13 The Patentability and Scope of Protection of Pharmaceutical Inventions Claiming Second Medical Use – the Japanese and European Approaches as Possible Paradigms for a Developing Country like Brazil(*)

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Progress in technology in the pharmaceutical area is often achieved by the development of further uses of an already known substance. Patent protection plays an important role by insuring investments in Research & Development (R&D) and in clinical trials necessary for the marketing of a new drug. The Examination Guidelines of the Japanese Patent Office (JPO) of 2005 have established some standards for the examination of patentability requirements of such inventions, classifying them as "inventions of products". There are discussions about the adequacy of the protection given to these kinds of inventions. The European Patent Office (EPO) has been accepting them under the so-called Swiss-Type claim wording since 1985. It has also clarified that such claims are towards an "effect" achieved by a substance (not to the production of a product). This led to the interpretation that such claims afford a product-by-new-use protection. In 2004 the EPO also dealt with the admissibility of claims concerning dosage regimes. The new European Patent Convention (EPC) 2000, in force as of December 13 of last year, introduces some changes that might lead to different practices by the EPO in the future. The research aims at analyzing the patterns of patentability and scope of protection of pharmaceutical inventions claiming second medical use in Japan and in Europe. The analysis intends to be helpful in the development of the Brazilian patent system, where the situation still remains unclear.

I Introduction

The purpose of this work is to analyze the patterns of patentability and scope of protection of pharmaceutical inventions claiming second medical use in Japan and in Europe. It takes into account the importance of these two players in the global context and the provisions of TRIPS Agreement, and it analyzes elements that can be helpful in developing the Brazilian patent system and its boundaries.

It is first described the overall scenario of the systems under investigation. Japan is an example that the introduction of an effective patent protection leads to increased R&D activities and, thus, economic growth, becoming one of the largest trading economy in the world. The Japanese government recognized the importance of improving the business environment to attract investments and developed a program to make Japan an "intellectual-property-based nation", by implementing measures to promote the creation and reinforce the patent protection for pharmaceuticals and other arts.

For a developing country, Brazil has an educational system and research organization relatively able to generate inventions and to benefit from a patent system. Brazilian universities and research institutions are pioneers in different projects. For example, the Empresa Brasileira de Pesquisa Agropecuária (EMBRAPA), a Brazilian governmental institution, was among the first entities in the world to

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understand and reveal the genome sequence of a living being, the bacterium Xilella fastigiosa, a pathogen that attacks citrus fruits.

The European Patent Convention (EPC) was signed in Munich in 1973 and provides for a centralized system for the granting of European patents. It establishes a system of 34 European Contracting States with extension to four other States that recognize the European patent. The EPO is the executive body of the system under the EPC and is responsible for granting European patents for the Contracting States to the EPC. Upon grant, a European patent has the effect of a national patent in the Contracting States which the applicant has designated at the filing of the application.

Then, the work describes the importance of the development of further applications of an already existing or known substance, being such inventions valuable technically and commercially. Patent protection plays an important role to promote the research on further medical uses, by insuring investments in R&D and in clinical trials necessary for the development of a new drug.

The term "first medical use" is used for a new medicinal use of a known substance that have not yet been used for medicinal purposes, as opposed to "second medical use", which refers to claims covering second medical indications of know substances already used for medicinal purposes. In the present work, the term "second medical use" designates not only second but also third and further medicinal uses of a known substance.

Grounded on the fundamental objective of the patent system, i.e. promotion of technical development for the benefit of the society as a whole, Japan and Europe developed one of the most important patent systems in the world. The analysis of the patentability patterns and scope of protection of inventions claiming second medical use under these two systems may serve as guidance and contribute to the development of a sound patent system in Brazil.

II The European System

In Europe, article 52(4) of the EPC 1973 prohibited patenting of methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body. Although these subject matters may be considered inventions, the provision explicitly determined that they will not be regarded as susceptible of industrial application. To support this provision is the policy argument that patents should not unduly hinder the activities of physician.

Since 1985 when it decided the G1/83, G5/83 and G6/83 cases, the European Patent Office (EPO) has been accepting the practice of the Swiss Federal Intellectual Property Office to protect second and subsequent medical indications "by means of a claim directed to the use of a substance or composition for the manufacture of a medicament for a specified (new) therapeutic application". It considered that, described as such, inventions would not fall under the prohibition of article 52(4), despite criticizing the assumption in the statutory text that these kinds of inventions do not have industrial applicability. The novelty and inventive step requirements are derived from the new and inventive use of the substance.

In another case, G2/88 the EPO has clarified that "a use claim in reality defines the use of a particular physical entity to achieve an 'effect', and does not define such a use to produce a 'product'". From this decision, it can be concluded that the protection conferred on the patentee covers the use of a particular physical entity to achieve an effect in the sense of a purpose-related product claim, leading to a product-by-new-use protection.

Since the G5/83 decision, the EPO has been granting patents under Swiss-type claims for: i) specific group of animals or subjects or a novel group of patients; ii) particular mode of administration, i.e. subcutaneous rather than intramuscular; and iii) new administration regimens, i.e.

certain dosage plan ("twice a day") or intermittent or cyclic treatment ("on and off") of disease with a known drug.

On December 13, 2007, the EPC 2000 came into force, introducing some changes on the EPC system, specially concerning procedural aspects. With regard to modifications on substantive patent law, it shifts the prohibition of patenting methods of treatment from article 52(4) – which ceases to exist – to the new article 53(c). Recognizing the criticism triggered by the EISAI decision, which considered that second medical use inventions can be industrial applicable, the new text simply prohibits the granting of patents on them, but still recognizes the patentability of products for use in methods of treatment.

Moreover, the new European Patent Convention (EPC) 2000, in article 54 (5), recognizes second medical use inventions as patentable inventions. It equates the treatment of substances for their first and subsequent use in a method referred to in article 53(c). It is expected that it would be possible to describe a claim directed to a product for a specific medical use.

Because a European patent is considered to be a "bundle of patents" to be enforced according to the laws of the Contracting States, it is important to analyze such national systems. In the present work, United Kingdom (UK) and Germany were chosen for the analysis, with special focus on patents on dosage regimes.

In the Bristol-Myers v. Baker Norton case, the Court of Appeal of the United Kingdom considered that the claim under discussion – consisting of a different dosage regime – was directed to a method of treatment of the human body and contravened Section 4 of the UK Patents Act 1977. The Court emphasized that the new use should be unconnected with the previously known uses.

In 1983, one year prior to the EPO's decision on G5/83 (EISAI), the German Federal Supreme Court in the Hydropiridine case, decided that a claim directed to the use of a known substance for the treatment of a new disease does not contravene Section 5(2) of the German Patent Act, which corresponds to article 52(4) of EPC 1973. The court recognized that these inventions are industrially applicable and established that a use claim does not need to be drafted in the Swiss-type form. With regard to dosage regimens, in the Carvedilol II in 2006, the Supreme Court held that a therapy plan for a patient including the prescribing and the administration of medicament is a method excluded from patentability by article 52(4) EPC and Section 5(2) German Patent Act.

III The Japanese System

The JPO in the current Examination Guidelines listed "methods for treatment of the human body by surgery or therapy and diagnostic methods practiced on the human body" as industrially inapplicable inventions. Like in Europe, the policy underlying this exclusion is to prevent patents from hindering physicians' activities in treating patients.

In order to solve the controversy and allow patents on pharmaceutical inventions claiming second medical use, the JPO considers them as an "invention of product", and, therefore, avoid them to be classified in the category of methods for treatment. Inventions consisting also of combination of two or more medicines, defined by a mode of medical treatment (dosage regimes) are also understood as "inventions of a product".

The Examination Guidelines establish as admissible claims: i) "A medicine for disease Z containing an effective component A"; ii) "A medical composition for disease Y containing an effective component B"; iii) "A medicine for disease W containing effective components C and D in combination"; and iv) "A kit for disease V comprising an injection agent including an effective component E, an oral agent including an effective component F, and an agent including an auxiliary component G".

Claims such "chemical compound X for treating disease A" are not regarded as medical use claim, but rather towards the

chemical compound. The medical use limitations are disregarded in the examination of novelty. On the other hand, in case of first medical use inventions, the claim can be described as "pharmaceutical composition containing substance X".

Representative embodiments or working examples are needed to show the feasibility of the claimed compounds to treat the diseases. The working examples required are mostly the result of the pharmacological tests (be it clinical, animal or in vitro), which must be submitted at the time of the filing of the application, under the penalty of rejection of the application for lack of enablement.

In order to fulfill the novelty requirement, the JPO established that the claimed medical uses of the known active ingredients should be novel over the prior art, meaning that: i) the compound should have a new specific pharmacological property; and ii) the medicinal use for a specific disease resulting from the property should be novel. Applications would be rejected on the basis of lack of novelty, in case the pharmacological effects are closely related, the new claimed medical use is general over the specific already known use, or the discovery of the working mechanism.

Inventions will be deemed not to accomplish with the inventive step requirement, if the claimed new medical uses and the prior art can be correlated with each other in view of the mechanism of the biological effect. With regard to combination drugs, a new combination may involve inventive step if such combination attains an unexpected remarkable effect – the unexpected effect must be synergistic, not only additive. Optimizing the dosing schedule or dosage to reduce toxicity and improve efficacy is considered by the Examination Guidelines a routine development of the manufacturer of a medicine. In such cases, the invention does not involve inventive step, unless an unexpected remarkable effect – to be shown by pharmacological test results – is attained. The invention must also be towards a new group of patients to be treated, a new dosage form, a new strength per dosage unit or a new kit.

IV The Brazilian Situation

The current industrial property law (Law 9279, of May 14, 1996) was enacted to comply with the obligations assumed by the Brazilian government when signing TRIPS. It establishes that inventions are patentable, provided that they meet the requirements of novelty, inventive step, industrial application, disclosure and they do not fall in the statutory prohibitions of article 10 (subject matter not patentable for lack of a patentability requirement) and 18 (subject matter excluded by an express legal bar, although constituting an invention). Different than the previous statute regulating industrial property (Law 5772, of December 21, 1971), it does not exclude products in the pharmaceutical filed from patentable subject matter.

Article 10, VIII of Law 9279/96 does not consider as inventions "operating or surgical techniques and therapeutic or diagnostic methods, for use on the human or animal body".

The Instituto Nacional da Propriedade Industrial (INPI) is the Brazilian Office competent for the examination and granting of patents. In addition, the law requires "prior approval" by the Agência Nacional de Vigilância Sanitária (ANVISA) – the regulatory agency responsible for the marketing approval of drugs – for the issuance of a patent in the pharmaceutical area. The "prior approval" requirement was definitely introduced in article 229-C of the Law 9279/96 on February 14, 2001 by the amending Law 10196/2001.

There is no legal guidance on the requirements for prior approval, nor any regulation implementing article 229-C. The ANVISA has decided on its own discretion to re-examine the patent applications on the same grounds already analyzed by the INPI. The patentability requirements such as novelty, inventive step and industrial

application are re-examined by ANVISA.

The INPI may allow patents on second use inventions, including in the pharmaceutical field, provided that such second use is novel and evidence inventive step. The current Examination Guidelines in the Biotechnology and Pharmaceutical Field defines what it is a second use invention. and allow patentability of such inventions under the Swiss-type form.

On November 26, 2003, ANVISA issued a decision about patent applications on pharmaceutical-related inventions, in which it states that the agency will not grant prior approval on inventions consisting of second medical uses. It considers that patents on second medical use inventions are harmful to public health, to the country's scientific and technological development, and that it may hinder access to medication by the population.

The conflicting understanding between the two governmental institutions, the INPI and ANVISA, led to the current discussions to review the INPI's Examination Guidelines. To the meetings were present representatives of the two governmental institutions, associations from the generic industry and the innovative industry, and practitioners.

On December 3, 2007, the Judge of the Federal District Court of Rio de Janeiro rendered a decision in a leading case, dealing for the first time with the issue of second medical use inventions. In the decision, the Judge states that new uses of pharmaceutical products do not represent therapeutic methods, and are not included among the prohibitions of article 10, VIII of Law 9279/96. In addition, he clarifies that he does not understand that a Swiss-type claim to protect a pharmaceutical second use invention should be considered a process claim, but understand that it should be considered as a product bound by its purpose.

V Conclusion

The basic belief governing the patent systems is that the possibility of protection for a limited period provides an incentive for people to innovate and invest. The social return from this incentive to innovate created by patent possibilities is an increase in the general knowledge and the creation of useful products from which, ultimately, the public benefits.

Nevertheless, the patentability of inventions in the pharmaceutical field raises controversies, especially in the developing countries, where pharmaceutical patents in general lead to increase of prices and affect consumer's access to medicine. Providing patent protection to second medical uses would have as purpose prolonging the life of existing products patents, being the privilege erroneous, because it does not cover an invention, but rather a simple discovery. Another argument criticizing such patents is that they consist of methods for medical treatment, which are excluded from patentable subject matter in some systems, like Europe, Japan and Brazil.

Not allowing patents on second medical uses may leads to even more damaging effects to the Brazilian pharmaceutical industry, which does not have the means to finance and perform the R&D activities and the clinical trials needed for the development of new drugs containing new chemical compounds. In contrast, the expenses needed for development of a drug based on new uses of known chemical compounds are much lower, since the initial tests for proving the safety of the substance have already been performed.

In light of the experience of Europe and Japan, second medical use inventions can be distinguished from methods for medical treatment and from mere discoveries. For such kinds of inventions, the incentive of patent protection is likely to be needed to encourage innovation.