Patentability Criteria and Typical Pharmaceutical Claims

Asian Regional Course for Judges on Intellectual Property and Public Health 2021

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Patentability Criteria

Nature and Scope of TRIPS Obligations

An important flexibility that can be construed from the terms of the TRIPS Agreement is with regard to the definition of the standards of patentability in national laws, and the rigour with which they are applied in determining whether a claimed invention is patentable. Weaknesses or gaps in such standards can allow ever-greening by the pharmaceutical industry – e.g. the obtaining of additional patents on a different crystalline form, a new formulation or new use of a known medicine – which may be enforced to block or delay the market entry of generic equivalents. Although several countries have fine-tuned their patentability standards in order to limit ever-greening, many countries still apply inappropriately broad criteria.

TRIPS obligates all WTO members to grant patents for any "invention" *in all fields of technology including pharmaceutical products* insofar as the technology is "novel", involves an "inventive step" and has "industrial applicability". However, TRIPS does not define what constitutes an invention, or the thresholds of novelty, inventive step and industrial applicability. Therefore, these thresholds can vary under different national laws and the policy objectives to be achieved through the patent law in the relevant industrial and social sector. With regard to pharmaceutical patents, strict thresholds may be established under national laws to ensure patents are only granted for genuine novel inventions that constitute advancement over the existing knowledge in the field, and not to incremental innovative developments that do not constitute inventive activity.

In addition, to the policy space that is available to WTO members to define what is an invention, and the standards of novelty, inventive step and industrial applicability, in terms of article 27.2 and 27.3 (see course pack on exclusions, exceptions and limitations).

Article 27 of TRIPS

> 1. *Subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application.4 Subject to*

paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced. For the purposes of this Article, the terms 'inventive step' and 'capable of industrial application' may be deemed by a Member to be synonymous with the terms 'non-obvious' and 'useful' respectively.

2. *Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect* ordre public *or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.*

3. *Members may also exclude from patentability:*

(a) diagnostic, therapeutic and surgical methods for the treatment of humans or animals;

(b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective sui generis system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO Agreement.

In addition to this, Article 29.1 of TRIPS requires members to make disclosure of the claimed invention in a patent application in a manner that is sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art. It also allows WTO members to require that such disclosure should be of such a standard that it indicates the best mode of carrying out the invention that is known to the applicant.

Article 29.1

Members shall require that an applicant for a patent shall disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art and may require the applicant to indicate the best mode for carrying out the invention known to the inventor at the filing date or, where priority is claimed, at the priority date of the application.

Major Considerations in Determining Patentability

- Does the claim constitute an invention?
- Does the invention fall within any of the exclusions from patentability under the law?
- Does the claim meet the requirements of novelty, inventive step and industrial applicability?

- Is the invention sufficiently disclosed to enable a person skilled in the art to perform the invention?

The determination of these questions in relation to each patent application will depend on how these criteria are defined or applied under national laws or appliable regulations, administrative guidelines, or patent examination practices.

Definition of *Invention*

The first requirement under art.27.1 of TRIPS is that a patent should be granted for a subject matter that constitutes an invention. However, the term is not defined in the TRIPS Agreement. The ordinary meaning of 'invention' suggests the output of an intellectual activity in the form of new knowledge of a technical nature. To invent is 'to create by thought, originate (new method, instrument, etc)'. It also suggests a distinction between creations and mere discoveries and, more generally, between inventions and other subject matter that does not qualify as such.

"Invention" has been defined in most countries in the region as an idea about solving a specific problem in a particular technical area, accompanied with a list of exclusions of inventions that are not considered to be patentable. Some countries, e.g., Thailand, define invention more broadly to include innovations and improvements of known products and processes. While most countries have generally excluded discoveries and methods of treatment from being considered as patentable inventions, India, Indonesia and the Philippines have specifically excluded new forms of known substances or compounds that do not result in increased efficacy from being regarded as inventions that are patentable.

The inclusion of provisions excluding certain claims on new uses of known substances as inventions that are not patentable is legitimate under the TRIPS Agreement. While article 27.1 of TRIPS requires patents to be made available without discrimination based on the field of technology, it allows differentiation between fields of technology, to set different thresholds on whether a claim can be regarded as a patentable invention.

Major Considerations in Interpreting "Invention"

- To be regarded as an invention a claim must encompass a technical effect, or in other words, have a technical character.
- Where the statutory provision is silent on whether new forms of known substances constitute inventions, judicial or quasi-judicial authorities may raise a presumption that such claims do not constitute inventions.
- Materials found in nature (such as genes) and properties and forms newly found in known products (e.g. the crystalline form of a compound of medical use) should not be deemed inventions.
- When it is determined that the patent application does not cover an invention, no further analysis of compliance with the patentability requirements is needed.

Definition of *Novelty*

The concept of novelty may be applied in different ways, depending on the legislation and interpretation by patent offices and courts Most countries in the region apply an absolute standard of novelty, i.e., an invention is considered to be novel when it is not anticipated by prior publication or use in the country or anywhere else in the world. The test is whether the invention as claimed is part of the prior art, or what is the existing prior art? In this regard, there is room for national policies to determine the scope of what has been disclosed and is therefore part of the 'prior art'.

The laws of most countries in the region specify that the prior art should be deemed to include applications filed in the same country that are published on or after the filing date of the application being examined. Nevertheless, there is scope for interpretation of other elements that could be considered to be part of the prior art.

For instance, the disclosure of an invention in the prior art may not have been made explicitly, but may be implicit in a prior art document. Implicit teachings can be considered part of the prior art, hence destroying the novelty of an invention. This approach is preferable to the 'photographic' approach to novelty, which is based on explicitly disclosed information. The photographic approach entails a rigid and formalistic assessment of novelty, which may lead to the unwarranted grant of patent rights. Novelty may also be excluded when the information available in the prior art discloses the essential elements of an invention, regardless of whether data enabling the execution of the invention were available. Thus, a feature or an element of claimed invention which already exists in the prior art cannot be novel regardless of whether its presence was expressly stated, known, or even whether it would have been recognizable.

Moreover, there is no limitation on the number of documents that could be taken into consideration in determining the scope of the prior art. Novelty can be derived from a combination of publications.

Patent offices in developing countries are often trained by patent offices from developed countries to grant patents on secondary applications over existing substances, based on legal fictions of novelty. An example of this are selection patents whereby the application claims one claim is specifically made from a range of claims in an earlier patent. provide an effective means of evergreening, since protection can be extended for the full length of a new patent, i.e. normally twenty additional years, despite the fact that novelty was actually lost when such items were first disclosed.

Major considerations in interpreting "novelty"

- Assessment of novelty should be based on what has been expressly disclosed in the prior art, as well as what has been implicitly or inherently disclosed in the prior art

- The discovery of a previously unknown property of a substance does not render the substance patentable.
- More than one document may be used to establish the lack of novelty.
- The determination of novelty should include information disclosed in patent applications filed in the same country that are published on or after the filing date of the application being examined.

Definition of *Inventive Step*

Generally, patent laws define inventive step (or non-obviousness) based on a legal fiction. They assume a judgment made by a person skilled in the art, with ordinary knowledge or expertise in a given technical field. The determination of the knowledge and capability of such a person is crucial to ensuring that the patent system rewards those who contribute new technical solutions, and to avoiding the grant of patents over minor or trivial developments

that may block innovation or exclude legitimate competition. This is particularly important in the pharmaceutical sector, where patents are often strategically used to deter the market entry of generic medicines at lower prices.

Inventive step should be interpreted not only on the basis of what is formally documented in the prior art, but also what an expert, such as a person trained and experienced in disciplines relevant to the pharmaceutical sector, could consider evident in the light of such prior art. Thus the identification of a pharmaceutically suitable salt to manufacture a medicine, or its formulation to ensure a certain release characteristic (e.g. slow release) of the active ingredient, are part of the common knowledge of people working in those fields. Only in very rare occasions will a salt or formulation, even if new, comply with a rigorously applied inventive-step requirement.

Person Skilled in the Art

The level of knowledge attributed to the fictional "person skilled in the art" is very critical to the determination of non-obviousness of a claimed invention. This is defined in varying terms under different patent laws and is therefore open to interpretation. For example, the patent law of Sri Lanka defines inventive step with reference to its non-obviousness to a person having *ordinary* skill in the art. On the other hand, some patent laws like that of India and the Philippines defines inventive step with reference to the claimed invention not being obvious to a person skilled in the art, but does not define the level of knowledge to be attributed to this fictional person. However, in India the patent examination guidelines attribute a certain level of knowledge to the hypothetical person skilled in the art , who is–

"… presumed to know all the prior arts as on that date, even non-patent prior art available to the public. He has knowledge of the technical advancement as on that

date, and the skill to perform experiments with the knowledge of state of the art. *He is not a dullard and has a certain modicum of creativity*."

Some other countries might also attribute the level of knowledge of a person skilled in the art in the statutes itself- For example, the patent law of Indonesia (article 7) defines inventive step with reference to whether the claimed invention is not predictable beforehand for someone who has "certain expertise" in the given technical field.

Thus, where there is lack of statutory guidance or ambiguity about the level of knowledge that the hypothetical person skilled in the art should be presumed to possess, the courts might be required to interpret the same. For example, in the US, in *KSR vs Teleflex* the court interpreted that the statutory reference to a person of ordinary skill in the art did not imply an automaton, but a person with some ordinary creativity, or as explained in the Indian patent examination guidelines mentioned above, a person with a certain modicum of creativity. Hence, inventive step could be assessed on the basis of whether a claimed invention is obvious to an expert or a team of experts with ordinary creativity in the relevant technical field.

The "Obvious to try" test

One of the main stages of pharmaceutical research includes experimenting in order to determine whether a selected compound has the desired therapeutic properties. Some compounds may have some properties which may be useful in treating certain diseases. However, it is only through experiment and testing that the effectiveness and safety of such compounds with the relevant properties can be established. It may sometimes be difficult or even impossible to predict with precision which of the selected compounds would have the desired effects. In such cases, courts apply a two-prong analysis: 1) was it obvious to try for a person skilled in the art: and 2) was there a reasonable expectation of success.

The first prong of the test, the "obvious to try" element, deals with situations where it is obvious to try a particular route or method. Such a situation may arise where the general disclosure in a patent application may raise a scientist's curiosity to undertake further research, but the disclosure itself does not contain a sufficient teaching of how to obtain a desired result. However, it is assumed that if a route or method disclosed in a patent application would be obvious to try to obtain certain results, the skilled person would be motivated to try it. If this is accompanied by a reasonable expectation that the method obvious to try is likely to be successful (even if not fully certain), then the conclusion could be drawn that the result is obvious and hence, non-inventive.

The "Problem-Solution" Approach

Patent examination practices in many countries have been influenced by the technical assistance provided by the European Patent Office which follows the "problem-solution" approach. Under this approach a claim can be construed to have an inventive step if a solution has been found to a problem or an unexpected advantage has been obtained. However, such an assumption is based on a legal fiction and the existence of an inventive step should not be assumed merely because a solution to a

problem has been found. The solution found must be the outcome of an inventive activity. With regard to pharmaceutical substances, mere claims that the proposed solution offers certain advantages such as increased bioavailability, low effective dosage forms, etc. are not sufficient in themselves to imply an inventive step.

Unexpected or Surprising Results

Pharmaceutical patent applications could also claim to be non-obvious on the ground of finding a surprising effect or unexpected results in course of its research. While such a finding may be an indicator of inventive step in some cases, it is not necessarily the case always. For example, in *Actavis vs. ICOS Corporation*, the UK Supreme Court ruled a patent claim on a low daily dosage range of an existing drug with an unexpected finding of reduced side effects at the claimed dosage range to be obvious, on the ground that exploring the lowest possible effective dosage range was obvious to try, and hence the result was born of a routine activity.

Major considerations in interpreting Inventive Step or Non-Obviousness

- Patents should only be granted when the claimed object is the result of an inventive activity.
- A claimed invention should be assessed in the light of the knowledge of an expert, or a team of experts, with ordinary creativity in the technical field, as the hypothetical person skilled in the art.
- A specific prior art document is not indispensable to prove that a claimed invention falls within the common knowledge, or that it is obvious for an expert in the field.
- A presumption may be raised that if a route or method would be obvious to try to obtain certain results in the light of the teaching of the patent, the skilled person would be motivated to try it. If this is accompanied with a reasonable expectation of success, the result, however unpredictable or surprising, will be obvious and non-inventive.
- The fact that a solution has been found to a problem or that an advantage has been obtained, even if unexpected, is not sufficient to prove the existence of such activity.

Definition of *Industrial Applicability*

Industrial applicability means that an invention can be made in an industry in accordance with the teachings disclosed in the patent. The patent laws of all countries in the region apply this concept with such understanding. Thus, a patent application describing a process that may be applied only in a laboratory, or how to use a medicine to achieve a certain therapeutic effect, would not be patentable. In the context of pharmaceutical substances, the industrial applicability requirement should rule out the patentability of inventions whose effects take place as the result of physiological or pharmacological actions that occur in the body. For instance, a new

therapeutic use of an existing medicine or changes in dosages of a known medicine would not be patentable.

Pharmaceutical companies generally file patent applications before completing clinical studies. Hence, the efficacy and safety of the drug has not been determined. Patent offices and courts generally accept this fact, but request that some evidence be provided to support an application. The courts can take into consideration the nature of the disease claimed to be treatable by the claimed utility. Claims for curing or preventing a disease generally require greater proof of utility compared to claims for method of treatment or treating a symptom; in the latter case, adequate test data can be sufficient evidence of utility.

Major considerations in interpreting Industrial Applicability

- To be patentable the invention must be capable of being made in an industry.
- The use or methods of use of a medicine, including the specification of a certain dose, and processes that do not allow a person skilled in the art to obtain a product in industry, should be deemed as lacking industrial applicability.

Sufficiency of Disclosure

An additional condition for the grant of a patent is the determination whether the invention has been sufficiently disclosed in the patent specification so as to allow a person skilled in the art to make or practice the claimed invention.

The requirement of sufficient disclosure is present in the patent laws of some countries in the region. For example, the Indian patent law requires the complete patent specification to disclose the best method of performing the claimed invention which is known to the applicant. The patent law of Sri Lanka requires the description in the patent application to disclose the invention in a manner that is sufficiently clear and complete for the invention to be carried out by a person having ordinary skill in the relevant field of technology, and particularly indicate the best mode of carrying out the invention that is known to the applicant.

It is noteworthy that while some patent laws require the disclosure to be sufficiently clear and complete for the invention to be carried out by a person with ordinary skill in the art, some other patent laws specifically require the disclosure of the best mode of performing the invention that is known to the applicant. Where the statutes are silent or ambiguous on the standard of sufficiency of disclosure requirement, an interpretation in favour of the best mode of performing the invention known to the applicant can be adopted.

Lack of sufficient disclosure is often a reason for the refusal of a patent application or the revocation of a patent. This is a matter of substance, not form. With regard to

pharmaceutical patent claims, it is a common practice to file so called Markush claims covering a range of compounds while only clearly disclosing a few specific compounds. Such claims could objected or limited on the ground of lack of sufficiency of disclosure. The same objection may be raised when a patent application generically claims formulations, salts, polymorphs, and so on without specifically characterizing them in the specification.

Similar to the inventive step requirement, the sufficiency of disclosure is also tested against the level of knowledge held by a person skilled in the art. However, the level of knowledge attributed to the person skilled in the art could vary in the two different contexts. Whereas for inventive step assessment it may be assumed that the person skilled in the art has some capacity of experimentation to derive what may be obvious from the teaching of the patent, in the case of sufficiency of disclosure it may be assumed that the person skilled in the art should be able to implement the teaching into reality without any undue burden of experimentation.

Major considerations in interpreting the standard of Sufficiency of Disclosure

- The disclosure of the claimed invention should be precise and clear enough for a person with average knowledge in the field to reproduce the invention without undue burden of experimentation.
- The disclosure should cover all the embodiments of the claimed invention and not only some of them, such as in a Markush claim.

Provisions Relating to Patentability Criteria in National Patent Laws

Criteria	India	Indonesia	Malaysia	Pakistan	The Philippines	Sri Lanka	Thailand	Viet Nam
Invention	New product/process involving inventive step and capable of industrial application, subject to exclusions under sections 3 and 4 (inventions not patentable)	The inventor's idea that is poured into a specific problem solving activity in a field of technology in the form of a product or process, or the improvement and development of a product or process, subject to exclusions under article 4	An invention means an idea of an inventor which permits in practice the solution to a specific problem in the field of technology. An invention may be or may relate to a product or process.	Invention means any new and useful product or process, in any field of technology and includes any new and useful improvement of either of them	A patentable invention is any technical solution of a problem in any field of human activity	Invention means an idea of an inventor which permits in practice the solution to a specific problem in a field of technology. An invention may be or may relate to a product or process.	No provision defining invention	An invention means a technical solution in form of a product or process which is intended to solve a problem by application of laws of nature
Exclusion of inventions not patentable (concerning new forms or uses of known substances)	Section 3(d) – mere discovery of new form of known substance which does not result in enhancement of known efficacy of that substance or new property/use of a known substance or mere use of a known process Section 3(e) – substance obtained by mere admixture resulting in	Article 4(f) – The invention does not cover findings (discovery) in the form of 1) new uses for existing and/or known products; and for 2) a new form of an existing compound that does not result in a significant increase in efficacy and there are known differences in the	No specific exclusion of new forms of known substances. Section 13 generally excludes discoveries and methods of treatment.	A patent shall not be granted for a new or subsequent use of a known product or process, and for mere change in physical appearance of a chemical product where the chemical formula or process of manufacture remains the same, provided that this clause	Section 22.1 - Discoveries are excluded, In the case of drugs and medicines, the mere discovery of a new form or new property of a known substance which does not result in the enhancement of the known efficacy of that substance, or the	No specific exclusion of new forms of known substances. Discoveries and methods of treatment are excluded	No specific exclusion of new forms of known substances. General provision on exclusions of inventions from patentability does not mention discoveries, but methods of treatment are excluded.	No specific exclusion of new forms of known substances. Discoveries and methods of treatment are excluded.

	mere aggregation of the properties of the components thereof or a process for producing such substance	associated chemical structure of the compound		shall not apply to an invention fulfilling the criteria of patentability	mere discovery of any new property/new use for a known substance is excluded			
Novelty	"new invention" means any invention or technology which has not been anticipated by publication in any document or used in the country or elsewhere in the world before the date of filing of patent application with complete specification	An invention is considered new if on the filing date the invention is not the same as the previously disclosed technology. The previously disclosed technology is a technology that has been announced within or outside Indonesia in written, oral description or through demonstration, use or other ways that enable an expert to implement the invention before the receipt date or priority date	An invention is new if it is not anticipated by prior art. Prior art shall consist of everything disclosed to the public, anywhere in the world, by written publication, oral disclosure, use or in any other way, before the priority date of the application concerned	An invention shall be considered new if it does not form part of the state of the art. The state of the art shall comprise everything disclosed to the public anywhere in the world by publication in tangible form, oral disclosure or in any other way	An invention shall not be considered new if it forms part of prior art. Prior art shall consist of everything that has been made available to the public anywhere in the world before the filing or priority date of concerned patent application	An invention is new if it is not anticipate by prior art. Prior art shall consist of everything disclosed to the public, anywhere in the world, by written publication, oral disclosure, use or in any other way, prior to the filing or priority date of the application	An invention is new if it does not form part of the state of the art. State of the art includes inventions widely known or used by others in the country before the date of application of the patent, an invention for which a patent was granted in Thailand or any other country, or applied for and published before the date of application of the patent	An invention shall be considered novel if it has not been publicly disclosed through use/written description/in any other form, inside or outside the country, before the relevant filing or priority date of an application
Inventive Step	Feature of an invention that involves technical advance as	An invention contains an inventive	An invention shall be considered as	An invention shall be considered as	An invention consists an inventive step if,	An invention shall be considered as	An invention shall be taken to involve an	An invention shall be considered

	compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art (explained further in patent examination guidelines)	step if the invention for someone who has certain expertise in the field of engineering is something that cannot be predicted beforehand	having an inventive step if, having regard to any matter which forms part of the prior art, such inventive step would not have been obvious to a person having ordinary skill in the art	having an inventive step if it is not obvious to a person skilled in the art prior to the date of application of the patent, having regard to any matter which forms part of the state of the art	having regard to prior art, it is not obvious to a person skilled in the art at the time of filing date or priority date of the application. In the case of drugs and medicines, there is no inventive step if the invention results from the mere discovery of a new form or new property of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of a new property/new use of a known substance	involving an inventive step if, having regard to the relevant prior art, such inventive step would have been obvious to a person having ordinary skill in the art	inventive step if it is not obvious to a person ordinary skilled in the art	involving an inventive step if , based on technical solutions already publicly disclosed (prior art), it constitutes an inventive progress and cannot be easily created by a person with average knowledge in the art
Industrial Applicability	The invention is capable of being made or used in an industry	The invention can be applied in industry if the invention can be implemented in industry as	An invention shall be considered industrially applicable if it can be made or used in any kind of	An invention shall be considered to be capable of industrial application if it is capable	An invention that can be produced or used in any industry	An invention shall be considered industrially applicable if it can be made or	An invention shall be taken to be capable of industrial application if it can be made	An invention shall be considered susceptible of industrial application if it is possible

		described in the application	industry	of being manufactured or otherwise industrially used		used in an industry	or used in any kind of industry including handicrafts, agriculture and commerce	to realize mass manufacture or production of products or repeated application of the process that is the subject matter of the invention, and to achieve stable results
Sufficiency of Disclosure	Every complete specification shall disclose the best method of performing the invention which is known to the applicant and for which he is entitled to claim protection	The description of the invention must clearly and completely disclose how the invention can be implemented by a person who is an expert in the field	The Patents Regulations requires the application to disclose the invention in such terms that it can be understood and in a manner sufficiently clear and complete for the invention to be evaluated and to be carried out by a person having ordinary skill in the art, describe the best mode contemplated by the applicant for carrying out the invention, and also describe	Every complete specification shall fully and particularly describe the invention and the method by which it is to be performed	The application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.	The description shall disclose the invention in a manner sufficiently clear and complete for the invention to be evaluated, and to be carried out by a person having ordinary skill in the relevant technology, and shall, in particular, indicate the best mode known to the applicant for carrying out the invention.	The application shall contain a detailed description of the invention in such full, concise, clear and exact terms as to enable any person ordinarily skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention and setting forth the best mode contemplated by the inventor to carry out his invention	The invention must be fully and clearly described to the extent that the invention may be realized by a person with average knowledge in the art

			the way in which the invention can be industrially applicable, and the way in which it can be made and used.					

Unique Elements of Pharmaceutical Patent Claims

While pharmaceutical patent claims have common features with inventions in other fields of technology, pharmaceutical patent claims have some unique elements determined by their intended use. In fact, a single drug may have a large portfolio of secondary patents besides the primary patent. There has been a proliferation of patent applications in the field of pharmaceuticals claiming polymorphs, salts, formulations, etc. and so on, which are often made to prevent generic competition rather than to protect genuine inventions. This strategy, known as evergreening, does not contribute to the technological pool, and they limit the market entry of generic products. This can have adverse consequences on availability, access and affordability of treatments and technologies. A number of countries in region have adopted legislation or policies for examining patent applications relating to pharmaceutical products and processes in a manner that accounts for public health considerations. The proper application of patentability standards can prevent the grant of 'poor quality' or trivial patents, which, by preventing the timely entry of generic competition, may harm public health.

Typical Claims Relating to Pharmaceuticals

Markush Claims

A claim made over a general chemical structure (formula) that may cover millions of alternative compounds that allow for the protection, under a single patent, of several variants of a claimed invention. In this way, sometimes millions of compounds may be covered through a single patent, while only disclosing examples of some of the compounds covered under the general formula. Recent studies show a growing use of Markush claims in several developing countries, where such claims accounted for more than 50 percent of all patent applications relating to pharmaceuticals. Such claims raise concerns regarding sufficiency of disclosure, and the true nature of the invention. It is also impossible to ensure full prior art search for establishing novelty and inventive step for the millions of compounds included in such a claim. Patent offices in many countries, including from the region, have adopted guidelines and practices to reduce the scope of such claims. These include requirements to ensure sufficiency of disclosure, and limiting the scope of the patent to the claimed embodiments that are actually enabled by the disclosure in the patent specification.

Selection Patents

Selection patents are claims made by selecting a subgroup of elements from a larger group on the grounds that a new, unexpected property has been found. For instance, if a Markush claim was admitted in relation to a set of pharmaceutical compounds, the patent owner might later file a new patent application covering one or more of such compounds. Thus, the patent owner may obtain a further 20-year monopoly simply by picking one or more compounds out of the generic formula.

The grant of selection patents, if allowed, implies that the coverage of a patent may be much wider than its disclosure. In other words, while the holder of the patent would get protection on all the embodiments of the basic patent, the subsequently selected elements (although protected) would be considered as not disclosed and, hence, novel. This argument was rejected by the Supreme Court of India in *Novartis AG v. Union of India & Others* (Judgment of 1 April 2013).

Patent offices and courts have considerable flexibility when dealing with selection patents. There is no obligation under the TRIPS Agreement to consider that the specific selection of disclosed compounds still eligible for patent protection based on the argument that a generic claim does not disclose its specific components. Hence, it can be interpreted that the selection of elements included in a disclosed group lacks novelty, such as in the case of compounds disclosed in a prior generic chemical structure or included within a numerical range. Patents should not be granted either in cases where a selection of elements is made from a list of known compounds, or where a selection is made of starting materials and alternative processes to obtain a compound.

Polymorphs

A chemical compound in its solid state may exist in more than one form or crystal structure. This is known as polymorphism. Some polymorph structures of the same compound may offer more thermodynamic stability to assure a reproducible bioavailability over the drug's shelf life, and in different storage conditions. Polymorphs of drug substances are obtained through standard crystallization methods with the intervention of variable thermodynamic and kinetic factors, such as temperature, humidity and time. Polymorphism is an inherent property of a substance, which is not invented but discovered through standard laboratory tests. They also cannot be construed to demonstrate inventive activity, as it is obvious for a person skilled in the art in the pharmaceutical sector to seek the most thermodynamically stable polymorph of the compound. Even if the process to obtain a polymorph may be difficult, it should be obvious to a person skilled in the art. However, a large number of

patent applications are filed claiming polymorphs. Patent offices and courts have become increasingly reluctant to grant such patents. The most notable example from the region is the claim on a polymorph (beta crystalline form) of imatinib mesylate which was rejected by the Indian patent office and upheld by the Supreme Court. In some countries, they are rejected as a matter of course.

Therefore, patents on polymorphs should be denied on the grounds of absence of a patentable invention or inventive activity. This conclusion may be reached even in cases where a document providing the basis for an inventive-step analysis in relation to the specific claimed polymorph is not identified; obtaining a polymorph is a routine activity in pharmaceutical production, carried out through methods widely known to a person skilled in the art. However, a process used for the preparation of a polymorph, if novel and involving inventive step, may be patentable.

Enantiomers

A large proportion of drugs in the market are chiral molecules, i.e., they exist as a pair of molecules that are mirror images of each other. Each of these pair of molecules is an enantiomer with the natural property of being able to rotate plane polarized light in a mutually opposite directions. In this way, enantiomers come together to form what is known as a racemic mixture, where the enantiomers are present in equal amounts. Sometime, one of the enantiomers may have properties that are pharmaceutically attractive and hence, the person skilled in the art can attempt to separate the enantiomer from the racemic mixture. A person skilled in organic chemistry in the pharmaceutical sector is well aware that the individual enantiomers in a racemic mixture frequently differ in their biological/therapeutic effects, and that the mixture's pharmacological activity is normally attributable to one of the enantiomers. It is also known that the inactive enantiomer may sometimes have undesirable or toxic side effects. The techniques applicable to separate enantiomers in a racemic mixture are well known. However, patent applications often claim an isolated enantiomer and its method of isolation.

When the racemic mixture is known, the patentability of individual enantiomers can be questioned on several grounds: 1) the enantiomer is inherently present in the racemic mixture; and 2) for a person skilled in pharmaceutical research and development it is obvious to try and isolate the therapeutically active enantiomer. Even if the process of isolation and purification of an enantiomer may be difficult, that is not an indicator of inventive activity.

Therefore isolated enantiomers should not be deemed patentable when the racemic mixture was previously disclosed. Processes for the separation and

purification of enantiomers may only be patented if novel and inventive. Any difficulty in developing and applying such processes is not by itself sufficient to prove inventive activity.

Salts

Pharmaceutically suitable salt of a compound in free base or acid form may be sought when the drug is not sufficiently soluble or stable, or when it is difficult to purify, handle or process during manufacturing. Different salts may lead to different solubility, bioavailability and efficacy, and to different organoleptic characteristics (such as taste, smell) or other properties. The choice of a salt for a particular drug is important in obtaining certain desirable characteristics related to stability, bioavailability, manufacturability and route of administration to the patient.

The preparation of pharmaceutically suitable salts is a mature technical field. The individual salt-forming acids and bases, their relevant properties and the processes for their preparation are familiar to any person with ordinary training in the formulation of pharmaceuticals. The discovery that that a particular salt has advantages over the free base/acid drug or other salts does not mean that it results from an inventive activity. The preparation of salts, with advantageous properties over the drug in its free base/acid form, is part of the common knowledge of a person skilled in the art. Thus, while a salt may be novel and industrially applicable, it will very rarely comply with the requirement of inventive step.

However, it has been common in the pharmaceutical industry to file patent applications on particular salts of a compound as a means of evergreening. If such patents are granted, generic drugs may be prevented from entering the market. Therefore, patent applications on particular salts should normally face an objection of lack of inventive step. Generic references to pharmaceutically acceptable salts in patent applications covering a compound should not be allowed either, as they would fail the sufficiency of disclosure requirement.

Ethers and Esters

Ethers and esters are two kinds of hydrocarbon bonds that can be derived from a chemical compound. Ethers and esters are generally more lipid soluble than salts, thereby altering tissue penetrability and sometimes the rate of release of a drug, as with steroids. Esters may use the safety or efficacy of a drug. However, ethers or esters would not generally enhance the therapeutic efficacy of a drug.

The preparation of ethers and esters of a compound is part of the common knowledge of a person skilled in pharmaceuticals. It is generally obvious to predict the claimed advantages that an ether or ester will provide compared.

to the free base or free acid compound. A skilled person would be able to anticipate the characteristics that may be achieved and how the compound will perform. Hence, like in the case of salts, the preparation of ethers or esters to achieve advantageous properties over the drug in its free base or acid form is part of the common knowledge of a person skilled in the art. Patent applications on particular ethers and esters will normally lack inventive step. Generic references to ethers or esters in patent applications covering an active ingredient or other subject matter should not be allowed.

Compositions

A large number of patent applications claim 'compositions' (or 'formulations') of known drugs. The active pharmaceutical ingredient made of the active compound is turned into different compositions as pills, injectibles, etc, by using pharmaceutically acceptable carriers or excipients – such as fillers or diluents, binders, stabilizing agents (such as pH regulators), disintegrants, and lubricants. The preparation of formulations is a mature technological field and falls within the competence of a person normally skilled in pharmaceutical formulation. The techniques for the preparation of compositions to ensure the delayed (e.g. using one or more enteric coating layers) or rapid release of an active ingredient are also well known. It is obvious for a person working in formulation to seek the most appropriate form for administering a drug. Similarly, the micronization of a drug (for instance, when it is poorly soluble) is a well-known method to improve drug delivery that only entails changes in the physical form. If granted, patents over formulations may obstruct the functioning of the generic market for the respective active ingredient, even if off-patent, particularly when a given composition is the most suitable for administration of a medicine. While a particular composition may have some advantageous effects (e.g. increased bioavailability, more stability during storage, inhibiting gastric acid secretion), this does not mean that its preparation results from an inventive activity. Formulation techniques are part of the common knowledge of the person skilled in the art. While some compositions may be novel, they would normally fail to satisfy the inventive step requirement. Therefore, the preparation of pharmaceutical compositions (formulations) requires the use of techniques and compounds commonly known to a person skilled in that field. Patent applications on compositions will normally confront an objection of lack of inventive step. Generic claims over compositions associated with new active ingredients, prodrugs, etc. with unspecified carriers or excipients will also be objectionable.

Doses

Some patent applications claim independently, or as part of a broader claim, the dose for administrating a particular drug. Patents over doses constitute

another form of evergreening, potentially blocking the marketing of generic versions when, for instance, the prescribed dose of a drug is included in the range covered by the patent. Often, claims of this type are drafted with the appearance of a claim covering composition and claim a formulation at a specific dosage. Dose-based claims are subject to objections of lack of industrial applicability. While they may be drafted in a manner that suggests a product claim, in reality they cover a method of medical treatment that, by definition, produces effects in the body and is deprived of industrial applicability. In addition to the lack of industrial applicability, in countries where methods of treatment are excluded from patentability, a dose-based claimed would be unacceptable. Hence, claims over the dose of a drug should be treated as a method of medical treatment, in spite of their appearance, for instance, as a composition (or combination) claim.

Combinations

Often two (or more) known drugs are combined in a single product, and patent protection over the combination is claimed. Many patent laws specifically exclude from patentability the juxtaposition or combination of known products, unless a new or synergistic effect may be found, such as when one of the drugs enhances or magnifies the therapeutic effects of the other. A typical example is the combination of certain doses of codeine with acetaminophen or ibuprofen to enhance pain relief. In the absence of such synergistic effects, a patent application on a combination of drugs will be rejected by many patent offices, or a patent will be revoked by courts. Patents on combination of drugs may be objected both on grounds of lack of novelty (e.g., where the use of the different drugs that are components of the combination was already in use in the medical profession to attain a certain therapeutic result before the patent application was filed) as well as lack of inventive step. Such claims may also be excluded as claims on methods of treatment.

In sum, combinations of known drugs may be considered a method of treatment and hence be deemed non- patentable because they lack industrial applicability or are excluded from protection under national law. In some cases, combination claims do not meet the novelty standard, such as when the combination was previously known and practised by the medical profession. In addition, such a combination will not satisfy the inventive step standard, unless a synergistic effect, justified by appropriate clinical tests, can be demonstrated. However, synergistic effects that may be reasonably expected from the combination of two or more drugs of known therapeutic classes do not meet the inventive step standard.

Prodrugs

Many medicines are commercialized as prodrugs. A prodrug is a precursor of a drug, which undergoes a chemical conversion by metabolic processes in the body before becoming therapeutically active. Prodrugs are often claimed independently from the active drug when a patent on the active drug has expired or is about to expire. In some cases, patent applications contain generic references to 'all prodrugs' of a given compound. The active moiety of the drug and prodrug is the same, hence the latter will generally lack inventive step. A prodrug may be regarded as the original drug 'in disguise' as noted by a British court in the case of hetacillin, an acetone adduct of ampicillin that is immediately hydrolyzed in the body to ampicillin. A key consideration under patent law is whether the development of a new prodrug is the outcome of an inventive activity or of routine research and experimentation. In examining claims over prodrugs, it should be determined whether the patent on the basic drug covers the prodrug. If this is the case, the new application will not be admissible. A claim on a prodrug will generally fail to meet the inventive step standard unless evidence is provided that it overcomes pharmaceutical or pharmacokinetically based problems of the parent drug in a non-evident manner. Generic claims over specified prodrugs should not be allowed.

Metabolites

An active metabolite is the compound that remains after a drug is metabolized by the body. Enzymes in the liver are responsible for chemically changing drug components into metabolites, which contain the same functional group as its parent drug. An active metabolite retains most, if not all, of the properties of its parent drug, until its carbon structure blends into larger structures or is reduced to smaller structures. Active metabolites may be identified, synthesized and commercialized as a product different from the parent drug. Often, patent applications on specific active metabolites are filed. In some cases, however, generic references to 'all metabolites' are included in patents claiming an active ingredient. Active metabolites cannot be deemed an invention because they are naturally produced through the metabolism. Although there may be advantages in administering an active metabolite compared to the parent drug, any advantages do not stem from an inventive activity. Isolating and characterizing a metabolite can be done using knowledge common to a person skilled in the pharmaceutical field. Moreover, an active metabolite may be deemed deprived of novelty, based on the concept of inherency.

New Medical Use

Claims over a new medical use of a known medicine (often called 'second use claims') account for a good part of the proliferation of pharmaceutical patents. When a patent is about to expire or has expired, pharmaceutical companies may attempt to extend their monopoly by applying for patents for one or more new therapeutic uses of an active ingredient. If granted, such patents may be used to prevent generic competition and to justify high prices for drugs that are actually off-patent. Second use' claims have been accepted in some jurisdictions. In Europe, for instance, on the basis of a fiction of novelty and industrial applicability, they were allowed if drafted as "use of a substance or composition X for the manufacture of a medicament for therapeutic application Z." This so-called Swiss-type claim gives the appearance of a claim to an invention with a technical character, which is actually absent. While some countries followed the EPO approach, some others explicitly exclude the patentability of new uses of known medicines. Knowing that an existing compound can also be used to treat other diseases or symptoms is not an invention, as the pharmacological effect is intrinsic to the compound. The new use is simply discovered through clinical trials or observation during the marketing period. Patentability of a use claim can be denied based on the grounds that it is a discovery rather than an invention. A claim on the new use of a medicine is equivalent to a claim on a method of medical treatment. The only contribution made in such a claim is information for the physician about the way to use a drug to achieve a new therapeutic effect. The effects take place in the body. There is no technical effect, since the claim does not cover the product and process of manufacture, but merely a given form of use. It does not matter how a claim relating to a new use of a drug is drafted; 94 it does not change its essence as a claim on method of treatment.

Exercise

- In your opinion, in determining whether a claim is patentable, what is the first question that should be considered?
- In determining whether a claim constitutes an invention, what should be the legal presumption concerning claims on new forms, use or property of a known substance?
- On what basis should the novelty of a patent claim be assessed? How should the scope of the prior art against which novelty is to be assessed be determined?
- In the assessment of inventive step or non-obviousness, what level of knowledge should be attributed to the fictional person skilled in the art?
- What should be the major considerations concerning inventive step determination on claims based on subsequent research in the light of the teaching in a patent?
- Can the existence of inventive step be presumed merely on the basis that a solution has been found to a problem or an unexpected advantage has been obtained?
- Can a patent claim on a new therapeutic use of an existing medicine or changes in dosages of a known medicine be deemed to be industrially applicable?
- What are the public policy objectives behind the requirement of sufficient disclosure of the invention claimed in a patent application? What should be the considerations in determining whether a patent specification sufficiently discloses the claimed invention, in the light of the public policy objectives of the disclosure requirement?
- Do you agree or disagree with the following statements
    - Patents on Markush claims should be limited to the claimed embodiments that are actually enabled by the disclosure in the patent specification.
    - A selection patent should be deemed to lack the requirement of novelty.
    - Discovery of a thermodynamically stable polymorph of a chemical compound that allows enhanced storability and bioavailability is a patentable invention.

- An isolated enantiomer from a known racemic mixture is the outcome of an inventive activity.
- The discovery of pharmaceutically suitable salts, ethers and esters of a compound are patentable inventions.
- A patent claim on a pharmaceutical composition offering some advantageous effect may be the outcome of an inventive activity.
- A patent claim on a particular dosage form of a drug can be denied on the ground of lack of industrial applicability, or excluded as a method of treatment.
- A prodrug can be patentable even if the active compound.
- A claim on a prodrug will generally fail to meet the inventive step standard unless evidence is provided that it overcomes pharmaceutical or pharmacokinetically based problems of the parent drug in a non-evident manner.
- Patent claims on the active metabolite of a drug can be deemed to lack novelty and inventive step.
- A patent claim on new medical use of a known medicine can be deemed to not constitute an invention or excluded from patentability as a method of treatment.

➢ What are the grounds on which a patent claim on a combination of known drugs be objected?