission or supplement referred to in subparagraph (3)(c)(iii).

(3.6) Those confidentiality rules are binding and enforceable by the Federal Court, which may award any remedy that it considers just if they are not respected.

(3.7) On motion of the first person or of the owner of the patent — or on its own initiative after giving an opportunity to be heard to that first person, that owner and the second person — the Federal Court may set aside or vary any or all of those confidentiality rules in any manner that it considers just.

(3.8) A second person who is, under subparagraph (3)(c)(iii) or paragraph (3)(d), required to serve or provide a document may — if there is reason to believe that the intended recipient of the document is not in Canada — refuse to do so unless that recipient attorns to the jurisdiction of the Federal Court with respect to the confidentiality of the information set out in the document.

(3.9) A second person who is, under subparagraph (3)(c)(iii) or paragraph (3)(d), required to serve or provide a document to a first person referred to in paragraph (3)(a) may — if there is reason to believe that the first person is required to forward the document to the owner of a patent who is not in Canada — require that the first person forward it only if that owner attorns to the jurisdiction of the Federal Court with respect to the confidentiality of the information set out in the document.

(4) A second person is not required to comply with

(a) subsection (1) in respect of a patent, or a certificate of supplementary protection that sets out the patent, that is added to the register in respect of the other drug on or after the date of filing of the submission referred to in that subsection, including one added under subsection 3(2.2) or (5); and

(b) subsection (2) in respect of a patent, or a certificate of supplementary protection that sets out the patent, that is added to the register in respect of the other drug on or after the date of filing of the supplement referred to in that subsection, including one added under subsection 3(2.2) or (5).

(5) For the purposes of subsections (3) and (4), if subsection (1) or (2) applies to a submission or supplement referred to in paragraph C.07.003(b) of the *Food and Drug Regulations*, if the drug to which the comparison or reference is made is an innovative drug within the meaning of subsection C.08.004.1(1) of those Regulations and if the date of filing of the submission or supplement is less than six years from the day on which the first notice of compliance was issued in respect of the innovative drug, the deemed date of filing of the submission or supplement is six years after the date of issuance of the notice of compliance.

(6) A second person who has served a notice of allegation on a first person under paragraph (3)(a) shall retract the notice of allegation and serve notice of the retraction on the first person within 90 days after either of the following dates:

(a) the date on which the Minister notifies the second person under paragraph C.08.004(3)(b) or C.08.004.01(3)(b), as the case may be, of the *Food and Drug Regulations* of their non-compliance with the requirements of section C.08.002, C.08.002.01, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1 of those Regulations; or

(b) the date of the cancellation by the second person of the submission or supplement to which the allegation relates.

(6.1) Within five days after the day on which the first person is served under subsection (6), they shall, if they are not the owner of any patent to which the notice of allegation relates, forward to the owner of that patent a copy of the notice of retraction.

(7) A person who brings an action under subsection 6(1) in response to a notice of allegation shall, if the notice is retracted in accordance with subsection (6), file without delay a notice of discontinuance.

Right of Action

6(1) The first person or an owner of a patent who receives a notice of allegation referred to in paragraph 5(3)(a) may, within 45 days after the day on which the first person is served with the notice, bring an action against the second person in the Federal Court for a declaration that the making, constructing, using or selling of a drug in accordance with the submission or supplement referred to in subsection 5(1) or (2) would infringe any patent or certificate of supplementary protection that is the subject of an allegation set out in that notice.

(2) If the person who brings an action under subsection (1) is not the owner of each patent — or of a patent that is set out in each certificate of supplementary protection — that is the subject of the action, the owner of each of those patents shall be or be made a party to the action.

(3) The second person may bring a counterclaim for a declaration

(a) under subsection 60(1) or (2) of the *Patent Act* in respect of any patent claim asserted in the action brought under subsection (1); or

(b) under 125(1) or (2) of that Act in respect of any claim, asserted in the action brought under subsection (1), in the patent set out in the certificate of supplementary protection in question in that action.

(4) If the Federal Court makes a declaration referred to in subsection (1), it may order any other remedy that is available under the *Patent Act*, or at law or in equity, in respect of infringement of a patent or a certificate of supplementary protection.

6.01 No action, other than one brought under subsection 6(1), may be brought against the second person for infringement of a patent or a certificate of supplementary protection that is the subject of a notice of allegation served under paragraph 5(3)(a) in relation to the making, constructing, using or selling of a drug in accordance with the submission or supplement referred to in subsection 5(1) or (2) unless the first person or the owner of the patent did not, within the 45-day period referred to in subsection 6(1), have a reasonable basis for bringing an action under that subsection.

6.02 No action may be joined to a given action brought under subsection 6(1) during any period during which the Minister shall not issue a notice of compliance because of paragraph 7(1)(d) other than

(a) another action brought under that subsection in relation to the submission or supplement in that given action; and

(b) an action brought in relation to a certificate of supplementary protection that is added to the register after the filing of the submission or supplement in that given action, if the patent that is set out in that certificate of supplementary protection is at issue in that given action.

6.03(1) If a second person makes a request under subsection 5(3.1), the person who brings the action must serve on the second person at the same time as their statement of claim,

(a) a document setting out the information referred to in paragraph (3.1)(a) and the documents referred to in paragraph (3.1)(b);

(b) a document setting out an explanation of the steps that have been and are being taken to locate that information or those documents, along with a statement that they will be provided as soon as feasible; or

(c) a document setting out the reasons for not providing them, if applicable.

(2) The person bringing the action may impose on the second person any reasonable rules for maintaining the confidentiality of the information set out in any document provided under paragraph (1)(a).

(3) Those confidentiality rules are binding and enforceable by the Federal Court, which may award any remedy that it considers just if they are not respected.

(4) On motion of the second person or on its own initiative, after giving an opportunity to be heard to the parties to the action, the Federal Court may set aside or vary any or all of those confidentiality rules in any manner that it considers just.

(5) Any person who is, under paragraph (1)(a), required to provide a document may — if there is reason to believe that the intended recipient of the document is not in Canada — refuse to provide it unless the recipient attorns to the jurisdiction of the Federal Court with respect to the confidentiality of the information set out in the document.

6.04(1) On the motion of a first person or owner of a patent who is a party to an action brought under subsection 6(1) or a counterclaim brought under subsection 6(3), the Federal Court may, at any time during the proceeding, order that the second person produce any portion of the submission or supplement that is relevant to determine if any patent or certificate of supplementary protection at issue would be infringed and any such portion that is changed.

(2) On the motion of a second person who is party to an action brought under subsection 6(1) or a counterclaim brought under subsection 6(3), the Federal Court may, at any time during the proceeding, order that the first person or owner of a patent produce a document setting out any information referred to in paragraph 5(3.1)(a) or any laboratory notebook, research report or other document that may be relevant to determine whether a particular property, advantage, or use asserted by the second person to be part of the invention was established as of the filing date of the application for the patent.

(3) The information set out in any document produced under subsection (1) or (2) shall be treated confidentially by the Federal Court subject to any conditions that it considers just.

6.05 The Minister shall, on the request of any party, verify that any portion of a submission or supplement that is referred to in subparagraph 5(3)(c)(iii) or paragraph 5(3)(d) or produced as a result of an order made under subsection 6.04(1) corresponds to the submission or supplement filed.

6.06 On the request, made by way of a motion, of a person who imposed rules referred to in subsection 5(3.5) or 6.03(2) for maintaining the confidentiality of the information set out in any document, the Federal Court shall treat that information confidentially subject to any conditions that it considers just.

6.07(1) In an action brought under subsection 6(1), the Federal Court may, on the motion of the second person, declare that a patent or certificate of supplementary protection is ineligible for inclusion on the register.

(2) The Minister may intervene as of right in the motion and make representations and call evidence that are relevant to any issue in the motion or to the factors that the Federal Court is entitled to take into consideration in determining the issue. The Minister may intervene as of right in any appeal arising from the decision made on the motion, whether the Minister intervened at the Federal Court or not.

(3) The Federal Court shall not, in whole or in part, dismiss the action solely on the basis that a patent or certificate of supplementary protection is ineligible for inclusion on the register.

(4) Subsection (1) does not apply in respect of a patent on a patent list that was submitted before June 17, 2006.

6.08 An action brought under subsection 6(1) may, on the motion of a second person, be dismissed, in whole or in part, on the ground that it is redundant, scandalous, frivolous or vexatious or is otherwise an abuse of process in respect of one or more patents or certificates of supplementary protection.

6.09 Every first person, second person and owner of a patent shall act diligently in carrying out their obligations under these Regulations and shall reasonably cooperate in expediting any action brought under subsection 6(1) or a counterclaim brought under subsection 6(3) to which they are a party.

6.1(1) An action brought under subsection 6(1) shall be a specially managed proceeding in accordance with the *Federal Courts Rules*.

(2) The case management judge who is assigned the specially managed proceeding shall conduct a case management conference as soon as feasible after the 10th day after proof of service of the statement of claim in the action is filed.

6.11(1) Any interlocutory order made in an action brought under subsection 6(1) or a counterclaim brought under subsection 6(3), including one that, in whole or in part, disposes of the action or counterclaim, may be appealed to the Federal Court of Appeal, with leave of that Court, and not to the Federal Court.

(2) The motion for leave to appeal shall be filed no later than 10 days after the day on which that interlocutory order is made.

6.12(1) In an action brought under subsection 6(1) or a counterclaim brought under subsection 6(3), the Federal Court may make any order in respect of costs, including on a solicitor-and-client basis, in accordance with the *Federal Courts Rules*.

(2) In addition to any other factor that the Federal Court may take into account in making an order in respect of costs, it may consider

(a) the diligence with which the parties have pursued the action;

(b) the extent to which they have reasonably cooperated in expediting the action;

(c) the certification of a patent list that includes a patent that should not have been included under section 4; and

(d) the failure of the first person to keep a patent list up to date in accordance with subsection 4(7).

6.13 The person who brings an action under subsection 6(1) shall provide to the Minister, as soon as feasible, a copy of the following documents in relation to the action:

(a) the statement of claim, including any amendments to it;

(b) any order made under subsection 6.04(1) or 7(8);

(c) any declaration referred to in subsection 6(1) or (3) or 6.07(1);

(d) the notice of motion and the motion record in respect of any motion referred to in subsection 6.07(1);

(e) any document discontinuing or dismissing the action, in whole or in part;

(f) any notice of appeal, including a motion or application for leave to appeal, in relation to any document referred to in paragraph (b), (c) or (e); and

(g) any judgment or order in an appeal, or a motion or application for leave to appeal, in relation to any document referred to in paragraph (b), (c) or (e).

Notice of Compliance

7(1) The Minister shall not issue a notice of compliance to a second person before the latest of

(a) the day after the expiry of all of the patents and certificates of supplementary protection in respect of which the second person is required to make a statement or allegation under subsection 5(1) or (2) and that are not the subject of an allegation;

(b) the day on which the second person complies with paragraph 5(3)(e);

(c) the 46th day after the day on which a notice of allegation under paragraph 5(3)(a) is served;

(d) the day after the expiry of the 24-month period that begins on the day on which an action is brought under subsection 6(1);

(e) the day after the expiry of all of the patents and certificates of supplementary protection in respect of which a declaration of infringement has been made in an action brought under subsection 6(1); and

(f) the day after the expiry of all of the certificates of supplementary protection, other than any that were held not to be infringed in an action referred to in paragraph (e), that

(i) set out a patent referred to in paragraph (a) or (e),

(ii) are not the subject of a statement or allegation made under subsection 5(1) or (2), and

(iii) are included on the register in respect of the same submission or supplement as the patent.

(2) Subsection (1) does not apply in respect of a patent or a certificate of supplementary protection if the Minister has been provided with evidence from the owner of the patent of their consent to the making, constructing, using or selling of the drug in Canada by the second person.

(3) Paragraphs (1)(a) to (d) do not apply in respect of a patent or certificate of supplementary protection if it is deleted from the register under any of paragraphs 3(2)(c) to (e) or subsection 3(2.3) or (3).

(4) Paragraph (1)(d) does not apply in respect of a patent or a certificate of supplementary protection that has been declared in the action referred to in that paragraph by the Federal Court to be ineligible for inclusion on the register.

(5) Paragraph (1)(d) does not apply if

(a) the action referred to in that paragraph is discontinued or dismissed; or

(b) each of the parties who brings an action referred to in subsection 6(1) in relation to a given notice of allegation provides, when they bring the action, a notice to the second person and the Minister that they renounce the application of that paragraph.

(6) A party may make the renouncement referred to in paragraph (5)(b) without prejudice to their right to proceed with the action or any other action for patent infringement or their entitlement to any remedy from the Federal Court or another court.

(7) A second person, or a first person or owner of a patent who receives a notice of allegation, shall, on request of the Minister, provide to the Minister without delay any information or document that the Minister requires to maintain the register in accordance with subsection 3(2), to determine the latest of the days referred to in subsection (1) and to determine whether any of subsections (2) to (5) apply.

(8) As long as the Federal Court has not made a declaration referred to in subsection 6(1), it may shorten or extend the 24-month period referred to in paragraph (1)(d) if it finds that a party has not acted diligently in carrying out their obligations under these Regulations or has not reasonably cooperated in expediting the action.

8 (1) A second person may apply to the Federal Court or another superior court of competent jurisdiction for an order requiring all plaintiffs in an action brought under subsection 6(1) to compensate the second person for the loss referred to in subsection (2).

(2) Subject to subsection (3), if an action brought under subsection 6(1) is discontinued or dismissed or if a declaration referred to in subsection 6(1) is reversed on appeal, all plaintiffs in the action are jointly and severally, or solidarily, liable to the second person for any loss suffered after the later of the day on which the notice of allegation was served, the service of which allowed that action to be brought, and of the day, as certified by the Minister, on which a notice of compliance would have been issued in the absence of these Regulations.

(3) The Federal Court or the other superior court may specify another day for the purpose of subsection (2) if it concludes that the other day is more appropriate, including being more appropriate because the certified day was, by the operation of *An Act to amend the Patent Act and the Food and Drugs Act (The Jean Chrétien Pledge to Africa)*, chapter 23 of the Statutes of Canada, 2004, earlier than it would otherwise have been.

(4) Subsections (1) to (3) do not apply if paragraph 7(1)(d) has no application because its application has been renounced under paragraph 7(5)(b).

(5) If the Federal Court or the other superior court orders a second person to be compensated for a loss referred to in subsection (2), the court may, in respect of that loss, make any order for relief by way of damages that the circumstances require.

(6) In assessing the amount of compensation — including any apportionment of that amount between the plaintiffs who are liable under subsection (2) — the court shall take into account all matters that it considers relevant to the assessment of the amount or the apportionment, including any conduct of the parties that contributed to delay the disposition of the action.

(7) No action or proceeding lies against Her Majesty in right of Canada in respect of any loss referred to in subsection (2).

8.1 A person who files a submission for a notice of compliance or a supplement to a submission for a notice of compliance in respect of a drug and who has reasonable grounds to believe that the making, constructing, using or selling of the drug might be alleged to infringe a patent or a certificate of supplementary protection is, if the submission or supplement directly or indirectly compares the drug with, or makes reference to, another drug marketed in Canada, an interested person

(a) for the purpose of subsection 60(1) of the *Patent Act* with respect to bringing an action for a declaration that the patent or any claim in the patent is invalid or void; or

(b) for the purpose of subsection 125(1) of that Act with respect to bringing an action for a declaration that the certificate of supplementary protection or any claim in the patent set out in it is invalid or void.

8.2 On receipt of a notice of allegation relating to a submission or supplement, a first person or owner of a patent may, under subsection 54(1) or 124(1) of the *Patent Act*, bring an action for infringement of a patent or certificate of supplementary protection — other than one that is the subject of an allegation set out in that notice — that could result from the making, constructing, using or selling of the drug in accordance with the submission or supplement.

Service

9(1) Service of any document referred to in these Regulations shall be effected personally or by registered mail.

(2) Service by registered mail shall be deemed to be effected on the addressee five days after mailing.

② C.08.004.1 Food of Food and Drug Regulations[20]

C.08.004.1 (1) The following definitions apply in this section.

abbreviated new drug submission includes an abbreviated extraordinary use new drug submission. (*présentation abrégée de drogue nouvelle*)

innovative drug means a drug that contains a medicinal ingredient not previously approved in a drug by the Minister and that is not a variation of a previously approved medicinal ingredient such as a salt, ester, enantiomer, solvate or polymorph. (*drogue innovante*)

new drug submission includes an extraordinary use new drug submission. (*présentation de drogue nouvelle*)

pediatric populations means the following groups: premature babies born before the 37th week of gestation; full-term babies from 0 to 27 days of age; and all children from 28 days to 2 years of age, 2 years plus 1 day to 11 years of age and 11 years plus 1 day to 18 years of age. (*population pédiatrique*)

(1.1) For the purposes of the definition *innovative drug* in subsection (1), a medicinal ingredient is not considered to be approved in a drug by reason of the Minister having issued or amended an authorization under the ISAD Interim Order in respect of a COVID-19 drug that contains the medicinal ingredient.

(2) The purpose of this section is to implement Articles 20.48 and 20.49 of the Agreement between Canada, the United States of America and the United Mexican States, as defined in the definition *Agreement* in section 2 of the *Canada–United States–Mexico Agreement Implementation Act*, and paragraph 3 of Article 39 of the Agreement on Trade-related Aspects of Intellectual Property Rights set out in Annex 1C to the Agreement Establishing the World Trade Organization, as defined in the definition *Agreement* in subsection 2(1) of the *World Trade Organization Agreement Implementation Act*.

(3) If a manufacturer seeks a notice of compliance for a new drug on the basis of a direct or indirect comparison between the new drug and an innovative drug,

> **(a)** the manufacturer may not file a new drug submission, a supplement to a new drug submission, an abbreviated new drug submission or a supplement to an abbreviated new drug submission in respect of the new drug before the end of a period of six years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug; and
>
> **(b)** the Minister shall not approve that submission or supplement and shall not issue a notice of compliance in respect of the new drug before the end of a period of eight years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug.

(4) The period specified in paragraph (3)(b) is lengthened to eight years and six months if

[20] Food and Drug Regulations（Justice Laws Website）
https://laws-lois.justice.gc.ca/PDF/C.R.C._c._870.pdf

(a) the innovator provides the Minister with the description and results of clinical trials relating to the use of the innovative drug in relevant pediatric populations in its first new drug submission for the innovative drug or in any supplement to that submission that is filed within five years after the issuance of the first notice of compliance for that innovative drug; and

(b) before the end of a period of six years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug, the Minister determines that the clinical trials were designed and conducted for the purpose of increasing knowledge of the use of the innovative drug in those pediatric populations and this knowledge would there-by provide a health benefit to members of those populations.

(5) Subsection (3) does not apply if the innovative drug is not being marketed in Canada.

(6) Paragraph (3)(a) does not apply to a manufacturer if the innovator consents to the filing of a new drug submission, a supplement to a new drug submission, an abbreviated new drug submission or a supplement to an abbreviated new drug submission by the manufacturer before the end of the period of six years specified in that paragraph.

(7) Paragraph (3)(a) does not apply to a manufacturer if the manufacturer files an application for authorization to sell its new drug under section C.07.003.

(8) Paragraph (3)(b) does not apply to a manufacturer if the innovator consents to the issuance of a notice of compliance to the manufacturer before the end of the period of eight years specified in that paragraph or of eight years and six months specified in subsection (4).

(9) The Minister shall maintain a register of innovative drugs that includes information relating to the matters specified in subsections (3) and (4).

③ Guidance Document – Patented Medicines (Notice of Compliance) Regulations[21]

7 章（1. Introduction; 2. Definition; 3. General Information; 4. Section 4 of the PM(NOC) Regulations; 5. Section 5 of the PM(NOC) Regulations; 6. Sections 6 and 7 of the PM(NOC) Regulations; 7. Maintenance of the Patent Register）からなる、2000 年 2 月 14 日施行、2018 年 4 月 5 日改正、2021 年 4 月 8 日改正されたガイダンス文書である。

[21] Guidance Document – Patented Medicines (Notice of Compliance) Regulations（カナダ政府ウェブサイト）https://www.canada.ca/content/dam/hc-sc/documents/services/drug-health-product-review-approval/drug-products/guidance-documents/pm-noc-regulations-guid-ld-eng.pdf

附属資料６：中国関連条文

① 専利法：第 4 次改正[22] 2021 年 6 月 1 日施行（仮訳）

第 76 条

薬品発売承認審査において、薬品発売許可申請者と関連専利権者又は利害関係者は、登録出願された薬品に係る専利権について紛争が生じた場合、関連当事者は人民法院に提訴し、登録出願された薬品の関連技術方案が他人の薬品専利権の保護範囲に含まれているかどうかを判決するように請求することができる。国務院薬品監督管理部門は規定された期限内に、人民法院による発効した判決により、関連薬品の発売許可を一時中止するかどうかの決定を下すことができる。

薬品発売許可申請者と関連専利権者又は利害関係者は、登録出願された薬品に係る専利権紛争について、国務院専利行政部門に行政裁決を請求することもできる。

国務院薬品監督管理部門は国務院専利行政部門と共同して、薬品販売の承認と薬品販売許可申請段階の専利権紛争解決の具体的な係合弁法を制定し、国務院に報告して承認を得てから施行する。

② 医薬品専利紛争の早期解決仕組みの実施弁法（＝医薬品特許紛争早期解決メカニズム行政裁決弁法）（試行）[23]（仮訳）（2021 年 7 月 4 日）

第 1 条

これらの措置は、医薬品特許権者の正当な権利と利益を保護し、新薬研究を奨励し、高レベルの後発医薬品の開発を促進し、医薬品特許紛争の早期解決メカニズムを確立するために策定される。

第 2 条

国家評議会の医薬品規制部門は、中国で登録および販売されている医薬品に関連する特許情報を登録するために、医薬品販売ライセンス保有者が中国に上場している医薬品の特許情報登録プラットフォームの確立を組織するものとする。

関連する特許情報が中国で販売されている医薬品特許情報登録プラットフォームに登録されていない場合、これらの措置は適用されない。

第 3 条

国家医薬品評価庁は、中国で販売されている医薬品の特許情報登録プラットフォームを確立および維持し、承認された医薬品の関連する特許情報を販売のために公表する責任がある。

第 4 条

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[22] 中华人民共和国专利法(2020 年修正)（ジェトロウェブサイト）
https://www.jetro.go.jp/ext_images/world/asia/cn/ip/law/pdf/regulation/regulation20210601.pdf

[23] 药品专利纠纷早期解决机制实施办法（试行）（中華人民共和国中央人民政府ウェブサイト）
https://view.officeapps.live.com/op/view.aspx?src=http%3A%2F%2Fwww.gov.cn%2Fzhengce%2Fzhengceku%2F2021-07%2F04%2F5622330%2Ffiles%2F4d1b47cd16164643844c3f75c93a5dd5.doc&wdOrigin=BROWSELINK

医薬品販売承認取得者は、医薬品登録証明書を取得してから 30 日以内に、医薬品名、投薬形態、明細書、販売承認取得者、関連特許番号、特許名、特許権者、特許ライセンシー、特許承認日、保護期間の満了日、特許のステータス、特許の種類、医薬品と関連する特許請求の対応、郵送先住所、連絡先、連絡先情報などを自己登録しなければならない。関連情報が変更された場合、医薬品販売承認取得者は、情報変更が有効になってから 30 日以内に更新を完了するものとする。
医薬品販売承認取得者は、登録された関連情報の信憑性、正確性、完全性に責任を負い、受け取った関連する異議を迅速に検証して処理し、記録するものとする。登録情報は、特許登録簿、特許ガゼット、および医薬品登録証明書の関連情報と一致している必要がある。医薬品使用の特許権は、承認された医薬品添付文書の適応症または機能と一致している必要がある。関連する特許保護範囲は、承認された薬の技術的解決策に対応するものを対象とする。関連情報の改訂は、理由を説明し、それらを公表するものとする。

第 5 条
化学薬品販売免許保持者は、医薬品の有効成分化合物の特許、有効成分を含む医薬組成物の特許、および医薬品使用の特許を中国上場医薬品特許情報登録プラットフォームに登録することができる。

第 6 条
化学後発医薬品の申請者は、医薬品販売承認の申請を行う場合、中国上場医薬品特許情報登録プラットホームに公開されている特許情報と比較して、後発医薬品の関連医薬品特許ごとに陳述するものとする。ステートメントは 4 つのカテゴリに分類される。
タイプ I の宣言：中国上場医薬品特許情報登録プラットフォームには、後発医薬品に関連する特許情報はない。
タイプ II の宣言：中国上場医薬品特許情報登録プラットフォームに含まれる後発医薬品に関連する特許権が終了または無効と宣言されたか、後発医薬品申請者が特許権者の関連する特許ライセンスを取得した。
タイプ III の宣言：中国の上場医薬品特許情報登録プラットフォームには後発医薬品に関連する特許が含まれており、後発医薬品申請者は、対応する特許権の満了前に申請された後発医薬品が一時的に上場されないことを約束する。
タイプ IV の宣言：中国上場医薬品特許情報登録プラットフォームに含まれる後発医薬品に関連する特許権は無効であると宣言されるか、後発医薬品は関連する特許権の保護の範囲に含まれない。
後発医薬品の申請者は、関連する声明の信憑性と正確性に責任がある。後発医薬品の申請が受理されてから 10 営業日以内に、国内の医薬品審査機関は、情報プラットフォーム上で申請情報と対応する声明を一般に開示するものとする。後発医薬品の申請者は、対応する声明と根拠を販売承認取得者に通知するものとする。声明および販売承認について保有者が特許権者でない場合、販売承認保有者は特許権者に通知するものとする。声明が関連特許権の保護の範囲に含まれない場合、声明の根拠には、後発医薬品の技術スキームと関連特許の関連クレームおよび関連技術データの比較表を含めるものとする。後発医薬品の申請者は、紙の資料に加えて、声明とその根拠を中国上場医薬

品特許情報登録プラットフォームに登録されている販売承認取得者の電子メールアドレスに送信し、関連する記録を保持する必要がある。

第 7 条

特許権者または利害関係者がタイプ IV の特許宣言に異議を唱える場合、国の医薬品評価機関が医薬品販売承認の申請書を発行した日から 45 日以内に、関連するかどうかを判断することができる。マーケティングに適用される医薬品の技術スキームは、関連する特許に該当する。人民法院で訴訟を起こすか、省議会の下の特許管理部門に行政裁定を要求する。関係者は、国務院の特許行政部の行政裁定に不満がある場合は、行政裁定を受けた後、法に基づき人民法院に訴訟を起こすことができます。

特許権者または利害関係者が所定の期限内に訴訟を提起するか、行政裁定を要求する場合、人民法院の日から 15 営業日以内に、訴訟または受理通知の写しを国の医薬品審査に提出するものとする。ケースを提出するか、省議会の下の特許管理部門がケースを受け入れる。評価機関と後発医薬品申請者に通知する。

第 8 条

人民法院による訴訟の写しまたは国務省の特許管理部門による受理の通知を受け取った後、国務省の薬物規制部門は、化学後発医薬品の登録の申請を 9 ヶ月の待機期間に設定するものとする。待機期間は、事件が人民法院に提起された日、または省議会の特許管理部門によって承認された日から 1 回だけ設定される。待機期間中、国家薬物評価機関は技術評価を停止しない。

特許権者または利害関係者が所定の期限内に訴訟を提起または行政裁定を要求しなかった場合、省議会の医薬品規制部門は、後発医薬品申請者が提出した結論および声明の技術的レビューに基づいて後発医薬品の販売を承認するかどうかを直接決定するものとする。申請者は、関連する規制に従って訴訟を起こすか、行政裁定を要求することができます。

第 9 条

待機期間をトリガーする化学後発医薬品登録申請については、特許権者または利害関係者、および化学後発医薬品申請者は、判断または決定のメカニズムを受け取ってから 10 営業日以内に関連文書を国内医薬品審査に提出するものとする。

技術審査に合格した化学後発医薬品登録申請については、国家医薬品審査機関は、人民法院の有効な判決または省議会の下での特許管理部門の行政決定と併せてこれに対処するものとする。

（1）当該特許権の保護範囲内にあることが確認された場合、当該化学後発医薬品の登録申請は、特許権期間満了前に行政審査及び承認リンクに転送される。

（2）当該特許権の保護の範囲外であることが確認された場合、または両当事者が和解に達した場合、当該化学後発医薬品登録申請書は、手順;

（3）関連する特許権が法律により無効である場合は、関連する化学後発医薬品登録申請書を、手順に従って行政審査および承認リンクに転送する。

（4）待機期間を超過した場合、国務院の薬物規制部門は、人民法院からの有効な判決または調停書、または省議会の特許管理部門の行政決定を受け取っておらず、関連する手順に従った行政審査および承認リンクへの化学後発医薬品登録申請;
（5）国家評議会の薬物規制部門が、行政審査および承認の期間中に人民法院の有効な判決または国家評議会の特許行政部門の行政決定を受け、それが範囲内にあることを確認した場合関連する特許権の保護については、本条第 2 段落の第 1 段落の規定に従い、関連する化学後発医薬品登録申請書を国の医薬品評価機関に提出するものとする。
国務省の医薬品規制部門が承認を一時停止する決定を下した後、人民法院が当初の行政判決を覆した場合、両当事者が和解した場合、関連する特許権が無効であると宣言された場合、または特許権者または利害関係者が訴訟または行政裁定の請求を取り下げた場合は、後発医薬品の申請を申請するものとする。省議会の医薬品規制部門に後発医薬品のリストの承認を申請することができ、省の医薬品規制部門に申請することができる。評議会は、承認するかどうかを決定する場合がある。

第 10 条
タイプ I およびタイプ II で宣言されたジェネリック化学薬品の登録申請については、国務院の医薬品規制部門は、技術審査の結論に従って販売を承認するかどうかを決定するものとする。上場を承認すると、対応する特許権と市場独占期間の満了後に、関連する医薬品を上場することができる。

第 11 条
特許に異議を申し立て、販売が承認された最初の化学後発医薬品には、市場独占期間が与えられる。国務省の医薬品規制部門は、特許の共同チャレンジが成功した場合を除き、医薬品の承認日から 12 か月以内に同じ種類の後発医薬品の販売を承認しない。市場独占権の期間は、異議申し立てを受けた医薬品の元の特許権の期間を超えない。市場独占期間中、国家医薬品評価機関は技術評価を停止しない。技術審査に合格した化学後発医薬品登録申請については、市場独占期間が満了する前に、関連する化学後発医薬品登録申請が行政承認リンクに転送される。
特許チャレンジの成功とは、化学後発医薬品の申請者がタイプ IV の宣言を提出し、特許権の無効化の要求に応じて、関連する特許権が無効であると宣言され、後発医薬品の販売が承認されることを意味する。

第 12 条
漢方薬および生物学的製剤の販売許可の保有者は、これらの措置の第 2 条、第 3 条、第 4 条、および第 7 条に従って関連する特許情報を登録するものとする。漢方薬は、漢方薬組成物の特許、漢方薬抽出物の特許、薬用の特許、有効成分の配列構造の特許、生物学的製剤の薬用の特許を登録することができる。
同じ名前、同じ処方箋、およびバイオシミラーの漢方薬の申請者は、これらの措置の第 6 条に従って関連する特許宣言を行うものとする。

第 13 条

同名、同式、バイオシミラーの漢方薬の登録申請については、国務省の医薬品規制部門が、技術審査の結論に基づいて販売を承認するかどうかを直接決定するものとする。人民法院または国務省の特許管理部門が、関連する技術的解決策が関連する特許権の保護の範囲内にあることを確認した場合、関連する医薬品は、対応する特許権の満了まで販売されない場合がある。

第 14 条
化学後発医薬品、同名・同処方の漢方薬、バイオシミラー医薬品の販売が承認された後、特許権者または利害関係者が、当該医薬品が対応する特許権を侵害し、紛争を引き起こすと信じる場合、特許法中華人民共和国の特許法およびその他の関連する法律および規制に従って解決するために使用されるものとする。法律に基づいて承認された医薬品の販売承認に関する決定は取り消されず、その有効性に影響はない。

第 15 条
虚偽の陳述およびその他の不正行為を提出する者は、保護の範囲が承認された医薬品とは関係がない、または中国上場医薬品特許情報登録プラットフォームに登録されるべき特許タイプに属さない特許を故意に登録する。特許権者の関連する特許権を侵害する関係者にその他の損失が生じた場合、当事者は法律に従って対応する責任を負うものとする。

第 16 条
これらの措置は、公布の日に発効するものとする。

③ 医薬品特許紛争の早期解決メカニズムの行政裁定規定[24]（仮訳）（2021 年 7 月 5 日）
第一条 これらの措置は、中華人民共和国特許法(以下、特許法という)及び関連法令及び規制に従って、医薬品上場審査及び承認の過程で特許紛争に関する行政判断(以下、医薬品特許紛争に関する行政判断という)の訴訟を法的に処理するために策定される。

第二条 国家知的財産局は、特許法第76条に基の行政裁定の処理を担当するものとする。国家知的財産局は、医薬品特許紛争の早期解決メカニズムに関する行政裁定委員会を設置し、医薬品特許紛争の早期解決メカニズムに関する行政裁定に関する作業を整理し、実施する。

第三条 事件処理員は、次の各号のいずれかに該当するときは、自ら避けるものとする。
(1) 当事者またはその代理人の近親者。
(2) 特許出願または特許権に利害関係を有すること。
(3) 当事者またはその代理人とのその他の関係が、公平なケースの処理に影響を与える可能性がある場合。

[24] 国家知识产权局 公告 国家知识产权局发布《药品专利纠纷早期解决机制行政裁决办法》的公告（第 435 号）（国家知识产权局ウェブサイト）
https://www.cnipa.gov.cn/art/2021/7/5/art_74_160566.html

当事者はまた、ケース処理担当者の回避を申請する権利があります。 当事者が回避を申請する場合、その理由を述べるものとする。
ケース担当者の回避は、ケース処理部門によって決定されます。

第四条 当事者が国家知的財産局に医薬品特許紛争に関する行政判断を求める場合、以下の条件を満たすものとする。
(1) 請求者は、特許法第76条に記載されている医薬品上場ライセンス申請者と、当該特許のライセンシーまたは登録医薬品上場ライセンス保有者を意味する利害関係者である。
(2) 明確な要求者を有すること。
(3) 明確な要求事項と具体的な事実と理由を有すること。
(4) 関連する特許情報は、中国上場医薬品特許情報登録プラットフォームに登録され、医薬品特許紛争の早期解決メカニズムの実施方法の関連規定に準拠しています。
(5) 人民裁判所は、以前に薬物特許紛争を提起しなかった。
(6) 医薬品上場許可の申請者が行政判断の申請をした場合、特許権者または利害関係者は、国家医薬品審査機関による医薬品上場許可の申請を公表した日から45日以内に、当該医薬品の特許紛争について人民裁判所に訴訟を起こしたり、行政裁定の要請を提起したりしない。
(7) 行政判断の要請は、上場許可を申請する医薬品技術スキームが特許権の保護範囲に収まるかどうかを確認することに限定されるものとする。

第五条 特許権者又は利害関係者が、上場許可の申請を求める医薬品関連技術プログラムが当該特許権の保護範囲に該当するときは、当該特許権の保護範囲に該当するときは、当該医薬品上場許可の申請者を被請求者とする。
特許権が複数の特許権者に帰属する場合、一部の共同特許権者は、当該団体の権利の放棄を明示的に表明する場合を除き、すべての特許権者によって請求されるものとする。
医薬品上場ライセンス保有者またはライセンス契約を独占的に実施しているライセンシーは、自分の名前で要求することができます。 独占的にライセンス契約を履行するライセンシーは、特許権者が要求しない限り、自分の名前で要求することができます。

第六条 医薬品上場許可の申請者は、上場許可の申請に係る医薬品関連技術スキームが当該特許権の保護範囲に該当しないことを確認するよう要求した場合、特許権者を請求者とする。

第七条 医薬品特許紛争に関する行政判断を国家知的財産局に求める場合、申請書及び以下の資料を提出しなければならない。
(1) 主体の資格証明書
(2) 中国上場医薬品特許情報登録プラットフォームによる関連特許の登録情報、国家医薬品審査機関情報プラットフォームが公表した医薬品上場許可申請、および関連する特許権の保護範囲に該当しない宣言および宣言の根拠。
(3) 請求者は、医薬品上場許可の申請者であり、また、登録を申請する医薬品関連技術プログラム

を提出し、機密情報を扱う技術スキームは、個別に提出し、宣言する必要があります。

第八条 要求には、以下の事項を記載しなければならない。
(1) 請求者の氏名、住所、法定代理人または主要責任者の氏名、連絡先電話番号、代理人に委託する者、代理人の氏名、代理人の名前、住所、連絡先電話番号。
(2) 請求者の氏名、住所、法定代理人の氏名、連絡先電話番号、その他の事項
(3) 特許番号、特許の種類、特許ステータス、特許権者、特許保護期間の満了日、および保護範囲に収まっているかどうかの認定を求める特定の請求を含む、中国上場医薬品特許情報登録プラットフォームに登録された関連特許情報。
(4) 国家医薬品審査機関情報プラットフォームが公表した登録医薬品の申請に関する情報と声明の種類。
(5) 登録を申請する医薬品技術スキームが関連する特許権の保護範囲に該当する理由。
(6) 証拠資料のリスト。
(7) 要求者または認可された代理人の署名(自然人)またはスタンプ(法人およびその他の組織)。 関連する証拠および証拠資料は、要求の附属書の形で提出することができます。

第九条 国家知的財産局は、要求及び関連資料を受領した後、登録を行い、要求書その他の資料を審査しなければならない。 要求および関連資料が不完全である場合、要求が所定の形式を使用していない場合、または要件を満たさない場合、要求者は5営業日以内に修正するよう通知しなければならない。 満了後に修正または修正後に同じ欠陥が残っている場合、行政判断の要求は受け付けられません。

第十条 医薬品特許紛争に関する行政判断の請求が、次の各号のいずれかに該当する場合、国家知的財産局は、請求者を受理し、通知しないものとする。
(1) 請求者の氏名、連絡先、その他の基本情報が不足しているか、特許情報が不足している場合。
(2) 要求者が不明確であること。
(3) 請求者及び請求者の主たる資格は、本措置の第4条、第5条及び第6条の関連規定に適合しない。
(4) 特許は、中国上場医薬品特許情報登録プラットフォームに登録された特許主題の種類に該当しないか、または第4種明細書の特許と矛盾する。
(5) 関連する特許に関する請求が国家知的財産局によって無効と宣言された場合。
(6) 請求に明示的に記載されていない特許請求、および行政判断の具体的な事項を要求すること。
(7) 請求者が行政裁定の根拠を指定しなかった場合、または提出された証拠と併せて行政判断の根拠を指定しなかった場合。
(8) 行政判断の要請は、上場許可を申請する1つ以上の医薬品技術プログラムまたは1つ以上の特許権に関するものである。
(9) 同じ医薬品特許紛争が人民裁判所によって提起された。

第十一条 当事者の要請が本措置の第4条の規定に合致する場合、国家知的財産局は、5営業日以内

に事件を提起し、請求者及び請求者に通知しなければならない。

第十二条 国家知的財産局は、当事者の申請に応じて、またはケース処理の必要性に応じて、関連する証拠を医薬品監督管理部門に検証することができる。

第十三条 国家知的財産局は、事件を審理するために合同会議グループを結成しなければならない。当事者の要請や事件の状況に応じて、合同チームは口頭または書面で審理することができる。
同じ当事者が、同じ医薬品に関連する複数の特許権について、多くの行政判断を求める場合、国家知的財産局は、合併して審理することができる。
国家知的財産局が口頭審理を行うことを決定した場合、口頭審理の少なくとも5営業日前までに、口頭審理の日時及び場所を当事者に通知しなければならない。 正当な理由なく参加を拒んだり、許可なく途中で撤退したりした場合、その要求は撤回とみなされます。 正当な理由なく参加を拒んだり、許可なく途中退場したりした場合、裁判を欠席する。

第十四条 医薬品特許紛争に関する行政裁定の手続において、特許に関する請求の一部が国家知的財産局によって無効と宣言された場合、行政判断は、有効な請求の維持に基づいて行われるものとする。 特許に関する請求が国家知的財産局によって完全に無効となった場合、行政判断の請求は却下される。

第十五条 国家知的財産局は、医薬品特許紛争に関する行政裁定のケースを処理する際に、当事者の希望に応じて調停を行うことができる。 調停の結果、当事者が合意に達した場合、国家知的財産局は、当事者の要請により調停書を作成することができる。 調停が成立しない場合、国家知的財産局は、適時に行政判断を下すものとする。

第十六条 当事者は、次の各号のいずれかに該当するときは、事件の処理の中止を申請することができ、国家知的財産局は、その権限に従って、その事件の処理を中断することを決定することができる。
(1) 当事者が死亡した場合、相続人が処理に参加するかどうかを示すのを待つ必要がある。
(2) 当事者が行政判断を求める能力を失った場合、法定代理人が決定されていない場合。
(3) 当事者である法人その他の団体が終了し、権利と義務の保有者が決定されていない場合。
(4) 当事者が不可抗力のために裁判に参加できない場合。
(5) その他、処理を中断する必要がある場合。
当事者が関連する特許の無効請求をした場合、国家知的財産局は、事件の処理を中断しないものとする

第十七条 国家知的財産局は、行政上の決定を下す前に、請求者がその要求を撤回することができる。 請求者が請求を撤回した場合、または請求が撤回されたとみなされる場合、医薬品特許紛争に関する行政判断手続きは終了します。

行政賞の結論が下された後、請求者が要求を撤回することは、行政賞の有効性に影響を与えない。

第十八条 国家知的財産局が行政判断を下した場合、上場医薬品技術プログラムの申請が関連する特許権の保護範囲に該当するか否かは、その根拠及び根拠を定めるものとする。
行政判断が下された後、当事者に送付し、国家医薬品監督管理部門にコピーし、政府情報公開規則及び関連規定に従って社会に公表しなければならない。 行政判断が公表されるときは、企業秘密に関する情報を削除するものとする。

第十九条 当事者は、国家知的財産局が下した医薬品特許紛争に関する行政判断に異議を申し立てた場合、法律に従って人民裁判所に訴訟を起こすことができる。

第二十条 当事者は、提供された証拠または証拠の真正性について責任を負うものとする。
当事者は、行政裁定手続において知られている企業秘密を秘密にしておく義務があり、その企業秘密を無断で開示、使用、または許可した場合、適切な法的責任を負うものとします。

第二十一条 医薬品特許紛争に関する行政判断のケース処理者及びその他の職員が、職権の乱用、職務の怠慢、私的詐欺、または業務の過程で知った企業秘密の漏洩は、犯罪に該当しない場合、法律に従って行政処分を受けるものとする。 犯罪が疑われる場合は、司法当局に付託する。

第二十二条 これらの措置が規定されていないときは、特許侵害紛争に関する国家知的財産局の行政措置及び行政判断の関連規定に従って実施されるものとする。

第二十三条 この措置は、国家知的財産局が解釈する責任を負うものとする。

第二十四条 この措置は、公布の日から施行する。

④ 登録申請医薬品に関連する特許紛争民事事件の審理における法律適用の若干問題に関する規定[25]（仮訳）

第一条 特許法第76条に基づく当事者による特許権の保護に関する紛争の確認に関する第一審の事件は、北京知的財産裁判所の管轄下に置かれるものとする。

第二条 特許法第76条に規定する関連特許とは、医薬品上場許可の審査及び承認及び医薬品上場許可の申請段階における特許権の紛争解決に関する国務院の関連管理部門による具体的な連絡方法(以下「連結措置」という。特許法第七十六条に規定する利害関係者とは、前項の特許のライセンシー及び関連医薬品の上場許可者をいう。

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[25] 最高人民法院关于审理申请注册的药品相关的专利权纠纷民事案件适用法律若干问题的规定（中華人民共和国最高人民法院ウェブサイト）
https://www.court.gov.cn/fabu-xiangqing-311791.html

第三条 特許権者又は利害関係者が特許法第七十六条に基づいて訴訟を起こした場合、民事訴訟法第百十九条第三項の規定により、次の資料を提出しなければならない。
(1) 国務院の関連行政部門が、特許名、特許番号、関連する特許請求の範囲など、接続方法に従って設置されたプラットフォームに登録された関連特許情報。
(2) 国務院の関連管理部門は、医薬品名、医薬品の種類、登録の種類、登録申請された医薬品と関連する上場医薬品との対応関係など、連結措置に基づいて設立されたプラットフォームに公表された登録医薬品の申請に関する情報を提供する。
(3) 医薬品上場許可申請者が、接続方法に従って行った4種類の声明および声明の根拠。医薬品上場許可の申請者は、第一審の回答期間内に、関連する特許権の保護範囲に該当するかどうかを判断するために必要な技術資料の写しを、国家医薬品審査機関に申告する。

第四条 特許権者又は利害関係者が、当該措置に定める期間内に人民裁判所に訴訟を起こさなかった場合、医薬品上場許可の申請者は、登録医薬品の申請が関連する特許権保護の範囲内に収まらなかったことを確認するため、人民裁判所に訴訟を起こすことができる。

第五条 当事者は、国務院の特許管理部門が特許法第76条に基づく行政裁定の要請を受理した理由として、特許法第76条に基づく訴訟を受理しない、または訴訟の停止を申請した場合、人民裁判所は支持しない。

第六条 当事者が特許法第76条に基づく訴訟を起こした後、人民裁判所は、国務院の特許管理部門が当該特許権の無効を宣言する申請を受理した理由として、訴訟の停止を申請した場合、通常、支持しない。

第七条 医薬品上場許可の申請者が、特許法第六十七条、第七十五条第二項等の規定の事情を主張する場合、人民裁判所は、審査の結果、登録を申請した医薬品関連技術プログラムが関連する特許権の保護範囲に該当していないことを確認することができると裁定することができる。

第八条 当事者は、訴訟で取得した企業秘密その他の機密保持を必要とするその他の商業情報を秘密にしておく義務を負い、その訴訟活動以外で無断で開示または使用または許可した場合、法律に従って民事責任を負うものとする。 民事訴訟法第111条に規定する状況を構成する場合、人民裁判所は、法律に従って処理しなければならない。

第九条 医薬品上場許可の申請者が人民裁判所に提出した登録申請に関する医薬品関連技術プログラムは、国家医薬品審査機関に申告した技術資料と著しく矛盾し、人民裁判所が事件を審理するのを妨げた場合、人民裁判所は、民事訴訟法第111条の規定に従って処理しなければならない。

第十条 特許権者又は利害関係者が、特許法第76条に規定する訴訟において行為の保全を申請し、特許権の有効期間中に特許法第11条に規定する行為を行う医薬品の上場許可を禁止するよう申請

者に求める場合、人民裁判所は、特許法及び民事訴訟法の関連規定に従って処理しなければならない。 人民裁判所は、医薬品の上場申請の禁止または審査・承認の申請を支持しない。

第十一条 人民裁判所は、特許権の侵害または特許権の侵害の確認に関する訴訟において、特許法第76条に基づく訴訟の効力発生判断により、関連する特許権の保護範囲に該当するか否かを認定する訴訟において、人民裁判所は、通常、その支援を行う。 ただし、侵害された医薬品技術スキームが登録を申請した医薬品関連技術プログラムと矛盾している、または新しい主張が成立したという証拠がある場合を除く。

第十二条 特許権者又は利害関係者は、特許権が無効と宣言されるか、または登録医薬品の申請に関する関連技術スキームが特許権の保護範囲に収まらず、特許法第76条に基定める訴訟を提起するか、または行政裁定を求める場合、医薬品上場許可の申請者は、北京知的財産裁判所に損害賠償の訴えをすることができる。

第十三条 人民裁判所は、法律に従い、国務院の関連行政部門が設置したプラットフォームに掲載された連絡先、住所、電子メール等への当事者への配達は、有効な配達とみなされるものとする。当事者が住所確認書を人民裁判所に提出した後、人民裁判所は、その確認書に記載されている配達住所に配達することができる。

第十四条 この規定は、2021 年 7 月 5 日から施行する。 裁判所が以前に発行した関連する司法解釈が本規定と矛盾する場合、この規定が優先される。

附属資料７：韓国関連条文

(i) 薬事法（仮訳）

第50条の2（医薬品に関する特許権の登載）

① 第 31 条第 2 項及び第 3 項に基づく品目許可又は同条第 9 項に基づく品目に関する変更許可（以下「品目許可又は変更許可」という）を受けた者は、食品医薬品安全処長が品目許可又は変更許可を受けた医薬品に関する特許権（以下「医薬品特許権」という）を登載・管理する医薬品特許目録(以下「特許目録」という)に医薬品特許権の登載を申請することができる。

② 第 1 項に基づき、特許目録に医薬品特許権の登載を申請しようとする者は、当該医薬品の品目許可若しくは変更許可を受けた日又は「特許法」第 87 条によって特許権の設定登録があった日から 30 日以内に次の各号の事項を記載した登載申請書に特許登載原簿の写し、「特許法」に基づく特許権者又は専用実施権者（以下「特許権者など」という）の同意書など、総理令で定める書類を添付して食品医薬品安全処長に提出しなければならない。

1. 医薬品の名称
2. 登載申請者の個人情報
3. 特許権者などの個人情報（国内に住所又は営業所を持たない場合、国内に住所又は営業所を持つ代理人の個人情報）
4. 特許番号
5. 特許権の存続期間満了日
6. 特許として保護を受けようとする事項（以下「特許請求項」という）
7. その他総理令で定める事項

③ 第 1 項に基づいて医薬品特許権の登載を申請した者は、申請に対する決定がある前に食品医薬品安全処長に第 2 項に基づく登載申請書の内容の変更を申請することができる。ただし、特許請求項を追加する場合には、第 2 項に基づく申請期間内に申請しなければならない。

④ 食品医薬品安全処長は、第 1 項に基づき登載を申請し、又は第 3 項に基づき登載申請書の内容の変更を申請した医薬品特許権が次の各号の対象及び要件をいずれも満たす場合には、医薬品の名称、特許権者などの個人情報、特許番号、特許存続期間など、総理令で定める事項を特許目録に登載し、これをインターネットのホームページに公開しなければならない。

1. 次の各目のいずれかに関するものであること
   イ．物質
   ロ．剤形
   ハ．組成物
   ニ．医薬的用途
2. 当該医薬品の品目許可又は変更許可を受けた事項と直接関連すること
3. 当該医薬品の品目許可日又は変更許可日以前に「特許法」第 42 条に基づいて出願されていること
4. 医薬品特許権が存続期間満了、無効、放棄などにより消滅していないこと
5. 当該医薬品の品目許可又は変更許可が有効であること

⑤ 食品医薬品安全処長は、第 4 項各号の対象及び要件を満たしているかを検討するために必要な場合、医薬品特許権の登載を申請した者に追加の資料の提出を命ずることができる。

第50条の3（登載事項の変更など）

① 第 50 条の 2 第 1 項に基づき、医薬品特許権の登載を申請して特許目録に医薬品特許権を登載した者（以下「特許権登載者」という）は、第 50 条の 2 第 4 項に基づき、特許目録に登載された事項（以下この条で「登載事項」という）の変更又は削除を食品医薬品安全処長に申請することができる。

② 登載事項のうち、特許目録に登載された特許権（以下「登載特許権」という）の存続期間満了日の変更は、その変更があった日から 30 日以内に申請しなければならない。ただし、食品医薬品安全処長は、特許権登載者の申請によって追加で 30 日以内の変更期間を付与することができる。

③ 食品医薬品安全処長は、第 1 項に基づく申請内容を確認した後、申請内容が適していると認められれば、登載事項を変更又は削除することができる。この場合、食品医薬品安全処長は、事前に特許目録に医薬品特許権が登載された医薬品（以下「登載医薬品」という）の特許権者など（以下「登載特許権者など」という）と登載医薬品の安全性・有効性に関する資料を根拠に医薬品の品目許可又は変更許可を申請した者など利害関係人の意見を聞かなければならない。

④ 食品医薬品安全処長は、次の各号のいずれかに該当する場合には、職権により登載事項を変更又は削除することができる。この場合、食品医薬品安全処長は、事前に特許権登載者の意見を聞かなければならない。

1. 特許権者などが同意を撤回した場合
2. 第 50 条の 2 第 4 項の対象及び要件が満たせなくなった場合
3. 偽りやその他不正な方法により医薬品特許権が登載された場合

⑤ 食品医薬品安全処長は、第3項及び第4項に基づいて登載事項を変更し、又は削除する場合、これをインターネットのホームページに公開しなければならない。

⑥ 第1項に基づく登載事項の変更・削除の申請の手続き、方法などに関して必要な事項は、総理令で定める。

第50条の4（品目許可などの申請事実の通知）

① 登載医薬品の安全性・有効性に関する資料を根拠に、第31条第2項又は第3項に基づいて医薬品の品目許可を申請し、又は同条第9項に基づいて効能・効果に関する変更許可を申請した者は、許可を申請した事実、許可申請日など、総理令で定める事項を特許権登載者と登載特許権者などに通知しなければならない。ただし、次の各号のいずれかに該当する場合には、この限りでない。

1. 登載特許権の存続期間が満了した場合
2. 登載特許権の存続期間が満了した後に医薬品を販売するために、品目許可又は変更許可を申請した場合
3. 特許権登載者と登載特許権者などが通知しないことに同意した場合
4. 第1号から第3号までの規定に準ずるもので、大統領令で定める場合

② 第1項のただし書きにもかかわらず、第1項第2号から第4号までの規定に基づく事由が消滅した

場合には、第1項の本文による通知をしなければならない。
③ 第1項又は第2項による通知は、特許目録に記載された特許権者など又はその代理人の国内の住所に到達すれば、行われたものとみなす。
④ 第1項又は第2項による通知は、品目許可又は変更許可の申請日から20日以内にしなければならない。その期限内に通知をしなかった場合には、品目許可又は変更許可を申請した者が特許権登載者又は登載特許権者などに通知した日のいずれか遅い日を品目許可又は変更許可の申請日とみなす。
⑤ 第1項又は第2項に基づき通知をした者はその通知した事実を証明することができる書類を遅滞なく食品医薬品安全処長に提出しなければならない。この場合、食品医薬品安全処長は通知された医薬品(以下「通知医薬品」という)の許可申請日、主成分、剤形など、総理令で定める事項をインターネットのホームページに公開しなければならない。
⑥ 食品医薬品安全処長は、第1項又は第2項による通知がされていない場合、当該品目許可又は変更許可をしてはならない。
⑦ 第1項による通知の方法、手続きなどについて必要な事項は、総理令で定める。

第50条の5（販売禁止の申請）
① 登載特許権者などは、第50条の4による通知を受けた日から45日以内に食品医薬品安全処長に次の各号の事項が記載された陳述書を添付して通知医薬品の販売禁止を申請することができる。
1. 販売禁止申請は正当に登載された特許権に基づいて行われていること
2. 第2項に基づく審判又は訴訟を善意により請求又は提起し、勝訴の見込みがあり、審判又は訴訟の手続きを不合理に遅延しないこと
② 登載特許権者などは、販売禁止を申請する前に通知医薬品を対象に登載特許権に関する次の各号のいずれかに該当する訴を提起し、又は審判を請求し、若しくは受けなければならない。
1.「特許法」第126条に基づく特許侵害の禁止又は予防請求の訴
2.「特許法」第135条に基づく権利範囲確認審判
③ 第1項にもかかわらず、既に第50条の6第1項に基づき、販売禁止をした医薬品については、追加的に販売禁止を申請することができない。ただし、第31条第9項による効能・効果に関する変更許可申請による通知医薬品に対しては、この限りではない。
④ 食品医薬品安全処長は、第1項による販売禁止の申請期間が経過するまで通知医薬品に対する品目許可又は変更許可をしてはならない。ただし、次の各号のいずれかに該当する場合には、この限りでない。
1. 販売禁止が申請された医薬品が登載特許権の権利範囲に属しないという旨の「特許法」第162条に基づく審決又は同法第189条に基づく判決があった場合
2. 登載特許権が無効という旨の「特許法」第162条に基づく審決又は同法第189条による判決があった場合
3. 医薬品特許権の登載が違法という旨の「行政審判法」第43条に基づく裁決又は「行政訴訟法」第3条によって提起された訴に対する法院の判決があった場合

⑤ 食品医薬品安全処長は、第 4 項各号の審決、裁決又は判決後、それに反する旨の審決又は判決がある場合、第 4 項のただし書きにもかかわらず通知医薬品に対する品目許可又は変更許可をしてはならない。
⑥ 販売禁止の申請方法及び手続きなどについて必要な事項は、総理令で定める。

第50条の6（販売禁止など）
① 第50条の5第1項に基づいて販売禁止申請を受けた食品医薬品安全処長は、販売禁止が申請された医薬品に対する品目許可又は変更許可をする際、次の各号のいずれかに該当する場合を除いては、第50条の4によって登載特許権者などが通知を受けた日(以下「通知を受けた日」という)から9カ月間販売を禁止しなければならない。
1. 第50条の5第1項による申請期間を遵守しない場合
2. 存続期間満了、放棄などにより消滅した特許権を基礎にした場合
3. 第50条の5第2項各号の訴訟を提起し、又は審判を請求し、若しくは受けずに申請した場合
4. 偽りやその他不正な方法により医薬品特許権が登載された場合
5. 第50条の4によって通知された医薬品が2つ以上で、通知された医薬品と次の各目の事項が同一である場合(以下「同一医薬品」という)であって、その同一医薬品の一部に対してのみ販売禁止申請をした場合
    イ．主成分及びその含量
    ロ．剤形
    ハ．用法・用量
    ニ．効能・効果
6. 販売禁止が申請された医薬品と同一医薬品で、既に登載医薬品の安全性・有効性に関する資料を根拠に品目許可又は変更許可を受け、販売が可能な医薬品が存在する場合
7. 第50条の5第4項各号のいずれかに該当する審決、裁決又は判決があった場合
8. 登載特許権が「特許法」第106条第1項、第106条の2第1項に該当し、又は同法第107条による裁定の対象となった場合と
② 食品医薬品安全処長は、通知医薬品に対する品目許可又は変更許可をする前に第 1 項第 7 号の審決、裁決又は判決について、これを取り消し、又は破棄する旨の審決又は判決（「特許法」第 178 条による再審の審決を含む）がある場合、第 1 項にもかかわらず、通知を受けた日から 9 カ月間販売を禁止しなければならない。
③ 第 1 項に基づく販売禁止の効力は、次に掲げる各号の日のいずれか早い日に消滅する。
1. 販売禁止が申請された医薬品が登載特許権の権利範囲に属しないという旨の審決日又は判決日
2. 販売禁止が申請された医薬品が登載特許権を侵害しないという旨の判決日
3. 登載特許権が無効という旨の審決日又は判決日
4. 医薬品特許権の登載が違法であるという旨の裁決日又は判決日
5. 第50条の5第2項各号のいずれかの審判又は訴訟が特許権者などの取下げ、取下げの同意、和解又は却下などにより終了した日
6. 第50条の5第2項各号のいずれかの審判又は訴訟と関連して仲裁又は調停が成立した日

7. 登載医薬品の品目許可又は変更許可の消滅日
8. 登載特許権の存続期間満了日
9. 登載特許権者などが販売禁止又は第50条の7に基づく優先販売品目許可と関連して「独占規制及び公正取引に関する法律」第3条の2第1項、第19条第1項又は第23条第1項に違反したという公正取引委員会の議決又は法院の判決があった日
10. 偽りや不正な方法により販売禁止を申請したと判明された日

④ 第1項から第3項までの規定による販売禁止又は消滅の手続きなどに関して必要な事項は、総理令で定める。

第50条の7(優先販売品目許可の申請)

① 50条の4に基づき通知をしなければならない者は、医薬品の品目許可又は変更許可を申請するとき、次の各号の要件をすべて満たした医薬品より優先して医薬品を販売することができる許可（以下、「優先販売品目許可」という）を食品医薬品安全処長に申請することができる。
1. 優先販売品目許可を申請する医薬品と同一医薬品であること
2. 登載医薬品の安全性・有効性に関する資料を根拠に品目許可又は変更許可を申請する医薬品のうち、登載医薬品と有効成分が同一の医薬品であること

② 優先販売品目許可を受けようとする者は、第1項に基づく申請をする前に、次の各号のいずれかに該当する審判を請求しなければならない。
1. 「特許法」第133条に基づく特許の無効審判
2. 「特許法」第134条に基づく特許権存続期間延長登録の無効審判
3. 「特許法」第135条に基づく権利範囲確認審判

③ 第 2 項各号の審判を請求する者は、遅滞なく特許審判番号など総理令で定める事項を食品医薬品安全処長に通知しなければならない。食品医薬品安全処長は通知を受けた事項をインターネットのホームページに公開することができる。

④ 優先販売品目許可を受けようとする者は、次の各号の事項を記載した優先販売品目許可申請書に第 2 項各号の審判請求書など、総理令で定める書類を添付して食品医薬品安全処長に提出しなければならない。
1. 申請者の個人情報
2. 特許番号
3. 特許審判番号
4. 審判請求日
5. その他総理令で定める事項

第50条の8（優先販売品目許可）

① 第50条の7に基づいて優先販売品目許可の申請を受けた食品医薬品安全処長は、申請者が次の各号の要件をすべて満たす場合、医薬品の品目許可又は変更許可と同時に優先販売品目許可をしなければならない。
1. 第50条の4に基づいて通知しなければならない医薬品の品目許可又は変更許可を申請した者の

中で、最も早い日に品目許可又は変更許可を申請した者であること（同日に申請した者が多数である場合はすべて同じ順位とみなす）。

2. 第50条の7第2項に基づいて審判を請求した者の中で、登載特許権について特許の無効、存続期間延長登録の無効又は当該医薬品が特許権利範囲に属しないという旨の審決又は審決を受けた者であること。ただし、通知を受けた日から9カ月が経過した日以降に審決又は判決を受けた者は除外する。

3. 第2号に基づく審決又は判決を受けた者の中で、次の各目の要件のいずれかに該当する者であること。

イ．最初に第50条7第2項各号の審判（以下、この号では「最初の審判」という）を請求した者であること

ロ．最初の審判が請求された日から14日以内に審判を請求した者であること

ハ．イ目又はロ目の要件に該当する者より先に第2号に基づく審決又は判決を受けた者であること

② 食品医薬品安全処長は、第 1 項に基づいて優先販売品目許可をする場合、優先販売品目許可医薬品の主成分、剤形、許可日など総理令で定める事項をインターネットのホームページに公開しなければならない。

第50条の9（同一医薬品などに対する販売禁止など）

① 食品医薬品安全処長は第50条の8第1項に基づいて優先販売品目許可をした場合、次の各号の要件をいずれも満たした医薬品に対する品目許可又は変更許可をする際に、第2項に基づく期間の間に販売を禁止することができる。

1. 優先販売品目許可を受けた医薬品と同一医薬品であること

2. 登載医薬品の安全性・有効性に関する資料を根拠に品目許可又は変更許可を申請した医薬品の中で、登載医薬品と有効成分が同一の医薬品であること

② 第1項に基づく販売禁止期間は、最初に優先販売品目許可を受けた者の販売可能日から9カ月が経過した日までとする。ただし、当該医薬品が「国民健康保険法」第41条第1項第2号に基づき療養手当を申請した薬剤である場合、2カ月の範囲内で延長することができる。

③ 第 1 項及び第 2 項に基づく販売禁止の方法及び手続きなどについて必要な事項は、総理令で定める。

第50条の10（同一医薬品などに対する販売禁止効力の消滅など）

① 第50条の9第1項に基づく販売禁止の効力は、次の各号のいずれか早い日に消滅される。

1. 優先販売品目許可を受けた医薬品の品目許可又は変更許可が消滅した日

2. 登載特許権が存続期間満了、無効であるという旨の審決又は判決の確定（優先販売品目許可を受けた者が請求又は提起した審判又は訴訟によるものは除外する）などにより消滅した日

② 食品医薬品安全処長は、次の各号のいずれかに該当する場合、第50条の9第1項に基づく販売禁止の効力を消滅させなければならない。この場合、食品医薬品安全処長は既に優先販売品目許可を受けた者の意見を聞かなければならない。

1. 第50条の8第1項第2号の審決又は判決に対し、これを取り消し、又は破棄する趣旨の判決(「特許法」第178条に基づく再審の審決を含む)がある場合
2. 優先販売品目許可医薬品を販売可能日から2カ月以内に正当な事由なしに販売していない場合
3. 優先販売品目許可を受けた者が販売禁止又は優先販売品目許可と関連し、「独占規制及び公正取引に関する法律」第3条の2第1項、第19条第1項又は第23条第1項を違反したという公正取引委員会の議決又は法院の判決がある場合
4. 偽りやその他の不正な方法により優先販売品目許可を受けた場合

③ 優先販売品目許可を受けた医薬品と同一医薬品の品目許可又は変更許可を申請した者などの利害関係者は、優先販売品目許可が第1項又は第2項各号のいずれかに該当するという旨の情報を食品医薬品安全処長に提供することができる。

④ 第 1 項から第 3 項までの規定に基づく販売禁止効力の消滅及び利害関係者の情報提供の方法、手続きなどについて必要な事項は総理令で定める。

第50条の11（影響評価）

① 食品医薬品安全処長は、第50条の6に基づく販売禁止及び優先販売品目許可など、この章において規定された事項が国内の製薬産業、保健政策、雇用増減などに及ぼす影響を分析・評価しなければならない。

② 食品医薬品安全処長は、第1項の影響評価のために必要と認めるときには、関係行政機関、教育・研究機関などに必要な資料を要請することができる。この場合、資料の要請を受けた関係行政機関の長、教育・研究機関の長などは、正当な事由がなければこれに従わなければならない。

③ 第1項に基づく影響評価を行うときには、海外事例を分析しなければならない。

④ 食品医薬品安全処長は、第1項に基づく影響評価の結果を公開し国会に報告しなければならない。

⑤ 第 1 項から第 4 項までに基づく影響評価の基準、方法、手続きなどに関し、必要な事項は総理令で定める。

第50条の12（登載医薬品の管理など）

① 食品医薬品安全処長は医薬品特許権と関連し、次の各号の事業を遂行する。
1. 登載医薬品の市場動向及び価格情報の収集
2. 中小企業の特許目録登載、優先販売品目許可などと関連した業務支援
3. 医薬品特許権と関連して製薬会社の能力強化に向けた教育
4. 登載医薬品と関連した特許情報の分析及び提供
5. この章に規定された事項と関連した海外事例及び政策の研究、統計の算出及び分析
6. その他に食品医薬品安全処長が必要と認める事項

② 食品医薬品安全処長は、第1項の事業遂行を他の機関に委託することができる。

③ 食品医薬品安全処長は、第1項の事業遂行のために必要と認める場合には、次の各号の機関に医薬品特許権などに関する資料の提供を要請することができ、要請を受けた機関は正当な事由がなければこれに従わなければならない。
1. 国家又は地方自治団体

2. 公共機関又は公共団体

第62条の2（医薬品に関する特許権の登載など）
① 法第50条の2第1項に基づいて特許目録に医薬品特許権の登載を申請しようとする者は、別紙第59号の2書式の医薬品特許目録登載申請書に第2項各号の書類（電子文書の申請書及び文書を含む）を添付し、食品医薬品安全処長に提出しなければならない。この場合、「電子政府法」第36条第1項による行政情報の共同利用を通じて第2項各号の書類が確認できるときは、その確認をもって添付資料を代えることができる。
② 法第50条の2法第50条の2第2項各号以外の部分において「総理令で定める書類」とは、次の各号の書類（電子文書を含む）をいう。
1. 特許登録原簿の写し
2. 登録広告用の特許公報の写し
3. 「特許法」に基づく特許権者又は専用実施権者（以下「特許権者など」という）の同意書
4. 特許権者などが代理人を選任する場合、その委任状
③ 法第50条の2第2項第7号の「総理令で定める事項」とは、法第50条の2第4項第2号の事項に関する詳細をいう。
④ 法第50条の2第3項に基づいて登載申請書の内容の変更を申請しようとする者は、別紙第59号の3書式の医薬品特許目録登載申請変更申請書（電子文書の申請書を含む）に変更事項が証明できる書類（電子文書を含む）を添付し、食品医薬品安全処長に提出しなければならない。
⑤ 法第50条の2第4項各号以外の部分の「総理令で定める事項」とは、次の各号の事項をいう。
1. 医薬品の名称
2. 特許目録に医薬品特許権を登載した者(以下「特許権登載者」という)の個人情報
3. 特許権者などの個人情報
4. 代理人の個人情報
5. 特許番号
6. 特許権の設定登録日及び存続期間満了日
7. 特許として保護を受けようとする事項（以下「特許請求項」という）

第62条の3（登載事項の変更など）
① 法第 50 条の 3 第 1 項に基づき、特許目録に登載された事項の変更又は削除を申請しようとする者は、別紙第 59 号の 4 書式の医薬品特許目録登載事項変更申請書（電子文書の申請書を含む）に変更事項が証明できる書類（電子文書を含む）を添付し、食品医薬品安全処長に提出しなければならない。
② 法第 50 条の 3 第 2 項ただし書きによる追加変更期間の付与を申請しようとする者は、その旨及び事由を記載した書類を食品医薬品安全処長に提出しなければならない。
③ 第 2 項により追加で付与された変更期間に特許目録に登載された事項の変更を申請しようとする者は、食品医薬品安全処長が定めて告示する手数料を払わなければならない。

第62条の4（品目許可など申請事実の通知）

① 法第 50 条の 4 に基づき登載医薬品の安全性・有効性に関する資料を根拠に法第 31 条第 2 項又は第 3 項による医薬品の品目許可を申請する、又は同条第 9 項による効能・効果に関する変更許可を申請した者は、次の各号の事項を記載した別紙第 59 号の 5 書式の品目許可申請事実通知書を特許権登載者と登載医薬品の特許権者など(以下「登載特許権者など」という)に通知しなければならない。

1. 品目許可又は変更許可の申請日
2. 特許目録に登載された特許権(以下「登載特許権」という)の存続期間満了前に医薬品を商業的に製造・輸入して販売する目的で登載医薬品の安全性・有効性に関する資料に基づいて品目許可又は変更許可を申請した事実
3. 登載特許権が無効である、又は品目許可若しくは変更許可を申請した医薬品が登載特許権を侵害しないという判断の根拠

② 法第 50 条の 4 第 5 項の後段において「総理令で定める事項」とは、次の各号の事項を言う。

1. 許可申請日
2. 主成分及びその含量
3. 剤形
4. 用法・容量
5. 効能・効果

第62条の5（販売禁止の申請）

① 法第50条の5第1項に基づき、販売禁止を申請しようとする者は、別紙第59号の6書式の販売禁止申請書（電子文書の申請書を含む）に法第50条の5第1項による陳述書と次の各号の事項が証明できる書類（電子文書を含む）を添付し、食品医薬品安全処長に提出しなければならない。

1. 法第50条の4による通知を受けた日
2. 法第50条の5第2項各号の訴を提起する、又は審判を請求し、若しくは受けた事
3. 法第50条の5第2項各号の訴又は審判に対する判決若しくは審決がある場合、その事実

第62条の6(販売禁止など)

① 食品医薬品安全処長は、法第50条5第1項に基づき、販売禁止の申請があった医薬品が販売禁止要件を満たす場合には、登載特許権者などと通知医薬品の品目許可又は変更許可を申請した者に販売禁止となった医薬品の名称及び販売禁止期間を知らせなければならない。

② 登載特許権者など又は販売禁止となった医薬品の品目許可又は変更許可を申請した者は、法第50条の6第3項第1号から第6号まで、第9号又は第10号の事由がある場合、これを遅滞なく食品医薬品安全処長に知らせなければならない。

③ 食品医薬品安全処長は、法第 50 条の 6 第 3 項各号の事由がある場合、販売禁止の効力が消滅されることを登載特許権者などと販売禁止となった医薬品の品目許可又は変更許可を申請した者に知らせなければならない。

第62条の7(優先販売品目許可の申請)

① 法第50条の7第1項に基づき優先販売品目許可を申請しようとする者は、別紙第59号の7書式の優先販売品目許可申請書(電子文書の申請書を含む)を食品医薬品安全処長に提出しなければならない。

② 法第 50 条の 7 第 3 項の前段において「総理令で定める事項」とは、次の各号をいう。

1. 特許番号
2. 特許審判番号
3. 審判請求日

③ 法第50条の7第4項各号以外の部分において「総理令で定める書類」とは、次の各号の書類(電子文書を含む)をいう。

1. 法第50条の7第2項各号の審判請求書に請求の趣旨及びその理由を記載したもの
2. 法第50条の7第2項各号の審判結果に不服する場合、請求の趣旨及び原因を記載した訴状
3. 法第50条の8第1項第2号の審決又は判決を受けた場合、これを証明できる書類
4. 品目許可申請医薬品が医薬品の同等性に対する立証が必要な医薬品の場合、同等性立証試験結果
5. 品目許可申請医薬品が第9条第6号の臨床試験成績に関する資料提出の医薬品である場合、臨床試験成績の結果

④ 法第 50 条の 7 第 4 項第 5 号において「総理令で定める事項」とは、次の各号の事項をいう。

1. 優先販売品目許可申請の医薬品に関する情報
2. 登載医薬品に関する情報

第62条の9(優先販売品目許可の申請)

① 食品医薬品安全処長は、法第50条の9第1項に基づく販売禁止期間について、優先販売品目許可を受けた医薬品と同一医薬品に対する品目許可又は変更許可を申請した者に通知しなければならない。

② 法第50条の9第2項及び法50条の10第2項第2号に基づく販売可能日は、次の各号の日のうちの遅い日とする。

1. 優先販売品目許可を受けた日
2. 法第50条の4第1項第2号に基づく登載特許権の存続期間満了日の翌日

③ 優先販売品目許可を受けた者は、当該医薬品に対し「国民健康保健法」第 41 条第 1 項第 2 号に基づいて療養手当を申請した場合、これを遅滞なく食品医薬品安全処長に通知しなければならない。

第62条の10（同一医薬品などに対する販売禁止効力の消滅など）

① 優先販売品目許可を受けた者は、法第 50 条の 10 第 1 項第 2 号又は第 2 項各号の事由がある場合、これを遅滞なく食品医薬品安全処長に通知しなければならない。

② 食品医薬品安全処長は、法第50条の10第1項に基づき販売禁止の効力が消滅された場合、又は同条第2項に基づき販売禁止の効力を消滅させる場合、優先販売品目許可を受けた者と、それにより販売禁止となった医薬品の品目許可又は変更許可を受けた者に販売禁止の効力が消滅された事実及び消滅した日を通知しなければならない。

第69条の2（関係機関への通知）
食品医薬品安全処長は大統領令で定める関係中央行政機関の長に、次の各号に関する事項を通知しなければならない。
1. 第50条の6第1項及び第2項に基づく医薬品の販売禁止処分及び同条第3項に基づく販売禁止効力の消滅
2. 優先販売品目許可及び第50条の10第1項及び第2項に基づく同一医薬品に対する販売禁止効力の消滅
3. 第 1 号又は第 2 号と関連した特許審判又は訴訟の開始及び終結

第69条の3（合意事項の報告）
次の各号のいずれかに該当する合意がある場合、合意の当事者は合意があった日から15日以内に合意当事者、合意内容、合意時期など、総理令で定める事項を食品医薬品安全処長及び公正取引委員会に報告しなければならない。
1. 登載医薬品の品目許可又は変更許可を受けた者若しくは登載特許権者などと通知医薬品に対する品目許可又は変更許可申請をした者との間で行った当該医薬品の製造又は販売に関する合意
2. 登載医薬品の品目許可又は変更許可を受けた者若しくは登載特許権者などと通知医薬品に対する品目許可又は変更許可申請をした者との間で行った優先販売品目許可の取得若しくはその消滅に関する合意
3. 通知医薬品に対する品目許可又は変更許可申請をした者の間で行った優先販売品目許可の取得又はその消滅に関する合意

第76条（許可の取消しと業務停止など）
① 医薬品などの製造業者、品目許可を受けた者、原料医薬品の登録をした者、輸入者、臨床試験又は生物学的な同等性試験の計画承認を受けた者又は薬局開設者や医薬品販売業者が、次の各号のいずれかに該当すれば、医薬品などの製造業者、品目許可を受けた者、原料医薬品の登録をした者、輸入者、臨床試験又は生物学的な同等性試験の計画承認を受けた者には、食品医薬品安全処長が、薬局開設者や医薬品販売業者には市長・郡守・区庁長がその許可・承認・登録の取消し又は委託製造販売業社・製造所の閉鎖（第 31 条第 4 項に基づき申告した場合のみ該当する。以下、第 77 条第 1 号と同じである）、品目製造禁止や品目輸入禁止を命じ、又は 1 年の範囲内で業務の全部若しくは一部の停止を命ずることができる（中略）。
5 の 3. 第 50 条の 4 第 1 項第 2 号を違反し、登載特許権の存続期間が満了した後に販売するために品目許可又は変更許可を申請した者が、当該期間が満了する前に医薬品を販売した場合
5 の 4. 第 50 条の 6 第 1 項・第 2 項又は第 50 条の 9 第 1 項に基づいて販売が禁止された医薬品を販売した場合（後略）

第82条（手数料）
（中略）
② 食品医薬品安全処の所管業務と関連し、次の各号に該当する者は、総理令で手数料を支払わな

ければならない。許可・更新・登録・申告・承認又はその他の総理令で定める事項を変更する場合にも同様である。
（中略）
2の2. 第50条の2、第50条の3、第50条の5 又は第50条の7に基づく医薬品特許権の登載、登載事項の変更、販売禁止又は優先販売品目許可を申請しようとする者
2の3. 第50条の3第2項ただし書きに基づく追加期間に登載事項の変更申請をしようとする者
3. その他の総理令で定める事項を要請する者

第82条の2（登載料）
① 特許権登載者は、総理令で定めるところにより医薬品特許権が登載された日を基準に毎年1年分の登載料を納付しなければならない。
② 食品医薬品安全処長は第1項に基づく登載料が納付されない場合、当該医薬品特許権を特許目録から削除しなければならない。
③ 第 1 項に基づく登載料の金額、納付方法及び納付期間などに必要な事項は総理令で定める。

第95条（罰則）
① 次の各号のいずれかに該当する者は1年以下の懲役又は1千万ウォン以下の罰金に処する（中略）。
9の2. 偽りやその他の不正な方法により第50条の2第4項に基づく登載を受けた者
9の3. 偽りやその他の不正な方法により第50条の5に基づく販売禁止の申請又は優先販売品目許可の申請をした者
（中略）
10の2. 偽りやその他の不正な方法により第69条の3に基づく合意事項を報告した者
（中略）
② 第 1 項の懲役と罰金は併科することができる。

第97条の2（過料）
① 正当な事由なしに第69条の3に基づく合意事項を報告しなかった者に対しては5千万ウォン以下の過料を賦課する。
② 第 1 項に基づく過料は、大統領令で定めるところにより食品医薬品安全処長が賦課・徴収する。

(ii) 薬事法施行令（仮訳）

第32条の5（品目許可など申請事実通知の例外事由）
法第 50 条の 4 第 1 項第 4 号（法第 42 条第 4 項で準用する場合を含む）で「大統領令で定める場合」とは、法第 50 条の 2 第 4 項第 1 号ニ目に基づく医薬的用途に関する登載特許権が法第 31 条第 2 項・第 3 項・第 9 項又は法第 42 条第 1 項に基づき製造販売又は輸入の品目許可又は変更許可を申請した医薬品の効能・効果に関するものでない場合をいう。

附属資料８：台湾関連条文

① 薬事法[26]（仮訳）

第 40 条の 2

中央衛生主務官庁は、新薬許可証を発行する際に、申請者より添付された公開済み発明の特許番号または出願番号を公開しなければならない。

新成分新薬許可証の発行日から 3 年以内に、他の薬商は、許可証所有者の同意なしに、その申請資料を引用し、承認審査を申請することができない。

前項期間満了日の翌日から、他の薬商はこの法律および関連法律に基づいて承認審査を申請することができる。規定に適合する場合、中央衛生主務官庁は、前項の新成分新薬許可証の発行日から 5 年後の翌日から、薬品許可証を発行することができる。

新成分新薬について、外国において販売承認を得てから 3 年以内に、中央衛生主務間著。宇に承認審査を申請する場合に限り、第 2 項の規定を適用することができる。

第 40 条の 3

中央衛生主務官庁により適応症の追加または変更が認められた薬品について、その適応症が追加または変更された日から 2 年以内に、他の薬商は、その申請資料を引用し、販売承認を申請することができない。

前項期間が満了した翌日から、他の薬商はこの法律および関連法律に基づいて販売承認を申請することができる。規定に適合する場合、中央衛生主務官庁は、前項の新規または変更された適応症の許可日の翌日から、許可証を発行することができる。ただし、前項における新規または変更された適応症の薬品許可証所有者が、当該新規または変更適応症について、国内において臨床試験を実施したことがある場合、中央衛生主務官庁は、その新規または変更された適応症の許可日から 5 年の翌日から、他の薬商に販売承認を発行することができる。

新規または変更適応症薬品が海外で販売承認審査を取得してから 2 年以内に、中央衛生主務官庁に販売承認審査を申請する場合に限り、第 1 項の規定を適用することができる。

第 48 条の 3

新薬許可証の所有者は、医薬に関わる特許情報を申告する必要があると認めた場合、その薬品許可証の取得日かの翌日から 45 日以内に、関連文書および資料を中央衛生主務官庁に申告すべきである。その期間を経て申告した場合は、この賞の規定を適用しない。

前項における医薬品特許は、以下の発明に限定されている。

1. 物質。
2. 組成物または製剤。
3. 医薬用途。

[26] 台湾薬事法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=L0030001

第 48 条の 4

前項における特許情報の内容は下記のとおりである。

1. 特許登録証書番号、特許の種類は医薬用途である場合、その請求項の番号も併せて説明しなければならない。
2. 特許権利満了日。
3. 特許権者の名前、国籍、住所、居場所または営業所について、代表者がいる場合は、その氏名。その特許に専用実施権許諾があり、かつ特許法に従い登録された場合は、被許諾者に関する前期資料。
4. 前号における特許権者または専用実施権被許諾者について、中華民国において住所、居場所及び営業所がない場合は、代理人を指定し、かつその代理人を指定し、かつその代理人の名前、住所、居場所またはその営業所を届けなければならない。

新薬許可証の所有者が特許権者と異なった場合、特許情報を申告する際に、特許権者の同意を得なければならない。特許権に専用実施権許諾があり、かつそれが特許法にしたがって登録された場合は、専用実施権被許諾者のみの同意を取得すればよい。

第 48 条の 5

新薬許可証の所有者が、中央衛生主務官庁より新薬許可証が発行されてから、特許主務官庁により審査されかつ公告された特許を取得する場合、それが第 48 条の 3 第 2 項に開示された特許権の種類に属したものである場合は、当該決定が公告された翌日から 45 日以内に、前条の規定に従って特許情報を届け出なければならない。期限を過ぎて届出を行う場合は、この章の規定を適用しない。

第 48 条の 6

新薬許可証の所有者は、次の何れかの状況が発生した日の翌日から 45 日以内に、当該掲載特許情報の変更または削除を行うものとする。

1. 特許権期間延長の申請が特許主務官庁により承認されかつ公告された場合。
2. 請求項更正の申請が特許主務官庁により承認されかつ公告された場合。
3. 特許権の取り消しが確定された場合。
4. 特許権が当然消滅した場合。
5. 第 48 条の 4 第 1 項第 3 号、第 4 号に定められた特許情報が変更された場合。

新薬薬品許可証所有者が特許権者または専用実施権被許諾者と異なった場合、前項に定められた事項を行う前に、第 48 条の第 2 項の規定に準用する。

第 48 条の 7

以下の状況の何れかに該当した場合、何人も書面にて理由を述べ、証拠を添付し、中央衛生官庁保険局に通知することができる。

1. 特許情報が公表された発明は、承認された薬品とは関係がない。
2. 特許情報が公表された発明は、第 48 条の 3 第 2 項の規定を満たさない。

3. 公表された特許情報には誤りがある。
4. 前条に定められた事情があるにもかかわらず、変更または削除はされていない。

中央衛生主務官庁は、前項の通知を受けた翌日の 20 日以内に、それを新薬許可証の所有者に転送しなければならない。

新薬許可証の所有者は、通知を受けた日の翌日から、書面にて理由を述べ、中央衛生主務官庁に返答し、かつ状況に応じて特許情報の変更または削除を行うことができる。

第 48 条の 8

中央衛生主務官庁は、西洋薬のパテントリンケージ登録システムを設置し、新薬許可証所有者より申告された特許情報を登録し、かつそれらを公開すべきである。特許情報の変更または削除も同じである。

登録された特許情報が前条に定められた事情に該当する場合、中央衛生主務官庁は、通知者の主張及び新薬薬品許可証所有者の書面返答を公開しなければならない。

第 48 条の 9

後発医薬品許可証申請者は、薬品許可証の申請時に、新薬許可所有者より登録された承認済み新薬の特許権について、中央衛生主務官庁に対し下記のいずれかの声明をしなければならない。

1. 当該新薬には特許情報が何ら掲載されていない。
2. 当該新薬に対応する特許権が消滅した。
3. 当該新薬に対応する特許権が消滅してから、初めて中央衛生主務官庁は薬品許可証を発行する。
4. 新薬に対応する特許権は取消されるべきであり、または薬品許可証を申請した後発医薬品は当該新薬に対応する特許権を侵害していない。

第 48 条の 10

後発医薬品許可証の申請が、前条第 1 号または第 2 号の声明のみに係り、かつ本法の規定を満たすという審査結果を得た場合は、中央衛生主務官庁が薬品許可証を発行する。

第 48 条の 11

後発医薬品許可証の申請案が第 48 条の 9 第 3 号の声明に該当し、かつ本法の規定を満たすという審査結果を得た場合は、当該新薬に関わるすべての特許権が消滅してから発行する。

第 48 条の 12

後発医薬品許可証の申請案が第 48 条の 9 第 4 号に関わる声明である場合、申請人は中央衛生主務官庁より発行された薬品許可証申請資料完備通知の送達日の翌日から 20 日以内に、書面にて新薬薬品許可証所有者及び中央衛生主務官庁に通知すべきである。新薬薬品許可証所有者が登録された特許権者、専用実施権被許諾者と異なった場合は、併せて通知しなければならない。

前項における通知にて、申請者は、その主張した特許取り消し事情または非侵害事情について理由を述べ、かつ証拠を添付しなければならない。

申請者が前二項の規定により通知しない場合、中央衛生主務官庁は当該後発医薬品許可証申請を却下すべきである。

第 48 条の 13

特許権者または専用実施権被許諾者は、前条第 1 項の通知を受けてから、掲載された特許権について侵害訴訟を提起しようとする場合、通知を受けた日の翌日から 45 日以内に訴えを提起し、かつそれを中央衛生主務官庁に通知しなければならない。

中央衛生主務官庁は、新薬薬品許可証所有者が前条第 1 項の通知を受けた日の翌日から 12 ヶ月以内に、薬品許可証の発行を停止すべきである。ただし、次のいずれかの状況があり、かつ本法の規定を満たす場合は、薬品許可証を発行することができる。

1. 特許権者または専用実施権被許諾者は、前条第 1 項の通知を受けてから 45 日以内に侵害訴訟を提起していない。
2. 特許権者または専用実施権被許諾者は、後発医薬品許可証申請日前に、掲載された特許権について侵害訴訟を提起していない。
3. 特許権者または専用実施権被許諾者が第 1 項の規定により提起した侵害訴訟は、裁判所により民事訴訟法第 249 条第 1 項または第 2 項の規定に基づき原告の訴えを却下すると裁定された。
4. 裁判所により、侵害訴訟に係属された特許権に取り消しの理由があり、また後発医薬品許可証申請人が非侵害であると認定された。
5. 後発医薬品許可証申請人が第 48 条の 9 第 4 号に基づき声明したすべての特許権について、特許主務官庁は無効審判成立の決定書を作成した。
6. 当事者により和解または調解の成立と合意された。
7. 後発医薬品許可証申請人が第 48 条の 9 第 4 号により声明したすべての特許権はその権利が当然消滅した。

前項第 1 号期間の計算は、特許権者または専用実施権被許諾者が通知を受けた日のうち、一番遅い日から起算する。

特許権者または専用実施権者が第 2 項に規定した 12 ヶ月の期間内に、登録された特許権について、侵害成立の確定判決を得た場合、中央衛生主務官庁は、当該特許権の権利消滅後、後発医薬品許可証を発行することができる。

特許権者または専用実施権許諾者が第 1 項の規定に基づき提起した侵害訴訟について、最初から不当な権利行使であるため、後発医薬品許可証の申請者が、薬品許可証の一時発行停止により損害を受けた場合は、損害賠償責任を負うべきである。

第 48 条の 14

後発医薬品許可証申請案について、その申請人及び薬品が同一の場合、中央衛生主務官庁が前条第 2 項の規定により薬品許可証の発行を一時停止する回数は、1 回に限られる。

第 48 条の 15

第 48 条の 13 第 2 項に定められた薬品許可証一時停止期間内に、中央衛生主務官庁は、後発医薬品許可申請案の審査手続きを完成した場合、その旨を後発医薬品許可申請人に通知しなければならない。

後発医薬品許可証の申請者は、前項の通知を受けた場合に、衛生福利部中央健康保険署に対し、保険収載及び薬価算定を申請することができる。ただし、中央衛生主務官庁が後発医薬品許可証を発行する前に、製造または輸入することはできない。

第 48 条の 16

第 48 条の 9 第 4 号により声明した後発医薬品許可証申請案のうち、その申請資料がもっとも早く完備したものは、12 ヶ月の独占期間を取得できる。中央衛生主務官庁は、上記期間の満了前に、他の後発医薬品許可証を発行することができない。

前項に規定する申請資料が完備した後発医薬品許可証申請案は、次のいずれかの事情がある場合、申請資料完備日があとである者の順序で候補となる。

1. 薬品許可証審査期間中に、第 48 条の 9 第 4 号のすべての声明を変更する。
2. 申請資料完備日の翌日から 12 ヶ月以内に第 1 項の薬品許可証審査完成通知を取得していない。
3. 第 48 条の 13 第 4 項の事情がある。

同じ日に 2 つ以上の後発医薬品許可証申請案が第 1 項に規定されたもっとも早く完備したものに該当する場合は、共同で 12 ヶ月の独占販売期間を取得できる。

第 48 条の 17

後発医薬品許可証所有者は、薬品許可証を受けた翌日から 6 ヶ月以内に販売を行い、かつ最初の販売日の翌日から 20 日以内に実際の販売日の証拠を添付し、中央衛生主務官庁は独占販売期間及びその開始日及び終了日を裁定する。

前項における独占販売期間は、薬品の実際販売日を開始日とする。

二つ以上の後発医薬品許可証申請案が共同で独占販売期間を取得した場合は、それらの最も早い実際販売日とする。

第 48 条の 18

独占販売期間を取得した後発医薬品許可証申請人に次の何れかの事情があった場合、中央衛生主務官庁は後発医薬品許可証を他の申請者に発行することができ、第 48 条の 16 第 1 項の制限を受けない。

1. 中央衛生主務官庁より通知された薬品許可証を受領期間内に受領していない。
2. 前条第 1 項の規定により取り扱っていない。
3. 第 48 条の 9 第 4 号により声明された特許権は、その権利が当然消滅する。

第 48 条の 19

新薬許可証申請者、新薬許可証所有者、後発医薬品許可証申請者、後発医薬品所有者、薬品特許権者及び専用実施権被許諾者の間で締結された和解協議またはその他の協議が、本章の薬品製造、

販売、独占販売期間規定に関わる場合、双方の当事者は、その事実が発生した翌日から 20 日以内に中央衛生主務官庁に申告するほか、協議が逆支払いに関わるものであれば、別途公平取引委員会に通報しなければならない。

前項における通報の方式、内容及び依拠すべき事項は、中央衛生主務官庁が公平取引委員会とともに省令を定める。

中央衛生主務官庁は、第 1 項の協議が公平取引法に違反する恐れがあると認定した場合、それを公平取引委員会に通報することができる。

第 48 条の 20

新成分新薬以外の新薬は、第 48 条の 9 から第 48 条の 15 における後発医薬品許可証申請に関連する規定を準用する。

第 48 条の 12 の後発医薬品許可証申請案は、以下のいずれかに該当した場合、第 48 条の 13 から第 48 条の 18 までの薬品許可証の一時停止及び独占販売期間の関連規定を適用しない。

1. 販売承認済みの新薬により掲載された特許権は存続しており、かつ第 48 条の 3 第 2 項第 2 号の医療用特許権に属すもの。

2. 後発医薬品許可証申請は、善寶における医薬用途特許権に対応した適応症を解除し、かつ後発医薬品が前項における特許権を侵害していないと声明する。

前項における適用症の排除、声明及び他の依拠事項は、中央衛生主務官庁が省令を定める。

第 48 条の 21

この法律の中華民国 106 年 12 月 29 日の修正条文実施前、第 48 条の 3 第 2 項に規定された医薬品特許権に該当し、かつ権利が消滅していない場合は、新薬薬品許可省所有者が、修正条文実施後 3 ヵ月以内に第 48 条の 4 の規定に基づき特許情報を申告することができる。

第 48 条の 22

第 48 条の 4 から第 48 条の 8 までの医薬品特許情報の申告方式及び内容、変更、削除、特許情報の登録及び公開、第 48 条の 9 の後発医薬品許可証申請者の声明、第 48 条の 12 の後発医薬品許可証申請者の書面通知方式及び内容、第 48 条の 15 の中央衛生主務官庁が完成した後発医薬品許可証申請案の審査手続きの通知方法及び内容、第 48 条の 16 から第 48 条の 18 までの独占販売期間の起算及び終了の事項及び他の依拠事項は、中央衛生主務官庁が省令を定める。

第 92 条の 1

新薬薬品許可証の所有者が第 48 条の 7 第 3 項により規定した期限内に返答せず、かつ中央衛生主務官庁より期限内に返答をするよう命じられ、期限内に返答をしない場合は、中央衛生主務官庁が三万台湾元以上五十万台湾元以下の罰金を処する。

第 48 条の 19 第 1 項又は第 2 項の規定における通報方式及び内容により通報しない場合は、中央衛生主務官庁が三万台湾元以上二百万台湾元以下の罰金を処する。

第 100 条

本法で定める罰金は、別途規定されている場合を除き、直轄市または県（市）の衛生主務官庁が処罰する。

第 100 条の 1

新薬薬品許可証所有者が第 48 条の 3 から第 48 条の 6 により特許情報を申告し、その内容が詐欺又は虚偽不実であり、刑事責任に関わる場合は、司法機関に移送する。

第 106 条

この法律は、公布日から施行する。

1996 年 5 月 7 日公布した 53 条改正規定の施行日は行政院が定める。2006 年 5 月 5 日の改正規定は、2006 年 7 月 1 日より施行する。

2017 年 12 月 29 日修正した第 4 条の 1、第 92 条の 1、第 100 条及び第 100 条の 1 の施行日は、行政院が定める。

② 医薬品パテントリンケージ施行弁法[27]（仮訳）

第 1 条（規定根拠）

本指針は、薬事法（以下、「本法」と称す）第 48 条の 20 第 3 項及び第 48 条の 22 の規定により定める。

第 2 条（指針適用範囲）

西洋薬に関わる薬品許可証申請及び発行事項について、本法第 4 章の 1 に関連するものは、本指針の規定に準ずる。本指針に規定されていないことは、その他の関連法令及び中央衛生主務官庁の公告事項の規定に準ずる。

第 3 条（申告特許権の範囲）

一、本法第 48 条の 3 第 2 項における医薬品特許権の発明は、その範囲は以下の通りである。

1. 物質：薬品製剤の有効成分である。多形体の異なる化合形態の発明（結晶多型発明）を含む。
2. 組成物または製剤：薬品製剤の有効成分の組み合わせまたは製剤。
3. 医薬用途：対応する薬品許可証に記載された適応症の全部またはその一部。

二、前項第 1 号における物質発明は、薬品製剤有効成分の異なる多形体に関するものである場合、販売承認審査において、当該多形体物質を有効成分とする薬品製剤が、同様の医療効果を有する試験資料証明を提出しなければならない。

三、薬品の製造工程、中間体、代謝物または包装は、第 1 項における医薬品特許権の発明に属さない。

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[27] 西藥專利連結施行辦法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030103

第 4 条（特許情報申告期間の起算日）

本法第 48 条の 5 における特許情報の申告について、その起算日の基礎である公告決定の査定日は、特許公報に記載される公告日とする。

第 5 条（特許情報申告方法）

一、新薬薬品許可証所有者は、本法第 48 条の 3 及び第 48 条の 4 の規定により特許情報を申告する際に、中央衛生主務官庁が設立した西洋薬パテントリンケージ登録システム（以下、「登録システム」と称す）において、添付資料一に規定したフォームに基づき記入し、下記の文書、資料と併せてスキャンし、アップロードしなければならない：

1. 特許登録証書または当該医薬品特許権が記載された特許公報。
2. 代理人を委任した場合、委任事実を証明できる証拠。
3. 特許権者または専用実施権者が同意する証明、専用実施許諾の証明
4. 申告情報の信ぴょう性を証明しうるその他の文献、資料。

二、前項の規定に基づき申告する医薬品特許情報の葉には、第 3 条第 2 項の多形体を除き、当該新薬が適用する特許請求項により限定された範囲に限られる。

薬品特許権が 2 つ以上ある場合、薬品特許権ごとに特許情報を逐一申告しなければならない。

医薬用途発明に属するものは、「当該医薬用途発明の請求項番号」、及び「各請求項番号が対応する薬品許可証に記載された適応症」を説明しなければならない。

三、中央衛生主務官庁は、必要があると認める場合、新薬薬品許可証所有者に第 1 項に定められた文献、資料の原本を提出するよう命じることができる。

第 6 条（登録情報の変更及び削除）

新薬薬品許可証所有者が、本法第 48 条の 6 または第 48 条の 7 規定により、掲載された薬品特許情報を変更または削除する場合、前条の規定を準用する。

第 7 条（登録情報に変更理由がある場合の通知、及び新薬許可証所有者の返答方法）

一、本法第 48 条の 7 第 1 項の規定に基づいて中央衛生主務官庁に通知する場合、それに添付される書面理由及び証拠資料は一式 2 通にする。

二、新薬薬品許可証所有者は、本法第 48 条の 7 第 3 項規定に基づいて、書面で中央衛生主務官庁に返答する場合、添付資料一のフォームに基づき、受けた通知、返答理由及び処理状況を登録システムにアップロードしなければならない。

第 8 条（後発医薬品許可証申請者による声明及び声明の変更）

一、後発医薬品許可証申請者が本法第 48 条の 9 規定により声明をする場合、添付資料二のフォームで記入した上、販売承認申請に添付すべき資料と併せて、中央衛生主務官庁に送付しなければならない。

二、前項における声明は、新薬が登録システムに示された特許権情報に対照しながら、記入しなければならない。特許権が医薬用途である場合、対応された請求項番号に基づいて、記入しなければならない。
三、申請者は、最初に本法第 48 条の 9 第 1 号ないし第 3 号の事情を声明したが、同条第 4 号の事情を声明することに変更する場合、改めて添付資料二の声明書を記入しなければならない。その際に、変更声明書が中央衛生主務官庁に届けられた日を申請日とする。

第 9 条（後発医薬品許可証申請者による声明が免除できる事情）
　後発医薬品許可証の申請の件について、下記の何れかの事情があり、かつ証拠を添付した場合、本法第 48 条の 9 規定による手続きを免除することができる。
　1. 薬品許可証申請の申請者と参照新薬薬品許可証所有者は同じ。
　2. 薬品許可証の申請は、新薬薬品特許権者または専用実施権者より、実施許諾を受けてから提出する。
　3. 参照新薬の薬品許可証は取り消しされ、または廃止、登録抹消された。

第 10 条（中央衛生主務官庁による申請資料完備通知）
一、本法第 48 条の 9 第 4 号の事情に基づき、声明をした後発医薬品許可証の申請について、中央衛生主務官庁は、申請資料の完備に関する返答を書面にて申請者に通知しなければならない。資料が完備した場合、登録システムに資料完備日を公開しなければならない。
二、参照新薬が同様である後発医薬品許可証申請は 2 件以上である場合、中央衛生主務官庁に届け出た日が異なる場合、中央衛生主務官庁は、送達期日の先後により、前項の返答を行わなければならない。届けた日が同じである場合、返答日も同じ日にしなければならない。

第 11 条（後発医薬品申請者が特許無効または非侵害を声明した場合の通知方法）
一、後発医薬品許可証申請者が本法第 48 条の 12 第 1 項の規定に基づき、書面通知を行う場合、特許権の取消理由、または非侵害理由について、説明し、かつ関連証明文献、資料を添付しなければならない。
二、前項における通知は、配達証明つき書留で郵便機構で配達し、全部（全員）送達後の翌日から 20 日以内に、配達証明の写し、またはその他の送達を証明できる文書を中央衛生主務官庁へ送達しなければならない。

第 12 条（特許権者または専用実施権者が提訴する場合の中央衛生主務官庁への通知方法）
一、特許権者または専用実施権者は、本法第 48 条の 13 の規定に基づき、登録された特許権で侵害訴訟を提起する場合、新薬薬品許可証所有者は、起訴日の翌日から 20 日以内に裁判所の受領印が捺印された起訴状の写しを、中央衛生主務官庁へ送達しなければならない。
二、新薬薬品許可証所有者は、本法第 48 条の 13 第 4 項に定められた侵害成立確定判決を有することを主張する場合、当該判決書の写し及び確定判決の証明を中央衛生主務官庁へ送達しなければならない。

第 13 条（後発医薬品許可証発行一時中止に解除事情がある場合の通知方法）

本法第 48 条の 13 第 2 項但し書各号事情の何れかを有する場合、後発医薬品許可証申請者は、各事情及び発生日を説明し、かつ関連証明文献、資料を中央衛生主務官庁へ送達して審査しなければならない。

第 14 条（後発医薬品許可証発行一時中止期間内に薬事審査が完成した場合の通知方法）

一、中央衛生主務官庁は、本法第 48 条の 15 第 1 項の規定により後発医薬品許可証申請者を通知する際に、書面で行わなければならない。

二、前項における通知の内藤は以下のとおりである：

1. 申請番号及びその薬品名称、剤型と剤量。
2. 申請資料完備日の日付。
3. 許可証発行条件。

第 15 条（後発医薬品の独占販売期間の公開及び起算日の決定）

一、中央衛生主務官庁は、本法第 48 条の 17 第 1 項により、独占販売期間及びその開始日、終了日を決定する際に、その決定内容を登録システムに公開しなければならない。

二、本法第 48 条の 17 第 2 項に規定する起算日は、最初の実際販売日に発行した統一発票に記載された日付に準ずる。

第 16 条（新成分新薬以外の新薬の適用方法及びバイオシミラーの準用）

一、本法第 48 条の 20 に定められた新成分新薬以外の新薬とは、新治療効果を有する新薬製剤及び新投与経路新薬である。

二、本指針における第 8 条ないし第 14 条の規定は、本法第 48 条の 20 第 1 項に基づき、新成分新薬以外の新薬薬品許可証の申請に準用する。

三、バイオシミラー薬品許可証の申請について、本法第 4 章の 1 施行前に中央衛生主務官庁により臨床試験実施許可を得たものを除き、本法第 4 章の 1 における後発医薬品許可証申請のパテントリンケージに関する規定を準用する。

四、前項におけるバイオシミラーとは、生物由来で製造され、かつ中央衛生主務官庁に販売承認審査を得たバイオ医薬品とは類似する製剤である。

第 17 条（後発医薬品申請者が医薬用途特許権の関連使用を排除し、かつ非侵害を声明する場合の対処）

一、後発医薬品許可証の申請につき、本法第 48 条の 20 第 2 項第 2 号による声明する場合、下記の事項を含まなければならない。

1. 登録システムに存続している参照新薬の特許権は、本法第 48 条の 3 第 2 項第 3 号に定めた医薬用途特許権しかない。
2. 前号特許権の請求項番号及び適応症
3. 後発医薬品申請案の適応症項目、及び参照薬品の医薬用途特許権を侵害していない旨

二、前項声明の書式及び内容は、添付資料二に従う。

第 18 条（本指針の実施日）

本指針の施行日期は、中央衛生主務官庁が別途に定める。

③ パテントリンケージ協議通報弁法[28]（仮訳）

第 1 条

これらの措置は、薬事法(以下、この法律)第 48 条第 19 条第 2 項に規定する。

第 2 条

1. 本契約の当事者は、この法律第 48 条第 19 条第 1 項の規定により通知し、書面及び中国語で記録するものとする。 その通知には、次のものを含める必要があります。

I. 当事者の氏名、国籍、居住地、居住地、または事業所。 代表者、氏名、居住地、または住居。

II. 協定の締結の目的。

III. 契約の発効日。

IV. 関係する医薬品ライセンス番号または申請番号。

V. 医薬品の製造、販売及び販売に関するこの法律第 IV 章の 1 つに関する独占的事実の発生日、期間、その他の関連事項に関する事項。

VI. 契約の内容に関する特許権の証明書番号の数。

VII. 利益の支払いに関する事項 公正取引委員会への通知の有無を示す逆の利子の支払いに関与する者。

2. 前項第 5 項の事実発生日は、本契約の発効日とする。 ただし、学名薬検査登録の申請日が協定の発効日以降である場合、検査登録申請日を事実発生日とする。

3. 第 1 項の通知は、この法律第 48 条第 19 条第 1 項の規定により、事実発生の日から二十日以内に行われるものとする。

第 3 条

中央保健当局は、前条の通知を受けた後、必要と認めた場合、契約の具体的な内容を書面で解釈するか、または合意の関連文書または資料を提出するよう、契約当事者に通知しなければならない。公平な取引委員会に通知せずに、逆の利益を含む者は、できるだけ早く当事者に通知しなければならない。

第 4 条

中央保健当局は、前二条の規定により得た事項及び文書及び資料を、本契約の内容が公正取引法に違反していると認めた場合には、この法律第 48 条第 19 条第 3 項の規定により、公正取引委員会に通知しなければならない。

第 5 条

この措置は、この法律が施行された日から施行される。

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[28] 西藥專利連結協議通報辦法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?pcode=L0030088

④ 専利法[29][30]（第 60 条の 1：2022 年 2 月 24 日 行政院により改正案を可決、2022 年 7 月 1 日施行）

第 60 条の 1

1. 医薬品ライセンス申請者が、薬事法第 48 条第 9 条第 4 項に規定する新薬のライセンス所有者により公開された特許権に対して宣言を行う場合、特許権者は、通知を受けた後、第 96 条第 1 項の規定により、侵害の除去または防止を求めることができる。

2. 特許権者は、薬事法第 48 条第 13 項に定める期間内に、前出願人に対して訴訟を起こさなかった場合、その出願人は、医薬品ライセンスを申請した医薬品が特許権を侵害したかどうかについて、確認の訴えを行うことができる。

[29] 台湾専利法（全國法規資料庫ウェブサイト）
https://law.moj.gov.tw/LawClass/LawAll.aspx?PCode=J0070007

[30] 增訂專利法第 60 條之 1，行政院定自 111 年 7 月 1 日施行（經濟部智慧財產局ウェブサイト）
https://www.tipo.gov.tw/tw/cp-86-910542-b0b28-1.html

諸外国のパテントリンケージ制度に関する調査報告書

令和４年１１月

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