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NEW APPROVAL PROCESS AND CURRENT CHALLENGES OF GENERIC DRUGS

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ABSTRACT

This article provides an overview of FDA's regulatory processes for drug development and approval, examines the issues and challenges facing the FDA in the near future. The FDA's improved processes for drug approval and post-market surveillance have achieved the goal of providing patients with timely access to effective drugs while minimizing the risk of drug-related harm. While the drug approval process remains at high risk and spans over multiple years, the FDA drug review and approval process has improved, with the median approval time for new molecular drugs been reduced from 19 months to 10 months. The overall cost to development of a drug remains quite high and has been estimated to range from $868M to $1,241M USD. Several new laws have been enacted, including the FDA Safety and Innovation Act (FDASIA) of 2013, which is designed to improve the drug approval process and enhance access to new medicines. The FDA drug approval process is not without controversy, as a number of well-known gastroenterology drugs have been withdrawn from the US market over the past few years. With the approval of the new FDASIA law, the FDA will continue to improve their processes and, working together with the ACG through the FDA-Related Matters Committee, continue to develop safe and effective drugs for our patients.

KEYWORDS: Patent, Food and drug adminstartion, Drug registration, Licence.

1. INTRODUCTION

A novel medicine is a pharmaceutical entity that lacks widespread recognition of its safety and efficacy for the intended purposes. Yet, this term has much broader scope than just a "novel" chemical substance. Drugs that have not yet been authorized for sale in the US by the FDA are considered novel drugs. This also applies to drugs that have been approved but have new therapeutic indications, a different way of administering them, a different schedule for when to take them, or a different dosage form.[1] A common pharmaceutical product is a medication specifically similar to the innovative pharmaceutical compound in terms of how it is administered, the amount of potency it contains, the quality

of the medication, its performance qualities, and its intended application. How Drugs are Developed and Approved When it comes to making sure that pharmaceuticals sold in the US are harmless and effective, main agency in charge of that is the FDA's Center for Drug Evaluation and Research provides cannot taking participate in chemical examination, the Department of Monitoring and Investigation does offer fundamental studies on the efficacy, safety, and quality of medications.[2] When compared to the other four FDA institutions, the CDER stands head and shoulders above the others. All medications, even those available without a prescription and those sold without a doctor's note, are within its purview. Please refer to the CDER Update on CDER actions, includes drug review indicators of performance and afterwards evaluations of risk, amongst others.[3] Human Pharmacological Interventions for the Betterment of Public Health1 The other four centers of the FDA oversee the regulation of food and cosmetics, biologics, veterinary pharmaceuticals, and medical and radiological equipment. Only the most inventive pharmaceutical firms are chosen to submit new medication applications in order to bring their cutting-edge products to the American medical market.[4] A pharmaceutical product protection and effectiveness must be shown through adequate testing, which drug's marketing company must provide. The sponsor's Nondisclosure Agreement (NDA), data, and suggested labeling are reviewed by an evaluation panel that includes CDER doctors, statisticians, chemists, pharmacologists, and other scientists.[5] The assessment & ultimate authorization of generic drugs may be achieved by filing an Additive New Drug Application (ANDA) to the Office of Generic Drugs, which operates under the FDA's Center for Drug Evaluation and Research. Upon acceptance, an application is granted the ability to manufacture and promote a generic medicine as a reliable, effective, and adequately priced choice for the American population. When compared to unique medicinal products, generic pharmaceutical products are almost identical in every way: dose form, asset, management route, pure, presentation geographies, and envisioned use. "Drug Price Competition and Patent Term Restoration Act of 1984," mandated the use of bioequivalence. By removing the need for expensive and recurrent clinical studies, this act speeds up the process of making more affordable generic medications by giving the FDA has the right to grant permission applications for the commercial manufacture of generic versions of brand-name products. medical treatments after reformulation For further details about the criteria for bioequivalence of generic pharmaceuticals, refer to the chapter headed "FDA Ensures Equivalence of Generic Drugs" in the book "From Test Tube to Patient: Improving Health Through Human Drugs." Additional information on the CDER's evaluation process for the harmless and bioequivalence of generic pharmaceutical products before they are approved for commercialization may be found on the website of the Headquarters of generic Drugs, which is a resource generic medicine makers. When reviewing applications for generic drugs, evaluators give precedence to facts on biologic equivalence, chemicals, microbiology, requests for factory inspections, or pharmacological labeling.

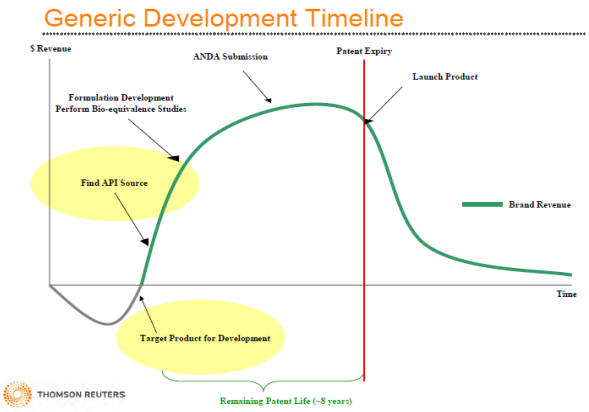

Fig. 1: Generic development timeline.

According to researcher IMS Health, the global pharmaceutical industry should anticipate see a growth rate of 5-7 percent in 2014, resulting in a market value of USD 880 billion. To protect the health and well-being of the general people, the pharmaceutical industry is subjected to comprehensive regulation. To keep up with the ever-evolving pharmaceutical industry and society's evolving demands, the present frameworks of drug regulation—including pharmaceutical drug laws, drug controlling organizations, medicine assessment tribunals, quality control labs, and Medicinal information centres have developed. A number of nations' drug laws were enacted in response to popular pressure, which prompted the implementation of stricter regulations meant to safeguard the populace.

Although drug legislation establishes the foundation for drug control, drug regulatory organizations depend on regulatory instruments such as standards and recommendations. the tools they need to put those laws into practice. The worldwide pharmaceutical regulations are now being harmonised but they may be classified into four primary groupings based on geographical location, development strategy, law, and marketing emphasis. North America Europe (including the European Union and Eastern Europe) Asia Pacific (except Japan, Australia, Gulf Cooperation Council, Latin America, Japan.

'Federal Food Drug and Cosmetic Act' are shown in Figure 2. Prior to the 1980s, inventors had the dominating position in the US pharmaceutical sector. Hatch-Waxman Act, is additionally referred to by the "Drug Price Competition and Patent Term Restoration Act of 1984," perhaps had a pivotal Significant contribution to the advancement of the generic sector in the US. The implementation of this regulation has significantly fostered the expansion and prosperity of generic enterprises inside the nation.

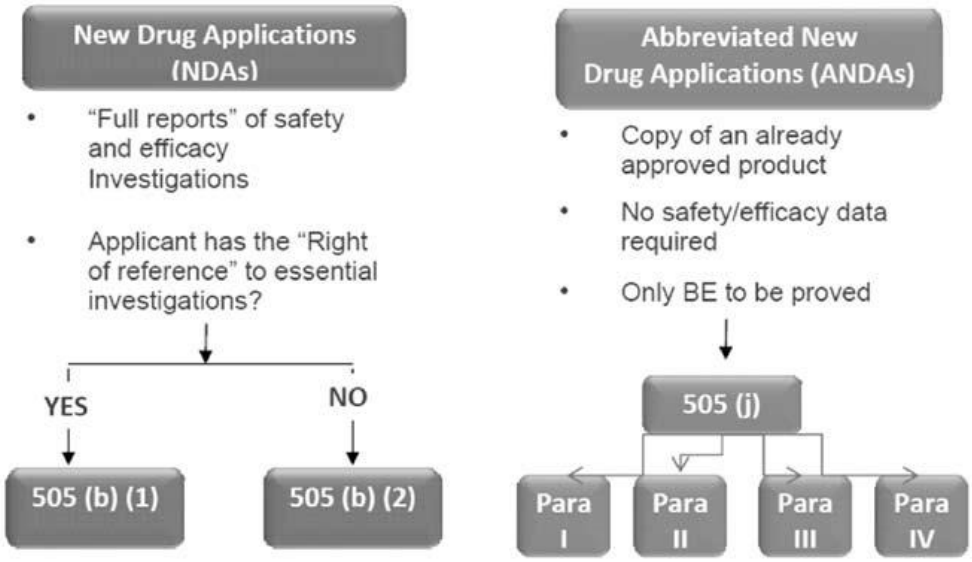

Fig. 2: Different Applications in USA.

2. OBJECTIVES OF THE WORK

The aim of this research is to identify the factors that influence the choice of a generic application, as well as the regulatory concerns associated with the development of generic drugs and the difficulties encountered throughout the approval process of generic products. Presenting a comprehensive examination of the Generic Drug Approval procedure in the US, the European Union, and Bharath, with a concentrate on explaining the distinctions among these

three nations. Every scientific investigation exhibits inherent principles and adheres to certain methodologies in order to achieve its objectives. Therefore, the selected approach significantly sets the results and implications of the research. Aim of this research was to clearly define the regulatory framework that governs the process of approving Generic Drugs in the US, European Union & India. The primary focus was on the application form, dates of approval, and the sequential order of stages in the generic medicine approval process. A variety of few instances of search engine results include Pharma Knowledge Base, Center for Pharmaceutical Information and Engineering Research, and appropriate Government websites like as the Food and Drug Administration Europe, Middle East, HMA, and CDSCO were used to gather the literature. The search query included phrases such as specific criteria for registering generic drugs, elements related to the pharmaceutical industry, names of regulatory bodies, and other variants. This analysis only includes patent data acquired from patent agencies specific to each country and the World Intellectual Property Organization.

3. REVIEW OF LITERTURE

J. Yoshasret al., 2021: The Pharmaceutical sector is subject to rigorous regulation. Prior to being released on the market, every pharmaceutical must get approval from Regulatory Authorities. The field of Pharmaceutical Regulatory Affairs is a unique and specialized domain of knowledge within the pharmaceutical industry. **Aliya Moin &, Sowjanya M 2020:** A pharmacological agent is a chemical compound indicated for the purpose of treating or diagnosing a specific medical ailment. In order to fulfill the standards established by the USFDA, the assessment of the effectiveness of a novel therapy requires meticulous and accurate testing, as well as clinical studies carried out over an extended period of time. Within the pharmaceutical industry, only medications that have received approval from the USFDA are allowed to be produced as prescription pharmaceuticals. **Jitendra Kumar Badjatya 2019:** Generic drugs refer to pharmaceuticals that have lost their patent protection and may now be manufactured by companies other than the original developers. The use of generic drugs has increased in recent years, mostly as a rational strategy to reduce costs in healthcare delivery. **Shweta Handoo,et al., 2018** There is significant variation in the regulatory standards across different nations worldwide. Hence, designing a comprehensive pharmaceutical product that can be simultaneously submitted for approval in all relevant nations is a formidable task for corporations. Before beginning the development process, it is essential to determine a properly defined regulatory plan for product development to prevent any significant unexpected events following its submission.

4. METHODOLGY

4.1. Patents: A patent is a document issued by the U.S. Patent and Trademark Office located in Arlington, Virginia, that grants to an inventor the legally enforceable right to exclude others from making, selling, distributing or using an invention in the U.S. territory. Congress allows this exclusive right, often considered a limited monopoly, to encourage the public disclosure of technical information and as an incentive for investing in their commercialization. Like other forms of property, the rights granted in the patent can be inherited, sold, rented, mortgaged and even taxed. When a patent expires or is held invalid, this exclusive right ceases. Congress has specified that a patent will be granted if the inventor files a timely application which adequately describes a novel and useful process, machine, manufacture or composition of matter, or any new and useful improvement thereof.

Types of Patent: There are three primary types of patent: Utility, Design, and Plant.

Utility Patents is the type of patent that is awarded to inventions that perform useful functions. Most of the patents that are issued are of this variety, and in fact most people who simply use the term "patent" are referring to a utility patent. Utility patents can be obtained for a thing, a method for making a thing, and/or a method for using a thing. Many times the news media will report that something that is quite old or well-known has been recently patented.

Design patents can be a useful tool in your intellectual property arsenal, particularly when you are attempting to create overlapping protection, thereby developing a true intellectual property portfolio. Having said this, it is important to know the limitations of design patents. Design patents do NOT protect an idea or an invention, but rather only protect ornamental design of exactly what is pictured.

4.2. Plant Patents: Patents to plants which are stable and reproduced by asexual reproduction, and not a potato or other edible tuber reproduced plant, are provided for by Title 35 United States Code, Section 161 which states: Whoever invents or discovers and asexually reproduces any distinct and new variety of plant, including cultivated sports, mutants, hybrids, and newly found seedlings, other than a tuber propagated plant or a plant found in an uncultivated state, may obtain a patent therefore, subject to the conditions and requirements of title. The subject matter of the application would be a plant which developed or discovered by applicant, and which has been found stable by asexual reproduction. To be patentable, it would also be required: That the plant was invented or discovered and, if discovered, that the discovery was made in a cultivated area That the plant is not a plant which is excluded by statute, where the part of the plant used for asexual reproduction is not a tuber food part, as with potato or Jerusalem artichoke. That the person or persons filing the application are those who actually invented the claimed plant; i.e., discovered or developed and identified or isolated the plant, and asexually reproduced the plant. That the plant has not been sold or released in the United States of America more than one year prior to the date of the application. That the plant has not been enabled to the public, i.e., by description in a printed publication in this country more than one year before the application for patent with an offer to sale; or by release or sale of the plant more than one year prior to application for patent. That the plant be shown to differ from known, related plants by at least one distinguishing characteristic, which is more than a difference caused by growing conditions or fertility levels, etc. The invention would not have been obvious to one skilled in the art at the time of invention by applicant. There are several types of patent or patent claim that are particularly relevant to pharmaceuticals.

These are: Product patent or claim

A “product patent” is a patent giving protection to a product as such, e.g. as an apparatus, a device or a chemical compound. If the patented product is a chemical compound, the patent is also called a “substance patent”. In the field of pharmaceutical inventions, a product patent gives protection to a chemical/biological compound (The active component of a medicine), also called a “New Chemical Entity” (NCE) or Active Pharmaceutical Ingredient (API).

Product by process patent or claim

This type of claim ‘claims’ a chemical or other process used to manufacture the drug whenever the drug is made by the patented process. It is the ‘next best’ type of claim as it also confers protection against importation of a product. However, the drug can be made and sold if another company can devise a commercially viable process not covered in the patent.

Process patent

This claims the chemical or other process used to manufacture the drug. The chemical product itself is not covered. Because of the difficulty of proving that another company is using the patented process, many countries have a 'burden of proof reversal' clause where the potential infringer has to prove that the patented process is not being used. In the USA, the patent law was amended to made importation of the product of a patented process an infringing act, although this is not generally the case.

Formulation patent

This claims the pharmaceutical dosage form on the drug, commonly also known as a composition but not to be confused with 'composition of matter' (see previously). It may take the form of a formulation of a particular drug or class of drugs, or a general formulation applicable to many drugs with different actions, such as slow release technologies, transdermal patches, etc. There may also be formulation process patents covering the manufacturing processes used to make the formulation.

Method of use

This covers the use of the drug to treat a disease. This type of claim is originally allowed in the USA and Germany, but is now being accepted in other countries including the UK. However, a careful wording of the claim in European patent application allows this type of claim. The European claim usually goes '... use of drug x to manufacture a pharmaceutical dosage form to treat ...', thereby avoiding a direct method of treatment claim.

Remember that not all types of claim are allowed in all countries and some countries do not have patent laws.

Second generation patent

A novel compound is patentable *per se* if its use is novel and inventive. A novel compound fulfilling these requirements may be protected *per se* by a "product patent" also called a "basic (compound) patent". "Secondary" or "second generation" patents are patents directed to new developments or improvements of the subject-matter of the basic patent.

If patenting strategy is carefully managed, secondary patents may bring, in some circumstances, extension of the term of protection around the product of interest. Basic patents and secondary patents may not belong to the same owner, sometimes having the effect that the owner of the basic patent is prevented from practicing certain embodiments falling into his own patent. However, careful management of patenting strategy around your product of interest can minimize the risk of being blocked by competitors' second generation patents.

This type of patent claim is now allowed in most commercially important countries, although it is a fairly recent event in many others. For instance, Japan, Switzerland, Sweden and Italy introduced product patent for pharmaceuticals in the 1970's, Austria in 1987, Portugal, Spain and Greece in 1992.

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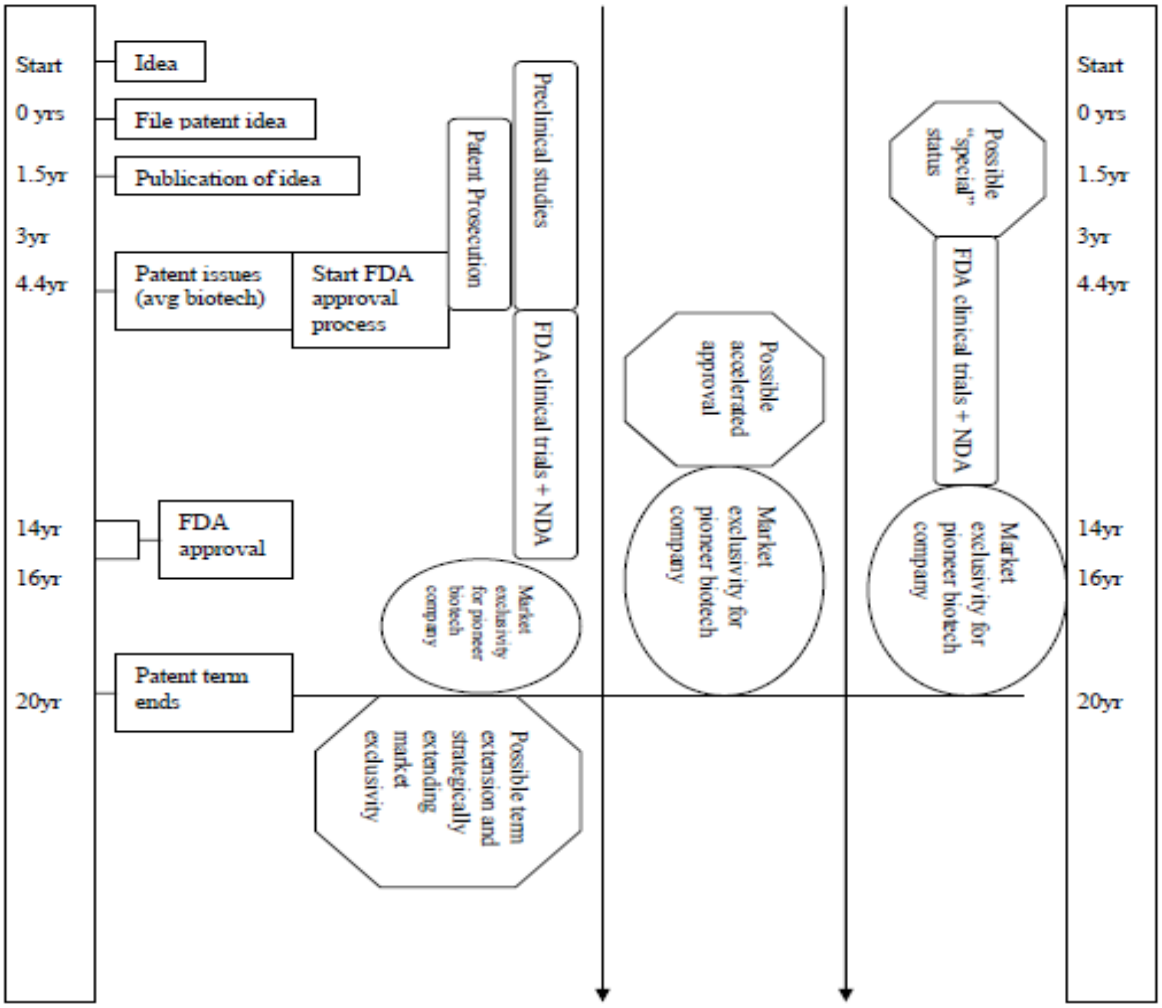

Fig. 3: Patent term.

Kinds of protection are available around a product

A product of interest may enjoy different types of protection, each of which may impact your intellectual property rights and your competitive advantage.

Different types of protection

Different types of protection may be obtained around a product, such as:

- ✓ Product (compound per se/composition of matter)
- ✓ Process (methods for manufacturing the product)
- ✓ Product by process (if the compound is novel)
- ✓ Use of the product or method of use protection (utility of the compound)
- ✓ Formulation of the product (e.g. cosmetic or pharmaceutical formulations)
- ✓ First and second medical use (for compounds found to be useful as a pharmaceutical).

The type of protection may differ from one country to another and therefore your Patent Attorney should give you advice on the type of protection you may aim for, based on your territorial commercial interests for example.

Some specific cases

Known compounds never used (or anticipated for use) in a medical indication

A compound that is known for use in a non-medical indications may still be patented for any medical indication and for a specific medical indication, in some countries (first medical use) if the inventor finds that it is useful as a pharmaceutical.

“Natural” products

Natural products may still be protected by patent claims framed in such a way as to distinguish the claimed product from the product as found in nature.

Basic patents

A basic patent generally protects a chemical (and eventually salts thereof) or a biological compound per se (composition of matter). It may further protect formulations of this compound, methods of using such a compound and methods of manufacturing it.

Secondary (follow-on) patents

Secondary patents protect “new developments” or “improvements” of the subject matter of the basic patent. Depending on when the secondary patent is filed (before or after the publication of the basic patent), the patentability requirements for the subject matter of the secondary patent are

(i) Novelty only with respect to the basic patent or

(ii) Both novelty and inventiveness (non-obviousness) with respect to the basic patent.

Secondary patents may be for example directed to:

- Purity/purified form of the compound

Deadlines for applying for such patent term extensions are quite short and are triggered by the market approval from the regulatory authorities.

Patent term extensions (PTE)

Patent term extension is available in the US, Japan, Israel, Australia, Taïwan, Korea and in some other countries for products subject to a regulatory approval.

Supplementary Protection Certificates (SPCs)

In Europe, the possibility of extension of the term of a patent to compensate for regulatory delays is offered by a Supplementary Protection Certificate. The aim of the supplementary protection certificate is to give 15 years of “effective patent protection”, defined as being the period during which a product can be sold while benefiting from the protection of either a patent or an SPC. The idea is to ensure that a patent holder can, if desired, market a patented product exclusively for at least 15 years. The SPC duration is such that it offers a maximum term of 15 years after the first market authorization for the product in the European Economic Area (EEA) and can give up to a maximum of 5 extra years from the normal patent expiry ("basic patent") in respect of a medicinal or plant protection product. The SPC does not extend the entire scope of the patent on which it is based but is limited to the product covered by the marketing authorization and for any medicinal use of the product that has been authorized. An SPC may be granted for

more than one compound per patent. Although SPCs are governed by an EU regulation, since patents are national, SPCs are national too. Therefore SPC applications should be nationally filed for on a country-by country basis.

Deadlines for applying for SPCs are triggered by the market approval by the regulatory authorities (either through centralized procedure via the European Medicines Agency (EMEA) or the approval in each country) or by the patent grant date whichever expires later.

Switzerland and Norway have their own patent extensions provisions which are similar to the SPC regulations existing in Europe.

Other types of exclusivity

Other ways of extending competitive advantage in the Biotech and pharmaceutical industries include Data exclusivity protection, Orphan drug protection and Pediatric exclusivity.

Strategies for optimizing patent product life

Complementary strategies to optimize product patent life require good communication, between Intellectual Property professionals, marketing decisionmakers and regulatory professionals.

Close follow-up of product development is essential

It is of utmost importance that patent attorneys/professionals are provided with the necessary information that may be crucial in the decision for filing "secondary" patent applications, for example. Relevant information can be provided through the following diligent process:

- Continuous monitoring of a product which is being developed;
- Monitoring the opportunities for matter that may support "second generation" patents (new process of manufacture, new formulation, new indications/new use, new regimen, new patient population, new route of administration etc…);
- Anticipating the possibilities opened to third parties seeking to work around your basic or secondary patents;
- Evaluating the competitive advantage of filing secondary patents, especially when you do not own the basic patent.

Active patent prosecution strategy

It is important to actively build-up your patent prosecution strategy. For example, a patent clustering strategy around your product of interest should be carefully managed through the timely filing of secondary patent applications and/or the filing of divisional applications, keeping in mind some country-specific provisions in terms of double-patenting, file-wrapper "estoppel" and restrictions on the filing deadline and content of divisional applications.

Diligent follow-up on marketing/regulatory status

In case of medicinal products or plant protection products subject to pending regulatory approval, coordinating marketing/regulatory approval information in all countries and patent strategy is crucial for optimizing patent life cycle management.

Careful follow-up on competition

Carefully sustained competitive intelligence around the product of interest is crucial to guide you in the decision to file secondary patents, particularly when you do not own the basic patent.

Analysis of the competitive landscape should take into account various strategies for optimizing patent product life mentioned above which are also available to your competitor.

Consideration of additional forms of protection in some countries

Other forms of protection may have to be considered, depending on your field of activity and on the countries where you are/intend to be commercially active. For example, filing utility model and design patents directed to a delivery device and/or a product package for the product of interest may provide a competitive advantage, in addition to the filing of the composition of matter patent.

In China for example, failure to file such utility model and design patents may create a loophole for third parties who may file such utility model and design patents around your product of interest. This can cause lengthy, costly and uncertain invalidation proceedings for the owner of the product patent. These troubles could be avoided by using such additional types of protection which have the advantage of enabling the owner of the product patent to stay one step ahead of potential competitors.

Role of the patent attorney

A patent attorney may cast a fresh eye upon your projects and propose possible patenting strategies, making use of a global view of patent life-cycle management. By virtue of his/her international contacts with foreign patent attorneys, the patent attorney can guide you in building a worldwide patent strategy adapted to your commercial needs.

As mentioned above, detailed information on product(s) under development, new developments, marketing plans and regulatory status are crucial information you may want to share with your patent attorney in order to enable him/her to provide you with the best advice adapted to your needs. His/her objective is to ensure optimum protection and, if possible, to extend protection to other embodiments of the invention and optimize your Intellectual Property rights' life.

6. RESULTS AND DISCUSSIONS

OPTIONS AVAILABLE TO ANDA APPLICANTS

An applicant pursuing an ANDA, with the aim of bypassing the thirty-month stay requirement, has limited negative legal options when they come across patents included in the Orange Book that do not provide protection for the particular NDA drug they are interested in. Nevertheless, some patents impose limitations on the drug to certain designs or allow for unauthorised use. In order to promptly dismiss the subsequent lawsuit by the NDA holder on the merits, so terminating the thirty-month stay, the applicant must provide a compelling argument to either the FDA or a court that certification under paragraph IV is superfluous, or must certify against all the patents listed in the Orange Book.

The regulations of the ANDA stipulate that certificates should only be granted for patents that assert ownership of the medication explicitly mentioned in the reference [Orange Book] or assert application of such medicine. The claim section of a patent must explicitly include all elements pertaining to the medicine, as defined by patent law, to establish its ownership. Specifically, a patent that includes both the constituents of the medicine and the constituents of the packaging does not provide exclusive ownership of the medication at the patent level. The directive explicitly defines that the term "drug" includes only drug products (such as prescribed medical forms) and drug substances (the active constituents). To obtain an Anti-Drug Agreement (ANDA), an applicant may argue to the FDA or a court that

certification against patents listed in the Orange book is not required if the patent includes aspects other than the dosage form or active ingredient, such as packaging or crystalline form components that are unrelated to the active ingredient. This is because the patents provide exclusive rights not only over the therapeutic product, but also over the active pharmaceutical ingredient. The ANDA applicant may suggest an alternative strategy by argumentating that the patents should be omitted from the Orange Book as they do not establish ownership of the drug. Furthermore, if the patents are revoked, the need for certification against the medicine will be rendered obsolete. Each of these approaches has its own distinct difficulties.

An applicant for an Anti-Drug Agreement (ANDA) is required by FDA regulatory interpretations to provide attestation for each patent included in the Orange Book. The FDA has determined that Congress explicitly intended for an ANDA applicant to only review the Orange Book to determine the existence of a relevant patent related to the specified medicine or its use. As to get the necessary certification according to the legislation, the FDA clarified that the Orange Book serves as a notification to prospective ANDA applicants about patents that might safeguard the unique pharmaceutical product.

The FDA's perspective is substantiated by the well-established procedure for contesting contested patents. The validity of an Orange Book entry may be contested by a systematic approach, wherein other parties possess a legitimate justification, such as mandatory certification, to contest a listing. The FDA regulations cited by the Abbott court, together with the official process for ANDA applicants to contest the relevance of information in the Orange Book, suggest that the FDA generally considers the code to mandate certification for all patents associated with a drug listed in the Orange Book.

Confirming the FDA's position on the matter is crucial for an ANDA applicant who anticipates approval without a substantial delay caused by a legal disagreement over the FDA's assessment. Resolving a legal battle that questions the FDA's need for certification of a certain Orange Book patent may take up to thirty months, rendering it unfeasible in avoiding schedule delays. Moreover, if an individual who is pursuing an accelerated patent application (ANDA) argues in court that they are not required to certify against a patent listed in the Orange Book, the FDA's position is significant because "the interpretation of a statute by an agency responsible for enforcement is delayed if it is reasonable and does not contradict the expressed intention of Congress."

Should the FDA require an ANDA application to obtain certification against any patent listed in the Orange Book, regardless of whether the patent specifically identifies the medicine or pharmaceutical product, the applicant may choose to remove a patent from the Orange Book before declining to certify against it. In its dicta, the Supreme Court observed that "ANDA's and paper NDA's must include one of the four certifications for each patent specified in the pioneer drug application." This suggests that patents not listed in the Orange Book do not need to be certified accordingly. Moreover, according to the FDA, an ANDA applicant is minimally required to refer to the Orange Book in order to determine the required certifications. Nevertheless, those seeking to file an ANDA have significant challenges in effectively having a patent formally withdrawn from the Orange Book. Under the rules, applicants to the ANDA have the right to challenge the correctness or pertinence of patent details. Under this rule, any party challenging a patent listing is required to notify the FDA of their reasons for disagreement over the inclusion of the patent. Fifty-s Accordingly, the FDA highly recommends that the applicant of the NDA should retract or modify their patent information. Should the proprietor of the NDA decline, the Orange Book will remain unaltered and the applicant of the

ANDA must provide proof against each patent indicated. The Act grants exclusive authority to the NDA holder over the listing of NDA patents, therefore barring any access to judicial recourse for ANDA applicants who fear that a patent is posted without proper authorization. A district court has the authority to make a declaratory judgement obligating a holder of a Non-Disclosure Agreement (NDA) to withdraw a patent from the Orange Book. Sixty The court in Ben Venue Laboratories, Inc. v. Novartis Pharmaceutical Corp. treated the FDA's decision to list a patent with considerable consideration, taking into account the FDA's history of rejecting patents.60 Nevertheless, the Court determined that being included in the Orange Book does not guarantee the accurate incorporation of a patent due to the limitations imposed by the FDA in terms of resources and inadequate competency to thoroughly evaluate applications.62. Therefore, a person pursuing an Anti-Denied Action (ANDA) might potentially circumvent the thirty-month stay requirement by contesting, via legal proceedings, the placement of a patent in the Orange Booklist. Legal procedures may be protracted, and a lawsuit contesting an Orange Book listing might lead to a delay in the acceptance of an ANDA that may be as or even more significant than the thirty-month stay requirement.

Denial of certification or removal of a patent from the Orange Book is a tactic that contends that the patents do not confer ownership of the NDA-approved medication or its intended use. Once patents demonstrate valid variations of the medication or drug usage, an ANDA application cannot claim exemption from attesting to these patents, regardless of whether the patents claim modifications that are not beneficial or unrelated to the proposed product of the patent applicant. In the absence of convincing evidence indicating that an ANDA applicant is not required to certify against a patent owned by an NDA holder or is unwilling to engage in a potentially protracted legal dispute to have a patent removed from the Orange book, the sole recourse is to certify against the patent owned by the NDA holder, wait for the lawsuit filed by the NDA holder to activate the thirty-month stay provision, and thereafter pursue the dismissal of the lawsuit without any delay. Regardless of the legitimacy of the NDA holder's claim or the absence of irrevocable damage that the NDA holder would suffer, the stay clause functions as a temporary prohibition issued to prevent the implementation of the ANDA.63% In order to avoid the injunction, the applicant for an Agreement to Dismiss (ANDA) must demonstrate that the lawsuit initiated by the NDA holder is certain to be unsuccessful, even if all the facts are in the NDA holder's advantage. A typical preliminary injunction requires the holder of a non-disclosure agreement (NDA) to demonstrate a high probability of the litigation being successful based on its merits.

INCENTIVES OF PATENT LAW

The present legislation of almost every nation clearly acknowledges the unique rights bestowed upon the creator of an invention or creative work, often known as intellectual property rights. Furthermore, the Constitution explicitly grants Congress the authority to promote the progress of science and practical arts by granting authors and inventors exclusive prerogative over their own works and discoveries for a certain period of time. Age 65 the fundamental inquiry in developing intellectual property systems is to ascertain the appropriate degree and duration of exclusivity that need to be bestowed.

Hence, the maximization of public utility may not be achieved. Application of a utilitarian or economic criterion to drug patents requires a very intricate equilibrium. Given utilitarian and humanitarian considerations, it is crucial that the development of extremely promising novel drugs continues to be a top priority. Therefore, it is recommended that the government strengthen the incentives towards the development of these novel treatments. On the other hand, the expenses incurred by a single inventor who has the only rights to market a medicine are also somewhat substantial. The

absence of significant price sensitivity in patient demand for a necessary therapy implies that the royalty associated with a drug monopoly might be quite expensive for customers. Nevertheless, Bayer effectively established a monopoly for a duration of thirty months over a product it did not create due to the inherent assumption of preliminary injunction effect included in the thirty-month stay rule. The incorporation of the thirty-month stay clause effectively intensified the adverse consequences of patent monopoly rules in intellectual property legislation, therefore impeding society from enjoying the advantages of any revolutionary breakthroughs. Furthermore, Elan's product was intentionally withheld from customers, in spite of its potential superiority over Bayer's patent, presuming that Bayer neglected to take into account the diverse range of South African Standards (SSA). Under such circumstances, the inclusion of a thirty-month stay clause may diminish the motivation for a firm like as Elan to engage in the advancement of groundbreaking pharmaceutical goods. Furthermore, the clause of a thirty-month stay does not especially promote the granting of patents for the crucial commercial medicinal breakthrough. Contrarily, it aggressively supports the notion of obtaining patents for "evergreening" and "trip wire" technology. Instead of investing resources in cultivating and identifying non-utilitarian sub-inventions that may serve as "trip wire" patents for pharmaceutical companies, it is more advantageous to focus on advancing practical fundamental medicine innovations to optimize societal utility and economic efficiency. One further issue with the thirty-month stay clause, from an economic or utility maximizing standpoint, is that it promotes pharmaceutical companies to focus on maximising profits via patents in general. An inherent constraint of patents is that their capacity to promote innovation is limited by the customers' capacity to financially support monopolistic rents. An economically efficient strategy would prioritize the development of pharmaceuticals that confer the greatest societal benefit while minimizing research expenditures, rather than prioritizing the development of drugs that primarily benefit the affluent segment of the population, even at a somewhat higher research expenditure. By reallocating capital generated from monopoly rents paid to patent holders towards direct government subsidies for pharmaceutical researchers specializing in developing drugs that specifically target the most severe diseases affecting the largest population, the public could improve efficiency beyond the current capabilities of the patent system.

An alternative method is to use an expedited FDA evaluation of novel pharmaceutical applications. By expediting the introduction of the NDA holder's product into the market, the adoption of an expedited evaluation of FDA new drug applications has the potential to significantly boost earnings. Companies consider expedited assessment to be a more highly appreciated and thus more efficient motivation than the ultimate postponement of market competition caused by the thirty-month stay clause. The potential value resulting from future delays in competition may span many years, so any benefits should be assessed based on the concepts of economic time value of money.

ANTITRUST LIMITATIONS

Antitrust law intervenes when a legal recourse is commenced to use the thirty-month stay provision in order to protect a monopoly. Indictments have been filed by the FTC against NDA holders who collude with an ANDA applicant to hinder the entry of generic medications into the market. Abbott Laboratories and Geneva Pharmaceuticals Inc. have been mandated by the FTC to commit to refraining from participating in arrangements in which an ANDA applicant confers exclusive rights or produces a generic product for an NDA holder. As part of ongoing patent litigation, the settlement mandates that the court must validate any arrangement for the payment of ANDA applicants by NDA holders in order to prohibit the manufacture of generic therapies.

FEDERAL TRADE COMMISSION STUDY

The FTC conducted a study to investigate whether the restrictions of 180-day exclusivity and 30-month stay in the Hatch-Waxman Amendments were intentionally used to hinder the availability of generic drugs to consumers, in response to allegations of anti-competitive behaviour by both brand-name and generic pharmaceutical companies. The Federal Trade Commission (FTC) published the findings of its investigation and proposed two primary recommendations in July 2002. The FTC suggested granting a single temporary 30-month suspension for each pharmaceutical product in the Andal Patent Application (ANDA) to combat allegations of patent infringement related to patents published in the "Orange Book" before the generic applicant's ANDA was filed. The FDA agrees with the FTC's conclusion that there has been a rise in the quantity of Authorizations for New Drug Applications (ANDAs) for which consecutive 30-month stays, as well as repeated 30-month stays, have been granted, in comparison to prior years. Furthermore, the current average number of patents being contested per generic medication application surpasses those from previous time periods.

An further proposal by the FTC involves the implementation of legislation mandating brand-name companies and initial generic applicants to provide written documentation of explicit agreements to the FTC. This response concerns the decision taken by the Federal Trade Commission on the partnership between manufacturers of well-known brands and original generic applicants to deliberately delay generic competition. There is no opposition to this concept from the FDA. This study is very relevant to our own thoughts throughout the generic goods application process, and the FDA agrees with the conclusions of the FTC research. The methodical collection of data on the resolution of legal conflicts over patents that were filed after the approval of Non-Disclosure Agreements (NDAs) serves as a clear example of this approach. The FTC investigation correctly recognized that the FDA does not possess the capacity to evaluate the appropriateness of patent titles.

Regulatory withdrawal by FDA

On June 12, 2003, President Bush, HHS Secretary Thompson, and FDA Commissioner McClellan proposed a new regulation to expedite the process of ensuring that consumers have access to safe and effective generic medications. The rule will go into effect after sixty days. This regulation proposal was first offered on October 24, 2002, in response to the FTC's recommendations and other adjustments that the Agency deemed advantageous to improving generic competition. The proposed law would limit a creative pharmaceutical enterprise to a rigorous 30-month window in which to submit a generic medicine application to the market or challenge a patent. The regulatory changes are expected to save customers $35 billion over the next 10 years. This aim will be reached by accelerating the availability of generic alternatives to some costly name-brand pharmaceuticals, therefore avoiding time-consuming legal problems. The revised regulations will be published as final rules in the Federal Register on June 18, 2003. The rule's implementation is set on August 18, 2003.

The rule specifies the following: each ANDA or 505(b)(2) application may only be filed for a maximum of 30 months; patents pertaining to metabolites, packaging, or intermediates are prohibited; certain patents claiming a different polymorphic form of the active ingredient described in the NDA are required; and test data demonstrating that a drug product containing the polymorph will function identically to the drug product described in the NDA is added as a requirement.

30-Month Stay Provisions

The final law limits prominent firms to a maximum of one 30-month stay. This is accomplished by establishing a deadline for generic enterprises to inform the patent holder and brand-name sponsor of a paragraph IV patent challenge, so commencing the 30-month stay process. Notifying the parties of a paragraph IV certification together with the first certification is critical if the prior certification and communication did not result in a full 30-month stay. An ANDA or 505(b)(2) application could only be updated to incorporate a paragraph IV certification if the patent owner and NDA holder were told of the certification ahead of time, or if the 30-month stay was insufficient. If the applicant modifies the certification before the 45-day period following the expiration of notice to the NDA holder and patent owner, and neither party has filed a patent lawsuit, the applicant for an ANDA or 505(b)(2) patent will not be considered to have provided a single notice of a paragraph IV certification and a complete opportunity for a 30-month stay. Brand-name corporations will be able to gain patents and challenge infringement allegations for as long as the FDA requires paragraph IV certificates from generic medicine applicants. They will be unable to block the approval of a generic version of a pharmaceutical, even if they file several patent applications or rely on later-awarded patents. Additional applications will not result in successive 30-month stays.

7. CONCLUSIONS

The statutory thirty-month stay of approval triggered by paragraph IV certification and subsequent patent infringement suit by the NDA holder is not efficient when evaluated under any of the prevalent norms justifying intellectual property regimes. The thirty-month stay provision allows NDA applicants to prevent generic drugs from entering the marketplace on the basis of expired patents, unsustainably broad readings of core patents on the NDA product, and "trip wire" or "evergreening" patents which do not reflect substantial change or improvement over an original patent but are prosecuted for the sole purpose of triggering the stay provision. The problems created by Hatch-Waxman Act's creation of the thirty-month stay provision should be addressed at many levels. First and most obviously, Congress should repeal the certification requirement for ANDA applicants. NDA holders would still be able to protect their innovations through standard patent law enforcement just like any other inventors. NDA holders would simply no longer benefit from special treatment. Even if Congress does not act, other entities can minimize the problems created by the thirty-month stay provision. The FDA should interpret Hatch-Waxman Act within statutory constraints in order to minimize the stay provision's effect. The FDA could reasonably interpret the Hatch-Waxman Act to only allow core patents directly covering the NDA product to be listed in the Orange Book, and rigorously review all patents submitted for inclusion in the Orange Book for suitability. Additionally, the FDA could evaluate the expiration of dates submitted to the Orange Book rather than simply taking applicants at their word. These two steps would eliminate the problem the stay provision being triggered by "trip-wire" patents and by expired patents. Third, courts should more freely exercise their discretion under the Hatch-Waxman Act to modify the length of the stay based on the plaintiff or defendant's failure "to cooperate reasonably in expediting the action. Courts could potentially, under this provision, reduce the length of the thirty-month stay to zero where the plaintiff's action has such an extremely small chance on the merits that the NDA's filing of the suit or the NDA holder's failure to settle the action for a nominal amount constitutes failure to expedite the action. By utilizing available discretion in this manner, the courts can reduce the problems caused by thirty-month stay provision while discouraging frivolous and nearly frivolous actions in their court. A court utilizing this discretion brings might analyze the thirty-month stay provision using standards similar to those historically accepted for preliminary injunctions. Fourth, the FTC and parties excluded from the generic drug market because of the thirty-month stay provision may seek remedies through antitrust laws in some cases. Although the burden of proving

that a claim is objectively baseless may not be easy to overcome and the process of litigating an antitrust trial may take well over thirty months, the possibility of treble damages calculated on the basis of the generic drug manufacturer's lost profits during the thirty months could bring enough pressure on NDA holders that at least the most frivolous patent cases would be settled. Finally, individual attorneys should refuse to pursue patent prosecution or litigation that has little merit even if the client desires to trigger the thirty-month stay provision. An attorney's interest in maintaining a professional reputation by advancing only positions with potential merit before the Patent and Trademark Office and before the Federal Courts along with the attorney's individual sense of morality and justice should serve, to some extent, to prevent the attorney from engaging in litigation and patent prosecution that is merely tactical. To best serve society, attorneys should aspire to substantively promoting justice and the state of the law of the law through client advocacy rather than invoking meritless suits merely because the suit serves a client's immediate interest such as triggering the thirty-month stay provision.

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