27 Generic Drug Entry and Coordination among Legal Systems: Drug Regulation, Intellectual Property Law, and Antitrust Policy

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Market entry of generic drugs assumes an important role as part of medical cost reductions, and raises issues that should be addressed by the three legal policy systems governing the structure of the pharmaceutical industry: drug regulations, intellectual property law, and antitrut policy. As material for comparative law, this analysis reviews the situation in the U.S. where legal systems of generic drug entry are the most developed and with the greatest number of precedent cases. Using a manner of cross-system analysis, it considers the various issues related to generic drug entry from the perspective of coordination among these three legal systems governing entry of generic drugs, rather than a direct analysis of the purpose for each individual legal system. Specific issues reviewed are: drug data exclusivity period for new drug applications, exemption from infringement for experimental use of patented drugs prior to patent expiration, legal commencement of marketing prior to patent expiration (including exhaustion), infringement litigation that abused procedures for listing patents in the U.S. FDA's Orange Book, and settlement of infringement litigation accompanied by agreements of reverse payments and delayed market entry.

Market entry of generic drugs, which takes an important roll in medical care cost reduction, has posed issues that should be addressed by one or all of three policies that stipulate the structure of the pharmaceutical industry: regulation of pharmaceuticals, intellectual property law, and anti-monopoly policy. This analysis reviews the situation in the U.S., where legal systems for market entry of generic drugs are the most developed and precedents have accumulated more than elsewhere, as material of comparative law systems, and considers various issues related to market entry of generic drugs not through analyzing the purposes of individual legal systems, but from the perspective of coordination among them. Purposes and means of the pharmaceutical affairs law (the FDA Act in the U.S.), patent law, and anti-monopoly law are supposedly distinguishable, but it cannot be denied that the purposes of these legal systems share a commonality.

The Pharmaceutical Affairs Law stipulates in Article 1 its purposes are: 1) to regulate the matters necessary for securing the quality, efficacy, and safety of pharmaceuticals; and, 2) to take the necessary steps for promoting research and development of pharmaceuticals and medical devices that are highly necessary. These purposes are common to patent law, which promotes research and development by granting exclusive rights for the purpose of development of industry, and anti-monopoly law,(*1) which indicates that high quality products and services desired by consumers are provided through free and fair

(*1) Precedents have determined that improvement of drug safety should be considered when judging violations of anti-monopoly law, since such improvements contribute to the public purpose under the anti-monopoly law. Especially in regard to pharmaceuticals, safety and efficacy are important attributes, which influence the business terms and conditions of products and services, and competitive pressures trigger acceleration of such competition.The Pharmaceutical Affairs Law stipulates in Article 1 its purposes are: 1) to regulate the matters necessary for securing the quality, efficacy, and safety of pharmaceuticals; and, 2) to take the necessary steps for promoting research and development of pharmaceuticals and medical devices that are highly necessary. These purposes are common to patent law, which promotes research and development by granting exclusive rights for the purpose of development of industry, and anti-monopoly law,(*1) which indicates that high quality products and services desired by consumers are provided through free and fair competition.

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In part II, new drug approval procedures in the U.S. are reviewed, and three issues are considered within the systems of pharmaceutical regulation and patent law.

The first issue concerns new drug product exclusivity. This system protects data of safety and efficacy, submitted by brand-name companies and patent holders, by prohibiting use of the information by generic drug companies for a certain length of time. The subject data of new drug product exclusivity are stipulated as data of new effective ingredients, new methods of clinical study, and so on. The issue involved with the relationship between pharmaceutical regulations and patent law arises here since the subject data share a resemblance to a portion of subject data under patent law. That means the issue becomes, how patent law relates to provisions in the pharmaceutical regulations when the patent term benefit is restored that was lost by regulatory procedures for new drug marketing. There are substantial differences. New drug product exclusivity protects rights not by disclosing information, but by prohibiting disclosure to third parties, while patent law grants exclusive rights as compensation for disclosing this information. New drug product exclusivity requires marketing approval as a new drug for commencement of exclusivity. This demonstrates that exclusivity is not for the protection of investment in research and development, but for the protection of investment in commercialization. To some extent, it is inappropriate to be concerned that protecting the patent with both bodies of law may create duplicated or excessive protection. When considering further the purpose of protecting commercialization investment, protection requirements will be considered in detail. For instance, it is rational to apply new drug product exclusivity to orphan drugs and children's drugs due to the narrow extent of their market sizes, while it is dubious to apply it to all efficacies whenever the route of administration or dosage is different. From the perspective of anti-monopoly law, how can new drug protect exclusivity be evaluated? There will be no problem if requirements are not manipulatable by applicants and it functions in an autonomous manner.

The second issue is exemption of production testing by generic drug makers prior to patent expiration of the pioneer, branded drug. The patent right is of no effect when a generic drug company intends to commence marketing after patent expiration and works with (analyzes, examines, and manufactures) the patented invention during the patent term to the extent necessary for submitting required information for a new drug approval. This exemption from patent right effect has been enacted in both the U.S. and Japan, and practically resolved by decisions of the Supreme Court. The justification reasoning remains an issue in Japan. The dominant counter-doctrine argues that the exemption is permitting infringement. This research points out that reasoning for justification of a research exemption shall not be considered as an issue solely of patent law, but it is natural to explain the reasoning in coordination with selling restriction laws (or the Pharmaceutical Affairs Law in the case of drugs) as well as with cases of patent term restoration(*2) which is permitted to brand-name drug companies. Moreover, this research considers evaluation of restrictions of patent right effect from the perspectives of the Pharmaceutical Affairs Law and anti-monopoly law. A greater number of applications for generic drugs indicate higher efficacy and safety of the patented drug, or, greater ease of safety improvements and other aspects. This is desirable in regard to quicker confirmation functions by competitors. Additionally, it is justified with respect to promoting research and

(*2) This refers to restoration of the length of a portion of the patent term that was not commercially exploitable due to necessary regulatory procedures for approval prior to commercial marketing. Section 2, Article 67 of the Japanese Patent Law; 35 U.S.C. §156.

development if generic drug companies intend to make improvements. Moreover, regarding an evaluation from the perspective of the Anti-Monopoly Act, there is low potential of an adverse impact on competition in the market for a patented product or a technology market when a research exemption is permitted to generic drug companies during the patent term.

The third issue is "legal" commencement of marketing before expiry of the patent right. In the U.S., generic drugs can be sold during the patent term if invalidity of the approved patent or non-infringement of the generic drug is certified by the applicant (so-called "Paragraph IV" certification). This system provides the opportunity to resolve infringement litigation prior to the market entry of the generic drug company and is rational under the Pharmaceutical Affairs Law. The system is also preferable from the perspective of anti-monopoly law to settle disputes among competitive companies over invalid patents, and conform to the system of patent law. However, this method also contains a significant impact for triggering settlements by the parties; the threat of the patent holder's injunction lawsuit is an effete tactic, since the lawsuit is filed prior to market entry by the generic drug company (i.e., the generic company cannot be ordered to suspend operations because they have not yet begun), hence the generic drug company does not carry the risk of unrecoverable sunk costs if it loses the lawsuit or until settlement. On the other hand, the branded drug company carries larger litigation risks since additional benefits of winning are small, even though the brand-name company pays legal costs and wins, but loses market share in the event of unsuccessful litigation. Therefore, incentives for the parties to settle become the reverse of normal infringement litigation.(*3)

In Japan, no clearly defined system permits generic drug companies to commence marketing during the patent term. It is, however, possible to commence marketing lawfully during the patent term under the condition that it becomes legal due to the first sale rule, that is to say, if a generic drug company purchases branded drugs, dissolves and recrystallizes the compound, and then sells them as their own generic drug (judgment by the Tokyo High Court of the Acyclovir case). Possible impacts from the judgment of the Intellectual Property High Court for the Canon Ink Tank case on the Acyclovir case are considered here. The judgment by the Intellectual Property High Court of the Canon Ink Tank case adopted the same criteria as the original decision in the Acyclovir case (the judgment by the District Court that was overturned on appeal), and clearly criticized the production approach theory. Precedents, however, have one consistent, practical rationale, which is determining whether duplicated benefit is generated, that lead to a conclusion regardless of issues such as the criteria for production are unclear in the production approach or that the first sale doctrine is not legally consistent. Based on this perspective, it is pointed out that there is no problem with recrystallization methodology under the Pharmaceutical Affairs Law.

Finally, new drug product exclusivity, a contentious issue also in Japan, is reviewed. New drug product exclusivity is enforced under the system of safety reexamination in Japan. As mentioned previously, new drug product exclusivity may assume different positions depending on whether accumulating investment for commercialization is adopted as the purpose of the system, or, ensuring safety. If the system's purpose is to ensure drug safety, it is acceptable to permit market entry of generic drug companies at an early stage and confirm drug safety with a wider range of patients. With respect to extending the period of new drug product exclusivity, international issues are pointed out in relation to broad scopes of protection and longer patent periods. A broader scope of new drug product exclusivity compared to Europe and the U.S. cannot be justified from the perspective of recovering

(*3) One opinion dominant in precedents is that this is a cause of reverse payments, mentioned later.

commercialization costs, but must be justified from the perspective of ensuring drug safety. In this context, it is necessary to recognize that the reexamination system functions to grant incentive, and then clarify the purpose of the system. If new drug product exclusivity is extended, Japanese drug companies will be motivated to postpone new drug approval applications in Japan and encourages foreign drug manufacturers to file their applications in Japan; this will accelerate the hollowing out of clinical studies conducted in Japan, and Japanese drug companies may lose benefits in the Japanese market.

In part III, U.S. cases of market entry by generic drugs regarded as anticompetitive interference are considered.

In the first case, a branded drug company abused procedures for listing patents in the U.S. Food and Drug Administration's Orange Book and filed infringement litigation for the sole purpose of delaying market entry by generic drug companies. It was alleged that irrelevant and frivolous patents were listed to stymie competitive market entries by generic drug companies, which was easily done since FDA has no ability or authority to investigate the efficacy and appropriateness of any patent listed in the Orange Book. After a patent is listed in the Orange Book, a generic drug company is subsequently required to respond to such patent by certifying the invalidity of the patent or their own non-infringement, etc. The branded drug company then files infringement litigation against such certification.(*4) The approval of the generic drug application is automatically suspended for 30 months if infringement litigation is filed, meaning that 30-month stays can be enforced multiple times simply by listing additional patents. This is clearly contrary to the purpose of the FDA Act. The U.S. FTC filed complaints against these cases of abuse, and concluded them with consent orders. FTC also recommended that the 30-month stay should be permitted only once, and to narrow the type of patents that are permitted listings in the Orange Book. In response to these recommendations, FDA amended regulations regarding listed patents. The revised FDA Act stipulated that the patents that a branded drug company can use as grounds of infringement litigation are limited only to patents for which information was submitted prior to the filing of the generic drug company's application, and that any patent after filing and before any amended applications cannot be grounds for litigation. This revision in practice limits the 30-month stay to occur only once. On the other hand, the revisions granted a generic drug company the legal means to dispute an inappropriately listed patent. Specifically, under the revised FDA Act drug applicants in counterclaims to infringement litigation filed by the patent holder can request court orders for the patent listing company to amend or eliminate such patent information.

Antitrust authorities took the initiative in promoting the enactment of the abovementioned law amendments because pharmaceutical regulations are often abused in an anticompetitive manner. Coordination between the Pharmaceutical Affairs Law and anti-monopoly law is well demonstrated by this case. Permitting consecutive 30-month stays by listing additional patents after filing infringement litigation does nothing to effectuate pharmaceutical review, and the possibility of filing infringement litigation after market approval of generic drugs still exists. Limiting the 30-month stay to once is justifiable.

The second case considered occurs commonly in actual practice: settlement of infringement litigation with reverse payment, in which a generic drug company delays its market entry for a certain period in exchange for cash payment from a brand-name company. This practice was initially accompanied by an agreement for 180-day exclusivity. 180-day exclusivity is a benefit

(*4) Patent law creates this right, and stipulates that the mere filing of an application by a generic drug company (ANDA) is itself an act of patent infringement. This is intended to resolve patent disputes prior to market entry of generic drug companies.

granted to the first applicant among generic drug companies filing a "Paragraph IV" abbreviated new drug application ("ANDA"). If multiple companies file certifications of patent invalidity or non-infringement (Paragraph IV certification) against the patent of the branded drug company, subsequent applications will not be approved (even though the application fulfills all substantial requirements) until 180 days after the date the first applicant commences marketing of the generic drug (or the date that a final decision on patent invalidity or non-infringement is determined for the first applicant). This regulation is intended as an incentive to the first generic drug company applicant that submits a Paragraph IV ANDA in order to trigger a challenge of the listed patent, by granting a benefit that also offsets the legal cost burden. However, if the first generic drug company does not commence marketing due to a reverse payment agreement and concludes infringement litigation with a permanent settlement, this intended purpose of the system is circumvented. Moreover, none of the subsequent generic drug companies that filed also can enter the market. At the outset, violations of anti-trust law were applicable to reverse payment agreements since these were interim settlements (which did not permanently resolve the patent disputes), but subsequently fewer cases committed violations of antitrust law due to the agreement.(*5)

Most legal theories suggest that a brand-name company engages in reverse payment when it is not confident of the validity of the patent held or of infringement. Legal theory assumes such a settlement is anticompetitive, and accepted only if the reverse payment is less than the anticipated legal costs. Case precedents deny such theories. Case precedents demonstrate that if the patent is valid and infringement exists, market entry of the generic drug company is not fundamentally allowed (i.e., there is no competitive situation). Assuming patent validity, there is no violation of antitrust law, since reverse payment settlements cannot restrict competition that does not exist.

However, since patent law stipulates that a patent shall be assumed valid, restraint of market entry by settlement is merely another enforcement of exclusivity based on the patent right. The contrast between lower court judgments and legal theory is the result of opposite stances for viewing the reverse payment situation: whether it should be assumed the patent is valid and infringement exists (precedent), or, whether it should be assumed the patent is invalid and no infringement exists (theory). With the former opinion, a presumption of infringement is unreasonable, while the presumption of patent effectiveness is acceptable. Critics of the latter state this opinion does not consider that terms of settlement are influenced by individual monetary resources or risk appetite and ignores the fact the settlements are triggered by the generally adverse results of infringement litigation that is systematically guaranteed by the Hatch/Waxman Amendments.

It is difficult to evaluate these opposing views from the perspectives of patent law and the Pharmaceutical Affairs Law. Hence, a viable solution may be to consider establishing rules, as are the criteria under anti-monopoly law, by comparing false positives when a competitive act is regarded in error as anticompetitive, and false negatives when an anticompetitive act is permitted in error as competitive. To some extent, reverse payment settlements may have a potential pro-competitive effect to create an economic condition in which lawsuit expenses (fixed costs) will increase resource allocation for research and development investment. However, this pro-competitive effect has a distant causal connection and should be proven by the respondent. At the same time, with respect to

(*5) The main reason for this trend is based on emphasizing consideration paid for the patent as a negative royalty, and because cases of simple reverse payment not accompanied by agreements of 180-day exclusivity have become the norm.

whether it is obvious or not that "anticompetitive" delays affect market entry, assuming so seems not to be easy based only on the fact of reverse payments, if the possibility of the generic drug company losing the lawsuit is considered. Therefore, it is necessary to verify various agreements accompanying a reverse payment as well as the infringement litigation process until the settlement. It should be noted that this approach requires proof of anticompetitive effect in each individual case and may prolong case processing.

If the same issue arises in Japan, it will be the case that delayed entry agreements are concluded in exchange for cash payments. This returns us to the contrast between theory and precedent in the U.S. Japan's Guidelines for Patent and Know-How Licensing Agreements refer to non-contestability, although they do not take into consideration vertical relationships and do not include a direct statement that may be construed as a suggestion for reverse payments. Assuming reverse payments are a type of licensing agreement may be to consider that a brand-name company is establishing a license with a negative royalty including special agreements that restrict the starting time of the license and force a generic drug company not to dispute patent effectiveness. Under these conditions, the license would not be granted if the patent were invalid, and the start of the license would not need to wait until patent expiration if the patent were valid. Either way, a reverse payment that permits market entry of a generic drug company after the expiry of patent term cannot be regarded as an execution of a patent right under patent law or violates the anti-monopoly law. For further consideration, establishment of criteria for these judgments is required, as it is in the case of the U.S.

This analysis reviews the abovementioned matters, points out that it is preferable to evaluate these legal systems multilaterally and simultaneously in order to regulate the structure of the pharmaceutical industry appropriately, and concludes with the point that role-sharing between the market and the law is beneficial for further review.