Impact of the EU-Andean Trade Agreements on Access to Medicines in Peru

IFARMA

Paper Series hai

Paper Series Reference 010-2009/01 prosperous

Published by:

Health Action International (HAI) Europe

Overtoom 60 II, 1054 HK Amsterdam. Netherlands. Tel: +31 20 683 3684 Fax: +31 20685 5002.

Health Action International (HAI) is an independent, European network working to increase access to essential medicines and improve their rational use through research excellence and evidence-based advocacy.

www.haiweb.org

IFARMA

Kr 13 # 32-51 Tower III ofic. Ed Bavaria 11-16. Bogotá DC – Colombia. Tel: (+571) 3381490 Fax: (+571) 3231472.

IFARMA Foundation is a research institute and consultancy with an international outlook, focusing on issues relating to medicines (access, use and quality). IFARMA is part of a network of organisations working on public health policies regarding medicines, particularly in Latin America.

IFARMA's research and ideas intend to be conducive to meaningful debate on public policy, contributing ideas and evidence to this debate. IFARMA operates under the approach that results of research on medicines should meet high quality standards, while at the same time reaching those who need it. Most importantly, results should be used correctly.

www.ifarma.org

Impact of the EU-Andean Trade Agreement on Access to Medicines in Peru

IFARMA

Main coordinator:

CAN EU Alliance on Access to Medicines:

Acción Internacional para la Salud, Latinoamérica & Caribe

Fundación IFARMA

Fundación Misión Salud

Health Action International, Europe

RED GE, Peru

Technical coordinators:

AIS-LAC and Fundación IFARMA

Coordinator:

Miguel Ernesto Cortes Gamba

Researchers:

Edson Meza Cornejo

Iván Rodríguez Bernate

Prelude

This study was commissioned by the CAN-EU Alliance on Access to Medicines during the early stages of the negotiation process toward an Association Agreement between the European Union (EU) and the Andean Community (CAN). The data used for the analyses on data exclusivity and supplementary patent protection (SPC) are based on the original demands by the EU in the initial rounds of negotiations. Since then, the EU, unable to fulfil these ambitions, has agreed to substantially lower its demands on data exclusivity and SPC. However, this study has served as a valuable advocacy tool, providing insight into how the EU's intellectual property (IP) trade agenda affects access to medicines and pinpointing areas of EU policy that other developing countries should take note of. The section on enforcement remains relevant to the later stages of the negotiations, which are ongoing.

Executive Summary

This study evaluates the foreseen impact on access to medicines in Peru from the intellectual property measures proposed by the European Union as part of the trade agreement that is being negotiated between the EU and some of the CAN countries. It specifically assesses the impact of increasing the effective duration of pharmaceutical patents and test data protection. Though these are the main measures set out in the European agenda, there are other measures that have a detrimental impact on Peru in particular, proposals concerning enforcement which could be just as negative and costly.

The analysis of the impact is based on the '*Guide to estimating the impact on access to medicines due to changes in intellectual property rights*', produced jointly by the World Health Organisation (WHO) and the Pan-American Health Organisation (PAHO). The guide outlines the *Intellectual property rights impact assessment* (IPRIA) model.

The most recent IPRIA studies were conducted in partnership with a consortium of organisations, including WHO, PAHO, the United Nations Development Programme (UNDP), the World Bank Institute (WBI) and the International Center for Trade and Sustainable Development (ICTSD), who have been refining the methodology. Colombia (2005, 2006, 2007), Guatemala (2005), Costa Rica (2005), Bolivia (2006), Costa Rica (2008), Dominican Republic (2008), Uruguay and Argentina are some of the studies that have been conducted with this model. In order to strengthen the methodology and how it is applied in different countries, a number of workshops have been organised (London, 2005; Malaysia, 2006; Thailand, 2006).

The IPRIA model uses the *scenario planning method* to establish the impact. The impact itself is the difference between the *basic scenario*, which describes the current situation (no changes to the IPR system), and *alternative scenarios,* which describe potential consequences of changing the IPR context.

It is estimated that the introduction of the two measures on data exclusivity and SPC would lead to an increase of 459 million USD in Peru's total pharmaceutical expenditure in 2025 and a cumulative increase in expenditure of 1267 million dollars (at present value, PV) for the same year. This represents the amount required to maintain the current consumption level. Consumption decrease would be caused by the result of an 11% increase in the number of API (Active pharmaceutical ingredients) protected, which in turn would lead to a 26% price increase.

Implementing the Supplementary Protection Certificates from Article 9.3 of the Intellectual Property Agreement Subgroup (thus extending the effective patent period by 4 years),[1] would lead to a 159 million USD increase in pharmaceutical expenditure in 2025.

At the same time, a 10-year test data exclusivity period, as proposed by the EU in Article 10.2 of the aforementioned subgroup, would lead to an increase of more than 300 million USD in medicines' expenditure in 2025 and a cumulative increase in expenditure of 899 million USD (at present value, PV) for the same year.

The total market can be divided into public and private sectors. The private sector would be more affected than the public one. In 2025, the private market would experience a 12% increase in the volume of active ingredients with IPR protection (both patented active ingredients and those with other IPR protection), which would cause a 27% increase in prices. This, in turn, would cause a 411 million USD (PV) increase in expenditure.

More medicines enter the private market than the public market, and it is estimated that, in 2025, the public sector would experience an 11% increase in the volume of medicines with IPR protection, which would lead to a 25% increase in prices and a 48 million USD increase in expenditure.

Importantly, when calculating patent duration, only the first patent for medicines is taken into consideration. However, medicines usually have secondary associated patents that extend, *per se*, the patent's monopoly period.

One of the most notable variables is the price of innovative products, which is 7.27 times the price of lower-priced generic competitors in the private market. On the other hand, national participation in patented medicines is currently zero, which calls into question the concept and reliability of technology transfer that may be featured in this provision.

It is worth noting that if the IPR enforcement measures proposed by the EU are implemented, this would not only strengthen the position of IPR holders, but would also greatly deter potential competitors. An environment that fails to encourage competition leads to high prices. This is particularly true if one considers that, in order to speed up dispute proceedings, the alleged infringer is not given the opportunity to be heard. This means that sentences could be passed based merely on presumptions.

[1] Text from the negotiation round in February 2009.

This has been demonstrated by recent events in the Netherlands and Germany, where generic medicines shipments in transit were seized even thought this medicine has not patent neither in the origin nor in the destination country.

Date	Medicine	Requesting party	Place of origin	Transit location	Final destination
Apr 2008	Atorvastatin	Warner-Lambert	India	Amsterdam	Colombia
Apr 2008	Sildenafil	Pfizer	India	Amsterdam	Colombia
Nov 2008	Valsartan	Novartis	India	Amsterdam	Colombia
Nov 2008	Atorvastatin	Warner-Lambert	India	Amsterdam	Peru
Nov 2008	Rivastigmine	Novartis	India	Amsterdam	Peru
Nov 2008	Olanzapine	Eli Lilly	India	Amsterdam	Peru
Jun 2009	Amoxicillin	GlaxoSmithKline	India	Frankfurt	Vanuatu

Of particular note is the seizure of Amoxicillin that was going from India to the island of Vanuatu, passing through Frankfurt, Germany. This medicine has been marketed for more than 20 years and does not have an applicable patent, or current data exclusivity in either the transit country or the final destination, and has been marketed by the INN, which means there would be no IPR infringement.

The enforcement measures contained in the EU proposal give IPR holders considerable opportunities to block potential competitors. Even though these competitors may not infringe any IPR rights, simply by being accused of such an infringement their goods can be seized or destroyed, and their commercial and financial networks, blocked. This is also due to the confusion created by IPR holders and the owners of registered trademarks, when it comes to generic, copied, counterfeit and pirated products.

To conclude, the aforementioned intellectual property protection provisions promote an increase of market share for protected products, thus extending periods of monopoly prices. This, in turn, hinders access to new pharmaceutical products.

In view of the above, it is worth remembering that "*medicines have an important social role, as they are an integral component in the achievement of a fundamental human right, the right to health. That is why they are considered as essential goods, in order to highlight the fact that everyone should have access to them."*[2]

[2] Velásquez, G. & Boulet, P. (2000). *"Globalización y acceso a los medicamentos: perspectivas sobre el Acuerdo ADPIC/OMC"*. [Globalisation and access to medicines; perspectives of the TRIPS/WTO Agreement. World Health Organisation (WHO), Department of Essential Medicines and Pharmaceutical policy. Geneva, Switzerland.

The United Nations member countries agreed, in one of the Millennium Development Goals aims: *“To provide access to essential medicines in developing countries at affordable prices, in cooperation with pharmaceutical companies.”* However, the EU proposal on intellectual property moves in the opposite direction, making it more difficult to ensure that people can benefit from the human right to health.

Introduction

In February 2009, round one of the trade agreement negotiations between Colombia, Ecuador and Peru and the European Union took place. By June 2009, four rounds had been held and a fifth will take place in Lima in July of this year.[3] At the end of Round one, which was held in Bogotá in February, both civil society groups and the Andean negotiating groups stated that the European proposal on intellectual property was severe. The European proposal offers more benefits for IPR holders than what is expressly stated in the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). These additional benefits include supplementary protection for patents and extending exclusivity protection for test data. In both cases, this leads to extended market exclusivity protection – i.e. monopolies.

However, these are not the only provisions contained in the EU proposal. IPR enforcement is another central feature of the proposal and its negative consequences for CAN countries could be just as significant, if not more so, than the provisions on data exclusivity and SPC.

The aim of this study is to evaluate the impact on expenditure and access to medicines in Peru of some of the provisions called for by the EU. Reference material includes the Draft Negotiating Test from the Bogotá Negotiation Round in February 2009, and *Health Protection in the European and Andean Association Agreement* by Xavier Seuba (2009),[4] which is particularly relevant for its discussion of IPR enforcement. The methodology used to calculate the impact is the *Intellectual Property Rights Impact Model*, which was based on the *Guide to estimating the impact on access to medicines due to changes in intellectual property rights* (WHO/PAHO 2005).[5]

[3] At the time of writing the negotiations were in an earlier stage then in the time of publishing. In October 2009, other rounds have taken place between only the EU and Peru and Colombia The Agreement negotiations began in September 2007, when the EU and CAN began negotiating an Association Agreement as blocs. This lasted until April 2008. In February 2009, when bloc negotiations failed, Colombia, Peru and Ecuador began the Multilateral Trade Agreement negotiations, where each country negotiates at their own pace with the EU.

[4] Seuba Hernández, Xavier (2009). *La protección de la salud en el nuevo Acuerdo de Asociación entre la Comunidad Andina (o algunos de sus Miembros) y la Comunidad Europea, a la luz de sus disposiciones en materia de propiedad intelectual y experiencias recientes.* [Health Protection in the European and Andean Association Agreement] , HAI Paper Series. www.haiweb.org

[5] Rovira, J. & Cortés, M. (2005) Intellectual Property Rights Impact Model, created based on the *Guía para estimar el impacto sobre el acceso a medicamentos, de cambios en los derechos de propiedad intelectual* [Guide to estimate the impact on access to medicines due to changes in intellectual property rights], WHO/PAHO.

This report does not provide a contextualisation of the trade agreements, the TRIPS agreement and how it affects access to medicines that are introduced to new audiences, and for this, we recommend the work of Velásquez & Correa (2008).[6]

This impact study considers the extension of effective patent periods as a result of supplementary protection and test data protection, for which the EU proposes a longer exclusive ownership period for the proprietor. The EU's proposal exceeds even that of the Trade Promotion Agreement (TPA) between Peru and the United States.

[6] Velásquez, Germán & Correa, Carlos (2008). *El acceso a medicamentos, en el contexto de los acuerdos internacionales de comercio y las nuevas reglas sobre la propiedad intelectual*.[Access to medicines in the context of international trade agreement and new regulations concerning intellectual property] Eds. Natalia Paredes and Francisco Rossi. Cinep; Bogota, Colombia.

Methodology

The impact presented in this study was calculated based on the 'Guide to estimating the impact on access to medicines due to changes in intellectual property rights'[7] produced jointly by the World Health Organisation (WHO) and the Pan-American Health Organisation (PAHO). This guide presents the Intellectual Property Rights Impact Assessment (IPRIA) model.

The IPRIA has been applied in different contexts in various countries, conducted in partnership with a consortium of organisations, including WHO, PAHO, the United Nations Development Programme (UNDP), the World Bank Institute (WBI) and the International Center for Trade and Sustainable Development (ICTSD), which have further refined the methodology. Examples of studies conducted include: Colombia (2005, 2006, 2007), Guatemala (2005), Costa Rica (2005), Bolivia (2006), Costa Rica (2008), Dominican Republic (2008), Uruguay and Argentina. A number of meetings and workshops have also been organised to enable its application in different countries (London, October 2005; Malaysia, June 2006; Thailand, November 2006).

The IPRIA model determines impact using the 'scenario planning method'. Impact represents the difference between the *basic scenario*, which describes the current situation (no changes to the IPR system) and its potential development into *alternative scenarios,* which describe situations that may occur as a result of certain changes to the IPR system.

The impacts that the model assessed for different time horizons are:

- **Level of medicine exclusivity in the market**
- **Impact on the average prices in the market**
- **Impact on pharmaceutical expenditure**
- **Impact on medicine consumption**

This report presents the IPRIA results for the articles taken from the EU proposal to the Andean countries, which refer to data protection and patents: Article 9.3 and Article 10.2.

Article 9.3 of the EU text proposes granting supplementary protection certificates, which would extend the effective patent period by approximately 4 years.

[7] ROVIRA, Joan, et al. "*Guía para estimar el impacto sobre el acceso a los medicamentos de cambios en los derechos de propiedad intelectual DPI*". [Guide to estimate the impact on access to medicines due to changes in intellectual property rights] WHO/PAHO 2005

Article 10.2 of the EU text proposes banning third parties from using test data for a minimum period of 8 years and a maximum of 11 years.

Articles 9.3 and 10.2, which are discussed by sub-group 11 during the negotiations (the intellectual property sub-group) are examined in detail in the next chapter.

Context and Created Scenarios

Basic Scenario

The intellectual property *status quo* in Peru has been taken as the basic scenario, corresponding to the introduction of the Trade Promotion Agreement (TPA) signed with the United States. The implementation of this agreement required 99 decrees, specifically Legislative Decrees 994 to 1092 of 2009. Some of these were modified by Law 29316 from the same year, others were considered unconstitutional and others have already been revoked by the Republic's Congress.[8]

A nominal duration of 20 years was established for patents, which is the same period indicated in the TRIPS agreement.

Data protection in the basic scenario sets a period of 5 years of exclusivity, which relates to the period given in Decree 1072 of 2009, the internal regulation that implements the terms of data protection negotiated in the TPA.

Alternative Scenario 1

The implementation of Supplementary Protection Certificates (SPC) as proposed in Article 9.3 of the EU text extends the effective patent period further than what is set out in the TRIPS Agreement and the TPA with the United States.

[8] See: Roca, Santiago (2009). Demócratas, salud pública y propiedad intelectual en el APC Perú-EE.UU. En la revista Puentes. ICTSD . Entre el comercio y el desarrollo sostenible. Mayo 2009. vol 10 No 2.

Article 9.3: Supplementary Protection Certificates

[EU Proposal]

1. "The Parties recognise that medicinal and plant protection products protected by a patent on their respective territory may be subject to an administrative authorisation procedure before being put on their market. They recognise that the period that elapses between the filing of the application for a patent and the first authorisation to place the product on their respective market, as defined for that purpose by the relevant legislation, may shorten the period of effective protection of the patent.

2. The Parties shall provide for a further period of protection for a medicinal or phytosanitary product which is protected by a patent and which has been subjected to an administrative authorisation procedure, that period being equal to that period referred to in Paragraph 1, second sentence, reduced by a period of five years.

3. Notwithstanding paragraph 2 and the possible extension for paediatric use pharmaceutical products, the additional protection period may not exceed five years".

According to the TRIPS Agreement and the TPA, a patent lasts 20 years. However, this is the period from the patent application until its market authorisation.[9] Therefore, the 20-year period described is in fact a nominal patent duration. The effective duration is the difference between the 20 years and the aforementioned period. For example, if it takes 4 years for a patent to get a market authorisation from the *Dirección General de Medicamentos, Insumos y Drogas* DIGEMID [Directorate-General for Medicines, Medical supplies and Drugs] from the moment that the application was submitted to the National Institute for the Defence of Competition and Protection of Intellectual Property (INDECOPI), then the patent will have an effective duration of 16 years.

This context illustrates the notion of Article 9.3, where paragraph 1 acknowledges that between the patent application and market authorisation for the medicine (the subject of the patent) there is a period of time that reduces the patent's effective period.

Paragraph 2 states that, if this period exceeds 5 years, the patent holder must be compensated for each additional year and finally, paragraph 3 states that compensation must be a maximum of 5 years.

[9] In Peru, patent applications are submitted to the Instituto Nacional de Defensa de la Competencia y de la Protección de la Propiedad Intelectual, INDECOPI [National Institute for the Defense of Competition and Protection of Intellectual Property]. The organisation that grants the registration required to market a medicine is the Dirección General de Medicamentos, Insumos y Drogas, DIGEMID [Directorate-General for Medicines, Medical supplies and Drugs].

To summarise, if the period between the patent application and market authorisation;

- is 0 to 5 years, the holder will not receive any compensation and the effective patent period shall be 15 to 20 years;
- is 6 to 10 years, the holder will receive compensation for each year the period is extended. I.e. in case of a 6-year period, compensation will be for 1 year. If the period is 7 years, the compensation will be for 2 years, and for 5 years in case of a 10-year period. This guarantees an effective patent period of 15 years;
- If the period exceeds 11 years, the compensation is for 5 years. For example, if the period is 11 years, the effective patent period will be 14 years; if the period is 12 years, the effective patent period will be 13 years.

Table 1 illustrates how the extension will impact the effective patent period in the United States if SPCs would be introduced. The period has been calculated from the first patent application until market authorisation of the medicine, for New Drug Approvals[10] by the Food and Drugs Administration (FDA) during 2005-2008, as shown in column 1. As a result, the effective patent period would increase by 3.9 years.

[10] New Drug Approvals, NDA

Table 1. Evaluation of duration for patents in the United States

PERIOD (YEARS)	PATENTS GRANTED		*EFFECTIVE DURATION WITHOUT SPC*	*EFFECTIVE DURATION WITH SPC*
	%	Accumulated		
2	2.29%	2%	18	18
3	1.14%	3%	17	17
4	2.86%	6%	16	16
5	2.86%	9%	15	15
6	6.29%	15%	14	15
7	6.29%	22%	13	15
8	5.71%	27%	12	15
9	6.86%	34%	11	15
10	9.71%	44%	10	15
11	8.00%	52%	9	14
12	5.71%	58%	8	13
13	12.00%	70%	7	12
14	12.57%	82%	6	11
15	7.43%	90%	5	10
16	6.29%	96%	4	9
17	1.14%	97%	3	8
18	1.71%	99%	2	7
20	1.14%	100%	0	5
WEIGHTED AVERAGE EFFECTIVE PATENT PERIOD			***9.06***	***12.98***

Sources: FDA and Orange Book. Total number of patents: 175 of 310 New Drugs in 2005-2008. The period relates to the difference between the patent application date and the market registration date.

It is important to clarify that the duration is calculated using the first patent. Nevertheless there could be further applications for several patents using Markush Claims and Selection Patent methods for the same pharmaceutical product (i.e. an active ingredient in a specific pharmaceutical form and concentration).[11] One example of this is the pharmaceutical product registered with the FDA in 2006 under the trade name Taclonex® (calcipotriene 0.005% and betamethasone dipropionate 0.064%, in a topical ointment), which obtained a second patent,

[11] The so-called 'Markush claims' refer to a chemical structure with multiple functionally equivalent chemical entities allowed in one or more parts of the compound. Markush claims may include a vast number (sometimes millions) of possible compounds. They may be used to obtain a wide patent coverage including a large number of compounds whose properties have not been tested, but only theoretically inferred from the equivalence with other compounds within the claim. Hence, the acceptance of Markush claims generate rights over an extremely broad set of compounds without prior testing or experimentation.ICTSD, WHO, UNCTAD (2006) Guídelines for the examination of pharmaceutical patents. Developing a Public health perspective. pp. 12-14.

not as a result of any product variation or innovation, but due to the aforementioned methods.[12]

Supplementary or additional protection provisions are not included in the TRIPS Agreement, in the regulations of CAN countries, nor in Peru's national regulations, including those related to the implementation of the TPA with the US. The additional protection proposed by the EU in Article 9.3 of the agreement has been used to configure the first alternative scenario of the IPRIA model. The second scenario relates to test data protection.

Alternative Scenario 2

This scenario corresponds to the extension of test data exclusivity[13] proposed by the EU in Article 10.2 of the Agreement. As will be analysed further in this document, by introducing this Article, test data exclusivity would increase by approximately 5 years compared to the period currently in force, according to Decree 1072 of 2009.

Article 10.2

[EU Proposal]

"Both parties shall enact and implement the legislation ensuring that any information submitted in order to obtain a marketing authorisation for a pharmaceutical product will remain undisclosed to third parties and benefit from a period of at least ten years of protection against unfair commercial use starting from the date of grant of marketing approval in either of the parties.

a) during a period of at least eight years, no person or entity (public or private), other than the person or entity who submitted such undisclosed data, will without the explicit consent of the person or entity who submitted this data, rely, directly or indirectly on such data, in support for an application for the authorisation to put a pharmaceutical product on the market.

b) During a ten-year period, any subsequent application for the authorisation to put a pharmaceutical product on the market would not be granted, unless the subsequent applicant submitted his/her own data (or data used with authorisation of the rights holder) meeting the same requirements as the first applicant. Products registered without submission of such data would be removed from the market until all requirements were met.

c) In addition, the ten year period referred to shall be extended to a maximum of eleven years if, during the first eight years, after obtaining authorisation in either of the Parties, the holder of the basic authorisation obtains an authorisation for one or more new therapeutic indications which are considered of significant clinical benefit in comparison with existing therapies.

[12] See the description in Appendix 3.

[13] Test data is the commonly used name for information concerning evidence that proves the safety and effectiveness of a pharmaceutical product.

In order for a New Pharmaceutical Product to be granted a marketing authorisation, the Health Authority carries out a pharmacological evaluation. For this purpose, the first seller must provide information proving the safety and effectiveness of the new drug. However, when the application for authorisation is not for a new Pharmaceutical Product, there is no need to provide such evidence, since the first seller will have already done so and the safety and effectiveness of the drug has already been confirmed.

Therefore, in order to obtain marketing authorisation for a medicine in Peru, a second, third or fourth producer must reference test data to DIGEMID (the Medicines Control Agency, an organisation that carries out a technical evaluation on the medicine).

Despite the previous procedure, Decree 1072 was introduced this year (as detailed above), which established a 5-year exclusivity period for the use of test data. Third parties must wait five years after this exclusivity protection is granted before they can use this information to obtain market authorisation for a generic version of the same medicine.

The EU proposal aims to extend this protection period even further, to a maximum of 11 years. Section “a” of Article 10.2 calls for an 8-year exclusivity period for the use of test data or undisclosed information. However, section “b” states that in the 2 years following the exclusivity period, test data cannot be used to support a market authorisation application for a generic version, unless the exclusivity holder grants permission to the third party who wishes to produce and market the generic. Therefore, the exclusivity period is in fact 10 years, since it is unlikely that the rights holder will grant any third party such permission.

Section “c” establishes an additional year of exclusivity if the holder registers a new indication for the same active ingredient. This study uses the 10-year period – 5 years more than what is currently granted – since there is no evidence to demonstrate in how many cases the additional year would be granted for new indications.

While test data protection is included in the TRIPS Agreement, there is no information regarding the exclusivity period for the use of this information. The TRIPS Agreement only requires that this information is protected against unfair commercial use.

Having now considered the three scenarios that will be evaluated – the basic scenario, alternative 1 and alternative 2 – the following section describes the variables that differentiate one from the other, and which therefore define their future path on the established time horizon. The introduction of a trade agreement containing both Article 9.3 and 10.2 would lead to an impact equal to the sum of the impacts calculated in scenarios 1 and 2. This cumulative impact is represented in alternative scenario 3 (a combination of both measures).

Defining Scenarios and their Variables

The aforementioned scenarios each have a set of variables by which they are defined and which enable the IPRIA model to be used to compare the evolution of the different scenarios. This provides results that show how appropriate or regressive an alternative may be, in terms of the prices which the private or institutional markets would pay and the expenditure involved.

Before defining the variables which configure each scenario, it is necessary to describe the availability of information and the approach used to complete this task.

The IPRIA model is currently being applied to the total medicine market in Peru, including both the private sector and the public sector, where large medicine purchases are made by organisations such as health service providers and health administrators, among others.

For the private market, a database of 560 Active Ingredients and their sales in values was used. The database was produced by the Intercontinental Marketing Service (IMS)-Interdata for 2007. In order to analyse the public market, a database of state procurements carried out by DIGEMID was used, which contains the amounts allocated to different public purchases. The period under evaluation was 2006-2008.

In order to establish the value of some of the variables, such as the percentage of products with data protection and patented products, information from the United States was used as a reference, particularly the FDA *New Drug Approvals* and their protection status, in accordance with the FDA Orange Book. This information was used not only because of the transparency and availability of information, (in contrast to the lack of local information) but also because it is believed that trade agreements can lead to a convergence in the proportion of patented medicines in developed and developing countries. It would have been ideal to have the EU information, but we were unable to gain access.

Having described the databases that provide the information for the appropriate application of the IPRIA, the different variables that constitute the model will now be described.

Simulation time frame

The implementation of the agreement is forecast for 2010 and the final simulation year for 2050, providing a time horizon of 40 years to capture the impact of the agreement's intellectual property provisions on medicines.

It is important to clarify that 2007 was used as the first simulation year for the private market, while 2008 was used for the public market, as these are the most recent years for which reliable information was available. Nonetheless, the period 2007-2009 evolved under the current *status quo*, i.e. under the basic scenario, and therefore this has no effect on the impact calculations.

❖ **Number of active ingredients available during the first simulation year**

The number of active ingredients that were on the relevant market in 2007 was defined as 80% of the total private market, based on information produced by IMS-Interdata. This gives a total of 560 active ingredients on the private market.

For the public market, the total number of active ingredients purchased by the Ministry of Health (MINSA) by public tender was used. See Table 3

Table 3

NUMBER OF ACTIVE INGREDIENTS	
YEAR	**Quantity**
2002	127
2004	126
2006	151

❖ **Total expenditure – total sales – in the first year**

As shown above, for the private sector, the model is applied to what is referred to as the relevant market, which represents a total expenditure of 521 million dollars. MINSA's total expenditure for the public market in 2008 was 97 million dollars.

❖ **Annual market growth rate in value**

In order to establish the annual growth of the private market in value the proxy used was the growth rate of the Gross Domestic Product (GDP) of pharmaceutical products and medicines, in USD as per 1994 prices.

Table 4

Pharmaceuticals and Medicines GDP		
USD in real terms in 1994		
Annual **Frequency**	**Coverage :** National	
Years	**Value**	**Growth**
2001	76,278,371	
2002	86,085,753	12.9%
2003	87,275,706	1.4%
2004	70,800,870	-18.9%
2005	80,309,851	13.4%
2006	98,204,571	22.3%
AVERAGE		**6.2%**

The public market growth rate is 4.2%, which is the total growth shown in Table 5.

Table 5

YEAR	VALUE	GROWTH
2005	86,835,887	
2006	89,130,527	2.6%
2007	103,216,060	15.8%
2008	97,068,222	-6.0%
AVERAGE		***4.2%***

Source: MINSA procurement of Medicines by Public Tender.

❖ **Discount rate**

The discount rate is the rate at which a monetary unit of value is discounted in order to obtain its present value (the value at t_0). Discounting is justified in economic analysis either by consumers' time preference or by the positive productivity of capital.

In order to achieve estimations for the present value and therefore appropriately contrast the different scenarios, a discount rate of 3% was used. Even though a discount rate of 11% for the country is suggested for public projects,[14] the rate of 3% was used as it is closer to a long-term interest rate.

[14] *Directiva General del Sistema Nacional de Inversión Pública, Resolución directoral No. 002-2009-EF_68.01*. [SNIP General Directive, Directoral Resolution No. 002-2009-EF_68.01]

❖ **National industry participation in market exclusivity**

This variable is defined using the percentage of national pharmaceutical producers, for all active ingredients with data exclusivity and active ingredients with patent protection.

Data exclusivity:

According to information provided by DIGEMID, as of June 2009, there were no molecules with exclusivity for their test data. This is because Decree 1072, which introduced this provision, has only been in force for 6 months. As a result, national industry participation in market exclusivity is 0%.

Patent protection:

It is worth highlighting that, in several countries, it is very difficult to accurately identify patented pharmaceutical products. In Peru, INDECOPI reports that no local pharmaceutical companies own a patented molecule.

The 0% value for this *national industry participation in market exclusivity* variable is the same for the public and private sectors.

❖ **National industry participation in the competitive market**

National industry participation in the competitive market is 25%, according to interviews with DIGEMID officials.

❖ **Year in which patents entered into force**

This parameter refers to the year in which the pharmaceutical patents were implemented in the WTO Member countries, which is 1994. Although in this year, medium and low income countries had special terms,[15] in Peru they were implemented in 1994 under CAN Decision 344.

❖ **Year in which test data exclusivity entered into force**

Decree 1072 of 2009 regulates issues relating to the protection of test data exclusivity in Peru. Therefore, 2009 is the year in which this measure entered into force.

[15] Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) World Trade Organization.

❖ **Nominal patent duration**

As previously described, the TRIPS Agreement and the US-Peru TPA establish a nominal period of 20 years and the agreement under negotiation with the EU does not call for a direct extension on this nominal patent duration. The EU does, however, request an extension of the effective duration, by means of Supplementary Protection Certificates (SPCs). Therefore, the value of this variable is 20 years for all scenarios, and the extension of the effective duration is captured in subsequent variables.

❖ **Time period between the active ingredient patent application and its marketing registration**

This variable provides the effective patent period, deducting this time from the nominal 20 year period.

Due to the difficulty in accessing information on patented medicines in Peru, the FDA's *New Drugs Approvals 2005-2008* is used as a reference for those medicines with patent protection.

Table 1 illustrates the period between the patent application and its marketing registration. It shows that the weighted average for the effective duration is 9.06 years, which indicates that the time between the patent application and its marketing registration is 10.94 years. This is the value which is used for the variable, both for the basic scenario and the alternative scenarios.

❖ **Extension of patent duration through compensation for delays in patent approval**

Basic Scenario:	0 years
Alternative Scenario 1:	3.9 years
Alternative Scenario 2:	0 years
Alternative Scenario 3:	3.9 years

As previously noted, the agreement does not call for an extension of the nominal patent period, but an extension of the real and effective duration, since the Supplementary Protection Certificates in Article 9.3 call for additional effective protection.

In the section presenting the scenarios, Article 9.3 has already been analysed, which states in brief that if the period between the patent application and the market authorisation:

- Is between 0 and 5 years, the holder shall not receive compensation and the effective patent period shall be between 15 and 20 years.

- Is between 6 and 10 years, the holder shall receive compensation for each year which the period is extended beyond 5 years. That is to say: if the period is 6 years, then compensation shall be for 1 year. If the period is 7 years, the compensation is for 2 years and if the period is 10 years, then the compensation is for 5 years. This guarantees an effective patent period of 15 years.

- If the period exceeds 11 years, the compensation is for 5 years. For example, if the period is 11 years, the patent effective period shall be 14 years; if the period is 12 years, the effective patent period shall be 13 years.

As mentioned before, implementation of the Supplementary Protection Certificates would lead to an average increase of 3.9 years in the effective patent period.

❖ **Proportion of active ingredients that enter the market with an extended patent period as a result of compensation for delays**

By accepting the agreement with the EU with the aforementioned requirements, 100% of new pharmaceuticals products would have additional protection.

❖ **Time period between the expiration of an active ingredient patent and the beginning of competition from generic manufacturers**

One aspect that has not been considered in the definition of the previous variables is Selection Patents and Markush Claims, which enable rights' holders to apply for a second patent on a specific pharmaceutical product; resulting in an extension of the market exclusivity (or monopoly) period. This can take place without the holder implementing their new additional protection right established by the SPC.

These second patents mean that the monopoly period increases to 4.05 years, in the case of FDA *New Drugs Approvals 2005-2008*. Therefore, this was the value used for this variable in all scenarios. It is not included as an impact of the agreement under negotiation, since it is the result of relaxed patentability criteria under the US TPA.

The delay in the entry of generics is not considered to be a result of generic producers' inability to adapt the new technology, since generic medicines can take between 5 months to 6 years to enter the market. However, the delay is a result of reasons outside of the agreement under negotiation:

- **Average delay in the entry of generics, as a result of the linkage between the Health authority and patent office**

The agreement with the EU does not establish measures for the patent-registry linkage, which does feature in the US-Peru TPA. Therefore the value for this variable is 0 years.

- **Proportion of active ingredients for which generic competition is delayed due to the aforementioned link**

For the same reason as the previous variable, this is set at 0%.

- **Exclusivity period for test data protection**

With regards to test data protection, as detailed in the definition of the scenarios, the basic scenario corresponds to Decree 1072 of 2009, which sets 'normal' exclusivity at 5 years. Despite any ambiguity caused by using 'normal', the 5-year exclusivity period is used for the basic scenario. Article 10.2 of the Agreement proposes an increase to 10 years, which is used in Alternative Scenario 2.

Basic Scenario:	5 years
Alternative Scenario 1:	5 years
Alternative Scenario 2:	10 years

- **Relative price of an active ingredient with market exclusivity and the same active ingredient in a competitive market**

The price differential between the active ingredient[16] in an pioneer version and its lower-priced generic version is used as a *proxy* for this variable. Using a selection of 20 medicines from the Essential Medicines List, the AIS-LAC study (2005)[17] established the price differential as 7.27 times.

- **Price elasticity of expenditure**

At this moment in time, there have been no studies on the elasticity of the Peruvian medicines' market, which is why two simulations were completed, one using an expenditure elasticity of zero (0) – i.e. expenditure on medicine remains the same despite increases in the general price index – and another simulation with an expenditure elasticity of minus one

[16] The term 'original medicine' is frequently used, however the use of the concept 'pioneer' is more suitable as this suggests it was the first to enter the market, whether globally or locally, whilst the term 'original' could suggest that the other medicines are fakes.

[17] AIS-LAC (2005*), Precios de medicamentos en el Perú* [Price of medicines in Peru]. www.aislac.org.

(-1) – i.e. expenditure increases in line with price. These two simulations were completed for the private and public sectors.

For the public market, expenditure elasticity is suspected to be much closer to zero, as it reflects the type of demand known as *needs-based demand, subject to cost minimisation strategies.* This means the required aggregated amount does not significantly decrease as a result of increases in the aggregated price, but requires the lower cost alternative of product substitutes.

- **Percentage of active ingredients protected by a (product) patent and/or with data exclusivity which will enter the market on an annual basis**

New active ingredients were chosen from the FDA *New Drugs Approvals Database 2005-2008* and their protection status was established in accordance with the Orange Book. Of the 105 active ingredients in the given period, 94.3% have some sort of protection, 69.5% have both types of protection, 11.4% have only patent protection and 13.33% have data protection.

Table 6

INTELLECTUAL PROPERTY PROTECTION OF ACTIVE INGREDIENTS APPROVED BY FDA (2005-2008)	
PATENTS AND DATA	69.52%
ONLY PATENT	11.43%
ONLY DATA	13.33%
NO PROTECTION	5.71%

Sources: FDA and Orange Book. Total of New Active Ingredients Approved: 105.

Results

As a direct result of applying the model, it is estimated that implementing the two measures would mean that, in order to maintain the current consumption levels in 2025, an increase of 459 million USD in Peru's total pharmaceutical expenditure is required or, there would need to be a 20% decrease in consumption. The consumption decrease is caused by an 11% increase in the number of IPR protected medicines, which in turn has led to a 26% price increase.

The extension of the effective patent period by 4 years, as a result of implementing the Supplementary Protection Certificates from Article 9.3 of the Intellectual Property Agreement Subgroup, could lead to an increase in pharmaceutical expenditure (PV) in 2025 of 159 million USD or a 9% decrease in consumption.

At the same time, a 10-year test data exclusivity period, as proposed by the EU in Article 10.2, would lead to an increase of more than 300 million USD in medicines' expenditure in 2025.

The total market can be broken down into institutional and private sectors. It is thought that the latter is affected to a greater degree. In 2025, the private market would experience a 12% increase in the volume of medicines with IPR protection (both patented medicines and those with IPR protection), which would cause a 27% increase in price. This, in turn, would require a 411 million USD increase in expenditure.

Given that the private market has a higher intake of medicines than the public market, it is estimated that the public sector would experience an 11% increase in 2025 in the volume of medicines with IPR protection, which would lead to a 25% increase in price and an increase in expenditure of 48 million USD.

Comparison with US Trade Promotion Agreement

By completing a comprehensive analysis of the different TRIPS Plus proposals, which have been advanced by developed countries in Peru and other Andean countries engaged in trade agreements, a complementarity has been identified between what was negotiated in the Trade Promotion Agreement with the United States (US TPA) and the trade agreement with the EU. This complementarity between the measures of the two proposals favours the multinational pharmaceutical industry, to the detriment of public health in Peru, since increased IPR for holders affects access to important pharmaceutical innovations.

On one hand, the US TPA calls for 1) Test data protection for five years, 2) An increased range of what can be patented by modifying patentability criteria,[18] and 3) Compensation for any delays in patent evaluation. These three measures would increase pharmaceutical expenditure, which in 2025 would amount to 1031 million USD.[19]

At the same time, the European proposal for the trade agreement[20] calls for enforcement measures, the impact of which has not been evaluated but is thought to be considerable and likely to complement the measures called for in the US TPA, in support of the multinational pharmaceutical industry. In addition to the enforcement provisions, these measures relate to 1) Extending patent monopolies by four years using Supplementary Protection Certificates, and 2) Extending data protection to 10 years. These two measures would have an impact estimated at 459 million USD.

Diagram 1

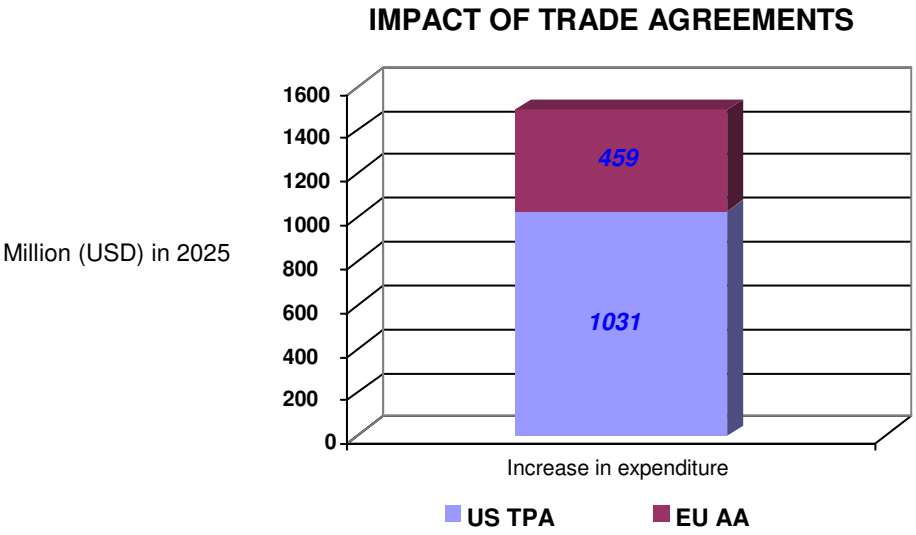

Table 7

IMPACT OF TRADE AGREEMENTS	
	Millions in 2025
EU AA	459 USD
US TPA	1031 USD

[18] By relaxing the patentability criteria, patents are being awarded for minor modifications on existing active ingredients, as shown in the examples in appendices 1 to 3.
[19] These impacts were calculated using information provided in this report.
[20] In the text from negotiation Round one, held in February in Bogotá.

The estimated impact of the European proposal for the agreement is described in more detail in the following tables. These tables contain the following columns:

Percentage of pharmaceutical products with protection. Shows the total percentage of the market that products with protection would occupy, whether from a patent or test data protection.

Price index. Indicates the impact the different changes in IPR would have on the price of medicines in the country. A value of 1 indicates no impact, higher values indicate directly related increases, E.g. a value of 1.3 indicates that prices would increase by 30%.

Expenditure variation. Indicates the overall budgetary change that must take place in the market in order to continue acquiring the same amount of medicines at the new prices.

Consumption reduction. Both for the institutional market and the total market, a reduction in consumption is expected to occur if expenditure is not adjusted to the increase in prices, which corresponds to an elasticity of 0.

Total Market

BASIC SCENARIO: TRIPS plus 2085	
YEAR	**ACTIVE INGREDIENTS WITH PROTECTION**
2010	7%
2015	22%
2020	28%
2025	28%
2030	25%

EFFECTS OF SCENARIO 1:
Patent extension using SPC

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1.00	0.00	0.00	0.00
2015	22%	1.00	0.00	0.00	0.00
2020	29%	1.02	19.76	14.28	-0.02
2025	31%	1.09	158.84	371.80	-0.08
2030	30%	1.13	319.97	1089.18	-0.12

EFFECTS OF SCENARIO 2:
Test data: (Formula 8+2+1, Art. 10.2)

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1.00	0.00	0.00	0.00
2015	24%	1.03	28.91	24.22	-0.03
2020	36%	1.18	233.95	489.54	-0.15
2025	35%	1.17	300.51	1388.34	-0.14
2030	31%	1.16	384.95	2363.55	-0.14

EFFECTS OF SCENARIO 3:
SPC + Data

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1.00	0.00	0.00	0.00
2015	24%	1.03	28.91	24.22	-0.03
2020	36%	1.19	253.71	528.03	-0.16
2025	39%	1.26	459.35	2288.18	-0.20
2030	37%	1.29	704.92	5740.90	-0.23

Private Market

BASIC SCENARIO: TRIPS plus 2085	
YEAR	**ACTIVE INGREDIENTS WITH PROTECTION**
2010	7%
2015	23%
2020	30%
2025	31%
2030	28%

EFFECTS OF SCENARIO 1:
Patent extension using SPC

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1.00	0.00		0%
2015	23%	1.00	0.00	0.00	0%
2020	31%	1.02	19.76	14.28	-2%
2025	35%	1.09	143.05	341.10	-9%
2030	34%	1.14	290.04	1000.37	-12%

EFFECTS OF SCENARIO 2:
Test data: (Formula 8+2+1, Art. 10.2)

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1,00	0,00		0%
2015	25%	1,03	28,91	24.22	-3%
2020	39%	1,18	207,49	430.42	-15%
2025	39%	1,17	268,22	1,224.70	-15%
2030	36%	1,17	348,05	2,097.64	-14%

EFFECTS OF SCENARIO 3:
SPC + Data

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1.00	0.00		0%
2015	25%	1.03	28.91	24.22	-3%
2020	40%	1.20	227.25	468.92	-17%
2025	43%	1.27	411.26	2,034.72	-21%
2030	42%	1.31	638.09	5,132.73	-23%

Public Market

BASIC SCENARIO: TRIPS plus 2085	
YEAR	**ACTIVE INGREDIENTS WITH PROTECTION**
2010	7%
2015	21%
2020	26%
2025	24%
2030	22%

EFFECTS OF SCENARIO 1:
Patent extension using SPC

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1.00	0.00		0%
2015	21%	1.00	0.00	0.00	0%
2020	26%	1.02	0.00	0.00	-2%
2025	28%	1.09	15.79	30.70	-8%
2030	26%	1.13	29.93	88.81	-11%

EFFECTS OF SCENARIO 2:
Test data: (Formula 8+2+1, Art. 10.2)

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1,00	0,00		0%
2015	22%	1,03	0,00	0,00	-3%
2020	33%	1,17	26,46	59,11	-15%
2025	31%	1,16	32,29	163.64	-14%
2030	27%	1,15	36,90	265.91	-13%

EFFECTS OF SCENARIO 3:
SPC + Data

YEAR	ACTIVE INGREDIENTS WITH PROTECTION	PRICE INDEX	INCREASE IN EXPENDITURE		DECREASE IN CONSUMPTION WITH EXPENDITURE ELASTICITY OF 0
			WITH EXPENDITURE ELASTICITY OF 1, FOR YEAR:	WITH EXPENDITURE ELASTICITY OF 1, ACCUMULATED (PV) FOR YEAR:	
2010	7%	1.00	0.00		0%
2015	22%	1.03	0.00	0.00	-3%
2020	33%	1.19	26.46	59.11	-16%
2025	35%	1.25	48.08	253.45	-20%
2030	32%	1.28	66.82	608.17	-22%

IPR Enforcement

The impacts calculated above do not address the issue of the measures proposed by the EU in relation to IPR enforcement, i.e. the requirements for exact and precise fulfilment of the IPR and the action that states would have to take in the event that such intellectual property rights were breached.

Although the impact of enforcement measures has not been estimated, it is still widely assumed that they have less of a detrimental effect than those measures that were evaluated. On the contrary, they can be just as negative and costly for the Peruvian State as the European proposal for extensions of patents and test data exclusivity. However, this impact estimation was not carried out as there is currently no transparent, clear methodology for such measurement. This methodology is currently being developed with the aim of promoting negotiations based on potential profits and losses as a result of the enforcement provisions.

In order to gain input for the development of this methodology, this section analyses the IPR enforcement provisions proposed by the EU in the agreement, according to the text from the negotiation round that took place in February 2009. The aim of this analysis is to identify and categorise the possible effects of the European proposal, in light of the studies on IPR enforcement carried out by Correa (2009), Muñoz & Tekeste (2008) and Seuba (2008).

Enforcement provisions proposed by the EU would have certain impacts in Colombia, Ecuador and Peru, which can be divided into two types. On one hand, the Andean countries would be responsible for the costs associated with implementing such measures, which could be a considerable amount of their budgets, bearing in mind that these are middle-income countries. These impacts are called *direct implementation effects* and include, amongst other things:

- The cost of modifying the regulatory framework.
- The periodic cost of training staff in accordance with the new regulations (judges, customs officers, patent office employees, medicine registration agency employees).
- The periodic cost of border measures (cost of increasing control of importation, exportation and re-exportation, the cost of the increased number of lawsuits, etc).

Furthermore, there is another type of effect that discourages generic competitors from entering the market, which would directly affect access to medicines by creating a

threatening environment for trade and lawful competition in the pharmaceutical industry. The average price of pharmaceutical products would therefore, increase, which would threaten the coverage of medicines in Colombia, Ecuador and Peru.

These effects, called *dissuasive effects*, are the result of strengthening the position of IPR holders, who can abuse such rights, and decreasing the rights of generic competitors. In the medium and long term, these *dissuasive effects* can have a greater negative impact than the implementation effects, since they pave the way for more concentrated markets.

Some of the dissuasive effects are the result of a combination of the following provisions proposed by the EU:

- An increase in applicants entitled to initiate processes in the event of any IPR breaches (strengthening the position of the holder).
- New precautionary and provisional measures for goods that constitute an alleged IPR infringement, arguing the need to protect them as legal evidence of such an infringement. (Strengthening the position of the holder, to the detriment of the position of the competitor.)
- Clear establishment of compensation and extreme criminal penalties for those who infringe an IPR. (Strengthening the position of the holder.)
- New border measures that explicitly include alleged patent infractions, which were not included in the TRIPS agreement, in addition to the many differentiation requirements that the generic competitor must meet – i.e. differentiating their names, logos, labelling and instructions from a registered trademark.
- The new border measures requiring that, if it is 'suspected' that a product infringes a patent or registered trademark in a country, it can be seized even if the product is not intended for that country's market, but is only in transit.

These provisions, which will be looked at in greater detail later, would not have such a considerable dissuasive effect if the concepts of counterfeit medicines and generic competitor medicines were clearly distinguished, both in the treaty and in practice. However, the EU's proposal for the agreement has certain grey areas that enable holders to abuse their IPR, appealing for infringements when there is no evidence.

In the following sections, the European proposals on enforcement provisions for the agreement are described in greater detail. Specific reference is made to Seuba (2008) who

analyses the enforcement measures of the aforementioned proposal, by comparing it with the TRIPS agreement.

Principal enforcement measures of the Agreement

Entitled applicants- Entitled applicants are understood to be holders or third parties who are authorised to call for legal proceedings to obtain IPR enforcement.

Article 14 of the European proposal in the Round one text establishes some explicit entitled applicants, who, in addition to IPR holders, can call for legal action. On this matter, Seuba (2008) states:

> *"[...] The TRIPS Agreement does not include within its entitled applicants third parties legally authorised to exercise a holder's rights, a matter left up to the nations themselves to decide. The European proposal does away with that decision-making power and expands and specifies the legitimacy when it includes among the "entitled applicants" "the holders of intellectual property rights", "all other persons authorised to use those rights, in particular licensees", "professional defence bodies", and, in the event the parties so recognise them, "intellectual property collective rights management bodies".* p. 48.

There is a cost involved in implementing this provision due to additional legal proceedings and periodic training will also be necessary for judges. Moreover, the threat and frequency of legal proceedings could dissuade generic competitors, who will have to take these risks into consideration in their costs.

Evidence of infringements- This refers mainly to the authority and commitment of legal authorities concerning the management of evidence presented by IPR holders, when they report an alleged infringement of their rights. In the case of medicines, evidence of the alleged violations would refer to batches and/or loads of medicines which an IPR holder considers are in violation of their rights.

The European proposal regarding the management of evidence (Articles 15 and 16) states that in order to protect evidence of infringements, goods that are presumed to be in violation of an IPR can be seized, along with materials or instruments used for their production or distribution and any related information. Where all these measures are not enough to protect evidence, Article 16 states that these can be seized without giving the alleged infringing party an opportunity to be heard.

This means that the provision not only increases the rights of holders, taking dramatic measures to defend their IPR, but also reduces the rights of the alleged infringing parties, since they are not given the opportunity to be heard before the authorities carry out the aforementioned seizures. Therefore, this measure not only has a great *dissuasive effect*, but also a high implementation cost, since it involves judges, police and customs agents who specialise in IPR.

Right to information concerning the infringement- This refers to the IPR holder's right to information concerning the infringement, since the EU proposal states that one of the holder's rights is to request information both from the infringer and also from those in possession of such information, those using the goods associated with the infringement or those who have supplied them on a commercial scale.

> *"The European proposal lacks the provision found in the TRIPS Agreement that allows infringing parties not to inform on third parties or distribution channels if this "would be out of proportion to the seriousness of the infringement." Secondly, what the TRIPS Agreement assumes to be a power of the state […] to authorise the "judicial authorities", the European proposal turns into a right of the claimant since it lays out that information may be ordered turned over in response to "a justified and proportionate request of the claimant".* Ibid. p. 53

Once again, this is a provision with a great dissuasive effect, as it increases holder's rights, to the detriment of the rights of the alleged infringers.

Damages and compensation for holders- This refers to damages caused by the IPR infringer and the type of compensation the infringer must pay to the IPR holder. On this matter, Seuba (2008) is very clear:

> *"Not only in the European proposal must there be "adequate" payment, but this must also encompass "all appropriate aspects", which at least includes profits made by the infringer and, lost profits and even "moral prejudice" suffered by the right's holder. The European proposal even goes as far as permitting a lump sum payment for damages caused".* Ibid. p. 54

Noting that this provision is aimed directly at actual infringers and not at 'alleged' infringers, it is possible to think that there are no major *dissuasive effects*. However, such effects are created by the lack of any explicit limits between the concept of generic and counterfeit products.

Penalties- The multilateral trade agreement between the EU and CAN countries began in September 2007, as part of an Association Agreement between the blocs. This lasted until April 2008. In February 2009, when bloc negotiations failed, Colombia, Ecuador and Peru began the multilateral trade agreement negotiations, allowing each country to negotiate with the EU at their own pace.

In Article 26 of the EU proposal for the Association Agreement, penalties are established for infringers, such as fines, the confiscation of products, the destruction of goods, closing down of any involved establishments and even incarceration.

The Agreement currently under negotiation considers establishing these types of penalties, although the associated article had yet to be specified, as of the February 2009 Round.

Border measures- One element of the enforcement measures are the so-called border measures, which refer to the customs authorities' duties in the event that a product infringing an IPR enters a given territory. These measures have a high impact, which is why they are usually analysed independently from the other enforcement provisions.

The border measures required by the TRIPS Agreement state that in a given country, an IPR holder can call upon the legal authorities to ensure that customs authorities seize a suspected counterfeit product that violates their rights, when it is believed that this will *be imported* into the aforementioned country. The European proposal goes further, since it states that the holder can make the aforementioned request when he believes that the aforementioned product is going to be *imported, exported, re-exported, enter or leave the customs territory* of the country where the holder claims there has been an infringement on their rights.

While the TRIPS agreement considers only 'counterfeit goods' within the border measures – i.e. those which bear exactly the same brand as the validly registered brand, or which fail to differentiate themselves from the registered brand – the European proposal for the Agreement also includes goods that are suspected of infringing a patent. In addition to this, the EU requires that generic products have a brand which is clearly different from a registered brand, and that they also have different logos, labels, stickers and instructions.

By implementing these measures, there is a chance that the generic version of a medicine that has a patent in an EU country will be at a disadvantage in international trade, since it will be difficult to export the product from this country or to pass through customs. This is perhaps the most evident dissuasive effect, if one bears in mind that the generic competitors

would have to establish new trading routes, which would in turn increase costs, making it less viable to market generic products.

In addition to the high dissuasive effect, there is also the cost of implementing these border measures, since it will be necessary to train judges and customs agents on IPR in Colombia, Ecuador and Peru. Furthermore, if this training is funded by the IPR holders, whether in the EU or Colombia, Ecuador and Peru, there is the risk of bias in their favour, facilitating abuse of their rights.

Medicines are already being seized for alleged IPR violations, without the enforcement of the treaties being negotiated by the EU and Colombia, Ecuador and Peru. This has been proven by recent events in the Netherlands and Germany, where generic medicines in transit were seized in these countries even though there was no patent in the country of destination, or in the country of origin.

Date	Medicine	Requesting party	Place of origin	Transit location	Final destination
Apr 2008	Atorvastatin	Warner-Lambert	India	Schiphol	Colombia
Apr 2008	Sildenafil	Pfizer	India	Schiphol	Colombia
Nov 2008	Valsartan	Novartis	India	Schiphol	Colombia
Nov 2008	Atorvastatin	Warner-Lambert	India	Schiphol	Peru
Nov 2008	Rivastigmine	Novartis	India	Schiphol	Peru
Nov 2008	Olanzapine	Eli Lilly	India	Schiphol	Peru
Jun 2009	Amoxicillin	GlaxoSmithKline	India	Frankfurt	Vanuatu

Of particular note is the seizure of Amoxicillin marketed in its generic form,[21] which was going from India to the island of Vanuatu, passing through Frankfurt. This medicine has been marketed for more than 20 years and does not have an applicable patent, or current data exclusivity in either the transit country or the final destination, and has been marketed by the INN, which means there would be no IPR infringement.

It is therefore clear that the measures proposed by the EU with regards to the IPR enforcement would create a regulatory framework that would not only disproportionately strengthen the position of IPR holders, but would also greatly deter potential competitors, since the cost of infringing an IPR would be so great that potential competitors would reconsider entering the market to avoid any type of penalty.

[21] The generic name or International Non-proprietary Name corresponds to the name of the active ingredient or molecule, and is not associated with the registered trademark of any holder.

This is particularly true if one considers that, in order to speed up the process, the alleged offender is not given the opportunity to be heard. This could lead to sentences being passed based merely on presumptions.

The way in which this is would deter competition is clear, given that in the pharmaceutical industry, a rights' holder laboratory specialising in new medicines in a certain therapeutic area can use different strategies in order to extend patents, such as *selection patents* and *Markush claims*. If these are combined, as seen in the appended examples, IPR can be guaranteed for periods of more than 20 years.

This would make it difficult for potential competitors to know the IP protection status of a medicine, even more so since a large percentage of generic medicine laboratories do not concentrate on smaller therapeutic areas but produce a wide range of such products.

The measures proposed by the EU regarding IPR enforcement give holders a new role, moving from a situation where they can prevent and sue the infringement of some rights to a situation where they can make the alleged infringement criminal, even when it has not been fully proven. This, therefore, reduces the alleged infringer's rights.

IPR holders would have a greater opportunity to block potential competitors. Even though these competitors may not be breaching any IPR rights, simply by being accused of infringement, their goods can be seized or destroyed, and their commercial and financial networks can be blocked. This is helped by the confusion created by IPR holders and the owners of registered trademarks, concerning the issues of generics, copies, counterfeits and pirated products.

APPENDIX 1

One example of a patent with a new formulation is that granted to the pharmaceutical form 'mups' (multiple unit pellets system) of omeprazole and esomeprazole. The mups system is a formulation in which each dose is divided into small units with modified release properties. To summarise, it is a modified release tablet of omeprazole and esomeprazole. Below is a summary of the patent document granted in the US and its claims. This can be viewed on www.uspto.gov.

Oral pharmaceutical multiple unit tableted dosage form

Patent number: WO 96/01623

Publication date: 1996-01-25

A new pharmaceutical multiple unit tableted dosage form containing omeprazole or one of its single enantiomers or an alkaline salt of omeprazole or one of its single enantiomers, a method for the manufacture of such a formulation, and the use of such a formulation in medicine.

Claims

1. An oral pharmaceutical multiple unit tableted dosage form comprising tablet excipients and individually enteric coating layered units of a core material containing active substance in the form of omeprazole or one of its single enantiomers or an alkaline salt of omeprazole or one of its single enantiomers, optionally mixed with alkaline compounds, covered with one or more layer(s), of which at least one is an enteric coating layer, whereby the enteric coating layer has mechanical properties such that the compression of the individual units mixed with the tablet excipients into the multiple unit tableted dosage form does not significantly affect the acid resistance of the individually enteric coating layered units.

2. A tableted dosage form according to claim 1, wherein the acid resistance of the individually enteric coating layered units is in coherence with the requirements on enteric coated articles defined in the United States Pharmacopeia.

3. A tableted dosage form according to claim 1, wherein the acid resistance of the individually enteric coating layered units does not decrease more than 10 % during the compression of the individual units into the multiple unit tableted dosage form.

4. A tableted dosage form according to claim 1, wherein the enteric coating layer covering the individual units comprises a plasticized enteric coating layer material.

5. A tableted dosage form according to claim 1, wherein the enteric coating layer covering the individual units has a thickness of at least 10pin.

6. A tableted dosage form according to claim 1, wherein the individually enteric coating layered units are further covered with an over-coating layer comprising pharmaceutically acceptable excipients.

7. A tableted dosage form according to claim 1, wherein the active substance is a magnesium salt of omeprazole having a degree of crystallinity which is higher than 70 % as determined by X-ray powder diffraction.

Taken from ICTSD, WHO, UNCTAD (2006) Op. Cit.

APPENDIX 2

An example of a patent for new dosage forms, granted for the sublingual form of Apomorphine which is given between 2.5 and 10Mg and dissolves within about 2 to 5 minutes.

Dosage forms and method for ameliorating male erectile dysfunction

Patent number: WO9528930

Publication date: 1995-11-02

Psychogenic impotence or erectile dysfunction can be identified in psychogenic male patients and can be ameliorated, without substantial undesirable side effects, by sublingual administration of apomorphine dosage forms that contain about 2.5 to about 10 milligrams of apomorphine and dissolve within a time period of about 2 to about 5 minutes.

Claims

1. A method of ameliorating erectile dysfunction in a psychogenic male patient which comprises administering to said patient apomorphine or a pharmaceutically acceptable acid addition salt thereof sublingually prior to sexual activity, and in an amount sufficient to induce an erection adequate for vaginal penetration but less than the amount that induces nausea.
2. The method in accordance with claim 1 wherein the amount of apomorphine administered is in the range of about 2.5 milligrams to about 10 milligrams.
3. The method in accordance with claim 1 wherein the amount of apomorphine administered is in the range of about 25 to about 60 micrograms per kilogram of body weight.
4. The method in accordance with claim 1 wherein apomorphine is administered as the hydrochloride salt.

Taken from ICTSD, WHO, UNCTAD (2006) Op. Cit.

APPENDIX 3

This appendix shows an example of two or more patents associated with one specific pharmaceutical product – i.e. an active ingredient, in a pharmaceutical form and a certain concentration. This could be the result of *selection patents, Markush claims* and *pharmaceutical composition patents.* The product in question is:

Taclonex® (calcipotriene 0.005% and betamethasone dipropionate 0.064%, topical ointment)

This medicine was approved for commercialisation in the US on January 9, 2006 and its Orange Book format description is shown in the table below:

Active Ingredient:	BETAMETHASONE DIPROPIONATE; CALCIPOTRIENE HYDRATE
Dosage Form;Route:	OINTMENT; TOPICAL
Proprietary Name:	TACLONEX
Applicant:	LEO PHARM
Strength:	0.064%; 0.005%
Application Number:	021852
Approval Date:	Jan 9, 2006

Source: OrangeBook, FDA.

As the following table shows, this specific product is associated with three different patents, in accordance with the number of patents shown in the table. Two of these have different expiration dates, i.e. patents 5763426 and 6753013 that expire in 2015 and 2020. Considering that the product entered the market in 2006, the first patent ensures an effective monopoly of 9 years, whereas the second ensures one of 14 years.

Appl No	Patent No	Patent Expiration
021852	5763426	Jun 09, 2015
021852	6753013	Jan 27, 2020
021852	6753013	Jan 27, 2020
021852	RE39706	Jun 09, 2015

Source: OrangeBook, FDA.

The number shown in the second column is assigned in the US by the U.S. Patent and Trademark Office (USPTO). By running a query in their database, the following patents can be found with their respective claims.

PATENT 1

United States Patent **5763426**

Crystalline form of a vitamin D analogue

The present invention relates to calcipotriol hydrate – a new crystalline form of calcipotriol – with superior technical properties and with superior stability.

Assignee: **Leo Pharmaceutical Products Ltd.** (Ballerup, **DE**)

PCT Filed: **January 15, 1993**

PCT Pub. No.: **WO94/15912**

PCT Pub. Date: **July 21, 1994**

Claims

1. Calcipotriol monohydrate characterized by its storage stability at 40.degree. C. after 12 months, its ready wettability and wet ball milling characteristics.
2. Pharmaceutical composition containing the compound of claim 1.
3. Pharmaceutical composition according to claim 2 which is a cream.
4. Pharmaceutical composition according to claim 2 which is a gel.
5. Pharmaceutical composition according to any one of claim 4, with a content of the active component of 1-100 .mu.g/g of the composition.
6. The method of preparing calcipotriol monohydrate which comprises dissolving calcipotriol in organic solvent and then adding water to the resulting solution to precipitate the hydrate, said hydrate being characterized by its storage stability at 40.degree. C., its ready wettability and wet ball milling characteristics.
7. In the preparation of a gel formulation which involves wet ball milling a calcipotriol component and adding the wet milled calcipotriol component to a gel base, the improvement which comprises wet milling calcipotriol hydrate as said component and using this wet milled hydrate for addition to said gel base, said hydrate being characterized by its storage stability at 40.degree. C. after 12 months, its ready wettability and wet ball milling characteristics.

* * * * *

PATENT 2

United States Patent **6753013**

Pharmaceutical composition

A pharmaceutical composition for dermal use, wherein the composition has a first pharmacologically active component A consisting of at least one vitamin D or vitamin D analogue, and a second pharmacologically active component B consisting of at least one corticosteroid, wherein the difference between the maximum stability pH of said first component A and the maximum stability pH of said second component B is at least 1. The composition can also have at least one solvent component C, where component C is compounds of the general formula R.sup.3 (OCH.sub.2 C(R.sup.1)H).sub.x OR.sup.2 (I), wherein x is in the range of 2-60, R.sup.1 in each of the x units independently is H or CH.sub.3, R.sup.2 is straight chain or branched C.sub.1-20 alkyl or benzoyl, and R.sup.3 is H or

phenylcarbonyloxy; di-(straight or branched)-C.sub.4-10 alkyl esters of C.sub.4 -C.sub.8 dicarboxylic acids; straight or branched C.sub.12-18 -alkyl benzoates; straight or branched C.sub.2-4 -alkyl esters of straight or branched C.sub.10-18 -alkanoic or -alkenoic acids; propylenglycol diesters with C.sub.8-14 -alkanoic acids; and branched primary C.sub.18-24 alkanols.

Assignee: **Leo Pharmaceutical Products, Ltd. A/S** (Ballerup, **DK**)

PCT Filed: **January 27, 2000**

PCT Pub. No.: **WO00/64450**

PCT Pub. Date: **November 02, 2000**

Claims

1. A pharmaceutical composition for dermal use, said composition comprising: a first pharmacologically active component A consisting of at least one vitamin D or vitamin D analogue selected from the group consisting of seocalcitol, calcipotriol, calcitriol, tacalcitol, maxacalcitol, paricalcitol, falecalcitriol, 1.alpha.,24S-dihydroxy-vitamin D2, 1(S),3(R)-dihydroxy-20(R)-[((3-(2-hydroxy-2-propyl)-phenyl)-methoxy)-methyl]- 9,10-seco-pregna-5(Z),7(E),10(19)-triene and mixtures thereof; and a second pharmacologically active component B consisting of at least one corticosteroid, wherein the difference between the maximum stability pH of said first component A and the maximum stability pH of said second component B is at least 1; and at least one solvent component C selected from the group consisting of: (i) compounds of the general formula R.sup.3 (OCH.sub.2 C(R.sup.1)H).sub.x OR.sup.2 (I) wherein x is in the range of 2-60, R.sup.1 in each of the x units independently is H or CH.sub.3, R.sup.2 is straight chain or branched C.sub.1-20 alkyl or benzoyl, and R.sup.3 is H or phenylcarbonyloxy; (ii) di-(straight or branched)-C.sub.4-10 alkyl esters of C.sub.4 -C.sub.8 dicarboxylic acids; (iii) straight or branched C.sub.12-18 -alkyl benzoates; (iv) straight or branched C.sub.2-4 -alkyl esters of straight or branched C.sub.10-18 -alkanoic or -alkenoic acids; (v) propylenglycol diesters with C.sub.8-14 -alkanoic acids; and (vi) branched primary C.sub.18-24 alkanols.
5. The composition according to claim 1 or 2, wherein said corticosteroid is selected from the group consisting of ***Betamethasone***, Clobetasol, Clobetasone, Desoximethasone, Diflucortolon, Diflorasone, Fluocinonid, Flumethasone, Fluocinolon, Fluticasone, Fluprednidene, Halcinonide, Hydrocortisone, Momethasone, Triamcinolon, and pharmaceutically acceptable esters and acetonides as well as mixtures thereof.

* * * * *

This second patent has another 21 claims, which are not shown in this summary.