



Guidelines on Patentability and Access to Medicines¹

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Abstract

The important relationship between the examination of patents carried out by national patent offices and the right of citizens to access to medicines hasn't always been well-understood. Too often these are viewed as to unrelated functions or responsibilities of the State . And the reason is clear: Patentability requirements are not defined by patent offices, but frequently by the courts, tribunals, legislation or treaty negotiators.³ This is the case when patent policy is implemented in isolation from, rather than guided by, public health policy. Today there is greater recognition that patent examiners and the examination of patents play a key role in facilitating or obstructing access to medicines. Given the impact of pharmaceutical patents on access to medicines, patent offices should continue to align their work in support of national health and medicine policies, using the freedom permitted by the TRIPS Agreement to define patentability requirements. The establishment of guidelines for the examination of pharmaceutical patents can constitute a valuable tool that is conducive to this objective.

This policy brief discusses the guidelines for the examination of pharmaceutical patents developed by

WHO that serve as a guide for the drafting of internal procedure manuals of national intellectual property offices for the examination of patentability of chemical-pharmaceutical inventions.

1. Introduction

In 1994, the creation of the World Trade Organization (WTO) resulted in the establishment of a new treaty, the broadest on intellectual property rights: the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement). This Agreement linked issues of intellectual property and trade for the first time and provided a multilateral mechanism to resolve disputes between States. The TRIPS Agreement requires all WTO Member States to incorporate into their legislation universal minimum standards for almost all rights in this domain: copyright, patents and trademarks.⁴ International agreements prior to the TRIPS Agreement did not specify minimum standards on intellectual property. Before the TRIPS Agreement, over 50 countries did not provide patent protection for pharmaceutical products; many provided patent protection for the processes but not the products and in a large number of countries, the duration was less than 20 years.⁵

Contents

| | |
|--------------------------------------|---|
| ABSTRACT | 1 |
| 1. INTRODUCTION | 1 |
| 2. THE PROBLEM | 2 |
| 3. A HISTORY OF THE GUIDELINES | 4 |
| 4. CONCLUSION | 6 |
| ENDNOTES..... | 7 |

A patent is “a title granted by the public authorities conferring a temporary monopoly for the exploitation of an invention upon the person who reveals it, furnishes a sufficiently clear and full description of it, and claims this monopoly.”⁶ As with any monopoly, it may lead to high prices that in turn may restrict access. The problem is compounded in the case of medicines, when patents confer a monopoly for a public good and essential products needed to prevent illness or death and improve health.

According to the TRIPS Agreement, the patentability requirements used by national intellectual property offices require a product or manufacturing process to meet the conditions necessary to grant patent protection, namely: novelty, inventive step and industrial applicability (utility). These three elements, however, are not defined in the TRIPS Agreement and WTO Member States are free to define these three criteria in a manner consistent with the public health objectives defined by each country.

According to the report of the United Nations High Commissioner for Human Rights “The requirements under the TRIPS Agreement for the grant of patents – novelty, inventive step and industrial applicability – are open to interpretation under national legislation and each country can decide according to local conditions. Consequently, the High Commissioner encourages interpretations of these requirements that do not lose sight of the public interest in the wide dissemination of knowledge...”⁷

Suggest to explain why this flexibility is important, i.e. avoid frivolous patents, evergreening, high costs of medicines, delay entry of follow-on drugs, etc.

It is important to note that a patent is a territorial right and that it is therefore possible to grant a patent for an invention in one country but that this can be legally rejected in another. At the same time, a patent that has been issued in one country can be revoked if it is demonstrated that the patent office ought not to have granted it. It is also important to highlight that in the pharmaceutical sphere, the situation is not *one product = one patent*. An invention can be protected by numerous patents; the production process for the product can also be protected by one or numerous patents; and in many countries a combination or

new clinical indication can be patented. As a result, a single medicine can be protected by a large number of patents.

It is widely held that patents are granted to protect new medicines to reward the innovation effort. However, the number of patents obtained annually to protect truly new pharmaceutical products is very low and falling. Moreover, of the thousands of patents that are granted for pharmaceutical products each year, a few are for new medicines – e.g. new molecular entities (NMEs).

All of the above led World Health Organization (WHO), in collaboration with the United Nations Conference on Trade and Development (UNCTAD), the United Nations Development Programme (UNDP) and the International Centre for Trade and Sustainable Development (ICTSD), to develop, in 2007, guidelines for the examination of pharmaceutical patents from a public health perspective.

The guidelines or directives were intended to contribute to improving the transparency and efficacy of the patent system for pharmaceutical products, so that countries could pay more attention to patent examination and granting procedures in order to avoid the negative effects of non-inventive developments on access to medicines.⁸

2. The Problem

Four major problems can be identified in the current use of the patent system to protect pharmaceutical innovation: reduction in innovation, high prices of medicines, lack of transparency in research and development costs, and proliferation of patents.

2.1 Reduction in pharmaceutical innovation

A study carried out by the journal *Prescrire* analysed the medicines that were introduced to the French market between 2006 and 2011 (six years), arriving at the conclusion that the number of molecules that produced significant therapeutic progress reduced drastically: 22 in 2006; 15, 10, 7, 4 in the following years up to 2011, which was a year in which *Prescrire* declared that only one medicine of significant therapeutic interest was brought to the market.⁹ Given that France is one of the largest pharmaceutical markets in the world, where the State also pays the bills for medicines, it can be supposed that the large majority of medicines that were released in the world between 2006 and 2011 were introduced into the

French market. In other words, the reduction in innovation confirmed in France is a good indicator of the global situation.

2.2 High prices of medicines

Oncologists from fifteen or so countries recently denounced the excessive prices of cancer treatments, which are necessary to save the lives of the patients, and urged that “moral implications” should prevail.¹⁰ According to this group of oncologists, of the 12 cancer treatments approved in 2012 by the United States Food and Drug Administration (FDA), 11 cost more than US\$ 100,000 per patient per year.

2.3 Lack of transparency in R&D costs

Since the 1950s, there have been some references to the costs of R&D for pharmaceutical products. According to some sources (see box below) these figures have increased from US\$ 1 million to US\$ 2.5 billion for the development of a single product. While there continues to be no clarity and transparency in this sphere, the difficulty that can lead to the high prices of medicines continues to be unresolved.

An article from the journal *BioSocieties*,¹³ a publication of the London School of Economics, argues that the real cost of R&D is, in fact, a fraction of the commonly quoted estimates. According to the authors

Average cost of research for a new pharmaceutical product*

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| 1950: | US\$ 1 million |
| 1970 & 1980: | Between US\$ 48 million and US\$ 54 million |
| 1991: | Tufts Center (Boston): US\$ 231 million |
| 2000: | Tufts Center: US\$ 473 million |
| 2002: | US\$ 802 million (double the cost in two years!) |
| 2008: | IFPMA: US\$ 900 million |
| 2012: | IFPMA: US\$ 1.3 billion |
| 2014: | Tufts Center (Boston): US\$ 2.56 billion |

*Prepared using diverse sources

In 2010, a group of English academics analysed the most prescribed drugs in the National Health Service (NHS) and calculated that approximately GBP 1 billion is wasted each year due to the prescription of patented “me too drugs”, for which there is an equally effective out of patent equivalent.¹¹ What is considered to be a waste of State funds resulting from the use of patented medicines in the British system is the reality in developing countries simply because of the impossibility of accessing the medicine for the majority of the population.

During the summer of 2014, a number of European countries, including France and Spain, spent many months negotiating with the company Gilead on the price of a new medicine for hepatitis C (known as brand name “Sovaldi”). The price fixed by Gilead was EUR 56,000 per patient for a twelve-week treatment, that is to say EUR 666 per tablet. According the newspaper *Le Monde* the price of each tablet was 280 times more than the production cost.¹² In France, it is calculated that 250,000 patients should receive this medicine, the cost of which would represent 7 per cent of the annual State medicine budget.

Light and Warburton, the average cost of R&D to develop a medicine varies between US\$13 million and US\$ 204 million depending on the type of product. The authors estimate an average cost of US\$ 43.4 million for R&D for each drug. And they conclude: “This is very far from the US\$ 802 million or US\$ 2.5 billion claimed by the industry.”

The Drugs for Neglected Diseases initiative (DNDi), founded by the non-governmental organization Médecins Sans Frontières (MSF) in 2004, recently published its research costs after 10 years of experience.¹⁴ Its figures are as follows:

- From EUR 6 million to 20 million to improve a treatment.
- From EUR 30 million to 40 million for a new chemical entity.

If this figure were to be adjusted as usually done for pharmaceutical R&D for infectious diseases to cover the risk of failure, the figures would be as follows:

- From EUR 10 million to 40 million to improve a treatment.

- From EUR 100 million to 150 million for a new chemical entity.

It is unfathomable that after 15 or more years of debate, there is still no consensus about the real costs of R&D for medicines. Until this issue is resolved, it will be difficult to advance constructive thinking that could determine the future of access to medicines. The differences in data between academia or non-profit initiatives, such as DNDi, and industry are between ONE and TEN.

2.4 Proliferation of patents

An investigation carried out by the European Union (EU) about the conduct and practices of the pharmaceutical industry between 2000 and 2007 found that a single medicine can be protected by up to 1300 patents or pending patent applications.¹⁵ The number of lawsuits between originator companies and generic companies has increased four-fold in the EU. These lawsuits delay the entry of the generic product by between six months and six years.¹⁶

A policy and strategy change at the patent office level could lead to significant changes. In Argentina, for example, after the introduction of new guidelines for the examination of pharmaceutical patents in 2012, the number of patents granted was 54, while in Mexico, a similar-sized market to Argentina, the number of patents applications in 2012 for pharmaceutical products was 2500.

3. WHO Guidelines for the Examination of Pharmaceutical Patents: A Public Health Perspective¹⁷

3.1 A History of the Guidelines

The fact that the TRIPS Agreement does not define novelty, inventive step and industrial applicability (utility) leaves countries significant room for manoeuvre. Therefore, patentability requirements represent the principal and most important flexibility allowed by the Agreement to protect public health and access to medicines. “Politicians and legislators have broad room for manoeuvre to give legal effect to those flexibilities.”¹⁸

In 2007 the WHO Essential Medicines Programme began to develop draft guidelines for the examination of pharmaceutical patents from a public

health perspective. Based on the first working document drafted by Professor Carlos Correa, a series of international, regional and national consultations took place with the participation of more than 50 countries.

3.2 Purpose of the Guidelines

The Guidelines for the examination of pharmaceutical patents developed by WHO are a guide for the drafting of internal procedure manuals of national intellectual property offices for the examination of patentability of chemical-pharmaceutical inventions.

It is a habitual practice of all patent offices around the world to set the level of patentability requirements that the examiners use for the examination of patents through patentability instructions or guidelines, which describe in detail the implementation of patent rights in specific circumstances.

The purpose of the guidelines for the examination of pharmaceutical patents is to provide a series of general guidelines for the examination of some common types of pharmaceutical patents granted. They respond to the growing concerns emerging in different circles¹⁹ about the proliferation of patents that protect minor variants, and in some obvious cases, existing medicines and processes (for example, changes to drug formulations and to salts, esters, ethers, isomers, polymorphs of existing molecules, and to combinations of known drugs with other known drugs), while the number of new chemical entities for pharmaceutical use is low and decreasing.²⁰ While those patents may be weak, or, if subjected to strict scrutiny, invalid, in many cases they can be used to prevent generic competition and, therefore, to reduce access to medicines.

The guidelines do not suggest the implementation of a new condition for patentability, but the taking into account of specific considerations related to innovation in pharmaceutical products when the common requirements of novelty, inventive step and industrial applicability (utility) are applied.

3.3 Content of the Guidelines

The guidelines for the examination of patents analyse and discuss the most common claims in the pharmaceutical sector. Transcribed below, for illustrative purposes, are the recommendations for each type of claim from a public health perspective that promote access to medicines.

- **Formulations and compositions**

Recommendation: New formulations and compositions, as well as processes for their preparation, should generally be deemed obvious in the light of the prior art, particularly when a single active ingredient is claimed in association with known or unspecified carriers or excipients. Exceptionally, claims of this type could be patentable if a truly unexpected or surprising effect is obtained, for instance, when a really difficult problem or a long standing need, such as a noticeable reduction in side effects, is solved in a non-obvious way, or when the solution found leads to a tremendous advantage compared to the state of the art.

- **Combinations**

Recommendation: Combinations of known active ingredients should be deemed non-inventive. If, however, a new and non-obvious synergistic effect is considered a basis for patentability, it should be properly demonstrated by biological tests and appropriately disclosed in the patent specifications.

- **Dosage/dose**

Recommendation: New doses of known products for the same or a different indication do not constitute inventions, particularly (but not only) in countries where methods of medical treatment are not patentable as such.

- **Salts, ethers and esters**

Recommendation: New salts, ethers, esters and other forms (e.g. amides) of existing pharmaceutical products should not be deemed patentable. This may not apply, exceptionally, when tests, appropriately conducted and described in the specifications, demonstrate unexpected advantages in properties such as an important difference in efficacy or side effects as compared to what was in the prior art. Processes for obtaining salts, ethers, esters and other forms should be deemed as non-patentable.

- **Polymorphs**

Recommendation: Polymorphism is an intrinsic property of matter in its solid state. Polymorphs are not created, but found. Patent offices should be aware of the possible unjustified extension of

the term of protection arising from the successive patenting of the active ingredient and its polymorphs, including hydrates/solvates. Processes to obtain polymorphs may be patentable in some cases if they are novel and meet the inventive step standard.

- **Markush claims**

Recommendation: Claims covering a large range of compounds should not be allowed. Patent offices should generally require patent applicants to provide sufficient information, such as fusion point, Infrared Absorption Spectrum (IR) or Nuclear Magnetic Resonance (NMR), obtained through true testing and experimentation to enable the reproduction by the disclosed method of each embodiment of the invention for which protection is sought. However, claims of limited scope could be granted if evidence is provided at least that, with the substitution of any member within the same family class, the same disclosed result would be obtained. The coverage of the patent should be limited to what is actually enabled by the disclosure in the specification.

- **Selection patents**

Recommendation: As a general rule, selection patents should not be granted if the selected components have already been disclosed or claimed and, hence, lack novelty. If an existing product were deemed patentable due to its unexpected advantages under the applicable law, the patentability of a selection could be considered when an inventive step is clearly present.

- **Analogy processes**

Recommendation: Non-novel or obvious pharmaceutical processes, regardless of whether the starting materials, intermediaries or the end product are novel or inventive, should be considered not patentable as such.

- **Enantiomers**

Recommendation: Single enantiomers should generally not be deemed patentable when the racemic mixture was known. However, processes for the obtention of enantiomers, if novel and inventive, may be patentable.

- **Active metabolites and prodrugs**

Recommendation: a) Active metabolites of drugs should generally not be deemed patentable separately from the active ingredient from which they are derived.

b) Patents over prodrugs, if granted, should disclaim the active ingredient as such, if previously disclosed or otherwise non-patentable. They should only be granted if the prodrug is specifically described and an unusual, non-predictable, effect was found. Like other subject matter claimed in a patent, a prodrug should be sufficiently supported by the information provided in the specifications. In addition, evidence may be required that the prodrug is inactive or less active than the compound to be released, that the generation of the active compound ensures an effective level of the drug and that it minimizes the direct metabolism of the prodrug as well as the gradual inactivity of the drug.

- **Method of treatment**

Recommendation: Methods of treatment, including for prevention, diagnosis or prophylaxis should be deemed non patentable where industrial applicability is required as a condition for patentability (including in cases where the patentability of such methods is not expressly excluded).

- **Use claims, including second indications**

Recommendation: Claims relating to the use, including the second indication, of a known pharmaceutical product can be refused, inter alia, on grounds of lack of novelty and industrial applicability.

4. Conclusion

National drugs policies, including matters related to intellectual property, are fundamental elements of a national health policy that endeavours to protect the right of all citizens to access to health care.

In order to develop new medicines, mechanisms promoting innovation and product development should be established, while at the same time it should be ensured that patients are able to quickly access the fruits of this research. In the context of essential medicines, innovation should be structurally linked to access. This means that the

research costs and final product price should be separate.

The effect of the introduction of pharmaceutical patents on access to medicines largely depends on the way in which the TRIPS Agreement is interpreted and implemented. This is why it is particularly important that when incorporating the provisions of the TRIPS Agreement, countries consider, inter alia, the following measures:

- a) The incorporation of the requirements of the TRIPS Agreement into national intellectual property legislation should take into account the principles of articles 7 and 8 in order to regulate intellectual property in a manner consistent with public health interests and minimize the economic and social costs that the changes can have on production, trade and access to medicines. These principles were ratified by the Doha Declaration (2001) on the TRIPS Agreement and public health;
- b) Defining the three patentability requirements – novelty, inventive step and industrial applicability (utility) – in a manner consistent with public health objectives;
- c) Integrating a mechanism to grant the compulsory licenses permitted by the Agreement into national legislation;
- d) Ensuring the import of products that have been legitimately placed on the market, under the principle of international exhaustion;
- e) Excluding naturally occurring substances from patentability (for not meeting the requirements for an “invention”)
- f) Limiting reversal of the burden of proof for process patents related to new chemical entities.

National intellectual property offices, through the examination of patents, play an important role in the access to medicines. The application of patentability requirements for medicines, given their public health dimension, should be considered with even more care than in the case of regular merchandise or luxury items. The first and most important step is to use the freedom permitted by the TRIPS Agreement to define the patentability requirements: novelty, inventive step and industrial applicability (utility) in a way “that do[es] not lose sight of public interest in the wide dissemination of knowledge (...)”²¹

If guidelines for the examination of pharmaceutical patents are implemented, in the manner analysed above, it is unlikely that the following types of patent applications for pharmaceutical products will be admissible by a national patent office:

- ◆ A new salt, ester, ether or polymorph, including hydrates and solvates, of an existing chemical entity;
- ◆ A single enantiomer of an existing chemical entity;
- ◆ A new combination of two or more active ingredients that are already available as individual entities;
- ◆ A new form of administration that enables a new administration route (for example, an injectable form when an oral tablet already exists);
- ◆ A new form of controlled release administration which already exists in uncontrolled release form;
- ◆ A new route for an existing form of administration (for example intravenous administration of a drug when subcutaneous administration has already been approved);
- ◆ A change in formulation.

Finally, patent offices should be aware that the decisions that they take in the examination of patents, although seemingly of a technical nature, can have definite consequences on people's lives and health. Erroneously granted patents can restrict access to medicines and be used to unduly limit competition.

Endnotes

1. Based on South Centre Research Papers No. 61 "Guidelines on Patentability and Access to Medicines", Geneva, March, 2015.
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3. Cf. Drahos, Peter "Trust me: Patent offices in developing countries", Centre for governance of knowledge and development, working paper, November 2007.
4. See Velásquez Boulet, Bulletin of WHO 1999, vol. 77, no. 3 "Essential drugs in the new international environment".
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7. The impact of the Agreement on Trade-Related Aspects of Intellectual Property Rights on human rights: Report of the High Commissioner, E/CN.4/Sub.2/2001/13, 27 June 2001, para 62.
8. C. Correa Op. cit.
9. Philippe EVEN, Bernard DEBRE, "Guide to the 4000 useful, useless and dangerous medicines" Ed. Cherche Midi, Paris, September 2012, p. 82.
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12. Santi, P. "Hépatite C: le nouveau hold-up des labos", in *Le Monde* 8 July 2014.
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17. For the complete text see: Correa C. "Guidelines for the examination of pharmaceutical patents: a public health perspective". WHO - ICTSD, UNCTAD, Geneva, March 2008.
18. Arias Eduardo, PPT on "Guidelines for the examination of patentability of chemical-pharmaceutical inventions, INPI, Argentina, 2014.
19. See, for example, Federal Trade Commission (FTC) (2003); Jaffe and Lerner (2004); Correa, 2001a.
20. The number of new molecular entities approved by the United States Food and Drug Administration of the (FDA) has fallen drastically since the mid-1990s (from 53 in 1996 to a low of 17 in 2002). See "CDER, NDAs approved in calendar years 1990-2004 by therapeutic potential and chemical type". United States Food and Drug Administration, 22 March 2005 (<http://www.fda.gov/cder/rdmt/pstable.htm>, accessed on 14 November 2005).

21. Op. cit. The impact of the Agreement on Trade-Related Aspects of Intellectual Property Rights on human rights: Report of the High Commissioner, E/CN.4/Sub.2/2001/13, 27 June 2001, para 62.

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