Patent Examination For Pharmaceutical Formulations

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January 1, 1995, was an important date for global trade history due to two events: the World Trade Organization (WTO) officially commenced under the Marrakesh Agreement, replacing the General Agreement on Tariffs and Trade (GATT); and the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) became effective as part of the Uruguay Round of GATT. The Uruguay Negotiation Round was the biggest negotiating mandate on trade ever agreed since the trading system was extended, notably in the areas of services and intellectual property. At that time, under the Thai Patent Act 1979, pharmaceutical products were excluded from patentability. Under the TRIPS Agreement, patentability became available in all countries party to the agreement, including Thailand, for any kind of invention, whether a product or process, in all fields of technology without discrimination.

As a WTO member, Thailand had an obligation to apply the TRIPS provisions to its national laws in order to establish minimum standards of intellectual property protection for foreign and domestic products and processes. As regards product patents for pharmaceutical products, Thailand implemented TRIPS on September 30, 1992, as an amendment to the Thai Patent Act, significantly increasing the level of pharmaceutical patent protection.

Application for zidovudine

On March 14, 1986, before the effective date of the Patent Act amendment in Thailand, a multinational pharmaceutical company filed a patent application for "Antiviral Nucleosides." The application originally contained 15 claims covering a process for preparation of zidovudine pharmaceutical formulation. The antiretroviral drug zidovudine (also known as AZT) is a nucleoside analog reverse transcriptase inhibitor whose role is to interfere with virus replication, namely the growth of either human T-lymphotropic virus type HI (HTLV-lll) or lymphadenopathy-associated virus (LAV), two pathogenic retroviruses which can play a role in the acquisition of acquired immune deficiency syndrome (AIDS). Zidovudine was first synthesized in 1964 by Dr. Jerome Horwitz, and in 1974, Wolfram Ostertag provided some evidence that zidovudine was active in a mouse cell cultures system transformed by Friend virus (a virus similar to HIV). Zidovudine is currently used in the "AIDS Cocktail" along with other AIDS drugs.

After the pre-grant publication of the application and the amendment of the Patent Act allowing the protection of pharmaceutical products became effective, the applicant submitted a claim amendment to the Thai Patent Office extending the number of claims from 15 to 26, with the intention to add the protection for zidovudine pharmaceutical formulation. By virtue of Section 39 of the amended Patent Act, the applicant argued that any application filed before the effective date of the 1992 amendment for which the Director-General had not yet issued an instruction shall be deemed to be filed under the amended Act. Additionally, the claim amendment did not enlarge the scope of the patent because the pharmaceutical formulation of zidovudine had been disclosed in and supported by the detailed description as originally filed.

Obviousness rejection

At the substantive examination step, the Director-General issued a rejection of the application on the ground of obviousness. The Director-General considered that although zidovudine per se was known in accordance with Dr. Horwitz's work, and its in vitro bioactivity was recognized in regard to Ostertag's work, the medical application against human retroviruses had not been reported. Therefore, the process for preparation of zidovudine pharmaceutical formulation was not anticipated and thus was novel. However, a process for preparation of pharmaceutical formulation by adding an active ingredient into pharmaceutically acceptable carriers was obvious to a person skilled in the art, making the application unpatentable.

Denial of new subject matter

The applicant submitted an appeal petition to the Board of Patents; however, the Board rejected the application on the same ground as the Director-General. Additionally, the Board considered the additional claims for the drug formulation product as an insertion of new subject matter, which was not allowed. The legal intention of Section 39 was to recognize the validity of applications filed prior to the amendment of the Thai Patent Act 1979, not to allow such applications to be evaluated under the revised procedures. The applicant then filed an appeal with the Civil Court in May 1997, seven months before the establishment of the Central Intellectual Property and International Trade Court, but again lost the case in the Civil and Appeal Courts for the same reasons as above. The applicant then brought the case to the Supreme Court.

Supreme Court decision

In Decision No. 1764/2549, the Supreme Court noted it was the common knowledge of persons in chemistry-related fields that in any pharmaceutical dosage forms, the pharmaceutical formulations could be prepared by adding an active ingredient, or its pharmaceutically acceptable derivatives, with pharmaceutically acceptable carriers. The claims in the "Antiviral Nucleosides" patent application failed to explicitly state the kinds of carriers as well as the steps in the formulation preparation process. Even though the corresponding patent for this application was granted in Europe, and the Thai Director-General may treat such examination result from any foreign patent office as having been done by a competent officer in order to facilitate the examination of a patent application, the Thai Examiner still had the power to conduct the examination in accordance with provisions of Thai law. Also, it is important to note that all patent applications for inventions have to go through substantive examination on a country-by-country basis. In the end, the Supreme Court ruled the application obvious and not patentable.

As the zidovudine case demonstrates, without explicit mention of discrete technology or a specific carrier, the process for preparing a formulation of a single active ingredient claimed in association with known or unspecified carriers or excipients claimed in the patent will fail the inventive step criteria if variations in composition and formulation are obvious to a person ordinarily skilled in the art. ❖