

Public Health Perspective on Intellectual Property and Access to Medicines

A compilation of studies prepared for WHO



Carlos M. Correa



SOUTH
CENTRE

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AND ACCESS TO MEDICINES**

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TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS	<i>xi</i>
PREFACE	<i>xiii</i>
CHAPTER I	
THE URUGUAY ROUND AND DRUGS.....	1
EXECUTIVE SUMMARY	1
INTRODUCTION.....	2
PATENTS.....	3
General Principles.....	4
Non-patentability: Biotechnology Based Drugs	5
Non-discrimination Clause	6
Rights Conferred: Imports	7
Rights Conferred: Protection of Products through Protection of the Process	8
Exceptions to Exclusive Rights	8
Granting of Compulsory Licences	9
Term of Protection.....	13
Reversal of the Burden of Proof	13
UNDISCLOSED INFORMATION	14
TRANSITIONAL PERIODS	16
General Grace Period.....	16
New Patentable Areas	16
Protection of Existing Subject Matter.....	17
Prior Compulsory Licenses and Application	17
Pharmaceutical and Agricultural Chemical Products	18
ENFORCEMENT AND SETTLEMENT OF DISPUTES.....	19
IMPLICATIONS FOR THE DEVELOPMENT, PRODUCTION AND MARKETING OF DRUGS	20
CONCLUSIONS	22
REFERENCES.....	24
CHAPTER II	
TRENDS IN DRUG PATENTING: CASE STUDIES	27

INTRODUCTION	27
THE CASES	30
1. Paroxetine.....	30
2. Amlodipine/Amlodipine Besylate.....	32
3. Alendronate	35
4. Clarithromycin	42
5. Omeprazole	45
6. Fluconazole	51
7. Ofloxacin/Levofloxacin.....	52
8. Fexofenadine	53
9. Recombinant Erythropoietin	55
CONCLUSIONS	57
REFERENCES	59
CHAPTER III	
PROTECTION OF DATA SUBMITTED FOR	
THE REGISTRATION OF PHARMACEUTICALS:	
IMPLEMENTING THE STANDARDS OF THE TRIPS AGREEMENT	61
EXECUTIVE SUMMARY	61
INTRODUCTION	62
DATA REQUIRED FOR THE REGISTRATION OF PHARMACEUTICALS	63
THE RATIONALE FOR DATA PROTECTION	65
Approaches to Data Protection	65
National Practices Before TRIPS	66
CONDITIONS OF PROTECTION UNDER TRIPS	68
Protection of Test Data Under the TRIPS Agreement	68
The Article 39.3 Conditions of Protection	69
NON-DISCLOSURE OBLIGATION	72
PROSCRIBED ACTS OF UNFAIR COMMERCIAL USE	74
The TRIPS Agreement Text	74
National Case Law.....	79
MEANS OF PROTECTION AGAINST UNFAIR COMMERCIAL USE	83
THE EXCLUSIVITY APPROACH.....	86
THE HISTORY OF THE TRIPS NEGOTIATIONS.....	90
CONCLUSIONS	91

ANNEX 1

Exclusive Use of Data and Compensation Under the U.S. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).....	93
--	----

REFERENCES	94
-------------------------	-----------

CHAPTER IV

IMPLICATIONS OF THE DOHA DECLARATION ON THE TRIPS AGREEMENT AND PUBLIC HEALTH.....	97
---	-----------

EXECUTIVE SUMMARY	97
--------------------------------	-----------

INTRODUCTION	98
---------------------------	-----------

SCOPE	101
--------------------	------------

THE ROLE OF TRIPS AND IPRS	102
---	------------

PUBLIC HEALTH MEASURES	103
-------------------------------------	------------

FLEXIBILITY IN TRIPS.....	106
----------------------------------	------------

Interpretation	107
----------------------	-----

Compulsory Licences	108
---------------------------	-----

Emergency	108
-----------------	-----

Exhaustion	110
------------------	-----

MEMBERS WITH INSUFFICIENT OR NO MANUFACTURING CAPACITIES.....	111
--	------------

Addressed Problem.....	112
------------------------	-----

Possible Approaches	115
---------------------------	-----

Safeguards	121
------------------	-----

Compulsory Licence in the Importing Country	122
---	-----

Economic Feasibility	122
----------------------------	-----

Legal Implementation	124
----------------------------	-----

TRANSFER OF TECHNOLOGY TO LDCs.....	124
--	------------

EXTENSION OF TRANSITIONAL PERIOD FOR LDCs.....	125
---	------------

SPECIAL TREATMENT UNDER TRIPS	129
--	------------

LEGAL STATUS OF THE DOHA DECLARATION	130
---	------------

ISSUES NOT COVERED IN THE DECLARATION	131
--	------------

CONCLUSIONS	131
--------------------------	------------

ANNEX 1

Doha Declaration on the TRIPS Agreement and Public Health	133
---	-----

ANNEX 2	
Levels of Development of Pharmaceutical Industry, by Country.....	135
REFERENCES	138

CHAPTER V	
IMPLEMENTATION OF THE WTO GENERAL COUNCIL	
DECISION ON PARAGRAPH 6 OF THE DOHA	
DECLARATION ON THE TRIPS AGREEMENT	
AND PUBLIC HEALTH	141

INTRODUCTION	141
---------------------------	------------

CIRCUMSTANCES IN WHICH THE DECISION MAY BE USED.....	143
Legal Status of the Decision	143
Amendment to National Laws	143
Patent Rights in Force.....	146
In What Circumstances Does the Decision Apply?	147
Covered Products.....	148
Which Countries Can Use the System?	149
For What Purposes Can the System Be Used?	149

COMPULSORY LICENCE IN THE IMPORTING COUNTRY	150
Notification of Intention to Use the System	150
Notification About Needed Products, Compulsory Licence	151
Establishing Lack of or Insufficient Manufacturing Capacity	152
Confirming the Intention to Grant a Compulsory Licence	153

COMPULSORY LICENCE IN THE EXPORTING COUNTRY	154
Amount Necessary to Meet Needs.....	154
Identification of Product(s).....	155
Notification by the Supplier.....	157
Notification by the Exporting Country	157

ANTI-DIVERSION MEASURES	158
--------------------------------------	------------

SUSPENSION OF THE SYSTEM	158
---------------------------------------	------------

CONCLUSIONS	159
--------------------------	------------

ANNEX 1	
Implementation of Paragraph 6 of the Doha Declaration	
on the TRIPS Agreement and Public Health	160

ANNEX 2	
Summary of Context and Steps Required to Use the System	165

CHAPTER VI	
GUIDELINES FOR THE EXAMINATION OF PHARMACEUTICAL PATENTS: DEVELOPING A PUBLIC HEALTH PERSPECTIVE	169
INTRODUCTION	169
DEFINING PATENTABILITY AND DISCLOSURE STANDARDS.....	170
TYPICAL CLAIMS RELATING TO PHARMACEUTICAL INVENTIONS.....	174
Formulations and Compositions	174
Combinations	176
Dosage/Dose	177
Salts, Ethers and Esters	178
Polymorphs	180
Markush Claims	182
Selection Patents	185
Analogy Processes	188
Enantiomers	189
Active Metabolites and Prodrugs	191
Methods of Treatment.....	192
Use Claims, Including Second Indications	194
MECHANISMS TO ENHANCE THE EXAMINATION OF PHARMACEUTICAL PATENTS FROM A PUBLIC HEALTH PERSPECTIVE	198
Pre- and Post-grant Opposition.....	198
Examination Rules and Procedures	200
CONCLUSIONS	201
ANNEX	203
REFERENCES	226

CHAPTER VII	
GUIDE FOR THE APPLICATION AND GRANTING OF COMPULSORY LICENCES AND AUTHORIZATION OF GOVERNMENT USE OF PHARMACEUTICAL PATENTS	229
INTRODUCTION	229
COMPULSORY LICENCES	231
Establishing the Need to Apply for a Compulsory Licence	231
Special Situation of Least Developed Countries.....	232
Determining the Patent Status of Required Products	233
Searching Patent Data	234
Establishing Whether the Acts to Be Performed Are Subject to Patent Rights	235
Articulating the Grounds for Compulsory Licences	235
Compulsory Licence Solely for Importation	236
Applying for a Compulsory Licence	236
Summary.....	242

Procedures for Granting a Compulsory Licence	242
Data Exclusivity	245
GOVERNMENT USE	246
Who Can Authorize the Use of a Patent?	246
Content of an Administrative Act Authorizing Government Use.....	246
Who Can Use the Patent(s)?	247
Notification of the Patent Owner	247
ANNEX 1	
Declaration on the TRIPS Agreement and Public Health.....	248
ANNEX 2	
Certification of Non-Recognition and Non-Enforceability of Patents and Data Protection in Respect of Pharmaceutical Products	250

ABBREVIATIONS AND ACRONYMS

ANDS	Abbreviated New Drug Submission
ARIPO	African Regional Industrial Property Organization
CLs	compulsory licences
DSU	Understanding on Rules and Procedures Governing the Settlement of Disputes
EC	European Commission
EMR	Exclusive Marketing Rights
EPA	Environmental Protection Agency
EPO	European Patent Office
EU	European Union
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FTAs	Free Trade Agreements
GATT	General Agreement on Tariffs and Trade
IIPi	International Intellectual Property Institute
IPRs	intellectual property rights
LDCs	least developed countries
MFN	most-favoured-nation
NAFTA	North American Free Trade Agreement
NDS	New Drug Submission
OAPI	Organisation Africaine de la Propriété Intellectuelle
SPS	Agreement on the Application of Sanitary and Phytosanitary Measures
TBT	Agreement on Technical Barriers to Trade
TRIPS	Agreement on Trade-Related Aspects of Intellectual Property Rights
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNCTAD	United Nations Conference on Trade and Development
UNDP	United Nations Development Programme
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

PREFACE

The purpose of this book is to facilitate the elaboration of national health policies and strategies to improve access to medicines, using fully the flexibilities allowed by the Agreement on Trade Related Aspects of Intellectual Property Rights ('TRIPS Agreement') of the World Trade Organization (WTO). It includes documents of the World Health Organization (WHO) written by Professor Carlos Correa and published between 1997 and 2009. As consultant to the WHO medicines department, Professor Correa helped to initiate and formulate WHO policy perspectives and to provide advice to Members States on intellectual property issues relating to the production and distribution of medicines. The content of this book illustrates the pioneer role that WHO played in identifying the public health implications of the binding rules introduced by the TRIPS Agreement.

Chapter I contains "The Uruguay Round and Drugs" (1997), the very first publication that examined how the TRIPS Agreement could affect access to medicines. This paper is based on a submission made to a conference organized in 1995 by Universidad Carlos III of Madrid with the WHO Drugs Action Programme (DAP).¹ The 40 page article, in particular, describes the "room for manoeuvre" left by the TRIPS Agreement to protect public health. This was probably the first document that specifically alerted the health sector of the possible implications of the TRIPS Agreement on public health and how to interpret it so as to preserve policy space for ensuring access to medicines. The WHO Assistant Director General stated in the preface to this document: "I consider this article a major contribution to the understanding of the influence of WTO TRIPS Agreement on WHO policies and strategies in regard to pharmaceutical products, food safety, blood products, medical devices and others".

Chapter II contains "Trends in Drug Patenting" (2001), a study prepared for the Department of Essential Medicines and Pharmaceutical Policies of WHO in the framework of the Network for Monitoring the Impact of Globalization and TRIPS on Access to Essential Drugs. It examines a number of specific cases of patenting in the area of medicines. It was one of the first studies documenting the practice of 'evergreening' by the pharmaceutical industry, that is, the filing of patents on formulations, salts, prodrugs, isomers, etc. of known drugs in order to delay the entry of generic versions. As a result of this practice, which distorts the objective of the patent system as an incentive for genuine innovations, thousands of patents have been granted in some countries despite that only a few new chemical entities are developed per year.

Chapter III incorporates the document on "Protection of Data Submitted for the Registration of Pharmaceuticals. Implementing the Standards of the TRIPS Agreement" (2002), jointly published by WHO and South Centre. The protection of data submitted for the registration of pharmaceuticals in the context of article 39.3 of the TRIPS Agreement has been an issue of a major practical importance for developing countries. Some developed countries and the pharmaceutical industry argued that Article 39.3 required WTO Members to confer exclusive rights to the originators of clinical data, thereby preventing other firms from using or relying on such data to obtain marketing approval of generic versions of the same medicine. Professor Correa, however, stated very clearly that "Countries are not obligated under Article

¹ Carlos M. Correa, "The Uruguay Round and drugs", WHO/TFHE/97.1, Distr: General, Original: English, 1997, p. 40.

39.3 of TRIPS, to confer exclusive rights on the originator of marketing approval data.” He provided a number of reasons to demonstrate that the ‘data exclusivity’ approach was not incorporated into the TRIPS Agreement. This paper was produced with the support of the Rockefeller Foundation and the draft was reviewed by Trevor Cook, Jim Keon, James Love, Jerome Reichman, Robert Weissman and Germán Velásquez. WHO also received comments from Octavio Espinoza (WIPO) Adrian Otten (WTO) and Jayashree Watal (WTO). The analysis provided in this document was instrumental in supporting governments that opted, as allowed by the TRIPS Agreement, to protect test data under the discipline of unfair competition without granting exclusive rights.

Chapter IV, “Implications of the Doha Declaration on the TRIPS Agreement and Public Health” (2002) is based on a paper commissioned by WHO shortly after the Doha Ministerial Declaration was adopted. It provides: (1) an overview of the declaration’s background; (2) an analysis of the Declaration’s content; (3) guidance to WTO Members by presenting possible options they may consider in resolving the problem posed in Paragraph 6 of the Declaration, and (4) a discussion of related issues not covered by the Declaration, such as the exceptions to patent rights (Article 30) and the protection of data submitted for registration (Article 39.3).

Chapter V contains the document on “Implementation of the WTO General Council Decision on Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health” (2004). It discusses the practical steps that need to be taken to use the mechanism established by paragraph 6 of the Doha Declaration. The document emphasized that the so-called “paragraph 6 problem” needed a stable international legal framework; transparency and predictability of the applicable rules in the exporting and importing countries; simple and speedy legal procedures in the exporting and importing countries; equality of opportunities for countries in need of medicines, even for products not patented in the importing country; facilitation of a multiplicity of potential suppliers of the required medicines, both from developed and developing countries; and broad coverage in terms of health problems and the range of medicines.

After more than 10 years of the adoption of the paragraph 6 decision, the system it created has only been used once by one country.

While the implementation of paragraph 6 was based on a complex system of compulsory licenses, there were other simpler and more straightforward options. Thus, in an intervention on 17 September 2002, the WHO representative to the WTO TRIPS Council stated: “Among the solutions being proposed, the limited exception under Article 30 is the most consistent with this public health principle. This solution will give WTO Members expeditious authorization, as requested by the Doha Declaration, to permit third parties to make, sell and export patented medicines and other health technologies to address public health needs.”

Chapter VI contains the “Guidelines for the Examination of Pharmaceutical Patents: Developing a Public Health Perspective”. In 2005, based on the mandate given by the World Health Assembly (WHA) through different resolutions, the WHO Essential Medicines Programme decided to develop 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 were held with the participants from more than 20 countries including representatives the South Centre, WHO, UNCTAD, ICTSD, the Lausanne Polytechnic School, WIPO, WTO, MSF and Third World

Network. Comments and contributions were also received from experts in public health and patents from Australia, United Kingdom and WHO.

In order to develop a legal and normative framework to grant pharmaceutical products patent protection that ensures a balance between the producers and the users of technological knowledge (as required by Article 7 of the TRIPS Agreement), several issues need to be carefully examined at the national level. The guidelines for the examination of patents are probably one of the major WHO contributions to tackle the challenge of access to medicines in the context of patent protection. As noted by 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...”²

Chapter VII, finally, incorporates a “Guide for the Application and Granting of Compulsory Licences and Authorization of Government Use of Pharmaceutical Patents” (2009). This paper was produced by WHO with the support of the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the Cooperation and Development of the French Ministry for Foreign Affairs. Despite that several WHA resolutions has recommended the full use of the flexibilities allowed by the TRIPS agreement, including the use of compulsory licenses, this document has not been widely distributed by WHO, probably because of a change of policy in the WHO Secretariat.

Compulsory licensing is, in effect, one of the important ‘flexibilities’ recognized under article 31 of the TRIPS Agreement. As stated in the introduction of this document, “Patents – as well as other intellectual property rights – confer exclusive rights. This means that the titleholder may exclude competition in the manufacture and sale of the protected products and, therefore, control the production and distribution of such products and their prices. (...). Like other rights, however, patent rights are not absolute. There are situations in which their exercise can be limited to protect public interests. Such situations may arise, in particular, in the area of public health, when access to needed pharmaceutical products must be ensured. “Compulsory licences” and “government use for non-commercial purposes” are mechanisms provided for in most laws worldwide to limit the exercise of exclusive patent rights – under the circumstances specified in the respective laws – which can specifically be used to address public health needs.” In the public health context, compulsory licensing can be used to enable domestic production and/or importation of generic medicines by both private and public sectors, as a means for overcoming patent barriers to access to affordable medicines. Since January 1995 – the general date of entry into force of the TRIPS Agreement – at least 12 developing and Least Developed Countries (LDCs) have granted compulsory licenses (CLs) or decided the public non-commercial use (known as ‘government use’) of patents.

All documents contained in the book, as well as Professor Correa’s articles in the Bulletin of the World Health Organization³, are available online on the website of WHO’s

² 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.

³ Bulletin of the World Health Organization, Editorial: “health and intellectual property rights” vol. 79, no. 5, 2001, p. 381-488; Bulletin of the World Health Organization. “Ownership of knowledge – the role of patents in pharmaceutical R&D.” 2004, 82(10): 784-786., available from: <http://www.who.int/bulletin/volumes/82/10/784.pdf>. Bulletin of the World Health Organization, 2006, vol.

Medicines department. Nevertheless, the South Centre considers that hard copies are important for many developing countries, as well for researches and students around the world.

Although this publication is intended to reproduce the papers as published, updates have been introduced when necessary.

The South Centre acknowledges and thanks the World Health Organization for granting permission to reprint the documents contained in this volume.

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South Centre, Geneva

CHAPTER I

THE URUGUAY ROUND AND DRUGS

EXECUTIVE SUMMARY

The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), which was negotiated as part of the Uruguay Round (1986-1994) may have great implications for the production of and access to drugs, especially in developing countries. The Round's Final Act signed in Marrakech in 1994, established the World Trade Organization (WTO) whose Member countries are bound to implement the principles and provisions laid down in the Agreement.

This paper comments on the possible effects of the Agreement on the development, production and marketing of drugs, as well as on access to them. In so doing, it refers to the 16 Articles (of the 73 Articles of the Agreement) which most concern the pharmaceutical sector.

Major patent provisions – The provisions on patents contain explicit obligations for Member countries and will have considerable impact on the drugs sector, although in varying degrees in different countries. One of the obligations is to grant both product and process patents in all fields of technology, thus eliminating the division between countries which grant patents to pharmaceutical industry and those which do not. The Agreement also requires that Member countries establish a minimum of 20 years patent protection.

What is patentable and what is not, especially in relation to biotechnological innovation, is discussed, as is patentability in relation to a product's origin and the interrelationship between product and process patents. Exceptions to exclusive rights conferred by patents and the grant of compulsory licences are both subject to certain conditions under the Agreement. The provisions on "undisclosed information" oblige to safeguard information submitted for approval of a pharmaceutical or agrochemical product, in order to protect it from unfair competition.

In connection with the latter provision is that of "undisclosed information" which gives countries the possibility to safeguard information submitted for approval of a product in order to protect the product from what may be considered unfair competition.

Transitional periods – After the TRIPS Agreement became effective on 1 January 1995, all Member countries of WTO had one-year transition period within which to fulfil their obligations under the Agreement. Developing countries which join the WTO have four additional years (total of five years) and least developed countries ten additional years (total of eleven years) to comply with the provisions of the Agreement. Transitional periods are also provided for specific acts within the provisions relating *inter alia* to pharmaceuticals.

Dispute settlement – An innovation of the Uruguay Round is to be found in the way in which disputes are settled. Previously, these were subject to "positive consensus" at each stage of the dispute process. The principle now in force is that of "negative consensus" which will allow each stage of the process to proceed unless there is a consensus against it.

Protection of public health – Finally, the principles embodied in Article 8 of the Agreement relating to the formulation or amendment of domestic laws and regulations, through which the Agreement must be implemented, explicitly recognize that measures necessary to protect public health may be adopted by countries, providing they are consistent with the Agreement’s provisions and implemented within the time limits laid down therein.

Conclusions – Following a detailed analysis of the effects of the new intellectual property rights relating to pharmaceuticals, especially in developing countries, the study concludes that:

- (a) Although protection of pharmaceutical products will be enhanced at a high standard, this will not necessarily be to the benefit of all countries;
- (b) An increase in research and development on new drugs will not take place in either developed or developing countries;
- (c) The transitional period for entry into force of the Agreement allows countries to temporarily limit the introduction of pharmaceutical patents; and
- (d) Measures to be borne in mind when incorporating the provisions of the Agreement into domestic legislation are (i) compulsory licences, (ii) international exhaustion of rights, and (iii) exclusion from patentability of certain substances.

INTRODUCTION

The agreements contained in the Final Act of the Uruguay Round will have a significant impact on the global production and marketing of goods and services. The effects will, however, vary according to the type of change introduced and the sector concerned. The production and marketing of drugs and health services may be affected at different levels and to a varying degree.

For the first time in the history of GATT, the results of the Uruguay Round include agreements on the liberalization of trade in services. The special feature of health services is, however, that they are not internationally traceable to any significant extent because of the virtually indispensable need for a physician patient relationship⁴ and the regulations on professional practice.⁵

The Uruguay Round provided the framework for the negotiation of a comprehensive Agreement on intellectual property rights (Agreement on Trade Related Aspects of Intellectual Property Rights).⁶ It is this component of the Final Act of the Uruguay Round that may have the greatest implications for the production of and access to drugs, especially in developing countries.

The negotiations and the results obtained in the area of intellectual property underline the all-encompassing nature of the Uruguay Round. Unlike the previous Rounds, it not only

⁴“Telemedicine” could however extend the supply of diagnostic services across borders or could make them available in countries or regions without the necessary infrastructure. The future of robot-assisted “telesurgery” is more questionable.

⁵ In some countries with a federal system, for example, physicians are not allowed to practice outside their authorized area. On the other hand, restrictions on direct foreign investment in health services do not appear to be more severe.

⁶ Hereinafter referred to as the “TRIPS Agreement.”

involved discussions on trade barriers at the border but also moved towards the harmonization of domestic policies (“beyond the border”), blurring the distinction between trade policy and other economic policies. In practice, the Uruguay Round has affected a series of policies which define a country’s competitive environment (Tussie, 1994).

The section of the TRIPS Agreement on patents will have the greatest effect in the drugs sector. It is the most detailed chapter and contains the most explicit obligations for Member countries. These include the obligation to grant patent protection in all fields of technology, thus eliminating the distinction between countries which grant patents to the pharmaceutical industry and those which do not. The pharmaceutical industry, like other industries, will have to confront a new international legal environment in which imitation will be more difficult and there will be increased opportunities to earn profits from inventions through the exercise of exclusive rights at the global level.

The TRIPS Agreement also includes for the first time in an international convention rules on restrictive practices in licensing agreements, as well as a multilateral system for protection of trade secrets that extends to information given to government authorities in order to obtain approval of pharmaceutical products. The Agreement also contains provisions on trademarks, which may have implications for the pharmaceutical industry.⁷

The aim of this study is to examine the possible effects of the TRIPS Agreement on the development, production and marketing of drugs, as well as access to them. Section 2 contains a brief summary of the content of the TRIPS Agreement relevant to patents. Section 3 reviews the main provisions on “confidential information” (trade secrets). Although the Agreement deals with other areas of intellectual property, these are the most relevant to the pharmaceutical sector. Section 4 concerns transitional periods and section 5 deals with the mechanism for the settlement of disputes and enforcement. Section 6 reviews the possible implications of the Agreement for innovation, direct foreign investment and the price of drugs. The analysis focuses on the effect of the new intellectual property rules in developing countries. Finally, the last section sets out the conclusions drawn.

PATENTS

The TRIPS Agreement lays down minimum standards for the protection of intellectual property, including operative and procedural rules to ensure the enforcement of rights. No Member may grant protection that is less than the levels laid down nor be obliged to give more extensive protection. The Agreement must be implemented according to the domestic laws of each country; it does not directly establish rights for individuals.

The Agreement explicitly recognizes that, in formulating or amending domestic laws and regulations, Members may “adopt measures necessary to protect public health ... provided that such measures are consistent” with the Agreement’s provisions (Article 8).

The question of patentability and exceptions was one of the major areas of negotiations of the TRIPS Agreement.⁸ From the beginning of the Uruguay Round, it was obvious that one

⁷ One of these provisions is the obligation to protect colours as a trademark, which may affect competition between products with a trademark and generic products in certain markets.

⁸ The text of the section on patents has been analysed in Correa (1994). See Castado and Cerro (1994) for an overall analysis of the Agreement.

of the essential aims of the industrialized countries, particularly the United States of America (USA), was to extend patentability to pharmaceutical products globally.

When the Round began, many countries did not confer protection on pharmaceutical products. Nevertheless, during the period which elapsed between the commencement of the Round in 1986 and its conclusion in 1994, this situation changed radically.

Some developing countries embarked upon economic restructuring and redefined their relations with industrialized countries, especially with regard to direct foreign investment. Changes in intellectual property were seen as components of a new framework for such relations and for attracting foreign capital.

In the majority of cases, however, changes in intellectual property law corresponded more to demands coming from outside than to endogenous motives. Many developing countries were subjected to strong pressure to amend their patent legislation exerted by the lobby of multinational pharmaceutical companies. The Government of the United States of America included intellectual property issues in its international agenda under the provisions of section 301 of the Trade and Tariffs Act (amended in 1988).⁹ Many developing countries, including Argentina, Brazil, Indonesia and Thailand, have been the subject of investigations or trade retaliations under this section.

From 1986 onwards, a new orientation in economic policy and a vigorous campaign by the USA combined to reduce substantially the number of countries which refused to grant patents in specific areas, especially in the field of pharmaceuticals. In Bolivia, Chile, China, Colombia, Ecuador, El Salvador, Indonesia, Mexico, Peru, South Korea, Taiwan, Thailand and Venezuela¹⁰ *inter alia* patent legislation was amended to this effect.

Pursuant to the TRIPS Agreement, three of the major pharmaceutical markets in developing countries (Argentina, Brazil and India) find themselves in this situation and will have to amend their patent legislation (within the time limits laid down in the Agreement).¹¹

General Principles

Article 27.1 of the TRIPS Agreement provides that any invention may be patented, whether for the product or a process “in all fields of technology”. It adds that “patents shall be available and patent rights enjoyable without discrimination as to ...the field of technology”.

This provision may be seen as one of the major concessions by developing countries in TRIPS. It puts an end to one of the most disputed issues in the history of patent law and has virtually global scope. It will not only have a direct impact on those countries which still do not allow drugs to be patented, but will also prevent any step backward in those countries which do allow such patentability, at least until the TRIPS Agreement is revised.

⁹ See Destler (1992) for an analysis of how this section is applied.

¹⁰ In the case of Bolivia, Colombia, Ecuador, Peru and Venezuela, it should be noted that the Common Industrial Property Regime applicable to them (Decision 344 of October 1993) does not allow pharmaceutical products which appear on the World Health Organization’s list of essential drugs to be patented (Article 7.e). Although this list which is periodically revised usually includes drugs with expired patents, it may also contain patented drugs.

¹¹ This is also the case of Egypt, Pakistan, Paraguay and Uruguay.

Non-patentability: Biotechnology Based Drugs

Article 27.2 and 27.3 both specify the exclusions from patentability which any country may establish in its domestic legislation, without being obliged to do so. Article 27.2, for example, states that:

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

Despite the seemingly general coverage of this provision, its application is subject to two restrictions.

On the one hand, an exclusion from patentability may only be permitted if the commercial exploitation of the prohibited invention is not allowed in the country concerned and if this non-exploitation is necessary to protect the interests mentioned in article 27.2. In other words, it would not be possible to declare that a particular object is not patentable while at the same time permitting its distribution or sale.

On the other hand, the provision prohibits other exclusions based on grounds which differ from those laid down in Article 27.2, even when these are prescribed by national law. The existence of a legal prohibition, if based on other grounds, will not be sufficient to sustain the non-patentability of an invention or category of invention.

Moreover, according to Article 27.3.

“Members may also exclude from patentability:

- Diagnostic therapeutic and surgical methods for the treatment of humans or animals;
- Plants and animals, other than microorganisms, and essentially biological processes for the production of plants or animals other than non biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective *sui generis* system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO Agreement.”

The present economic importance of the inventions which could be excluded from protection under Article 27.3 (a) is low. In the USA, only a few medical processes have been patented (it is one of the few countries which allows this) for methods that are rarely used (Berman and Lambrecht, 1991). Furthermore, patents for such methods are particularly difficult to enforce.

Correctly interpreted, the exclusion mentioned in Article 27.3 (a) would not apply to any apparatus used for diagnostic or therapeutic purposes not to “diagnostic kits”, one of the main biotechnology based products on the market today.

The exclusion referred to in Article 27.3 (b) reflects the significant differences even among industrialized countries, with regard to patents for plants and animals. The EEC proposals in GATT which the Article in question reflects to a certain extent were aimed at maintaining the present position of the member countries of the European Patent Convention in connection with the non-patentability of animal races and plant varieties and the “essentially biological processes” for their production.

The possible exclusion of “essentially biological processes” is limited by the reference to “non biological and microbiological” processes. The concept of microbiological processes as exceptions to the exclusion is present in European legislation and in the laws of various other countries. Its aim is to restrict the exclusion from patentability to traditional methods of breeding and improvement, while keeping the obligation to protect, for example, inventions based on radiation.

The Agreement does not specify if the replication of a substance which already exists in nature can be patented or not. This is of special importance for the biotechnology-based pharmaceutical industry in connection with products such as interferon, TPA (Tissue Plasminogen Activator) and growth hormones. The possible patentability of products which “copy” substances already existing in nature has given rise to animated discussion and different solutions among the industrialized countries.¹²

Although the USA and some European countries tend to acknowledge that a substance existing in nature can be patented provided that it is isolated and in purified form, other countries consider that such cases do not involve an “invention” but simply a “discovery” and cannot therefore give rise to individual intellectual property rights.

The TRIPS Agreement allows for the interpretation that such substances are not inventions, which would mean that drugs based on the replication of human proteins or other matter existing in nature would not be patentable.

Article 27.3 (b) is the only provision in the TRIPS Agreement subject to an early review (four years after the Agreement enters into force). This period is even shorter than the transitional period for developing countries (Article 65). This solution shows how difficult it was to reach an agreement on the biotechnology related issues. It also means that, in the short term, countries could once again be called on to extend patent protection to various categories of biotechnological innovation.

Non-discrimination Clause

Article 27.1 contains a non-discrimination clause that refers both to the availability of patents and the enjoyment of patent rights. It was introduced into the text as a compromise during the final stages of the negotiations. The Article states that: “patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced”.

As mentioned above, this clause allows the patentability of all types of invention irrespective of the industrial sector or technological field to which they belong. It also prohibits any differential treatment based on the place of invention such as the one included until

¹² See the special issue of the *Revista del Derecho Industrial*, year 12, no. 24, Buenos Aires.

recently, for example, in the Canadian patent law, in connection with the granting of compulsory licences for pharmaceutical products.

In many countries, the system of granting compulsory licences could also be affected by the prohibition on discrimination according to the product's origin (locally manufactured or imported). The aim of the text's drafters was to weaken or eliminate the obligation to work the patented invention, one of the traditional foundations of the patent system. Such an obligation justified the granting of patents in developing countries as this was seen as a mechanism for the promotion of investment and the transfer of technology to developing countries (Penrose, 1974).

The weakening of the obligation to work the patent resulting from the TRIPS Agreement is undoubtedly consistent with the trend towards internationalization of production and marketing by multinational companies.¹³ Having chosen to locate production in a certain place, their strategy is to supply global markets under monopolies conferred by patents, exporting finished or semi-finished products¹⁴ rather than transferring technology or making direct foreign investment (Correa, 1989).

Rights Conferred: Imports

Article 28 establishes the rights that a patent should confer on its owner. It takes into account the two traditional categories of inventions: products and processes.

Patents for products confer the right to prevent third parties from "making, using, offering for sale, selling or importing for these purposes that product" without the owner's consent (Article 28.1 (a)).

One important aspect of this provision is that it expressly refers to importation as one of the exclusive rights of the patent owner. Nevertheless, the footnote contains a cross reference to Article 6 of the Agreement, which allows Members to provide for the exhaustion of intellectual property rights subject to national and most favoured nation treatment. Exhaustion may only apply to acts occurring within a country ("national exhaustion"), in a group of countries or a region ("regional exhaustion") or in the global market as a whole ("international exhaustion").

Recent legislative reform in a number of countries has established the principle of international exhaustion with the aim of introducing a certain degree of competition into the market. To give an example, if a patented product is sold in country A at a price of \$100 and in country B the same (legitimate) product is sold at \$80, this principle allows any interested party in country A to import the product from country B without the consent of the patent's owner.

The adoption of this principle may be of particular importance in the area of drugs in order to prevent discrimination or price abuse by the owners of patents. A point which merits further consideration is whether the principle could also be extended to cases where a product is imported from a country in which the patent owner has not been able to obtain protection (because there is no possibility of obtaining a patent, for example) or has not sought protection, or protection is no longer possible because the patent has expired, or for other reasons.

¹³ See Chesnais (1994) on recent trends towards internationalization.

¹⁴ After pharmaceutical patents had been recognized in Chile, for example, it was noted that some foreign subsidiaries which formulated drugs locally were dismantled and the market was supplied directly through imports.

Rights Conferred: Protection of Products through Protection of the Process

Article 28.2(b), on the other hand, provides for the extension of the protection conferred on a process to the product “obtained directly by that process”. This extension, not yet recognized by many countries, together with reversal of the burden of proof mentioned below, will in many instances lead to a substantial strengthening of the patent rights concerning process inventions.

This means that the granting of a process patent, even for a product already known but not patented, may result in a monopoly of the market in the product concerned.

This would be possible if the process used to manufacture the product were totally or partly unique and irreplaceable. The extension of process protection to a product will no doubt be the cause of frequent lawsuits and threats to independent pharmaceutical companies.¹⁵

Exceptions to Exclusive Rights

Exceptions to patent rights must meet three conditions. Firstly, they must be limited, even where their scope, term or other aspects are not specified. Secondly, they must not unreasonably conflict with the normal exploitation of a patent. Thirdly, they must not unreasonably prejudice the legitimate interests of the patent owner. These three conditions have to be applied, however, taking into account “the legitimate interests of third parties”.

This text obviously calls for a case by case analysis of the exceptions that may be allowed. Based on the present status of comparative patent law, the following exceptions may be deemed legitimate pursuant to Article 30:

- a) importation of a product that has been put on sale by the owner of the patent or with his consent or in a country where patent protection does not exist;
- b) acts done privately and on a non-commercial scale or for a non-commercial purpose;
- c) use of the invention for research and experimentation or for teaching purposes;
- d) preparation of drugs for individual cases according to a prescription;
- e) use of the invention by a third party who started or carried out serious preparations before the application for the patent (or its publication);
- f) experiments carried out in order to obtain health approval before marketing a drug.

With regard to the latter, the United States Drug Price Competition and Patent Term Restoration Act permits the carrying out of tests to establish the bio equivalence of generic products before the relevant patent expires. Its purpose is to help producers of generic drugs to market their products as soon as the patent expires.

Public interest, or more explicitly public health, may be deemed to be another legitimate reason for suspending exclusive rights in accordance with the “principles” laid down in Article 8 of the Agreement.

¹⁵ Pfizer is presently suing a number of Latin companies in order to prevent the sale of an unpatented product whose manufacturing process was granted a patent. One of the companies it is suing manufactures under a process licence from a Spanish company (Prescription Monitor, vol. 2, no. 1, 1995).

Granting of Compulsory Licences

The Agreement does not refer to the widely accepted notion of “non-voluntary” or “compulsory” licences. It should be noted that 96 countries allow for one form or another of compulsory licences. Nevertheless, Article 31 on “Other Use Without Authorization of the Right Holder” contains a detailed set of conditions and limitations for the granting of such licences. In this Article, the industrialized countries have tried to limit the opportunities for use of the compulsory licence system even though its actual application has been rather limited in the past.

Grounds for granting compulsory licences

Article 31 does not interfere with domestic legislation regarding the grounds for the granting of compulsory licences. Although it mentions some specific grounds (national emergency, anti-competitive practices, dependent patents, etc.), it does not limit the Members’ right to apply this remedy to different situations; it only lays down the conditions to be met “where the law of a Member allows for other use”.

Consequently, a compulsory licence could be granted on the following grounds, *inter alia*.

Public health and nutrition or other reasons of public interest

Article 8 (“Principles”) of the Agreement specifically recognizes the sovereign right of Members to “adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development, provided that such measures are consistent with the provisions of this Agreement”.

Many countries, including some developed countries, provide for compulsory licences in their legislation. The legal provisions are usually drafted in general terms so as to allow them to be applied flexibly. The Agreement does not prevent the granting of compulsory licences on the grounds indicated, provided that the criteria laid down in Articles 27.1 and 31 are respected.

Non voluntary licences may not be established for a special technological field *per se* (for example, foodstuffs), but only in relation to products and processes for certain purposes. A compulsory licence system could, for instance, include different technologies whose access and use affect health needs such as manufacturing processes and pharmaceutical products, hospital equipment and materials, diagnostic elements and other items relevant to this purpose.

National emergency and extreme urgency

These motives are specifically mentioned in Article 31 (b). Basically, they could be considered as being covered by other general formulations such as “public interest”. In such cases, prior negotiations with the right holder can be avoided.

Public non-commercial use

In this case, a government is directly interested in using the patented invention. The Government of the USA has used such licences, for example, through NASA and in other

instances of military interest. Such licences may also be used in other areas (for example, the production of drugs). In order to remain legitimate, use must be non-commercial, even though this does not exclude the possible participation of a private contractor.

Anti-competitive practices

Exclusive rights conferred by patents can lead to various forms of abuse of a dominant market position. Compulsory licences to prevent or punish anti-competitive practices have been granted in many cases in the USA on the basis of its anti-trust legislation. Recent legislative reform in Latin America (Andean Group, Argentina, Chile) has expressly included these types of licences. They are also mentioned in Article 31 (k) of the Agreement. For them to be applied, a judicial or administrative procedure must determine that an anti-competitive practice exists. Domestic laws can of course define the cases in which the granting of such a licence is justified. This will usually be when the price received by the patent owner is excessive or licences are granted subject to unreasonable restrictions or when other acts carried out constitute abuse.

Article 31(k) provides for the possibility that licences for anti-competitive practices be subject to special rules regarding remuneration to the patent owner. Thus, according to the judicial and administrative practice in the USA compulsory licences might be granted “royalty free” (Fugate, 1991).

Dependent patents

Article 31(l) contains detailed provisions on compulsory licenses based on dependent patents. It defines a number of criteria for their granting: the technical and economic importance of the “second patent” (it must involve “an important technical advance of considerable economic significance”); granting of a “cross licence on reasonable terms” to the owner of the “first patent”; non assignability of the licence (except with the assignment of the “second patent”). These conditions tend to restrict the ways in which improvement patents have been used in some countries to promote access to patented technology by national companies. In this connection, the evaluation of the economic and technical importance of the second invention will be a key factor in the practical functioning of this system.

Environmental protection

One of the most pressing issues in the world today is the degradation of the environment. Important efforts are being made at the national and international levels to prevent activities that are harmful to nature and to formulate effective measures to protect the environment. In the patents sphere, the granting of compulsory licences could help to increase the use of environmentally sound technologies, as well as of technologies conceived for environmental protection. The international community made proposals in Agenda 21 to promote the use of such technologies under compulsory licences in developing countries.

Refusal of a voluntary licence

The TRIPS Agreement also authorizes the granting of a compulsory licence when the owner of a patent has refused a reasonable commercial offer, which he has been given a reasonable amount of time to consider. The adoption of this “refusal to deal” principle may be of particular importance as a dissuasive element. A patent owner should exercise caution when refusing a

voluntary licence if the law contains an effective mechanism that gives an authorization to use a patent to a third party who has acted within reasonable commercial parameters.

There is of course a broad margin for evaluating whether or not an application for a licence, and its refusal, are reasonable; this implies the need for detailed regulations on this type of licence, taking into account the aim of promoting dissemination of technology and avoiding monopolistic positions in respect of medicines.

Other grounds

As mentioned above, the Agreement is not limiting as to the grounds for granting compulsory licences. In other words, domestic law can define the grounds for granting such licences, including those that are not mentioned in the TRIPS Agreement, which is only indicative in this respect.

The only sector in which there are limitations on the type of compulsory licence that may be granted is the semiconductor sector, where compulsory licences may only be granted for “public non-commercial use or to remedy a practice determined after judicial or administrative process to be anti-competitive” (Article 31 (c)).

Conditions for the granting of compulsory licences

The Agreement devotes particular attention to the conditions under which a compulsory licence may be granted.

- Such a licence should be granted taking into consideration “its individual merits” (Article 21 (a)). This means that decisions have to be taken on each individual application and that they cannot apply in general to certain types of patents defined by their category, owner or in any other way.
- Before granting a licence, the proposed licensee should have made efforts “to obtain authorization from the right holder on reasonable commercial terms and conditions”, and it is a condition that “such efforts have not been successful within a reasonable period of time” (Article 31 (b)). This provision makes it mandatory to hold prior commercial negotiations with the patent owner. Nevertheless, Article 31 allows exceptions in cases of national emergency or other circumstances of extreme urgency, as well as for “public non-commercial use” or where a licence is granted to remedy anti-competitive practices.
- The scope and duration of use “shall be limited to the purpose for which it was authorized” (Article 31 (c)). This clause means that a licence may be limited both in terms of scope (for example, to certain categories or types of product) and duration. Nevertheless, nothing prevents an application for a licence lasting until the date of expiry of the patent. In fact, this practice has been generally accepted under the Paris Convention until now. For a licensee who invests in production or marketing, it will usually be essential to obtain a licence for the whole term of the patent.

Another important point is that the Agreement does not limit the purpose for which a compulsory license may be granted. In other words, it may be granted for importation as well as for local production of a patented product. In some cases (licence to remedy the abuse of a dominant market position or to protect public health), importation may in fact be the only way of fulfilling the purpose for which the authorization was granted. Moreover in developing

countries there will be cases in which local industry might start making up formulations under licence on the basis of importation of the active ingredients whose manufacture is not viable for reasons of scale or technology.

- As prescribed in the majority of legislations, any authorization should be non-exclusive and non-assignable, except with regard to that part of the company that uses it. The non-exclusive character of a licence means that the holder may import or industrially work the invention in parallel with the licensee, by himself or by means of other voluntary licensees. It also means that more than one compulsory licence can be granted for a given patent.
- Licences should be granted “predominantly for the supply of the domestic market” (Article 31 (f)). This provision (which may not be applicable to licences granted in order to remedy anticompetitive practices); if applied restrictively, may mean that it is not viable to produce locally any substances in which economies of scale play an important role.
- One important change is introduced regarding the term of licences as usually applied at present. Article 31 (g) states that a compulsory licence can be terminated “if and when the circumstances which led to it cease to exist and are unlikely to recur”. Consequently, the competent authorities must have the authority to review, upon motivated request, the continued existence of these circumstances. Nevertheless, termination is subject to “protection of the legitimate interests of persons” authorized to use the invention. Without this last condition, the Article in question would have totally weakened the potential of any system for the granting of compulsory licenses. Protection of the legitimate interests of the licensee should be taken to mean that the latter cannot be deprived of his right to hold a licence if he has made serious preparations to use the invention or has created production or marketing facilities. If a reasonable degree of certainty is not guaranteed, no one would be interested in applying for a licence that could be terminated at any time. Paradoxically, the licensee most affected might be precisely the one who has made the greatest contribution to remedying the situation that gave rise to the granting of the licence.
- The owner of the patent must be paid “adequate remuneration in the circumstances of each case, taking into account the economic value of the authorization” (Article 31(h)). This provision would apply in principle to any kind of compulsory licence. For licences granted to remedy anticompetitive practices, however, the need to correct such practices “may be taken into account in determining the amount of remuneration” (Article 31 (k)). Since the aim is to restore healthy competition, this provision envisages the possibility of fixing reduced remuneration in order to make it easier for third parties to apply for and obtain a licence for this purpose. A licence free of royalties may also be granted (Mendes da Costa, 1992), as has been done by authorities in some cases to remedy anti-competitive practices.¹⁶

There is still wide scope for interpretation at the national level of the criteria used to determine when the remuneration is deemed to be “adequate”. The provision undoubtedly establishes two elements for this interpretation: on the one hand, the adequacy of the amount must be determined by the circumstances of each case and, on the other, it is necessary to take into account – as a decisive but not unique factor – “the economic value of the authorization”. Consequently, the circumstances of the licensee and of the country where he operates, as well

¹⁶ On example of a “royalty free” compulsory licence is that granted by the USA Federal Trade Commission in 1990 to the French company Rhone-Poulenc for five years.

as the purpose of the licence, have to be taken into account when establishing a fair remuneration. A license granted to meet public health or other needs must be subjected to parameters other than those applicable when only purely commercial and industrial interests are involved. The “economic value” will differ, *inter alia*, depending on the size of the market to be supplied (usually the domestic market); the age of the technology; the rate of obsolescence in the sector concerned; the degree of competition from substitute products; and the coverage of the patent.

The word “adequate” also needs to be clarified in order to give more precise guidance to national judicial and administrative authorities. One possible interpretation is that it simply means the remuneration that the patent owner could obtain in a transaction between independent parties. This is not, however, the true meaning of the word in the original English text.¹⁷ A more appropriate interpretation would be to distinguish the value of the actual contribution made by the holder to the development of the invention, deducting any contributions by third parties, subsidies or other contributions which the patent owner may have received. The extent of amortization of research and development costs at the time of granting the licence also has to be calculated.

The patent owner must be given the possibility of having the “legal validity” of any decision relating to the granting of a licence or to the remuneration reviewed by an administrative authority at a higher level or by judicial authority (Article 31(i) and 8g)). This right does not, however, prevent a Member country from granting a licence subject to subsequent revision, so any appeal against the decision granting the licence does not suspend its immediate effect. This is particularly important in cases related to public interest and to remedy anti-competitive practices.

Term of Protection

The Agreement will have a powerful harmonizing effect at the global level in respect of the term of patent rights. Article 33 establishes a minimum of 20 years from the date of filing of the patent application. This provision will prohibit any special period determined on the basis of the field of technology, the extent of the exploitation of the invention or on any other grounds.

On the other hand, there is no obligation whatsoever to extend the term of protection beyond this minimum as has been done, however, in the USA and Europe) for pharmaceutical patents.

Reversal of the Burden of Proof

Article 34 provides for reversal of the burden of proof in civil litigation involving process patents. This provision is of special importance for the pharmaceutical industry. The text’s wording itself indicates the difficulties encountered in achieving a consensus on this aspect. The reversal of the burden of proof can have a negative effect on motivation in small scale and medium scale industries due to the risk of facing legal problems and high litigation costs.

¹⁷ See Harry Small (1991) regarding the concept of “adequate remuneration”. It is interesting to note that this is the only provision in the Agreement referring to “adequate” remuneration. Articles 14.4 and 70.4 use the word “equitable” remuneration instead.

This problem affects small companies both in developing and developed countries. It has been noted in the USA, for example, that “large firms are more likely to be able to threaten litigation and to defend against litigation. There have been at least some cases of ‘strategic litigation’ in which a large firm uses the threat of litigation costs to deter a start up” (Barton, 1995).

According to the first sentence of Article 34.1, it is the judge who will have the authority “to order the defendant to prove that the process to obtain an identical product is different from the patented process”. This would have been a reasonable solution since it would have given the judge the opportunity to assess, in the circumstances of each case, the extent to which reversal is justified. However, the provision goes on to establish a legal presumption. It allows countries to choose between two hypotheses, but in both of them “any identical product when produced without the consent of the patent owner shall ... be deemed to have been obtained by the patented process”.

The first hypothesis is that the product obtained by the patented process is “new”. The Members may interpret the degree of newness required. In principle, newness means according to the usual term of patent law, even if the product is not patentable as such. It has to be assessed at the time when the lawsuit is initiated.

According to the second hypothesis there must be “a substantial likelihood that the identical products was made by the process and the owner of the patent has been unable through reasonable efforts to determine the process actually used. In this case, the product might not be “new”, thus the scope of the provision is broader than in the first hypothesis because it applies to all products previously available. The requirement regarding “reasonable efforts” by the patent owner has to be evaluated by the judge in each particular case; if it is applied correctly, it could help to restrict any abuse by the patent owner to resort to reversal of the burden of proof.¹⁸

Finally, it should be pointed out that this provision has to be interpreted and applied in the light of Article 29. The invention of the process must be described clearly and completely since this is a condition for ensuring that any potential infringer is aware of the extent to which his acts are legitimate or not.

UNDISCLOSED INFORMATION

Section 7 of Part II of the TRIPS Agreement contains specific provisions on “undisclosed information”. According to Article 1.2, this constitutes a category of “intellectual property” in the same way as patents, trademarks and other forms dealt with in the Agreement. Article 39.1 provides that, in order to ensure effective protection against unfair competition, Member countries shall protect undisclosed information and data submitted to governmental agencies in order to obtain approval for the sale of pharmaceutical or agricultural chemical products.

There are two general considerations regarding this topic. Firstly, the Agreement subordinates “undisclosed information” to the rules on unfair competition in accordance with Article 10 *bis* of the Paris Convention. By adopting this approach, the Agreement clearly avoids treating undisclosed information as “property”, as proposed by the USA in prior

¹⁸ Nevertheless, the first hypothesis in Article 34.1 provides greater legal assurance and is therefore the one which would be most desirable in domestic legislation.

informal proposals. The conceptual framework adopted is consistent with prevailing ideas on this subject in Europe, Japan and many developing countries. The fact that “undisclosed information” is considered as a “category” of intellectual property does not mean that there is an exclusive right.

Secondly, it should be noted that the text does not utilize the words “know how” or “trade secrets”. Perhaps the difficulty in achieving a common and acceptable understanding of the meaning of these words encouraged the adoption of the wording used, which does not specify the technical or commercial nature of the information but only that it is “undisclosed”. Article 39 therefore applies to any commercial information, provided that it meets the requirements laid down in Article 39.2

Article 39.2 specifies the conditions required for information to be considered as “undisclosed: it must be secret, have a commercial value and be subject to reasonable steps, under the circumstances in each particular case, to keep it secret. The conditions laid down are essentially based on the relevant legislation enacted in many States in the USA. The footnote to this Article defines practices which “at least” have to be considered “contrary to honest commercial practice”, thereby limiting the possibility of divergent interpretations. The practices mentioned include those which may result from contractual or like relations (breach of contract, breach of confidence and inducement to breach), as well as the acquisition of undisclosed information by third parties who knew or were grossly negligent in failing to know such practices were involved in the acquisition.

Although Article 39.1 refers to “undisclosed information” and other “data submitted” to governments as two separate aspects, it seems clear that in the latter case the information must also be “undisclosed” in order to be included within the terms of the Agreement. The scope of Article 39.3 is sectoral: it only protects information submitted as a condition for approving the marketing of pharmaceutical or agricultural chemical products “which utilize new chemical entities”. This means, first of all, that information that is already in the public domain (for example, because it has been published in scientific reviews) and is submitted in order to obtain marketing approval does not fall under this section. Secondly, as mentioned above in connection with the reversal of the burden of proof, in such cases a “new” entity can be taken to mean an entity not included in the state of the art.

In the light of the foregoing analysis, the scope of the obligation laid down in Article 39.3 is limited by the type of novelty of the products concerned and the purpose of the submission of data (only for marketing approval). Furthermore, these provisions state that, in order to seek protection, “considerable effort” must have been made to create the information. Unlike the wording of Article 70.4, which refers to “significant investments”, the expression used in the former case is much broader. A reasonable explanation would be that of the “effort” made must not only be significant in economic terms but also from a technical and scientific point of view, essentially meaning experimental activities.

The protection envisaged has two purposes. One is to try to prevent “unfair commercial use” of the information protected. This means that it would be possible to prevent a third person, for example, from using the results of tests submitted by another company as a basis for making a separate application to obtain marketing approval if these data were obtained using unfair trade practices. The third person concerned could obviously draw up the data and information independently or obtain them from other sources.

The duplication of tests (which often implies the suffering of animals) in order to obtain results that are already known would of course be questionable from a social cost-benefit standpoint. This provision would not, however, prevent governments using information submitted by one company in order to assess information submitted by other companies, as is permitted, for example, in the case of approval for the marketing of generic drugs under the United States Drug Price Competition and Patent Term Restoration Act (1984).

In addition, protection against the disclosure of confidential information has to be ensured. Since any disclosure by third parties is already covered in Article 39.2, the obligation not to reveal data contained in Article 39.3 appears to be directed at government authorities. Two exceptions to this obligation are envisaged:

- Where the disclosure is necessary to protect the public; and
- Where steps have been taken to ensure that the information will not be used in a way that is commercially unfair.

Subject to these exceptions, disclosure would be allowed, for example, to enable the holder of a compulsory licence to obtain marketing approval, especially when the purpose of the licence is to remedy anti-competitive practices or to meet public health requirements.

It should be noted that the original position adopted by the developing countries in the TRIPS negotiations was to reject any form of protection to know how in the text of the Agreement. At the other extreme, some industrialized countries made proposals aimed at establishing a minimum period of protection (five years) to safeguard tests and data submitted for marketing approval. The text of the Agreement as adopted represents a compromise which gives ample opportunity for implementation at the national level. Nevertheless, it is undoubtedly a complex matter and for many countries it involves new obligations that do not only affect the private sector but also government bodies responsible for approving drugs.

TRANSITIONAL PERIODS

General Grace Period

All members of the World Trade Organization will have one year after the date of entry into force of the Agreement in which to fulfil the obligations on the protection of intellectual property (Article 65.1). Developing countries will have an additional period of four years, except for obligations concerning national treatment and most favoured nation treatment, which will become applicable after the expiry of the afore-mentioned one year period (Article 65.2). Least developed country Members have an additional period of ten years, which can be extended upon “duly motivated request” (Article 66.1)

New Patentable Areas

In addition to the general transitional period for developing countries mentioned in the previous paragraph, there is a further period of five years for countries that are obliged to extend product patent protection to areas of technology not so protected on the general date of application of the Agreement for that particular country (Article 65.4). This clause will apply to countries that only grant process patent protection or no protection at all in the pharmaceuticals sector. These

provisions will only apply to countries which, on the aforementioned date of entry into force of the Agreement, do not confer product patent protection (see Article 65.5).

Protection of Existing Subject Matter

The possible retroactive recognition of patent rights was a considerable source of dispute during the TRIPS negotiations. The Agreement adopted a negative approach to such recognition, eliminating “pipeline” type solutions as proposed by the USA. Articles 70.1 and 70.3 state that the Agreement does not give rise to obligations in respects of acts which occurred before the date of application of the Agreement for a Member (Article 70.1) and does not oblige a Member to restore protection to subject matter which on that date has fallen into the public domain. This means that Members are not obliged to confer protection on inventions that have become public (whether through private acts, publication by foreign patent offices or in any other way) before that date.

Article 70.4 confirms the application of the Agreement for the future; it allows special treatment for acts which involved significant investment before the Agreement was ratified by the Member. In such cases, the Member must provide for “equitable remuneration” to the right holder, but it may exclude or limit the applicability of other measures (for example, interruption of use or sale of a protected product). There can be little doubt that national authorities will have to interpret the meaning of “significant investment” and “equitable remuneration”, which in any event will be subject to judicial review (Article 41.4). It is obvious that the significance of investment will have to be defined according to factors such as the size of the company in question, the type of product and the production facilities needed, as well as the cost of installation or utilization of the product entitled to protection. In order to determine “equitable remuneration”, consideration will have to be given *inter alia* to the extent of development of the technology, the amount of the research and development costs written off and any subsidies granted to the patent owner in order to carry out the research which resulted in the protected technology.

Prior Compulsory Licenses and Application

Compulsory licenses granted by a government before the date on which the Agreement “became known” do not need to respect the provisions of Article 31. The same applies to compulsory licenses in a specific field of technology and which would be regarded as discriminatory under Article 27.1 (see Article 70.6). The use of an ill-defined point in time (the moment at which the Agreement “became known”) is confusing. This provision has apparently been adopted in order to accelerate the abolition of “automatic” licenses for drugs in Canadian legislation, which allowed the development of a large generic drugs industry in Canada.

According to Article 70.7, if a patent application is awaiting approval at the time the Agreement enters into force in a Member country, it will be possible to amend the application to claim “any enhanced protection provided under the provisions of this Agreement” (Article 70.7). Such an amendment may not, however, include “new matter”. The major issue here is whether an application for a process patent may be changed into an application for a product patent. Since the distinction between a manufacturing process and a product is clearly defined, the change would imply the incorporation of new matter not included in the original claim. The answer should therefore be in the negative. On the other hand, the applicant may, for example, apply for protection for twenty years (Article 33) if the term of the patent previously applied for is less.

Pharmaceutical and Agricultural Chemical Products

The importance of patent protection for pharmaceutical and agricultural chemical products is underlined by special transitional provisions which establish rights not granted to patent owners in other fields of technology. This special treatment is in the following form.

Firstly, applications for pharmaceutical and agricultural chemical products may be filed in a Member country (according to Article 70.8) as from the date of entry into force of the Agreement. However, the patents will only be granted after the Agreement has become binding for the Member in question and (although the relevant provision does not explicitly mention this) after the expiry of the transitional periods set out in Article 65. The time elapsing between the application and the granting of the patent may therefore be considerable. Nevertheless, Article 70.8 manages to preserve the novelty of the application through a legal artifice based on determination of its novelty (and other patentability criteria) as though it had been evaluated on the date of filing the application in the Member country (or the date of priority if available and claimed) and not on the date when it was in fact evaluated. Patents granted in this way will last for the remainder of the term of the patent, calculated from the date of filing and in accordance to the twenty year period established in Article 33.

Secondly, irrespective of the fact that the aforementioned transitional periods extend the possibilities for not patentability in developing countries for a total period of ten years after the date of entry into force of the Agreement, Article 70.9 limits this overall period for pharmaceutical and agricultural chemical products. It establishes the right to obtain “exclusive marketing rights” for these products before a patent has been granted. These rights which appear to be inspired by the “certificates” granted in EEC countries in order to extend the term of pharmaceutical patents¹⁹ can be obtained provided that the following criteria are met:

- a patent application has been filed in a Member country after the entry into force of the Agreement;
- an application has been filed in another Member country after the entry into force of the Agreement and a patent has been granted;
- marketing approval for the protected product has been obtained in the other Member country concerned;
- marketing approval has been obtained in the Member country referred to in subparagraph (a).

If these requirements are met, the Member concerned must grant these “exclusive marketing rights” for a period of five years after marketing approval has been obtained in that particular country. These rights will be terminated, however, if (a) the corresponding patent is eventually granted, or (b) the patent application is rejected in the country concerned.

The Agreement does not mention the content and scope of these “exclusive marketing rights”. To what extent could the holders of such rights prevent others from marketing the product concerned? What recourse would they have against infringement? Would the provisions on granting compulsory licenses be applicable? What procedures would be available to third parties wishing to use the invention, for example, for experiments, tests, marketing

¹⁹ See the decision of 19 December 1991 by the Council of Europe, which establishes an additional protection certificate for pharmaceutical patents that have expired.

approval, etc.? There needs to be an in depth analysis of these and other questions relating to the implications of Article 70.9.

It is nevertheless relevant to mention that penal remedies are usually reserved for procedures related to patents; the holder of such exclusive rights may only have recourse to civil proceedings. In addition, the holder of the rights may not be placed in a better position than the owner of the patent and, consequently, the abuse of a dominant position, public health requirements or other justified grounds could be a sufficient argument to limit the exclusive rights using means like compulsory licenses (or revocation in cases of abuse). Finally, exclusive marketing rights should be interpreted as not restricting production for export to third countries.

The economic impact of Article 70.9 will vary according to the time needed for the approval and registration required to obtain exclusive marketing rights for a given product. In the pharmaceuticals sector, the carrying out of clinical and pre-clinical tests in order to demonstrate the usefulness and safety of a drug, in addition to the time required for government procedures, which is quite long in the USA and other industrialized countries, often delays the introduction of new products for several years. There are, however, indications that this period is becoming shorter, particularly for biotechnology-based products.

ENFORCEMENT AND SETTLEMENT OF DISPUTES

In addition to its operative provisions, the TRIPS Agreement contains a series of procedural rules aimed at ensuring enforcement of the protection of intellectual property rights.

If a member considers another member is not fulfilling its obligations under the Agreement, it can initiate the mechanism for the settlement of disputes provided for in the "Dispute Settlement Understanding". The new rules for this mechanism ensure that a decision is taken relatively quickly and that any unfavourable verdict is decided upon by "negative consensus". This means that, for a decision to be rejected by a panel, there must be a consensus to do so. In other words, a decision against a particular country may be adopted because there is no consensus to reject it.

Once the dispute settlement mechanism has been exhausted, the country concerned may apply trade sanctions against the country which is deemed to be infringing. Actions such as those taken under Section 301 of the aforementioned United States Act become illegitimate, even for sectors other than those affected by the fulfilment ("cross-retaliation").

Lastly, it should be borne in mind that the TRIPS Agreement lays down minimum standards and that, at the same time, no member country can be obliged to grant "more extensive protection" than required by the Agreement (Article 1). This signifies that any unilateral action on the part of governments requiring higher standards of protection than those required by the Agreement or the application of trade retaliations on such grounds will clearly be unlawful within the framework of the WTO.

IMPLICATIONS FOR THE DEVELOPMENT, PRODUCTION AND MARKETING OF DRUGS

The negotiations on intellectual property within the GATT framework were promoted by the governments of the industrialized countries, particularly the USA, in order to respond to the demands made by their domestic industry. Associations in the pharmaceuticals, semiconductor and audio-visual sectors, among others, made unstinting efforts to raise the standards of intellectual property protection in general and, in particular, to obtain the recognition and strengthening of rights in developing countries which did not allow for such protection.

As has been seen, the Uruguay Round gave industrialized countries and the aforementioned industrial associations the opportunity to lay down universal minimum standards and at the same time to legitimize the trade retaliation mechanism applied by the USA under section 301 of the Trade Act. For the pharmaceutical industry in particular, the Round afforded the opportunity to overcome the resistance of those countries which refused to allow patent protection for pharmaceutical products. At the end of the 1970s, more than 80 countries did not provide any protections or only protected pharmaceutical processes (and not products). The USA pharmaceutical industry, moreover, considered that adequate and comprehensive patent protection was only available in 16 countries (White, 1979).

The arguments put forward by developed countries in favour of the extension and strengthening of patent protections included the positive impact this would have on the rate of innovation, as well on the transfer of technology to and direct foreign investment in developing countries. Some of these issues are discussed below.

One of the main arguments in seeking universal and effective patent protection for pharmaceutical products has been the failure of developing countries to contribute towards the cost of research and development (R&D) by innovating companies.²⁰ This would have a negative impact on the availability of resources to continue R&D efforts by innovating companies.

Global recognition of pharmaceutical patents will undoubtedly increase the earnings of companies owning such patents in the form of royalties and profits (Nogues, 1990). It is unlikely, however, that this increase will to any significant extent lead to an increase in global pharmaceutical innovation.

In 1990, the developing countries' share of global production of pharmaceutical products (formulations) was 18.4 per cent (Ballance, Pogany and Forstner, 1992). A large part of this production was carried out in these countries by the same multinationals which, in general, control two thirds or more of the markets in developing countries.²¹ Another large segment corresponds to "generic" products, for which no patents are in force. Estimates of the market share of formulations supplied by domestic companies by replicating products of multinational companies vary greatly, between 10 per cent and one third of the total domestic

²⁰ Although these countries have not contributed in the form of payment of royalties, in many cases they have contributed indirectly but significantly through the surcharges paid for the importation of active ingredients. In the case of Argentina, for example, annual average flows due to over-invoicing in the mid-1980s were estimated at US\$ 80 million (Bisang, 1991), an amount equivalent to the amount estimated by the Pharmaceutical Manufacturers' Association as the annual losses of the USA pharmaceutical companies due to the nonpatentability of drugs (Nogues, 1991).

²¹ In the cases of Brazil and Mexico, for example, foreign companies account for 80 per cent or more of the market for formulations. Argentina and India are the most important exceptions because domestic companies account for a large share of the market.

market (Nogues, 1990). This means that, even if all developing countries recognized pharmaceutical patents, the impact on pharmaceutical innovation will be marginal and will hardly justify the economic and social costs to be borne by these countries.²²

In addition, according to a study of the Office of Technology Assessment (OTA, Washington), it can be assumed that on average a new drug put on sale in the USA market during the period 1981-1983 earned an amount in dollars after tax of around US\$ 36 million more than the amount involved in its R&D. According to this study, “the long term persistence in the industry as a whole of dollar earnings that are higher than the amount required to justify cost and the R&D risk is proof of the unnecessary power or price fixing for ethical pharmaceutical products” (OTA, 1993, p. 3).

To summarize, it is not possible to sustain the argument that the introduction of pharmaceutical patents in developing countries which excluded them from protection is justified by the increase in R&D by companies which will benefit from increased earnings in the form of profits and royalties.

Neither can it be expected that there will be an increase in R&D in developing countries because, if the cost of R&D for a new drug is around US\$ 150-200 million, as estimated, in developing countries there is no company with a sales volume (not less than US\$ 400 million per annum) that would allow it to make such investment. Although large pharmaceutical companies have decentralized some of their activities to R&D centres in countries other than that where they have their headquarters, the transfer of such activities to developing countries is insignificant (United Nations, 1992).

A study of inventions related to drugs carried out between 1950 and 1989 in 95 countries which recognize patents for pharmaceutical products shows that 91.7 per cent of them are to be found in 16 countries, and in 64 countries there have been no inventions at all (Challu, 1991a). In other words, the existence of patent protection, as can be expected, will not lead to a greater capacity for innovation if other conditions are not present, particularly as far as the scientific and technological infrastructure is concerned. Even in South Korea, one of the countries which has seen the most spectacular increase in R&D capacity over the past twenty years, the impact of the introduction of patents had a negative effect on the majority of Korean pharmaceutical companies (Kim, Ro and Yu, 1994).

The positive impact of the adoption of patents on direct foreign investment and the transfer of technology is equally questionable. There is, on the one hand, no conclusive evidence that greater protection leads to greater flows of direct foreign investment. In the pharmaceutical sector, in particular, the cases of Brazil and Turkey show precisely the opposite (United Nations, 1993). There is even evidence that pharmaceutical plants have been dismantled by foreign subsidiaries after the introduction of pharmaceutical patents. It is likely that local production of formulations in developing countries will progressively be replaced by imports of finished products (or bulk products), in other words, trade in drugs will increasingly

²² There are no reliable figures on the losses actually suffered by pharmaceutical companies. According to the survey by the United States International Trade Commission, losses of royalties and other revenue by the pharmaceutical industry because of inadequate patent protection amounted to US\$ 232 million in 1986. The Commission admits that these estimates may be “biased and self-serving” (USITC, 1988, Table 5, p. 1). In 1987, the industry’s R&D expenditures amounted to US\$ 5.5 billion (OTA, 1993, Table 2.2); at the very best, generalized granting of protection would have allowed these expenditures to be increased by 4.2 per cent, assuming that the total additional earnings were devoted to R&D.

replace direct foreign investment and the granting of licences to local companies in these countries.

For the time being, the only likely effect to the introduction of pharmaceutical patents as a result of the amendments to patent legislation in developing countries and the changes introduced in order to comply with the TRIPS Agreement will be higher drug prices. This will happen unless effective systems of compulsory licences and international exhaustion of rights and established.

For example, Subramanian noted that the price of drugs in Malaysia, where patent protection exists, is 20 to 760 per cent higher than in India, where there is no such protection. In Malaysia, prices are fixed according to the principle of “what the market can bear” (Subramanian, 1992). The impact of the introduction of patents in India may be incalculable: even with prices that are extremely low in comparison with those in other countries, only 30 per cent of the population can afford to buy modern drugs. According to the Indian Ministry of Trade, “patents for products will increase prices for drugs between five and ten times” (Karandikar, 1994).

The information shown in the studies by Noguez (1990) and Challu (1991a and b) coincides with this scenario of increased prices. In the case of Italy, following the introduction of patents for pharmaceutical products in 1978, drug prices increased on average by more than 200 per cent (Challu, 1991b).

Finally, it has been argued that concessions by developing countries in the area of intellectual property represent the “price” for the advantages they will obtain under the Uruguay Round as a whole, particularly in respect of market access. However, the balance of the agreements²³ on tariff reduction, agriculture and textiles shows very poor results, barely favourable, for developing countries. The reduction of tariffs on products that are mainly traded within industries and companies and among industrialized countries is much greater (from 43 to 62 per cent) than the reduction in tariffs on products which constitute the major exports of developing countries (around 20 per cent on average). The tariff structure in industrialized countries after the Round continues to discriminate against agriculture and textiles products.²⁴ In addition, the possibility given to importing countries to apply safeguard measures makes even more uncertain the advantages that might be gained.

CONCLUSIONS

This study shows that the TRIPS Agreement contains provisions which, on the one hand, will require amendments to patent legislation in many developing countries in the direction of broadening and reinforcing the protection of pharmaceutical products. On the other hand, the Agreement will “freeze” the level of protection at a high standard that cannot be changed if and until the Agreement is revised.

The adoption of the Agreement has undoubtedly involved a major concession on the part of those countries which refused to grant patents for drugs in order to avoid the effects of

²³ The analysis which follows is based on Agosin and Tussie, 1994.

²⁴ For example, in the USA the average overall tariff (excluding that for oil and natural gas) after the Uruguay Round will be 5.5 per cent, but will rise to 7 per cent for non-tropical agricultural products and 16.9 per cent for textiles and clothing. In the European Union, the figures will be 6.9, 16.8 and 10.1 per cent respectively.

market monopolies derived from exclusive rights. The information available briefly referred to in the precedent section, shows that the universalization of pharmaceutical patents will not lead to increased R&D on new drugs by large companies nor to the possibility that this will be carried out to any significant degree in developing countries. Neither will developing countries receive increased flows or direct foreign investment or transfer of technology.

Countries which, on the date the Agreement entered into force, did not confer protection still have the possibility of limiting the introduction of pharmaceutical patents under the conditions laid down in the Agreement. Even though the transitional period for pharmaceutical and agricultural chemical products is ten years for developing countries, it has been made subject to the ambiguous notion of “exclusive marketing rights” which, incorrectly interpreted, could cancel out the advantages of the transitional period. In this connection, it is important to specify the scope of such rights and distinguish them sufficiently from the rights conferred by patents.²⁵

The effect of introducing pharmaceutical patents will undoubtedly depend on the degree of competition existing in the therapeutic/products categories concerned and the forms of production of formulations and competition existing in each domestic market. The form in which patent rights are implemented will also have a decisive impact. This is why it is particularly important that, when incorporating the provisions of the TRIPS Agreement in domestic legislation, countries should consider the following measures *inter alia*:

- a) including in domestic legislation a series of compulsory licences to act as an effective deterrent to monopolistic practices and encourage access to licences by local companies under reasonable conditions;
- b) Guaranteeing the importation of products legitimately sold on the principle of international exhaustion;
- c) Excluding from patentability substances which exist in nature, including biotechnology-based drugs;
- d) Restricting reversal of the burden of proof to process patents for new chemical entities.

In incorporating the provisions of the Agreement, attention must be paid to the principles of Article 8 in order to regulate intellectual property in a manner that is compatible with the interests of public health and minimizes the economic and social costs which such changes might have for the production and marketing of drugs and access thereto.

²⁵ This is likely to be one of the first issues to be tackled by the Council for TRIPS established under the Agreement to monitor its implementation.

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CHAPTER II

TRENDS IN DRUG PATENTING: CASE STUDIES

INTRODUCTION

The patent system was devised in order to reward inventiveness, encourage technical progress and foster the dissemination of innovations. The restriction on the free movement of ideas that the granting of a patent entails is usually justified by the inventor's contribution to society and by the need to recover the investment necessary for invention (Gutterman, 1997; Granstrand, 1999; Le Bas, 1999). There is no doubt that the development and exploitation of numerous contributions to technology have been closely linked to, although not necessarily determined by, the possibility of obtaining exclusive rights to exploit inventions (Archibugi and Malaman, 1991).

Nonetheless, if we observe how the patent system operates nowadays, it is apparent that the attainment of its main objectives, which are in themselves valid, is increasingly offset by serious shortcomings in the system's design and management. One increasingly widespread view is that the patent system (especially as it operates in the United States of America) is in crisis and that there is a danger of it stifling the very innovation it is supposed to foster.¹ The National Academies of the United States have taken up the criticism levelled by many academics and sectors of industry (Barton 2000) and have expressed their concern in relation to the low standards, especially as regards non-obviousness and usefulness, applied in the examination and granting of patents, as a result of which many "low quality" patents with broad coverage are being granted.²

Lester Thurow, an economist at MIT, has also expressed serious doubts about the efficacy of the patent system for ensuring a satisfactory rate of innovation at the lowest social cost. He wonders why patent rights of equal effect and duration should be granted to inventors who have made different contributions, some of them significant and others less so, and how is it possible to ensure that patents actually encourage, rather than hold back innovation. He also advocates differential treatment for the developing countries, which are basically dependent on foreign technology (Thurow, 1997).

In fact, thousands of patents are granted each year in the United States for minor developments, trivial ideas, or for substances (including genes) that already exist in nature and which have merely been *discovered* but not *invented* by their would-be "owner". In 1999, the United States Patent Office granted over 160.000 patents, twice the number granted ten years before.

¹ See, Gleick, 2000, p. 44; The Economist, April 8, p. 17.

² The National Academies, Board on Science, Technology and Economic Policy, "Request for proposals for research on intellectual property in the knowledge-based economy", 23 March 2000.

This is the fruit of loose criteria for patentability,³ of the excessive flexibility of the patent office in assessing the degree of non obviousness, novelty and usefulness of the applications submitted to it and of shortcomings in the examination procedure.⁴ In addition, new areas have emerged, such as *software* and “methods of doing business”, where patents, in the view of some, are likely to jeopardize the so called “new economy” (Gleick, 2000, p. 44).

Other patent offices throughout the world are following suit, occasionally in the mistaken belief that an examination conducted by the patent office of a highly industrialized country provides a guarantee of quality. Many of the patents granted are astounding, not so much for their inventiveness as for their triviality.⁵

Nevertheless, patents for trivial inventions are no great worry, when their economic value is scant or limited. The problem arises, however, when the same lax criteria and deficient examination are applied in areas of great economic and social importance. Even if the patent granted is weak and questionable, if the firm that owns it is sufficiently wealthy, in many cases it will aggressively assert its rights against potential competitors, and will elbow out of the market small and medium-sized firms which lack the means to take on costly and lengthy litigation.⁶

In the pharmaceutical field, only a few (several dozen) “new chemical entities” (i.e. molecules not pre-existing) are developed and patented each year. Nonetheless, thousands of patents are granted annually in this sector.⁷ This paradox can be explained by the enormous capacity that the sector’s major firms have built up not only for developing authentic inventions, but also for taking out patents on secondary, occasionally trivial developments, in order to extend their monopoly over a product or process, beyond that allowed by the original patent.⁸ One example will illustrate this type of problem.

Some five years after having patented cimetidine, SmithKline & French obtained a new patent for a polymorph (a particular crystalline form of the molecule), which had in fact actually been described in the original patent. The effect of this patent would have been to delay for several years the marketing of generic products. The patent was challenged – with success – before the courts in several countries on grounds of lack of novelty, thereby aborting the attempt to extend the monopoly of the original patent. Had the patent remained in force, the public would have been denied access to the drug at more competitive prices even after the original patent expiry.

There are various ways in which barriers are frequently raised around products in the public domain, or patents on the point of expiring, with the aim of preventing legitimate

³ The adoption of a notion of local innovation for knowledge disseminated by means other than publication outside the United States has led, for example, to the patenting of plants and knowledge widely used in developing countries (Correa, 1999; The Crucible, 2000).

⁴ For example, less than 50% of the examinations conducted by the Office refer to relevant background bibliography; the examination is by and large limited to analyzing previous patents. See, Aharonian, 2000.

⁵ Examples of some of the patents granted in the United States include an “invention” to inhibit the intake of food and consisting of a pair of elastic bands across the mouth, allowing wearers to breathe but preventing the intake of food (US 4,883,072); a patent for a hunting device consisting of a cape and a hat serving as a decoy for prey (US 5,197,216); a patent for a hat for four-legged animals (US 4,967,317). See, Feinberg, 1994.

⁶ Barton has drawn attention to the use of these “strategic litigation” practices. See, Barton, 1995.

⁷ The chemical and pharmaceutical industry accounts for about one third of the patents granted each year in the USA (Aharonian, 2000).

⁸ See, Zaveri, 1998; Keayla, 1999; Cook, Doyle and Jabbari, 1991.

competition. One of them is the patenting of polymorphs, described above. Other means employed to artificially delay the marketing of competing products include the patenting of:

- a) A *pharmaceutical form*, i.e. a particular way of administering an active ingredient, which may be unpatented,⁹ in combination with certain additives;
- b) “*Selection*” inventions: these occur when a single element or group of elements of an already known large group are selected in order to take out a patent based, for example, on a feature that was not specifically described in an earlier patent for the larger group;
- c) “*Analogy*” processes: this relates to processes that are not in themselves inventive, but which allow a product with inventive features to be obtained;
- d) *Combinations* of known products;
- e) *Optical isomers*: this takes advantage of the property of many chemical compounds to present two mirror forms. Frequently, after the mixture of both forms has been patented (“racemic” mixture) an application is made for a patent for the most active isomer;
- f) *Active metabolites*: this involves patenting the active metabolite of a particular compound that produces the desired effect in the body;¹⁰
- g) *Prodrugs*: these are compounds which, although themselves inactive, produce a therapeutically active ingredient when metabolized in the body;
- h) New *salts* of known substances;
- i) Variants of known *manufacturing processes*;
- j) New *uses* for known products.¹¹

The legal approaches and administrative and judicial practices observed in respect of these different forms of protection vary significantly in different jurisdictions. There is considerable margin for manoeuvre to allow each country to determine its own patent policy. Ideally, it should seek to afford protection to developments that are truly innovative, and reject those that are designed to block competition and delay the marketing of alternative products that are cheaper for consumers.

This study examines a number of specific cases in the area of drugs that, on the basis of objective technical considerations, illustrate types of patenting that potentially divert patents from their real purpose – to encourage and reward a genuinely inventive effort.

⁹ The practical consequences of this type of patent may be significant. For example, in Thailand - where there are serious problems of HIV infection-there is no current patent for didanosine (“ddl”) as such. Nevertheless, the firm Bristol Myers Squibb (which did not discover the product, but obtained it under licence from a federal United States laboratory) patented a formulation of “ddl” thereby blocking the Thai Government’s attempts to purchase the drug at a price that was more affordable to its population. The Thai Government is currently examining the possibility of granting a mandatory licence or of challenging the patent validity.

¹⁰ For example, after terfenadine had been on sale for several years, a patent was obtained for the relevant active metabolite. The courts decided that it was an unacceptable attempt to extend the original patent.

¹¹ An example of a patent for the *use* of a known drug is AZT (“Retrovir”), which was synthesized in 1964 by the Michigan Cancer Foundation as a possible anti-cancer drug. Another more recent example is sildenafil (“Viagra”).

THE CASES

1. Paroxetine

Paroxetine is an antidepressant compound through its inhibiting effect on uptake of the 5-hydroxy-triptamine neurotransmitter. Chemically, the product is identified as (3S-trans)-3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl) piperidine.

The compound has been known both in its basic form and in the form of its pharmaceutically acceptable salts since at least 1977 with the publication of United States patent 4,007,196 (which invokes United Kingdom application priority No. 4496/73 of 30 January 1973), belonging to the Danish company A/S Ferrosan. The patent makes explicit reference to the paroxetine base and to its maleate, but the other salts with a pharmaceutically acceptable acid are covered by reference in the general formula. Although the patent gives no example of the preparation of paroxetine hydrochloride, it does refer to a procedure for preparing N-methyl paroxetine hydrochloride using a widespread general technique for preparing hydrochlorides.

During the period 1979-1985, the Ferrosan company supplied paroxetine hydrochloride to numerous research groups working on the biochemistry and pharmacology of antidepressants; the supplies were public, as is indicated by several articles, of which at least 11 were published by the research groups in scientific journals. For example, in 1979, Ferrosan's own investigators published a paper on the pharmacokinetics of paroxetine in humans, which referred to the administration of oral doses of paroxetine hydrochloride (*Acta Pharmacologica et Toxicologica*, **44**, 289-295 (1979)).

In May 1984, a licensing agreement was signed between Ferrosan and SmithKline Beecham (at the time Beecham). Subsequently, and with the expiry date for the Ferrosan paroxetine patent not far off (United Kingdom priority, 1973), Beecham attempted to extend the protection for paroxetine by means of several patents, including:

- 1) With 1985 UK priority, Beecham applied and obtained patent EP 233.403 claiming crystalline paroxetine hydrochloride hemihydrate. The product patent was granted without it being clear in what way it was different from the already known paroxetine hydrochloride or what the benefits of the allegedly new product were in comparison with that already known.
- 2) With 1995 GB priority, Beecham requested protection through application WO 96/24595 for four different forms of paroxetine hydrochloride anhydrate, and for various paroxetine hydrochloride solvates.
- 3) With 1997 GB priority documents, Beecham requested protection under WO 98/31365 for free-flowing paroxetine hydrochloride obtained using the "spray-dried" technique.
- 4) With 1998 GB priority documentation, SmithKline Beecham requested protection, through WO 99/47519, for a crystalline form of paroxetine free base, paroxetine free base in substantially pure form and paroxetine free base which is substantially solvent free.
- 5) With prior 1998 GB documentation, SmithKline Beecham requested protection through WO 99/40084, for salts of paroxetine with various acids selected from the group consisting of sulphuric, oxalic, fumaric, propionic, formic, glutamic, succinic, benzoic, citric, nitric, phosphoric, tartaric, 4-methylbenzenesulfonic, hypophosphorous, lactic and mandelic acids and glycine.

In addition to endeavouring to protect every possible form of paroxetine base and of paroxetine salts with different acids in various forms (free-flowing, crystalline, hydrates, anhydrides and solvates, including different polymorphs of some of these), SmithKline attempted to block other alternatives to the use of the product as a pure solid, by applying for protection of the use of paroxetine in liquid form or as a solid absorbed in or by another solid.

Thus, in WO 99/26625 (invoking 1997 priority) the company attempted to patent an oral swallow capsule containing paroxetine as the free base or a pharmaceutically acceptable salt or solvate thereof in solution in a carrier, while in WO 99/48499 (invoking 1998 priority) it claimed paroxetine or a pharmaceutically acceptable derivative thereof adsorbed on or absorbed by a solid carrier. Finally, SmithKline Beecham rounded off the circle by claiming paroxetine maleate, a product which had been explicitly described in Ferrosan's expired patent US 4,007,196.

In SmithKline Beecham's application WO 99/52901, the authors claim that although example 2 in US 4,007,196 describes treatment of the paroxetine base dissolved in ether with a solution of maleic acid in ether to produce a crystalline product which is recrystallized from ethanol-ether to give paroxetine maleate with a melting point of 136-138°C, the patent gives no further data that allow the structure to be determined unambiguously.

In this way, they claim "surprisingly" to have discovered "novel" maleate salts of paroxetine.

Although paroxetine maleate and paroxetine hydrochloride were known from the description in US 4,007,196 and from the samples made by Ferrosan itself between 1979 and 1985 respectively, SmithKline Beecham has deployed a barrage of patents which for the moment prevent paroxetine hydrochloride from being marketed until EP 223 403 expires, i.e. at least until 2006 in the European designated countries without SPC¹² (Belgium, Germany, Greece, Spain, Luxembourg, the Netherlands, Sweden and The United Kingdom) or until June 2008 in Switzerland and Liechtenstein, October 2009 in France and December 2012 in Italy, where SPCs were granted.

It should be borne in mind that Ferrosan's basic patents claiming paroxetine and its pharmaceutically acceptable salts, equivalent to US 4,007,196, have already expired or are about to expire in those European Countries. For example, in Belgium, Luxembourg, the Netherlands, Switzerland, the United Kingdom, Spain and Germany, the equivalent patents expired between 1992 and 1999, depending on the country (in some of them, SPCs were granted, extending the patent until 1999). In France the patent expires in January 2001 and in Sweden in April 2002.

Because all the methods of producing paroxetine hydrochloride by crystallization of the salt in not completely dry solvents produce in any case the hemihydrate crystalline form, to prevent competition from generic drugs using distinct forms of it, Beecham has blocked the amorphous or anhydrate forms of paroxetine hydrochloride.

Finally, anticipating action by more intrepid competitors who might have imagined to market paroxetine salts other than hydrochloride (HCL), Beecham patented other salts even

¹²"Special Protection Certificate".

though they had no benefits other than those already known, and again patented the maleate salt, first described by Ferrosan.

In short, this case illustrates how it may be possible to extend the patent protection for an active ingredient, through processes for producing salts that add little or nothing in terms of innovation, occasionally resorting to well-known techniques.

2. Amlodipine/Amlodipine Besylate

Amlodipine is a dihydropyridine calcium-channel blocker developed by the Pfizer corporation that is used in the management of hypertension and angina pectoris.

The active ingredient was patented by the company in Europe under patent No. EP 089.167 B:

Patent for Amlodipine, EP 089.167

Patent EP No.:	089.167 B
Application No.:	83301227-1
Application date:	08/03/83
Publication date:	15/10/86
Priority No.:	GB 82-07180(11/03/82)
Title:	“Dihydropyridine anti-ischæmic and antihypertensive agents, processes for their production and pharmaceutical compositions containing them”
Inventors:	Campbell S. F., Cross P. E., Stubbs J. K.
Int. classification:	C 07 D 211/90

This European patent designates Austria, Belgium, Switzerland, Germany, France, the United Kingdom, Italy, Liechtenstein, Luxembourg, the Netherlands and Sweden. Although its original date of expiry was 8 March 2003, according to the information on the NPS and Inpadoc data bases, extensions have been applied for and granted in Belgium, Switzerland, France, the United Kingdom, Italy, Liechtenstein, Luxembourg, the Netherlands and Sweden. In Germany, an application was made for an SPC on 11 May 1993 (No. 16909.00.00), but has not yet been granted.

The expiry dates of patent EP 089.167 B in each of those countries are:

8 March 2003	in Austria
8 March 2003	in principle, in Germany (SPC applied for)
8 March 2004	in Belgium and Luxembourg (SPC granted)
7 March 2004	in the United Kingdom and the Netherlands (SPC granted)
26 March 2005	in Switzerland and Liechtenstein (SPC granted)

17 January 2006	in Sweden (SPC granted)
21 August 2007	in France (SCP granted)
2 April 2010	in Italy (SCP granted)

The equivalent US patent is US 4,572,909, valid until 1 August 2006.

In this first group of patents, Pfizer claimed compounds according to claim 1 and the pharmaceutically acceptable acid addition salts thereof, which included amlodipine and its salts.

The description indicated that the pharmaceutically acceptable acid addition salts of the compounds of the patent are those formed from acids which form non-toxic addition salts containing pharmaceutically acceptable anions, such as the hydrochloride, hydrobromide, sulphate, phosphate or acid phosphate, acetate, maleate, fumarate, lactate, tartrate, citrate and gluconate salts.

The compound and its preparation, amlodipine and its maleate salt, are described in the submission.

Four years after the application for the amlodipine product patent, Pfizer “unexpectedly found” that the addition salt of amlodipine which possesses numerous benefits is not one of those cited in the previous patent, but the benzene sulfonate salt or besylate.

For this reason, it patented it under European Patent EP 244 944 B and equivalent patents:

Patent for Amlodipine Besylate, EP 244 944:

Patent:	244 944B
Application No.:	87302767.6
Date of filing:	31 March 1987
Date granted:	24 January 1990
Priority:	GB860335 (4 April 1986)
Title:	“Salts of amlodipine”
Inventors:	Davison E., Wells J. I.
Int. classification:	C07D 211/90

This European patent designates Austria, Belgium, Switzerland, Germany, Spain, France, the United Kingdom, Greece, Italy, Liechtenstein, Luxembourg, the Netherlands and Sweden. The patent’s date of expiry in each country is:

31 March 2007	in Austria, Belgium, Switzerland, Germany, Spain, the United Kingdom, Greece, Liechtenstein, Luxembourg, the Netherlands and Sweden;
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21 August 2007 in France (SCP granted);

2 April 2010 in Italy (SCP granted).

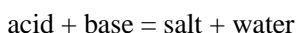
Moreover, in the United States, Pfizer protected the product under patent US 4,879,303, which will be in force until 25 March 2007.

In 1990, Pfizer launched the product on the market in its amlodipine besylate form. As a result, because Pfizer took out separate patents for the active ingredient amlodipine and its besylate salt as separate products, the generic product will not only have to wait until the patent for amlodipine (the actual active ingredient) expires, but also until the patent for the besylate salt expires, some 1 to 4 years later.

In some countries where it was not possible to patent the pharmaceutical product, Pfizer Limited obtained a patent for the production process of an amlodipine besylate salt. For example, in Argentina, it obtained Patent No. AR 242.562 on 30 April 1993. The application was based on the priority of an application made in the United Kingdom (GB 86-8335), which protected the pharmaceutical product, something not possible in Argentina under the legislation in force at the time of the application.

The Argentine patent protects a procedure for the preparation of amlodipine besylate by reacting the amlodipine base with a solution of benzenesulfonic acid or its ammonium salt in an inert solvent. Contingently, the patent protects the preparation of the pharmaceutical formulations of besylate obtained by the procedure described, in the form of tablets, capsules and aqueous solutions for parenteral administration.

The procedure for obtaining amlodipine besylate claimed and described in patent AR242.562 is a simple chemical reaction: the production of a salt from an acid with a base. This reaction is described by the simple formula:



which is to be found in elementary chemistry textbooks.¹³

This formula applies to both inorganic and organic compounds; the production of salts from organic acids, such as carboxylic and sulfonic acid, is one of the basic principles of organic chemistry. In the case of the preparation of amlodipine besylate, the acid is a sulfonic aromatic organic acid, benzenesulfonic acid to be precise, and the base is a nitrogen organic base, called amlodipine base.

The reaction that produces the salt from a carboxylic or sulfonic acid is one of the most elementary chemical reactions and is an indispensable resource for processing organic substances for formulation as agricultural compounds, pesticides or pharmaceuticals. Moreover, in patent literature, the production of salts is considered to be a wholly familiar process, and in most cases, when a patent claims a synthetic process, the production of the salt is simply mentioned on completion of the definition of the process claimed, in terms such as

¹³ See, for example *The Chemistry of Organic Compounds* by Carl Noller, second edition, 1968, chapter 11; *Química orgánica*, by Robert T. Morrison and Robert N. Boyd, second Spanish edition (Addison-Wesley Iberoamericana, México, 1987).

“the pharmaceutically acceptable salts are obtained” or “agriculturally acceptable salts are produced”, or “and its salts”. Normally, there is no need to specify the method of preparation, since it is obvious to anyone as a matter of course. When an organic nitrogen base (amlodipine base) reacts with an organic acid (benzenesulfonic acid), the salt (amlodipine besylate) is inevitably formed.

In the case of the patent under consideration, there is no novelty or inventive step. The process for obtaining the salts described in the patent was already familiar before the date of application and of its priority, to any specialist and even to any secondary school or university student of chemistry.

Thus, in patent ES 521.728 of 12 April 1984, concerning the processes for obtaining sultamicillin benzenesulfonate, Pfizer states that the benzenesulfonate (or besylate) is obtained by “the usual methods for the preparation of acid addition salts of aminopenicillins”. The patent is based on an even earlier US patent application No. 371156 (of 23 April 1982) which was granted under No. US 4,432,987, the description of which states that the salts are prepared by standard methods known in the art for preparing acid addition salts of aminopenicillins; for example, by contacting the free base of sultamicillin with an equimolar amount of the appropriate acid, i.e., benzenesulfonic acid or 4-chlorobenzenesulfonic acid in the presence of a suitable solvent. Preparation by metathesis of salt forms in which an inorganic salt is formed, for example, by reaction of a hydrohalide addition salt of sultamicillin with an alkali metal or alkaline earth salt of the appropriate sulfonic acid is also described. The description also refers to a further method of preparing the salt, by reaction of an amino-protected precursor of sultamicillin (such as an enamine-protecting group) in the presence of the requisite benzenesulfonic acid under conditions which allow the removal of the amino-protecting group.

In some countries, the doctrine known as “analogy processes” has been put forward; under this doctrine, a patent may be granted if the product obtained by the process is novel and of inventive merit, even if the procedure itself does not meet these criteria. In other words, the novelty and inventive character of the product could “impregnate” the procedure, even if it lacks them.

This doctrine is founded upon a legal fiction that disregards, however, the clear distinction made by patent law between “the product” and “the procedure”.

This example also highlights the practice of developing and protecting salts as a means of extending the monopoly over a product, and the use of “analogy processes” to obtain protection for elementary processes for making salts which are in the public domain.

3. Alendronate

Alendronate, or alendronate sodium, or 4-Amino-1-hydroxybutane-1,1-diylbis(phosphonic acid), is a product used to treat and prevent osteoporosis.

The product has no patent protection and was described for the first time by M. I. Kabachnik and collaborators in *Izv Akad. Nauk. SSR, Ser. Khim* (1978), **2**, 433-7.

Subsequently, the Italian company Instituto Gentili discovered that certain diphosphonic acids, including alendronic acid and its alkaline metal salts are useful for treating urolithiasis and as inhibitors of bone resorption.

With a 1982 priority, it patented the pharmaceutical compounds containing alendronic acid and its salts (GB 2,118,042) or the pharmaceutical compounds containing alendronic acid and its salts to inhibit bone resorption (DE 3,313,049), and a method of treatment of urolithiasis and inhibiting bone resorption which consists of administering to a patient in need thereof an effective amount of alendronic acid (US 4,621,077).

There are equivalents for this patent in Belgium (expires on 14 April 2008), France (expires on 10 April 2008), Hong Kong (expires with the UK patent), Italy (expires on 15 April 2007), Japan (expires on 13 April 2003), Luxembourg (expires on 13 April 2008), the Netherlands (expires on 15 April 2003, SPC requested), Sweden (expires on 15 April 2008), Switzerland (expires on 25 March 2003, SPC requested) the United Kingdom (expires on 29 March 2008), the United States (expires on 4 August 2007) and Germany (expires on 12 April 2003, SPC requested).

The company granted a world-wide licence to develop the product to Merck & Co.

Even though the preparation of this alendronic acid compound by treatment of 4-aminobutyric acid with phosphorous acid (H_3PO_3) and phosphorous trichloride (PCl_3), phosphorous pentachloride (PCl_5), or phosphorous oxychloride ($POCl_3$), had already been described by M. I. Kabachnik and Collaborators in *Izv Akad. Nauk. SSR, Ser. Khim* (1978), **2**, 433-7, and by Henkel Koffman in European patent EP 039 033, and in equivalents such as US4,407,761 (all of which invoked German priority of 28 April 1980), the firms Instituto Gentili and Merck & Co. took out new patents to protect procedures for the preparation of this compound. These include:

US patent No.:	4,705,651
Application No.:	786815
Application date:	11 October 1985
Date granted:	10 November 1987
Approx. exp. date:	10 November 2004
Priorities:	IT 23362, A784 (29 October 1984)
Inventors:	Giorgio Staibano
Assignee:	Instituto Gentili
International class:	C O7F 009/38
Patent family:	
AT 391,702	IT 1,196,315
BE 903,5	JP 61/109794
CH 663,791	LU 86,133
DE 3,535,404	NL 85/02949
FR 2,572,406	SE 464,084
HK 9100128	GB 2,166,741

This patent protects an improved process for the preparation of alendronic acid which consists of reacting 4-aminobutyric acid, H_3PO_3 and PCl in a molar ratio of 1:1.25:2, and in the absence of solvents. This patent will not expire until 11 October 2005.

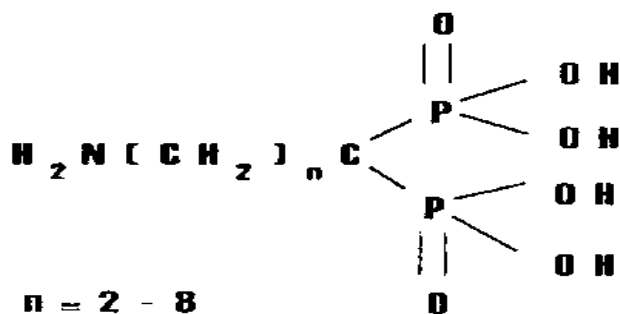
According to the authors, the molar ratio of the components allows the reaction mixture to be kept fluid, and the product is recovered by dilution with C_1 - C_3 alcohol.

However, according to Gentili itself, the procedure described is unsuitable to an industrial scale application, because of the problem presented by the viscosity of the reaction mixture, which poses problems of stirring and hydrolysis. To resolve them, Gentili applied for an improvement on US patent 4,705,651 via the following European patent:

EP patent No.:	0494 844
Application No.:	92830001.1
Date of filing:	2 January 1992
Date of pub. of appl.:	15 July 1992
Date granted:	19 April 1995
Approx. exp. date:	2 January 2012
Designated contracting States:	AT, BE, CH, DE, DK, ES, FR, GB, GR, LI, LU, MC, NL, PT, SE
Priorities:	IT 080191 F191000003 (8 January 1991)
Inventor:	Guaianai-Ricci, G.
Assignee:	Instituto Gentili
International class.:	C07F9/38
Patent family:	
CA 2,058,905	ES 2,072,126T
JP 04/342596	IT 1,246,992

This patent claims an improved process for the preparation of diphosphonic acids having the formula 2 wherein n is comprised between 2 and 8, and of its alkaline salts in mono or bi-basic form (see figure 1).

Figure 1



The process comprises the following stages a) melting a mixture of aminocarboxylic acid and phosphorous acid in the absence of a solvent; b) adding dropwise phosphorous trihalide; c) addition of an hydrolyzing agent selected between water and a strong, not oxydizing acid, and d) recovering the diphosphonic acid thus produced. The process is characterized in that the molar ratio between aminocarboxylic acid, phosphorous acid and phosphorous trihalide in the reaction mixture is comprised between 1:3:2 and 1:20:6.

Claim No. 7 protects the process where the aminodiphosphonic acid produced is alendronic acid. Example No. 4 of the description sets out the preparation of alendronic acid by reaction of 4-aminobutyric acid, phosphorous trichloride and phosphorous acid.

This patent will not expire until January 2002 in all the designated European States, which include Spain, Austria, Germany, Belgium, Denmark, France, the United Kingdom, Greece and Portugal. Equivalents have been found in Canada and Japan.

Merck & Co. also possesses patents covering the preparation of this compound:

EP patent No.	402 152
Application No.:	19900306238
Application date:	8 June 1990
Date appl. published:	12 December 1990
Date granted:	2 November 1995
Approx. date of expiry:	8 June 2010
Designated States:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
Priorities:	US 363820 (9 June 1989)
Inventors:	Kieczkowski G., Jobson R.
Assignee:	Merck & Co.
International class.:	CO7F9/38
Patent family:	
AU 625,704	NO 902,559
CA 2,018,477	NZ 233,972
FI 902,845	PT 94,306
IL 94,612	US 4,922.007
JP 03/101684	ZA 90/04446
LV 11472	ES 2,080,116T
IE 69564	KH 9600695
HU 211908	

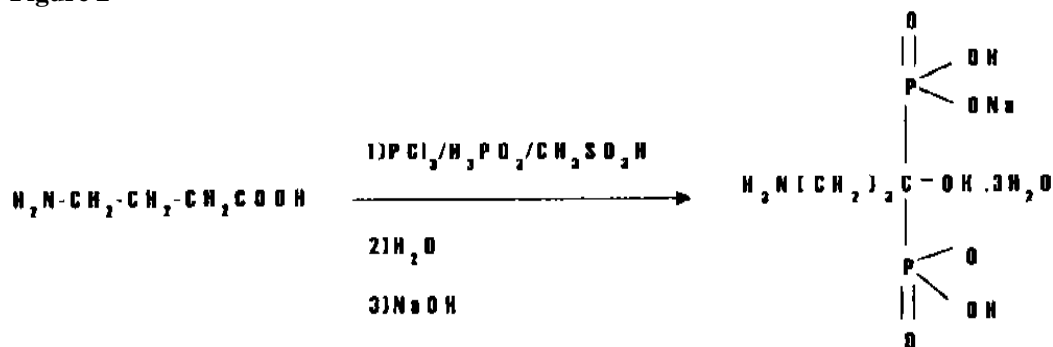
In this European patent, Merck not only claims a process for the preparation of alendronate, but the product itself, in its crystalline trihydrate form of monosodium alendronic acid salt.

This European patent claims for Austria, Germany, Belgium, Switzerland, Denmark, France, the United Kingdom, Italy, Liechtenstein, Luxembourg, the Netherlands and Sweden, but not for Spain or Greece, alendronic acid monosodium salt trihydrate.

It also claims for these countries, and for Spain and Greece, a procedure for obtaining this compound, comprising:

- a) Reacting 4-aminobutyric acid with a mixture of HP_3PO_3 and PCL_3 in the presence of $\text{CH}_3\text{SO}_3\text{H}$ at a temperature below 85°C ;
- b) Treating it with water;
- c) Cooling to $0\text{-}5^\circ\text{C}$;
- d) Recovering the compound by filtration, washing with water and 95% ethanol and air drying (see figure 2).

Figure 2



According to the authors, the methane sulfonic acid ensures the homogeneity of the reaction mixture, increases the yield of the process and allows the salt to be obtained without the need to isolate the acid. Claims 4 and 5, protect the process when the compound recovered is alendronic acid monosodium salt trihydrate and alendronic acid respectively.

Equivalents to the European patent have been presented in many countries, such as Canada, Japan, Australia, Norway, Portugal, Finland, South Africa, Israel, Ireland, New Zealand, Latvia and the United States.

The equivalent United States patent, number 4,922,007, claims only the process for the preparation of 4-amino-1-hydroxybutylidene-1,1-biphosphonic acid or salts thereof, but NOT alendronic acid monosodium salt trihydrate itself. The process comprises:

- reacting 4-aminobutyric acid with a mixture of HP_3PO_3 and PCl_3 in the presence of $\text{CH}_3\text{SO}_3\text{H}$;
- recovering the acid or salt.

Merck subsequently presented a variant of the process claimed in the earlier European patent EP 402 152:

EP patent No.:	462 663
Application No.:	91201490.9
Date of filing:	14 June 1991
Date of pub. of appl.:	27 December 1991
Date granted:	27 September 1995
Approx. date of expiry:	14 June 2011
Designated States:	AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
Priority:	US540997 (20 June 1990)
Inventor:	Kieczkowski G
Assignee:	Merck & Co.
Patent family:	
AU 642,264	NO 91/02395
CA 2,044,923	PT 97,963
FI 9103008	US 5,019,651
JP 05/132492	ZA 91/04708
LV 11471	ES 2,079,026

NZ	238,493	IL	98462
IE	69171	HK	9600644
RO	112355		

The patent claims a process for preparing alendronic acid or its salts:

- a) reacting 4-aminobutyric acid with a mixture of phosphorous acid and PCl_3 in the presence of methanesulfonic acid;
- b) contacting the mixture from step a) with an aqueous hydrolysis mixture;
- c) recovering said acid or salts thereof; which is characterized by the maintenance of the pH in the range of 4 to 10 during step b).

This patent will remain in force until June 2011 in all the designated States, which include Austria, Belgium, Switzerland, Germany, Spain, France, the United Kingdom, Greece, Italy, Liechtenstein, Luxembourg, the Netherlands and Sweden. Equivalents have also been found in Australia, Canada, Finland, Japan, Norway, Portugal, South Africa, Latvia New Zealand, Israel, Ireland, Hong Kong and Romania.

The equivalent US patent, No. 5,019,561 runs until 20 June 2010. It claims a process for preparing 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid (ABP) or salts thereof, comprising:

- a) reacting 4-aminobutyric acid with a mixture of phosphorous acid and PCl_3 in the presence of methanesulfonic acid;
- b) contacting the mixture from step (a) with an aqueous hydrolysis mixture, wherein the pH is maintained in the range of 4 to 10 during the contacting;
- c) recovering said acid or salts thereof.

A claim is also made for the process comprising:

- a) reacting 4-aminobutyric acid with a mixture of H_3PO_3 and PCl_3 in the presence of $\text{CH}_3\text{SO}_3\text{H}$ at a temperature of about 65°C ;
- b) contacting the resulting mixture from Step (a) with an aqueous phosphate buffer at a temperature in the range of $0\text{-}20^\circ\text{C}$, and maintaining the pH between 6-8 during the contacting;
b-2) heating the resulting mixture from Step (b) at the boiling point; and
- c) recovering said acid or salts thereof.

In addition to claiming the product in its crystalline alendronic acid monosodium salt trihydrate form and/or processes for its preparation, Merck attempts to protect the galenical composition of the tablets marketed under the Fosfamax trade name, through application PCT WO 94/12200. This application designates, *inter alia*, Spain, Japan, the United Kingdom, France, Germany, Portugal, Italy, Ireland and the United States.

This PCT application claims a pharmaceutical composition comprising between 0.5 and 40% by weight of alendronic acid or its salts and between 60 and 95% by weight of processing aids, essentially consisting of anhydrous lactose, microcrystalline cellulose, croscarmallose sodium and magnesium stearate. It also claims a composition comprising about 0.5 to 40% by weight of alendronic acid or its salts, 10 to 80% by weight of anhydrous lactose, 5 to 50% by weight of microcrystalline cellulose, 0.5 to 10% by weight of croscarmallose sodium and 0.1 to

5% by weight of magnesium stearate. It further claims a process for the preparation of a tablet containing alendronic acid or its salts which involves forming a mixture containing alendronic acid and a diluent selected from anhydrous lactose, a dry binder, a disintegrant and optionally one or more additional ingredients selected from the group consisting of compression aids, flavours, flavour enhancers, sweeteners and preservatives, lubricating the mixture with a lubricant and compressing the lubricated mixture. The method claimed is a direct dry mix compression process.

The application for PCT WO 94/12200 in other countries has been studied; it is being examined as EP 690 719 in Europe.

In the United States, Merck's PCT application has given rise to three patents: US 5,358,941, US 5,681,590 and US 5,882,656.

In claim 1, US 5,358,941 which is in force until December 2012, describes a composition comprising about 0.5 to 40% by weight of alendronic acid or its salts and from about 60 to 99.5% by weight of excipients consisting essentially of anhydrous lactose, microcrystalline cellulose, croscarmallose sodium and magnesium stearate. It also claims the pharmaceutical composition comprising about 0.5 to 40% by weight of alendronic acid or its salts, about 10 to 80% by weight of anhydrous lactose, about 5 to 50% by weight of microcrystalline cellulose, about 0.5 to 10% by weight of croscarmallose sodium; and about 0.1 to 5% by weight of magnesium stearate.

United States patent No. 5,681,590, which is in force until December 2012, claims a process for the preparation of a tablet containing alendronic acid or its salts, comprising forming a mixture by mixing the active ingredient with a diluent, selected from anhydrous lactose, or hydrous fast flow lactose, a dry binder, a disintegrant, and optionally one or more additional ingredients selected from the group consisting of compression aids, flavours, flavour enhancers, sweeteners and preservatives, lubricating the mixture with a lubricant; and compressing the resultant lubricated mixture into a desired tablet form. The method claimed is a dry mix formulation.

Finally, patent US 5,882,656 claims, in the United States, a pharmaceutical composition comprising by weight, about 0.5 to 40% of alendronic acid and its salts and from about 60 to 99.5% by weight of excipients comprising a diluent, a binder, a disintegrant, and a lubricant.

The PCT has also given rise to patents or equivalent applications in Mexico, Australia, Norway, New Zealand, Bulgaria, Slovakia, Finland, Hungary, Israel, the Czech Republic, South Africa, Canada, Romania and Japan.

To sum up: alendronic acid was a product that became known through a description made in 1978. The Italian firm Instituto Gentili discovered that alendronic acid and its alkaline metal salts are useful in treating urolithiasis and in inhibiting bone resorption. It patented, with 1982 priority, the pharmaceutical compositions containing alendronic acid and its salts in US patent 4,621,077 and equivalents. These patents should originally have remained in force in Europe and in the United States until 2003, but extensions of the deadline have been obtained until 2007-2008, depending on the country.

It should be emphasized that the Gentili patents do not claim only the pharmaceutical compositions containing alendronic acid, but also those containing its salts. Example three

describes the preparation of alendronic acid using the method patented by Henkel, while example five describes the preparation of the sodium salt of a product analogous to alendronic acid by treating the corresponding acid with NaOH.

Gentili granted a licence to Merck, who took advantage of the fact that sodium alendronate had not been identified in the Gentili patents; seven years after the Gentili discovery, Merck patented as a product, under patent EP 402 152 (and equivalents) the self-evident result of treating alendronic acid with an alkaline metal base; of course, the product launched on the market as “FOSAMAX” is nothing else than alendronic acid monosodium salt trihydrate; this resulted in an additional two to three years protection beyond the expiry date of the patents for the Gentili pharmaceutical preparations.

In addition to this extended protection, Merck made separate patent claims invoking a 1992 priority, as in application WO 94/12200, for the galenical composition (conventional tablets produced by dry mix using common techniques) contained in the FOSAMAX specialty which had been on the market since November 1993. If these are granted, as they have been in the United States, they will enjoy patent protection until 2012 or 2013.

When the Gentili patents expire between 2007-2008, the generic product will still have to contend with at least two Merck product patents covering monosodium trihydrate (2010) and the tablets containing it (2012-2013).

The case of alendronic acid is illustrative of the simultaneous use of a variety of means - including salts, procedures and formulations- to achieve broad protection and to extend it for more than 30 years after the basic product was first described.

4. Clarithromycin

Clarithromycin or 6-*O* Methylerythromycin A is a semisynthetic macrolide antibiotic derived from erythromycin A, presenting greater stability in acid conditions and greater antibiotic activity than erythromycin A.

The Japanese company Taisho Pharmaceutical is the holder of the product patent family, which includes European patent EP 041 355. The company has granted a licence to Abbott for the development of the product world-wide, except in Japan, Korea and Taiwan. The product was first launched in 1990 in Ireland.

European patent EP 041 355 will run until May 2001 in Germany, Belgium, Austria, France, the United Kingdom, Italy, the Netherlands, Liechtenstein, Sweden and Switzerland. However, SPCs have been granted in some of these countries, as a result of which the expiry dates of the patent are: 19 November 2004 in the United Kingdom and the Netherlands, 20 November 2004 in Germany, Austria and Belgium, 4 October 2005 in Switzerland and Liechtenstein, 27 May 2006 in Sweden and 27 May 2008 in France.

Equivalent patents have been found in Japan and in the United States. The equivalent United States patent, US 4,331,803, will run until 23 May 2005.

The Japanese equivalents, JP 63/002274 and JP 61/052839 will be in force until 4 June 2000 and 1 September 2004 respectively.

Taisho also holds other later patents that claim new processes for synthesizing clarithromycin: EP 147 062 A, EP 158 467 B, EP 180 415 B, EP 195 960 B, EP 260 938 B and EP 272 110 B.

Abbott also holds five PCX applications relating to the preparation of clarithromycin, WO 97/36912, WO 97/36913, WO 98/35976 and WO 99/12946, and of United States patents US 5,852,180 and US 5,892,008, also relating to the preparation of clarithromycin.

As regards the process for synthesizing clarithromycin described in the above documents, there are four general process for alkylation of 6-OH from erythromycin A.

In the first of them, described in patents EP 041 355 and EP 147 062, a derivative of erythromycin A (3'-demethylerythromycin A) protected in its 2'-OH and 3'-NHCH₃ positions, is subjected to methylation. The second consists of methylating a derivative of erythromycin A in *O*-substitute-oxime form, favouring the 6-OH position in alkylation (EP 158 467, EP 180 415, EP 195 960, EP 260 938, EP 272 110, EP 342 990, WO 97/36912, WO 97/36913, WO 97/38000, WO 98/35976 and US 5,852,180). The third consists of methylating 9-hydrazone erythromycin A and 9-azine erythromycin A derivatives (WO 99/12946). The fourth consists of methylating a 9-hydroxy erythromycin A derivate (US5,892,008).

Patents EP 180 415, EP 195 960, EP 260 938, EP 272 110, WO 96/36912, WO 97/36913, WO 98/35976 and US 5,852,180 describe and claim methods that depend on the procedure of patent EP 158 476, since this patent claims the basic method for introducing the 6-OH group used in those patents. They also claim intermediates or precursors of clarithromycin.

The synthesis of clarithromycin described in the family of product patents, as in EP 041 355, and in the family of later procedure patents, as in EP 147 062, basically consists of a process of 6-*O* alkylation of a derivative of erythromycin A protected in positions 2' and 3', (2'-*O*,N-bis(benzyloxycarbonyl)-N-demethylerythromycin A)-in the presence of an alkylating agent and an alkali metal hydride, alkali metal amide or butyl lithium ...base in anhydrous conditions, to derive 6-*O*-methyl-2',3'-*O*,N-bis(benzyloxycarbonyl)-N-demethylerythromycin A **3**. The protecting group is then removed using H₂ on Pd/C to obtain 6-*O*-methyl-N-demethylerythromycin A **2**. Finally, compound **2** is methylated with formaldehyde under reducing conditions (H₂-Pd/C)¹⁴

According to Taisho's inventors, the processes described in the previous patents have a serious drawback, the low selectivity of the *O*-alkylation process. To improve it, Taisho developed a new approach consisting of *O*-methylating the 6-OH group of a derivative of erythromycin A in the form of oxime.

Thus, patent EP 158 467 and equivalents develop and claim a new process for the selective methylation of the hydroxyl group at the 6-position of an erythromycin A derivative, comprising converting an erythromycin A derivative into an erythromycin A 9-oxime derivative and reacting this with a methylating agent in the presence of a base, where the methylating agent is methyl iodide, methyl bromide, methyl chloride, dimethyl sulfate, methyl *p*-toluenesulfonate or methanesulfonate, and the base potassium hydroxide, sodium hydroxide, potassium hydride or sodium hydride.

¹⁴ See Carlos M. Correa, *Trends in Drug Patenting: Case Studies* (Buenos Aires, Ediciones Corregidor, 2001) Figure 3, p. 41.

Details of this European patent are given below:

EP patent No.:	158 467 B1
Application No.:	85301997.4
Date of filing:	22 March 1985
Date of pub. of appl.:	16 October 1985
Date granted:	5 July 1989
Approx. date of expiry:	22 March 2005
Designated States:	AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE.
Priority:	JP 68509//84 (6 April 1984)
Inventors:	Watanabe Y., Morimoto S., Goi M., Mitsukuchi M., Adachi T., Nakagami J., Asaka T., Eguchi T.
Assignee:	Taisho Pharmaceutical
International class.:	C 07 H 17/08
Patent family:	
AR 240,833	PT 80,237
AU 567,803	RU 1,577,700
CA 1,225,637	ZA 85/02349
CN 1,009,001	KR 91/7572
DK 85/01523	ES 541,898
FI 77,250	US 4,672,109
HK 94/996	DE 3,571,323
JP 05/003475	

This patent will remain in force in Austria, Belgium, Switzerland, Germany, France, the United Kingdom, Italy, Liechtenstein, Luxembourg, the Netherlands and Sweden until March 2005.

Equivalents exist in Argentina, Australia, Canada, China, Korea, Denmark, Spain, the United States, Finland, Hong Kong, Japan, Portugal, Russia and South Africa.

The United States equivalent, US 4,672,109, will be in force until 5 April 2005.

This means that when the product patent for clarithromycin expires, it will not be possible to market the product unless it is prepared by the method described in the product patent family, a process which, according to Taisho, is impractical for obtaining a product of quality.

Moreover, invoking 1996 and 1997 priority, and 16-17 years after the protection of clarithromycin by the Taisho patents invoking 1980 priority, and after numerous patents describing other methods of synthesizing the product, Abbott has presented three PCT applications describing and claiming crystal forms of clarithromycin: WO 98/04573 (Form I), WO 98/04574 (Form II) and WO 98/31699 (solvate form 0). The three PCTs designate many countries.

In short, this case illustrates how patents may be used to cover manufacturing process, and complementarily, crystal forms, as a strategy to extend patent protection in time, beyond the expiry of the basic product patent.

5. Omeprazole

Omeprazole, 5-methoxy-2-[[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole is an inhibitor of secretion of gastric acid, developed by the Swedish firm Aktiebolaget Hassle.

The product patent family for omeprazole belongs to the Haessle company, and invokes priority SE 78-4231 (14 April 1978) in Europe. In Europe, Haessle protected the invention through patent EP 005 129, in which it protected, among other claims, omeprazole or its pharmaceutically acceptable salts and pharmaceutical preparations containing them. The United States equivalents to EP 005 129 are US 4,255,431, US 4,337,257 and US 4,508,905.

The expiry date of EP 005 129 in each country, and of the equivalent patents in the same family are shown in a table below.

Although the description and claims describe omeprazole, there are no examples of salts of the compound.

The compound is very labile and decomposes easily, especially in an acid environment. This is why, when it is administered orally, it needs to be protected from the stomach's highly acid environment. For this reason, Astra developed and patented under EP 247 903, a colour-stable oral pharmaceutical preparation containing omeprazole as an active ingredient; the preparation is characterized by being formed of a core, in the form of a small pill or tablet containing omeprazole with an alkaline reacting substance or alkaline reacting salt of omeprazole, optionally with an alkaline reacting substance. The core is covered with one or more inert separating layers containing excipients that are water soluble or rapidly disintegrating in water or water-soluble polymers used for film-coating applications, which may optionally contain pH buffering compounds between the alkaline reacting core, and an outer enteric coating.

This patent was applied for on 16 April 1987 and granted on 7 January 1993. It designates Austria, Belgium, Switzerland, Germany, Spain, France, the United Kingdom, Greece, Italy, Liechtenstein, Luxembourg, the Netherlands and Sweden.

Equivalents exist in Australia, Canada, the Czech Republic, China, Korea, Denmark, the United States, Finland, Hungary, Israel, Japan, Norway, Portugal, Russia, Singapore and South Africa.

The expiry date of EP 247 983 in each country, and of the equivalent patents of the same family, are given below.

Germany was one of the first countries in which the patent for omeprazole expired, in April 1999, and in which generic versions of Astra's Prilosec or Mopral have been put on the market. Astra had applied for and obtained an SPC extending the patent until 21 March 2003. However, the SPC was subsequently revoked and declared null and void by a decision of the German Patent Court, dated June 1997. An appeal against the decision was lodged with the German Court of Appeal, which recently referred the case to the European Court of Justice.

The company has requested, and in some cases secured, protective measures to halt the sale of these generic versions, for alleged infringement of EP 247 983.

Astra is not only the holder of the above patents, but of many others relating to this product.

A telling example is patent EP 124 495, which invokes 1983 priority, claiming omeprazole salts *per se*.

Patent EP No.:	124 495 B
Application No.:	84850066.6
Application date:	28 February 1984
Date granted:	14 January 1987
Approx. expiry date:	28 February 2004
Priorities:	SE 83-8301182 (4 March 1983)
Designated States:	AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
Inventor:	Brändström A. E.
Assignee:	Aktiebolaget Hässle
International class.:	C 07 D 401/12
Patent family:	
AT 24,907	IL 70,985
AU 563,842	JP 03/013233
BG 44,538	KR 87/01005
BG 60,837	LT 2,253
CA 1,264,751	NO 160,204
CS 241,150	NZ 207,348
DD 221,459	PH 21,352
DE 3,462,036	PL 142,748
DK 160,044	PT 78,191
ES 530,242	RO 88,721
FI 83,649	RU 1,314,953
GB 2,137,616	SI 84/10397
GR 79,828	SG 90/00014
HK 90/135	HU 193,557
US 4,738,974	
HR 93/0428	YU 43,345
IE 57,326	ZA 84/01202

The patent claims the lithium, sodium, potassium, magnesium, calcium salts of omeprazole, a process for their manufacture, the pharmaceutical salts containing it, and its use to inhibit gastric acid secretion, to provide gastrointestinal cytoprotective effects and to treat gastrointestinal inflammatory diseases in humans and mammals and in humans.

According to the authors' description in the patent, these novel alkaline salts of omeprazole are more stable during storage than the corresponding neutral form of omeprazole; they state, for example, that the magnesium salts are specially preferred for the preparation of tablets, while the sodium salts are preferred for the formulation of liquid pharmaceutical preparations.

This European patent and its equivalents were submitted 5 years after omeprazole or its pharmaceutically acceptable salts had been patented under EP 005 129.

Not only are separate claims made for omeprazole and its sodium or magnesium salts, but Astra again attempted to patent, under WO 99/08500 (November 1998 priority), WO 99/00380 (June 1997 priority) and WO 95/01977 (July 1993 priority), specific polymorphic forms of omeprazole, sodium omeprazole and magnesium omeprazole, respectively, characterized by having a degree of crystallinity which is higher than 70 per cent, many years after the products had become known.

A further front in this vast field of omeprazole patents involves a push towards the development of enantiomerically pure forms of the compound or of its salts.

For example, Astra is currently in the process of registering the drug perprazole, which is an optical isomer of omeprazole. Omeprazole is a sulfoxide, and consequently a chiral compound, since sulphur is a stereogenic centre; it is a racemic mixture and perprazole is one of the two isomers of the racemic mixture.

In this case, perprazole was not patented by Astra itself but by another firm, Byk Gulden, which described and patented (+)-omeprazole and (-)-omeprazole through WO 92/08716. Although through WO 98/54171, (Swedish priority of December 1986), Astra claims S-omeprazole in a neutral form, characterized by being in a solid state.

Astra has done the same with the (+) and (-) isomers of omeprazole salts, which are protected under Astra's PCT application relating to WO 94/27988, invoking 1993 priority. This strategy of extending product life by means of new patents continued with the submission of WO 98/54171, which describes and claims the magnesium salt of the S-enantiomer of omeprazole trihydrate or omeprazole (-)-enantiomer.

Lastly, it should be mentioned that Astra has patented new oral pharmaceutical formulations of omeprazole. Omeprazole pellets, protected by patent EP 247 983 are dosed and administered in capsule form. Astra has now designed a new form known as "MUPS" (multiunit pellet system) whereby the pellets are dosed and administered in tablet form.

In WO 96/01623, Astra claims an oral pharmaceutical multiple unit tableted dosage form comprising tablet excipients and pellets formed by core material containing 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 layers, at least one of which 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. A specific claim is made where the active substance is a magnesium salt of omeprazole having a degree of crystallinity which is higher than 70 per cent as determined by X-ray powder diffraction, and where the active substance is an alkaline salt of (+) omeprazole or (-) omeprazole, preferable a magnesium salt.

This patent, which was applied for on 7 June 1995, designates, *inter alia*, Australia, Brazil, Canada, the Slovak Republic, the Czech Republic, China, Korea, the United States (US 5,817,338), Finland, Hungary, Japan, Mexico, Norway, Russia and Singapore. There is also an equivalent in South Africa.

In Europe, an application has been made under EP 723 436 A, designating Austria, Belgium, Switzerland, Germany, Denmark, Spain, France, the United Kingdom, Greece, Ireland, Italy, Liechtenstein, Luxembourg, Monaco, the Netherlands, Portugal and Sweden.

The new pharmaceutical form presents no tangible advantage. Its purpose is probably to eliminate competition from alternative products produced by competitors.

In Germany and in some 20 other countries, Astra has already withdrawn the capsules containing omeprazole pellets from the market and has replaced them with the MUPS tablets. As a result, when the product patent for omeprazole expires, the generic products will have no reference on the market; this hinders or may hinder the processing and/or approval of the generic product by the relevant health authority. Some health authorities have already declared that they will not authorize generic versions of products the original form of which is no longer on the market, even if it has been present recently.

AstraZeneca itself has stated, according to the journal *Scrip* (issue No. 2497 of 10 December 1999) that the launch of the new MUPS formulation has led to a revitalization of the Losec brand, and was a further barrier to generic entry. Losec MUPS has been launched in around 20 countries.

In practice, this strategy is also designed to prevent parallel imports. It is common for Losec to be introduced into northern Europe from other cheaper markets in southern Europe. For example, withdrawing Losec in the United Kingdom and replacing it with MUPS prevents parallel imports of Losec, because the code of ethics of British pharmaceutical chemists stipulates that unless a prescription indicates the generic name of the compound, a chemist will not dispense an imported medicament if the name is different from that on the prescription (see, *Scrip*, No. 2494, 1 December 1999).

Omeprazole

Country	Product patent or patent for the equivalent process Expiry date	Pellets Patent Expiry date
Germany	EP 005.129 a 03/04/1999 21/03/2003*	EP 247.983; EP 496.437 2 16/04/2007
Argentina	Unpatented	AR 240.250 30/03/2005
Austria	AT 389.995 b 14/08/2007	EP 247.983 16/04/2007
Austria	AT 375.365 c 14/12/2001	EP 496.437 16/04/2007
Austria	AT 374.471 d 14/09/2001 **	
Australia	AU 529.654 10/04/95***	AU 601.974 22/04/2007
Belgium	EP 005 129 16/11/2002*	EP 247 983; EP 496 437 16/04/2007
Brazil	Unpatented	Unpatented
Bulgaria	Unpatented	Unpatented

Country	Product patent or patent for the equivalent process Expiry date	Pellets Patent Expiry date
Canada	CA 1,127,158 06/07/99	CA 1,292,693 03/12/2008
China	Unknown	CN 1,020,852 30/04/2002
Cyprus	CY 1,232 03/04/99	CY 1,810 16/04/2007
Korea	Unknown	KR 91/4579 29/04/2007
Croatia	Unknown	HR 92/0854 01/01/2002
Cuba	Unpatented	Unpatented
Denmark	DK 150,510 (11/04/99)****	DK 169,988 28/04/2007
Egypt	Unpatented	Unpatented
Spain	Unpatented,	ES 2,006,457; ES 2,091,971 16/04/2007
Finland	FI 65,067 21/03/2003*	FI 90.393 29/04/2007
Philippines	Unpatented	Unpatented
France	EP 005 129 14/04/2004*	EP 247 983; EP 496 437 16/04/2007
United Kingdom	EP 005 129 14/04/2002*	EP 247 983; EP 496 437 16/04/2007
Greece	Unpatented	EP 247 983; EP 496 437 16/04/2007
Hong Kong	HK 84/00152 03/04/99	HK 94/1352 16/04/2007
Honduras	Unknown	Unknown
Netherlands	EP 005 129 15/11/2002*	EP 247 983; EP 496 437 16/04/2007
Hungary	HU 179,022 13/04/99	HU 196,708 29/04/2007
India	Unpatented	Unpatented
Indonesia	Unknown	Unknown
Ireland	IE 48,370 15/04/2002*	IE 61,416 27/04/2007
Israel	Unpatented	IL 82,911 18/06/2007
Italy	EP 005129 01/03/2010*	EP 496 437 16/04/2007
Italy		EP 247 983 01/03/2010*
Japan	JP 60/034956; JP 63/053191 03/01/2004; 14/04/99***	JP 05/069807 30/04/2007

Country	Product patent or patent for the equivalent process Expiry date	Pellets Patent Expiry date
Latvia	LV 93/853; LV 93/883; LV 93/881; LV 93/882 13/04/99	LV 10.357 29/04/2007
Liechtenstein	Unpatented	EP 247.983; EP 496.437 16/04/2007
Lithuania	Unknown	LT 3,699 28/12/2008
Luxembourg	EP 005.129 16/11/2002*	EP 247 983; EP 496 437 16/04/2007
Malaysia	MY 85/74 03/04/99	Unpatented
Morocco	Unknown	Unknown
Mexico	MX? 03/04/99	Unpatented
Norway	NO 152,216 10/04/99	NO 174,239 29/04/2007
New Zealand	NZ 190,203 17/04/99	NZ 220,096 26/04/2007
Poland	Unpatented	PL 151.631 29/04/2002
Portugal	Unpatented	PT 84785 29/04/2007
Czech Republic	CZ 261,851; CZ 261,872 CZ 261,873; CZ 261,874 13/04/94	Unpatented
Slovak Republic	SK 261,851; SK 261,872 SK 261,873; SK 261,874 13/04/94	Unpatented
Romania	Unpatented	Unknown
Singapore	SG 83/00633 03/04/99	SG 94/1542 16/04/2007
Sweden	EP 005 129 04/02/2003 *	EP 247 983; EP 496 437 16/04/2007
Switzerland	EP 005 129 03/04/99	EP 247 983; EP 496 437 16/04/2007
South Africa	ZA 79/01586 02/04/99	ZA 87/2378 31/03/2007
Turkey	Unpatented	Unpatented
Soviet Union	SU 873,879; SU 873,880; SU 878,196; SU 895,292 13/04/99	SU 1,820,837 29/04/2007
Ukraine	UA 4909; UA 4910; UA 4776; UA 4908 13/04/99	

Country	Product patent or patent for the equivalent process Expiry date	Pellets Patent Expiry date
USA	US 4,255,431 05/04/2001	US 4,786,505 20/04/2007
Yugoslavia	Unpatented	YU 46,192 01/01/2002

Notes: The data for the table are taken from data bases (WPI, INPADOC, CIBEPAT, NEW PORT and DRUGPAT) which do not cover 100 per cent of the patent data for the countries listed; these data need to be reconfirmed by patent data from the countries themselves. Moreover, the expiry dates for the patents are simply indicative, and also need to be confirmed by data from the countries.

- * SPC extension
- ** SPC requested
- *** Possible extension
- **** SPC refused

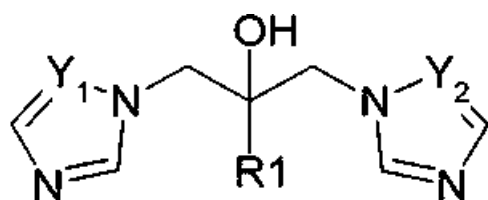
- a SPC for sodium omeprazole, 21 March 2003; SPC for omeprazole refused and under appeal.
- b Patent AT 389,995 claims a specific use for omeprazole.
- c Patent AT 375,365 claims a generic process for synthesizing omeprazole.
- d Patent AT 374,471 claims a specific process for synthesizing omeprazole.
- e EP 496 437 is a divisional patent of EP 247 983.

To sum up, this case illustrates the use of a wide range of methods for broadening and extending patent protection, including the use of patent protection for polymorphs, isomers and pharmaceutical formulations.

6. Fluconazole

ICI is the holder of the patent family which includes United Kingdom patent GB 2,078,719 claiming compounds of the formula indicated in figure 4, wherein R₁ is alkyl, cycloalkyl, aryl or aralkyl any of which may be optionally substituted, Y₁ and Y₂ are =CH- or =N-, and their acid addition salts, metal complexes, ethers and esters.

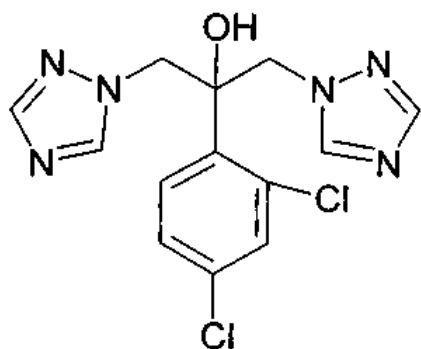
Figure 4



Priorities of June 1980 and of March and May 1981 are invoked.

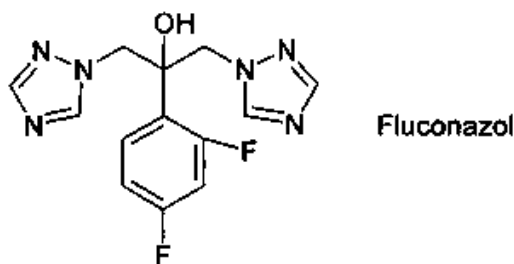
The compounds have fungicidal activity. One of the compounds specifically described and claimed is 1,3-Bis-(1,2,4)-triazolyl-2-(2,4-dichlorophenyl)-propan-2-ol having the structure indicated in figure 5.

Figure 5



The Pfizer Company subsequently developed a new fungicide which, although covered generically by the product patents claimed by ICI, had not been specified; Pfizer described and specifically claimed the product in a patent family invoking British priorities of June and October 1981 and March 1982. The product, the fungicide fluconazole, is claimed in EP 0069 442. The product is solely distinguished from that in the previous formula, by having 2 fluoride atoms in place of the chloride atoms on the benzene ring (see figure 6).

Figure 6



According to Pfizer, “fluconazole chloride” is teratogenic, whereas fluconazole is not.

This example illustrates the technique of “selective inventions”, whereby an application is made for a product (or process) patent that has already been more broadly described in an earlier patent, on the basis of alleged novel and inventive characteristics or effects.

7. Ofloxacin/Levofloxacin

It is common practice nowadays to patent separately the pure enantiomeric forms of a compound whose racemic form is already known.

An enantiomer free of its mirror image, which is the mixture found in a racemate, is not a new compound in relation to the racemic mixture, since 50 per cent of it is formed by each of them.

None the less, product patents are granted for each of the enantiomers. Not only is the product not novel, its pharmacological action, whether beneficial, equal or harmful, in comparison with the racemate, is quite foreseeable; all that is required is to determine which of

the enantiomeric pair has properties that are better than (or even equal to) or worse than the racemate.

Products that exhibit pharmacological activity interact with optically active and asymmetric macromolecules, such as proteins, polynucleotides or glycolipids that act as receptors and which consequently exhibit stereochemical specificity.

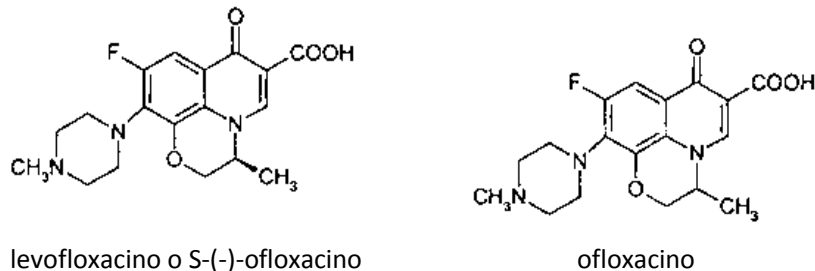
As a result, isomers of the same compound exhibit different action. It is well known that the use of pure enantiomers in place of the racemate is frequently beneficial when one of the enantiomers, known as the *eutomer* “bonds better” and the other, known as the *distomer* has undesired effects which may include the following: 1) Contributing to adverse reactions; 2) antagonizing or diluting the pharmacological action of the eutomer; 3) metabolizing into compounds whose action is not beneficial; and/or 4) metabolizing into toxic compounds.

Daiichi’s levofloxacin is one of the many examples that exist. This compound is S-(!)-9-Fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-*de*]-[1,4]-benzoxazine-6-carboxylic acid:

It is claimed under Daiichi’s United States patent 5,053,407, which is in force until 1 October 2008.

Levofloxacin is the S(-)- isomer of ofloxacin, which is protected in the United States by patent US 4,382,892, in force until 2 September 2003 (see figure 7).

Figure 7



According to Daiichi, the S(-) isomer of the racemic ofloxacin possesses an antimicrobial activity about 2 times higher than that of the racemic mixture and an acute toxicity weaker than that of the racemate. The R(+)-compound exhibits an antimicrobial activity of only about 1/10 to 1/100 times that of the racemate, whereas it possesses an acute toxicity substantially equal to that of the mixture.

The example of ofloxacin is a clear illustration of the use of optical isomers to achieve broader and longer patent protection.

8. Fexofenadine

Fexofenadine is the active metabolite of terfenadine developed by Marion Merrel Dow. It is used as an antihistaminic. It has become known as a result of Merrel Dow’s efforts to prevent the development of generic products based on terfenadine, on the grounds that the patent for fexofenadine was infringed when patients were given terfenadine.

United States patent US 4,254,129, owned by Merrel Dow claims fexofenadine as a product and describes a process for obtaining the compound. Although this patent expired on 10 April 1999, a Waxman/Hacht extension of 679 days has been granted, as a result of which the patent will now expire on 18 February 2001. Equivalents exist in Australia, Austria, Belgium, Germany, Canada, Denmark, Spain, the Philippines, France, the United Kingdom, Ireland, Israel, Italy, the Netherlands, Japan, Norway, New Zealand, Switzerland, Sweden and South Africa.

Moreover, Merrel Dow holds various international patent applications relating to fexofenadine. For example, WO 93/21156 and WO 95/00480 claim processes for obtaining the product, WO 95/31436 describes an optical resolution process and WO 95/31437 claims polymorphs and pseudomorphs of the anhydride and hydrate forms of fexofenadine hydrochloride. They have all been extended to many countries, and if granted, will expire in 2013.

Hoechst Marion Roussel is the holder of applications EP 864 653 and WO 99/47693 relating to procedures for the preparation of fexofenadine by the bioconversion of terfenadine using fungi of the *Cunninghamella* or *Absidia* species and *Absydia corymbifera* LCP 63-1800 or *Streptomyces platensis* NRRL 2364 strains.

Another firm, Albany, is the holder of PCT application WO 95/00482 describing and claiming a process for providing substantially pure fexofenadine. According to the authors, under the Merrel patents referred to above, fexofenadine is obtained in an inseparable mixture with regioisomers in which the 4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-1-hydroxybutyl group is attached at either of the three aromatic carbons which are meta or para to the dimethylacetate substituent. The process claimed under WO 95/00482 makes it possible to obtain the pure form of the regioisomer, i.e. fexofenadine. The equivalent United States patent, US 5,578,610, which runs until 2013, is a product patent claiming the above process and pure fexofenadine.

Moreover, Albany holds applications WO 97/22344 and WO 97/23213 relating to other fexofenadine preparation procedures.

As regards processes for synthesizing the product, Sepracor holds WO 98/33789 claiming a process for the preparation of fexofenadine.

Lastly, patents relating to the galenical formulations and/or uses of fexofenadine, and held by Merrel Dow, Sepracor, McNeil-PPC, Procter & Gamble, Schering, Warner-Lambert, Alza, Asta, Axia, Hermes Fabrik and Hoechst have been found. WO 94/03179 and the United States equivalents US 5,375,693 (3 August 2012), held by Sepracor, claim a method for treating allergic rhinitis in humans while avoiding the concomitant liability of cardiac arrhythmia associated with the administration of terfenadine, comprising administering a therapeutically effective amount of racemic terfenadine carboxylate alone or associated with a nonsteroidal anti-inflammatory agent or non-narcotic analgesic.

In this case, in order to market a generic product (fexofenadine is protected in the United States until 2001), it will be necessary to overcome the technical drawback of a process described in the product patent family which supposedly provides a mixture of isomers that are difficult to separate. It should also be borne in mind the numerous patents or patent applications claiming new methods of synthesizing which – in some cases – claim the use of a precursor

that is substantially pure of its undesirable isomer (which to an expert is obvious to avoid the formation of mixtures) and even a product patent protecting *substantially pure* fexofenadine until 2013 in the United States.

9. Recombinant Erythropoietin

Erythropoietin (EPO) has been at the centre of an intense legal battle over the rights to its genetic code sequence and over the method of obtaining it. Although this battle concerned two United States firms, its repercussions were felt in other countries, including those in Latin America.

Genetics Institute (GI) obtained United States patent 4,677,195 relating to a process for purifying EPO, which in 1991 was declared null and void by the relevant Federal court (*Scrip* No. 2001, 1995, p. 11). A divisional patent belonging to the same owner (No. 5,322,837) met with the same fate. On 28 October 1996, the United States Court of Appeal ruled that the rights of Amgen Inc. overrode those of Genetics Institute (*Scrip* No. 2719, 1996, p. 14).

The sequence of the gene coding EPO was obtained for the first time by the United States firm Kirin Amgen (hereinafter referred to as Amgen), which took out patent US 4,703,008, applied for on 30 November 1984, and in which it described the amino acid sequence corresponding to human EPO.

Amgen obtained United States patent number 4,703,008 for a process for obtaining erythropoietin on 27 October 1987; in 1995, it obtained patent number 5,441,868 (*Scrip* No. 2054, 1995, p. 13), and in 1996 it was awarded patent number 5,547,933 (*Scrip* No. 2166, 1996, p. 25).

As a result, GI has been unable to market erythropoietin in the United States. With respect to Genetics Institute's failed attempt to be recognized as the "inventor" of a process for obtaining erythropoietin, Cárdenas y Espinosa has noted that "in 1991, Amgen applied to the Federal Circuit Court of Appeal to have GI (Genetics Institute's) patent over EPO invalidated; the Court reversed the decision of the Boston court, thereby invalidating GI's patent over EPO as a naturally occurring substance, thus leaving the market for EPO in the hands of Amgen Inc." (Cárdenas y Espinosa, 1997, p. 63; annex P).

In Europe as in the United States, Genetics Institute has failed to obtain patent protection for EPO. For example, patent EP 205 564 relating to a "method for the production of erythropoietin" was revoked in October 1996 as a result of the opposition of five firms, including Boehringer, Johnson & Johnson and Janssen-Cilag (*Scrip* No. 2179, 1996, p. 141). The patent was based on exactly the same United States applications, numbers 677,813 of 4 December 1984, 688,622 of 3 January 1985 and 693,258 of 22 January 1985, which were never granted in the United States.

Genetics Institute has faced litigation in at least France, Belgium, Spain, the United Kingdom and the Netherlands for infringement of the patents granted in Europe to its competitors Amgen and Kirin-Brewery Co.

In spite of the above, GI obtained patents for process relating to erythropoietin in a number of developing countries, such as Argentina and Chile, where it has attempted to use

them to exclude any alternative supplies of the product, including from licensees of Amgen, the firm recognized in the United States as the holder of patent rights over EPO.

GI's patents relating to EPO in Argentina and Chile were obtained on the basis of the same applications that were refused in the United States.

In Argentina, patent 235,470¹⁵ claims a recombinant method of producing EPO. It does not claim the sequence of EPO as such, as this was prohibited by article 4 of Act No. 111, in force at the time.

The recombinant technique was widespread before the patent application was made (and before its priority); it became a routine method of biotechnology towards the middle of the 1980s. When the patent application was made, the technique was described in contemporary students' textbooks and in numerous earlier scientific publications. It could be carried out in any laboratory anywhere in the world using standard methods that were in no way novel. In other words, the technique was obvious to any specialist in the field.

Moreover, human EPO was identified at the beginning of the last century. Studies of the protein were widely known well before GI's patent. As early as in 1972, the World Health Organization laid down international standards for the preparation of human EPO.

As already mentioned, GI cannot be considered to have been the first to have obtained the amino acid sequence that constitutes human EPO, as claimed in claim number 1 of its patent.

Nor can any novelty be claimed for the culture medium of the host cells, simply because the patent is wholly generic in this respect and makes no claim for a particular medium. It merely claims "an appropriate culture medium". Furthermore, the use of mammal cells for the type of cloning described in the patent had already been described in the literature before the date of application and the priority.

The method claimed in Argentine patent 235,470 is described in a generic form, weaving together knowledge that was already widely known from the state of the art at the time of the priority invoked. This means that any averaged skilled specialist was capable of adapting the state of the art to obtain recombinant human EPO in the same way as for other proteins. At the date of the application (and of the priority), it was obvious to any technician with average skills that human EPO could be obtained by a recombinant method such as that described in the patent. The recombinant method can be used with any type of human protein, and in fact human EPO had already been obtained by this method before the dates of application and of priority invoked.

In addition, the generic method described does not allow a pharmaceutically acceptable product to be obtained; first of all, the description is insufficient to allow the invention to be realised, secondly, the detailed description concerns *in vitro* assays, but does not demonstrate the capacity to utilize the product obtained to carry out *in vivo* the patented method. In other words, it is a technically unimaginative, purely experimental laboratory method that is unsuitable for industrial application. Proof of this is provided by the detailed description which states that the method makes it possible to obtain a 60 per cent pure product, which is

¹⁵ The equivalent patent granted in Chile is number 36,298, of 16 December 1988.

unacceptable for use in humans, for whom an extremely high degree of purity, close to 100 per cent, is required.

The recombinant procedure is defined in such general terms as to include every existing micro-organism capable of being genetically modified with the human EPO gene. The claims made in patent number 235,470 are presented in a purely functional manner without a proper description of the different elements and steps of the patented process. The result of this is that the claims cover **an unlimited number of possible processes** for obtaining EPO. By claiming patent rights over all possible methods of production, the patent is in fact a product patent.

As has already been pointed out, and as Amgen's patent number 4,703,008 and GI's Spanish application, number 549,539 reveal, it was perfectly possible to provide a fuller and more precise description of the method of obtaining EPO; it was probably avoided in this case in order unduly to extend the monopoly conferred by the patent.

In short, the GI patent provides an unsatisfactory and inadequate description of a **generic method** for obtaining human EPO which is none other than the genetic engineering technique already known at the date of the application and of the priority. The patent does not make it possible to obtain erythropoietin as an industrial product. The detailed description and claims are marred by numerous inaccuracies and gaps making it impossible to reproduce the method to obtain the product, even with the unacceptable degree of purity (for an industrial product) that would be achieved with this process.

These considerations notwithstanding, GI has attempted to use this patent to block the production and sale of human EPO in Argentina and Chile.

CONCLUSIONS

The cases examined illustrate some of the patenting practices used in the pharmaceutical sector that may be detrimental to competition, and in particular affect the early access to cheaper alternative products by the public.

The cases cover a broad range of products whose value as medicaments is different. Their common trait is the use of the occasionally excessive flexibility of the patent system to set up barriers to legitimate competition.

It is nowadays generally accepted that the purpose of the patent system is to make it possible to recoup the investment made in research and development through a temporary monopoly over the invention. Although the system was conceived to encourage genuinely "inventive" innovations, in practice, as several of the cases examined reveal, it is frequently used to protect minor, often trivial developments.

There is no question that patents are valuable as a means of rewarding genuinely inventive, occasionally costly R&D activity. However, the analysis made shows how the system is blighted by the granting of patents of dubious worth that make a negligible contribution or no contribution at all to technological progress, whose sole purpose is to serve as a barrier to legitimate third-party competition. If governments wish to have a credible and sound patent system, they need to make a considerable effort to define rigorous criteria for patentability, and especially to apply them in a responsible and consistent manner.

The examples given also suggest that a substantial part of the R&D budget that pharmaceutical firms claim is devoted to the development of new products is, in reality, allocated to developing a vast array of patents around existing products, with the clear intent of expanding and/or extending over time the exercise of exclusive rights.

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CHAPTER III

PROTECTION OF DATA SUBMITTED FOR THE REGISTRATION OF PHARMACEUTICALS: IMPLEMENTING THE STANDARDS OF THE TRIPS AGREEMENT

EXECUTIVE SUMMARY

1. As a condition for registering pharmaceutical products, national authorities normally require registrants to submit data relating to drugs' quality, safety and efficacy ("test data"), as well as information on the composition and physical and chemical characteristics of the product. A particularly important issue is the direct or indirect use of the data for subsequent registration of products similar to those originally registered.
2. The World Trade Organization's Trade Related Aspects of Intellectual Property Agreement (TRIPS), Article 39.3, requires member countries to establish protections for submitted test data. But this requirement is in fact narrowly drawn, and countries maintain substantial flexibility in implementation. The public interest in limiting protections for data is to promote competition, and to ensure that data protections do not become the means to block the timely entrance of generic competitors to off-patent drugs. Generic competitors drive down price, thereby promoting greater accessibility of medicines.
3. Article 39.3 requires governments to provide protection to marketing approval data only under certain conditions. Test data must be protected if national authorities require its submission. Article 39.3 does not require protection be given to already public data. Protection is required only for new chemical entities. Members have considerable discretion in defining "new," and may exclude applications for second indications, formulations and dosage forms. And, prior to granting protection, national regulatory authorities may request the applicant to prove that the information for which protection is sought is the result of significant investment.
4. Article 39.3 requires countries to protect against "unfair commercial use" of marketing approval data. Countries have considerable discretion to define "unfair" in the context of their own national laws and culture. Use by the government to assess the efficacy and toxicity of a pharmaceutical or agrochemical product is not a commercial use subject to Article 39.3. Granting marketing approval to a second entrant, based on the second product's similarity to a previously approved first product, is not a proscribed "use" under Article 39.3. These interpretations are supported by United States and Canadian Supreme Court decisions interpreting national laws.
5. Countries can meet their obligations to protect against "unfair commercial use" under Article 39.3 by barring "dishonest" uses of test data. This would require, for example, proscribing situations in which a competitor obtains the results of testing data through fraud, breach of confidence or other "dishonest" practices, and *uses* them to submit an application for marketing approval for its own benefit. It would also apply in cases where the government provides access to undisclosed testing data in order to provide an advantage to a firm which did not produce them or share their cost.

6. Countries are not obligated under Article 39.3 to confer exclusive rights on the originator of marketing approval data.
7. The pharmaceutical industry and some countries have argued for much broader coverage of Article 39.3, and for a requirement that countries confer exclusive rights on originators of marketing approval data. But these positions are not well grounded in either the text or negotiating history of TRIPS. TRIPS negotiators specifically considered and rejected language requiring grants of exclusive rights to test data.

INTRODUCTION

As a condition for registering pharmaceutical products, national authorities normally require registrants to submit data relating to a drug's quality, safety and efficacy as well as to its physical and chemical characteristics. A particularly important issue is third parties' use of the data for subsequent registration of products similar to those originally registered.

In some jurisdictions, the data submitted for the registration of pharmaceutical (and agrochemical products), are subject to a *sui generis* system of protection, based on a temporary right to the exclusive use of such data by the first applicant (generally the company that developed a new product). In such a system, other companies (often "generics" manufacturers) cannot rely on the data submitted by the first applicant for the purpose of registering a similar product for commercial use. The rationale for this exclusivity model is to permit the originator of data to recover the investments made for their development. The underlying assumption is that, without such protection, private firms would have no incentive to bear the considerable costs of producing the required data.

In other countries, however, health authorities are permitted to rely on data submitted by the first applicant to process and approve third parties' subsequent applications for a similar product,¹ subject to evidence that its physico-chemical attributes are equivalent to those of the first applicant's product. This approach emphasizes that the registration of products should not erect barriers to otherwise legitimate competition. It holds, instead, that the registration system should promote price competition and access to more affordable medicines.

The issue of data protection is especially relevant for off-patent products as well as for products, such as biologicals, that are often difficult to patent. In cases where the product is patented, the patent holder can, in principle, exclude **any** competition during the lifetime of the patent – a period of exclusion which will generally run longer than that afforded by data protections. Data protection rules are of particular importance to many developing countries that until recently did not provide patent protection for pharmaceuticals (and to those under the transitional periods of the WTO's TRIPS Agreement, which still do not provide pharmaceutical patent protection). In these countries, there is a large pool of unpatented pharmaceutical products. Data protection systems could, if they provided exclusivity, become a partial substitute for patent protection in these cases and nullify, in practice, the transitional periods granted to developing countries.

Before the entry into force of the TRIPS Agreement, countries had considerable latitude to determine rules for the protection of test data. The Agreement introduced the first

¹ In some cases, national authorities are allowed to rely on the registration made in a foreign country to approve subsequent applications.

international standard on the subject, as contained in its Article 39.3.² But the Agreement is not a “uniform law” – it only establishes broad parameters for national rules. An important question is the extent to which the Agreement allows WTO Member countries freedom to apply different approaches for the protection of test data and, in particular, the extent to which a competitive model – i.e., protection without exclusivity – is compatible with the minimum standards set forth in Article 39.3.

To properly interpret Article 39.3, the Vienna Convention on the Law of the Treaties instructs that the ordinary meaning and context of the terms used, and the object and purpose of the treaty must be carefully considered. The history of the negotiation is also an important complementary element for interpretation (Article 31 (2) of the Vienna Convention).

The first section of this paper describes the different stages of drug development and the testing required for marketing approval of new pharmaceutical products. The second section discusses the rationale for test data protection. The third section examines the conditions, established by Article 39.3 of TRIPS, under which protection must be given to marketing approval data. The fourth section examines the concept of “unfair commercial use” of data – the conduct proscribed by Article 39.3. The fifth section examines the legal means that States may adopt to provide protection against commercial use. The sixth section offers a brief analysis of the negotiating history of Article 39.3, which provides the backdrop for interpretation of the TRIPS Agreement’s data protection obligations. A final, concluding section assesses the obligations on countries to provide marketing approval protection under the TRIPS Agreement, and reviews the flexibilities available to Member countries.

DATA REQUIRED FOR THE REGISTRATION OF PHARMACEUTICALS

The development of a **new** drug involves different stages, during which a variety of data are produced.

The “discovery” stage involves the synthesis or isolation of new chemicals. Initial screening tests determine whether the new chemicals possess sufficient biological activity to be worthy of further investigation. The nature of pharmaceutical research has changed dramatically in the last twenty years with the application of the “rational drug design” method and the use of combinatorial chemistry. With discovery by design, scientists use knowledge about the causes of human disorders, the properties of drug compounds, and their action in the human organism to conceptualize the structure of an “ideal” molecule that is expected to restore the altered equilibrium. Laboratory chemists then search for substances whose molecular structures match as closely as possible the theoretical model (Gambardella, 1995, p. 23). This methodology reduces the cost of the “discovery” stage, but does not eliminate the need for bioassay, animal and other tests of the new drugs.

Once a promising new chemical is identified, its non-toxicity and efficacy must be confirmed. The testing procedures involve different stages and phases (see Box 1).

² The full text of Article 39.3 reads: “Members, when requiring as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.”

On the basis of the results of these tests, national authorities can assess whether to grant marketing authorization for a new chemical entity. All the safety and efficacy tests must normally be completed before the authority approves the product. The authority may also require additional clinical tests. In 1980, the duration of these studies varied from about 1 to 7 years and averaged slightly less than 3 years. This period has been significantly reduced since then (Raggett, 1996, p. 26).

Box 1
Testing New Drugs

Preclinical Stage

In the preclinical stage, the new chemical entity (NCE) is tested in animals to assess its pharmacodynamic, pharmacokinetic and toxicological profile. Results of these tests are studied carefully before tests in human beings are carried out.

Safety and Efficacy Testing

The types of tests, the procedures to be used, and the standards to be met to demonstrate safety and efficacy may vary among therapeutic classes and even among drugs for use within a therapeutic class. This stage includes different phases.

In *Phase I* chemical testing, a small group of healthy volunteers receive dosages of the investigational drug for a short period of time. The primary purpose is to look for evidence of toxicity or unexpected undesirable reactions, and to study the bioavailability and pharmacokinetics of the NCE/drug applied to patients.

Phase II of clinical testing has a similar purpose to phase I, but considering the therapeutic context. Its primary objective is to ascertain the effectiveness of the investigational drug.

Phase III clinical trials are conducted on a large number of patients; they often involve several hundred human subjects and are conducted for substantial periods. These tests are designed to determine the efficacy of the investigational drug and to uncover any unanticipated side effects that the drug may have, considering age and gender influence, drug interactions and specific dosage for different indications.

While the phase III trials are under way, long-term animal toxicity studies are undertaken to determine the effects of prolonged exposure and the effects on subsequent generations. The duration of the studies vary widely among therapeutic classes. For drugs that affect the reproductive system or that will be used over long periods of time, animal toxicity studies are typically expensive and lengthy.

In addition to test data, national authorities require information on the quantitative and qualitative composition and other attributes of the product, as well as on manufacturing methods.

Marketing approval is generally granted for a specific drug used for a specific therapy. Changing the composition of the drug, combining it with other drugs in a single product or selling the drug for a different therapeutic purpose requires new approval.

THE RATIONALE FOR DATA PROTECTION

Approaches to Data Protection

A basic element of data protection is the obligation imposed on third parties not to disclose the data; that is, to keep them confidential.

Some health specialists have argued against any concealment of data submitted for the approval of pharmaceuticals (Olilla and Hamminki, 1996, p. 169). In their view, non-disclosure contradicts the right of the public to be informed about the efficacy and safety of approved pharmaceuticals. According to this opinion, the concealment of data on clinical, pharmacological and toxicological experiments retards the development of knowledge, and poses risks that consumers of a drug may be injured unnecessarily. Since confidentiality prevents the scientific community from scrutinizing the scientific basis of a licensing decision, it is not possible to determine whether there is commercial bias in the information, or whether it meets high standards. Drug companies have an interest in not publishing research that is not favourable to their products, and may even try to hinder the publication of such studies (Dukes, 1996, p. 149).

Other experts emphasize that health authorities should be able to use and rely on registration data submitted for similar products, or on the existence of a prior registration elsewhere.³ If the regulatory body is not free, when assessing a file, to use all the knowledge available to it, including data from other files and published information, a great deal of *repetitive* toxicological and clinical investigation will be required, which will be wasteful and in the case of animal testing, ethically questionable (Dukes, 1996, p. 146).

According to this position, when the authorities already know the characteristics and effects of the product (due to the first registration), it is not rational from the society's point of view to duplicate tests to recreate existing information. All that the authorities need for the second application is confirmation that the second product is **similar** to the first product. How to prove similarity is a matter for national regulation; some countries require bio-equivalence and bio-availability tests, while others are satisfied with the proof of chemical similarity and prior registration.

This position is also grounded in the pro-competitive effects of low entry barriers for pharmaceutical products. If producers (particularly generics manufacturers) are obliged to repeat long and costly testing, competition will be reduced because of time delays and, more importantly, because some small and medium firms – especially local firms in developing countries – will lack the resources to undertake such testing. This reduces competition and the affordability of medicines that – by definition – are off-patent and, therefore, should be broadly available at the lowest possible price.

The research-based industry has, however, argued for stronger test data protection, using both equity and health policy arguments. The industry position argues that the manufacturer has invested, often heavily, in conducting tests and deserves a return on investment. Where patent law fails to provide protection (for example, because the patent on an active component is shortly to expire, or because the drug is based on a combination of known substances used in

³ In this case, the authority bases its decision on the fact that a foreign country has granted registration, and on the proof of equivalence in terms of the physical and chemical characteristics and other relevant attributes of the product.

novel manner) data exclusivity is a necessary barrier to competitors rapidly producing and registering an exact copy of the drug.

In accordance with this view,

“equity demands that protection be provided for data, which can cost the original submitter several million dollars to produce. Disclosing this data to the public or allowing its use by another applicant unfairly denies the compiler of the data the value of its efforts and grants an economic advantage to later applicants for marketing approval, enabling them to avoid the cost of developing test data for their own products. Countries that allow such unfair advantages to later applicants discourage developers of new pharmaceuticals and agricultural chemicals from seeking to introduce their state-of-the-art products in the country’s market. So, not only is such protection required by the TRIPS Agreement, it is both equitable and wise from a public and health policy standpoint” (Priapantja, 2000, p. 4).

Finally, consumer groups such as the Trans-Atlantic Consumer Dialogue have proposed that, since data exclusivity is intended to protect investment, companies seeking data exclusivity should be required to disclose the amount actually invested. This would enhance transparency and allow the establishment of a relation between the actual investment and the protection provided (WHO, 2000, p. 40).

In the light of these contrasting approaches, a key issue is the extent to which, under the TRIPS Agreement, Member countries are obliged to provide exclusivity, and whether authorities can rely on the data from a prior registration or on a registration made in a foreign country.

National Practices Before TRIPS

Companies originating data for the registration of new products have requested from national health authorities and generally obtained protection of submitted data against disclosure. Confidentiality is essentially intended to protect secret information from misappropriation by third parties. However, problems with secrecy in drug regulation have historically raised public concern in several countries, including Great Britain, New Zealand, Germany, Sweden and the USA (Ollila and Hamminki, 1996, p. 168).

Historically, some health authorities relied on the first application data for the evaluation of second-entrant applications for similar products. Some companies brought legal action against the authorities arguing that reliance on the knowledge derived from one file to evaluate another one (e.g., a generic equivalent) caused them commercial injury.

In a number of court cases relating to *Cimetidine* decided in the United Kingdom, Australia and New Zealand, first entrants originating registration data invoked the ordinary law of confidential information to prevent regulatory authorities from relying on the originator’s file when assessing an application for the approval of an equivalent drug by a generic competitor. Courts were, however, reluctant to apply such law (Cook, 2000, p. 5).

As a result of industry lobbying, some developed countries established *sui generis* protections for test data submitted for the approval of pharmaceuticals (and agrochemicals).

Under different modalities, they adopted the concept of *exclusive* use of the test data by the originator company. The U.S. adopted a regulatory data protection regime for pesticides,⁴ and in 1984 regulatory exclusivity provisions for medicines. The U.S. health registration regulations provide for five years of exclusivity for new chemical entities, and three years for data filed in support of authorizations based on new clinical research relating to chemical entities which had already been approved for therapeutic use.⁵

In the European Union (EU), the Member States have provided exclusivity protection for the data filed in support of marketing authorizations for pharmaceuticals since 1987. One of the original objectives of this regime was to compensate for the lack of patent protection for pharmaceuticals in some Member States (Portugal, Spain), but it was maintained after those countries introduced such protection (Watal, 2001, p. 201). During the exclusivity period, health authorities cannot rely on an originator's test to approve other applications without the originator's consent.⁶ The minimum period of such protection is six years, but 10 years is obligatory for "high technology products" (most biotechnology products), and also for new chemical entity authorizations granted by the European Medicines Evaluation Agency

⁴ This regime limits exclusivity by allowing third parties to use originator's test data if compensation is paid. In case of disagreement, the amount is determined through arbitration. See in Annex 1 a summary of the relevant legislation.

⁵ In October 1997, the U.S. Senate held hearings on "Health Registration Data Exclusivity, Biomedical Research, and Restrictions on the Introduction of Generic Drugs" (Subcommittee on Labor, Health and Human Services and Education and Related Agencies, Committee on Appropriations). These hearings considered a proposal for a voluntary five-year extension of the U.S. data exclusivity period, coupled with a 6 per cent R&D commitment from the company electing to take the extension. The U.S. Congress did not adopt this proposal.

⁶ Article 8 of Directive 65/65, as amended by Directive 87/21/EEC, establishes that "without prejudice to the law relating to the protection of industrial and commercial property:

- (a) The applicant shall not be required to provide the results of pharmaceutical and toxicological tests or the results of clinical trials if he can demonstrate:
 - i. either that the proprietary medicinal product is essentially similar to a product authorized in the country concerned by the application and that the person responsible for the marketing of the original proprietary medicinal product has consented to the pharmacological, toxicological or clinical references contained in the file on the original proprietary medicinal product being used for the purpose of examining the application in question;
 - ii. or by detailed references to published scientific literature presented in accordance with the second paragraph of Article 1 of Directive 75/318/EEC that the constituent or constituents of the proprietary medicinal product have a well-established medicinal use, with recognized efficacy and an acceptable level of safety;
 - iii. or that the proprietary medicinal product is essentially similar to a product which has been authorized within the Community, in accordance with Community provisions in force, for not less than six years and is marketed in the Member State for which the application is made; this period shall be extended to 10 years in the case of high-technology medicinal products within the meaning of Part A in the Annex to Directive 87/22/EEC or of a medicinal product within the meaning of Part B in the Annex to that Directive for which the procedure laid down in Article 2 thereof has been followed; furthermore, a Member State may also extend this period to 10 years by a single Decision covering all the products marketed on its territory where it considers this necessary in the interest of public health. Member states are at liberty not to apply the abovementioned six-year period beyond the date of expiry of a patent protecting the original product. However, where the proprietary medicinal product is intended for a different therapeutic use from that of the other proprietary medicinal products marketed or is to be administered by different routes or in different doses, the results of appropriate pharmacological and toxicological tests and/or of appropriate clinical trials must be provided.
- (b) In the case of new proprietary medicinal products containing known constituents not hitherto used in combination for therapeutic purposes, the results of pharmacological and toxicological tests and of clinical trials relating to that combination must be provided, but it shall not be necessary to provide references relating to each individual constituent".

(EMEA). EMEA may also grant 10 years exclusive protection for test data related to medicines administered by means of “new delivery systems which ... constitute a significant innovation”, and “medicinal products containing a new substance or an entirely new indication which...is of significant therapeutic interest” (Cook, 2000, p. 18).

Most Member States (Belgium, France, Germany, Italy, the United Kingdom, the Netherlands and Sweden) have applied the 10-year period to *all* medicinal products (Dodds Smith, 2000, p. 113). Moreover, the “data exclusivity that this affords can, if a marketing authorization is obtained only late in the life of a patent, extend beyond patent expiry. The only qualification to this is an option available to those few Member States which have not availed themselves of the 10-year period for all medicinal products, and which can also elect for such data exclusivity ‘not to extend beyond patent expiry’” (Cook, 2000, p. 18).

Article 1711 of the North American Free Trade Agreement (NAFTA) of 1992 also establishes an exclusivity standard, requiring signatory countries to provide a minimum five years exclusivity period counted from the date of marketing approval. This model was followed in 1993 by the Andean Group countries under Decision 344 (“Common Regime on Industrial Property”).

At the time of conclusion of the TRIPS Agreement, few countries had adopted the exclusivity approach developed in the United States and Europe. At the time, most countries in the world did not provide for exclusivity and most allowed the national health authorities to *rely* on test data submitted by the first applicant to approve subsequent applications on “similar” products.⁷ In some countries (e.g. Argentina, Singapore, Taiwan, and the territory of Hong Kong) it was sufficient to prove that a similar product had been approved or commercialized in a foreign country.

CONDITIONS OF PROTECTION UNDER TRIPS

The TRIPS Agreement establishes a minimum international standard for the protection of marketing approval data. WTO Member countries need to determine what is actually needed to fulfil their obligations under the Agreement. Understanding the obligations imposed by Article 39.3 requires a close reading of the text, an assessment of each of its components, as well as a review of the negotiating history and national practice. The remainder of this paper turns to these tasks.

Protection of Test Data Under the TRIPS Agreement

The inclusion of test data as a category of intellectual property in TRIPS does not mean countries must provide exclusivity protections for such data.

⁷ Though the time of the adoption of the Agreement is to be taken into account, according to general principles of international law, for the interpretation of its obligations, it should be noted that even today, after the expiration of all except the transitional period for LDCs, only a minority of the WTO Members apparently confer data exclusivity (see, e.g. the February 2000 Pharma submission to the USTR on Section 301, at www.pharma.org). New Zealand introduced an exclusivity period in 1994, as part of implementing legislation of the TRIPS Agreement, and Australia did it in 1998 as a result of U.S. action under “Special 301” of U.S. Trade Act. The Andean Group countries, instead, revised Decision 344 in 2000 and eliminated the exclusivity period. A special exclusivity granted under the “Safety Monitoring Program” in Thailand was also abolished in January 2001.

According to Article 1.2 of the TRIPS Agreement, the protection of test data is a category of “intellectual property” like patents, copyrights and trademarks. The structure of Article 39 suggests that the regime for test data has been conceived by the negotiating parties as a **particular** case in the framework of the protection of “undisclosed” information. In this sense, the protection conferred cannot be properly deemed a *sui generis* system.

The categorization of test data as a subject matter of “intellectual property” does not mean that Article 39.3 puts their protection on the same footing as other intellectual property rights. In particular, it cannot be inferred that such protection requires *exclusive* rights. Though in most instances intellectual property rights confer an *ius excluendi*, this is far from being an absolute rule. It is well accepted, for example, that trade secrets protection in the framework of unfair competition does not give rise to a right to exclude. Nor does the protection of geographical indications under the TRIPS Agreement entail the granting of such faculty.⁸ Likewise, there are many situations in which copyright protection only allows the title-holder to claim remuneration, but not to prohibit unauthorized acts.

As Article 39.3 itself indicates (see below), test data protection is a reward for the **investment** in data production, rather than for the creativity or inventiveness involved in generating the data. Test data are developed in accordance with standard protocols and procedures, involving a systematic compilation of factual information. Though the testing may refer to a novel drug, the test results themselves are merely the outcome of routine scientific practices.

Thus, the inclusion of test data in the TRIPS Agreement as a category of “intellectual property” does not determine the nature of the protection conferred. In particular, it does not indicate that such data should be protected through grant of exclusive rights.

The Article 39.3 Conditions of Protection

1. Data necessary for marketing approval

A basic premise for the application of Article 39.3 is that **test data must only be protected if national authorities require their submission** for obtaining marketing approval of pharmaceuticals or agrochemical products. The first sentence of this article states:

“Members, when requiring, as a condition of approving the marketing of...”

Given the territoriality of the intellectual property system – a feature that the TRIPS Agreement has not altered – the obligation to protect test data only arises in the Member countries where national regulations require the submission of such data. If a Member country opts not to require those data, Article 39.3 will be not apply.

In addition, the submission of data must be **necessary** to obtain approval. Data voluntarily submitted by an applicant, or in excess of what is required for approval, are not subject to protection under Article 39.3.

⁸ See article 22.2 of the TRIPS Agreement.

2. Protected data

The subject matter of the protection under this article is written material which details the results of scientific health and safety testing of drugs and agrochemicals, in relation to human, animal and plant health, impact on the environment and efficacy of use. The provision covers tests and other data that may be required by the authorities. These “other” data may include, for instance, manufacturing, conservation and packaging methods and conditions, but only to the extent that submission of this information is **necessary** to obtain marketing approval.

3. Undisclosed data

Article 39.3 does not require protection be given to public data submitted for marketing approval. To qualify for protection under Article 39.3, the pertinent information must be “undisclosed”. This means that information that is already public does not fall within the scope of this article. Any requirement for the submission of published or otherwise disclosed information to national regulators shall not generate any private right limiting the use of such information by the government or third parties, since the information would be in the public domain.

While a substantial part of the information on tests relating to safety and efficacy of approved drugs becomes publicly available – because the information is published in scientific journals,⁹ or made public by the health authority,¹⁰ – many data remain confidential such as data relating to some of the product’s physical and chemical attributes and manufacturing processes.

Given that under Article 39.3 protection is only conferred on undisclosed information, it will be necessary to determine in cases of controversy which of the information accompanying an application for marketing approval is confidential and need to be protected, and which is not. The undisclosed or disclosed nature of information is an **objective** feature, and it is not dependent on the qualification given by the applicant to the information that it is submitted. Hence, any applicant’s declaration that all or certain information is “confidential” or “undisclosed” should be subject to scrutiny.

4. New chemical entities

Another important condition for the application of Article 39.3 is that the data must refer to a “new chemical entity”. The Agreement does not define the term “new”. While the term presumably does not impose a patent standard of novelty, Member countries may choose under the Agreement to apply such a standard.

It may be also held that the test for newness under Article 39.3 refers to the date of application for approval. Thus, a chemical entity may be deemed “new” if there were no prior

⁹ In the case of the EU regulations (Directive 65/65, as amended) the possibility of obtaining market approval on the basis of published literature has been interpreted very restrictively. It only applies where a product has a well-established medicinal use and the documentation submitted by the applicant covers **all** aspects of the safety and efficacy assessment (Dodds-Smith, 2000, p. 111).

¹⁰ For instance, the European Medicines Evaluation Agency (EMA) publishes summaries of clinical trials in the “European Public Assessment Report” (EPAR). However, no detailed information on toxicological/pharmaceutical tests or clinical trials is published which could be used for registration by another company. The manufacturing process is not published either.

application for approval of the same drug, or where the same drug was not previously known in commerce.

Article 39.3 does not clarify either whether newness should be absolute (universal) or relative (local), that is, whether “new” would mean the **first** application in the world or in the Member country where it was filed (Cook, 2000, p. 6).

Occasionally, a product which is known and used in a certain field (e.g. chemical industry), may find a new application in the pharmaceutical sector. Such a new therapeutic product (generally known as “first indication”) may be deemed not to constitute a “new chemical entity”, since the chemical was already known. Alternatively, the newness may be assessed within a particular regulatory framework, and without regard to the fact that the same chemical may have been used in the context of another regulatory framework (Cook, 2000, p. 6).

All the above interpretations are equally permissible. The TRIPS Agreement deliberately avoids defining the concept of “new chemical entity”. This is one of the clear areas in which Member countries enjoy room for manoeuvre to implement the Agreement’s provisions.

Based on the ordinary meaning of the terms used, it may be also interpreted that there is no obligation to provide for protection when the test data were developed for a new **use** of a pharmaceutical product (generally called a “second indication”). In this case, it is the application or method of use of a known chemical entity that is new, but not the entity as such.

Similarly, Article 39.3 would not apply in cases where approval is sought for new indications, dosage forms, combinations, new forms of administration, crystalline forms, isomers, etc. of existing drugs, since there would be no novel chemical entity involved. The European Court of Justice indirectly addressed this issue in the “*Squibb*” case.¹¹ The Court held that a (second) product is “essentially similar” to an earlier approved product if the second product has “the same qualitative and quantitative composition in terms of active principles”, “the same pharmaceutical form” and is bio-equivalent to the first product, “unless it is apparent in the light of scientific knowledge that it differs significantly from the original product as regards safety or efficacy”. In these cases, the original applicant does not receive new periods of so-called “marketing exclusivity” for each new indication, dosage form or dosage schedule (Jones and Nittenberg, 1998/1999, p. 152).

5. Considerable effort (investment)

The subject matter of the protection under Article 39.3 is test data which cover matters such as toxicology, clinical trials for the pharmaceuticals and field trials for agrochemicals. Because this information is not “invented” or “created”, the TRIPS Agreement does not define any substantive standard for granting protection (like inventive step or novelty). It simply mandates protection when the process of obtaining the data involved “a considerable effort”.

¹¹ The ECJ decision was given in response to questions referred to it from the English High Court in relation to three cases. In all of them, the research-based pharmaceutical companies had made changes to certain aspects of their products and obtained marketing approval for each change. Subsequently, generic companies sought to rely not only on the original versions of the products but also on the products which had been approved more recently. The Medicines Control Agency acceded to certain of the generic companies’ requests, but not all of them (Jones and Nittenberg, 1998/1999, p. 152). See also Dodds-Smith, 2000, p. 112.

The text is vague about the type of effort involved (technical, economic?) and also with respect to its magnitude (when would it be deemed “considerable”?). As mentioned, the proponents of this formulation intended to protect the **investment** made in producing test data. The extension of intellectual property beyond its boundaries so as to protect investment, and not intellectual contributions¹² disrupts the essence of a system conceived to reward the creators of original ideas and new inventions.¹³ Even if it may be argued that “free riding” or “unfair use” of such data by third parties may create unfair advantages or unjust enrichment, it is not the role of the intellectual property system to solve competition problems that do not relate to the creation or use of ideas. Nonetheless, Article 39.3 exists. And it includes the considerable effort standard. Inclusion of this standard suggests national regulatory authorities may request the applicant prove that the information for which protection is sought is the result of considerable effort.

NON-DISCLOSURE OBLIGATION

Since the TRIPS Agreement’s obligations with regard to test data protection relates exclusively to undisclosed information, it seems clear that WTO Members’ obligations are limited to information, effectively requested by and submitted to the government, which was at the time of submission, and later remains, “undisclosed”.

The non-disclosure obligation requires that the test data be protected against “disclosure” unless:

- a) it is necessary to protect the public; or
- b) steps are taken to ensure that the data are protected against unfair commercial use.

The application of the first exception is subject to a “necessity test”. In determining necessity, GATT/WTO rules and jurisprudence generally provide deference to Member countries to determine when a necessity arises, but impose an often heavy burden of proof on the Member invoking it (Trebilcock and Howse, 1999, p. 140; Correa, 2000).

The second exception would permit a Member to disclose any information, if its unfair commercial use can be prevented. The key questions are what constitutes unfair use and how that protection can be guaranteed. This issue is discussed below.

Article 39.3 aims at preserving the confidentiality of the information submitted for marketing approval without any time limit. There is no indication in the provision about the duration of the obligation, certainly a weak point in the text. In principle, the confidentiality obligation continues until the information becomes known. It may also be possible, however, for a Member to establish a maximum period of confidentiality.

¹² An investment-based system was adopted by the European Community in the form of a *sui generis* regime for the protection of data bases. Despite the efforts of WIPO, however, no agreement has been reached so far to adopt an international convention modelled on the European approach. A bill on the matter proposed in the United States has also found strong opposition, particularly from the scientific and librarian communities (Reichman and Uhler, 1999).

¹³ According to the Trans Atlantic Consumer Dialogue (TACD), “data exclusivity provisions are part of a growing class of *sui generis* forms of protection that are designed to protect investment, rather than innovation. Because data exclusivity is not a reward for invention (which is already rewarded by patents) but rather a protection of investment, there should be greater transparency of the basis for the protection and a reasonable relationship between the investment and the protection” (available at www.tacd.org).

In any case, as mentioned above, because of the public health implications of the release into the market of a new drug, a substantial part of, but not all, the results of safety and efficacy tests and other data become available to the public. Some public health specialists have strongly opposed the possibility of keeping confidential pharmaceutical data, such as information obtained during pre-clinical tests. It has been argued that

“The earliest point in the career of the drug when one obtains a glimpse as to which its adverse effects might be is, without doubt, the phase of pharmacological and toxicological studies in animals. Very properly, the community requires of the pharmaceutical industry that the work performed at this stage be conscientiously carried out and painstakingly reported when the drug is submitted to Drug Control Authorities...Very improperly, the community then goes on to tolerate a situation whereby these reports, having been used for this purpose, are then commonly deposited in confidential archives where they are inaccessible to the medical world at large...It follows that when the first clinical evidence of a particular and unexpected side effect reaches us there is often no simple and direct means of comparing it with what has been reported in dogs, rabbits and mice. If these data were public property, it might be simpler to identify at an early stage those adverse reaction reports from the clinics which, because they run parallel to animal findings, deserve particular attention....” (Dukes, 1977).

Public health concerns were only marginally present in the negotiation of the TRIPS Agreement.¹⁴ The non-disclosure obligation was established on the basis of commercial considerations, without a proper weighing of public health interests in the openness of drug information (see Box 2).

Box 2

The Benefits of Openness of Drug Information¹⁵

The importance of access to information

Full availability of information is essential if all parties involved in health care are to participate effectively. Openness facilitates adequate feedback, proper setting of priorities and development of trust. A culture of openness protects conscientious individuals working in organizations of all kinds.

Knowledge relating to all drugs evolves constantly, as do standards and expectations relating to them, their producers and health care providers. However thorough the investigations made before a drug is licensed and marketed, much more will be learned about its efficacy, proper use and risks once it is marketed and used on a much larger scale.

Almost no new element of knowledge emerges suddenly; as a rule it begins with impressions and hypotheses. Where these arise – for example, in reports of possible serious side effects in the journals – all existing relevant information will need to be mobilized to verify or discount this evidence so that the trust can be established as quickly as possible. Much of the information needed for that purpose, including data on both animal and human experience, is

¹⁴ See, e.g., Article 8.1.

¹⁵ Extracts from the Statement of the “International Working Group on transparency and accountability in drug regulation” (Uppsala, 11-14 September, 1996).

unpublished and lies only within the files of agencies. By using it, the truth can be established much more quickly than if one is reliant purely on published evidence.

Consequences of excessive secrecy in drug regulation

If a substantial part of the information existing on drugs remains hidden within regulatory agencies, and sometimes fragmented between them, the development of knowledge will be impeded. This is particularly dangerous where suspicion arises of a hitherto unknown risk.

Malpractice can be hidden from view; legal discovery in the course of litigation has for example revealed cases of falsification or suppression of unfavourable data by certain companies, or submission of inconsistent files on the same drug to different agencies. Secrecy facilitates the circulation and use of sub-standard drugs.

Where a drug is subject to negative findings, the failure of a drug agency to explain its conclusions or provide background data, can leave the way clear for the sometimes very different and emphatic account given from the manufacturer. In a climate of secrecy and mistrust, the public is unlikely to believe even accurate and meticulously prepared official statements – assuming that they cannot be taken at face value and that some relevant information has probably been withheld.

The incomplete availability and irregular release of information promotes a climate in which suspicion is generated and in which sensational and poorly founded stories on drugs break in the popular press, their reliability cannot be checked and unnecessary panic can be caused.

Secrecy has consequences which can be wasteful and even inhumane; scientific work, e.g., in humans or animals which has already been performed by one company but hidden within regulatory files, may be repeated unnecessarily.

If drug utilization data are not available irrational drug use may continue unrecognized and unchecked.

If research is sponsored by companies, unfavourable or unclear results may be withheld or the research itself may be stopped.

PROSCRIBED ACTS OF UNFAIR COMMERCIAL USE

The TRIPS Agreement Text

One of the crucial interpretative issues in Article 39.3 is whether the reliance by a national authority on data submitted by one company (the “originator”) to evaluate a subsequent application by another company (a “follower”), constitutes an “unfair commercial use” of the information.

The expression “*unfair commercial use*” is not defined in Article 39. Pursuant to Article 31 (1) of the Vienna Convention, its interpretation should be based on the ordinary meaning of the terms of the treaty in their context and in the light of the agreement’s object and purpose.

1. “Unfair”

The ordinary meaning of “unfair” is “*not equitable or honest or impartial or according to rules*”¹⁶. In the case of Article 39.3, this concept must be understood in the light of Article 10 *bis* of the Paris Convention.

The concept of “unfair” is relative to the values of a particular society at a given point in time. It varies among Members, and this variation is in fact one of the premises on which the discipline of unfair competition is grounded. There is no absolute, universal rule to determine when certain practices should be deemed “unfair”:

“Morality, which is the source of the law of unfair competition, is a simple notion in theory only. In fact it reflects customs and habits anchored in the spirit of a particular community. There is no clearly objective standard of feeling, instincts, or attitudes toward a certain conduct. Therefore, specific prescriptions involving uniform evaluation of certain acts are extremely difficult.

The pressures existing in the various countries for the suppression of acts of unfair competition differ greatly. Generally, the development of law of unfair competition depends on active and intense competition in the marketplace by competing enterprises. It is the pressure of conflicting interests which leads to the establishment of clear rules of law. This pressure is not uniform in all countries and indeed it is evolving continuously” (Ladas, 1975, p. 1685-1686).

Ladas concludes his treatise’s discussion of the issue by indicating that:

We look for a standard by which we may judge the act complained of. This is an objective standard: the honest practices in the course of trade in the particular community and at the particular time” (Ladas, 1975, p. 1689).

Given this diversity, it is likely that different countries will judge certain situations differently, depending on their values and competitive advantages. Some countries may consider it an “unfair practice” for a “follower” company to commercially benefit from the data produced by the originator, via a marketing approval system based on “similarity”; or hold that such commercial benefit gives rise to claims of “unjust enrichment” leading to a compensation for the use of the data. In others, it may be regarded as the legitimate exploitation of an externality created during legitimate competition in the market. As noted by Kamperman Sanders,

5. *“Where exploitation of another’s achievements becomes inequitable, unfair competition law acts provides a remedy. This means that the mere fact that another’s achievement is being exploited does not call for any impediment on the basis of unfair competition provisions. On the contrary, appropriating and building on others’ achievements is the cornerstone of cultural and economic development. The axiom of freedom to copy epitomizes the principles of the free market system”.*

¹⁶ *The Concise Oxford Dictionary*, Seventh Edition, Oxford University Press, Oxford, 1989.

Certainly, specific regulations could be adopted at the international level in order to harmonize the treatment of these cases. The United States made such a proposal in the TRIPS negotiations,¹⁷ but it was not incorporated into the final text of the TRIPS Agreement. The U.S. proposal would have obliged countries to prevent any use of test data, without the consent of the right holder or on payment of “the reasonable value of the use”, if that use led to the “commercial or competitive benefit of the government or of any person”. This provision would have obliged countries to prevent **any** practice that would create such benefit. The final proposal, by contrast, used the term “unfair commercial practices”. The rejection of the US proposal indicates that the negotiating parties deliberately opted under Article 39.3 to mandate regulation of certain **types** of practices (those that are commercially **unfair**) and not to prevent any practice based on its possible **effects** on benefits allocation.

In other words, Article 39.3 only applies when a competitor obtains a benefit or advantage from the use of the originator’s testing data **as the result of unfair commercial practices**. It is the qualification of the practice that counts, not the mere existence of an advantage or benefit. Such qualification is left to Members’ discretion; it is part of the room for manoeuvre that they retained when signing the Agreement.

There are many instances in which the production of goods, notably intangibles, in a competitive environment generate externalities that benefit competitors. In describing the nature of competition, Ladas has noted that:

“it is an undeniable fact of modern business life that successful manufacturers or traders have to cope with the danger of having the goodwill of their business, their connection with the purchasing public, interfered with by competitors...In a competitive economy it is to be expected that each manufacturer or trader necessarily seeks to maintain and improve his market position by obtaining the benefit of a public demand, even though this demand be created by other manufacturers or traders...”

“...where does lawful competition end and unlawful competition begin? The fact that a competitor may derive a profit from his act of competition or cause monetary loss to another is not, in itself, unlawful. The dictum “no one should reap where he has not sown” requires delicate application. Progress would be paralyzed and monopoly would become general if we should attempt to prevent persons from using the work or experience of others. We must encourage people in the same trade or industry to compete for the custom of the public on the most favourable terms. The issue is whether the means employed in such competition are fair and lawful. An act may lack tact or taste but not be dishonest” (Ladas, 1975, pp. 1676, 1677 and 1689).

Many countries do not treat commercialization of a “similar” product approved by reference to a previous registration, or by reliance on data submitted by the originator company, as an unfair commercial practice, but some do. Under Article 39.3, each approach is valid. Article 39.3 mandates protection against “unfair commercial practices”, but permits Member countries to determine which practices will be deemed commercially unfair. As mentioned, differences among countries are likely to exist, consistent with Article 10 *bis* of the Paris Convention.

¹⁷ See below the history of the negotiation of article 39.3.

2. “Commercial”

Article 39.3 only covers “commercial” uses. This requirement clearly excludes use by the government, notably by the national health authority to assess the efficacy and toxicity of a pharmaceutical or agrochemical product.

In the view of the European Union, however, there is a substantial difference between the underlying principle in Article 39.1, which refers to relationships between competitors and Article 39.3, which includes governmental acts:

“The main question of interpretation is what is meant by “unfair commercial use”. Clearly, this concept is different from the concept of “unfair competition”, as used in Article 39.1 with a reference to Article 10 bis of the Paris Convention on the protection of Industrial Property, and which relates to behaviour among competitors. Protection of registration data is a government function. Article 39.3 does not indicate whether the notion of “unfair commercial use” refers to unfair commercial use by generic manufacturers to those who have submitted the data (usually research-based pharmaceutical industry) or to use by regulatory authorities of these data to the benefit of competitors. Protecting data against “unfair commercial use” is also different from protecting them from disclosure, since the latter is a separate and distinct obligation under Article 39.3” (EU, 2001, p. 3).

The EU argument, however, disregards that Article 39 **develops** and does not add to Article 10 *bis* of the Paris Convention. It only incorporates **examples of the general principle contained in paragraph (2) of Article 10 bis**.

In addition, though the use by the governments will **indirectly** have commercial consequences (the entry of a competitor in the market), it does not represent a **commercial** activity as such, but a legitimate State practice. In order to be “commercial”, the use of the information should be made by an entity which is actually in commerce. As also noted by Ladas,

“The general clause of Article 10bis, in establishing as its foundation “honest usages,” looks to the relations between competitors and to the interests of customers, and these provide an objective test which reflects an evolving pattern of competition in most of the present world... By definition, competition in commerce refers to the efforts of two or more persons, acting independently, to secure the custom of third parties, with the results that one may increase the sale of his goods and reduce the sale of the goods of the other” (Ladas. 1975, p. 1688).

The same concept underlies the WIPO “Model Provisions on Protection Against Unfair Competition” which, in relation to data protection, suggests the adoption by national laws of the following provision:

“Use or Disclosure of Secret Information Submitted for Procedure of Approval of Marketing: Any act or practice, in the course of industrial or commercial activities, shall be considered an act of unfair competition if it consists or results in an unfair commercial use of secret test or other data, the origination of which have been submitted to a competent authority for the

purposes of obtaining approval of the marketing of pharmaceutical or agricultural chemical products which utilize new chemical entities” (emphasis added) (WIPO, 1996).

3. “Use”

Finally, for Article 39.3 to apply there must be “use” of the information submitted by the originator.¹⁸

4. Analysing “Unfair Commercial Use”

Thus, given the flexibility inherent in Article 39.3, and depending on the applicable legal system, national laws can follow different approaches for the approval of a second-entry marketing application. They may:

- a) require the second-entrant to produce its own testing and other data or to obtain an authorization of use from the “originator” of the data;
- b) allow the second-entrant to rely on the “originator’s” data against payment of a compensation to the “originator” (when the “originator” has not given his consent for the use of the data);¹⁹
- c) examine and rely upon the data submitted by the “originator” to evaluate the second-entrant application;
- d) approve a second entry marketing application without examining or otherwise relying upon confidential information submitted by the originator.

In all cases, the authorities will normally require that the second-entrant prove that his product is similar or “essentially similar” to the already registered product (in terms of its physical and chemical characteristics and attributes).²⁰ Different types of bioequivalence studies are generally required for this purpose.²¹

In cases a) and b) the data receive specific protection, either on the basis of exclusivity or compensation. In case c) the second-entrant does not *use* the data; it is the authority that examines and relies on the data in its possession. In case d), finally, there is no “use” at all, since the authority does not use the testing and other data (which it may not even possess); it merely relies on public information and/or on the existence of a prior (domestic or foreign) marketing approval.

Neither in cases c) or d) is there a “commercial use” of the data. A contrary interpretation holds that even indirect reliance on data by a national authority constitutes a form

¹⁸ In one of the texts under consideration by the negotiating parties in July 1990, the broader concept of “exploitation” was proposed (but not finally adopted). The text read:

“3Aa. Parties, when requiring the publication or submission of undisclosed information consisting of test [or other] data, the origination of which involves a considerable effort, shall protect such data against unfair exploitation by competitors. The protection shall last for a reasonable time commensurate with the efforts involved in the origination of the data, the nature of the data, and the expenditure involved in their preparation, and shall take no account of the availability of other forms of protection”.

¹⁹ This compulsory licence approach is the one applicable, under certain circumstances, in accordance with the U.S. FIFRA. See Annex 1.

²⁰ See, e.g., article 4.8 (a)(ii) of the EC Directive 65/65/EEC.

²¹ In some countries, bio-availability studies are also required for the approval of generic versions of existing products.

of commercial use. Under this interpretation, the competent authority must be proscribed from “using” the data to support, clear or otherwise review second entrant applications for marketing approval for a set amount of time unless authorized by the “originator” (WHO, 2000, p. 39).

According to this interpretation, national authority reliance on the data submitted by the originator in order to assess a subsequent application constitutes “unfair commercial use”, even when neither the authority nor the competitor actually “use” the data without the originator’s authorization (for instance, when approval is given without any re-examination of the data). In the U.S. complaint against Australia, for instance, the USA argued that relying on the innovator’s data allowed free-riding by generic drug companies on

“the innovator company’s investment in developing the test data and thus puts the innovator company at a competitive disadvantage...The U.S. claims that Article 39 para.(3) means that generic companies are not allowed to derive commercial benefit from the innovator’s test data” (Priapantja, 2000, p. 6).

Under this view, the fact that a competitor obtains a commercial benefit or advantage constitutes an “unfair commercial use” of the data, notwithstanding that actual use may not occur and that the practice as such may not be “dishonest” or contrary to a country’s prevailing values of morality or fairness in commercial activities.

This latter interpretation, however, clearly goes beyond what the provision mandates. It does introduce an obligation not negotiated during the Uruguay Round that, in practice, would limit legitimate competition and thereby erect barriers to the access to medicines.

National Case Law

Available national case law supports the view that granting marketing approval to a second entrant, based on the second product’s similarity to a previously approved first product, is not a proscribed “use” under Article 39.3.

The nature and extent of data exclusivity rights were examined in two important decisions by the U.S. Supreme Court (*Ruckelshaus v. Monsanto Co.*, 467 US 986, 104 S.Ct.2862, June 26, 1984) and the Canadian Federal Court of Appeal (*Bayer Inc. v. The General Attorney of Canada, the Minister of Health, Apotex Inc. and Novopharm Ltd.*, May 19, 1999). The second decision, in particular, examined the extent to which a national health authority can *rely on* the originator’s data, *even when an exclusivity period applies*.

The *Ruckelshaus v. Monsanto Co.* case relates to the protection of data submitted for the registration of an agrochemical product. Though a subsequent applicant was obliged to compensate for the use of Monsanto’s original data, Monsanto argued that such use undermined its reasonable “investment backed expectations” and was unconstitutional. A basic argument of the plaintiff was that the possibility given to a competitor of using the data against payment of a compensation nullified its “reasonable investment-backed expectation”. However, the Supreme Court described the extensive practice of relying on data submitted by the first applicant in the United States, and rejected Monsanto’s complaint (see Box 3).

Box 3

Relying on data: the U.S. Supreme Court decision in *Ruckelshaus v. Monsanto Co.*

The Supreme Court considered that Monsanto could not have had a reasonable, investment-backed expectation that the Environmental Protection Agency (EPA) would keep the data confidential beyond the limits prescribed in the amended statute itself. Monsanto was on notice of the manner in which EPA was authorized to use and disclose any data turned over to it by an applicant for registration.

Excerpts from the Court's decision:

- “In addition, Monsanto was aware that information relating to formulae of products could be revealed by EPA to “any Federal agency consulted and [could] be revealed at a public hearing or in findings of fact” issued by EPA “when necessary to carry out” EPA’s duties under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) § 10(B)²². The statute also gave Monsanto notice that much of the health, safety, and efficacy data provided by it could be disclosed according to the data-consideration and data-disclosure provisions in the statute. Monsanto chose to submit the requisite data in order to receive a registration, it can hardly argue that its reasonable investment-backed expectations are disturbed when EPA acts to use or disclose the data in a manner that was authorized by law at the time of the submission.”
- “Because the market for Monsanto’s pesticide products is an international one, Monsanto could decide to forego registration in the United States and sell a pesticide only in foreign markets. Presumably, it will do so in those situations where it deems the data to be protected from disclosure more valuable than the right to sell in the United States.”
- “*A fortiori*, the Trade Secrets Act cannot be construed as any sort of assurance against internal agency use of submitted data during consideration of the application of a subsequent applicant for registration. Indeed, there is some evidence that the practice of using data submitted by one company during consideration of the application of a subsequent applicant was widespread and well known. Thus, with respect to any data that Monsanto submitted to EPA prior to the effective date of the 1972 amendments to FIFRA, we hold that Monsanto could not have had a “reasonable investment-backed expectation” that EPA would maintain those data in strictest confidence and would use them exclusively for the purpose of considering the Monsanto application in connection with which the data were submitted.”
- “When Monsanto provided data to EPA during this period, it was with the understanding, embodied in the FIFRA, that EPA was free to use any of submitted data that were not trade secrets in considering the application of another, provided that EPA required the subsequent applicant to pay “reasonable compensation” to the original submitter. § 3(c)(1)(D), 86 Stat. 979. But the statute also gave Monsanto explicit assurance that EPA was prohibited in connection with the application of another, to use any data submitted by an applicant if both the applicant and EPA determined the data to constitute trade secrets.”

²² See a summary of FIFRA in Annex 1.

The U.S. Supreme Court in this case recognized that the authority could use the data submitted by the originator to assess second-entrant applications. According to the law applicable at the time of the complaint, Monsanto was entitled to compensation, but not to exclusive use of the data. The solution has probably not substantially changed in the United States despite the adoption of the Second Restatement of Unfair Competition Law (1997). In the absence of a specific provision granting an exclusivity period as currently provided for medicines by U.S. law, relying on data to approve subsequent applications would not be considered an illegitimate misappropriation of trade secrets.²³

The General Court Appeal of Canada decided a second and more significant case on issues related to data exclusivity. Despite the fact that NAFTA provisions, as mentioned before, provide for a minimum term of exclusivity, the Court found legitimate the approval of a subsequent application on the basis of a prior registration. The court argued that the health authority neither requested undisclosed information a second time nor examined it; the authority just checked whether the original and subsequent products were indeed the same (see Box 4). The issue was decided under Canadian law and NAFTA Article 1711 on “Trade Secrets”, which establishes the following:

“5. If a Party requires, as a condition for approving the marketing of pharmaceutical or agricultural chemical products that utilize new chemical entities, the submission of undisclosed test or other data necessary to determine whether the use of such data involves considerable effort, the Party shall protect against disclosure of the data of persons making such submission, where the origination of such data involve considerable efforts, except where the disclosure is necessary to protect the public or unless steps are taken to ensure that the data is protected against unfair commercial use.

6. Each Party shall provide that for data subject to paragraph 5 that are submitted to the Party after the date of entry into force of this Agreement, no person other than the person that submitted them may, without the latter’s permission, rely on such data in support of an application for the product approval during a reasonable period of time after their submission. For this purpose, a reasonable period shall normally mean not less than five years from the date on which the Party granted approval to the person that produced the data for approval to market its product, taking account of the nature of the data and the person’s efforts and expenditures in producing them. Subject to this provision, there shall be no limitation on any Party to implement abbreviated approval procedures for such products on the basis of bioequivalence and bioavailability studies.

7. Where a Party relies on a marketing approval granted by another Party, the reasonable period of exclusive use of the data submitted in connection with obtaining the approval relied on shall begin with the date of the first marketing approval relied on”.

²³ Personal communication by Prof. J. Reichman (Duke University), October 2001.

Box 4

Canadian Federal Court of Appeal: the Bayer case

The Federal Court of Appeal held, *inter alia*, the following:

“When a generic manufacturer files an Abbreviated New Drug Submission (ANDS), the safety and effectiveness of the generic product may be demonstrated by showing that the product is the pharmaceutical and bioequivalent of the innovator’s product. If the generic manufacturer is able to do so solely by comparing its product with the innovator’s product which is being publicly marketed, the Minister will not have to examine or rely upon confidential information filed as part of the innovator’s New Drug Submission (NDS). In such case, the minimum five year market protection referred to in the regulation will not apply.

“On the other hand, if in order to be satisfied of the safety and effectiveness of the generic product, the Minister examines and relies upon information filed by the innovator in its NDS, the minimum five years market protection for the innovator will apply. This is because the safety and effectiveness of the generic product will only be established by reference to confidential information provided to the Minister by the innovator. It is only this use of that confidential information by the Minister on behalf of the generic manufacturer that gives rise to the minimum five years protection from competition for the innovator.

“The appellant says that whenever an ANDS is filed by a generic manufacturer comparing the generic product with the innovator’s product, the Minister must implicitly be examining and relying upon the confidential information filed by the innovator in its NDS. We do not read subsection C.08.004.1(1) in this way. To do so would be to interpret it as invariably providing a minimum five years of market protection to an innovator when an ANDS is filed by a generic manufacturer. Rather, the regulation contemplates that the Minister may or may not examine and rely upon confidential information filed by the innovator. The appellant’s argument reads out of the regulation the option given to the Minister as to whether or not to examine and rely on the confidential information filed by the innovator.

“The NAFTA provisions are intended to protect trade secrets. If the generic manufacturer exercises the option of having the Minister examine the confidential information filed by the innovator in support of its application for a Notice of Compliance, it is, in effect, relying on that information within the meaning of section 6 of Article 1711. It is apparent that if confidential data is not relied upon, the trade secrets provisions of the NAFTA are not applicable. Specifically, if a generic manufacturer is able to establish the safety and effectiveness of its product on the basis of bioequivalence or bioavailability studies without the Minister having to examine and rely upon confidential data filed by the innovator, there is no reason or justification for the minimum five years protection from competition. This interpretation of subsection C.08.004.01(1) is consonant with section 5 and 6 of Article 1711 of the NAFTA.

“If a generic manufacturer compares its product to an innovator’s product solely on the basis of public information, providing the innovator with protection from competition for a minimum of five years is tantamount to granting it the protection a patent would provide. Put another way, even if the Minister did not examine and rely on the innovator’s confidential information, the innovator would be entitled to the minimum of five years protection from

competition. The words of subsection C.08.004.1(1) cannot be construed to yield such a result.”

The Court, in sum, concluded that, under Canadian law and NAFTA, if the health authority actually uses the data submitted by the originator on behalf of the generic manufacturer in order to assess the latter’s application, the minimum five years protection from the competition for the innovator applies. But if the authority does not examine and rely on that confidential or trade secret information on behalf of the generic manufacturer, there is no use of data and the exclusivity provision is not applicable.

If despite the express provision of exclusivity, the mere reliance on a prior registration without use of the data does not allow to claim exclusivity, *a fortiori* the same conclusion should be reached when the exclusivity is not specifically established, as in the case of Article 39.3.

In sum, whatever the desire of some of the TRIPS negotiating parties might have been, the expression “unfair commercial use”, reasonable interpreted, does not sustain a reading that Article 39.3 requires the provision of exclusivity, or of a compensation. It has left wide room for manoeuvre for Member countries to determine:

- a) when such a use exists, and
- b) the means of protection (see next section)

An “unfair commercial use” may be determined to exist, for instance, in situations in which a competitor obtains through fraud, breach of confidence or other “dishonest” practices, the results of testing data and *uses* them to submit an application for marketing approval in its own benefit. It would also apply in cases where the government provides access to undisclosed testing data in order to provide an advantage to a firm which did not produce them or share their cost.²⁴

MEANS OF PROTECTION AGAINST UNFAIR COMMERCIAL USE

A key issue for the application of Article 39.3 is to determine the nature and extent of the obligation to protect “against unfair commercial use”. As noted, the interpretation of this rule has created considerable controversy.

The TRIPS Agreement mandates the protection of “undisclosed information” in the framework of the discipline of “unfair competition”. Article 39.1 of Agreement stipulates that

“in the course of ensuring effective protection against unfair competition as provided in Article 10bis of the Paris Convention (1967) Members shall protect ...the data submitted to governments or governmental agencies in accordance with paragraph 3”.

²⁴ This would represent a violation of the non-disclosure obligation as well as an “unfair commercial use”.

Article 10 *bis* of the Paris Convention requires protection against “unfair competition”, defined as

“any act of competition contrary to honest commercial practices in industrial or commercial matters”.

The discipline of unfair competition protects fairness in commercial activities. As mentioned, there are no universal moral values or a unique concept of what is “honest” in commercial behaviour. The definition of what constitutes “fair” or “honest” practices varies among countries. They may include competitor’s misrepresentation, fraud threats, defamation, disparagement, enticement of employees, betrayal of confidential information commercial bribery, among others. In many but not all jurisdictions, the misappropriation of trade secrets is regulated under unfair competition law, as is the case with the TRIPS Agreement.

The present status of international competition law in the Paris Convention is outlined in Box 5.

Box 5

International protection against unfair competition under the Paris Convention

- Pursuant to Art.10 bis (1), the contracting states are obliged to ensure citizens of other contracting states “effective protection against unfair competition”.
- In Art.10 bis (2) (general clause), unfair competition is defined as any act of competition which is “contrary to honest practices in industrial or commercial matters”.
- Three cases are named in Art.10 bis (3) which “in particular shall be prohibited”, namely creating the risk of confusion, discrediting competitors through false allegations and making misleading indications or allegations about one’s own goods. This list is not enumerative, so that other competitive acts can also be covered by the general clause.
- Pursuant to Art.10 bis (1) of the Paris Convention, appropriate legal remedies must be made available to the citizens of other contracting states, in order to ensure the effective repression of acts contravening Art.10 bis; these must also include the power of federations and associations to take legal action (Art.10 *ter* (2)).

Source: Henning-Bodewig, 1999, p. 173.

Under the discipline of unfair competition, protection is not based on the existence of “property” rights. Hence, the provision of protection under such discipline does not give rise to claims of property rights, including in respect of trade secrets and data submitted for marketing approval. There is only “possession” of this information. The TRIPS Agreement itself, in Article 39.3 refers to undisclosed information “under the control” of a person, in clear contrast to the concept used in the sections relating to other categories of intellectual property rights.²⁵ A comparison between patents and trade secrets protection illustrates this important difference (see Box 6).

²⁵ See, e.g., articles 16.1 and 28.1 which refer to the “owner” of a trademark and of a patent, respectively.

Box 6

Patents vs. undisclosed information

- A patent confers property rights.
- A patent owner obtains the exclusive use of his/her rights. This means he/she is the only one who can use the invention, commercialize the product, etc. A patent owner can prevent any other person from using that invention. Even if a third party has developed the same product in an independent manner, without knowing or relying on the technology of the patent owner, the former is not allowed to use it, since the exclusive rights conferred are absolute.
- In the case of undisclosed information, under most legal systems, there is only “possession” of certain information.
- The value of undisclosed information does not lie in the inventive step or novelty – even a list of clients can be protected, though obviously this is not an invention – but in the fact that the undisclosed information has commercial value and in the fact that it is secret.
- Unlike patents, which in general last for 20 years from the filing date, in the case of undisclosed information there is no defined time limit. Undisclosed information is protected as long as it is kept undisclosed. The duration of the protection, therefore, depends on the factual situation, not on any legal provision.

Though during the TRIPS negotiations the United States suggested the consideration of undisclosed information as “property” – in accordance with the concepts developed in its own legal system – that approach did not find support, particularly from European and developing countries.²⁶

The TRIPS Agreement clearly does not treat undisclosed information as “property”.²⁷ The fact that TRIPS deems “undisclosed information” to be a “category” of intellectual property does not imply, as mentioned before, the existence of a property right.²⁸

Because the TRIPS agreement embraces an unfair competition approach to undisclosed information, a logic consequence of the Agreement is that Article 39 does not obligate countries to confer *exclusive* rights.

Exclusive rights are merely one “TRIPS-plus” option to deal with issues covered by Article 39.3. There are heavy costs and ethical concerns associated with such an approach, however. In the absence of mechanisms that permit the use of the data, an exclusive rights system leads to the need for competitors to duplicate tests (often involving suffering of animals) in order to reach results that are already known.

²⁶ On the different approaches in continental and common law with regard to trade secrets, see Coleman, 1992; Font Segura, 1999.

²⁷ According to Engelberg, U.S. law does not recognize “any property rights in the data submitted to support an application for approval of a new drug... The non-patent, market exclusivity provisions of the Drug Competition Act of 1984 were created as an arbitrary means of providing investment incentive for the development of drug products that had little or no patent protection and not as a purposeful determination to create a new form of intellectual property based on undisclosed data”.

²⁸ It is generally accepted, particularly under European law, that unfair competition is one of the disciplines of industrial property, and it is in this sense that article 1.2 should be interpreted.

The Article 39.3 obligation may be implemented through less onerous means, such as through the legal faculty to impede the use of information acquired through dishonest practices (e.g. espionage, breach of confidence), as background for an independent submission for marketing approval.

Implementing legislation may also require the subsequent user to pay compensation, without providing for exclusive rights. The U.S. FIFRA, for instance, recognizes the possibility of using the originator's test data for the approval of a subsequent application, without the originator's consent but with payment of compensation. The law thus establishes a form of compulsory licensing for such data. The United States required such a compulsory licence – without payment of compensation – in approving Dow Chemical's acquisition of Rugby-Darby Group Companies. Approval of the merger was contingent on the issuance of a licence for registration data to all potential competitors (see Box 7).

Box 7

Compulsory licensing in the U.S. involving test data

Acquisition of shares of Rugby-Darby Group Companies by Dow Chemical Co.

The Federal Trade Commission required Dow to license to potential entrants, intangible dicyclomine assets, including all formulations, patents, trade secrets, technology, know-how, specifications, designs, drawings, processes, quality control data, research materials, technical information, management information systems, software, *the Drug Master File*, and all information relating to the United States Food and Drug Administration Approvals that are not part of the acquired company's physical facilities or other tangible assets.

Source: www.cptech.org

In sum, Article 39.3 – interpreted according to the ordinary meaning of the words used, in their context (notably Article 39.1) and taking into account the object and purpose of the Agreement as expressed in Articles 7 and 8 – does not require the granting of exclusive rights.²⁹ The obligation that it imposes may be satisfied by other means, not specified in the Agreement. As stated by UNCTAD in relation to data covered by Article 39.3,

“authorities are not prevented... from using knowledge of such data, for instance, to assess subsequent applications by third parties for the registration of similar products” (UNCTAD, 1996, p. 48).

THE EXCLUSIVITY APPROACH

The pharmaceutical industry, the United States and the European Union disagree with the contention that Article 39.3 does not require the granting of exclusive rights. According to the industry, the only way to effectively protect test data against unfair commercial use is to provide an exclusivity period for the use of the data:

²⁹ See also Watal (2001) who concludes that “in the end in the TRIPS text there is no clear obligation not to rely on the test data for the second or subsequent applicants nor a fixed duration of market exclusivity, failing which the first registrant is assured reasonable compensation. This is a clear contrast to the corresponding provisions in NAFTA” (p. 199).

“To have a meaningful purpose this provision (Article 39.3) must be interpreted to require the protection of data against use by the competitors. Even if there is some concern about government use of such data in a commercial manner, it is minuscule in comparison to the problem of competitors’ use of the data. Consequently, in light of the maxim of statutory construction that a provision will be interpreted so that no part will be inoperative or superfluous, void or insignificant, Article 39 para.(3) must be interpreted to provide protection against the use of data by competitors for some period of time” (Priapantja, 2000, p. 4).

The Office of the U.S. Trade Representative (USTR) has interpreted Article 39.3 of the TRIPS Agreement to mean that

“the data will not be used to support, clear or otherwise review other applications for marketing approval for a set amount of time unless authorised by the original submitter of the data. Any other definition of this term would be inconsistent with logic and the negotiating history of the provision ”.³⁰

The United States maintained this position, for instance, in its complaint (initiated in April 1996), under Special 301 Section of U.S. Trade Act, against Australia.³¹ Australia did not grant exclusivity, and generic companies only had to demonstrate bio-equivalence in order to obtain marketing approval of a similar product. In addition, Australian authorities granted certificates of free sale which permitted generic companies to export to other countries where marketing approval was automatically granted on the basis of the Australian certificates.

The U.S. argued that the Australian regime violated Article 39.3. The U.S. pressure forced an amendment to the Australian law. Under the Therapeutic Goods Legislation Amendment Act 1998 (No.34, 1998) test data in Australia now have five years of “exclusivity”. During this time, another company wishing to register a generic copy of an originator’s product will be required to seek the agreement of the originator company to use its data, or to develop its own data package (Priapantja, 2000, p. 6).

The exclusivity approach was also incorporated, as a result of U.S. demands, in the USA-Jordan Agreement on the Establishment of a Free Trade Area (Washington D.C., 24 October, 2000), according to which “in situations where there is reliance on evidence of approval in another country, Jordan shall at a minimum protect such information against unfair commercial use for the same period of time the other country is protecting such information against unfair commercial use” (Article 22, fn. 11)³².

³⁰ Office of the General Counsel, U.S. Trade Representative, “The protection of Undisclosed Test Data in Accordance with TRIPS Article 39.3”, unattributed paper for submission in bilateral discussions with Australia (May 1995).

³¹ This case was not brought to a panel resolution under the WTO’s Dispute Settlement Understanding (DSU) rules. The U.S. instead threatened to impose unilateral trade sanctions on Australia, even though TRIPS had already entered into force in both countries. The U.S. also applied economic sanctions to Argentina in 1997, arguing Argentina maintained insufficient protection of confidential information. More recently, the U.S. has started consultations under the DSU on, *inter alia*, Argentina’s compliance with Article 39.3.

³² In addition, this Agreement establishes a TRIPS-plus standard in relation to the concept of “new chemical entities”: it is understood that such concept “shall also include protection for new uses for old chemical entities for a period of three years” (article 22, fn. 10). The U.S. has also criticized the amendment of the Thai “Safety Monitoring Programme” (SMP) established in 1993 as a result of USTR demands aimed at ensuring a two years minimum exclusivity period for drugs patented abroad between 1986 and September 1991. In January 2001 the SMP was amended and generics companies were allowed to conduct bioequivalence studies at any

The EU argues, similarly, that Article 39.3 established an exclusivity obligation. All that is left to Member countries, according to the EU, is the determination of the *duration* thereof.³³

“the only way to guarantee that no “unfair commercial use” within the meaning of Article 39.3 shall be made is to provide that regulatory authorities should not rely on these data for a reasonable period of time, the determination of what is a reasonable period of time being left to the discretion of the Members.

4. *In theory, Article 39.3 appears to give Members the discretion to provide for different means of data protection, although it is very difficult to imagine other ways than non-reliance over a certain period of time, except for a (temporary) refusal to grant any second market approval to similar products (even if the second applicant submits its own data), as is the case in at least one WTO Member and maybe for an obligation to pay as a compensation for reliance on proprietary data without having to obtain consent from the first applicant. The question remains whether such payment would indeed be sufficient to guarantee that any “unfair commercial use” of test data takes place. For instance, it would be essential that such payment reflects the investments made by the original applicant – which may not always be easy to establish.*

In theory, any country maintaining an effective system to implement obligations under 39.3 even if different from non-reliance over time, would not be in breach of its TRIPS obligations, but we are not aware of many alternatives and it is clear that what the TRIPS-negotiations had in mind was data exclusivity over a certain period of time. On the other hand, as it does not set any time limit, Article 39.3 would not prevent a country from providing for data exclusivity for an unlimited period of time” (EU, 2001, pp. 4-5).

The EU position suffers from several shortcomings, however. First, had the negotiating parties agreed to embrace the concept of exclusivity, they simply could have done so explicitly. The TRIPS Agreement’s obligations in relation to copyrights, trademarks, industrial designs, patents and integrated circuits (via incorporation of the Washington Treaty), all explicitly provide for exclusivity.

The EU admits that there was substantial disagreement during negotiations:

“It must be admitted that the following of Article 39.3 does not, from a prima facie reading, appear to impose data exclusivity during a certain period of time. This lack of clarity is the obvious result of a difficult negotiation process where divergences of views arose between developing and industrialized countries as to the necessity of EC/U.S. like type of data protection as well as among industrialized countries on the length of the data exclusivity period” (EU, 2001, p. 3).

time regardless of whether or not the original products are under the SMP. If the original products are under the SMP, however, those generic products must also be under the SMP. According to the Thai authorities, the SMP had led to unaffordable high prices for new drugs. In the USTR view, this reform would mean the relinquishment of the benefits affording data protection in accordance with the US-Thai 1993 Bilateral Agreement, and would create – at least until a “satisfactorily TRIPS-consistent Trade Secrets Law is enacted and implemented in Thailand – an unacceptable gap in data protection coverage (Kwa, 2001, pp. 49-50).

³³ See also Lobato García-Miján, 2000.

The disagreement among the parties was, however, more substantial than that argued by the EU, and there was no international established practice on which to rely. The negotiating history of Article 39.3 reveals that the parties considered at length, but did not adopt, text which clearly required exclusivity for test data.

Second, if the negotiating parties only left the Members the freedom to determine the **duration** of the exclusivity period, on what basis could a panel or the Appellate Body establish an “adequate” duration? The basic rule of Article 3.2 of the WTO’s Dispute Settlement Understanding prohibits dispute settlement bodies from adding to or subtracting from WTO agreement rights.³⁴ The EU itself admits that there was disagreement among the developed countries even about the duration of such period:

“Would this be 5 years (as in the case inter alia in US), 4 years or 3 years? This remains an open question”.

As noted by Watal,

5. *“It can be argued that if the intention had been to have such exclusive marketing rights, this term, which is used in Article 70.9 of TRIPS, would have been used here too. Further, given the differences in the TRIPS and NAFTA texts of this provision, it is clear that the scope and purpose in TRIPS is intended to be more limited as otherwise the text would have been as specific. No additional obligations, which are not present in the text, can be imported through interpretation. Therefore, a reasonable interpretation would be that the obligation on the authorities would be to keep the test data secret and to prohibit others from accessing this test data for unfair commercial use, such as sale to rival firms”* (Watal, 2001, p. 204).

In sum, Article 39.3 clearly requires some form of protection for test data. Its main purpose is not to prevent the commercial use of such data by governments, but the use by competitors. The wording, context and purpose of the article does not support an interpretation that the required protection can be implemented only on the basis of an exclusivity protection. This interpretation is confirmed by the history of the negotiation of the TRIPS Agreement, as reviewed below.³⁵

³⁴ Article 3.2: “Recommendations and rulings by the Dispute Settlement Body cannot add to or diminish the rights and obligations provided in the covered agreements”.

³⁵ The suggested interpretation has also been held by the Africa Group, Barbados, Bolivia, Brazil, Dominican Republic, Ecuador, Honduras, India, Indonesia, Jamaica, Pakistan, Paraguay, Philippines, Peru, Sri Lanka, Thailand and Venezuela in a recent submission to the Council of TRIPS on “TRIPS and Public Health”: “**Protection of Test Data:** Article 39.3 of the TRIPS Agreement leaves considerable room for Member countries to implement the obligation to protect test data against unfair competition practices. The Agreement provides that “undisclosed information” is regulated under the discipline of unfair competition, as contained in article 10 *bis* of the Paris Convention. With this provision, the Agreement clearly avoids the treatment of undisclosed information as a “property” and does not require granting “exclusive” rights to the owner of the data” (para. 39) (IP/C/W/296, 19 June, 2001).

THE HISTORY OF THE TRIPS NEGOTIATIONS

The history of the TRIPS Agreement negotiations also provides important evidence for interpreting Article 39.3. Such history has been accepted in recent WTO jurisprudence as an interpretative source under Article 31 (2) of the Vienna Convention on the Law of the treaties. It has been used to **confirm** the interpretation reached by the application of the principles of Article 31 (1) of the Convention.³⁶

An early precedent of Article 39.3 can be found in the “Statement of Views of the European, Japanese and United States Business Communities”,³⁷ which also influenced the drafting of other articles of the TRIPS Agreement. In their submission, the business communities advocated for the protection of test data as follows:

“1. Information required by a government to be disclosed by any party shall not be used commercially or further disclosed without the consent of the owner.

2 Information disclosed to a government as a condition for registration of a product shall be reserved for the exclusive use of the registrant for a reasonable period from the day when government approval based on the information was given. The reasonable period shall be adequate to protect the commercial interests of the registrant”.

This proposal clearly specified the obligation to establish a data exclusivity period. The same approach was reflected in the U.S. proposal:

*“Contracting parties which require that trade secrets be submitted to carry out governmental functions, shall not use the trade secrets for the commercial or competitive benefit of the government or of any person other than the right-holder except with the right holder’s consent, on payment of the reasonable value of the use, or if a reasonable period of exclusive use is given to the right-holder”.*³⁸

It is interesting to note that this proposal referred to the “commercial or competitive benefit” obtained by a third party, rather than to “unfair commercial use” as is the Agreement’s text. The proposal is based on the effects of the use (the creation of a benefit), while Article 39.3 is based on an ethical qualification of the use as “unfair”. The U.S. proposal turned on whether a commercial or competitive benefit (independently of the qualification of the use that generated it) was obtained; under Article 39.3, the key issue is whether there is unfairness in the use (as provided by Article 10 *bis* of the Paris Convention) and not whether a third party obtains a benefit.

The negotiating parties considered requiring test data exclusivity, but rejected this approach. Bracketed text under consideration at the Brussels Ministerial Meeting (December 1990) would have required not less than five years of data exclusivity. The draft read as follows:

³⁶ See, e.g. the panel report in *United States-Section 110(5) of the Copyright U.S. Copyright Act*, WT/DS160/R, 15 June 2000, para. 6.50; *United States-Section 211 Omnibus Appropriations Act of 1998*, WT/DS176/R, 6 August, 2001, para.8.378.

³⁷ See Annex III of Beier and Schricker, 1989.

³⁸ See MTN.GNG/NG11/W/70, reproduced in Correa and Yusuf, 1998.

*“Parties, when requiring, as a condition of approving the marketing of new pharmaceutical products or of a new agricultural chemical product, the submission of undisclosed test or other data, the originator of which involves a considerable effort, shall [protect such data against unfair commercial use. Unless the person submitting the information agrees, the data may not be relied upon for the approval of competing products for a reasonable time, generally no less than five years, commensurate with the efforts involved in the origination of the data, their nature, and the expenditure involved in their preparation. In addition, Parties shall] protect such data against disclosure, except where necessary to protect the public”.*³⁹

Notably, this text also explicitly included a prohibition on **reliance** on the data submitted by the originator. But this concept disappeared from the final text. The negotiating history of Article 39.3, in sum, does not support the thesis that it was intended to provide exclusive rights.⁴⁰ On the contrary, it shows that such concept was rejected. It is also suggestive in this sense that the most active proponents of such approach are currently proposing to **review** the TRIPS Agreement in order to include an exclusivity period.⁴¹

CONCLUSIONS

The use by health authorities and competitors of test data which must be submitted to obtain marketing approval of pharmaceutical (and agrochemical) products has been subject to specific regulations in several jurisdictions. Some developed countries, notably the U.S. and EU, have established data protection regulations based on the exclusive use of such data by the originator company. In other countries, however, off-patent generic products can be approved by relying on the data available to health authorities or by reference to a prior registration either domestic or in third countries. In all cases, the physical and chemical similarity (or essential similarity) with the registered product must be demonstrated.

The TRIPS Agreement has obliged WTO Member countries to treat test data as a component of “intellectual property”. However, the rationale for test data protection is the investment made in data production, rather than their creative or inventive content.

Article 39.3 of the TRIPS Agreement requires data protection against disclosure and “unfair commercial use”. Article 39.3 develops Article 10 *bis* of the Paris Convention; that is, it requires the protection of data against dishonest commercial practices.

The non-disclosure obligation admits exceptions where necessary to protect the public, and in other cases where measures are adopted to ensure that the information is not used in an

³⁹ See Gervais, 1998, pp. 182-183.

⁴⁰ The EU has pointed out that “according to one commentator, the U.S. negotiations finally decided to drop the more explicit language of above drafts because they did not view such wording as essential because, in any event, “the accepted definition at the time of protection against unfair commercial use included non-reliance for a fixed period of time for new chemical entities” (EU, 2001, p. 4).

⁴¹ In its position paper on the WTO Millennium Round, the International Federation of Pharmaceutical Manufacturers’ Association (IFPMA) has called, *inter alia*, for the adoption of a 10-year data exclusivity period (see “What is at stake in Seattle”, in www.pharma.org). See also IIPi (2000), where it is noted that Article 39.3 “requires WTO Members to protect health registration data from disclosure or unfair commercial use, but its exact boundaries of “unfair commercial use” are not entirely clear (p. 26).

unfair commercial manner. Considerable room has been left to Members for defining the grounds for the application of these exceptions.

In implementing the obligation to protect against unfair commercial use, the Member States can determine, in accordance with their own values and practices, the standards demarcating dishonest commercial practices. Further, the TRIPS Agreement has deferred to Members the determination of the legal means to be used in order to make such protection effective. Hence, Members may opt for means of protection against unfair commercial use which allow for the approval of “similar” products without the use of the data or relying on them. Members may also opt, but are not obliged to, grant “TRIPS-plus” protection on the basis of data exclusivity, as some countries currently do.

In making such choices, policymakers will have to weigh the protection of the interests of originator companies against the importance of creating a competitive environment in order to increase access to medicines that are outside patent protection. From a public health perspective, the introduction of TRIPS-plus standards does not seem the best approach for developing countries.

In sum, developing countries should carefully consider the scope of regulations on approval of pharmaceutical products. Such regulations should be enacted with a pro-competitive intent, in a manner that maximizes legitimate competition and access to drugs, while respecting the legitimate interests of the originators of data in accordance with the standards of protection established by the TRIPS Agreement.

ANNEX 1

Exclusive Use of Data and Compensation Under the U.S. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)

1. Under the “exclusive use” provision, some data are temporarily protected from use by a data submitter’s competitors. FIFRA § 3(c) (1) (D) (i). Registrants are granted a ten-year period of exclusive use for data on new active ingredients first registered after September 30, 1978. FIFRA § 3(c) (1) (D) (i). During that period, no other applicant may use the data to support an application for registration. To be eligible for exclusive use, data must pertain to a “new” complete data package. The second registrant, however, is not necessarily required to duplicate exactly the original submitter’s data package.
2. Under the “data compensation” provision, most data can be used by any company willing to pay compensation to the data submitter. FIFRA § 3(c) (1) (D) (ii). Compensation is required whenever data submitted after December 31, 1969 is considered by EPA in support of another company’s registration. § 3(c) (1) (D) (ii). The duty to pay compensation, however, ends fifteen years after the data are submitted, after which no further payment is required for use of the data. § 3(c) (1) (D) (iii). In the case of an active ingredient subject to exclusive use protection, the data are subject to compensation for five years after the ten-year period of exclusivity expires.
3. Under the “joint data development” provision, two or more registrants can agree to develop jointly, or to share the cost of, new data needed for re-registration or to respond to data call-ins. FIFRA § 3(c) (2) (B) (ii). Registrants may agree to develop jointly new data needed by EPA for re-registration. FIFRA § 3(e) (2) (B) (ii). Applicants for re-registration which are not developing re-registration data either alone or jointly must offer to share in the cost of the data being developed by other registrants. See FIFRA §§ 4(d) (3) (B) (ii), 4(e) (1) (H) (ii). FIFRA does not establish a formula or standard for determining the amount of compensation under § 3(c) (1) (D) or the manner in which costs should be shared under § 3(c) (1) (D). Instead, the statute leaves it to the parties themselves to work out compensation or cost sharing arrangements, or to agree upon a dispute resolution procedure. Any party, however, has the right to initiate binding arbitration proceedings in order to resolve a data compensation or cost sharing dispute. FIFRA § 3(d) (1) (D) (ii), 3(c) (2) (B) (iii).
4. Under FIFRA’s binding arbitration provisions, data compensation or cost sharing disputes can be resolved by a neutral arbitrator. FIFRA § 3(c) (1) (D) (ii), 3(c) (2) (B) (iii). In the *Thomas v. Union Carbide Agricultural Products Co.*, 473 U.S. 568 (1985) case, several pesticide manufacturers challenged the FIFRA arbitration system on the grounds that it delegated too much power to an arbitrator to determine compensation, without review of the soundness of arbitration awards by the federal courts. The Supreme Court concluded that this delegation of adjudicatory power to arbitrators, rather than the courts, does not violate the “separation of powers” required by the Constitution. 473 U.S. at 592-93. A federal district court subsequently held that the lack of a standard in FIFRA for measuring compensation is not unconstitutional. *PPG Industries v. Stauffer Chemical Co.*, 637 F. Supp. 85 (D.D.C.1986), *appeal dismissed*, No. 86-5502 (D.C. Cir.Nov.4, 1987).

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CHAPTER IV

IMPLICATIONS OF THE DOHA DECLARATION ON THE TRIPS AGREEMENT AND PUBLIC HEALTH

EXECUTIVE SUMMARY

1. The adoption of the Doha Ministerial Declaration on TRIPS and Public Health was the outcome of carefully elaborated strategy by developing countries and a significant achievement for those nations.
2. The Doha Declaration recognizes the “gravity” of the public health problems afflicting many developing and LDCs, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics. But the Declaration reflects the concerns of developing countries and LDCs about the implications of the TRIPS Agreement with regard to public health in general, without limitation to certain diseases.
3. While acknowledging the role of intellectual property protection “for the development of new medicines”, the Declaration specifically recognizes concerns about its effects on prices.
4. The Declaration affirms that “the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health”, and that it should be interpreted accordingly.
5. In establishing that Public Health is a clearly stated purpose of the Agreement, the Doha Declaration establishes a specific rule of interpretation that gives content to the general interpretive provisions of the Vienna Convention on the Law of the Treaties on which GATT/WTO jurisprudence has been built up. Therefore, in cases of ambiguity, panels and the Appellate Body should opt for interpretations that are effectively “supportive of WTO Members' right to protect Public Health”.
6. The confirmation that the TRIPS Agreement has left room for flexibility at the national level has important political and legal implications. It indicates that the pressures to impede the use of available flexibilities run counter to the spirit and purpose of the TRIPS Agreement. In legal terms, it means that panels and the Appellate Body must interpret the Agreement and the laws and regulations adopted to implement it in light of the public health needs of individual Members.
7. The Declaration clarifies that “public health crises” can represent “a national emergency or other circumstances of extreme urgency”, and that an “emergency” may be either a short-term problem, or a long-lasting situation. The Declaration also places the burden on a complaining Member to prove that an emergency or urgency does not exist.
8. The Doha Declaration clarifies Members’ right to adopt an international principle of exhaustion of rights (determining the rules by which parallel imports may be accepted). The Declaration states that “the effect of the provisions in the TRIPS Agreement ... is to leave each Member free to establish its own regime for such exhaustion without challenge”.

9. The Declaration recognizes an unresolved problem relating to TRIPS and Public Health – the use of compulsory licensing in countries with little or no manufacturing capacity or insufficient market demand – and commits the governing body of the TRIPS, the TRIPS Council, to reach a solution in 2002.

10. In considering various approaches to the problem of compulsory licensing in countries with little or no manufacturing capacity or insufficient market demand, Members must be mindful of choosing an approach that provides adequate incentives for the production and export of the medicines in need.

11. Desirable features of any possible solution to the problem of compulsory licensing in countries with little or no manufacturing capacity or insufficient market demand would include: a stable international legal framework; transparency and predictability of the applicable rules in the exporting and importing countries; simple and speedy legal procedures in the exporting and importing countries; equality of opportunities for countries in need of medicines, even for products not patented in the importing country; facilitation of a multiplicity of potential suppliers of the required medicines, both from developed and developing countries; and broad coverage in terms of health problems and the range of medicines.

12. The Doha Declaration permits LDCs to opt for an extension of the transitional period provided for under Article 66.1 of the TRIPS Agreement in relation to pharmaceutical patents. However, because all but a few LDCs already grant patent protection to pharmaceuticals, this apparent concession to LDCs may have little practical effect.

13. It is implicit within the Doha Declaration that differentiation in patent rules may be necessary to protect public health. The singling out of public health, and in particular pharmaceuticals, as an issue needing special attention in TRIPS implementation constitutes recognition that public health-related patents may be treated differently from other patents.

14. The Doha Declaration is a strong political statement that can make it easier for developing countries to adopt measures necessary to ensure access to health care without the fear of being dragged into a legal battle. The Declaration is also a Ministerial decision with legal effects on the Members and on the WTO bodies, particularly the Dispute Settlement Body and the Council for TRIPS.

INTRODUCTION

At the Doha World Trade Organization (WTO) Ministerial Conference (9-14 November 2001), the WTO Members took the unprecedented step of adopting a special declaration¹ on issues related to the Agreement on Trade-Related Aspects of Intellectual Property (TRIPS) and Public Health.² Discussion on this declaration was one of the outstanding issues at the Conference,³

¹ Paragraph 17 of the general Ministerial Declaration states: “We stress the importance we attach to implementation and interpretation of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) in a manner supportive of public health, by promoting both access to existing medicines and research and development into new medicines and, in this connection, are adopting a separate Declaration”.

² “Doha Ministerial Declaration on the TRIPS Agreement and Public Health” (hereinafter “the Doha Declaration”), WT/MIN(01)/DEC/W/2, 14 November 2001 (see the full text in Annex 1).

³ The Director General of WTO emphasized the importance of this issue on the opening day of the Conference, indicating that agreement on public health and TRIPS was the “deal breaker” of the new round. Pascal Lamy,

which launched a new round of trade negotiations on a broad range of issues.⁴ This was the first outcome of a process that started in early 2001 when, upon the request of the African Group, the Council for TRIPS agreed to deal specifically with the relationship between the TRIPS Agreement and Public Health.

The African Group's request, supported by other developing countries, reflected growing concerns about the implications of the TRIPS Agreement (particularly the Agreement's provisions on patents) with regard to access to drugs. The HIV crisis in Sub-Saharan African countries, the attempts by the pharmaceutical industry, backed by some governments,⁵ to block the implementation of TRIPS-compatible measures by the South African Government, and the complaint brought by the USA against Brazil in relation to compulsory licences,⁶ were perceived as manifestations of a conflict between the recognition of intellectual property rights (IPRs) and essential public health objectives. Although one of the stated goals of the TRIPS Agreement was to reduce tensions arising from intellectual property protection,⁷ intellectual property protection for pharmaceuticals and its effects on public health, and access to drugs in particular, remained a highly controversial issue.⁸

The developing countries' move to specifically address public health issues at the Council for TRIPS was grounded on the conviction that the TRIPS Agreement should not prevent Members from adopting measures necessary to ensure access to medicines and to satisfy other public health needs. Several documents, particularly by WHO⁹ and UNCTAD,¹⁰ as well as extensive academic work¹¹ and NGO statements,¹² had highlighted the flexibility allowed by the TRIPS Agreement, especially in relation to exceptions to patent rights, parallel imports and compulsory licensing. The developing countries sought a declaration, not because of the lack of clarity in the Agreement, but as a result of the obstacles that the authorities in those countries had experienced when trying to make effective use of such flexibility at the national level.

the EU Commissioner for Trade, stated at the Conference that "... we must also find the right mix of trade and other policies – consider the passion surrounding our debate of TRIPS and Access to Medicines, which has risen so dramatically to become a clearly defining issue for us this week, and rightly so".

⁴ Including implementation, agriculture, services, industrial tariffs, subsidies, anti-dumping, regional trade agreements and environment.

⁵ US Public Law 105-277 (105th Congress, 1999) established that "...None of the funds appropriated under this heading may be available for assistance for the central Government of the Republic of South Africa, until the Secretary of State reports in writing to the appropriate committees of the Congress on the steps being taken by the United States Government to work with the Government of the Republic of South Africa to negotiate the repeal, suspension, or termination of section 15 (c) of South Africa's Medicines and Related Substances Control Amendment Act No. 90 of 1997". After the adoption of the TRIPS Agreement, the US Government continued to list countries according to the Special 301 section of the US Trade Act, in many cases challenging provisions in national laws relevant to public health.

⁶ The declared intention of the Brazilian Government was to procure anti-retrovirals at prices lower than those charged by patent owners, in the framework of its government-supported program against AIDS. The USA withdrew its complaint upon an agreement with the Brazilian government in March 2001.

⁷ See the Preamble of the Agreement, paragraph 7: "*Emphasizing* the importance of reducing tensions by reaching strengthened commitments to resolve disputes on trade-related intellectual property issues through multilateral procedures".

⁸ See e.g., Abbott, 2002a.

⁹ See, e.g., Velasquez and Boulet (1999).

¹⁰ UNCTAD (1996).

¹¹ See an annotated bibliography in WHO (2001).

¹² See, e.g., Oxfam (2002), Médecins Sans Frontières (2001); VSO (2001).

The relationship between public health and the TRIPS Agreement had been examined in 1996 by the World Health Assembly, which addressed the subject in a resolution on the Revised Drug Strategy.¹³ Subsequent resolutions adopted by the World Health Assembly in 2001¹⁴, addressed the need to evaluate the impact of the TRIPS Agreement on access to drugs, local manufacturing capacity and the development of new drugs.¹⁵

The Council for TRIPS systematically considered the relationship between public health and TRIPS for the first time in a special session in June 2001. A number of developing countries¹⁶ and the European Commission and its Member States¹⁷ each submitted documents to the Council. In August and September 2001, the TRIPS Council held additional sessions for discussions on this issue. At the June meeting, the African Group and other developing countries¹⁸ presented a draft text for a ministerial declaration on the TRIPS Agreement and Public Health. This proposal was a comprehensive text addressing political principles to ensure that the TRIPS Agreement does not undermine the legitimate right of WTO Members to formulate their own public health policies, as well as practical clarifications for provisions related to compulsory licensing, parallel importation, production for export to a country with insufficient production capacity, and data protection (Article 39.3 of the TRIPS Agreement). The text also included a proposal for evaluation of the effects of the TRIPS Agreement, with particular emphasis on access to medicines and research and development for the prevention and treatment of diseases predominantly affecting people in developing and least developed countries (LDCs). The USA, Japan, Switzerland, Australia and Canada circulated a non-paper with alternative text stressing the importance of intellectual property protection for research and development, arguing that intellectual property contributes to public health objectives globally. An EC non-paper was also circulated that proposed possible solutions to the problem of production for exports to fulfil a compulsory licence in a country with no or insufficient production capacity. Negotiations on these texts took place at the General Council.

The eventual adoption of a declaration on Public Health and TRIPS was the outcome of a carefully elaborated strategy by developing countries.¹⁹ Despite the initial resistance by some developed countries,²⁰ the Doha Declaration was adopted by consensus, on the basis of last minute compromises and a delicate balance in wording.²¹

¹³ WHO was mandated "to report on the impact of the work of the WTO with respect to national drug policies and essential drugs and make recommendations for collaboration between WTO and WHO, as appropriate" (Resolution WHA49.14, 25 May 1996).

¹⁴ Resolutions WHA54.10 and WHA54.11.

¹⁵ The UN Sub-Commission for the Promotion and Protection of Human Rights also pointed out the "apparent conflicts between the intellectual property rights regime embodied in the TRIPS Agreement, on the one hand, and international human rights law, on the other", including human rights to food, health and self-determination (Commission on Human Rights, Sub-Commission on the Promotion and Protection of Human Rights, Fifty-second session, Agenda item 4, The Realization of Economic, Social and Cultural Rights, Intellectual Property Rights and Human Rights).

¹⁶ See the submission by the African Group, Barbados, Bolivia, Brazil, Cuba, Dominican Republic, Ecuador, Honduras, India, Indonesia, Jamaica, Pakistan, Paraguay, Philippines, Peru, Sri Lanka, Thailand and Venezuela (IP/C/W/296).

¹⁷ See IP/C/W/280, 12 June 2001.

¹⁸ Bangladesh, Barbados, Bolivia, Brazil, Cuba, Dominican Republic, Ecuador, Haiti, Honduras, India, Indonesia, Jamaica, Pakistan, Paraguay, Philippines, Peru, Sri Lanka, Thailand, and Venezuela.

¹⁹ "Doha is a concrete success to which developing countries and NGOs can point. Whether Doha represents a significant shift in the power of developing countries to influence the standard-setting process in intellectual property within WTO remains a matter of conjecture" (Drahos, 2002, p. 26).

²⁰ For some observers, the "anthrax crisis" shifted the balance to the public interest side in the Doha debate on public health and TRIPS (see, e.g., South Centre, 2001, p. 11). "The US was suddenly faced with a situation

SCOPE

The Doha Declaration includes preambular provisions (paragraphs 1 to 4), a provision aimed at confirming the interpretation of certain rules of the TRIPS Agreement (paragraph 5), and two operative provisions requiring action by the Council for TRIPS in relation to countries with no or insufficient manufacturing capacity in pharmaceuticals (paragraph 6), and for the extension of the transitional period for LDCs in relation to the protection of pharmaceutical products (paragraph 7).

The problems addressed by the Doha Declaration are defined in paragraph 1 in broad terms. Members recognize the “gravity” of the public health problems afflicting many developing and LDCs, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics.

Doha Declaration on TRIPS and Public Health: Paragraph 1

1. We recognize the gravity of the public health problems afflicting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics.

While some developed countries attempted to limit the scope of the Declaration²² to the HIV/AIDS crisis, the adopted text reflects the concerns of developing countries and LDCs about the implications of the TRIPS Agreement with regard to public health in general, without limitation to certain diseases. The reference to some specific “epidemics”²³ does not imply that the Declaration is limited to them. It covers any “public health problem”, including those that may be derived from diseases that affect the population in developing as well as developed countries, such as asthma or cancer.

Further, though access to medicines was the main preoccupation that led to the Doha Declaration, the Declaration covers not only medicines, but any product, method or technology for health care. Thus, the Declaration applies to pharmaceutical products, processes and uses, surgical, therapeutic and diagnostic methods,²⁴ diagnostic kits as well as medical equipment.

where there was a perceived need for immediate and widespread access to a product still on-patent, where the exclusive owner of that patent, Bayer in this case, appeared unable or unwilling to offer enough supplies to meet immediate demand. The US Government’s first instinct was to consider the compulsory licence option and seek out alternative manufacturers.” (Kettler, 2002, p. 9) The Canadian government also took actions to ensure supply of the anti-anthrax drug despite the patent held by Bayer (see, e.g., Harmon, 2001).

²¹ Developing countries, in particular, abandoned for study their original position asking for the declaration to state that “*Nothing in the TRIPS Agreement shall prevent Members from taking measures to protect public health*” (IP/C/W/312, WT/GC/W/450, 4 October 2001), which had been one of the main points of contention during the preparatory work.

²² The disagreement on the scope of the declaration was reflected in the partly bracketed title of the draft declaration (“access to medicines”) (“public health”). Throughout the negotiations, the USA, supported by Switzerland, proposed a text that referred to “health crisis”, “pandemics” and “infectious disease” only. See ’t Hoen, 2001, p. 13.

²³ “Epidemic” is a disease prevalent among a community at a special time; one of the draft texts of the Declaration alluded instead to “pandemics”, that is, a disease prevalent over the whole of the country or over the whole world (*The Concise Oxford Dictionary*, pp. 324 and 738).

²⁴ It should be noted that WTO Members can exclude these methods from patentability (see Article 27.3 (a) of the TRIPS Agreement).

Finally, while patents have been the focus of the debate on this issue, the Declaration applies to all areas of intellectual property covered by the TRIPS Agreement, including protection of test data submitted for the marketing approval of pharmaceuticals.²⁵

THE ROLE OF TRIPS AND IPRS

Doha Declaration on TRIPS and Public Health: Paragraphs 2 and 3

2. We stress the need for the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) to be part of the wider national and international action to address these problems.
3. We recognize that intellectual property protection is important for the development of new medicines. We also recognize the concerns about its effects on prices.

Paragraphs 2 and 3 of the Doha Declaration express the Members' view with regard to the role of TRIPS and IPRs in the context of public health.

Paragraph 2 stresses “the need for” the TRIPS Agreement “to be part of the wider national and international action to address these problems”. This statement, read in conjunction with paragraph 4, seems to indicate that the extent to which the Agreement is part of the problem or of the solution to public health needs, crucially depends on the way in which the Agreement is implemented and interpreted. This paragraph suggests that intellectual property rights are one but not the only factor that affects public health and, in particular, access to drugs.²⁶

The first sentence of paragraph 3 alludes to the “important” role of intellectual property protection “for the development of new medicines”. Unlike other preambular paragraphs, this one specifically refers to “medicines”.²⁷ This statement – welcomed by the pharmaceutical industry – is balanced by the second sentence, which recognizes one of the troubling effects of patent protection: its impact on prices.

The patent system is designed to enable patent holders to set prices higher than those that would be obtained in a competitive market. The Doha Declaration recognizes that the high prices of medicines caused by patent protection are part of the grave problems that afflict developing countries and LDCs and is a “concern” that needs to be addressed. The consensus achieved on patent protection's impact on drug prices may be considered one of the major political achievements of the developing countries in the Doha Ministerial Declaration.

²⁵ See para. 7 of the Declaration.

²⁶ Some analyses, particularly by the pharmaceutical industry, have stressed that access to drugs is fundamentally determined by non-IPR factors, such as health infrastructure and medical services. See, e.g., IPI. See also the US submission to the Council of TRIPS (IP/C/W/340, 14 March 2002).

²⁷ The crucial role of patents in inciting research in drug development has been the subject of extensive academic work, See, e.g. Kettler, 2002.

PUBLIC HEALTH MEASURES

Doha Declaration on TRIPS and Public Health: Paragraph 4

4. We agree that the TRIPS Agreement does not and should not prevent members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all.

In this connection, we reaffirm the right of WTO members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose.

Paragraph 4 of the Doha Declaration was one of the most controversial provisions of the document and the subject of intense negotiations during the preparations for and at the Ministerial Conference in Doha. Developing countries' negotiating target was, as mentioned above, to obtain recognition that nothing in the TRIPS Agreement shall be interpreted as preventing Members from adopting measures necessary to protect public health.

Developing countries were essentially seeking a declaration recognizing their right to implement certain pro-competitive measures, notably compulsory licences and parallel imports, as needed to enhance access to health care. They were frustrated by the opposition and pressure exerted on some countries by the pharmaceutical industry and governments.²⁸ Moreover, some felt that the final proviso in Article 8.1 establishing that any measures adopted, *inter alia*, to protect public health should be consistent with the provisions of the TRIPS Agreement,²⁹ provided less protection for public health than under the corresponding exceptions of Article XX (b) of GATT³⁰ and the Sanitary and Phytosanitary Measures and Technical Barriers to Trade agreements.

Developed countries did not view the TRIPS Agreement as representing a barrier to the achievement of public health objectives, and they were not prepared to undermine any of the obligations under the Agreement.³¹ According to the EU, "the TRIPS Agreement cannot be held responsible for the health crisis in developing countries, while it must not stand in the way for action to combat the crisis". The EU was, consequently, "ready to contribute constructively to any debate concerning the interpretation of its provisions"³²

²⁸ See, e.g., Drahos, 2002.

²⁹ TRIPS Article 8.1: "Members may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development, provided that such measures are consistent with the provisions of this Agreement."

³⁰ GATT Article XX: "Subject to the requirement that such measures are not applied in a manner which would constitute a means of arbitrary or unjustifiable discrimination between countries where the same conditions prevail, or a disguised restriction on international trade, nothing in this Agreement shall be construed to prevent the adoption or enforcement by any contracting party of measures:

...

(b) necessary to protect human, animal or plant life or health;"

³¹ See, e.g., the statement by the US delegation at the special session of the Council for TRIPS of 21 June 2001, IP/C/M/31.

³² IP/C/W/280.

The text, drafted by the chair of the WTO General Council, which provided the basis for the negotiations in Doha, offered two options for paragraph 4:

Option 1

[Nothing in the TRIPS Agreement shall prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement shall be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to ensure access to medicines for all.

In this connection, we reaffirm the right of WTO Members to use, to the full, the provisions in the TRIPS Agreement which provide flexibility for this purpose.]

Option 2

[We affirm a Member's ability to use, to the full, the provisions in the TRIPS Agreement which provide flexibility to address public health crises such as HIV/AIDS and other pandemics, and to that end, that a Member is able to take measures necessary to address these public health crises, in particular to secure affordable access to medicines. Further, we agree that this Declaration does not add to or diminish the rights and obligations of Members provided in the TRIPS Agreement. With a view to facilitating the use of this flexibility by providing greater certainty, we agree on the following clarifications.]³³

The wording of the first part of paragraph 4 reflects the delicate compromise reached in Doha. It reaffirms Members' rights to take measures "to protect public health", in a much less elaborated way than article XX (b) of GATT and the respective provisions in the SPS and TBT agreements.³⁴

A possible interpretation for paragraph 4 is that the TRIPS Agreement does not raise conflicts with public health. Paragraph 4 would constitute a statement of fact ("the TRIPS Agreement does not ... prevent ...") rather than a rebalancing of the Agreement in the sense that public health overrides commercial interests. Thus, for the European Commission, "the issue is not whether or not intellectual property overrides public health or vice versa. Intellectual property and public health can and should be mutually supportive because without effective medicines, public health policies would be hampered".³⁵ In the view of the European Commission, the statement contained in paragraph 4 "is important in order to give meaning to the obvious principle that a Member's right (or indeed duty) to pursue public health objectives and policies is unaffected by the TRIPS Agreement".³⁶

In order to give meaning to paragraph 4, however, it is possible to interpret that the intention of the Members was to indicate that in cases where there is conflict between IPRs and

³³ During the negotiating process, the European Commission proposed the following compromise text for paragraph 4: "*Nothing in the TRIPS Agreement prevents Members from pursuing and achieving public health objectives. Accordingly, the TRIPS Agreement shall be interpreted and implemented in a manner supportive of WTO Members' ability to enhance access to affordable medicines for all in the context of public health objectives*".

³⁴ The "necessity" test, central to those provisions, is not mentioned in the Doha Declaration. On the application of such test in GATT/WTO jurisprudence, see e.g., Correa (2000b).

³⁵ European Commission, 2001, p. 2.

³⁶ Ibid.

public health, the former should not be an obstacle to the realization of the latter.³⁷ A possible reading of this paragraph is that such a conflict may arise, and this is precisely why “the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health”.

As mentioned, a basic issue underlying the discussions leading to the Doha Declaration was the extent to which the final proviso of article 8.1 would mean that intellectual property can override public health. One possible interpretation of this proviso is that, unlike Article XX (b) of the GATT, under the TRIPS Agreement Public Health and other reasons enumerated in Article 8.1 permit Members to adopt measures (e.g. commercialization and price controls), but not to derogate obligations relating to the availability or enforcement of IPRs. However, in the light of paragraph 4 of the Doha Declaration, it may be argued that Article 8.1 would not prevent derogation from certain obligations under the TRIPS Agreement if necessary to address public health needs.

The realization of public health becomes, with the Doha Declaration, a clearly stated **purpose** of the Agreement. In affirming that the TRIPS Agreement, “can and should be interpreted and implemented in a manner supportive of WTO Members’ right to protect public health and, in particular, to promote access to medicines for all”, paragraph 4 gives guidance to panels and the Appellate Body for the interpretation of the Agreement’s provisions in cases involving public health issues. In doing so, Members have developed a specific **rule of interpretation** that gives content to the general interpretive provisions of the Vienna Convention on the Law of the Treaties (hereinafter “the Vienna Convention”) on which GATT/WTO jurisprudence has been built up.³⁸ Therefore, in cases of ambiguity, or where more than one interpretation were possible, panels and the Appellate Body should opt for the interpretation that is effectively “supportive of WTO Members’ right to protect public health”.

It also should be noted that paragraph 4 makes a specific reference to the issue of “access to medicines for all”, indicating that in the interpretation of the Agreement’s obligations, special attention should be given to the achievement of this goal.

Finally, paragraph 4 alludes to the **implementation** of the Agreement, and not only to its interpretation. Implementation takes place at the national level, but is influenced by actions taken by other governments, either in the context of bilateral dealings or in the multilateral framework. The important message of the Declaration in this regard is that the Agreement can be implemented³⁹ in a manner supportive of WTO Members’ right to protect public health. As

³⁷ The Brazilian delegation pointed out at the Doha Ministerial Conference that “in the area of intellectual property, different readings of the TRIPS Agreement have given rise to tensions. To a certain extent, it is natural that conflicts of interests should reflect themselves in divergent interpretations of common rules. But the commercial exploitation of knowledge must not be valued more highly than human life. There are circumstances in which the conflict of interests will require that the State exercise its supreme political responsibility... Brazil promotes and upholds intellectual property rights... However, if circumstances so require it, Brazil, like many other countries, will not hesitate to make full use of the flexibility afforded by the TRIPS Agreement to legitimately safeguard the health of its citizens.” See also, e.g. ‘t Hoen (2001), p. 11; Raja, p. 2002, 14, and the Joint Statement of 14 November 2001, by MSF, Oxfam, TWN, CPT, Consumers International, HAI and The Third World Network Third World Economics, No. 268, 1-15 November 2001.

³⁸ As stated by a panel, the TRIPS Agreement has a “relatively self-contained, *sui generis* status within the WTO”, but it is “an integral part of the WTO system, which itself builds upon the experience of over nearly half a century under the GATT 1947”. See *USA – India – Patent Protection for Agricultural and Chemical Products*, WT/DS50/R, adopted on 16 January 1998, para. 7.19.

³⁹ Since implementation is in the last instance an obligation imposed on Member States, the logical reading of the second sentence of paragraph 4 is that the Agreement should be interpreted and can be implemented in a

a result, other Members should restrain from any action that hinders the exercise of such rights by Members, especially developing countries and LDCs.

According to this paragraph, however, Members not only **can** implement the TRIPS Agreement “in a manner supportive of WTO Members’ right to protect public health”, but they **should** also implement it in that way. This means that all Member countries, including developed countries, are bound to contribute to the solution of the public health problems addressed by the Doha Declaration.⁴⁰ One possible way of doing so would be, for instance, by adopting measures to allow the export of medicines needed in a country with no or insufficient manufacturing capacity, an issue which paragraph 6 of the Declaration requires Members to address (see below).

FLEXIBILITY IN TRIPS

The second part of paragraph 4 of the Doha Declaration reflects one of the main concerns of developing countries in the process leading to the Doha Ministerial.

The concept of “flexibility”⁴¹ as applied to the obligations imposed by the TRIPS Agreement, has been central to several analyses of the TRIPS Agreement⁴² and to the position of developing countries at the Council for TRIPS in the special sessions on TRIPS and health.⁴³ Spelling out some of the available flexibility was the main objective of the Declaration.

The Declaration stresses the flexibility “for this purpose”, that is, for the purpose of adopting measures to protect public health. As indicated by the coverage of paragraph 5, Members, only specified, in a non-exhaustive manner, some of the aspects of the Agreement that provide for such a flexibility (“...we recognize that these flexibilities *include*...”).⁴⁴

The confirmation that the TRIPS Agreement has left room for flexibility at the national level has important political and legal implications. It indicates that the pressures to impede the use of available flexibilities run counter to the spirit and purpose of the TRIPS Agreement, especially in the light of the recognized “gravity of the problems” faced in the area of public health by developing countries and LDCs. In legal terms, such confirmation means that panels and the Appellate Body must interpret the Agreement and the laws and regulations adopted to implement it in light of the public health needs of individual Member States.

manner supportive of WTO Members' right to protect public health.

⁴⁰ See also Paragraph 17 of the general Doha Ministerial Declaration, as quoted in footnote 1 above.

⁴¹ “Flexible” means “easily led, manageable, adaptable, versatile, supple, complacent” (*Concise Oxford Dictionary*, p. 373).

⁴² See, e.g., Correa (2000a); Reichman (1997).

⁴³ The European Commission also held, in its submission of 12 June 2001, that “In the view of the EC and their Member States, the Agreement’s objectives, principles and purpose (set out in Articles 7 and 8), special transitional arrangements and other provisions give these countries a sufficiently wide margin of discretion in implementing it. This margin enables them to set up an intellectual property regime that meets their policy needs and is capable of responding to public health concerns” (IP/C/W/280).

⁴⁴ Note that both the developing countries’ and the EC submissions to the special session of 20 June 2001, mentioned other aspects where members enjoy flexibility, such as the “Bolar provision” and the protection of data submitted for the marketing approval of pharmaceuticals (Article 39.3 of the Agreement). See IP/C/W/296 and IP/C/W/280.

Interpretation

Doha Declaration on TRIPS and Public Health: Sub-paragraph 5 (a)

5. Accordingly and in the light of paragraph 4 above, while maintaining our commitments in the TRIPS Agreement, we recognize that these flexibilities include:

a. In applying the customary rules of interpretation of public international law, each provision of the TRIPS Agreement shall be read in the light of the object and purpose of the Agreement as expressed, in particular, in its objectives and principles.

The objective of developing countries in proposing sub-paragraph 5(a) of the Doha Declaration was to stress the importance of TRIPS Articles 7 and 8 in the interpretation of the Agreement, particularly in the light of Article 31 of the Vienna Convention.⁴⁵ They attained their objective without ignoring, however, that other provisions of the Agreement also contribute to the determination of its object and purpose.

That TRIPS purposes are elaborated in its Articles 7 and 8, but also in other provisions of the Agreement has, in fact, already been recognized in TRIPS/WTO jurisprudence. In the *Canada-Patent protection of pharmaceutical products case*,⁴⁶ the WTO dispute settlement panel argued, in connection with Article 30 of the TRIPS Agreement, that “the goals and the limitations stated in Articles 7 and 8” as well as those of “other provisions of the TRIPS Agreement which indicate its object and purposes ... must obviously be borne in mind” when examining the conditions set forth by said Article. The panel thus determined that Articles 7 and 8 express the “object and purpose” of the TRIPS Agreement, but that these are not the only provisions establishing the Agreement’s objectives.

It is also relevant to note that the EC and their Member States emphasized the key role of Articles 7 and 8 in the interpretation of the TRIPS Agreement, in its submission to the Council for TRIPS of 12 June 2001.⁴⁷ It stated that

“Although Articles 7 and 8 were not drafted as general exception clauses, they are important for interpreting other provisions of the Agreement, including where measures are taken by Members to meet health objectives”.

In fact, the Doha Declaration goes beyond merely confirming the relevance of Articles 7 and 8 for the interpretation of the TRIPS Agreement. It provides an **understanding** about the purpose of the TRIPS Agreement in relation to public health issues, which should guide any future rulings by panels and the Appellate Body dealing with such issues.

⁴⁵ It is unclear why this interpretive rule has been considered as one of the “flexibilities” in paragraph 5. In fact, such rule, properly applied, should ensure that due deference to national law is given in appropriate cases; that is, that the flexibility left to Member States is respected by the DSB.

⁴⁶ WT/DS114/R, 17 March 2000 (hereinafter the “EC-Canada case”).

⁴⁷ See IP/C/W/280.

Compulsory Licences

Doha Declaration on TRIPS and Public Health: Sub-paragraph 5 (b)

5. Accordingly and in the light of paragraph 4 above, while maintaining our commitments in the TRIPS Agreement, we recognize that these flexibilities include:

...

b. Each Member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted.

Developing countries have identified compulsory licensing as one of the key instruments that may limit the exclusive rights of the patent owner when needed to fulfil certain objectives of public policy, particularly in order to ensure the availability of alternative sources for the supply of medicines at lower prices.⁴⁸

Sub-paragraph 5 (b) of the Doha Declaration deals with an issue central to the interests of developing countries. It simply states what is apparent: Article 31 sets forth a number of **conditions** for the granting of compulsory licences (case-by-case determination; prior negotiation, in certain cases, with the patent owner; remuneration, etc.), but it does not limit the **grounds** on which such licences can be granted. Though Article 31 refers to some of the possible grounds (such as emergency and anti-competitive practices) for issuing compulsory licences, it leaves Members full freedom to stipulate other grounds, such as non-working, public health or public interest.

Though sub-paragraph 5 (b) does not add anything substantively to the understanding of TRIPS, the Doha Declaration specifically employs the expression “compulsory licence”, which is not found in the TRIPS Agreement itself.⁴⁹ The use of this terminology may help to create awareness, particularly among health ministries in developing countries and LDCs, about the possible utilization of compulsory licences to meet public health and other objectives.⁵⁰

Emergency

Doha Declaration on TRIPS and Public Health: Sub-paragraph 5 (c)

5. Accordingly and in the light of paragraph 4 above, while maintaining our commitments in the TRIPS Agreement, we recognize that these flexibilities include:

...

c. Each member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.

⁴⁸ See, e.g., Velasquez and Boulet, 1999; Correa (2000a).

⁴⁹ TRIPS Article 31 is entitled “[O]ther use without authorization of the right holder”.

⁵⁰ Despite the fact that the governmental use for a non-commercial purpose of a patent is not mentioned in the commented paragraph, such mechanism can also be important to attain public health objectives.

Paragraph 5 (c) of the Doha Declaration states what is an unquestionable right of Members States: the right to determine “what constitutes a national emergency or other circumstances of extreme urgency”. Such determination may be relevant for the granting of compulsory licences, the establishment of exceptions under Article 30, or the adoption of other measures permitted under Article 8.1 of the Agreement.⁵¹

Paragraph 5 (c) also includes a presumption:

“it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency”.

This provision is important for three reasons. First, it clarifies that “public health crises” can represent “a national emergency or other circumstances of extreme urgency”, thereby allowing for the granting of compulsory licences when provided for under national law⁵² and, pursuant to TRIPS Article 31 (b), without the obligation for prior negotiation with the patent owner.

Second, the reference to “HIV/AIDS, tuberculosis, malaria and other epidemics” indicates that an “emergency” may be not only a short-term problem, but a long-lasting situation, as is the case with the epidemics specifically mentioned for illustrative purposes. This recognition may be deemed an important achievement for developing countries in the Doha Declaration, since it implies that specific measures to deal with an emergency may be adopted and maintained as long as the underlying situation persists, without temporal constraints.

Third, if a Member complains about the qualification of a specific situation by another Member as a “national emergency or other circumstances of extreme urgency”, the language of paragraph 5 (c) places the burden on the complaining Member to prove that such emergency or urgency does not exist. This represents an important difference with respect to earlier GATT/WTO jurisprudence outside of the TRIPS context that, under the “necessity test”, put the burden of proof on the Member invoking an exception to its obligations.⁵³

⁵¹ In May 2002, the Minister of Justice, Legal and Parliamentary Affairs of Zimbabwe issued a Declaration of Period of Emergency (HIV/AIDS) (Notice, 2002). In view of the rapid spread of HIV/AIDS among the population of Zimbabwe, the Minister declared “an emergency for a period of six months, with effect from the date of promulgation of this notice, for the purpose of enabling the State or a person authorised by the Minister under section 34 of the Act (a) to make or use any patented drug, including any anti-retroviral drug, used in the treatment of persons suffering from HIV/AIDS or HIV/AIDS-related conditions; (b) to import any generic drug used in the treatment of persons suffering from HIV/AIDS or HIV/AIDS-related conditions”. A Declaration of Sanitary Emergency until 31 December 2002 was also issued by the Executive Power of Argentina (Decree 486, 12 March, 2002), but it does not make explicit reference to patent law provisions.

⁵² A survey covering the patent laws of 70 developing countries indicates that only 13 have provided for national emergency or health emergency as specific grounds for the granting of compulsory licences. See Thorpe, 2002.

⁵³ See, Correa, 2000b.

Exhaustion

Doha Declaration on TRIPS and Public Health: Sub-paragraph 5 (d)

5. Accordingly and in the light of paragraph 4 above, while maintaining our commitments in the TRIPS Agreement, we recognize that these flexibilities include:

...

d. The effect of the provisions in the TRIPS Agreement that are relevant to the exhaustion of intellectual property rights is to leave each member free to establish its own regime for such exhaustion without challenge, subject to the MFN and national treatment provisions of Articles 3 and 4.

The authorization of parallel imports under an international principle of exhaustion has also been regarded by developing countries as a key component of a patent system sensitive to public health needs. This was one of the key issues raised by pharmaceutical companies against South Africa in the already mentioned case.⁵⁴

Developing countries were keen to clarify in the Doha Declaration the Members' right to adopt an **international** principle of exhaustion of rights,⁵⁵ in accordance with article 6 of the Agreement. Paragraph 5 (d) provides the sought-after clarification. It specifically states that "the effect of the provisions in the TRIPS Agreement... is to leave each Member free to establish its own regime for such exhaustion **without** challenge" (emphasis added).

Though this paragraph does not add substantively to the TRIPS Agreement, it certainly reassures Members wishing to apply an international exhaustion principle that it would be legitimate and fully consistent with the Agreement to do so.

It is necessary to stress that in order to take advantage of this and other flexibilities allowed by the TRIPS Agreement – and confirmed by the Doha Declaration – national laws must incorporate the appropriate rules in the form of compulsory licences, exceptions and other relevant provisions. Such flexibilities do not automatically translate themselves into national regimes, and do not protect governments (or private parties) from legal actions based on national laws and regulations that fail to make use of the TRIPS Agreement's flexibilities. For example, specific legal provisions allowing for parallel imports would be normally necessary in order to benefit from the principle of international exhaustion of rights.⁵⁶

A survey of patent laws in developing countries shows that many of such countries have not or only partially used the flexibilities allowed by the TRIPS Agreement.⁵⁷ The effective implementation of the Doha Declaration in those countries, therefore, would call for an

⁵⁴ See, e.g. Bond, 1999.

⁵⁵ This principle permits the import of a patented product into a country without the authorization of the title holder or his licensees, to the extent that the product has been put on the market elsewhere in a legitimate manner. See, e.g., Velásquez and Boulet, 1999.

⁵⁶ Though in some countries this principle may result from jurisprudential elaboration, it may take a long time to test what the legal solution is. The ensuing uncertainty is likely to discourage or effectively prevent the use of such a mechanism as a means to obtain medicines at lower prices than those domestically available.

⁵⁷ See Thorpe, 2002.

amendment to national laws so as to incorporate the exceptions and safeguards necessary to protect public health.⁵⁸

MEMBERS WITH INSUFFICIENT OR NO MANUFACTURING CAPACITIES

Doha Declaration on TRIPS and Public Health: Paragraph 6

6. We recognize that WTO members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement. We instruct the Council for TRIPS to find an expeditious solution to this problem and to report to the General Council before the end of 2002.

In paragraph 6 the Doha Declaration instructs the Council for TRIPS to address a delicate issue: how can Members lacking or with insufficient manufacturing capacities make effective use of compulsory licensing. The Declaration requests the Council for TRIPS “to find an expeditious solution to this problem and to report to the General Council before the end of 2002”. As discussed below, in order to be effective such a solution should be economically viable, and not only legally acceptable.

A major limitation in compulsory licensing rules under Article 31 (f) of the TRIPS Agreement is the requirement that a product made under a compulsory licence be supplied predominantly to the licensee's domestic market,⁵⁹ unless the licence were issued to remedy anti-competitive practices (Article 31 (k) of the Agreement). This means, in practical terms, that Members with large markets, like India, the UK or the USA, typically could easily grant compulsory licences for the supply of patented medicines to meet public health needs (for instance, those arising from the threat of bioterrorism). However, for Member countries with small markets, like the African countries where the AIDS crisis is most severe, it might be extremely difficult to establish economically viable production if the manufactured product has to be “predominantly” sold in the local market.

The basic problem underlying paragraph 6 is that many developing countries lack or have an insufficient capacity to manufacture medicines on their own. As indicated in Annex 2,⁶⁰ manufacturing capacities in pharmaceuticals are distributed very unevenly in the world. Not many countries have the capacity to produce both active ingredients and formulations, and very few countries maintain significant research and development capabilities.

Given that only a few developing countries have substantial manufacturing capacity in pharmaceuticals, once the TRIPS Agreement becomes fully operative (after 2005), many countries may face difficulties in acquiring medicines at affordable prices. Today, for example, some countries, such as India, do not provide patent protections for pharmaceutical products,

⁵⁸ For possible options for such a reform, see, e.g. Correa, 2000c.

⁵⁹ TRIPS Article 31: “Where the law of a Member allows for other use of the subject matter of a patent without the authorization of the right holder, including use by the government or third parties authorized by the government, the following provisions shall be respected:

...

(f) any such use shall be authorized predominantly for the supply of the domestic market of the Member authorizing such use”.

⁶⁰ See also WHO, 2000, p. 32.

and produce generic versions at a fraction of the price of the patented product. A Member country where the price of patented products is high has the option of issuing a compulsory licence to permit import from such countries. The problem is that, as countries fully comply with the TRIPS Agreement by 2005 at the latest, they will no longer be able to produce and export cheap generic copies of patented medicines. Consequently, the sources of affordable new medicines will dry up and countries without sufficient manufacturing capacity and market demand will not be able to grant a compulsory licence either for the local production or for the importation of such medicines: they will become entirely dependent on the expensive patented versions.⁶¹

This problem had been raised by developing countries during the special sessions on TRIPS and health at the Council for TRIPS, and by the EC and their Member States in its submission of 12 June 2001. Developing countries argued that “nothing in the TRIPS Agreement prevents Members from granting compulsory licences for foreign suppliers to provide medicines in the domestic market... In this respect, the reading of Article 31 (f) should confirm that nothing in the TRIPS Agreement will prevent Members from granting compulsory licences to supply foreign markets”.⁶²

The EC and their Member States noted the problems posed by the limitation imposed by Article 31 (f). A Member is free to grant a compulsory licence for the importation of goods which are under patent in its own territory, as long as the imported goods have been produced in a country where they are not patented, or where the term of protection has expired. However, when a patent exists in the potential supplier country, the patent owner may block exports to the country in need of the medicines.⁶³ Moreover, since Article 31 (f) requires that a compulsory licensee predominantly supply the domestic market, that provision would prevent the granting of a compulsory licence exclusively or mainly to export to a country in need of certain medicines.

Addressed Problem

To determine the problem addressed under paragraph 6, it must be read in the context of paragraphs 1 to 4 of the Doha Declaration. As mentioned above, though the Declaration specially refers to the problems resulting “from HIV/AIDS, tuberculosis, malaria and other epidemics”, it is intended to provide solutions to “health problems” in general. There is nothing in paragraph 6 limiting its application to cases of crises or public emergency.

Paragraph 6 refers to “manufacturing” capacities in the pharmaceutical sector. “Manufacturing” is the “making of articles by physical labour or machinery, **especially on large scale**”.⁶⁴ This suggests – based on the ordinary meaning of the words used, as mandated by the Vienna Convention – that the Declaration is intended to address the problems that arise when production on a large scale, that is, in an economically viable manner, cannot be conducted.

The pharmaceutical sector includes – as indicated in Annex 2 – both the manufacturing of **active ingredients** (that is, the compounds that possess therapeutic activity) as well as of finished products or **pharmaceutical formulations** (active ingredients and the excipients

⁶¹ See, e.g., Oxfam, 2002.

⁶² See IP/C/W/296.

⁶³ See IP/C/W/280.

⁶⁴ *The Concise Oxford Dictionary*, p. 617 (emphasis added).

added, as necessary, for the administration of a medicine to a patient). Paragraph 6 does not distinguish between these two categories of activities. It should be interpreted, therefore, that paragraph 6 addresses the lack of or insufficient capacity either to produce active ingredients or pharmaceutical formulations or both.

A country may have the technical capacity to produce active ingredients or formulations, but such production may not be economically viable. One of the main objectives of the Doha Declaration is to “promote access to medicines for all” (paragraph 4). This objective would not be achieved if low-priced medicines (and other health-care products) could not be produced because meaningful economies of scale were out of reach. A “solution” under paragraph 6 may be illusory if it does not benefit countries where manufacturing may be technically feasible but not economically viable.

The determination of the coverage of paragraph 6 raises other interpretive issues, namely:

- (a) Does paragraph 6 refer to medicines only, or does it encompass any health care product? To the extent that a product is expended through pharmacies (such as diagnostic kits), it will fall under the ordinary meaning of a “pharmaceutical” product.⁶⁵
- (b) Does the notion of “capacity”⁶⁶ refers to the general capacity to manufacture or to the capacity to manufacture a particular product? A country may have manufacturing capacity **in general** to produce active ingredients or formulations, but lack the equipment, technology or access to the intermediate chemicals necessary to produce a **particular** product. For instance, some countries may be able to manufacture relatively simple drugs, but not anti-retrovirals, where production and quality control standards are extraordinarily important because of the risk of drug resistance and/or toxicity. A reasonable reading of paragraph 6 suggests that it is intended to address both the cases of general and particular lack or insufficient capacity, since otherwise it would not be possible for the concerned country to address its “health problems” (paragraph 1) and to “protect public health” (paragraph 4).

Under this interpretation, the solution to be worked out in line with paragraph 6 should not be based on the determination of categories of Member countries with or without manufacturing capacity, or with or without a sufficient manufacturing capacity. Rather a solution should apply to any Member, or at least to **any** developing country or LDC where the effective use of compulsory licensing is not possible because of capacity limitations and insufficient market demand.

- (c) Who can receive compulsory licences in the exporting or the importing country? Pursuant to paragraph 6, recipients clearly may include State as well as commercial entities. There is no limitation under Article 31 in this respect, and it would be contrary to the objective of the Doha Declaration to exclude the possibility of granting the required compulsory licence to a for-profit entity.

⁶⁵ “Pharmaceutical” is “of or engaged in pharmacy; of the use or sale of medicinal drugs” (The Concise Oxford Dictionary, p. 768). It also opens the possibility, given the broad scope of the Doha Declaration, as mentioned above, for Members to discuss the inclusion of other products, such as testing equipment.

⁶⁶ “Capacity” is the “power of containing, receiving, experiencing or producing” (The Concise Oxford Dictionary, p. 136).

- (d) Where should potential suppliers of medicines be located? Potential suppliers of the required medicines may be located in developed and developing countries alike.⁶⁷ The purpose of the Doha Declaration is to alleviate grave public health problems, independent of the location of the source of supply. Hence, in order to effectively implement the Declaration, both developed and developing countries should introduce legislative changes, as necessary, to allow exports to countries in need.
- (e) Can countries where no patent protection exists benefit from a solution under paragraph 6? Since a compulsory licence can only be granted when a patent exists, paragraph 6 seems to relate only to cases where a pharmaceutical patent is in force in the importing country. This would include cases where product or process patents have been granted,⁶⁸ but would exclude and seriously disadvantage⁶⁹ countries where no patent protection for pharmaceuticals is granted,⁷⁰ or even countries where such protection exists but where the needed product or process is, for any reason,⁷¹ off-patent. Finding a solution to the problems of these latter countries will be an essential component in the implementation of the Doha Declaration, if not specifically under paragraph 6, as a part of the “action” necessary to address the public health problems that afflict developing countries and LDCs (see paragraphs 1 and 2 of the Declaration).⁷²
- (f) Does paragraph 6 cover cases where an authorization for governmental use has been accorded? Though it is possible to distinguish between “compulsory licences” and authorizations for governmental use,⁷³ their effect is similar and they are jointly treated in Article 31 of the TRIPS Agreement. There is no reason to exclude government use authorizations from the coverage of paragraph 6.

Box 1

Designing a Solution to the Paragraph 6 Problem

In considering approaches to implement paragraph 6, it is vital to consider the efficiency and workability of alternative approaches. This will not only depend on the decisions adopted in the framework of WTO but, crucially, on the steps taken at the national level to introduce legislative changes necessary to implement the adopted solution.

⁶⁷ Thus, in July 2000, a Canadian generic pharmaceutical manufacturer announced that it could supply, at cost, alternatives to the major AIDS treatments for developing countries within months, if the Canadian Federal Government granted the needed compulsory licences under the Patent Act.

⁶⁸ It would also cover cases where patents on new uses have been conferred, if admissible under the relevant national law.

⁶⁹ See the joint letter sent on January 28, 2002 to the TRIPS Council members by Consumer Project on Technology, Médecins Sans Frontières, Third World Network, Oxfam, Health Gap Coalition and Essential Action.

⁷⁰ As discussed below, LDCs have been authorized by the Doha Declaration to delay such protection until 2016.

⁷¹ Because a patent has not been applied for, has been rejected or cancelled.

⁷² It should be noted that nothing would prevent the Council for TRIPS from considering a situation not expressly mentioned in paragraph 6 of the Declaration.

⁷³ While in the case of compulsory licence a private party may be authorized to use and commercialize the invention for a profit, under governmental use the exploitation of the invention should be made to satisfy a governmental need, for non-profit purposes. This includes the case – for example – in which a private company produces a patented drug, as a subcontractor, to supply the government, who distributes the drug through public hospitals.

Some of the desired features of any possible solution would include:

- stability of the international legal framework, in order to ensure a long-term solution;
- transparency and predictability of the applicable rules in the exporting and importing countries, so as to provide the required incentives to the private sector to act within the established framework;
- simple and speedy legal procedures in the exporting and importing countries, to allow for the fast supply of needed medicines, with the required quantity and quality;
- equality of opportunities for countries in need of medicines, even for products not patented in the importing country and for countries which are not WTO Members;⁷⁴
- facilitation of a multiplicity of potential suppliers of the required medicines, both from developed and developing countries;
- broad coverage in terms of health problems and the range of medicines (not limited to certain diseases or products).

In addition, the legal solution should not be encumbered with limitative conditions that could deprive it of practical value, nor should it limit the grounds for granting compulsory licences.

Possible Approaches

Different approaches may be followed in order to address the problem posed by lack of or insufficient manufacturing capacity in pharmaceuticals. The main options include:

- a. To amend⁷⁵ Article 31 (f), in order to allow for the granting of a compulsory licence which is not “predominantly” for the domestic market;
- b. To provide for a specific exception for exports under Article 30 of the TRIPS Agreement,⁷⁶ possibly by means of an authoritative interpretation;⁷⁷
- c. To agree on a moratorium with regard to complaints against countries that export some medicines to countries in need, under certain conditions;⁷⁸
- d. To declare exports to a country eligible under paragraph 6 as non-judicable under the WTO rules;⁷⁹
- e. To allow a Member to issue a compulsory licence to a manufacturer in another country, provided the government of that other country recognized the licence (which it would not be obliged to do under the Agreement),⁸⁰ and provided that all the goods manufactured under the licence were exported to the country granting the licence.⁸¹

⁷⁴ There are a significant number of countries which are not members of the WTO (while many are negotiating accession) that may face the problems addressed in paragraph 6.

⁷⁵ In the absence of consensus, an amendment to a WTO Multilateral Trade Agreement must be approved by a two-thirds majority, but it only becomes binding on Members that accepted it. An amendment may also be adopted by a three-fourths majority as binding on all Members, but any Member which has not accepted it shall be free to withdraw from the WTO or to remain as a Member with the consent of the Ministerial Conference (Article X.1 and 2 of the Agreement Establishing the WTO).

⁷⁶ See the letter of 28 January 2002 sent to the Members of the Council for TRIPS by Consumer Project on Technology, Médecins Sans Frontières, Third World Network, Oxfam, Health Gap Coalition and Essential Action.

⁷⁷ An authoritative interpretation needs to be adopted by a three-fourths majority of Members, and should not be used “in a manner that would undermine the amendments provision of article X” (article IX.2 of the WTO Agreement).

⁷⁸ Proposed by the USA delegation at the March 2002 session of the Council for TRIPS.

⁷⁹ Unlike the moratorium, this solution would be permanent. See, e.g. Attaran, 2002.

⁸⁰ The effective application of this option faces jurisdictional barriers. An authority in a given country can only

Other options include the transfer of technology in order to create manufacturing capacity in the country in need,⁸² the creation of a “regional pharmaceutical supply centre”,⁸³ and the establishment of “pharmaceutical production export zones”.⁸⁴

Some of the options mentioned above have been examined at the session of the Council for TRIPS held in March 2002 (see Box 2).

Box 2

Proposals relating to implementation of Paragraph 6 discussed at the Council for TRIPS (March 2002)

The EC and their Member States submitted two possible options to address the paragraph 6 problem:⁸⁵

- 1) an amendment to Article 31 of the TRIPS Agreement in order to carve out an exception to Article 31 (f) for exports under compulsory licences, under certain conditions, of products needed to combat serious public health problems; or
- 2) an interpretation of the limited exceptions clause of Article 30 of the TRIPS Agreement in a way to allow production for export, to certain countries and under certain conditions, of products needed to combat serious public health problems;

Option (1) would be subject to three conditions: criteria ensuring that importing countries actually face serious public health problems, safeguards against re-exportation of the cut-price generics, particularly to rich countries, and reporting requirements that would inform trading partners of such action.

Option (2) would be subject to two minimum conditions: the entirety of the product must be exported to the country with the public health problem, and re-export from the importing country would be prohibited.⁸⁶

- 3) The USA proposed a moratorium whereby WTO Members would agree not to bring a WTO complaint against countries that export some medicines to countries in need, so long as certain other conditions are met.⁸⁷

grant a compulsory licence valid in that country. There is no obligation on other countries to admit extraterritorial effects of such a grant. This could be done, however, under the concept of “Comity See”, e.g., Abbott, 2002b, p. 29.

⁸¹ See IP/C/W/280.

⁸² According to the statement by Kenya on behalf of developing countries at the March 2002 session of the Council for TRIPS, “any expeditious solution to address the problem acknowledged in Paragraph 6 should not detract the TRIPS Council from the need to consider measures that support the acquisition of all necessary technology and the building of a sound technological base including in respect of medical technology; this is the proven sustainable way to address the public health and public policy concerns of developing countries and least developed countries”. This would be, however, a long-term solution and not an “expeditious” solution as envisaged under paragraph 6.

⁸³ See Reichman, 2002.

⁸⁴ See, e.g., Abbott, 2002b.

⁸⁵ See IP/C/W/339, 4 March 2002.

⁸⁶ In addition, the EC and their Member States indicated that the Article 30 exception should conform with other TRIPS provisions, in particular Article 27.1.

⁸⁷ According to the USA submission, any solution should only apply to epidemics referred to in the Doha Declaration – HIV/AIDS, tuberculosis and malaria – and only to countries with insufficient or no

On behalf of the African Group, Brazil, Cuba, Dominican Republic, Ecuador, Honduras, India, Indonesia, Jamaica, Malaysia, Sri Lanka and Thailand, Kenya made a statement suggesting, as possible options, an amendment to Article 31 in order to eliminate paragraph "f", or to develop an authoritative interpretation that would recognize the right of Members to allow the production without the consent of the patent holder to address public health needs in another country, under Article 30 of the TRIPS Agreement.

It is beyond the remit of this study to examine thoroughly the merits of the different options mentioned above. In the light of the previous analysis, however, some of the advantages and disadvantages of the proposals described in Box 1 are considered in more detail.

(a) Article 31 (f)

Article 31 (f) prevents the granting of a compulsory licence exclusively or mainly to export to a country in need of certain medicines.⁸⁸

The option based on the amendment of Article 31 (f) of the TRIPS Agreement would require three steps: (a) a political decision to open the Agreement to renegotiation and an approval of the agreed modification; (b) a change in the national law of the potential exporting country in order to delete the "predominantly" requirement already incorporated in many laws, and to specify as a ground for a compulsory licence the need to address a paragraph 6 situation, and (c) the granting in the exporting country of a compulsory licence upon request of an interested party.

The first step may encounter political resistance by those countries that are reluctant to amend any part of the Agreement, because of the risk of stimulating the renegotiation of other provisions. The second step is likely to require action by national parliaments. Legislative processes are generally complex and lengthy. In addition, though domestic producers may benefit from new export opportunities, an amendment to the national compulsory licence system may be perceived as benefiting mainly the population in a foreign country, and may fail to gain sufficient political support. Finally, if the law were amended, the government would still need to exercise its power to grant a particular compulsory licence, provided that requests were made for that purpose.

Where there was a request for a compulsory licence, it would be necessary to undertake a prior negotiation on commercially reasonable terms with the patent holder, and to determine the level of royalty compensation to be paid upon issuance of a compulsory licence. Moreover, the granting authority may have to make a determination of the level of "capacity" of the importing country and of the public health need, if these conditions were required under the Article 31 (f) amendment and/or under the national law. Compulsory licence procedures, in

pharmaceutical manufacturing capability. The USA also questioned whether commercial entities should be allowed to produce under such licences. See IP/C/W/340, 14 March 2002.

⁸⁸ It is interesting to note, however, that some developed countries provide for compulsory licences or governmental use for export without the limitation imposed by Article 31 (f). Such is the case of Article 168 of the Australian Patent Act and Article 55 (2) of the Patent Act of New Zealand, which permit exports under an agreement with a foreign country to supply products required for the defence of that country. Article 48B(d)(i) of the UK Patent Act provides for a compulsory licence in respect of a patent whose proprietor is not a WTO proprietor when the owner's failure to licence the patent on reasonable grounds means that a market for the export a patented product made in the UK is not being supplied.

addition, may be costly and burdensome, and may be subject to industry's opposition and give rise to political pressures at the bilateral level.

A possible solution based on an amendment to Article 31 (f) may also provide for double compensation to be paid to the patent holder (in both the importing and exporting countries), thus increasing the cost and possibly reducing access to the products in need.

The three-step process required for the compulsory licence option may mean that a practical solution may be years away, and does not constitute an "expeditious" solution.

(b) Article 30

Article 30 allows Members to provide for limited exceptions to the exclusive rights conferred by a patent, that is, to define acts that would not be deemed as infringing when made without the authorization of the patent owner. Such exceptions may include, for instance, acts of experimentation and the request for marketing approval of a pharmaceutical product before the expiration of the patent (known as the "Bolar exception").⁸⁹

An Article 30 solution may be more streamlined and easier to implement than an Article 31 (f) solution, since no amendment and parliamentary approval is involved, and the exporting country would not be bound to grant case-by-case compulsory licences.

The solution based on an interpretation of Article 30 avoids two of the three steps mentioned above and the double compensation issue. There is no need to amend the Agreement; the TRIPS Council could simply provide an authoritative interpretation. An amendment to national law in exporting countries would be required (a step that may encounter the same type of difficulties as mentioned above), but once provided, the exception could be invoked without the need to obtain, case-by-case, a compulsory licence from the government of the exporting country. The exception could be invoked at any time, and without time limit, by any third party. Finally, compensation would only be payable under the compulsory licence in the importing country.

An Article 30 solution must overcome possible objections about the consistency of an exports exception with the conditions of Article 30,⁹⁰ which have been narrowly interpreted by a panel in the EC-Canada case.⁹¹

⁸⁹ See, e.g., Velasquez and Boulet, 1999.

⁹⁰ A possible difficulty is that any interpretation may be read across to other Articles of TRIPS. See IP/C/W/340.

⁹¹ WT/DS114/R, 17 March 2000.

The panel provided an interpretation of what "limited" means in Article 30:

"The word "exception" by itself connotes a limited derogation, one that does not undercut the body of rules from which it is made. When a treaty uses the term "limited exception", the word "limited" must be given a meaning separate from the limitation implicit in the word "exception" itself. The term "limited exception" must therefore be read to connote a narrow exception – one which makes only a small diminution of the rights in question (para. 7.30)

In the absence of other indications, the Panel concluded that it would be justified in reading the text literally, focusing on the extent to which legal rights have been curtailed, rather than the size or extent of the economic impact. In support of this conclusion, the Panel noted that the following two conditions of Article 30 ask more particularly about the economic impact of the exception, and provide two sets of standards by which such impact may be judged. The term "limited exceptions" is the only

It must be noted, however, that the interpretation given by a panel (or the Appellate Body) to a particular provision does not bind Members, who may depart from such interpretation in exercising their “exclusive authority to adopt interpretations” (Article IX.2 of the WTO Agreement). In fact, in adopting the Doha Declaration, Members have established a precedent for reading the exception in Article 30 in a broader way than the panel in the EC-Canada case, whenever public health issues are at stake. In effect, since the TRIPS Agreement is “a part of the wider national and international action” to address public health problems (paragraph 2 of the Doha Declaration), the panels and the Appellate Body should consider the public-health implications of exceptions to the patent owner’s exclusive rights.

An export exception, if circumscribed to situations defined in accordance with paragraph 6, may be reasonably deemed to fall under the three conditions stipulated by Article 30. The exception

- would be “limited” to specified circumstances;
- would “not unreasonably conflict with a normal exploitation of the invention” since, though exportation is a normal mode of exploiting an invention, supplying of a market at low prices by a third party may not conflict with such exploitation (which is normally made in order to obtain the monopolistic rent generated by patent protection);
- would not “unreasonably prejudice the legitimate interests of the patent owner”, to the extent that safeguards are adopted in order to avoid diversion to other markets;
- would positively “take account of the legitimate interests of third parties” (consumers in the importing country).⁹²

(c) *Moratorium*

A moratorium⁹³ does not imply any change of the substantive treaty obligations; it only temporarily suspends their operation.⁹⁴ The moratorium approach offers an “expeditious”

one of the three conditions in Article 30 under which the extent of the curtailment of rights as such is dealt with” (para. 7.31).

The panel also considered what “normal exploitation” means. It argued that:

“The normal practice of exploitation by patent owners, as with owners of any other intellectual property right, is to exclude all forms of competition that could detract significantly from the economic returns anticipated from a patent’s grant of market exclusivity. The specific forms of patent exploitation are not static, of course, for to be effective exploitation must adapt to changing forms of competition due to technological development and the evolution of marketing practices. Protection of all normal exploitation practices is a key element of the policy reflected in all patent laws” (para. 7.55).

Finally, the panel indicated that “legitimate interests” must be “construed as a concept broader than legal interests” (para 7.71), but did not address what “unreasonably” means, since the panel’s analysis led to the conclusion that there was not in the case “conflict” with the normal exploitation of a patent, and therefore it was not necessary to elucidate whether the Canadian exception was reasonable or not. If a conflict of such kind were found, however, the way in which “unreasonably” were to be interpreted would acquire crucial importance and become a delicate issue. For an interpretation of Article 30 in the context of paragraph 6, see Abbott, 2002b.

⁹² Questions may also arise as to whether – given the territoriality of patent grants – the interests of the consumers in a foreign country may be deemed a “legitimate interest” for the purposes of Article 30. Canada held, in this regard, in the EC-Canada case that “[a]s the TRIPS system was designed to be international and so to extend across borders there was no reason why the legitimate interests of the third parties in other countries could not be taken into account when applying a limited exception under Article 30” (para.4.38(d)).

response to the problem posed by paragraph 6, but not a “solution”, since it would not be straightforward enough either to induce potential exporting countries to change their legislation to permit production for export, or to induce generic manufacturers to invest in creating or increasing export capacity. In addition, it is unclear what procedures would be applied in order to adopt a moratorium, and whether formal changes to the TRIPS Agreement would be necessary.⁹⁵

Though most waivers apply to just one named contracting party, in GATT history at least two waivers were framed in general terms to apply to any contracting party who fulfilled the criteria. At their eleventh session, the Contracting Parties formulated a series of guidelines for the issuance of waivers, partly as a response to the perception that a waiver could produce an effect substantially the same as an amendment (Jackson, 2000, p. 29).⁹⁶ In exceptional circumstances, the Ministerial Conference can, by a three-fourth majority, waive an obligation imposed on a Member, for a determined period. A waiver is bureaucratic to administer, since it requires regular renewal by the Ministerial Conference if granted for a period of more than one year.⁹⁷

The main characteristics and some implications of the three above-examined proposed solutions are presented in Table 1.

Table 1

The main proposed solutions in comparison

Option	Steps to achieve	Conditions ⁹⁸	Considerations	Considerations
a) <u>To amend</u> Article 31 (f) to carve out an exception for exports under CL, <u>or</u> to remove limitations on export entirely.	a) Agreement to reopen TRIPS and approval of amendment b) Changes in national laws c) Grant of CL	a) Criteria to ensure importing countries face serious public health problems b) Safeguards against re-exportation of CL product c) Reporting of action to trading partners	* Requires granting of two CLs * Requires compensation in exporting and importing countries * Changes in CL legislation in importing countries may be required	*Would require exporting country to assess “capacity” of importing country *Subject to pressures both in importing and exporting * Granting of licence case-by-case

⁹³ A “moratorium” is “a period during which an obligor has a legal right to delay meeting an obligation” (*Blacks’ Law Dictionary*, Abridged Sixth Edition, St. Paul, Minnesota, West Publishing, 1991, p. 698).

⁹⁴ See Article 57 of the Vienna Convention of the Law of Treaties.

⁹⁵ See, e.g. Article 64.2 of the TRIPS Agreement, which established a five years moratorium for “non-violation” complaints.

⁹⁶ Procedures adopted November 1, 1956, *Basic Instruments and Selected Documents*, 5th Supplement, 25.

⁹⁷ See Article IX. 3 and 4 of the Agreement.

⁹⁸ According to proposals by the USA and the EC and their Member States.

<p>b) To <u>interpret</u> limited exceptions clause of Article 30 to allow production for export to countries with no or inefficient manufacturing capacity</p>	<p>a) Authoritative interpretation (¾ vote) b) Change in national laws of exporting countries c) Change in CL legislation in importing countries may be required</p>	<p>a) Entirety of the product must be exported to countries with the public health problem b) Prohibition of re-export.</p>	<p>*Export country not required to do a case-by-case decision *No amendment of TRIPS needed *Compensation payable only in importing country</p>	<p>*Any party can invoke the exception, at any time, in exporting country</p>
<p>c) <u>Moratorium</u> on WTO complaints/ disputes</p>	<p>Ministerial Conference/ Amendment</p>	<p>Criteria to be established</p>	<p>*Not a solution, as such, since it is only temporary *The criteria could be disputable even if mechanism is not</p>	

Abbreviation: CL = compulsory licence

As indicated in the precedent Table, an Article 30-based solution would be more straightforward than one based on Article 31 (f). Some Members may fear that an authoritative interpretation of Article 30 might spill over into unforeseen categories of intellectual property, particularly copyright, because of the existence of a similar exceptions provision. However, appropriate wording may be adopted in order to avoid an unintended reading of such an interpretation.

Safeguards

If developed countries agreed to any of these solutions, they are likely to demand the establishment of certain “safeguards”, as indicated in the submissions by the USA and the EC and their Member States to the Council for TRIPS of March 2002. Such safeguards would aim at ensuring that any agreed solution is not utilized to attain objectives other than those related to the protection of public health in the countries with no or insufficient manufacturing capacity for the economically viable production of pharmaceuticals.

A basic safeguard would be the provision of mechanisms to prevent the diversion of products exported to a country qualifying under paragraph 6 to other countries,⁹⁹ and that the

⁹⁹ However, it may be excessive (due to complexity and costs) to impose the burden of monitoring and preventing such a diversion on the importing country in need of pharmaceuticals. The European Commission has noted that “the industry acknowledges that to date there is no re-importation of medicines from the poorest developing countries into the EU, i.e. the problem of re-importation is still largely theoretical” (European Commission, 2002, p. 10). In addition, restrictions on the export of products may violate Article XI of GATT (prohibitions or restrictions on the importation or exportation of products).

entire output of the relevant pharmaceuticals manufactured be exported to the Member in need. The notification to other Members of actions taken has also been mentioned.¹⁰⁰

Compulsory Licence in the Importing Country

In order to import a patented product, the country in need may apply the international exhaustion principle and allow parallel imports or grant a compulsory licence either to **import** or to **manufacture** the protected product. The understanding given by the Members to paragraph 6 in some of the proposals mentioned above clearly implies that a compulsory licence can be satisfied by imports, and not only by local production.¹⁰¹

A review of the patent laws of seventy developing countries and LDCs (Table 2) indicates that the majority provide for compulsory licences in case of failure to exploit or to do it on reasonable terms – in line with Article 5A of the Paris Convention – while only 13 provide for grounds relating to public interest and/or national emergency or health emergency.

Table 2

Grounds for compulsory licences in developing countries and LDCs

Grounds for granting compulsory licences	Countries providing such grounds	Total
Failure to exploit or exploit on reasonable terms	16 + OAPI	32
Public interest	8 + Andean	13
National emergency or health emergency	8 + Andean	13
Remedy anti-competitive practices, unfair competition	6 + Andean	11
Failure to obtain licence under reasonable terms	4	4
Failure to work domestically	2	2
No apparent provisions	2	2

Source: Thorpe, 2002.

Though more detailed research on national laws is required, this information suggests that in order to make operative any solution under paragraph 6, many developing countries and LDCs would need to amend their national patent laws.

Economic Feasibility

For any possible solution under paragraph 6 to work, it is crucial that the designed legal framework provide the adequate incentives for the production and export of the medicines in

¹⁰⁰ See IP/C/W/340. One additional question might be if, in order to be validated under a paragraph 6 exception, certain pricing conditions would be attached to the exported products.

¹⁰¹ Some national laws require, however, the compulsory licensee to locally produce the invention. Unless amended, such legislation can make illusory a solution under paragraph 6 based on either Article 31 (f) or Article 30, since in both cases the assumption is that the compulsory licensee is able to import in order to execute his licence.

need. Overcoming the normative obstacles to exports would not mean much if no firms were interested in supplying the required pharmaceuticals at a low cost.

Generic companies operate today as suppliers of off-patent medicines, and have not generally used the compulsory licence system to get access to patented products. Their main interest lies in the rapid introduction of products after patent expiry, relying – where available – on “Bolar” type exceptions. In case a need emerges in a country under paragraph 6, a generic company would need to develop and implement a method for the production, on viable economic terms, of the active ingredient. In addition, a suitable formulation would need to be developed and approval obtained in the importing country. Offering the required drug would require considerable investment and time. A premise of paragraph 6 is that the drugs would have to be supplied at **low cost**, making the realization of economies of scale an essential condition for the implementation of any acceptable solution. In the already mentioned EC-Canada case, Canada argued that

“Both the brand name and generic pharmaceutical industries were global in nature. Very few countries had fully integrated brand name or generic drug industries within their borders. Even in large countries, generic producers frequently had to obtain ingredients such as fine chemicals from producers in other countries. Many countries had no generic industries at all and had to obtain generic (as well as brand name) products from other countries. Smaller countries that did have generic industries did not have domestic markets sufficiently large to enable those industries to operate on an economic scale. Those industries had to export in order to be able to manufacture in sufficient quantities to achieve economies of scale, so that domestic consumers could receive the benefits of cost-effective generic products” (para. 4.38 (a)).

If individual countries with small markets look for supplies under a solution (whatever it is) under paragraph 6, generic companies may lack sufficient incentives to incur the necessary costs of development and marketing of a low cost version of the patented drug. A good diplomatic solution to the problem posed by paragraph 6, therefore, may not necessarily provide effective relief to the countries in need. An option to address this problem would be for several countries to pool their buying power of certain drugs, in order to allow potential suppliers to realize economies of scale (Engelberg, 2002). The time at which a request under paragraph 6 is made may also make a difference. Generic companies may be more inclined to satisfy requests when the relevant patent is about to expire (and therefore investments made may be soon recovered in other markets) than in cases where the patent will still be valid for a long period.

The economic feasibility of supply may also depend on the importing country's regime for protection of data submitted for marketing approval. If the local regulation strictly follows Article 39.3¹⁰² of the TRIPS Agreement and provides protection against unfair commercial use of such data, but not an exclusivity period, the registration of the generic product may be relatively simple and straightforward.¹⁰³ However, if a TRIPS-plus approach is adopted, and the registration of subsequent products is banned until a period of exclusivity expires – as is the case in the USA and Europe – the entry of the generic product may be delayed or frustrated.

¹⁰² See on this issue, Correa, 2002.

¹⁰³ Depending also on the kind of studies required to prove the “similarity” of the product with the original one, such as bioequivalence and bioavailability tests.

Generic companies may not be willing to make the substantial investment needed to duplicate the tests necessary to prove efficacy and safety.

Legal Implementation

Changes in the TRIPS Agreement, or new interpretations, do not translate automatically into changes in national laws. Therefore, any solution found at the Council for TRIPS is likely to call for amendments to national laws in potential exporting countries in order to become operative. All potentially exporting countries, including developed countries, should appropriately amend national law to facilitate effective implementation of the Council for TRIPS solution to the paragraph 6 problem.

The implementation of an effective solution under paragraph 6 may also depend on the conditions under which compulsory licences are granted in the importing country. The remuneration to be paid to the patent holder should be such that it does not nullify the aim of the licence, to ensure the supply of low cost pharmaceuticals. In addition, national governments should carefully implement Article 31 (g)¹⁰⁴ of the TRIPS Agreement, in a manner that does not undermine the incentives to apply for and execute a compulsory licence.¹⁰⁵

TRANSFER OF TECHNOLOGY TO LDCS

Doha Declaration on TRIPS and Public Health: Paragraph 7

We reaffirm the commitment of developed-country members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country members pursuant to Article 66.2. We also agree that the least-developed country members will not be obliged, with respect to pharmaceutical products, to implement or apply Sections 5 and 7 of Part II of the TRIPS Agreement or to enforce rights provided for under these Sections until 1 January 2016, without prejudice to the right of least-developed country members to seek other extensions of the transition periods as provided for in Article 66.1 of the TRIPS Agreement. We instruct the Council for TRIPS to take the necessary action to give effect to this pursuant to Article 66.1 of the TRIPS Agreement.

Paragraph 7 of the Doha Declaration reaffirmed

“the commitment of developed-country Members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country Members pursuant to Article 66.2.”

LDCs have repeatedly raised concerns at the Council for TRIPS about the lack of effective action by developed countries to comply with Article 66.2 of the TRIPS Agreement.¹⁰⁶

¹⁰⁴ TRIPS Article 31 (g): “[The] authorization for such use shall be liable, subject to adequate protection of the legitimate interests of the persons so authorized, to be terminated if and when the circumstances which led to it cease to exist and are unlikely to recur. The competent authority shall have the authority to review, upon motivated request, the continued existence of these circumstances”.

¹⁰⁵ This also applies, of course, to a possible solution under Article 31 (f).

¹⁰⁶ Also note that paragraph 11.2 of the Implementation Decision adopted on 14 November.

Though some developed countries provide different forms of technical assistance on IPR-related issues, LDCs have repeatedly noted that no or little action has been taken by developed countries to specifically implement their obligations under Article 66.2. It remains to be seen whether the reaffirmation in the Doha Declaration of such obligations has a practical impact on developed countries' actions in this area.

Though the wording in paragraph 7 is broad, its inclusion in the Doha Declaration indicates that effective incentives should be granted in developed countries in order to specifically foster the transfer to LDCs of health-related technologies, including pharmaceutical technologies.

EXTENSION OF TRANSITIONAL PERIOD FOR LDCs

The Doha Declaration permits LDCs to opt for an extension of the transitional period provided for under Article 66.1 of the TRIPS Agreement. Paragraph 7 establishes the grounds for an extension of the transitional period for LDCs¹⁰⁷ in relation to pharmaceutical patents only. It contains a “duly motivated request” – in the terms of Article 66.1 of the TRIPS Agreement¹⁰⁸ – on the basis of which the Council for TRIPS must give effect to that extension. LDCs do not need to individually follow the procedure provided for under Article 66.1 to enjoy this period. The Declaration, however, explicitly preserves the right of LDCs to request extensions for other matters (not related to pharmaceutical patents) in accordance with Article 66.1's procedure,¹⁰⁹ without diminishing their right to request further extensions for pharmaceutical patents after 2016.

This extension applies to “pharmaceutical products”. However, the protection conferred to a patented process encompasses, according to Article 28.1 (b) of the TRIPS Agreement, the protection of the products directly obtained with such process. Hence, the extension of the transitional period should also be deemed to apply to process patents.¹¹⁰ Likewise, extension

2001 states the following: “Reaffirming that the provisions of Article 66.2 of the TRIPS Agreement are mandatory, it is agreed that the TRIPS Council shall put in place a mechanism for ensuring the monitoring and full implementation of the obligations in question. To this end, developed-country members shall submit prior to the end of 2002 detailed reports on the functioning in practice of the incentives provided to their enterprises for the transfer of technology in pursuance of their commitments under Article 66.2. These submissions shall be subject to a review in the TRIPS Council and information shall be updated by Members annually”. For information on home country measures encouraging transfer of technology, see IP/C/W/132, Add. 1-7.

¹⁰⁷ Though this paragraph does not amend Article 66.1 of the Agreement, it does innovate with regard to the procedure applicable for the extension of the transitional period for LDCs.

¹⁰⁸ TRIPS Article 66.1. “In view of the special needs and requirements of least-developed country Members, their economic, financial and administrative constraints, and their need for flexibility to create a viable technological base, such Members shall not be required to apply the provisions of this Agreement, other than Articles 3, 4 and 5, for a period of 10 years from the date of application as defined under paragraph 1 of Article 65. The Council for TRIPS shall, upon duly motivated request by a least-developed country Member, accord extensions of this period”.

¹⁰⁹ In fact, it would have seem more logical to extend the transitional period for all fields of technology since, unless individual extensions are accorded, LDCs would be required anyway to bear the costs of granting patents in other sectors.

¹¹⁰ This is also the interpretation of the European Commission, who held that “all least developed Members benefit from the extension of the transition period from 1.1. 2006 to 1.1.2016 (and probably beyond) with regard to product and process patent protection and its enforcement” (European Commission, 2001, p. 4). Also note that the USA delegation, while submitting their proposal for paragraph 7 at the Doha Ministerial Conference did not refer to product patent protection only: “We recommend granting the least-developed countries a 10-year extension to 2016, to come into full compliance with *pharmaceutical-related patent*

would apply to cases involving a second indication of a pharmaceutical product, since claims are generally drafted in these cases as product claims on the basis of the “Swiss-claims” formulation.¹¹¹

The extension of the transitional period applies in relation to Sections 5 (patents) and 7 (undisclosed information) of Part II of the TRIPS Agreement, and to the enforcement of such rights.

An important practical aspect is to determine which are the LDCs that can effectively benefit from paragraph 7 of the Doha Declaration. Out of thirty African LDCs, only two¹¹² do not currently grant patents for pharmaceuticals.¹¹³ These would be, in principle, the only African LDCs that can benefit from this paragraph, unless they amend their legislation.

Twelve out of the 34 African LDCs are members of the Organisation Africaine de la Propriété Intellectuelle (OAPI) and 10 of the African Regional Industrial Property Organization (ARIPO).

Table 3 indicates that 12 out of the 16 members of OAPI are LDCs. Figure 1 illustrates the patents granted by OAPI over a year period from 1984 to 1996. Also indicated is the proportion of these patents relating to pharmaceuticals.¹¹⁴ Figure 1 shows the increase of the number of patents granted in such fields since 1991.

Table 3

Current membership of OAPI

<i>Benin</i>	<i>Burkina Faso</i>	Cameroon	<i>Central African Republic</i>
<i>Chad</i>	Congo	Côte d’Ivoire	<i>Equatorial Guinea</i>
Gabon	<i>Guinea</i>	<i>Guinea Bissau</i>	<i>Mali</i>
<i>Mauritania</i>	<i>Niger</i>	<i>Senegal</i>	<i>Togo</i>

Note: [Countries in italics are United Nations designated Least Developed Countries (LDCs)]

There are 10 LDCs among ARIPO's members (see Table 4). Figure 2 illustrates the patents granted by ARIPO from 1985 to 1999.¹¹⁵

obligations under TRIPS” (emphasis added). See also Vandoren, 2002, p. 10.

¹¹¹ See Correa (2000c).

¹¹² Angola and Eritrea. See Thorpe, 2002.

¹¹³ The majority of non-African LDCs also seem to confer patent protection for pharmaceutical products, due to the application of their ex-metropolis’ legislation (personal communication from WIPO).

¹¹⁴ The data include patents classified under IPC classification mark A61K (preparations for medical, dental, or toilet purposes) or having a corresponding patent filed elsewhere classified under mark A61K. Since medicinal-related inventions can also be classified under other marks, the figures shown should only be taken to represent the bottom end of possible medicinal-related patents.

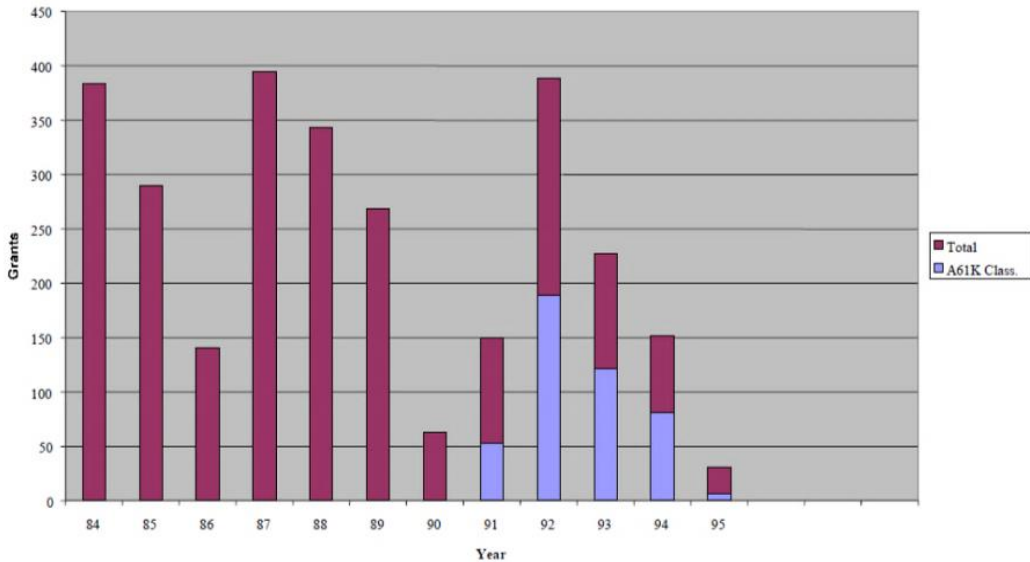
¹¹⁵ Also indicated is the proportion of these patents classified under IPC classification mark A61K (preparations for medical, dental, or toilet purposes) or having a corresponding patent filed elsewhere classified under mark A61K.

Table 4
Current Membership of ARIPO

Botswana	<i>Gambia</i>	Ghana	Kenya
<i>Lesotho</i>	<i>Malawi</i>	<i>Mozambique</i>	<i>Sierra Leone</i>
<i>Somalia</i>	<i>Sudan</i>	Swaziland	<i>United Republic of Tanzania</i>
<i>Uganda</i>	<i>Zambia</i>	Zimbabwe	

Note: [Countries in italics are United Nations designated Least Developed Countries (LDCs)]

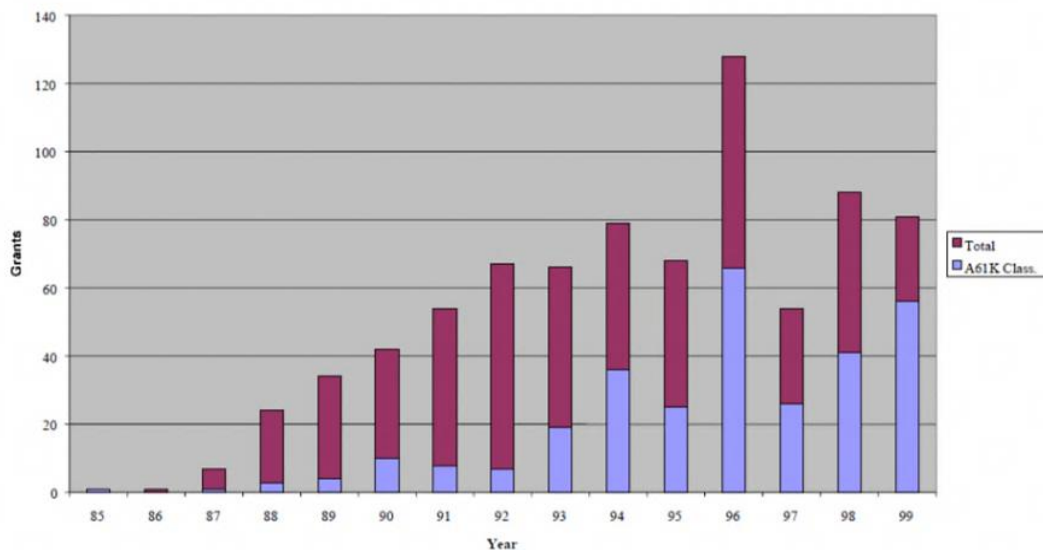
Figure 1
Patents Granted by OAPI



LDCs that already grant pharmaceutical patents could, however, amend their legislation and not grant product patents until 2016,¹¹⁶ since they are not constrained by the "freezing clause" of Article 65.5 of the TRIPS Agreement.

¹¹⁶ Such a change, where possible, is likely to raise some complex legal issues under the relevant national laws, including of a constitutional nature. In the case of the LDCs members of OAPI, the use of the additional traditional period would require the amendment of the Libreville Agreement of 1962 (amended in 1977 and 1999). The OAPI establishes a uniform law and a centralized system of examination and registration. In contrast, the African Industrial Property Organization (ARIPO), provides for a centralized system of examination and registration, but it does not establish a common regional law and all designated States are given a chance to refuse an application before granting by the Regional Office. See, e.g., Chirambo, 2002.

Figure 2
Patents Granted by ARIPO



Another crucial point is whether LDCs will be obliged to grant exclusive marketing rights (EMRs) under Article 70.9 of the TRIPS Agreement during the extended transitional period.¹¹⁷ Paragraph 7 does not explicitly exclude the application of that provision. If LDCs were bound to grant EMRs,¹¹⁸ the value of the concession made by the Doha Declaration to LDCs would be very limited, since access to medicines and other products could be effectively blocked for at least five years.

An alternative interpretation for paragraph 7 is possible. Since EMRs do not constitute a category of intellectual property rights (as enumerated in Article 1.2 of the TRIPS Agreement), the granting of such rights only provides one way of **enforcing** foreign patent rights. As mentioned, paragraph 7 exempts LDCs from the enforcement of rights provided for in accordance with the patents section of the TRIPS Agreement. Under this interpretation, LDCs would be exempted from compliance with Article 70.9.

In addition, in relation to those LDCs that **did grant** patent protection for pharmaceutical products as of the entry into force of the WTO Agreement,¹¹⁹ the chapeau of Article 70.8 of the TRIPS Agreement makes it clear that the mailbox obligation applies to members that did “not make available as of the date of entry into force of the WTO Agreement patent protection for pharmaceutical and agricultural chemical products.” Article 70.8, literally

¹¹⁷ TRIPS Article 70.9. “Where a product is the subject of a patent application in a Member in accordance with paragraph 8(a), exclusive marketing rights shall be granted, notwithstanding the provisions of Part VI, for a period of five years after obtaining marketing approval in that Member or until a product patent is granted or rejected in that Member, whichever period is shorter, provided that, subsequent to the entry into force of the WTO Agreement, a patent application has been filed and a patent granted for that product in another Member and marketing approval obtained in such other Member”.

¹¹⁸ Article 70.8 makes it clear that its application (and that of Article 70.9 which provides for EMRs) proceeds “notwithstanding the provisions of Part IV” which includes Article 66.1.

¹¹⁹ 1 January 1995.

interpreted, means that those LDCs who granted such a protection would not be subject to the obligation to grant exclusive marketing rights.

SPECIAL TREATMENT UNDER TRIPS

The non-discrimination clause contained in Article 27.1 of the TRIPS Agreement¹²⁰ has often been mentioned as preventing any differentiation under patent law in the treatment of various products or sectors. This interpretation would suggest that any solution under paragraph 6 would likely violate Article 27.1's non-discrimination clause.

However, as stated by the panel in the EC-Canada case¹²¹ Article 27.1 prohibits "discrimination," as opposed to "differentiation". The panel held that:

"Article 27 prohibits only discrimination as the place of invention, the field of technology, and whether products are imported or produced locally. Article 27 does not prohibit *bona fide* exceptions to deal with problems that may exist only in certain product areas. Moreover, to the extent the prohibition of discrimination does limit the ability to target certain products in dealing with certain of the important national policies referred to in Articles 7 and 8.1, that fact may well constitute a deliberate limitation rather than frustration of purpose" (para 7.92).¹²²

It is implicit within the Doha Declaration that differentiation in patent rules may be necessary to protect public health. The singling out of public health, and in particular pharmaceuticals (paragraphs 6 and 7), as an issue needing special attention in TRIPS implementation constitutes recognition that public health-related patents deserve to be treated differently from other patents.

The French patent law provides an interesting example of a patent law that differentiates the treatment of pharmaceutical products on public health grounds. It provides that:

*"Where the interest of public health demand, patents granted for medicines or for processes for obtaining medicines, for products necessary in obtaining such medicines or for processes for manufacturing such products may be subject to ex officio licences in accordance with Article L. 613-16 in the event of such medicines being made available to the public in insufficient quantity or quality or at (abnormally high prices) by order of the Minister responsible for industrial property at the request of the Minister responsible for health".*¹²³

Moreover, public health is not a "field of technology", but a problem area that may be addressed with products originating in different technological fields, such as equipment, software, diagnostic kits, medicines, and a large variety of devices used for medical treatment.

¹²⁰ TRIPS Article 27.1 "Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced".

¹²¹ WT/DS114/R, 17 March 2000.

¹²² The USA also held in the same case, based on the panel report on Section 337, that "differential treatment was not necessarily treatment that was inconsistent with TRIPS requirements" (para. 5.36 (b)(3)(ii), WT/DS114/R).

¹²³ Article L. 613-16.

LEGAL STATUS OF THE DOHA DECLARATION

The Doha Declaration is a strong political statement that can make it easier for developing countries to adopt measures necessary to ensure access to health care without the fear of being dragged into a legal battle.¹²⁴ The Declaration is also a Ministerial decision¹²⁵ with legal effects on the Member States and on the WTO bodies, particularly the Dispute Settlement Body and the Council for TRIPS.¹²⁶ It states the purpose of the TRIPS Agreement in the area of public health, interprets the TRIPS Agreement with regard to some important aspects, instructs the Council for TRIPS to take action, and decides on the implementation of the transitional provisions for LDCs.

A “declaration” has no specific legal status in the framework of WTO law;¹²⁷ it is not strictly an authoritative interpretation in terms of Article IX.2 of the Marrakesh Agreement Establishing the WTO. However, given the content and mode of approval of the Doha Declaration, it can be argued that it has the same effects as an authoritative interpretation. In particular, in providing an agreed understanding on certain aspects of the TRIPS Agreement in paragraph 5, Members have created a binding precedent for future panels and Appellate Body reports. According to the European Commission,

“in the case of disputes (e.g. in the context of WTO dispute settlement procedures) Members can avail themselves of the comfort provided by this Declaration. Panellists are likely to take account of the provisions of the TRIPS Agreement themselves as well as of this complementary Declaration, which, although it was not meant to affect Members’ rights and obligations, expresses the Members’ views and intentions. Hence, the Declaration is part of the context of the TRIPS Agreement, which, according to the rules of treaty interpretation, has to be taken into account when interpreting the Agreement”.¹²⁸

Moreover, the Declaration can be regarded as a “subsequent agreement” between the parties regarding the interpretation of a treaty or the application of its provisions, under Article 31.3 (a) of the Vienna Convention on the Law of the Treaties.

Any WTO Member could bring a complaint under the DSU on issues covered by the Doha Declaration,¹²⁹ and it would be theoretically possible for a panel or the Appellate Body to

¹²⁴ See e.g. Weisbrot, 2002, p. 16; Raja, 2001, p. 14.

¹²⁵ See article IX.1 of the WTO Agreement.

¹²⁶ It should be noted that the Ministerial Conference rejected proposed language (“Desiring to clarify the provisions of the TRIPS Agreement, while preserving the rights and obligations of Members under the Agreement”) that would have suggested that the Declaration would only clarify provisions of the TRIPS Agreement.

¹²⁷ The WTO adopted several “declarations” prior to the document examined here: “Declaration on the Contribution of The World Trade Organization to Achieving Greater Coherence In Global Economic Policymaking”; “Declaration on the Relationship of the World Trade Organization with the International Monetary Fund”; “Declaration on the Dispute Settlement Pursuant to the Agreement on Implementation of Article VI of the General Agreement on Tariffs and Trade 1994 or Part V of the Agreement on Subsidies and Countervailing Measures”.

¹²⁸ European Commission, 2001, p. 2. See also Vandoren (2002), who notes that “the Declaration provides comfort to Members in the case of disputes... A Member whose legislation is being challenged by another Member because of alleged incompatibility with the TRIPS Agreement can refer to the contents of this Declaration in support of the measures under dispute, where relevant...and panellists are likely to take account of this complementary Declaration as well as the provisions of the TRIPS Agreement in their decisions” (p. 8).

¹²⁹ See Gillespie-White, 2001.

find an inconsistency between the Doha Declaration and the TRIPS Agreement itself. This is unlikely, however, since in adopting the Declaration, Members have exercised their exclusive competence to interpret a WTO agreement,¹³⁰ and it would be extremely difficult to challenge the adopted interpretation.

It should be stressed, however, as mentioned above, that the Doha Declaration is not self-executing and both developed and developing countries should adopt the legal amendments necessary to implement it. Developing countries, in particular, should ensure that they are using to the full extent possible the flexibilities allowed by the TRIPS Agreement to protect public health and facilitate access to health care by all.

ISSUES NOT COVERED IN THE DECLARATION

The Doha Declaration does not cover all the areas where flexibility of the TRIPS Agreement exists, such as the exceptions to patent rights (Article 30) and the protection of data submitted for the registration of pharmaceutical (and agrochemical) products (Article 39.3). Nor does it refer to the room left to Members to determine the patentability standards in ways that prevent patenting strategies aiming at expanding or temporally extending the protection conferred in the pharmaceutical field.¹³¹

Proposals made in the pre-Doha negotiation phase by different Members included, *inter alia*, language on the need to prevent diversion of drugs sold at discounted prices in developing countries to high-income markets,¹³² and to ensure that data protection requirements of Article 39.3 do not become a barrier to the registration and introduction of generic drugs and the use of compulsory licensing.¹³³ The USA proposed a five year moratorium on dispute settlement action in relation to “non-violation” complaints, which was limited to Sub-Saharan African countries.¹³⁴

CONCLUSIONS

The Doha Declaration addresses real and urgent problems faced by many developing countries in the area of public health. It is not intended to amend the TRIPS Agreement in any substantial manner. Rather, it aims to clarify the relationship between the TRIPS Agreement and Public Health policies of Member countries, and confirm the rights that Members have retained under the Agreement, particularly by defining the flexibility allowed in certain key areas.

The Declaration addresses most of the concerns of developing countries on the issue of public health. The ambiguous wording used in some paragraphs – particularly in paragraph 4 – was the obvious price paid to build a consensus for the adoption of the Declaration. Despite such wording, the Declaration makes it clear that a conflict may exist between TRIPS standards

¹³⁰ Panels and the Appellate Body can only “clarify” the provisions of the WTO agreements; they “cannot add or diminish the rights and obligations provided in the covered agreements” (article 3.2 of the Dispute Settlement Understanding).

¹³¹ See, e.g., Correa, 2001.

¹³² The EC regretted that this issue was not dealt with by the Conference (European Commission, 2001, p. 6).

¹³³ See IP/C/W/296.

¹³⁴ Acceptance of this proposal would have implied that Article 64 of the TRIPS Agreement on “non-violation” complaints could be immediately applied to any other Member, something that most Members rejected since the scope and modalities of such complaints have not been determined yet by the Ministerial Conference.

and public health, and has reaffirmed the right of Members, particularly developing countries, to take measures necessary to protect public health. The Declaration has set the ground for a differentiation of intellectual property policies when necessary to protect health.

Though an important political document, the Doha Declaration also has legal effects, equivalent to those of an authoritative interpretation under WTO rules.

As the mandate given in paragraphs 6 and 7 illustrates, the Doha Declaration represents, rather than the end of a process, the initial step for rethinking the TRIPS Agreement in light of the public interest.

Paragraph 6 aims at addressing a problem created by the extension of patent protection for pharmaceutical products to all WTO Members, irrespective of their level of development and of their pharmaceutical manufacturing capacity. While many different legal approaches may be developed, an effective solution must create the right economic conditions for countries with no or insufficient manufacturing capacity to obtain pharmaceutical products at low cost. Likewise, the TRIPS Agreement will continue to create tensions in the public health area, if the case of countries where no patent protection exists is not also a part of viable legal and economic solution.

All WTO Members should, in due time, take the steps, as necessary, to implement the Doha Declaration. Amendments to national laws should be introduced in order to facilitate exports of needed pharmaceuticals under paragraph 6 of the Declaration. Developing countries should be encouraged (and the relevant technical assistance provided) to review their legislation in order to ensure that the flexibilities, as clarified in the Declaration, as well as other flexibilities allowed by the TRIPS Agreement, are incorporated in national laws and effectively used to address public health concerns.

The situation of LDCs received special attention at the Doha Conference, but the paragraph 7 action item did not represent any significant improvement for the great majority of them. Hence, the problems faced by LDCs to gain access to needed pharmaceuticals are likely to require further consideration by the WTO Members, in order to accomplish the objectives sought by the Doha Declaration.

ANNEX 1
Doha Declaration on the TRIPS Agreement and Public Health

WORLD TRADE

WT/MIN(01)/DEC/W/2

ORGANIZATION

14 November 2001

(01-5770)

MINISTERIAL CONFERENCE Fourth Session

Doha, 9 - 14 November 2001

DECLARATION ON THE TRIPS AGREEMENT AND PUBLIC HEALTH

Adopted on 14 November 2001

1. We recognize the gravity of the public health problems afflicting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics.

2. We stress the need for the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) to be part of the wider national and international action to address these problems.

3. We recognize that intellectual property protection is important for the development of new medicines. We also recognize the concerns about its effects on prices.

4. We agree that the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all.

In this connection, we reaffirm the right of WTO Members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose.

5. Accordingly and in the light of paragraph 4 above, while maintaining our commitments in the TRIPS Agreement, we recognize that these flexibilities include:

- (a) In applying the customary rules of interpretation of public international law, each provision of the TRIPS Agreement shall be read in the light of the object and purpose of the Agreement as expressed, in particular, in its objectives and principles.
- (b) Each Member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted.
- (c) Each Member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.

- (d) The effect of the provisions in the TRIPS Agreement that are relevant to the exhaustion of intellectual property rights is to leave each Member free to establish its own regime for such exhaustion without challenge, subject to the MFN and national treatment provisions of Articles 3 and 4.

6. We recognize that WTO Members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement. We instruct the Council for TRIPS to find an expeditious solution to this problem and to report to the General Council before the end of 2002.

7. We reaffirm the commitment of developed-country Members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country Members pursuant to Article 66.2. We also agree that the least-developed country Members will not be obliged, with respect to pharmaceutical products, to implement or apply Sections 5 and 7 of Part II of the TRIPS Agreement or to enforce rights provided for under these Sections until 1 January 2016, without prejudice to the right of least-developed country Members to seek other extensions of the transition periods as provided for in Article 66.1 of the TRIPS Agreement. We instruct the Council for TRIPS to take the necessary action to give effect to this pursuant to Article 66.1 of the TRIPS Agreement.

ANNEX 2
Levels of Development of Pharmaceutical Industry, by Country

Sophisticated Pharmaceutical Industry and Research Base	Innovative Capabilities	Reproductive Capabilities – Active Ingredients and Finished Products	Reproductive Capabilities – Finished Products from Imported Ingredients only	No Pharmaceutical Industry
Belgium France Germany Italy Japan Netherlands Sweden Switzerland United Kingdom United States	Argentina Australia Austria Canada China Denmark Finland Hungary India Ireland Israel Mexico Portugal Republic of Korea Spain USSR Yugoslavia	Bahamas Bolivia Brazil Bulgaria Cuba Czechoslovakia Egypt Indonesia Macau, China Norway Poland Puerto Rico Romania Turkey	Afghanistan Albania Algeria Angola Bangladesh Barbados Belize Benin Brunei Cambodia Cameroon Cape Verde Chile Colombia Costa Rica Côte d'Ivoire Cyprus Democratic People's Republic of Korea Dominican Republic Ecuador El Salvador Ethiopia Fiji Gambia Ghana Greece Guatemala Guyana Haiti Honduras Hong Kong, China Iran (Islamic Republic of) Iraq Jamaica Jordan	Andorra Antigua and Barbuda Aruba Bahrain Bermuda Bhutan Botswana British Virgin Islands Burkina Faso Burundi Central African Republic Chad Comoros Congo Cook Islands Djibouti Dominica Equatorial Guinea Faeroe Islands French Guyana French Polynesia Gabon Greenland Grenada Guadeloupe Guam Guinea Guinea-Bissau Iceland Laos Libyan Arab Jamahiriya Liechtenstein Luxembourg Maldives

Sophisticated Pharmaceutical Industry and Research Base	Innovative Capabilities	Reproductive Capabilities – Active Ingredients and Finished Products	Reproductive Capabilities – Finished Products from Imported Ingredients only	No Pharmaceutical Industry
			Kenya Kiribati Kuwait Lebanon Lesotho Liberia Madagascar Malawi Malaysia Mali Malta Mauritius Mongolia Morocco Mozambique Myanmar Namibia Nepal New Zealand Nicaragua Niger Nigeria Pakistan Panama Papua New Guinea Paraguay Peru Philippines Saudi Arabia Seychelles Sierra Leone Singapore Solomon Islands Somalia South Africa Sri Lanka Sudan Syrian Arab Republic Chinese Taipei Thailand Tonga	Martinique Mauritania Mayotte Micronesia Nauru Netherland Antilles New Caledonia Niue Oman Qatar Reunion Rwanda St. Kitts and Nevis St. Lucia St. Vincent & Grenadines Samoa San Marino Sao Tome and Principe Senegal Suriname Swaziland Togo Tuvalu US Virgin Island Vanuatu Western Samoa

Sophisticated Pharmaceutical Industry and Research Base	Innovative Capabilities	Reproductive Capabilities – Active Ingredients and Finished Products	Reproductive Capabilities – Finished Products from Imported Ingredients only	No Pharmaceutical Industry
			Trinidad and Tobago Tunisia Uganda United Arab Emirates United Republic of Tanzania Uruguay Venezuela Viet Nam Yemen Zaire Zambia Zanzibar Zimbabwe	

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CHAPTER V

IMPLEMENTATION OF THE WTO GENERAL COUNCIL DECISION ON PARAGRAPH 6 OF THE DOHA DECLARATION ON THE TRIPS AGREEMENT AND PUBLIC HEALTH

INTRODUCTION

Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health,¹ adopted at the Fourth World Trade Organization (WTO) Ministerial Conference (9-14 November 2001), instructed the WTO Council for TRIPS (Trade-Related Aspects of Intellectual Property Rights) to address how WTO Members lacking or with insufficient manufacturing capacities in pharmaceuticals can make effective use of compulsory licensing. Many developing countries and the least developed countries (LDCs) cannot produce either active ingredients or formulations, due to lack of technology, equipment, human resources or economic viability of domestic production. While these countries may issue compulsory licences to import generic versions of patent-protected medicines, TRIPS rules impose constraints on the ability of countries to authorize exports of such products. Paragraph 6 promised a solution to the export problem caused by these constraints.

Currently, some developing country Members of WTO do not yet provide patent protection for pharmaceutical products. Some companies in these countries produce generic versions of pharmaceuticals at prices significantly lower than those offered by brand name companies. Those products may legally be exported freely to other countries, provided that a) they are not covered by patents in the importing country; or b) if the product is patent protected in the importing country, that a compulsory licence is granted there. The problem is that, as product patents for pharmaceuticals become enforceable in accordance with the TRIPS Agreement,² countries with industrial and export capacity will face legal obstacles to produce and export cheap generic copies of patented medicines.

If a product is deemed covered in an exporting country by the exclusive rights granted to the patent owner, production for export could take place under a compulsory licence.³ However, the TRIPS Agreement establishes that, unless a compulsory licence is granted to remedy anti-competitive practices (Article 31(k)), it must "predominantly" supply the licensee's domestic market (Article 31(f)). This means that if a company received a request to manufacture and export a product that is covered in the manufacturing country by a third party's patent, it would not be able to do so (in the absence of patent owner authorization), to the extent that production were predominantly for export and not for the manufacturer's domestic market.

¹ WT/MIN(01)/DEC/2, 20 November 2001, hereinafter "the Doha Declaration".

² By 2005 at the latest, all WTO Members (except least developed countries) must provide patent protection for pharmaceutical products.

³ Production for export, however, may be deemed admissible under Article 30 of the TRIPS Agreement. See, e.g. Commission on Intellectual Property Rights, *Integrating Intellectual Property Rights and Development Policy*, London, 2002, available on the Internet at www.iprcommission.org; Correa C, *Implications of the Doha Declaration on the TRIPS Agreement and Public Health*, Geneva, WHO, Health Economics and Drugs, EDM Series No. 12, 2002.

As a result of these legal constraints and, although countries without sufficient manufacturing capacity in pharmaceuticals could issue a compulsory licence for the importation of products they cannot manufacture, they will not be able to find export sources of affordable new medicines.

The Doha Declaration directed the Council for TRIPS "to find an expeditious solution to this problem and to report to the General Council before the end of 2002". An agreement to address the problem was finally reached on 30 August 2003,⁴ based on a compromise developed by the Chair of the TRIPS Council⁵ and on a "Statement" by the Chair of the General Council⁶ that "represents several key shared understandings of Members regarding the Decision to be taken and the way in which it will be interpreted and implemented".

This paper examines the ways in which the Decision can be implemented in prospective importing and exporting countries. It is addressed to policy-makers and to potential suppliers and purchasers of pharmaceutical products.⁷ The analysis is motivated by a desire to serve a number of public health objectives, namely the need to ensure:

- a rapid and effective response to public health needs;
- equality of opportunities for countries in need, irrespective of the patent status of a drug in the importing country, and without regard to its membership in the WTO;⁸
- the sustainability of quality supply at affordable prices;
- the facilitation of a multiplicity of potential suppliers, both from developed and developing countries, which can compete to drive prices down; and
- provision of a wide range of pharmaceutical products to meet an array of health problems.

In implementing the Decision it should also be borne in mind that the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being, as defined in the Constitution of the World Health Organization.⁹ Progressive realization of that right involves access to health facilities, care, treatment and support, including access to affordable medicines.¹⁰

This paper proceeds according to the following plan: the first section details the legal status of the Decision and the circumstances in which the Decision may be used. This section considers amendments to national laws needed to implement the Decision; the circumstances in

⁴ See WT/L/540, available on the Internet at www.wto.org (hereinafter "the Decision"). The Decision is reproduced in Annex 1.

⁵ See the text of the Statement by the Chairman of the Council for TRIPS of 16 December 2002 (JOB(02)/217).

⁶ See WT/GC/M/82, para. 29, available on the Internet at www.wto.org.

⁷ Importation under the Decision may be undertaken by governments as well as by nongovernmental organizations (NGOs), public or private hospitals, companies and other entities.

⁸ There is a significant number of countries which are not members of the WTO (while many are negotiating accession) that may face the problems addressed in paragraph 6.

⁹ For a description of the sources and scope of the right to health, see Report of the Special Rapporteur of the Commission on Human Rights on *The right of everyone to the enjoyment of the highest attainable standard of physical and mental health*, E/CN.4/2003/58, 13 February 2003, paras. 10-36.

¹⁰ As interpreted by the Committee on Economic, Social and Cultural Rights (CESCR), access to essential medicines constitutes a core element of the right to the highest attainable standard of health under the International Covenant on Economic, Social and Cultural Rights. See CESCR General Comment 14 (E/C.12/2000/4), para. 43.

which the Decision may be invoked; the products covered by the Decision; the countries which may use the Decision; and the purposes for which Members may use the Decision.

The second section considers the steps that an importing country must undertake to employ the Decision. These include required notifications to the TRIPS Council and confirming its intent to issue a compulsory licence.

The third section considers the steps required of an exporting country. These include issuance of a compulsory licence and required notifications by the exporting supplier and the exporting country.

The next section reviews the obligations on an importing country to take measures to prevent diversion of imported goods to other markets once it has employed the system.

A further section discusses the issue of suspension of the system.

A brief concluding section is followed by an annex summarizing the context and steps required to use the system established by the Decision.

CIRCUMSTANCES IN WHICH THE DECISION MAY BE USED

Legal Status of the Decision

The Decision adopted by the WTO General Council implements interim waivers with regard to the obligations set out in paragraphs (f) and (h) of Article 31 of the TRIPS Agreement. The Council for TRIPS shall review annually the functioning of the system set out in this Decision "with a view to ensuring its effective operation and shall annually report on its operation to the General Council" (paragraph 8). This waiver shall terminate on the date on which an amendment to the TRIPS Agreement replacing its provisions takes effect for a Member.¹¹ The TRIPS Council was mandated to initiate, by the end of 2003, work on the preparation of such an amendment with a view to its adoption within six months, "on the understanding that the amendment will be based, where appropriate, on this Decision" (paragraph 11).

The Decision does not affect the use of the flexibilities allowed by the TRIPS Agreement, including the adoption of other avenues to facilitate the export and importation of cheaper pharmaceutical products, such as on the basis of Article 30 of the TRIPS Agreement.¹²

Amendment to National Laws

A waiver does not imply any change of substantive treaty obligations; it only temporarily suspends their operation (Article 57 of the Vienna Convention on the Law of Treaties). A WTO

¹¹ The purpose of this linkage has been to provide legal certainty and encourage countries to implement the Decision as soon as possible. So far, only a handful of countries are reported to have taken action in order to amend national laws and allow exports under the Decision.

¹² According to para 9, "This Decision is without prejudice to the rights, obligations and flexibilities that Members have under the provisions of the TRIPS Agreement other than paragraphs (f) and (h) of Article 31, including those reaffirmed by the Declaration, and to their interpretation. It is also without prejudice to the extent to which pharmaceutical products produced under a compulsory licence can be exported under the present provisions of Article 31 (f) of the TRIPS Agreement".

waiver means that a Member shall not initiate a complaint against another Member if the latter acted under the terms of the adopted waiver. However, to the extent that a Member's national law is not revised to implement the terms of the waiver,¹³ patent owners may invoke provisions in the national law to block the export of a patented drug by other companies. Whether generic drug makers will actually be able to export under the terms of the Decision, therefore, will depend on the extent to which national laws allow for it.

Under the adopted system, and in a manner fully consistent with the TRIPS Agreement, countries may grant a compulsory licence¹⁴ to import a patented drug. However, some developing countries provide for the granting of compulsory licences for the manufacture of patented subject matter, and not for importation. Hence, in order to make any solution under paragraph 6 operational, those developing countries would need to amend their compulsory licence laws to provide for importation.

The Decision does not waive the application of Article 31 (b) of the TRIPS Agreement, which requires that prior to granting a compulsory licence, licence applicants make efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and within a reasonable period of time. This requirement may be waived by national law in the case of a national emergency or other urgent circumstances or in cases of public non-commercial use. National laws may also determine that in cases where Article 31 (b) cannot be waived and the Decision is to be applied, the period of time be shorter than in normal situations so as to expedite access to needed pharmaceutical products.¹⁵

Similarly, amendments to national laws will be necessary in the prospective exporting countries. Compulsory licences are granted under grounds specified in national laws. The supply of export markets is not an accepted ground in most national laws. Moreover, Article 31 (f) of the TRIPS Agreement requires that compulsory licences be issued "predominantly" for the domestic market. National laws in exporting countries must be amended to permit paragraph 6 compulsory licences exclusively to supply a foreign country.

The need to apply the Decision will arise when the patent owner does not agree to supply a patented pharmaceutical product to a country with insufficient or no manufacturing capacity in pharmaceuticals, at an affordable price or under other suitable conditions. Whatever humanitarian reasons¹⁶ underpin the country's demand for a given pharmaceutical product, nothing in the adopted system compels the patent owner to supply it or to forego the owner's rights under national laws.

In this context, the patent owner may eventually exercise his rights to appeal a decision granting a compulsory licence in both the importing and exporting country. In some countries, such appeal may not suspend the immediate execution of the compulsory licence. In others, this may not be the case¹⁷ and the patent owner may obtain an injunction and thereby delay exports

¹³ So far only two countries (Canada and Norway) have adopted legislative changes to implement the Decision. See Canada's Bill C-9, passed by the House of Commons on 4 May 2004, which amended the Patent Act and the Food and Drugs Act, and the amendment of 14 May 2004 to the Norwegian Regulations of 20 December 1996 No. 1162 relating to the patent act.

¹⁴ As mentioned below, the Decision also applies in cases of government use for non-commercial purposes.

¹⁵ The Preamble of the Decision recognizes "where eligible importing Members seek to obtain supplies under the system set out in this Decision, the importance of a rapid response to those needs consistent with the provisions of this Decision".

¹⁶ See the Statement by the Chair of the General Council accompanying the Decision.

¹⁷ The experience of the Philippines is illustrative in this regard. One hundred and twenty petitions for

or imports under the compulsory licence until a final administrative or judicial decision is taken. National patents laws, hence, will have to be amended, as necessary, in order to allow for an effective and rapid application of the Decision to address public health needs, particularly in cases of national emergency or urgency. In undertaking such an amendment, prospective exporting and importing countries should both consider establishing a short period for fulfilling the obligation under Article 31 (b) of the TRIPS Agreement¹⁸ for a prior negotiation with the patent owner.¹⁹ Although Article 31 (b) has not been waived, as mentioned below, exporting countries may consider that compliance with Article 31 (b) should not be required when the importing country resorts to public non-commercial use or grants a compulsory licence on grounds of a national emergency or other circumstances of extreme urgency.

The waiver granted by the Decision with respect to payment of compensation in the importing country (Article 31 (h) of the TRIPS Agreement) may also need to be implemented through a legal revision, in order to prevent patent owners' potential claims of compensation according to the national law.

Implementation of the Decision may not only require making specific changes to national laws, but also ensuring that countries do not assume TRIPS-plus obligations under bilateral or regional treaties. Bilateral agreements established by the USA with some developing and developed countries (e.g. Australia, the Central American countries, Chile, Jordan, Morocco), for instance, require the protection of data under a sui generis regime of data exclusivity for at least five years from the date of the first approval of a pharmaceutical product in the country. Some bilateral agreements, moreover, establish "linkage" requirements, so that, without the consent and acquiescence of the patent owner, national health authorities are prevented from granting marketing approval for a generic product as long as a patent over the product is in force.

The implications of these obligations are quite significant, and may delay introduction of generic products, even where compulsory licences are issued. Under the data exclusivity terms, if a compulsory licence were granted in a country to import a pharmaceutical product, a generic company would have to develop on its own all the test data as required for approval. This is a very lengthy, costly, duplicative and wasteful process given that the data have already been generated by a brand-name company, and will create an enormous obstacle to the use of the Decision. Moreover, the "linkage" between patent protection and marketing approval seems to erect an almost insurmountable barrier to the execution of a compulsory licence or government

compulsory licences were filed under the old Philippine patent law, out of which 51 compulsory licences were granted. However, the beneficiary companies were unable to market the products due to appellate proceedings that delayed the execution of the decision. The delay in the proceedings also led to the dismissal of 23 applications. Fourteen petitions were also dismissed due to a compromise agreement between the parties. Eight petitions were dismissed because the patent expired while the petitions were still pending. The only compulsory licence granted after the new Philippine Intellectual Property Code took effect on 1 January 1998 was a compulsory licence petition filed on 8 December 1991 when the old patent law was in effect. This petition was finally granted on 19 December 2001, i.e. after a period of ten years. The rest of the petitions filed under the old Philippine patent law are still pending (communication from Susan Villanueva, College of law, Philippines, 26 September 2003, on file with the author).

¹⁸ Since prior efforts to obtain a compulsory licence would have to be made, in some cases, both in the importing and exporting country, and given the need to provide a rapid response, coordination on this matter may be envisaged between the two countries.

¹⁹ Canadian Bill C-9 requires the applicant of the compulsory licence to provide a declaration showing that at least thirty days before filing the application it sought a voluntary licence from the patent owner on reasonable terms and that his effort were unsuccessful (section 21.04.3 (c)).

non-commercial use, since the compulsory licensee or government would be authorized to use the patented invention but not to obtain the regulatory approval to make it available. Countries willing to use the Decision (as importers or exporters) would have to devise ways, including crafting specific exceptions, to overcome these restrictions.

Finally, it is to be noted that the implementation of the Decision through appropriate amendments to national laws, as necessary, should not be regarded as a matter of mere convenience or political choice. The Decision creates international obligations that must be complied with in good faith.²⁰ States' human right obligations are also relevant in this context for both importing and exporting countries. For instance, under the International Covenant on Economic, Social and Cultural Rights, the State parties' obligations to take steps towards the full realization of the right to health include: (a) a domestic obligation to fulfil the right to health, which requires States to adopt appropriate legislative and administrative measures towards the full realization of the right to health (General Comment No. 14, para. 33), and (b) an international obligation to take steps, individually and through international assistance and cooperation, especially economic and technical, towards the full realization of the rights recognized in the Covenant, including the right to the highest attainable standard of health (General Comment No. 14, paras 38-39).²¹

In sum, WTO Members should review their domestic laws in order to determine what amendments are required in order to implement the Decision, and undertake the necessary legal adaptations. Such review should consider the procedures for granting compulsory licences, in order to ensure their timely granting and that their execution could not be prevented by appeals or other legal actions.

Patent Rights in Force

The Decision will apply when the required pharmaceutical products are patented, at least in the exporting country.

Patents may be obtained not only in relation to active ingredients, but also in respect of formulations, pharmaceutical salts, isomers, polymorphs, combinations, manufacturing processes, etc. In some countries the new use of a known product may also be patented (as a "second indication"). There are cases in which an active ingredient is off-patent, but the pharmaceutical product that contains it, its method or manufacture or use, is patented, even many years after the expiration of the original patent. In other cases, a patent on the active ingredient may coexist (though not necessarily for exactly the same period) with many other patents on the product.

Whenever this is the case, the application of the Decision may require the granting of compulsory licences on a set of patents, not just on a single patent. If the coverage of the licence is not comprehensive, patent holders may complain that export or import of the product is not permitted.

²⁰ See Vienna Convention on the Law of Treaties (Article 26).

²¹ Thus, Paul Hunt, the Special Rapporteur of the Commission on Human Rights, issued a press release lauding the Canadian Bill as an example of the fulfilment of such obligation of international assistance and cooperation. See also E/CN.4/2004/49/Add.1, particularly the discussion of the impact of the 30 August 2003 Decision therein (para. 43).

Given the territoriality of the patent system and that the same patents are not necessarily applied for and obtained in all countries, and that the scope of the approved claims (with regard to the same invention) may also vary from country to country, the set of patents to be subject to compulsory licences may not be exactly the same in the exporting and importing countries. In addition, it will be necessary to determine whether the relevant patents are in force. They not only elapse due to the expiry of the term of protection, but also due to the lack of timely payment of maintenance fees.²²

Importing and exporting countries alike may overcome these problems by specifying that the compulsory licences apply to all patents on the product, its processes of manufacture and uses.

In What Circumstances Does the Decision Apply?

The Decision may be applied when:

- a) the required pharmaceutical product is subject to one or more patents validly in force in the exporting country;
- b) the relevant patents are not subject in the exporting country to a compulsory licence to remedy anti-competitive practices that allows the licensee to export (Article 31 (k) of the TRIPS Agreement, in which case Article 31 (f) does not apply, and there is no need to employ the Decision waiver). Similarly, if a compulsory licence has been issued under which the licensee is predominantly supplying the domestic market, the licensee may supply an importing country with the non-predominant share of its production, and therefore without resort to the Decision waiver.

The Decision would be applicable whether or not the relevant products and processes are patented in the importing country.

If the required pharmaceutical product, or the process for its manufacture, is not patented in the importing country or the patent has expired or been revoked, there is no need to grant a compulsory licence in the importing country. But the Decision applies in order to allow the granting of such a licence in the exporting country.

A particular case may arise in LDCs, which can delay the recognition of pharmaceutical patents until 2016. LDCs that make use of this extension may consider granted pharmaceutical patents non-enforceable until that date. If, despite this possibility, patents on needed pharmaceutical products are enforced, they can grant compulsory licences to use the system set forth by the Decision.

If the product or process for its manufacture is patented in the importing country, then the importing country must issue a compulsory licence pursuant to the special conditions set forth in the Decision.

The Decision will not apply if the relevant product is off-patent in the exporting country, since a waiver of Article 31 (f) is not required. In this case, and if the product were patented in the importing country, a compulsory licence should only be granted in the importing country,

²² Most countries in the world provide for the automatic expiry of patents when the patent owner fails to pay the specified maintenance fees. Some laws allow for the rehabilitation of expired patents, but this is facultative (see Article 5 bis of the Paris Convention).

under the ordinary terms allowed by the national law. There would be no need to comply with the special conditions established by the Decision.

Covered Products

According to paragraph 1 (a) of the Decision, a "pharmaceutical product" is defined as "any patented product, or product manufactured through a patented process, of the pharmaceutical sector needed to address the public health problems as recognized in paragraph 1 of the Declaration". Several elements in this paragraph are important.

First, the Decision may apply either when a patent covers a product or a manufacturing process.

Second, it applies to products "of the pharmaceutical sector" in general, without any limitation as to the types of products (e.g. synthesized chemical products or biologicals), their characterization as essential medicines, or the kind of diseases they are intended to treat. The Decision clarifies that this concept includes "active ingredients necessary for its manufacture". The Decision may be applied in relation to a patent covering a pharmaceutical formulation or the process for its manufacture. The Decision also clarifies that "diagnostic kits needed for its use would be included". This wording may be interpreted as including reagents, diagnosis and monitoring kits. Microbicides can also be considered as covered products.

Vaccines are not specifically mentioned in the Decision. It may be argued that, had the drafters the intention to exclude them, an exception would have been expressly established. According to its ordinary meaning, "pharmaceutical" means "of or engaged in pharmacy; of the use or sale of medicinal drugs".²³ Vaccines may be delivered at a pharmacy, are produced by pharmaceutical firms, and are crucial to address public health problems in developing countries. In view of the very purpose of the Declaration, the term "product ... of the pharmaceutical sector" should, hence, be read as including vaccines.²⁴

Third, the definition of pharmaceutical product refers to Paragraph 1 of the Declaration, which recognizes "the gravity of the public health problems afflicting many developing and least developed countries, **especially** those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics" (emphasis **added**). As the negotiation of the Decision made clear, it applies to pharmaceutical products for any disease. The three mentioned epidemics are only special cases – that certainly deserve particular attention – but the system established by the Decision is not limited to products related to them. Similarly, the Decision is not limited to "grave" diseases, since "gravity" in paragraph 1 of the Declaration is generally referred to "the public health problems" and is not intended to qualify the type of diseases to be addressed.

It is unclear whether a patent covering a therapeutic use (generally called "second indication") is covered by the Decision. The protected invention in this case is a method of treatment and not a product as such.²⁵ However, such patents can be effectively used to restrict access to the products for important therapeutic purposes. In the absence of an exception, and

²³ *The Concise Oxford Dictionary*, p. 768.

²⁴ See, e.g. Vandoren P and Van Eeckhaute JC, The WTO Decision on Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, *The Journal of World Intellectual Property*, vol. 6, no. 6, November 2003, p. 784.

²⁵ For instance, AZT – an important antiretroviral – was developed in the 1950s, and later on its use for HIV/AIDS was patented in many countries.

in view of the intended objectives of the Decision, it seems reasonable to interpret that the Decision can also be applied in these cases.

Which Countries Can Use the System?

The Decision defines the "eligible importing Member[s]". They include:

- a) Any least developed country Member. The only qualification is that the LDC must be a WTO Member;
- b) Any other Member that has made a notification to the Council for TRIPS of its intention to use the system as an importer. As discussed below, the notification may be unqualified or qualified.

The Chair's Statement indicates that the following Members have agreed to opt out of using the system as importers: Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Japan, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom and the United States of America. Until their accession to the European Union, the Czech Republic, Cyprus, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, the Slovak Republic and Slovenia agreed that they would only use the system as importers in situations of national emergency or other circumstances of extreme urgency. These countries further agreed that upon their accession to the European Union, they would opt out of using the system as importers.

Other WTO Members have agreed that they would only use the system as importers in situations of national emergency or other circumstances of extreme urgency: Hong Kong, China; Israel; Korea; Kuwait; Macao, China; Mexico; Qatar; Singapore; the Separate Customs Territory of Taiwan, Penghu, Kinmen and Matsu; Turkey; and the United Arab Emirates.

For What Purposes Can the System Be Used?

LDCs can use the system to import pharmaceutical products under a compulsory licence granted according to any of the grounds authorized by their national laws. As the Doha Declaration has expressly confirmed, WTO Members are free to determine such grounds, which may include, *inter alia*, non-working, public interest, public health, remedying anti-competitive practices, emergency, and refusal to deal. It is clear that while a public health emergency may be one of the grounds for granting a compulsory licence, Member countries may invoke any other ground for that purpose.

The same applies to any other Member, except those Members who opt out of the system, or designate that they will use the system for limited purposes, such as in the case of national emergency.

A question arises as to the extent to which the wording in the Chair's Statement may limit the reasons for which a compulsory licence may be issued. The Statement indicates that the system "should be used in good faith to protect public health and, without prejudice to paragraph 6 of the Decision, not be an instrument to pursue industrial or commercial policy objectives".

At the same time, paragraph 7 of the Decision states that "Members recognize the desirability of promoting the transfer of technology and capacity building in the pharmaceutical

sector in order to overcome the problem identified in paragraph 6 of the Declaration". Paragraph 6 of the Decision aims at "harnessing economies of scale for the purposes of enhancing purchasing power for, and facilitating the local production of, pharmaceutical products" in the context of some regional trade agreements.

This wording suggests that industrial and commercial policy objectives should not be pursued by Member countries under the system established by the Decision, but that Members recognize such objectives cannot be excluded altogether. Thus, eligible importing Members may grant compulsory licences to foster the development of capacity in their pharmaceutical industry as a sustainable way to address their public health problems, for instance by importing active ingredients under the Decision for the local formulation of medicines.

Further, it seems clear that prospective suppliers of pharmaceutical products under the Decision include private companies, notably from countries where a strong generics industry has developed. Such companies will not make the needed investments nor bear the opportunity costs of supplying products under the Decision, unless they are able to obtain some commercial benefit.

COMPULSORY LICENCE IN THE IMPORTING COUNTRY

Notification of Intention to Use the System

Implementation of the Decision involves two kinds of notifications to the Council for TRIPS: a general notification about the intention to be an eligible importing Member, and a specific notification about the products, quantities, etc. that it intends to import.²⁶ This second type of notification is examined below. In both cases, "[t]hese notifications are for the sake of transparency and information only... [They] do not amount to authorization requests; Members concerned will not need to be approved by any WTO body in order to be able to use the system. They can automatically use the system once they have made the notifications".²⁷

The notification to the Council for TRIPS by a prospective importer Member is about the intention to use the Decision, and not about its actual use. This notification seems to be a condition to qualify as an "eligible importing Member". It is not a requirement for LDCs, however, which automatically qualify as eligible importing Members.

The notification may be unqualified, when the Member does not declare any limitations to its potential use of the system, or it may be qualified, when the Member voluntarily states that it will only use the system in a limited way. This limitation may be expressed in terms of the grounds of the compulsory licences (e.g. national emergency or other circumstances of extreme urgency) or otherwise. There is nothing in the Decision preventing a Member from changing, at any time, the terms of its notification. Thus, a Member that declared it would only make limited use of the system may later notify the TRIPS Council of its intention to expand its use.

²⁶ Except as required by Article 31 (b), where applicable, there is no obligation to notify the patent owner about the intention to grant a compulsory licence and the conditions thereof. Likewise, there is no obligation to offer the patent owner the option to supply the required products under the terms and conditions established for the compulsory licence, as proposed in Canadian Bill C-56 (2003).

²⁷ Vandoren, Van Eeckhaute, *op. cit.*, p. 789.

The effect of the notification is declaratory. A Member can declare itself an "eligible importing Member". Footnote 2 of the Decision clarifies that this notification "does not need to be approved by a WTO body in order to use the system set out in this Decision". This means that neither the Council for TRIPS nor any other WTO body is entitled to review, approve or reject a notification and the specific terms under which it is made.

Notification About Needed Products, Compulsory Licence

The second notification to be made by the eligible importing Member²⁸ relates to the importation of particular product(s).²⁹ It must include three elements:

Needed products

The would-be importing country is bound to notify the Council for TRIPS of:

- i) the names of the needed product(s): the generic names of the required pharmaceuticals are to be mentioned;
- ii) the "expected quantities": the notified quantities may not exactly correspond to the quantity of product finally requested or purchased. However, importing countries should carefully assess the quantities needed since, as mentioned below, the corresponding compulsory licence in the exporting country can be granted only for a specified amount.

The specification of quantities may be made in different ways. It may refer to the number of pills or other doses, to a quantity of active ingredients (e.g. 50 kilograms of drug X), to the number of patients to be treated over a period of time, or to other parameters.

The obligation to specify the expected quantity only applies to the notification. It does not refer to the specific terms of the compulsory licence. The compulsory licence issued in the importing country is not required to establish a determined quantity. The authorization could be given to import whatever is required over the duration of the compulsory licence. It would be too cumbersome for the importing country to issue a compulsory licence each time it needs to import a given quantity of a product.

A situation may arise in which the notified "expected" quantities may not correspond to the quantities effectively imported. A country may need, in particular, to import more than expected because it had underestimated its needs. This discord would not affect the right to import, so long as the compulsory licence was not limited to the amounts specified in the TRIPS Council notification.

The application of the Decision does not exclude the application of tendering procedures by the importing country. Moreover, there is no obligation on the importing country to determine a specific timeframe in which importation would take place.

²⁸ This notification also is for transparency purposes only and does not amount to an authorization request.

²⁹ "Joint notifications providing the information required under this subparagraph may be made by the regional organizations referred to in paragraph 6 of this Decision on behalf of eligible importing Members using the system that are parties to them, with the agreement of those parties" (footnote 4 of the Decision).

Establishing Lack of or Insufficient Manufacturing Capacity

This requirement does not apply to LDCs.

For other countries, the insufficient or no manufacturing capacity is not to be assessed in general, but for the particular pharmaceutical product(s) required.

There are two alternative ways to establish these circumstances, as set out in the Annex to the Decision:

- i) The first option applies when the Member has established that it has no manufacturing capacity in the pharmaceutical sector;
- ii) The second option applies when the Member has some pharmaceutical manufacturing capacity, has examined its capacity and found that, excluding any capacity owned or controlled by the patent owner, it is currently insufficient for the purposes of meeting its needs.

What manufacturing capacity means in either of the options is open to interpretation. In a market economy, pharmaceutical manufacturing capacity has two dimensions: technical capability (dependent on availability of technology, trained personnel, equipment, access to raw materials, etc.) and the economic feasibility of production. The technical capability alone does not make it possible to undertake production. The Decision recognizes this limitation and, in particular, the importance of economies of scale in its paragraph 6,³⁰ thereby suggesting that assessment of the existence of manufacturing capacity should not be limited to technical aspects.

A Member country may establish its lack of or insufficient manufacturing capacity and use the system to procure an active ingredient, even though it may have manufacturing capacity to formulate the corresponding product. Formulation is a less technically arduous process and occurs later in the production chain than manufacture of active ingredients.

It is important to note that the Decision does not determine particular criteria or methods to establish the lack of or insufficient capacity. This is a matter of self-assessment,³¹ the outcome of which cannot be challenged by another Member and cannot be subject to review, reversed or rejected by the Council for TRIPS. The Chair's Statement indicates that "[t]o promote transparency and avoid controversy, notifications under paragraph 2(a)(ii) of the Decision would include information on how the Member in question had established, in accordance with the Annex, that it has insufficient or no manufacturing capacities in the pharmaceutical sector". The Statement, however, does not amend the Decision. It only suggests that Members' communicate information, for instance, about the type of analysis made, but not about the criteria or method employed, the data used, or the way in which conclusions were reached.³²

³⁰ "With a view to harnessing economies of scale for the purposes of enhancing purchasing power for, and facilitating the local production of, pharmaceutical products ...".

³¹ Vandoren, Van Eeckhaute, *op. cit.*, p. 785.

³² The following types of notifications would indicate **how** the assessment was made: "The Department/Ministry of ... has [reviewed information in its possession and] [, upon consultations with experts in the field of pharmaceuticals,] found that there is currently no capacity to manufacture [product(s)] in the country." OR "The Department/Ministry of ... has undertaken an enquiry among pharmaceutical producers established in [country] and determined that, excluding the patent owner's facilities, there is currently no capacity in the country to manufacture [product(s)] for the purposes of meeting its needs."

Confirming the Intention to Grant a Compulsory Licence

Finally, where a pharmaceutical product is patented in its territory, the importing country must notify the Council for TRIPS that it has granted or intends to grant a compulsory licence. It would be sufficient to notify the Council that the competent authority intends to grant a compulsory licence. There is no specified timeframe in which the compulsory licence must be issued after the notification is made.

The only condition imposed on the compulsory licence to be granted is that it be "in accordance with Article 31 of the TRIPS Agreement".³³ Hence, the importing country has to respect the conditions set out in this Article. It is not bound to apply more stringent conditions. In particular, there is no obligation to limit the compulsory licence to a limited quantity of the required product(s). The compulsory licence may be granted – as in any other situation – for the lifetime of the patent, subject only to the requirement of Article 31 (g) that the licence may be terminated under certain circumstances, "subject to adequate protection of the legitimate interests" of the compulsory licensee.

In addition, there is no obligation in the importing country to provide compensation to the patent holder. The Decision waives application of Article 31 (h) and stipulates that compensation must be paid in the exporting country.

However, the Decision does not waive the application of Article 31 (b) of the TRIPS Agreement, despite the fact that countries willing to use the system would not be looking for a voluntary licence (unless some phases of production are locally made) but to purchase the final product. This can make the application of that provision a rather futile exercise.

It is to be noted that, although paragraph 6 of the Doha Declaration and the Decision refer to "compulsory licences", the system established by the Decision applies to any use without authorization of the right holder as contemplated in Article 31 of the TRIPS Agreement. This means that the importing country (as well as the exporting country) may apply the system on the basis of an authorization for **public non-commercial use**, and not necessarily under a compulsory licence granted to a third party. For such use without the authorization of the patent holder – often known as "government use" or "crown use" – the obligation for prior negotiation with the patent holder under Article 31 (b) is waived in all cases. In these cases, Members may also limit the remedies available to permit patent holders to seek compensation, without possibility of injunction (Article 44.2 of the TRIPS Agreement).

As mentioned before, notification of the grant of a compulsory licence, or the intention to grant a compulsory licence, is for informational purposes only. The importing country is not required to prove that the conditions provided for by Article 31 have been met, nor can the Council for TRIPS review or contest the content of the notification.³⁴

³³ A question may be raised as to whether this condition means that a compulsory licence may be granted to import pharmaceutical products under Article 31 even in cases where the national legislation does not provide for such grant or for the execution of the licence through importation. The adopted waiver means that a Member country will not have the right to complain against another Member not complying with Article 31 (f) or (h) but would not prevent, in principle, the patent owner from interfering with the granting of a compulsory licence if inconsistent with national law.

³⁴ However, the Statement by the Chair of the General Council indicates that:

- "In accordance with the normal practice of the TRIPS Council, notifications made under the system shall be brought to the attention of its next meeting.
- Any Member may bring any matter related to the interpretation or implementation of the Decision,

The notification will be made publicly available by the WTO Secretariat through a page on the WTO web site dedicated to the Decision. If the notification was made before the granting of the compulsory licence by the importing country, there is no need to make another notification after grant of the licence.

COMPULSORY LICENCE IN THE EXPORTING COUNTRY

The Decision requires the exporting country to grant a compulsory licence.

The Decision does not waive the Article 31 (b) requirement that, prior to issuance of a compulsory licence, a request for a voluntary licence be made to the patent owner.³⁵

If the request for the voluntary licence is unsuccessful, the interested supplier would have to apply for a compulsory licence under the applicable national rules. The competent national authority would have to decide on the application and determine the remuneration to be paid. As mentioned above, this would require that the national law in the exporting country provide for the possibility of issuing a compulsory licence to satisfy a demand on the terms set out in the Decision.

The patent owner may appeal the government's decision to grant a compulsory licence. Depending on procedural rules in the exporting country, an appeal may not interfere with the immediate execution of the licence, or it may prevent the applicant from using the licence until the decision is confirmed. If the appeal does not suspend the execution of the licence, the applicant may start production and export but at the risk of a later claim for damages by the patent owner, if the decision to grant the compulsory licence were reversed.

The Decision sets out with some detail the conditions under which a compulsory licence can be issued by the exporting Member.

Amount Necessary to Meet Needs

The compulsory licence must be granted only to produce and export "the amount necessary to meet the needs of the eligible importing Member(s)". In addition, the entirety of the production under licence shall be exported to the Member(s) which has notified its needs to the Council for TRIPS.

The "needs" are established by the importing country. The amount to be supplied is that actually agreed upon with the importing country (which autonomously determines what its needs are) and not necessarily what was indicated in the notification by the importing country (which only needs to specify the "expected" quantities, as previously mentioned). The "amount necessary to meet the needs" may be established on the basis of several criteria, depending on

including issues related to diversion, to the TRIPS Council for expeditious review, with a view to taking appropriate action.

- If any Member has concerns that the terms of the Decision have not been fully complied with, the Member may also utilize the good offices of the Director-General or Chair of the TRIPS Council, with a view to finding a mutually acceptable solution".

³⁵ As previously mentioned, it may be argued that the exporting country is entitled to consider the situation in the importing country as an emergency, or to recognize public non-commercial use, thus waiving the obligation for prior negotiations as required by Article 31 (b) of the TRIPS Agreement. This possibility would speed up the application of the system.

the degree to which the needs of the eligible importing country can be determined *ex ante*. For instance, it may be based on a specified number of units of products when the needs can be precisely determined, or on the basis of patients to be treated or hospitals to be supplied over a period of time. In order to avoid the transaction costs and delays involved in obtaining a compulsory licence, it might also be possible to consider the granting of an amendable compulsory licence that expands the quantity to be supplied based on subsequent requests notified by the importing country(ies).

Given that one of the concerns underpinning the Decision is the risk of diversion, the criteria to determine quantities to be supplied should be established in good faith and be sufficient to determine the extent of use of the patented invention.

Identification of Product(s)

(i) Labelling and marks

The Decision requires that the products to be supplied under the Decision be clearly identified "through specific labelling or marking". The purpose of the label or mark is to make the products identifiable in case there is diversion to other markets. This requirement may be satisfied by literally stating on the label that a product has been produced under the Decision,³⁶ but the requirement does not impose any specific indication. Hence, the supplier may choose what phrase or sign to utilize to make the products identifiable.

(ii) Packaging, colouring and shaping

Products should not only be identifiable but also distinguishable, presumably from the branded products. This is to be achieved, according to the Decision, through special packaging and/or the colouring/shaping of the products themselves.

Despite the apparent ambiguity of the expression "colouring/shaping", it is clear that these requirements are not cumulative.³⁷ It will be up to the supplier to choose whether to distinguish through packaging, colouring or shaping.

The differences in packaging, colouring or shaping should be those reasonably necessary to enable the distinction to be made. The Decision does not state, however, who should be able to distinguish the products. The requirements may be differently implemented depending on whether the products are to be distinguishable to customs authorities, distributors and retailers, medical doctors, or the general public. Since the objective of this provision is not to protect consumers but to protect pharmaceutical companies against diversion,³⁸ the differences should be those sufficient for customs authorities or pharmaceutical manufacturers (in the case of active ingredients) to distinguish the products. In addition, it is to be noted that while special packaging is not likely to impose a heavy burden on suppliers, changes in colour or shape may

³⁶ For instance, by indicating in the label "Product made for country X under the WTO General Council Decision of 30 August 2003 (WT/L/540)".

³⁷ See the second paragraph of the Statement by the Chair of the General Council where reference is explicitly made to "packaging ... colouring **or** shaping" (emphasis added).

³⁸ See the second paragraph of the Statement by the Chair of the General Council which indicates that "Members recognize that the purpose of the Decision would be defeated if products supplied under this Decision are diverted from the markets for which they are intended. Therefore, all reasonable measures should be taken to prevent such diversion in accordance with the relevant paragraphs of the Decision".

require new bioequivalence and bioavailability studies (if such studies had already been made before) thereby delaying the supply of the products and increasing their prices.

The Decision seems to refer to differentiation of finished products only. However, the Statement indicates that "the provisions of paragraph 2(b)(ii) apply not only to formulated pharmaceuticals produced and supplied under the system but also to active ingredients produced and supplied under the system and to finished products produced using such active ingredients". Whatever the legal value of the Statement (an issue not addressed in this document), the differentiation of an active ingredient by shape may be impossible (since it would normally be provided in powder, liquid or other amorphous form), while differentiation by colour would require inclusion of unnecessary additives and would change the chemical composition of the product. Packaging would seem the only reasonable option for differentiation of active ingredients. Since they are traded between specialized companies, however, differentiation of active ingredients, as opposed to finished products, may not be necessary to prevent diversion.

The obligation to distinguish the products is not absolute. Exporters do not need to distinguish the products when doing so (i) is not feasible, or (ii) will have a significant impact on price.

There are no parameters in the Decision to determine what constitutes a "significant impact on price". Since the Decision's aim is to address the public health needs of Member countries – in the framework of the overall objective of the Doha Declaration to ensure access to medicines for all (paragraph 4) – the significance of the increase in price should be assessed from the perspective of the purchaser. Any increase in price may be "significant" for the purchaser and limit its capacity to address public health needs, particularly in the case of expensive products or purchases in big volumes.

Nor does the Decision specify who should assess whether the impact is significant. It is apparently the supplier who is expected to make this judgment, which should be made taking the purchasers' interests into account.

The Statement indicates that "[i]t is the understanding of Members that in general special packaging and/or special colouring or shaping should not have a significant impact on the price of pharmaceuticals". This ambiguous statement may be read as a recognition that special packaging, colouring or shaping generally does not have a significant impact, or as a normative statement emphasizing the idea that the use of such distinction should not have such a negative impact. This second reading corresponds to the literal wording of the text. Though it may be seen as redundant, it does clarify that colouring and shaping are alternative and not cumulative, and expresses the Members' concern that the distinction of products must not significantly increase prices.

It is important to note that obtaining a compulsory licence may not be sufficient for a company to be able to export a pharmaceutical product under the system, as national health regulations generally require prior approval from national drug regulatory agencies for the production of medicines for export.

Notification by the Supplier

Under the terms of the compulsory licence granted in the supplying country, the supplier should post on a web site certain information before shipment begins. The licensee may use its own web site or the page on the WTO web site dedicated to the Decision. The information must include (i) the quantities being supplied to each destination, and (ii) the distinguishing features of the product(s).

The obligation to provide information is limited to the "distinguishing features", and does not encompass other information about the product. It may include, for instance, an image showing the product as packaged or its label, or indication of its colour or shape, depending on the distinguishing characteristic chosen by the supplier.

Notification by the Exporting Country

In addition to the supplier's notification, the exporting country must notify the Council for TRIPS of the grant of the licence. As in the case of the notification by the importing country, this notification does not need to be approved by any WTO body (footnote 8 of the Decision). The Council for TRIPS has no authority to review the notification nor to object to the grounds and conditions under which the compulsory licence has been granted. Nor can it observe deficiencies in the notification either (for instance, if some of the required information was missing).³⁹ The notification will be made available publicly by the WTO Secretariat through a page on the WTO web site dedicated to the Decision.

The notification must contain the following:

- the name and address of the licensee;
- the product(s) for which the licence has been granted;
- the quantity(ies) for which it has been granted;
- the country(ies) to which the product(s) is (are) to be supplied;
- the duration of the licence;
- the address of the web site where the supplier will post the information referred to in paragraph 2 (b)(iii) of the Decision.

The specified content of the notification suggests that, although a compulsory licence is to be granted for a limited quantity only, a single compulsory licence may cover the production for and export to more than one country. Several importing countries may, in fact, pool their purchasing power for a set of pharmaceutical products, in order to obtain better prices. The Decision also allows a country member of a regional trade agreement, at least half of which is made up of LDCs, to re-export products acquired under the system established by the Decision to other developing or LDC parties to the regional trade agreement that "share the health problem in question" (paragraph 6(i)). The main advantage created by this provision is that the waiver of Article 31 (f) applies to all members of the trade agreement and there is no need to notify the Council for TRIPS each time that an export is made. However, this exception only

³⁹ The Statement by the Chair of the General Council, however, indicates that "[a]ny Member may bring any matter related to the interpretation or implementation of the Decision, including issues related to diversion, to the TRIPS Council for expeditious review, with a view to taking appropriate action." In addition, "if any Member has concerns that the terms of the Decision have not been fully complied with, the Member may also utilize the good offices of the Director-General or Chair of the TRIPS Council, with a view to finding a mutually acceptable solution".

applies to some regional trade agreements in Africa, and not to the bigger regional markets in Asia and Latin America, where more significant economies of scale could be attained. Moreover, the Decision does not allow the supplier to supply all or some of the eligible members of the regional trade agreement. The exception applies only to permit an importing trade agreement member to re-export to others.

The duration of the compulsory licence is to be determined by the exporting country's government. It would be logical to provide for its termination upon the effective supply of the required quantities of a given product, in order to avoid the burden and cost of requiring repeated compulsory licences if delivery takes place over a period of time.

ANTI-DIVERSION MEASURES

According to paragraph 4 of the Decision, "in order to ensure that the products imported under the system set out in this Decision are used for the public health purposes underlying their importation, eligible importing Members shall take reasonable measures within their means, proportionate to their administrative capacities and to the risk of trade diversion to prevent re-exportation of the products that have actually been imported into their territories under the system. In the event that an eligible importing Member that is a developing country Member or a least-developed country Member experiences difficulty in implementing this provision, developed country Members shall provide, on request and on mutually agreed terms and conditions, technical and financial cooperation in order to facilitate its implementation".

The Statement emphasizes that "the purpose of the Decision would be defeated if products supplied under this Decision are diverted from the markets for which they are intended" and indicates that "all reasonable measures should be taken to prevent such diversion in accordance with the relevant paragraphs of the Decision". Though the wording here appears somehow stronger than in the Decision, it neither alters the content nor the nature of the best efforts obligation imposed by the latter. It will be the prerogative of the importing country to determine what is:

- reasonable within the Member's means;
- proportionate to its administrative capacities;
- proportionate to the risk of trade diversion.

General measures on pharmaceuticals need not be adopted, but only those necessary in relation to "products that have actually been imported into their territories under the system".

SUSPENSION OF THE SYSTEM

The second alternative in the Annex to the Decision indicates that "When it is established that such [manufacturing] capacity has become sufficient to meet the Member's needs, the system shall no longer apply". This condition applies only when a country has determined that it has insufficient manufacturing capacity; it does not apply when the determination was that the country lacks manufacturing capacity altogether.

This Decision does not mention who is to make the determination that the capacity has become sufficient nor the applicable procedures. Since it is the importing county itself which

determines insufficient capacity and the Council for TRIPS has no power to review this determination, it is logical to interpret that the importing country should also make the determination that capacity has become sufficient. Given that lack or insufficient capacity is to be established per product, and that compulsory licences are issued to import a specified quantity of a needed pharmaceutical product(s), the determination that capacity has become sufficient would not affect the future use of the system with regard to other product(s).

CONCLUSIONS

The WTO General Council Decision allows Member countries to grant compulsory licences for the export of pharmaceutical products without the restriction established by Article 31 (f) of the TRIPS Agreement, and permits the importing country not to provide compensation to the patent owner where a compulsory licence is granted. The Decision may be also applied on the basis of government non-commercial use, an avenue that in many instances may be quicker, simpler and more effective than the granting of a compulsory licence.

In addition to the steps and procedures stipulated by the Decision, legislative changes are likely to be necessary in both the exporting and importing countries in order to implement the Decision. The conditions under which a compulsory licence can be obtained will influence the speed and cost of making the system operative. Recourse to non-commercial government use may be the most appropriate way in many cases, as the requirement of Article 31 (b) may be waived. A summary of some of the issues to be considered and the steps to be taken to make the system operational are included in Annex 2.

Finally, countries willing to use the Decision should ensure that legal obstacles are not erected through data exclusivity obligations, the “linkage” between product patents and drug registration, or through other regulations.

ANNEX 1

WORLD TRADE

ORGANIZATION

WT/L/540

2 September 2003

(03-4582)

**IMPLEMENTATION OF PARAGRAPH 6 OF THE DOHA DECLARATION ON
THE TRIPS AGREEMENT AND PUBLIC HEALTH**

Decision of 30 August 2003*

The General Council,

Having regard to paragraphs 1, 3 and 4 of Article IX of the Marrakesh Agreement Establishing the World Trade Organization ("the WTO Agreement");

Conducting the functions of the Ministerial Conference in the interval between meetings pursuant to paragraph 2 of Article IV of the WTO Agreement;

Noting the Declaration on the TRIPS Agreement and Public Health (WT/MIN(01)/DEC/2) (the "Declaration") and, in particular, the instruction of the Ministerial Conference to the Council for TRIPS contained in paragraph 6 of the Declaration to find an expeditious solution to the problem of the difficulties that WTO Members with insufficient or no manufacturing capacities in the pharmaceutical sector could face in making effective use of compulsory licensing under the TRIPS Agreement and to report to the General Council before the end of 2002;

Recognizing, where eligible importing Members seek to obtain supplies under the system set out in this Decision, the importance of a rapid response to those needs consistent with the provisions of this Decision;

Noting that, in the light of the foregoing, exceptional circumstances exist justifying waivers from the obligations set out in paragraphs (f) and (h) of Article 31 of the TRIPS Agreement with respect to pharmaceutical products;

Decides as follows:

1. For the purposes of this Decision:
 - (a) "pharmaceutical product" means any patented product, or product manufactured through a patented process, of the pharmaceutical sector needed to address the

* This Decision was adopted by the General Council in the light of a statement read out by the Chairman, which can be found in JOB(03)/177. This statement will be reproduced in the minutes of the General Council to be issued as WT/GC/M/82.

public health problems as recognized in paragraph 1 of the Declaration. It is understood that active ingredients necessary for its manufacture and diagnostic kits needed for its use would be included⁴⁰;

- (b) "eligible importing Member" means any least-developed country Member, and any other Member that has made a notification⁴¹ to the Council for TRIPS of its intention to use the system as an importer, it being understood that a Member may notify at any time that it will use the system in whole or in a limited way, for example only in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use. It is noted that some Members will not use the system set out in this Decision as importing Members⁴² and that some other Members have stated that, if they use the system, it would be in no more than situations of national emergency or other circumstances of extreme urgency;
- (c) "exporting Member" means a Member using the system set out in this Decision to produce pharmaceutical products for, and export them to, an eligible importing Member.

2. The obligations of an exporting Member under Article 31(f) of the TRIPS Agreement shall be waived with respect to the grant by it of a compulsory licence to the extent necessary for the purposes of production of a pharmaceutical product(s) and its export to an eligible importing Member(s) in accordance with the terms set out below in this paragraph:

- (a) the eligible importing Member(s)⁴³ has made a notification² to the Council for TRIPS, that:
 - (i) specifies the names and expected quantities of the product(s) needed⁴⁴;
 - (ii) confirms that the eligible importing Member in question, other than a least-developed country Member, has established that it has insufficient or no manufacturing capacities in the pharmaceutical sector for the product(s) in question in one of the ways set out in the Annex to this Decision; and
 - (iii) confirms that, where a pharmaceutical product is patented in its territory, it has granted or intends to grant a compulsory licence in accordance with Article 31 of the TRIPS Agreement and the provisions of this Decision⁴⁵;

⁴⁰ This subparagraph is without prejudice to subparagraph 1(b).

⁴¹ It is understood that this notification does not need to be approved by a WTO body in order to use the system set out in this Decision.

⁴² Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Japan, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom and the United States.

⁴³ Joint notifications providing the information required under this subparagraph may be made by the regional organizations referred to in paragraph 6 of this Decision on behalf of eligible importing Members using the system that are parties to them, with the agreement of those parties.

⁴⁴ The notification will be made available publicly by the WTO Secretariat through a page on the WTO website dedicated to this Decision.

⁴⁵ This subparagraph is without prejudice to Article 66.1 of the TRIPS Agreement.

- (b) the compulsory licence issued by the exporting Member under this Decision shall contain the following conditions:
- (i) only the amount necessary to meet the needs of the eligible importing Member(s) may be manufactured under the licence and the entirety of this production shall be exported to the Member(s) which has notified its needs to the Council for TRIPS;
 - (ii) products produced under the licence shall be clearly identified as being produced under the system set out in this Decision through specific labelling or marking. Suppliers should distinguish such products through special packaging and/or special colouring/ shaping of the products themselves, provided that such distinction is feasible and does not have a significant impact on price; and
 - (iii) before shipment begins, the licensee shall post on a website⁴⁶ the following information:
 - the quantities being supplied to each destination as referred to in indent (i) above; and
 - the distinguishing features of the product(s) referred to in indent (ii) above;
- (c) the exporting Member shall notify⁴⁷ the Council for TRIPS of the grant of the licence, including the conditions attached to it.⁴⁸ The information provided shall include the name and address of the licensee, the product(s) for which the licence has been granted, the quantity(ies) for which it has been granted, the country(ies) to which the product(s) is (are) to be supplied and the duration of the licence. The notification shall also indicate the address of the website referred to in subparagraph (b)(iii) above.

3. Where a compulsory licence is granted by an exporting Member under the system set out in this Decision, adequate remuneration pursuant to Article 31(h) of the TRIPS Agreement shall be paid in that Member taking into account the economic value to the importing Member of the use that has been authorized in the exporting Member. Where a compulsory licence is granted for the same products in the eligible importing Member, the obligation of that Member under Article 31(h) shall be waived in respect of those products for which remuneration in accordance with the first sentence of this paragraph is paid in the exporting Member.

4. In order to ensure that the products imported under the system set out in this Decision are used for the public health purposes underlying their importation, eligible importing Members shall take reasonable measures within their means, proportionate to their administrative capacities and to the risk of trade diversion to prevent re-exportation of the

⁴⁶ The licensee may use for this purpose its own website or, with the assistance of the WTO Secretariat, the page on the WTO website dedicated to this Decision.

⁴⁷ It is understood that this notification does not need to be approved by a WTO body in order to use the system set out in this Decision.

⁴⁸ The notification will be made available publicly by the WTO Secretariat through a page on the WTO website dedicated to this Decision.

products that have actually been imported into their territories under the system. In the event that an eligible importing Member that is a developing country Member or a least-developed country Member experiences difficulty in implementing this provision, developed country Members shall provide, on request and on mutually agreed terms and conditions, technical and financial cooperation in order to facilitate its implementation.

5. Members shall ensure the availability of effective legal means to prevent the importation into, and sale in, their territories of products produced under the system set out in this Decision and diverted to their markets inconsistently with its provisions, using the means already required to be available under the TRIPS Agreement. If any Member considers that such measures are proving insufficient for this purpose, the matter may be reviewed in the Council for TRIPS at the request of that Member.

6. With a view to harnessing economies of scale for the purposes of enhancing purchasing power for, and facilitating the local production of, pharmaceutical products:

- (i) where a developing or least-developed country WTO Member is a party to a regional trade agreement within the meaning of Article XXIV of the GATT 1994 and the Decision of 28 November 1979 on Differential and More Favourable Treatment Reciprocity and Fuller Participation of Developing Countries (L/4903), at least half of the current membership of which is made up of countries presently on the United Nations list of least-developed countries, the obligation of that Member under Article 31(f) of the TRIPS Agreement shall be waived to the extent necessary to enable a pharmaceutical product produced or imported under a compulsory licence in that Member to be exported to the markets of those other developing or least-developed country parties to the regional trade agreement that share the health problem in question. It is understood that this will not prejudice the territorial nature of the patent rights in question;
- (ii) it is recognized that the development of systems providing for the grant of regional patents to be applicable in the above Members should be promoted. To this end, developed country Members undertake to provide technical cooperation in accordance with Article 67 of the TRIPS Agreement, including in conjunction with other relevant intergovernmental organizations.

7. Members recognize the desirability of promoting the transfer of technology and capacity building in the pharmaceutical sector in order to overcome the problem identified in paragraph 6 of the Declaration. To this end, eligible importing Members and exporting Members are encouraged to use the system set out in this Decision in a way which would promote this objective. Members undertake to cooperate in paying special attention to the transfer of technology and capacity building in the pharmaceutical sector in the work to be undertaken pursuant to Article 66.2 of the TRIPS Agreement, paragraph 7 of the Declaration and any other relevant work of the Council for TRIPS.

8. The Council for TRIPS shall review annually the functioning of the system set out in this Decision with a view to ensuring its effective operation and shall annually report on its operation to the General Council. This review shall be deemed to fulfil the review requirements of Article IX:4 of the WTO Agreement.

9. This Decision is without prejudice to the rights, obligations and flexibilities that Members have under the provisions of the TRIPS Agreement other than paragraphs (f) and (h) of Article 31, including those reaffirmed by the Declaration, and to their interpretation. It is also without prejudice to the extent to which pharmaceutical products produced under a compulsory licence can be exported under the present provisions of Article 31(f) of the TRIPS Agreement.

10. Members shall not challenge any measures taken in conformity with the provisions of the waivers contained in this Decision under subparagraphs 1(b) and 1(c) of Article XXIII of GATT 1994.

11. This Decision, including the waivers granted in it, shall terminate for each Member on the date on which an amendment to the TRIPS Agreement replacing its provisions takes effect for that Member. The TRIPS Council shall initiate by the end of 2003 work on the preparation of such an amendment with a view to its adoption within six months, on the understanding that the amendment will be based, where appropriate, on this Decision and on the further understanding that it will not be part of the negotiations referred to in paragraph 45 of the Doha Ministerial Declaration (WT/MIN(01)/DEC/1).

ANNEX

Assessment of Manufacturing Capacities in the Pharmaceutical Sector

Least-developed country Members are deemed to have insufficient or no manufacturing capacities in the pharmaceutical sector.

For other eligible importing Members insufficient or no manufacturing capacities for the product(s) in question may be established in either of the following ways:

(i) the Member in question has established that it has no manufacturing capacity in the pharmaceutical sector;

OR

(ii) where the Member has some manufacturing capacity in this sector, it has examined this capacity and found that, excluding any capacity owned or controlled by the patent owner, it is currently insufficient for the purposes of meeting its needs. When it is established that such capacity has become sufficient to meet the Member's needs, the system shall no longer apply.

ANNEX 2

Summary of Context and Steps Required to Use the System

Issues to be considered

- There is no need to follow the Decision procedures if there is an agreement by the patent owner or his voluntary licensee to supply the required pharmaceutical product(s) at prices agreeable to the importing country. The need to use the Decision arises if the patent owner refuses to supply on mutually agreed conditions.
- If an agreement with the patent owner is not reached, the prospective importing country should determine which patents are relevant in the importing and exporting country and their legal status. This may not be a simple task since, as previously mentioned, several patents usually protect, directly or indirectly, a product. Moreover, patents expire after the specified period of duration and for lack of payment of maintenance fees. Before taking action, the existence of enforceable patents should be confirmed. An option that governments may follow when Article 31(b) is not applicable (e.g. in cases of emergency), is to grant a compulsory licence covering all patents (whether identified or not) relating to a product (including processes and, if relevant, indications) that would be infringed in case of importation.⁴⁹
- The possibility of using the Decision will depend on certain aspects of the national patent laws in the importing and exporting countries. The law in the importing country must provide for compulsory licences under which imports can be made to address public health needs, and the law in the exporting country must allow for exports in cases (not covered by Article 31 (k) of the TRIPS Agreement) where export markets are predominantly supplied. The national law in the importing country should also permit the implementation of the waiver of Article 31 (h) regarding compensation to the patent owner when products are being imported pursuant to the Decision.
- A dissatisfied patent owner may use the legal mechanisms available under the laws of the importing and/or exporting country to challenge the compulsory licence, the compensation to be paid (in the exporting country) or other aspects of the transactions made under the Decision.

Context

Access to needed product refused	Refusal of the patent owner to supply drugs at a price acceptable to importing country
Patent status in the importing and exporting country	Identification and analysis of relevant patents and of their validity
Compulsory licence (CL) to import allowed by national law in importing country	Law in the importing country allows for the granting of CL to import in order to satisfy public health needs; in cases of emergency, for public interest, to remedy anti-competitive practices, for non-commercial government use or on other grounds

⁴⁹ See, e.g. the notice of authorization for the exploitation of patented inventions issued by the Government of Malaysia on 29 October 2003 relating to didanosine, zidovudine and lamivudine, and the compulsory licence granted by the Government of Mozambique (No. 01/MIC/04) in May 2004.

Implementation of waiver on compensation (Article 31 (h) of the TRIPS Agreement)	Law in the importing country has been adapted to use the waiver relating to the compensation to the patent owner
CL for export allowed by national law in exporting country	Exporting country's law has been amended, as necessary, to implement waiver of Article 31 (f) of the TRIPS Agreement

Steps in the Importing Member Country

The steps for the importing country to use the Decision are summarized in the following table. As previously mentioned, differences exist in some aspects of the procedures depending on whether the importing country is a LDC or a developing country not falling within this category. The steps indicated below are not necessarily sequential (for instance, the notification of the importing country can be made before or after the granting of a compulsory licence).

Steps to use Decision	LDCs	Other Members
Notification of intention to use the system	Not required	Notification with or without limitations
Establishing lack of or insufficient manufacturing capacity	Not required	Required
Notification of product's name and quantities, intention to grant or granting of CL and lack of or insufficient manufacturing capacity	Notification of lack of or insufficient manufacturing capacity not required	Required
Preliminary procedures to obtain a CL if relevant patents are in force in the importing country	Unless the prior request of a voluntary licence does not apply, an entity in the importing country must seek a voluntary licence from the patent owner	Unless the prior request of a voluntary licence does not apply, an entity in the importing country must seek a voluntary licence from the patent owner
Application for and processing of CL request	Compliance with national laws	Compliance with national laws
Granting of CL in importing country, before or after the notification	CL may be for unlimited quantity, as long the patent is in force, and without compensation	CL may be for unlimited quantity, as long the patent is in force, and without compensation
Review of CL	The granting of a CL may be challenged by the patent owner and subject to review by a higher authority. Depending on national law,	The granting of a CL may be challenged by the patent owner and subject to review by a higher authority. Depending on national law, the review need not suspend

Steps to use Decision	LDCs	Other Members
	the review need not suspend the execution of the licence	the execution of the licence
Registration of products with health authority in the importing country	Proof of bioequivalence and bioavailability, if required by national law If, in the importing country, data exclusivity is granted with regard to data submitted for the registration of medicines, the data holder's authorization would be required, unless the use of such data is included ⁵⁰ in the CL ⁵¹	Proof of bioequivalence and bioavailability, if required by national law If, in the importing country, data exclusivity is granted with regard to data submitted for the registration of medicines, the data holder's authorization would be required, unless the use of such data is included in the CL
Anti-diversion measures in the importing country	Adoption of reasonable measures within their means, proportionate to their administrative capacities and to the risk of trade diversion to prevent re-exportation of the products that have actually been imported into their territories under the system	Adoption of reasonable measures within their means, proportionate to their administrative capacities and to the risk of trade diversion to prevent re-exportation of the products that have actually been imported into their territories under the system

Steps in the Exporting Member country

In addition to a possible legislative change, a number of actions need to be taken by the prospective supplier and exporting country in order to apply the Decision.

Steps to use Decision	Actions required
Preliminary procedures to obtain a CL	Unless the prior request of a voluntary licence does not apply, an entity in the exporting country must seek a voluntary licence from the patent owner
Application for a CL	Only for a limited amount Entirety of production for export
Granting of CL including determination of compensation to patent owner	Compliance with national laws
Review of CL	The granting of a CL may be challenged by the patent owner and subject to review by a higher authority. The review need not suspend the execution of the licence

⁵⁰ There are precedents of this kind in the USA. See Correa, C (1999), *Intellectual property rights and the use of compulsory licenses: options for developing countries*, Trade-Related Agenda, Development and Equity, Working Paper No. 5, Geneva, South Centre, 1999, p. 16.

⁵¹ Provisions allowing the use of data in cases of the granting of a compulsory licence may need to be incorporated into national laws, in order to prevent legal challenges that could otherwise block the exploitation of the licence.

Steps to use Decision	Actions required
Notification by exporting country	Information about the conditions attached to the CL, including the name and address of the licensee, the product(s) for which the licence has been granted, the quantity(ies) for which it has been granted, the country(ies) to which the product(s) is (are) to be supplied, the duration of the licence and the address of the web site where the supplier will post information about shipment
Production and product differentiation	Develop the chemistry and formulate the drug (when produced by the licensee for the first time), and investigate the shape, colouring, labelling and packaging of the patent-holder's product in the importing country in order to differentiate the product for export
Notification by the supplier before shipment	Information about quantities and distinguishing features of products

CHAPTER VI

GUIDELINES FOR THE EXAMINATION OF PHARMACEUTICAL PATENTS: DEVELOPING A PUBLIC HEALTH PERSPECTIVE

INTRODUCTION

The pharmaceutical sector is a major user of the patent system. While only a small – and declining – number of new chemical entities are approved annually, thousands of patents are applied for to protect variants of existing products, processes of manufacture or, where admitted, second indications of known pharmaceutical products.

Since patents confer exclusive rights regarding the production, sale and use of the patented subject matter, they can be used to restrain competition and set prices higher than those that would have existed if competitive products were available. This is the very purpose of the patent system, which is generally justified as necessary to encourage investments to develop new products and processes.¹

Given the substantial effects that patents can have on competition and, hence, prices of medicines, the criteria that are applied to examine and grant pharmaceutical patents are extremely relevant for public health policies, and not only a matter of concern for patent and industrial policy. Policy makers in the health area, as well as patent examiners, should be aware that decisions relating to the grant of a patent (which is generally presumed valid until proven to the contrary) can directly affect the health and lives of the people of the country where the patent is granted and enforced.

The purpose of this document is to provide a set of general guidelines for the assessment of some of the common types of pharmaceutical patent claims. It responds to growing concerns in different circles² about the proliferation of patents that protect minor, and in some cases obvious, variants of existing drugs or processes (such as changes in the drug formulation, salts, esters, ethers, isomers, polymorphs of known molecules, combinations of a known drug with other known drugs) while the number of new chemical entities of pharmaceutical use is small and declining.³ Although such patents may be weak or, if subject to strict scrutiny, invalid, they can be effectively used in many cases to prevent generic competition thereby reducing access to medicines.

¹ On the functions of the patent system, see Commission on Intellectual Property Rights, Innovation and Public Health, Public Health, Innovation and Intellectual Property Rights, World Health Organization (available at www.who.int) 2006 (hereinafter ‘CIPIH’).

² See, e.g. Federal Trade Commission (FTC) (2003); Jaffe and Lerner (2004); Correa, (2001a).

³ The number of new molecular entities (NMEs) approved by the US Food and Drug Administration drastically declined since the mid-1990s (from 53 in 1996 to a minimum 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 14 November 2005).

While recognizing the importance that pharmaceutical follow-on innovation may have in certain cases,⁴ the present guidelines aim to increase the capacity of patent offices, public health and drug regulatory authorities, as well as of civil society, to evaluate and take the necessary actions, as appropriate under national laws, to protect public health in cases where patent applications or grants cover subject matter that does not deserve the reward of a patent monopoly. This document is ultimately intended to provide support to national patent offices by highlighting the areas in which poor decisions have often been made, including in economically important countries. The complexity and cost of overturning bad decisions generally pose insurmountable barriers to those who are affected. These guidelines aim, hence, at contributing to a sound analysis of pharmaceutical patents based on a rational application of the patentability standards.

First, the document briefly discusses the scope allowed to WTO Member countries by the TRIPS Agreement to determine the standards under which the novelty and inventive step of claimed inventions are assessed. Second, it provides examples of different categories of patent claims for pharmaceutical products,⁵ indicates the practice of some patent offices, and includes recommendations for each category of claims. The proposed recommendations suggest elements for the development of public health-sensitive guidelines for the evaluation and review of pharmaceuticals patents at the national level. Analysis of particular cases and possible exceptions to the general recommendations made herein should be further undertaken and elaborated in the light of the national applicable law, particularly as regards the concept of ‘invention’ and patentability criteria. Finally, the document addresses some of the mechanisms that may be adopted to incorporate public health perspectives into procedures for the granting and review of pharmaceutical patents.

It is acknowledged that the issues dealt with are complex and that any one of them would require a more detailed elaboration, as done in some of the bibliography mentioned in the text. It is outside the remit of this document to undertake such detailed elaboration, since its purpose is only to provide an overview of problematic areas of patentability and possible ways of generally addressing them.⁶

The guidelines, as proposed in this document, do not suggest the application of a new requirement of patentability, but rather to take into account, in applying the ordinary requirements of novelty, inventive step and industrial applicability (or utility), specific considerations relating to innovation in pharmaceuticals.

DEFINING PATENTABILITY AND DISCLOSURE STANDARDS

The ordinary meaning of ‘invention’ relates to the output of an intellectual activity in the form of new knowledge of a technical nature. To invent is ‘to create by thought, originate (new

⁴ CIPIH, p. 17. However, patents may, in some circumstances, deter follow on innovation, especially when outputs of up-stream science are patented. See, e.g. Commission on Intellectual Property Rights (2002); Sampath (2005), p. 29.

⁵ The examples include the abstract and one or more claims as an illustration. There has been no intention to judge the validity of the patents mentioned (or any of their claims) in particular jurisdictions. The examples have been selected with the assistance of Lic. Romina Gomez (Faculty of Exact and Natural Sciences, University of Buenos Aires).

⁶ This document does not address issues relating to the patentability of pharmaceutically relevant biotechnological inventions, such as those relating to human proteins or genes.

method, instrument, etc.)'.⁷ It also suggests a distinction between creations and mere discoveries and, more generally, between inventions and other subject matter that is not the outcome of an inventive process.⁸

Most patent laws in the world do not define what an invention is. Rather than a gap this has often been regarded as essential to allow a progressive adaptation of patent law to the advancement of science and technology.⁹ Exceptionally, some patent laws include a definition of 'invention'. For instance, the Mexican patent law considers as an invention all human creation that permits the transformation of matter or energy that exists in nature, for the benefit of man and to satisfy his concrete needs (Article 15).¹⁰ The law in Chinese Taipei refers to 'a high-level creation of technical concept(s) by which natural rules are utilized' (Article 19). These definitions seem to suggest that an invention supposes creating rather than discovering something that was previously undisclosed. In other jurisdictions, however, discoveries that are useful to solve a problem are patentable.¹¹

In fact, the concept of invention as applied in various countries significantly differs. The TRIPS Agreement, however, does not seem to interfere with such diversity. The wording of Article 27.1 indicates that Members have been left room to interpret in good faith the concept of 'invention' within their legal systems,¹² subject only to the application of the rules for interpretation set out by the Vienna Convention on the Law of the Treaties.¹³ Members may require the existence of an invention as a precondition for patentability.¹⁴

Whatever the definition of invention, the crucial issue is that a patent must contain a non-obvious technical contribution to the state of the art, whereby a technical problem is solved by technical means.

Subject to the same aforementioned interpretation rules, the TRIPS Agreement also allows WTO Member countries to adopt their own definitions of the patentability standards. Article 27.1 prescribes, in effect, that patents "shall be available for any inventions ... provided that they are new, involve an inventive step and are capable of industrial application", but does not contain any specification about the precise way in which these criteria are to be applied.

The general terms used in Article 27.1 have permitted Member countries to keep different criteria to assess patentability. The definition of such criteria constitutes a key aspect of patent policy, with implications in other areas, such as industrial and public health policies. Obviously, the narrower the novelty standard, the lower the bar to assess inventive step, and the

⁷ The Concise Oxford Dictionary, 1989, p. 527.

⁸ Many patent laws make such a distinction. For instance, Article 52 (2) of the European Patent Convention stipulates that '[T]he following in particular shall not be regarded as inventions within the meaning of paragraph 1: (a) discoveries, scientific theories and mathematical methods; (b) aesthetic creations; (c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers; (d) presentations of information'.

⁹ See, e.g. Burnier (1981), p. 22.

¹⁰ The same concept is contained in the Argentine patent law (Article 4(a)).

¹¹ The European Patent Convention, for instance, is interpreted to only exclude from patentability discoveries as such. See, e.g. Cook (2002), p. 179.

¹² See Straus (1996), p. 187.

¹³ See Articles 31 and 32 of the Convention. The method of interpretation codified by this Convention has been extensively used in GATT/WTO jurisprudence, including with regard to the TRIPS Agreement. See, e.g. Frankel (2006).

¹⁴ As suggested by decision in the UK and by the European Patent Office. See, e.g. Bently and Sherman (2001), pp. 370-371.

broader the concept of industrial applicability or utility, the greater the number of applications that may be granted in a particular country. A greater number of grants made on the basis of low standards of patentability may lead to unnecessary limitations on competition without any significant trade-off in terms of more innovation to address society's needs.

Although most countries in the world apply an absolute novelty requirement (that is, disclosure in any form anywhere in the world before the filing date will prevent the granting of a patent) some countries maintain a double standard of novelty depending on whether the disclosure of the invention has taken place within or outside their territory.¹⁵

In practice, the concept of novelty is narrowly construed by some patent offices, requiring an almost 'photographic' disclosure of the invention in a single prior document in order to consider that novelty does not exist. For experienced patent applicants, overcoming novelty barriers may be just a matter of clever design of patent applications.

WTO Members, however, are not constrained to apply a particular concept of novelty, and can adopt a notion that objectively reflects whether the claimed invention is genuinely new or not. For instance, they may consider non-novel an invention that is not described *expressis verbis* in a document but which may be derived thereof, as well as inventions just selected from a family of already disclosed products (the so called 'selection inventions').¹⁶ In addition, novelty may not be normally claimed if a feature was present in a known substance and was inherent thereto, even though that feature was not mentioned in the prior art.¹⁷

Defining 'non-obviousness/inventive step' is one of the most critical aspects of a patent regime, as it determines the level of technical contribution required to obtain a patent and the corresponding limitation on competition. Patent examiners need to consider not only what is disclosed in the prior art but also what a person skilled in the art (such as a person trained and experienced in pharmaceutical formulation) could consider obvious in the light of such prior art. As the TRIPS Agreement does not define this concept either, Member countries are free to determine whether they want a system under which a myriad of incremental innovations¹⁸ are

¹⁵ According to US law, for example, "[A] person shall be entitled to a patent unless the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States ..." (35 U.S.C section 102). In responding to a question about the novelty standard applied under this Section, the US held that in the TRIPS Agreement there was 'no prescription as to how WTO Members define what inventions are to be considered "new" within their domestic systems' and, hence, that its legislation was 'perfectly consistent with the provisions of the TRIPS Agreement' (document IP/Q3/USA/1, May 1, 1998).

¹⁶ See below.

¹⁷ See e.g., the decision by the Opposition Division of the European Patent Office of 20-1-05 revoking EP-B-1049467 (relating to compositions of 'Celecoxib'); see also in *re Benner*, 174 F.2d 938, 942 (C.C.P.A.1949) ("[N]o provision has been made in the patent statutes for granting a patent upon an old product based solely upon discovery of a new use for such product."); in *re Cruciferous Sprout Litig.*, 301 F.3d1343, 1349-50 (Fed. Cir. 2002) (inventor's recognition of substances that render broccoli and cauliflower particularly healthy does not permit patent on identifying broccoli seeds or preparing broccoli as a food product); *ABBOTT LABORATORIES and CENTRAL GLASS COMPANY, LTD. v. BAXTER PHARMACEUTICAL PRODUCTS, INC. and BAXTER HEALTHCARE CORP*, United States Court of Appeals for the Federal Circuit, 9 November 2006.

¹⁸ 'Incremental innovations' (as opposed to 'major' innovations) are modifications, such as improvements or adaptations of existing products and processes. Irrespective of their practical usefulness, such improvements may be obvious to develop for a person having ordinary skills in the art.

patentable,¹⁹ or one aimed at rewarding more substantive departures from the prior art.²⁰ Patent offices and courts can apply more or less lax or stringent criteria to determine non-obviousness/inventive step.

The best policy from the perspective of public health would seem to be the application of a strict standard of inventiveness²¹ so as to promote genuine innovations and prevent unwarranted limitations to competition and access to existing drugs. This implies that the ‘person skilled in the art’ should be deemed to have some specialized knowledge and not simply somebody with very general or ordinary knowledge in the relevant technical field.²² A person skilled in the art is not just an expert in his technical field but a person who should have some degree of imagination and intuition. He should not only rely on the documents found in the novelty search, but apply his experience and his knowledge. Such an examiner should be particularly strict when examining the inventive step.

Finally, inventions must be susceptible of industrial applicability, since the aim of patent law is to protect technical solutions to a given problem, not abstract knowledge. In some countries, such as the United States, it is sufficient to show that the invention has utility, which obviously allows for a broader scope of patentability than the narrower concept of ‘industrial applicability’. Like in the case of novelty and inventive step, the TRIPS Agreement does not define what criteria should be applied to determine industrial applicability or utility. The application of these requirements is problematic in chemistry and biosciences in the absence of concrete experimentation, since these are empirical sciences with low predictive capacity about the specific properties of obtainable substances. Patent claims should contain, as a minimum, a technically viable solution and not merely an unresolved problem or a speculative or intended result.

Another important element in the assessment of patent applications or grants is the disclosure of the invention. In accordance with Article 29.1 of the TRIPS Agreement,

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

¹⁹ Scherer noted almost two decades ago: ‘As the bleary-eyed reviewer of some 15,000 patent abstracts in connection with research... I was struck by how narrowly incremental (adaptive?) most "inventions" are’ (Scherer, 1987, p. 124).

²⁰ In an early US court decision Justice Bradley stated that “[I]t was never the object of [the patent] laws to grant a monopoly for every trifling device, every shadow of a shade, of an idea, which would naturally and spontaneously occur to any skilled mechanic or operator in the ordinary progress or manufactures” (Atlantic Works v. Brady, 107 U.S. (17 Otto) 192, 1883). Fifty years later Justice Douglas stated that a new device, to be patentable, “must reveal the flash of creative genius” (Cuno Engineering Corp., 314U.S. 84, 51 U.S.P.Q. 1, 1941) (quoted in Chisum, Donald and Jacobs, Michael (1992)). The US policy on the matter has significantly changed, however, since these statements were made, as the patent office and courts applied a less rigorous concept of non-obviousness. See, e.g., Federal Trade Commission (FTC) (2003); Jaffe and Lerner (2004).

²¹ See, e.g. World Bank (2001), p. 147, recommending that developing countries generally apply strict criteria for the granting of patents.

²² Finding a solution to a problem should not be deemed as a basis for patentability, unless the solution is non-obvious. On the problem-solution approach applied by the European Patent Office, see Cook, *op. cit.* pp. 208-210.

Lack of sufficient disclosure may be a reason for refusal of an application or invalidation of a patent. This requirement has particular importance in the chemical and pharmaceutical fields to enable the reproduction of the invention during the patent term (for instance, in the case of a compulsory license) or after patent's expiry. A special consideration should be given to cases in which a large number (sometimes millions) of compounds belonging to a group characterized by common elements is claimed.²³

Finally, a general rule in patent law is that the patent must cover a single inventive concept, that is, there must be 'unity of invention'. This means that the claimed subject matter should share the same technical features understood as the contributions that each of the claimed inventions, considered as a whole, makes over the prior art.²⁴

In sum, the ways in which national laws conceptualize what an invention is, and how the patentability standards and the requirements regarding disclosure and unity of invention are applied, will certainly be key to determine whether different types of claims relating to pharmaceutical inventions are admissible or not.

TYPICAL CLAIMS RELATING TO PHARMACEUTICAL INVENTIONS

A patent claim relating to a pharmaceutical product may relate to an active ingredient as such independently of or jointly with formulations, salts, prodrugs, isomers, etc., or cover any of these subject matters separately. It may also solely cover a manufacturing process or include both a process and a product. In some countries, as noted below, use-related claims are admissible. The following sections include some considerations for the evaluation of different types of claims that are typical in this area.

In undertaking such evaluation it will be important to bear in mind that while the development of new molecules of pharmaceutical use may encompass various levels of inventive steps, pharmaceutical techniques for the preparation of medicines in different forms and dosages are generally well known and part of the pool of knowledge in possession of a 'person skilled in the art'. Hence, there is a narrow range of developments that could be considered genuinely inventive in this field in view of the state of the art.

Formulations and Compositions²⁵

The same active ingredient may be presented in different dosage forms, for instance, as tablets, capsules, ointment or aqueous solutions for parenteral administration, which in turn can be formulated using different pharmaceutically acceptable excipients.

A large number of patents claim formulations of new or existing drugs, often including specifications of dose or concentration, either as the principal claim or in subordination to claims over the active ingredients or their uses. 'Composition claims' cover active ingredients and pharmaceutically acceptable carriers or excipients such as fillers, binders, disintegrants and lubricants.

²³ This paper does not deal with issues relating to the breadth of patent claims, except in relation to the so-called 'Markush claims'. Such issues also deserve a careful and systematic analysis. See, e.g. Merges (1996), pp. 120-144.

²⁴ See Bently and Sherman (2001), pp. 370-371.

²⁵ See examples 1 to 10 in the Annex.

Patents granted solely on the basis of formulation or composition claims do not protect the active ingredients as such, and different formulations or compositions comprising the same ingredients may – if they are in the public domain – be commercialized by competing companies. However, such patents may be used to discourage competition through ‘strategic’ litigation, that is, by alleging infringement and requesting provisional injunctions that block commercialization until a final decision is made.

Formulation or composition claims are deemed acceptable by some patent offices, under certain conditions. This is, for instance, the case of the United Kingdom (see Box 1).

Box 1

Examination Guidelines for Patent Applications relating to Medical Inventions in the UK Patent Office (March 2004), Claims to pharmaceutical compositions, Compositions adapted to a particular use, Paragraph 11431

Known substances may be protected by *per se* product claims to pharmaceutical compositions containing them, if the composition is in a form which is novel and inventive over any known products. In particular, a claim may be made to a medicament having a form of administration which is novel and distinct from the previous use. For example, an anti-eczema ointment containing X would be regarded as clearly distinct from a tablet containing X for controlling blood pressure.²⁶ The ointment is new because X has never been formulated in this form before, and it would be inventive if the previous use of X would not suggest its use in topical form.

In some cases, a particular claimed formulation is associated with certain effects, such as controlled release in blood of a drug.²⁷ Achieving such effects is generally part of the ordinary skill of a person knowledgeable in the formulation of pharmaceuticals, unless there are exceptional circumstances, such as the use in a product of a new excipient that produces a truly unexpected or surprising effect, for instance, a noticeable reduction in side effects or an extraordinary improvement in drug release,²⁸ such as a sub-dermal device that will release insulin for a long period.

In India, the patent office has considered that the Patent Act denies claims to compositions obtained by mere admixture resulting in the aggregation of the properties of the components therefrom. Thus, a novel pharmaceutical composition with a single active ingredient (known or novel) with an inert carrier is not patentable in India as there is no synergy between the components viz. the active compound and the inert carrier (see Box 2). The existence of synergy, however, should not be considered *per se* as demonstrating inventive step, if the composition is obvious to a person skilled in the art.

As a general rule, formulation techniques and the range of compounds that may be used for developing pharmaceutically viable products in different forms are well known to a person

²⁶ This example refers to a case where there is a new indication for a known product with a different therapeutic effect.

²⁷ For example, a prolonged release (PR) dosage form.

²⁸ Most regulatory authorities would not allow such a product to be registered unless there were demonstrated benefits to the patient such as reduced incidence of adverse effects or prolonged efficacy leading to reduced frequency of dosing. In some cases, however, prolonged release dosage forms may add an undesirable variability.

skilled in the art. For instance, it is not inventive to use particular stabilizing agents (such as pH regulators) or some compounds to improve bio-availability, as these are well known. In some cases, certain salts are preferred for the preparation of particular formulations, such as tablets, while other salts may be preferred for the formulation of liquid pharmaceutical preparations. In most cases, it is likely that the claimed inventions in this field lack inventive step.

Similarly, claims relating to pharmacokinetic parameters, micronisation of a known product or particles distribution within a given diameter or weight should not generally be deemed admissible. As mentioned above, the existence or not of inventive step is not to be determined exclusively on the basis of documentation in the prior art, but taking into account the average knowledge of a person trained and experienced in pharmaceutical formulation.

Finally, it should be noted that processes to prepare formulations or compositions are generally well known and routinely applied. Hence, claims over such processes would rarely be inventive. Likewise, simple experiments/trials are not sufficient to support patentability.

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.

Box 2

**Draft Manual of Patent Practice and Procedure. Patent Office, India - 2005.
Annexure – 1. 6.0 Pharmaceutical Compositions**

- 6.1 The pharmaceutical compositions other than mere admixtures resulting in the aggregation of properties of the ingredients, but having synergistic effect may normally be patentable.
- 6.2 The known pharmaceutical compositions in different new dosages and different form such as capsules, tablets, syrups, suspensions etc., are not patentable under sections 2(1)(j), 3(d) and 3(e) of the Act.
- 6.3 New use of known substance or its new use in a pharmaceutical composition is not normally patentable.
- 6.4 Any method of using pharmaceutical composition is not patentable.

Combinations²⁹

Claims are sometimes directed to combinations of previously known active ingredients.³⁰ In some cases, the specific covered compounds and quantities are indicated,³¹ while in others they

²⁹ See examples 11 to 13 in the Annex.

³⁰ For instance, CIPLA, the Indian pharmaceutical firm, filed a PCT application for the combination of three antiretrovirals: efavirenz (EFV), zidovudine (AZT) and lamivudine (3TC) and their analogues. Another

generally refer to a category of therapeutic compounds, such as antacids. If claims on combinations are accepted subsequent to a patent on the relevant active ingredient/s, the patent owner may be able to indirectly extend the term of protection granted under the basic patent.

In some countries, combination claims are rejected unless the combination generates a new and non-obvious synergy or distinct effect. If a synergistic effect is to be relied on to allow patentability, it must be possessed by everything covered by the claims,³² appropriately described and proven in the patent specification (for instance, on the basis of biological tests) and be the manifestation of an inventive step. A new synergy need not be considered, as such, as inventive, since it may be obvious for a person skilled in the art. Moreover, the synergy between two or more drugs may be deemed a 'discovery' rather than an 'invention', since the synergy takes place in the body and is found through clinical trials.

It is also to be noted that, in some cases, combination claims may in practical terms be equivalent to claims over medical treatments (the patentability of which is excluded in most countries), to the extent that they only provide a method of administering a combination of existing drugs. Also, combining drugs to avoid resistance is normal practice in pharmaceutical development and should generally be seen as evident to a person with average skills in the field.

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/Dose³³

Some patent applications claim inventions consisting of the dosage for administration to patients of an existing product, including pediatric dosages. Although drafted as product claims, these claims have the same effect as claims over methods for medical treatment,³⁴ as the subject matter is not a product or process but the way in which a product is therapeutically used.

Some countries admit patents on dosages under certain circumstances. For instance, the UK Guidelines allows for the patenting of a dosage where there is a new medical indication and the dosage is substantially different from that for the known use (see Box 3). The UK approach is only valid, however, where second indication patents are permitted.³⁵ When the only contribution made by the applicant is a new dosage for the same use of a drug, the subject

example is the application filed by GlaxoSmithKline for the tablet formulation of the combination of zidovudine (AZT) and lamivudine (3TC), also known under the brand name 'Combivir'.

³¹ For instance, claims on the combination of aspirin 325 mg + carisoprodol 200 mg + codeine phosphate 16 mg were granted in the USA, with expiry date 13/08/2002.

³² See Glaxo Group Ltd.'s Patent [2004]RPC 43. Report of Patent, Design and Trade Mark Cases (RPC). The RPC is published by Sweet & Maxwell on behalf of the Patent Office (UK).

³³ See example 14 to 16 in the Annex.

³⁴ A method of medical treatment (or therapeutic method) is a set of steps that may include the administration of a medicine, applied to the human (or animal) body to treat or cure a disease.

³⁵ See an analysis of this issue below.

matter would not be patentable. The same would apply if the dosage refers to a new use,³⁶ to the extent that a new use is not patentable.

Moreover, changes in dosages would rarely be of an inventive nature and may be considered as not meeting the industrial applicability standard, since the invention would only have effects on the body and not technical effects.

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.

Box 3

Examination Guidelines for Patent Applications relating to Medical Inventions in the UK Patent Office (March 2004), Claims to pharmaceutical compositions, Claims to unit dosage forms, Paragraph 120

It may be possible in cases where the required dosage for a new medical use is markedly different from that for the known use, to allow a claim to a unit dosage form containing the known active ingredient in such an amount that the unit dosage form is novel and not obvious to have been made up in that amount for the prior art use. Thus if the new medical use requires a dose of, for example, ten times (or one tenth) that for the prior art use, then a claim to a unit dosage form might be judged to be novel and inventive and allowable. In assessing the inventiveness of such claims it should be remembered that dosages required are usually related to body weight so that children's doses are smaller than those for adults.

Salts, Ethers and Esters³⁷

Frequently, pharmaceutical patents protect new salts of known active ingredients. Salts are normally formed to increase stability or solubility of the drug. It is common knowledge in the pharmaceutical field that salts result in different solubility and, therefore, in different bioavailability. If an active ingredient is an acid or base, then any chemistry student knows how to make a salt, and can make predictions about its likely physicochemical properties. Patents on salts are one of the main avenues for the 'evergreening'³⁸ of pharmaceutical patents.

There may be exceptional cases in which new salts present unexpected advantages in properties as compared to what is in the prior art. Such advantages should be supported by information about the results of appropriate tests incorporated into the patent specifications.

The processes for forming salts are also normally obvious to a person trained in the field. There may be very exceptional cases where forming a salt (for instance, with optimal crystalline characteristics) of complex molecules require special skills and may be eventually

³⁶ It is possible for an active ingredient to have different indications at different doses. For example clonidine is used to treat hypertension in a regimen of 150-300 micrograms twice daily, but at 25 micrograms twice daily for migraine prophylaxis.

³⁷ See examples 17 to 19 in the Annex.

³⁸ 'Evergreening' is a patenting strategy consisting of acquiring patents on minor, often trivial, modifications of existing pharmaceutical products or processes in order to indirectly extend the period of patent protection over previously patented compounds.

patentable as a process. However, the complexity of a process does not provide sufficient ground for claiming inventive step.

Similarly, ethers³⁹ as well as esters of known alcohols, although fundamentally different to salts,⁴⁰ are generally subject to the same objection of obviousness.⁴¹

The Indian patent office has issued draft guidelines specifically providing criteria for the examination of applications relating to hydrates, salts and other derivatives (see Box 4). The amendment introduced to the Indian Patent Act in 2005, moreover, incorporated a specific provision with regard to claims regarding salts, esters and other ‘forms’ of existing products.

Box 4

**Draft Manual of Patent Practice and Procedure. Patent Office, India – 2005
Annexure – 1**

5.6. HYDRATES AND OTHER SUBSTANCES ETC:

Hydrates, acid addition salts and other derivatives, which are routinely prepared *prima facie*, lack inventive step. However where there is a problem, like stability, absorption etc., and there is a long standing problem in preparing the derivatives, patentability of such process may be considered.

The clear objective of the amendment to the Indian Patent Act is to limit the proliferation of patents around existing pharmaceutical products. It provides in section 3(d) that the following shall not be treated as an invention within the meaning of the Act:

the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.

Explanation – For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy.⁴²

³⁹ See Wegner (1994), p. 283.

⁴⁰ Salt forms can affect stability, dissolution rate and manufacturing properties (e.g. powder flow in a hopper). Esters and ethers are generally more lipid soluble than are salts, thus altering tissue penetrability and sometimes rate of release (for example steroids have quite different topical potencies when administered as esters). In some cases, the use of esters may confer an advantage in terms of safety and efficacy.

⁴¹ See, e.g. *Ex parte Korten*, 71 USPQ 173 (1946) quoted in Wegner (1994), p. 283, who also quotes a later case where an ester of a known alcohol was deemed patentable because the motivation to esterify it could not be presumed to necessarily exist.

⁴² Some comments on this provision seem pertinent here. In accordance with this provision, if not significantly different in properties with regard to efficacy, salts, esters and ethers are considered to be the same substance and, hence, no separate patent could be granted. Establishing such differences with regard to efficacy (which is not a technical effect, but the result of the use of the substance in the body) would not be sufficient, however, to obtain a patent, since in any case the novelty, inventive step and utility requirements should be met. In other

Any special claims made by an applicant regarding, for instance, a faster therapeutic response of a new salt, should be supported by clinical data that demonstrate this effect. The more special claims that are made, the more data should be required to examine the viability of the application. It is critical that the new data be properly assessed. Health regulatory authorities have the appropriate expertise in these matters; hence, an articulated cooperation with patent offices in examining these applications might, as discussed below, facilitate the task of the patent offices and improve the quality of their decisions.

Recommendation: New salts, ethers, esters and other forms of existing pharmaceutical products can generally be obtained with ordinary skills and are not inventive. This may not apply, exceptionally, when tests, appropriately conducted and described in the specifications, demonstrate unexpected advantages in properties as compared to what was in the prior art.

Polymorphs⁴³

Some therapeutically active ingredients present polymorphic forms, that is, they may exist in different physical forms (as amorphous solid and/or in different crystalline forms), which may have different properties more or less pharmaceutically significant (such as solubility and therefore bioavailability). Polymorphism is a natural property: polymorphs are not ‘created’ or ‘invented’; they are discovered normally as part of routine experimentation related to drug formulation. They result from the conditions under which a compound is obtained.⁴⁴ Any compound that presents polymorphism will naturally tend to its more stable form,⁴⁵ even without any human intervention.

The significance of different polymorphs is almost entirely in their relative rate of dissolution (in theory the extent of dissolution can be affected too but this is rarely of practical significance). Occasionally there is an effect on long-term stability if the most stable polymorph had not been selected for development in the first place. The practical effect of changing the polymorph is, consequently, on the dissolution rate of the finished product and, potentially, an effect on bioavailability, or a change in the long term stability profile. There could also be in some cases manufacturing advantages in choosing a particular polymorph. However, there is no question of an effect on safety or efficacy, since the active ingredient is the same.

words, an increased efficacy would only prove that the substance is different, and not that it is patentable. An important issue is how a difference in efficacy is to be determined, since at the time of filing a patent application the results of clinical tests are generally not yet available. In the USA, for instance, the Court of Appeals for the Federal Circuit reversed in *re Brana* (51 F.3d 1560, Fed. Cir. 1995) a decision of the US Patent and Trademark Office (USPTO) holding that a compound was useful enough to be granted a patent, even without the approval of the FDA at that stage (the USPTO had rejected the patent application as it had not yet been approved by the FDA for Phase II clinical trials). In a more recent case, the Court held that where there is “no indication that one skilled in [the] art would accept without question statements [as to the effects of the claimed drug products] and no evidence has been presented to demonstrate that the claimed products do have those effects” the applicant has failed to demonstrate sufficient utility and therefore cannot establish enablement (*Novak*, 306 F.2d at 928; *Rasmusson and Reynolds v. SmithKline Beecham*, June 27, 2005).

⁴³ See examples 20 to 23 in the Annex.

⁴⁴ The usual process for finding new polymorphs is to recrystallise the active pharmaceutical ingredient from different solvents, or under different recrystallisation conditions such as temperature or rate of stirring.

⁴⁵ Many polymorphs are metastable, that is they have short-term stability, which reduces their utility from a manufacturing and storage perspective. An ordinary skilled chemist that develops a new substance for pharmaceutical use will normally seek to identify the most stable polymorph. On some technical aspects relating to polymorphism, see *Dunitz* (1995) pp. 193-200; *Bernstein* (1999), pp. 3440-3461.

Independent patent applications on polymorphs have become increasingly frequent and controversial, as patents thereon can be used to obstruct or delay the entry of generic competition. Polymorphs can be deemed within the prior art – and therefore non-patentable – if they are inevitably obtainable following the process of the basic patent on the active ingredient. Moreover, the possibility of discovering different crystals is obvious when polymorphism is found.

A well-known example of a dispute on a polymorph patent related to cimetidine. The patent holder applied for a patent on a polymorph of cimetidine approximately five years after the patent on the active ingredient was granted. That polymorph patent, however, was cancelled in the UK and other countries on the grounds that the polymorph was inevitably obtained by applying the process already claimed in the original patent.⁴⁶ Another example is the case of ranitidine (see example 22 in the annex). The patentee obtained in the United States a patent for a polymorph expiring in 2002 as opposed to 1995 for the main patent.⁴⁷

Polymorph claims are accepted in many countries. For instance, the EPO regularly grants patents on newly identified polymorphic forms, in line with the practice of the German Patent Office and the Federal Patent Court. According to the “Kristallformen” case, products of the same chemical formula are not identical if they differ in some reliable parameter.⁴⁸ Patents over polymorphs have been rejected, however, in other jurisdictions.⁴⁹ The Indian draft guidelines for patent examination, for instance, provide specific criteria for assessing claims of such forms (see Box 5).

Solvates, including hydrates, were originally considered as “pseudo-polymorphs”.⁵⁰ Nevertheless, according to the International Conference of Harmonization (ICH) of 1999, they are to be deemed ‘polymorphs’.⁵¹ Hydrates/solvates will rarely be inventive, as they are obvious to produce in most situations. Hence, claims relating to changes in the content of water in known molecules (deriving in mono-hydrates, bi-hydrates, etc.) should generally be considered non-inventive and not patentable.

It should also be noted that for most solvates and polymorphs, like for new salt forms, only data on quality and, where required, bioequivalence are needed, that is, no more data than

⁴⁶ See, e.g. Cook, Doyle and Jabbari (1991), p. 89; Hansen and Hirsch (1997), p. 113.

⁴⁷ See, e.g. Cook, Doyle and Jabbari (1991), p. 90; Grubb (1999), p. 205.

⁴⁸ See Hansen and Hirsch (1997), p. 112.

⁴⁹ See, for instance, the decision by the Superintendencia de Industria y Comercio of Colombia regarding crystalline forms of atorvastatin (Tribunal de Justicia de la Comunidad Andina, Proceso No. 151-IP-2005. Interpretación prejudicial de las disposiciones previstas en los artículos 1, 4 y 7 de la Decisión 344 de la Comisión del Acuerdo de Cartagena, así como en los artículos 45 y 48 y en la Disposición Transitoria Primera de la Decisión 486 de la Comisión de la Comunidad Andina, con fundamento en la solicitud formulada por el Consejo de Estado de la República de Colombia, Sala de lo Contencioso Administrativo, Sección Primera. Expediente: No. 2003-00255).

⁵⁰ Substances that can be described as polymorphs of each other have the same chemical composition, whereas a solvate and a non-solvate do not. Indeed different solvates have different chemical compositions.

⁵¹ “Polymorphic forms: Some new drug substances exist in different crystalline forms which differ in their physical properties. Polymorphism may also include solvation or hydration products (also known as pseudopolymorphs) and amorphous forms. Differences in these forms could, in some cases, affect the quality or performance of the new drug products. In cases where differences exist which have been shown to affect drug product performance, bioavailability or stability, then the appropriate solid state should be specified” (Specifications: Test Procedures & Acceptance. Criteria for New Drug Substances and New Drug Products: Chemical substances Q6A, ICH 1999).

for the approval of a generic product. This is the reason why in many jurisdictions these variants of a substance are deemed to be the ‘same’ substance for health regulatory purposes.⁵²

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.

Box 5

**Draft Manual of Patent Practice and Procedure. Patent Office, India – 2005
Annexure – 1**

5.3 POLYMORPHS

5.3.1 Some compounds present in polymorphic forms, i.e., they crystallize in diverse forms. Such forms can be deemed within the prior art and therefore not patentable. However, process patent may be allowed for the new polymorph, if the polymorph is prepared by a novel process involving inventive step.

5.3.2. Some therapeutically active ingredients present polymorphic forms, that is, they may crystallize in diverse forms, which may have different properties that are more or less significant in terms of their therapeutic use. Such forms can be deemed within the prior art – and therefore non-patentable – if they were inevitably obtained following the process of the basic patent on the active ingredient or were covered by a previous product patent.

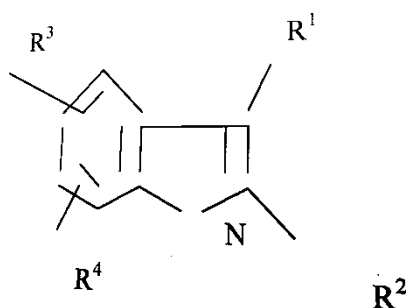
Markush Claims

Often broad (“generic”) patent claims are drafted covering a family of a large number (sometimes thousands or millions) of possible compounds. 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 generates rights over an extremely broad set of compounds without prior testing or experimentation.

⁵² As quoted above, the recent reform of the Indian Patent Act provides that polymorphs, *inter alia*, ‘shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy’ (Section 3 (d)).

An example of a Markush claim is the following:

Claim 1: The compounds of the general formula



Wherein, R₁ is selected from phenyl, pyridyl, thiazolyl, thioalkyl, alkoxy and methyl; R₂-R₄ are methyl, tolyl or phenyl... the compounds are used as a pharmaceutical for increasing the oxygen-intaking capability of blood.

Explanation: In the general formula, indolyl is the main structure unit common to all the Markush compounds, and all the compounds have the same use. Therefore, this Markush claim possesses unity of invention.⁵³

Patent examination guidelines of several countries include detailed instructions to deal with this type of claims (see Boxes 6 and 7).

In addition to the ordinary issues relating to the patentability requirements, the consideration of Markush claims raises issues of disclosure and enablement, since the patent applicant has effectively obtained only a few of the possible elements of the group. Given that a search of prior art for millions of compounds is virtually impossible, the search of the patent office and the corresponding patent grant should be limited to what has been actually assessed and supported by the examples provided in the specification.

Recommendation: Claims covering a large range of compounds should not be allowed. Patent offices should 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. 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.

⁵³ Chinese Guidelines, Chapter 10. Several Provisions for the Examination of Applications for Patent for Invention in the Field of Chemistry.

Box 6

Manual of Patent Examining Procedure (MPEP), Eighth Edition, August 2001 – Latest Revision October 2005 – 800 Restriction in Applications Filed Under 35 U.S.C. 111; Double Patenting, 803.02 Markush Claims [R-3]⁵⁴

If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, the examiner may require a provisional election of a single species prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. As in the prevailing practice, a second action on the rejected claims would be made final.

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn

⁵⁴ <http://www.uspto.gov/web/offices/pac/mpep/index.htm>.

from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be re-examined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the re-examination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

Box 7

Guidelines for Examination in the European Patent Office, Part C, Chapter III (Claims), (7) Unity of invention, (7.4a) Markush grouping⁵⁵

Where a single claim defines (chemical or non-chemical) alternatives, i.e. a so-called "Markush grouping", unity of invention should be considered to be present if the alternatives are of a similar nature (see III, 3.7).

When the Markush grouping is for alternatives of chemical compounds, they should be regarded as being of a similar nature where:

- (i) all alternatives have a common property or activity, and
- (ii) a common structure is present, i.e. a significant structural element is shared by all of the alternatives, or all alternatives belong to a recognised class of chemical compounds in the art to which the invention pertains.

A "significant structural element is shared by all of the alternatives" where the compounds share a common chemical structure which occupies a large portion of their structures, or, in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art. The structural element may be a single component or a combination of individual components linked together. The alternatives belong to a "recognised class of chemical compounds" if there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention, i.e. that each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

Selection Patents⁵⁶

A "selection patent" is a patent under which a single element or a small segment within a large known group is "selected" and independently claimed based on a particular feature not mentioned in the large group. A "selection invention" may be applied for, for instance, when a

⁵⁵ http://www.european-patent-office.org/legal/gui_lines/e/index.htm.

⁵⁶ See example 24 in the Annex.

range of products characterized as having n-carbon atoms has been patented, and later on a patent on a specific range (e.g. C₁-C₄) is claimed.

If a large group of elements is patented, the patent owner may use the selection patent to extend the term of protection for the selected subset beyond the expiration of the original patent.⁵⁷ While accepted in some jurisdictions when the selected elements possess a surprising advantage, selection patents have been denied when the supposed advantage is a property shared by all or nearly all the large group.

Although differences exist in the treatment of these claims by patent offices, including between the EPO and some national patent offices in Europe, the admission of selection patents is subject to limitations in most jurisdictions (see the EPO and UK Guidelines in Boxes 8, 9, and 10).

Box 8

Guidelines for examination in the European Patent Office, Part C, Chapter IV – Annex (Examples relating to the requirement of inventive step indicators), (3.1) Obvious and consequently non-inventive selection among a number of known possibilities

3.1 Obvious and consequently non-inventive selection among a number of known possibilities: (iv) The invention consists merely in selecting particular chemical compounds or compositions (including alloys) from a broad field.

Example: The prior art includes disclosure of a chemical compound characterized by a specified structure including a substituent group designated "R". This substituent "R" is defined so as to embrace entire ranges of broadly-defined radical groups such as all alkyl or aryl radicals either unsubstituted or substituted by halogen and/or hydroxy, although for practical reasons only a very small number of specific examples are given. The invention consists in the selection of a particular radical or particular group of radicals from amongst those referred to, as the substituent "R" (the selected radical or group of radicals not being specifically disclosed in the prior art document since the question would then be one of lack of novelty rather than obviousness). The resulting compounds

(a) are not described as having, nor shown to possess, any advantageous properties not possessed by the prior art examples; or

(b) are described as possessing advantageous properties compared with the compounds specifically referred to in the prior art but these properties are ones which the person skilled in the art would expect such compounds to possess, so that he is likely to be led to make this selection.

⁵⁷ However, a selection patent may be applied for by a third party, and not necessarily by the owner of the original patent. This may raise issues of patent-dependency and eventually trigger the application of compulsory licenses. See Article 31(l) of the TRIPS Agreement.

Box 9

Examination Guidelines for Patent Applications relating to Biotechnological Inventions in the UK Patent Office (May 2005), Inventive step – Paragraphs 24,⁵⁸ Section 3 of the Manual of Patent Practice, paragraph 3.27⁵⁹

A "selection" invention should meet the criteria laid down in I G Farbenindustrie AG's Patent, 47 RPC 289 at pages 322-3, namely,

- (1) the selection must be based on some substantial advantage gained or some substantial disadvantage avoided,
- (2) substantially all the selected members must possess the advantage in question, and
- (3) the selection must be in respect of a quality of special character which can fairly be said to be peculiar to the selected group; this is not necessarily nullified if it transpires that some other members of the class from which the selection is made have this quality, but the claim may be invalid if it is found that the quality is common to many other members in addition to those selected.

In Germany, the Bundesgerichtshof has held that even in a relatively large generic group of compounds, disclosure of the group is, to the skilled chemist, fully equivalent to a disclosure of each compound within the group.⁶⁰ Selection inventions in the normal sense of the word may, hence, be regarded as unpatentable in Germany.

If a previous patent contains, for instance, a Markush-type claim with a large number of possible compounds without a detailed disclosure, and the compounds claimed in a subsequent patent are not found by simple experiments and show an unexpected advantage, far enough away from the completely disclosed compounds in the previous patent, an issue of inventive step will essentially arise in considering the patentability of the selection.

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.⁶¹ If unexpected advantages of existing products were deemed patentable under the applicable law, the patentability of a selection could be considered when an inventive step is present.⁶²

⁵⁸ <http://www.patent.gov.uk/patent/reference/biotechguide/index.htm>.

⁵⁹ <http://www.patent.gov.uk/patent/reference/mpp/ss1-6.pdf>.

⁶⁰ 'A compound, in the sense of Patent Law, is every chemical entity that can be reliably differentiated from another chemical entity, through the provision of sufficient, suitable parameters. Fundamentally, compounds having the same chemical composition are identical. This does not apply for special forms of compounds having the same chemical composition, if these forms could not be produced, despite their chemical composition being known' (Grubb (1999), pp. 197-199).

⁶¹ When a prior claim or document in the prior art includes a range, for instance, in the form of C₁-C₄ or 50° to 75° of temperature, all the comprised possibilities (e.g. C₂ and C₃; 60° of temperature) should be deemed disclosed and, hence, not patentable as a 'selection'.

⁶² The patentability of a selection will proceed in this case if an exception to the strict principles of novelty were allowed under the applicable law. See, e.g. Cook, op. cit., p. 291.

Box 10

**Guidelines for examination in the European Patent Office, Part C, Chapter IV, (9.)
Inventive step, (9.12) Dependent claims; claims in different categories**

...[I]f a claim to a product is new and non-obvious there is no need to investigate the novelty and non-obviousness of any claims for a process which inevitably results in the manufacture of that product or of any claims for a use of that product. In particular, analogy processes, i.e. processes which themselves would otherwise not involve an inventive step, are nevertheless patentable insofar as they provide a novel and inventive product (see T 119/82, OJ 5/1984,217). It should, however, be noted that in cases where the product, process and use claims have different effective dates, a separate examination as to novelty and inventive step may still be necessary in view of intermediate documents.

Analogy Processes

Products and processes are two distinct categories of eligible subject matter for the purposes of patent protection. The patentability of each of them must be evaluated according to their own properties and characteristics. However, manufacturing processes (often called ‘analogy processes’) that are not by themselves novel or inventive but which are used for the preparation of new or inventive but unpatented compound are deemed patentable in some jurisdictions under a legal fiction (see box on EPO guidelines). The doctrine of analogy processes expands the possibility of appropriation of knowledge in the public domain.⁶³

In the United States, the patent office has held “analogy process” claims to be unpatentable unless they were inventive in themselves,⁶⁴ but legislation carved out an exception for biotechnology. A statutory amendment to the US law in 1993 determined that a biotechnological process claim would be non-obvious if it involved new and non-obvious starting materials or produced a new and non-obvious result.⁶⁵ While this solution was only targeted to biotechnology, it has been extended by case law to other fields of technology.⁶⁶

An example of a patent probably granted on the basis of an implicit application of the concept of analogy process is patent AR 242.562 on the process for obtaining amlodipine besylate. The claimed and described process is a simple chemical reaction: the production of a salt from an acid with a base. This reaction is described by the simple formula: acid + base = salt + water, which can be found in elementary chemistry textbooks.⁶⁷

The application of the doctrine of analogy processes may lead to the protection of non-patentable pharmaceuticals,⁶⁸ as the TRIPS Agreement (Article 28.1(b)) requires the extension of patent protection to the products directly obtained with a patented process.

⁶³ A different situation arises when a compound has to be produced by a large number of consecutive steps (chemical reactions). It may be inventive to produce this compound by another much more efficient route (comprising less steps), even if this individual chemical reactions as such were known for other compounds.

⁶⁴ See, e.g. Grubb (1999), p. 206.

⁶⁵ See, e.g. Dratler, §2.03[3].

⁶⁶ See, e.g. Grubb (1999), p. 207.

⁶⁷ The validity of this patent has been challenged before Argentine courts (decision still pending).

⁶⁸ This situation may arise, in particular, in countries that did not grant patent protection for pharmaceutical products before the TRIPS Agreement obliged the granting of patents in all fields of technology (Article 27.1).

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.

Enantiomers⁶⁹

Enantiomers (or optical isomers⁷⁰) behave in relation to one another as an image does to its mirror image. In organic chemistry, enantiomers spontaneously occur, for example, in compounds that comprise a carbon atom with four different substituents.⁷¹ This property has been exploited in the patent field by often claiming, first, the “racemic” mixture of both enantiomers, and later claiming⁷² rights over the most active enantiomer,⁷³ thus evergreening the originally obtained protection.

It is routine to test whether one or the other enantiomer in isolation is more active than the racemic mixture of both, as it is expected that one optical isomer will typically have much higher activity than the other, so that superior activity for at least one of the isomers as compared to the racemate is to be expected.⁷⁴ When the chemical formula of a compound with enantiomers is disclosed, the novelty of the latter is also lost as the formula necessarily reveals the existence of the enantiomers.⁷⁵

Some patent offices, such as EPO, have considered that enantiomers of known racemates may be deemed novel, but that its patentability is a matter of inventive step. A single enantiomer (of an active ingredient that was previously registered with the health authority as a racemate) may be registered in its own right if it is of adequate quality, safety and efficacy.⁷⁶

⁶⁹ See examples 25 and 26 in the Annex.

⁷⁰ Enantiomers are “stereoisomers whose mirror images cannot be superimposed. Enantiomers have identical physical and chemical properties except that they rotate the plane of polarized light in opposite directions and behave differently in a chiral environment”. ‘Stereoisomers’ are compounds made up of the same atoms bonded in the same sequence but having different orientations in space. [...]”. See http://www.hc-sc.gc.ca/dhp-mpps/alt_formats/hpfbdgpsa/pdf/prodpharma/stereo_e.pdf.

⁷¹ During the synthesis of asymmetric molecules equal amounts of enantiomeric pairs will always form, except when one of the starting materials or reagents is itself a single enantiomer. In other words, unequal amounts of enantiomers will form only if the chemist deliberately selects starting materials or reagents that are single enantiomers.

⁷² See, e.g. Hansen and Hirsch (1997), p. 113. It is estimated that over a quarter of known pharmaceuticals present this property. See, e.g. Cook, Doyle and Jabbari (1991), p. 84.

⁷³ Although the patent on an isolated enantiomer would not normally be deemed infringed by the commercialization of the racemic mixture, promotion of the enantiomer as more advantageous than the latter may massively drive prescribing doctors towards the new product.

⁷⁴ See, e.g. Grubb (1999), pp. 199-200; Hansen and Hirsch (1997), pp. 113-118. For instance, esomeprazole is the S-enantiomer of omeprazole. Improved efficacy of this single enantiomer over the racemic mixture of omeprazole has been claimed (see, e.g. <http://en.wikipedia.org/wiki/Esomeprazole>). Another example is citalopram and escitalopram.

⁷⁵ An enantiomer might have in some cases useful properties that are not the same as those of the racemate, which useful properties could not have been predicted but were masked in the racemate by the other enantiomer. It will depend on the applicable national law whether the identification of such properties could provide the basis for obtaining a patent or whether it would be considered a non-patentable discovery or anticipated in the prior art.

⁷⁶ For instance, it might be found that one enantiomer is leading to adverse reactions, so using its mirror image alone confers an advantage in terms of safety. It’s often the case that the two enantiomers in a pair have a different safety and efficacy profile. (e.g. 3-hydroxy-tyrosine and levodopa. D-dopa is highly toxic). Article 10(2)(b) of the 2001/83/EC Directive (as amended by Directive 2004/27/EC) provides that for abridged applications by generic companies, different salts, esters, ethers, isomers, mixtures of isomers, complexes or

But this does not equate to a patentable invention, since the enantiomers were present in the racemate⁷⁷ and the latter's pharmacological/therapeutic activity was based almost entirely (if not entirely) on the active enantiomer. The draft guidelines for patent examination of India provide some criteria for the evaluation of claims of this kind (see Box 11).

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.

Box 11

**Draft Manual of Patent Practice and Procedure. Patent Office, India – 2005
Annexure – 1**

5.0 Patentability of various forms of chemical substances:

5.1 Isomers

5.1.1. Isomers are different compounds that have the same molecular formula which may be broadly divided into two kinds namely structural isomers or positional isomers and stereo isomers.

5.1.2. Structural Isomers or positional isomers may be structurally similar or dissimilar compounds. The simplest examples are butane and isobutane and ethanol and dimethyl ether. In the former case the compounds are having structural and functional similarity. In the second set of compounds, although they have the same molecular formula but are structurally and functionally different. Such isomers even having close structural similarity may be considered to be novel over the prior art. But when such chemical compounds have close structural similarity, similar functional similarities and if it is found that the enabling methods are available, a case of obviousness may be made.

5.1.3. Isomers having the same empirical formula but having structural differences may be considered novel and may not normally offend "obviousness" as they are structurally different.

An example is that cyclohexylstyrene is not considered prima facie obvious over prior art isohexyl styrene.

5.1.4. Stereo Isomers are prima facie obvious. Once a racemic compound is known, its enantiomers are obvious because a person skilled in the art knows that a compound having a chiral centre exists in two optically active forms. Hence product patent may not be granted for the enantiomers. When a new compound is claimed for the first time in its optically active pure form, product patent may be granted. In a case (S)-enantiomer of a compound, capable of producing antidiabetic effects was claimed. The cited prior art disclosed the racemate of the same compound which was claimed for the same purpose and was not allowed.

derivatives of an active ingredient, are considered to be essentially similar drugs unless they differ significantly in properties with regard to safety and/or efficacy.

⁷⁷ This applies to the individual isomers (cis and trans) that are components of the existing mixture.

Active Metabolites and Prodrugs⁷⁸

In some cases, pharmaceutical compounds generate an active metabolite, which is the product of the compound's metabolism in the body.⁷⁹ Metabolites are derivatives from the active ingredients that are produced in the body, and cannot be deemed as 'created' or 'invented'. However, active metabolites can have different safety and efficacy profiles to those of the parent molecule.⁸⁰

On the other hand, when metabolized in the body, inactive compounds (called "prodrugs") can produce a therapeutically active ingredient.⁸¹ In some cases, patent claims cover a drug and its prodrug/s.⁸² In situations where the active ingredient is not patented, a patent over a prodrug as such may extend control by the patentee over the market of the active ingredient that is metabolized. A prodrug may be regarded as the original drug 'in disguise'.⁸³

In the case of terfenadine, which had been sold for many years in the United Kingdom as an antihistamine drug, the patent holder obtained a further patent on the active metabolite fexofenadine and attempted to block competition in the market of terfenadine, after the patent for the latter had expired. This was deemed to be an unacceptable attempt to extend patent protection.⁸⁴

Specific guidelines to deal with metabolites and prodrugs have been developed by some patent offices (see Box 12).

Box 12

Draft Manual of Patent Practice and Procedure. Patent Office, India – 2005 Annexure – 1

5.4 METABOLITES: Metabolites are the compounds that are formed inside a living body during metabolic reaction. The types of metabolites are:

- (i) Active metabolites formed from inactive precursors (e.g. Dopa & Cyclophosphamide)
- (ii) Active metabolites formed from precursors that show mechanism of action that is

⁷⁸ See examples 27 to 34 in the Annex.

⁷⁹ An example is nelfinavir and its active metabolite M8.

⁸⁰ When an active metabolite of an existing product is registered with the health authority in its own right, it is possible that a full set of new safety and efficacy data will be required, similar to that which was generated for the parent compound. There are cases where an active metabolite has been registered for a different indication to that of the parent drug (for example, the primary indication for temazepam, an active metabolite of diazepam, is as a hypnotic whereas the primary indication for diazepam itself is anxiety).

⁸¹ Some examples are the following: enalapril is converted by esterase to the active enalaprilat; valaciclovir is converted by esterase to the active aciclovir; levodopa is converted by DOPA decarboxylase to the active dopamine; fosamprenavir calcium is a pro-drug of the protease inhibitor and antiretroviral drug amprenavir.

⁸² In some cases, the prodrug might have benefits in terms of being more readily administered than the active compound.

⁸³ In the UK, for instance, it was held that sales of hetacillin, an acetone adduct of ampicillin which was immediately hydrolyzed in the body to ampicillin, infringed the ampicillin patent, because it was "ampicillin in disguise" (Grubb (1999), p. 211).

⁸⁴ See, e.g. Grubb (1999), pp. 212-213. The decision however, did not invalidate the patent to the active metabolite when produced other than by metabolism. Another conflict arose with regard to a Bristol Myers patent over the monohydrate form of cephalosporin, which is metabolized in the body from a semi-hydrate form developed by Zenith. See, e.g., Soto Vázquez, Cárdenas y Espinosa, Parra Cervantes y Cassaigne Hernández (2001), p. 54.

different from that of parent compound (e.g. Buspirone & 1-pyrimidyl piperazine Fenflouromine & norfenfleuromine)

(iii) Active metabolites which contribute to the duration of action of the parent compound (e.g. Hexamethylmelamine & Clobazam)

(iv) Active metabolites that show antagonistic effect on the activity of the parent compound (e.g. Trezodone & m-chlorophenyl piperazine, Aspirin & salicylate)

5.4.1 A metabolite is **unpatentable** since giving the drug to a patient naturally and inevitably results in formation of that metabolite.

5.5 PRODRUGS:

5.5.1 Prodrugs are inactive compounds that can produce an active ingredient when metabolized in the body. Hence prodrugs and metabolites are interlinked. When metabolized in the body, inactive compounds (pro-drug) can produce a therapeutically active ingredient. It must be determined whether the patent on the compound covers the prodrug and the extent to which claims relating to certain compounds should also be allowed to include their prodrugs. The inventive aspects of prodrug may be decided based on the **merits of the case**.

5.5.2 However, if there is a marked improvement over the primary drug, prodrugs may be patentable.

One possible way of dealing with patents over prodrugs – which may be novel and inventive in some cases – is to allow them when the patentability standards are met, provided that the active ingredient is properly disclaimed (that is, excluded from the patent claims).

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. 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.

Methods of Treatment⁸⁵

Some patents claim methods of treatment, including prophylaxis, cure, relief of pain, diagnosis or surgical methods. These claims do not cover a product *per se*, but the way in which it is used in order to obtain certain effects. National patent policies considerably differ on this subject and, in some cases, adopt a very expansive approach (see Japan Guidelines below in Box 13).

In many cases, a method of treatment claim is not apparent at first sight since reference may be made, for instance, to compositions which are not characterized by their chemical

⁸⁵ See examples 35 to 40 in the Annex.

structure or intrinsic characteristics but by their dosage or form of administration. It is important, hence, to carefully examine the claims in order to identify and appropriately deal with cases in which under the appearance of product claims it is a method of treatment that is actually disclosed.

The TRIPS Agreement (Article 27.2) explicitly allows Members to exclude therapeutic, diagnostic and surgical methods from patent protection, and many countries do follow this approach. If such exclusion has been provided for, claims describing such methods or claims that are equivalent thereto should be refused.

Even in the absence of a specific exclusion from patentability, such methods should be deemed not patentable in countries where the standard of industrial applicability applies, since they only produce effects on the body and have no industrial application.⁸⁶ The same would apply to the case of cosmetic methods.

In cases where aspects of a therapeutic method are undistinguishable from a non-therapeutic method (for instance a method for cleaning teeth), the EPO jurisprudence has tended to consider it of therapeutic and, hence, non-patentable nature.⁸⁷

Box 13

**Examination Guidelines for Patent and Utility Model in Japan. Part VII:
Examination guidelines for inventions in specific fields, Chapter 3 Medicinal
Inventions, (2.1) Industrial Applicability⁸⁸**

As a medicinal invention means “an invention of a product.”, it does not come under the category of “methods for treatment of the human body by surgery or therapy and Diagnostic methods practiced on the human body” despite the fact that the application possibly involves the administration of a dosage to a human body or the spreading on the human body, and it is considered to be an “industrially applicable invention.” It should be noted that a medicinal invention defined by combination of two or more medicines, or defined by a mode of medical treatment such as a dosing interval, a given dose, or the like is handled in the same way because it is also “an invention of a product” (Refer to the Examination Guidelines Part II, Chapter 1, 2.1 “Industrial Applicability”).

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).

⁸⁶ The medical profession is not an industry, as stated in a landmark decision by the German Federal Supreme Court in Operation for baldness (38 BGHZ 313, 1968 GRUR 142). See, e.g. Thomas (2003), p. 850.

⁸⁷ See Thomas (2003), p. 870.

⁸⁸ http://www.jpo.go.jp/tetuzuki_e/t_tokkyo_e/Guidelines/PartVII-3.pdf.

Box 14

Guidelines for examination in the European Patent Office, Part C, Chapter IV (Patentability). (4.) Industrial application, (4.2) Surgery, therapy and diagnostic methods⁸⁹

"Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body shall not be regarded as inventions which are susceptible of industrial application. This provision shall not apply to products, in particular substances or compositions, for use in any of these methods." Hence, patents may be obtained for surgical, therapeutic or diagnostic instruments or apparatuses for use in such methods. The manufacture of prostheses or artificial limbs could be patentable. For instance, a method of manufacturing insoles in order to correct the posture or a method of manufacturing an artificial limb should be patentable. In both cases, taking the imprint of the footplate or a moulding of the stump on which an artificial limb is fitted is clearly not of a surgical nature and does not require the presence of a medically qualified person. Furthermore, the insoles as well as the artificial limb are manufactured outside the body. However, a method of manufacturing an endoprosthesis outside the body, but requiring a surgical step to be carried out for taking measurements, would be excluded from patentability under Art. 52(4) EPC (see T 1005/98, not published in OJ).

Art. 52(4)

Patents may also be obtained for new products for use in these methods of treatment or diagnosis, particularly substances or compositions. However, in the case of a known substance or composition, this may only be patented for use in these methods if the known substance or composition was not previously disclosed for use in surgery, therapy or diagnostic methods practiced on the human or animal body ("first medical use"). The same substance or composition cannot subsequently be patented for any other use of that kind. A claim to a known substance or composition for the first use in surgical, therapeutic and/or diagnostic methods should be in a form such as: "Substance or composition X" followed by the indication of the use, for instance "... for use as a medicament", "... as an antibacterial agent" or "... for curing disease Y". In contrast to what is stated in general in III, 4.8, these types of claims will be regarded as restricted to the substance or composition when presented or packaged for the use. Art. 54(5) thus provides for an exception from the general principle that product claims can only be obtained for (absolutely) novel products. However, this does not mean that product claims for the first medical use need not fulfil all other requirements of patentability, especially that of inventive step (see T 128/82, OJ 4/1984, 164).

Use Claims, Including Second Indications

Patenting of the medical use of a product, including first and second indications⁹⁰ of a known medicinal product has become common practice in the pharmaceutical field. According to a literal interpretation of the TRIPS Agreement,⁹¹ which only obliges to grant patents over products and processes, Members should be under no obligation to grant use claims, including second indications.

⁸⁹ http://www.european-patent-office.org/legal/gui_lines/e/c_iv_4_2.htm.

⁹⁰ A well-known example of a 'second indication' patent relates to sildenafil citrate. Another example is zidovudine, developed as an anticancer drug and then covered by patent as a HIV drug.

⁹¹ As required by the Vienna Convention on the Law of the Treaties.

The European Patent Office (EPO) jurisprudence has distinguished between a claim to a composition adapted for a given use, as opposed to one suitable for such a use (see the following Box 15).

The EPO Guidelines also refer to the case of "pack" or "kit of parts" claims, which are usually used where the invention comprises the administration of two or more different drug compositions at particular time intervals, or merely simultaneously or sequentially. A claim of this form was considered by the EPO Board of Appeal in T 09/81[56]. It was held in this case that the combination was novel and inventive, but needed to be "purpose limited" – i.e. in the first medical use format – to distinguish it from a medical kit, collection or package containing the two agents together for their known independent uses.

Box 15

Examination Guidelines for Patent Applications relating to Medical Inventions in the UK Patent Office (March 2004), Claims to Pharmaceutical Compositions, Compositions adapted to a particular use, Paragraph 114.

A claim to a formulation "adapted for only topical, to the exclusion of oral and injectable administration" was accepted by the EPO in T 289/84.⁹² In this case, the Board of Appeal held that there was a difference in meaning between a claim to composition adapted for topical use, as opposed to one suitable for such a use. Both eye drops and injectable formulations typically consist of sterile aqueous solutions, so either might be "suitable" for the other use. However, an eye-drop formulation was not "adapted" for use as an injectable solution or vice versa – injectable solutions had to both be sterile and pyrogen-free, whereas eye-drops do not need to be pyrogen-free but have a very narrow range of acceptable pH. However, a claim to a composition "adapted to" a specific use should be objected to on clarity grounds as being defined by its intended result, unless it would be clear to the person skilled in the art as to what is meant.

As illustrated in the boxes below, the European Patent Convention and the law of some countries allow for the patenting of the first pharmaceutical indication of a known product. Second indications are accepted under European jurisprudence and in other countries when framed in accordance with the so called 'Swiss' claims.⁹³ However, the patenting of a new use of a known product including, in particular, second indications, expands the scope of protection inconsistently with the novelty requirement.⁹⁴

In addition to the lack of novelty, there are other possible objections to the patentability of second indications:

- there is no industrial applicability, since what is new is an identified effect on the body, not the product as such or its method of manufacture;

⁹² EPO Board of Appeal, 10 November 1986, Case number: T 0289/84-3.3.1, Application number: EP80104029.

⁹³ The formulation of these claims, deemed to have been first introduced by the Swiss patent office, is of the type 'use of x for the manufacture of product y to treat disease z'. See examples 41 and 42 in the Annex.

⁹⁴ However, this formula suffers from "the logical objection that it lacks novelty, since it claims the use of the compound for preparation of a medicament, and normally the medicament itself will be the same as that already used for the first pharmaceutical indication" (Grubb (1999), p. 221).

- a patent covering the second medical indication of a known product is substantially equivalent to a patent over a method of therapeutic treatment.

Admitting the patentability of second indications extends the protection of pharmaceuticals to cases where no new product has been developed. Many countries reject claims over such indications (see illustrative legislation in the Boxes 16, 17, and 18).

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.

Box 16

Examination Guidelines for Patent Applications relating to Medical Inventions in the UK Patent Office (March 2004). First medical use, Section 2(6), Paragraph 64

Section 2(6) protects the first medical use only. Even if the claim defines a substance "for use in" the treatment of a specific disease, the claim will not be novel if that substance has been used in the treatment of any other disease previously. ... First medical use claims are normally used in cases where the substance is known. However, first (and second) medical use claims are acceptable for new compounds, for example, as a fall-back in the event of a prior disclosure of the compound coming to light after grant.

Therapy, Guidelines for determining whether a method is "treatment by therapy", Paragraph 18.

The intention underlying [Article 52(4)] is to ensure that nobody who wants to use methods specified in this Article as part of the medical treatment of humans or animals should be prevented from this by patents. T 24/91 THOMPSON/Cornea OJEPO 1995, 512

Second Medical Use, Swiss-type claims, Paragraph 79.

".... [I]t is legitimate in principle to allow claims directed to the use of a substance ... for the manufacture of a medicament for a specified new and inventive therapeutic application, even in a case where the process of manufacture as such does not differ from known processes using the same active ingredient." G 05/83 EISAI/Second medical use OJEPO 1985, 64

Second Medical Use, Second medical use – forms of claim, Paragraph 80.

The use of X in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of Y.

The use of X in the preparation of an anti-Y agent in ready-to-use drug form for treating or preventing Y.

The use of X in the manufacture of an anti-Y agent in a package together with instructions for its use in the treatment of Y.

Second Medical Use, Second medical use – forms of claim, Paragraph 81.

Unacceptable second medical use claims.

Substance X for use in the treatment of medical condition Y. The use of substance X in the treatment of disease Y.

Package containing as an active pharmaceutical agent substance X together with instructions for treating condition Y.

Box 17

Guidelines for examination in the European Patent Office, Part C, Chapter IV (Patentability), (4.) Industrial application, (4.2) Surgery, therapy and diagnostic methods

Art. 54(5)

A claim in the form "Use of substance or composition X for the treatment of disease Y ..." will be regarded as relating to a method for treatment explicitly excluded from patentability by Art. 52(4) and therefore will not be accepted.

Art. 82

If an application discloses for the first time a number of distinct surgical, therapeutic or diagnostic uses for a known substance or composition, normally in the one application independent claims each directed to the substance or composition for one of the various uses may be allowed; i.e. an a priori objection of lack of unity of invention should not, as a general rule, be raised (see III, 7.6).

A claim in the form "Use of a substance or composition X for the manufacture of a medicament for therapeutic application Z" is allowable for either a first or "subsequent" (second or further) such application ("second medical use"-type of claim or "Swiss-type" claim), if this application is new and inventive (cf. G 5/83, OJ 3/1985, 64). The same applies to claims in the form "Method for manufacturing a medicament intended for therapeutic application Z, characterised in that the substance X is used" or the substantive equivalents therefrom (see T 958/94, OJ 6/1997, 241). In cases where an applicant simultaneously discloses more than one "subsequent" therapeutic use, claims of the above type directed to these different uses are allowable in the one application, but only if they form a single general inventive concept (Art. 82). Regarding use or method claims of the above type, it should also be noted that a mere pharmaceutical effect does not necessarily imply a therapeutic application. For instance, the selective occupation of a specific receptor by a given substance cannot be considered in itself as a therapeutic application; indeed, the discovery that a substance selectively binds a receptor, even if representing an important piece of scientific knowledge, still needs to find an application in the form of a defined, real treatment of a pathological condition in order to make a technical contribution to the art and to be considered as an invention eligible for patent protection (see T 241/95, OJ 2/2001, 103). See also III, 4.14, for the functional definition of a pathological condition.

Box 18

Decision 486, Common Regime on Industrial Property, Andean Community of Nations

Products or processes already patented and included in the state of the art within the meaning of Article 16 of this Decision may not be the subject of new patents on the sole ground of having been put to a use different from that originally contemplated by the initial patent (Article 21).

Indian Patent Act (as amended in 2005)

The following shall not be treated as an invention within the meaning of the Act: "...the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant" (Section 3(d)).

MECHANISMS TO ENHANCE THE EXAMINATION OF PHARMACEUTICAL PATENTS FROM A PUBLIC HEALTH PERSPECTIVE

There are several measures that countries can implement in order to incorporate a public health perspective into patent examination procedures. Such measures include pre- and post-grant opposition and the adoption of special examination criteria and procedures.⁹⁵

Pre- and Post-grant Opposition

Patents are granted, even in countries where substantive examination takes place, without the State's guarantee about the utility of the invention or the validity of the patent. However, challenging the validity of a granted patent before judicial courts is costly, and obtaining a decision may take years. This gives a major advantage to title holders, since third parties – especially small and medium enterprises in developing countries or the public that may be affected by a wrongly granted patent – will be reluctant or unable to bear the cost and take the risk of litigation.⁹⁶ Wrongly granted patents that unduly block competition and prejudice consumers may, hence, remain in force for the full period of the grant.

To address this problem and enhance the examination of patents, many patent laws provide for the possibility of filing observations or an opposition to the granting of a patent

⁹⁵ Other measures may include reducing the legal standard for proving a patent invalid in court. For instance, in the United States currently such standard is "clear and convincing evidence", which is much tougher than a "preponderance of the evidence" standard. See e.g. FTC (2003); Pamela Samuelson, Legally Speaking: Why Reform the U.S. Patent System? 47 Communications of the ACM, June 2004, available at <http://www.sims.berkeley.edu/~pam/papers/cacm%20patent%20reform.pdf>. Patent quality may also be enhanced by establishing an obligation on the applicant to inform about the grant or refusal of corresponding foreign patent applications (as allowed by Article 29.2 of the TRIPS Agreement), and by prescribing ways of describing prior art in the patent specifications. Peer review mechanisms can also be used. For instance, under The Community Patent Review project (<http://dotank.nyls.edu/communitypatent>) it is proposed to establish a system for researchers to be informed whenever patent applications in their areas of expertise are published. They could then voluntarily use an electronic bulletin-board to post any prior publications that might be relevant. This project has been under consideration of the US Patent and Trademark Office and is backed by some large US firms, such as IBM (see Editorial, Nature, 441, 256, 18 May 2006).

⁹⁶ Moreover, if a patent is invalidated as a result of a legal challenge, the decision would benefit all competitors in a given field, thus giving incentives to potential challengers to reach an agreement with the title-holder rather than bearing alone the costs of litigation.

application. Such a presentation can be made after the publication of the application (or a summary thereof) within a specified term or, if allowed by the applicable law, at any time before the approval of the application. Of course, the longer the period, the greater the opportunities for the patent office to receive observations from third parties, as the existence or relevance of some patent applications may not be immediately recognized. The admissible observations generally relate to non-compliance with any of the patentability requirements, but may also include insufficiency of disclosure and other reasons.

Pre-grant opposition mechanisms help examiners to improve the analysis they undertake, as third parties can bring to their attention precedents that may not have been identified, and lead to the granting of more solid patents while avoiding the creation of rights over developments that are not really inventive. As noted by the US Federal Trade Commission, the circumstances in which patents are granted "suggest that an overly strong presumption of a patent's validity is inappropriate" and that "it does not seem sensible to treat an issued patent as though it had met some higher standard of patentability".⁹⁷

Filing a pre-grant opposition or observations requires capacity to monitor published patent applications and the skills necessary to make the search and analysis of precedents that may be opposed. This requires enhancing the technical knowledge of domestic pharmaceutical companies, ministries of health and civil society to deal with the intricacies of patent law and claims' drafting and interpretation.

A key issue is also the extent to which the information contained in the publication about a patent application is sufficient for interested parties to identify those situations in which an opposition should be submitted. In many cases, the published abstracts and other data about a patent application do not properly characterize a claimed pharmaceutical invention. For instance, the majority of abstracts relating to pharmaceutical inventions do not include the International Nonproprietary Name (INN) that identifies the relevant compounds, but rather report the chemical formula, chemical names or other names that do not allow an easy identification of the patent as related to the compound.⁹⁸

Pre-grant procedures should be implemented in a manner that does not obstruct bona fide patent applications. In some countries, the person who files a pre-grant opposition or observations can participate in some way in the ensuing procedures (*inter-partes* procedures). In others, they must be considered by the examiner, but the person who submitted them does not become party (*ex-parte* procedures).

In some countries post-grant re-examination mechanisms before the administration exist. In the USA, for instance, the validity of a patent may be challenged, based on prior art precedents. These procedures, however, have been rarely used in the USA⁹⁹ and may take a long time (and generate significant expenses, particularly lawyers' fees). Post-grant procedures

⁹⁷ FTC (2003), p. 8. Orrin Hatch and Patrick Leahy, chairmen of the U.S. Senate's intellectual-property panel, introduced in August 2006 the 'Patent Reform Act of 2006' that, in order to stave off excessive litigation, proposes an enhanced "post-grant opposition" system that would allow outsiders to dispute the validity of a patent before a board of administrative judges within the Patent Office.

⁹⁸ An INN is generally not available when a patent for the compound is first filed. It is assigned later in the development process.

⁹⁹ FTC, op. cit, p. 27. There are currently initiatives in the USA to introduce changes to the patent law, *inter alia*, in order to make the post-grant procedures more effective. See, e.g. <http://www.law.com/jsp/article.jsp?id=1124109330603>. See also Bill S.3818 submitted by Senators Hatch and Leahy.

are also available, *inter alia*, at the EPO.¹⁰⁰ The use of these procedures is particularly intense in areas of high patenting activity and the likelihood of opposition increases with patent value.¹⁰¹

The availability of post-grant administrative procedures is also important to enhance the quality of patents granted, as these procedures may generally be completed at a lower cost and in a shorter time than court procedures.

In sum, it is advisable that national laws provide for mechanisms of pre- and/or post-grant opposition. The effectiveness of such mechanisms may be significantly enhanced if the published patent applications or their summaries include all relevant data for the identification of the subject matter of the application. In particular, patent offices should require that all patent applications (and their summaries) related to pharmaceuticals include the INN, where available.

Examination Rules and Procedures

Countries may adopt different types of measures to increase the quality of patents granted in the pharmaceutical and other sectors. Despite the fact that the TRIPS Agreement bans discrimination between fields of technology (Article 27.1), a justified differentiation is viable.¹⁰² This is particularly so in the area of public health, as indicated by the Doha Declaration on the TRIPS Agreement and Public Health.¹⁰³ The singling out of public health and, in particular, pharmaceuticals as an issue that needs special attention in the implementation of the TRIPS Agreement, constitutes a clear recognition that public health-related patents and other forms of intellectual property rights can be treated differently if necessary to protect public health.

Special rules for the examination and grant of pharmaceutical patents may be established in national laws and regulations, as well as in guidelines of patent offices. Such rules may include the definition of specific criteria for the approval of patent applications, as adopted by the amendment to the Indian law of 2005.

In addition to prescribing criteria to be applied by the patent offices, it would be desirable to develop a close cooperation between, on the one hand, the ministries of health and health regulatory authorities and, on the other, the patent offices; for the examination of pharmaceutical patent applications. Moreover, the intervention of authorities competent in the area of public health can be envisaged. For instance, in Brazil, a provisional measure by the President (14 December 1999) subsequently converted into Federal Law 10.196 of 14 February 2001, introduced into the Industrial Property Code a requirement of “prior consent” by the

¹⁰⁰ In the case of India, in accordance with the amended Patents Act, unlike as under the Patents Act, 1970, patents can be opposed even before grant, but full-scale proceedings for opposition can start only after the patent is granted.

¹⁰¹ See Harhoff and Reitzig (2002).

¹⁰² In a WTO case between the EC and Canada, it was held that: “Article 27 prohibits only discrimination as the place of invention, the field of technology, and whether products are imported or produced locally. Article 27 does not prohibit bona fide exceptions to deal with problems that may exist only in certain product areas. Moreover, to the extent the prohibition of discrimination does limit the ability to target certain products in dealing with certain of the important national policies referred to in Articles 7 and 8.1, that fact may well constitute a deliberate limitation rather than frustration of purpose” (WT/DS114/R, 17 March 2000, para 7.92).

¹⁰³ WT/MIN(01)/DEC/W/2, 14 November 2001, available at www.wto.org.

National Sanitary Supervision Agency (ANVISA) for the granting of pharmaceutical patents. A similar requirement has been established in Paraguay.

CONCLUSIONS

Whether subject to the TRIPS Agreement or not, countries can determine their own criteria to assess patent applications consistently with their public health policies. Patent regimes are generally part of national technological and industrial strategies, but it is also crucial to design them consistently with public health strategies. It is important, in particular, that the scope of patentability be congruent with public health policies, and that governments be aware that unduly expanding what can be patented may distort competition and reduce access to medicines. Patents over minor developments may be effectively used to discourage or block competition, as generic producers, purchasing agencies and consumers, especially in developing countries, generally lack the substantial technical and financial resources needed to challenge wrongly granted patents or defend against infringement claims.

The analysis and criteria presented in this document intend to provide general guidance to patent offices and other bodies that participate in the examination of pharmaceutical patents, in a way that is consistent with patent law and, at the same time, congruent with public health objectives, in particular with the right of access to medicines by all. They should be further refined and adjusted to national legislation, as appropriate.

As discussed above, it is unlikely that the following classes of product patent applications be admissible:

- 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 single entities;
- A new dosage form that allows a new route of administration (e.g. an injection when an oral tablet already exists);
- A controlled release dosage form when a non-controlled release dosage form already exists;
- A new route of administration of an existing dosage form (e.g. intravenous administration of an injection when subcutaneous administration is already approved);
- A change in formulation.

In order to be able to implement these guidelines, or otherwise preserve the capacity to determine the criteria for the examination of pharmaceutical patents, countries should not adhere to international instruments¹⁰⁴ that may erode the flexibilities currently allowed by the TRIPS Agreement for that purpose, such as the capacity to define the concept of invention and the criteria to apply the standards of patentability, notably with regard to the level of inventive step.

¹⁰⁴ With regard to initiatives for the harmonization of substantive patent law, see Carlos Correa (2005).

An indispensable requirement for dealing with patent applications with a public health perspective is obviously to adequately train and retain qualified examiners. Training provided by patent offices of developed countries may increase examiners' technical skills, but also induce standards of evaluation that may lead to an undue expansion in the scope of patentability of pharmaceuticals.

Finally, patent examiners should be aware that the decisions they take, although apparently technical in nature, may have very practical implications for the health and life of people, as wrongly granted patents can be used to unduly restrict competition and limit access to needed medicines.

ANNEX

• EXAMPLE 1

Oral administration forms of a medicament containing pantoprazole

Patent number: HK1005851

Publication date: 1999-01-29

The invention relates to oral presentation forms for pantoprazole, which consist of a core, an intermediate layer and an outer layer which is resistant to gastric juice.

Claims

1. An orally administrable medicament in pellet or tablet form which is resistant to gastric juice, and in which each pellet or tablet consists of a core in which active compound or its physiologically-tolerated salt is in admixture with binder, filler and, optionally, a member selected from the group consisting of another tablet auxiliary and a basic physiologically-tolerated inorganic compound, an inert water-soluble intermediate layer surrounding the core and an outer layer which is resistant to gastric juice, wherein the active compound is pantoprazole, the binder is polyvinylpyrrolidone and/or hydroxypropylmethylcellulose and, optionally, the filler is mannitol.

• EXAMPLE 2

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 10µm.
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.

• **EXAMPLE 3**

Didanosine granula composition and its preparation method

Patent number: CN1565422 (WO0003696) Publication date: 2005-01-19

The invention discloses an AIDS drug didanosine granula composition and its preparation method, the particle composition comprises a therapeutically effective dosage of inosine, acid preparation, filler and binder.

Claims

1. An enteric coated pharmaceutical composition comprising a core in the form of a tablet and having an enteric coating surrounding said core, said core comprising an acid labile medicament, a binder or filler, a disintegrant, and a lubricant, said enteric coating comprising a methacrylic acid copolymer, and a plasticizer, and imparting protection to said core so that said core is afforded protection in a low pH environment of 3 or less while capable of releasing medicament at a pH of 4.5 or higher.

• **EXAMPLE 4**

Extended release formulation containing venlafaxine

Patent number: EP0797991

Publication date: 1997-10-01

This invention relates to a 24 hour extended release dosage formulation and unit dosage form thereof of venlafaxine hydrochloride, an antidepressant, which provides better control of blood plasma levels than conventional tablet formulations which must be administered two or more times a day and further provides a lower incidence of nausea and vomiting than the conventional tablets.

Claims

1. An encapsulated, extended release formulation of venlafaxine hydrochloride comprising a hard gelatine capsule containing a therapeutically effective amount of spheroids comprised of venlafaxine hydrochloride, microcrystalline cellulose and hydroxypropylmethylcellulose coated with ethyl cellulose and hydroxypropylmethylcellulose.

- **EXAMPLE 5**

Antibiotic preparations

Patent number: GB1479655

Publication date: 1977-07-13

A powder which may be dispersed in water to yield an orally administrable pharmaceutical composition comprises (a) particles of particle size 5 to 500Å comprising a water-soluble acid addition salt of an in vivo hydrolysable ester of a penicillin or cephalosporin which has an amino group in the acetylamino side chain which particles are at least 50% coated with a pharmaceutically acceptable water-insoluble coating agent and (b) a water-soluble salt of a weak organic acid, the weight ratio (a):(b) being from 5:1 to 1:5. The salt (b) may be included within the penicillin, or cephalosporin particles. The antibiotic may be ampicillin phthalidyl ester hydrochloride or ampicillin pivaloyloxy-methyl ester hydrochloride. The weak acid salt may be disodium citrate or trisodium citrate. The coating agent may be ethyl cellulose, poly(dimethylaminoethylmethacrylate) or poly-(vinyl acetal diethylaminoacetate). Other ingredients specified include monmorillonite clay, preservative, flavouring and caster sugar.

Claims

1. A powder which may be reconstituted into an orally administrable pharmaceutical composition in suspension or solution form by the addition of water which powder contains (a) fine particles of a water-soluble acid addition salt of an in vivo hydrolysable ester of a penicillin or cephalosporin which has an amino group in the acetylamino side chain and which fine particles are substantially or wholly coated by a pharmaceutically acceptable water-insoluble coating agent, (b) a water-soluble salt of a weak organic acid and (c) conventional carriers; the weight ratio of penicillin or cephalosporin derivative to water-soluble salt of a weak organic acid being from 5:1 to 1:5.

- **EXAMPLE 6**

Celecoxib compositions

Patent number: WO0032189

Publication date: 2000-06-08

Pharmaceutical compositions are provided comprising one or more orally deliverable dose units, each comprising particulate celecoxib in an amount of about 10 mg to about 1000 mg in

intimate mixture with one or more pharmaceutically acceptable excipients. The compositions are useful in treatment or prophylaxis of cyclooxygenase-2 mediated conditions and disorders.

Claims

1. pharmaceutical composition comprising one or more orally deliverable dose units, each comprising particulate celecoxib in an amount of about 10 mg to about 1000 mg in intimate mixture with one or more pharmaceutically acceptable excipients, wherein a single dose unit, upon oral administration to a fasting subject, provides a time course of blood serum concentration of celecoxib characterized by at least one of
 - (a) a time to reach 100 ng/ml not greater than about 0.5 h after administration;
 - (b) a time to reach maximum concentration (T_{max}) not greater than about 3 h after administration;
 - (c) a duration of time wherein concentration remains above 100 ng/ml not less than about 12 h;
 - (d) a terminal half-life (T_{1/2}) not less than about 10 h; and
 - (e) a maximum concentration (C_{max}) not less than about 200 ng/ml.
2. A composition of Claim 1 wherein the time course of blood serum concentration of celecoxib is characterized by a T_{max} not greater than about 3 h, preferably not greater than about 2 h, and more preferably not greater than about 1.7 h, after administration.
3. A composition of Claim 1 wherein the C_{max} is not less than about 200 ng/ml, preferably not less than about 400 ng/ml.
4. A pharmaceutical composition comprising one or more orally deliverable dose units, each comprising particulate celecoxib in an amount of about 10 mg to about 1000 mg in intimate mixture with one or more pharmaceutically acceptable excipients, and having relative bioavailability not less than about 50%, preferably not less than about 70%, by comparison with an orally delivered solution containing an equivalent amount of celecoxib.
5. A pharmaceutical composition comprising one or more orally deliverable dose units, each comprising particulate celecoxib in an amount of about 10 mg to about 1000 mg in intimate mixture with one or more pharmaceutically acceptable excipients, and having a distribution of celecoxib particle sizes such that 50% of the particles is less than 200 pLm, preferably less than 100 urn, more preferably less than 40 nm, and most preferably less than 25 um, in the longest dimension of said particles.

• **EXAMPLE 7**

Oral pediatric Trimethobenzamide formulations and methods

Patent number: WO03072021A2

Publication date: 2003-09-04

Oral pediatric trimethobenzamide compositions and methods for treating and controlling nausea and/ or vomiting are disclosed in warm blooded animals, especially humans including children. The oral pediatric trimethobenzamide compositions and methods of the present invention are believed to be at least as effective as a 200 mg intramuscular I.M. trimethobenzamide HCl injectable formulation when administered at a dose of about 100 mg. In addition, an oral pediatric composition containing about 120 mg of trimethobenzamide HCl

is believed to be uniquely approximately bioequivalent to a 200 mg intramuscular I.M. trimethobenzamide HCl injectable formulation when administered at a dose of about 100 mg.

Claims

1. An oral pediatric trimethobenzamide composition for treating and controlling nausea and/or vomiting in a child comprising trimethobenzamide and a suitable pharmaceutical excipient, wherein said oral pediatric trimethobenzamide composition is at least about as effective as a 200 mg intramuscular (I.M.) trimethobenzamide HCl injectable formulation when administered in a dose of about 100 mg to treat and control nausea and/or vomiting.
2. An oral pediatric trimethobenzamide composition of claim 1, wherein said trimethobenzamide is present in an amount greater than 120 mg.

• **EXAMPLE 8**

Taxol for use in cancer therapy

Patent number: EP0584001

Publication date: 1994-02-23

The invention concerns products containing taxol for use in cancer therapy. According to this invention, the products contain an anti-neoplastically effective amount of taxol and sufficient medications to prevent severe anaphylactic-like reactions and are formulated and packaged for separate or sequential or simultaneous use in cancer therapy with a patient over a period of about 24 hours or less. These products find application in the treatment of all types of cancers, treatable by taxol.

Claims

1. Products containing an anti-neoplastically effective amount of taxol and sufficient medications to prevent severe anaphylactic-like reactions formulated and packaged for separate or sequential or simultaneous use in cancer therapy with a patient over a period of about 24 hours or less.

• **EXAMPLE 9**

Pharmaceutical composition

Patent number: WO2004010993

Publication date: 2004-02-05

The instant invention provides a pharmaceutical composition comprised of a cholesterol absorption inhibitor and an HMG-CoA reductase inhibitor, one or more anti-oxidants, microcrystalline cellulose, hydroxypropyl methylcellulose, magnesium stearate and lactose. The composition need not contain ascorbic acid in order to obtain desirable stability.

Claims

1. A pharmaceutical composition comprised of from 1% to 20% by weight of ezetimibe; from 1% to 80% by weight of simvastatin; and from 0.01% to 2% by weight of BHA.
2. The composition of claim 1 comprised of from 1.25% to 10% of ezetimibe, and from 1% to 20% of simvastatin.
3. The composition of claim 2 comprised of from 5% to 10% of simvastatin.
4. The composition of claim 1 comprised of 0.01% to 0.05% of BHA
5. The composition of claim 4 comprised of about 0.02% of BHA
6. The composition of claim 1 further comprised of 0.2% or less by weight of propyl gallate.
7. The composition of claim 6 comprised of from 0.001% to 0.05% by weight of propyl gallate.

• **EXAMPLE 10**

Modified release ibuprofen dosage form

Patent number: WO2006039692

Publication date: 2006-04-13

The present invention is a solid dosage form for oral administration of ibuprofen comprising a modified release formulation of ibuprofen which provides an immediate burst effect and thereafter a sustained release of sufficient ibuprofen to maintain blood levels at least 6.4g/ml over an extended period of at least 8 hours following administration of a single dose. The dosage form releases ibuprofen at a rate sufficient to initially deliver an effective amount of ibuprofen within about 2.0 hours following administration. The dosage form then subsequently delivers the remaining amount of ibuprofen at a relatively constant rate sufficient to maintain a level of ibuprofen over a predetermined delivery period of for at least 8 hours.

Claims

1. A solid dosage form for modified oral administration of ibuprofen comprising: a hydrophilic polymer; 300 to 800 mg of ibuprofen in the solid dosage form uniformly dispersed in said polymer; a dissolution additive dispersed in said hydrophilic polymer in an amount in the range of 10% to 35% by weight of the ibuprofen, said dissolution additive comprising an alkali metal salt, an amino acid having a neutral to alkaline side chain, croscarmellose or a salt thereof, or a combination of any two of such dissolution additives; and an inert formulation additive dispersed in said hydrophilic polymer in an amount in the range of 15% to 75% by weight of the ibuprofen, said formulation additive comprising microcrystalline cellulose, silica, magnesium stearate, stearic acid, lactose, pre-gelatinized starch, dicalcium phosphate or a combination of any of them, wherein at least 20% of the ibuprofen is released within 2 hours following oral administration or exposure to an agitated aqueous medium of a single dosage unit, then thereafter releases ibuprofen at a relatively constant rate over a period of at least 8 hours, and wherein at least 70% of the ibuprofen is released over a period of not more than 14 hours following such administration or exposure.
2. The solid dosage form of claim 1, wherein ibuprofen is present in each dosage form in an amount of about 300mg, 400mg or 600 mg.

• **EXAMPLE 11**

Novel combination

Patent number: US 20050065176

Publication date: 2005-03-24

Combinations comprising

- a) an activator of soluble guanylate cyclase and
- b) an inhibitor of angiotensin converting enzyme (ACE) are useful for treating hypertension.

Claims

1. The use of a combination of an activator of soluble guanylate cyclase and an inhibitor of angiotensin converting enzyme (ACE) for the preparation of a medicament for the palliative, curative or prophylactic treatment of a cardiovascular or metabolic disorder.
11. A pharmaceutical composition comprising an activator of soluble guanylate cyclase and an inhibitor of angiotensin converting enzyme (ACE).
12. A pharmaceutical combination for simultaneous, separate or sequential administration for treating hypertension, comprising an activator of soluble guanylate cyclase and an inhibitor of angiotensin converting enzyme (ACE).

• **EXAMPLE 12**

Pharmaceutical composition containing a statin and aspirin

Patent number: EP1071403 B1

Publication date: 2005-07-27

A pharmaceutical composition is provided which is useful for cholesterol lowering and reducing the risk of a myocardial infarction, which includes a statin, such as pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin or fluvastatin, in combination with aspirin, in a manner to minimize interaction of aspirin with the statin and minimize side effects of aspirin. A method for lowering cholesterol and reducing risk of a myocardial infarction employing such composition is also provided.

Claims

1. A pharmaceutical composition comprising a statin cholesterol lowering agent and aspirin in a formulation to reduce statin:aspirin interaction wherein the statin and aspirin are formulated together in a bi-layered tablet, the aspirin being present in a first layer, and the statin being present in a second layer.
2. The pharmaceutical composition as defined in claim 1 wherein the layer containing the statin also includes one or more buffering agents.
3. The pharmaceutical composition as defined in claim 1 wherein the tablet includes a core and a coating layer surrounding said core and wherein one of the statin and aspirin is present in the core and the other is present in the coating layer surrounding the core.

• **EXAMPLE 13**

Composition comprising a tramadol compound and acetaminophen and its use

Patent number: EP0566709 B1

Publication date: 1998-12-08

This invention relates to a composition comprising a tramadol material and acetaminophen, and its use. As used herein tramadol refers to various forms of tramadol. The compositions are pharmacologically useful in treating pain and tussive conditions. The compositions are also subject to less opioid side-effects such as abuse liability, tolerance, constipation and respiratory depression. Furthermore, where the components of the compositions are within certain ratios the pharmacological effects of the compositions are superadditive (synergistic).

Claims

1. A pharmaceutical composition comprising a tramadol compound and acetaminophen.
2. The pharmaceutical composition of claim 1 wherein the tramadol compound and acetaminophen are in a ratio that is sufficient to provide a synergistic pharmacological effect.

• **EXAMPLE 14**

Composition comprising 5-[4-[2-(n-methyl-n-2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione

Patent number: WO9855122

Publication date: 1998-12-10

A pharmaceutical composition comprising Compound (I), characterised in that the composition comprises 2 to 12 mg of Compound (I) in a pharmaceutically acceptable form and optionally a pharmaceutically acceptable carrier therefor, the use of such a composition in medicine, processes for the preparation of such a composition and intermediate composition useful in such a process.

Claims

1. A pharmaceutical composition comprising 5-[4-[2-(N-methyl-N(pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (hereinafter 'Compound (I)'), characterised in that the composition comprises 2 to 12 mg of Compound (I) in a pharmaceutically acceptable form and optionally a pharmaceutically acceptable carrier therefor.
2. A composition according to claim 1, which comprises 2 to 4 mg of Compound (I) in a pharmaceutically acceptable form.
3. A composition according to claim 1, which comprises 4 to 8 mg of Compound (I) in a pharmaceutically acceptable form.

4. A composition according to claim 1, which comprises 8 to 12 mg of Compound (I) in a pharmaceutically acceptable form.
5. A composition according to claim 1, which comprises 2 mg of Compound (I) in a pharmaceutically acceptable form.
6. A composition according to claim 1, which comprises 4 mg of Compound (I) in a pharmaceutically acceptable form.
7. A composition according to claim 1, which comprises 8 mg of Compound (I) in a pharmaceutically acceptable form.

• **EXAMPLE 15**

High dose ibandronate formulation

Patent number: US2004121007

Publication date: 2004-06-24

The invention relates to a high dose oral formulation of bisphosphonates and to a process for the preparation of such formulations.

Claims

1. A pharmaceutical composition containing as active substance up to about 250 mg of bisphosphonates or a pharmaceutically acceptable salt thereof for oral application.
4. A pharmaceutical composition according to claim 1 comprising the equivalent of 150 mg bisphosphonates or a pharmaceutically acceptable salt thereof as active substance.
5. A pharmaceutical composition according to claim 1 comprising the equivalent of 100 mg bisphosphonates or a pharmaceutically acceptable salt thereof as active substance.
6. A pharmaceutical composition according to claim 1, wherein the active substance is ibandronic acid or a pharmaceutically acceptable salt thereof.

• **EXAMPLE 16**

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.

• **EXAMPLE 17**

Salts of amlodipine

Patent number: GB19860008335

Publication date: 1993-04-30

Improved pharmaceutical salts of amlodipine, particularly the besylate salt, and pharmaceutical compositions thereof. These salts find utility as anti-*ischaemic* and anti-hypertensive agents.

Claims

1. The besylate salt of amlodipine.

• **EXAMPLE 18**

Paroxetine methanesulfonate

Patent number: GB2336364

Publication date: 1999-10-20

Paroxetine methanesulfonate is a novel compound having pharmaceutical activity. It may be obtained as a 1:1 solvate with acetonitrile and it can be converted to paroxetine hydrochloride.

Claims

1. Paroxetine methanesulfonate.

• **EXAMPLE 19**

Bisulfate salt of HIV protease inhibitor (atazanavir)

Patent number: US6087383

Publication date: 2000-07-11

The present invention provides the crystalline bisulfate salt of the formula which is found to have unexpectedly high solubility/dissolution rate and oral bioavailability relative to the free base form of this azapeptide HIV protease inhibitor compound.

Claims

1. The bisulfate salt having the formula.
2. A pharmaceutical dosage form comprising the bisulfate salt of claim 1 and a pharmaceutically acceptable carrier.

• **EXAMPLE 20**

Intermediates and process for preparing olanzapine

Patent number: EP0831098

Publication date: 1998-03-25

The present invention provides a process for preparing olanzapine and intermediates thereof.

Claims

1. A compound which is an olanzapine dihydrate.
2. A compound of Claim 1 wherein the dihydrate is an intermediate for preparing Form II olanzapine.
3. A compound of Claim 1 wherein the dihydrate is crystalline Dihydrate B olanzapine polymorph having a typical x-ray powder diffraction pattern as represented by the following interplanar spacings (d) as set forth in Table 2 [omitted].

• **EXAMPLE 21**

Crystalline polymorphic form of irinotecan hydrochloride

Patent number: WO03074527

Publication date: 2003-09-12

This invention relates to a novel crystalline polymorphic form of irinotecan hydrochloride. A process for preparing this novel polymorphic form, pharmaceutical compositions comprising it as an active ingredient and the use of the same and its pharmaceutical compositions as a therapeutic agent is also within the scope of the present invention.

Claims

1. Polymorphic form of crystalline irinotecan hydrochloride of formula:

EMI21.1 characterized by providing an X-ray powder diffraction pattern comprising 20 angle values of about 9.15; about 10.00; about 11.80; about 12.20; about 13.00 and about 13.40.

• **EXAMPLE 22**

Ranitidine

Patent number: US4521431

Publication date: 1985-06-04

A novel crystal form of ranitidine (N-[2-[[[5-(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl- N'-methyl 1-2-nitro-1,1-ethenediamine) hydrochloride, designated Form 2, and having favourable filtration and drying characteristics, is characterized by its infra-red spectrum and/or by its x-ray powder diffraction patterns.

Claims

Form 2 ranitidine hydrochloride characterised by an infra-red spectrum as a mull in mineral oil showing the following main peaks [table omitted]

• **EXAMPLE 23**

Cephadroxil monohydrate

Patent Number: US4504657

Publication date: 1985-03-12

A novel crystalline monohydrate of 7-[D- α -amino- α -(p-hydroxyphenyl)acetamido]-3-cephem-4-carboxylic acid is prepared and found to be a stable useful form of the cephalosporin antibiotic especially advantageous for pharmaceutical formulations.

Claims

1. Crystalline 7-[D- α -amino- α -(p-hydroxyphenyl)acetamido]-3-methyl-3-cephem-4-carboxylic acid monohydrate exhibiting essentially the following x-ray diffraction properties:

Line	Spacing d(A)	Relative Intensity
1	8.84	
1002	7.88 403 7.27 424 6.89 155 6.08 706 5.56 57 5.35 638 4.98 389 4.73 2610 4.43 1811 4.10	
6112	3.95 513 3.79 7014 3.66 515 3.55 1216 3.45 7417 3.30 1118 3.18 1419 3.09 1620 3.03	
2921	2.93 822 2.85 2623 2.76 1924 2.67 925 2.59 2826 2.51 1227 2.46 1328 2.41 229 2.35	
1230	2.30 231 2.20 1532 2.17 1133 2.12 734 2.05 435 1.99 436 1.95 1437 1.90	
10		

• **EXAMPLE 24**

Heterocyclic compounds

Patent number: GB2078719

Publication date: 1982-01-13

Fungicidal compounds of the formula [] wherein R1 is an optionally substituted-alkyl, -cycloalkyl, -aryl or -aralkyl group, Y1 and Y2 are =CH- or =N-; and salts, metal complexes, ethers and esters thereof.

Claims

1. A compound selected from the group consisting of compounds having the formula: III [omitted] wherein R1 is selected from the group consisting of: phenyl or benzyl substituted with one or more of the following: halogen, alkyl or haloalkyl each containing from 1 to 5 carbon atoms, alkoxy or haloalkoxy each containing from 1 to 4 carbon atoms, nitro, cyano, hydroxy, alkylthio containing from 1 to 40 carbon atoms, vinyl, phenyl or phenoxy; and wherein the alkyl moiety of the benzyl is unsubstituted, or substituted with alkyl containing from 1 to 4 carbon atoms, phenyl or chlorophenyl, Y1 and Y2 are =CH or =N; and salts, metal complexes, methyl, ethyl, propyl, butyl, phenyl, benzyl, p-chlorobenzyl, allyl and propargyl ethers and acetate, pivaloate, benzoate, tosylate and mesylate esters thereof.

• **EXAMPLE 25**

Substantially pure enantiomers of 2-azabicyclo(2,2,1)hept-5-en-3-one

Patent number: US5498625

Publication date: 1996-03-12

Lactams of 1-amino-3-carboxylic acid cyclic compounds are produced in enantiomeric form, together with an enantiomer of the corresponding ring-opened amino-acid or ester, by reaction of the racemic lactam with a novel lactamase. The products are useful in the synthesis of chiral carbocyclic nucleotides. The enantiomer is preferably 2-azabicyclo(2,2,1)hept-5-en-3-one. It is desirable to isolate the enantiomer comprising predominantly the (+) enantiomer and a residual amount of the (-) enantiomer, wherein the (+) enantiomer is present in an enantiomeric excess of at least about 88% over the (-) enantiomer or the enantiomer comprising predominantly the (-) enantiomer and a residual amount of the (+) enantiomer, wherein the (-) enantiomer is present in an enantiomeric excess of at least about 98% over the (+) enantiomer.

Claims

1. 2-Azabicyclo(2,2,1)hept-5-en-3-one, comprising predominantly the (+) enantiomer and a residual amount of the (-) enantiomer, wherein the (+) enantiomer is present in an enantiomeric excess of at least about 88% over the (-) enantiomer.
2. The 2-azabicyclo-[2,2,1]hept-5-en-3-one of claim 1, formed by a process comprising the steps of reacting a racemate of 2-azabicyclo(2,2,1)hept-5-en-3-one with an enzyme having

lactamase activity or a microorganism having lactamase activity which stereoselectively cleaves the (-) enantiomer thereby forming the (-) enantiomer of 4-amino-cyclopent-2-ene-1-carboxylic acid or an ester thereof, and then isolating the 2-azabicyclo(2,2,1)hept-5-en-3-one having an enantiomeric excess of the (+) enantiomer.

• **EXAMPLE 26**

New enantiomers and their isolation

Patent number: EP0347066B1

Publication date: 1995-03-15

The novel (+) enantiomer of 1-(3-dimethylaminopropyl)-1-(4 min -fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile as well as acid addition salts thereof are described as valuable antidepressants, geriatrics or in the treatment of obesity and alcoholism. Novel intermediates and a method for the preparation of the (+) enantiomer as well as the racemic mixture are described.

Claims

1. (+)-1-(3-dimethylaminopropyl)-1-(4'-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile having the general formula and non-toxic acid addition salts thereof.
6. A method for the preparation of a compound as defined in claim 1, which comprises, converting(-)-4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxy methyl)benzocarbonitrile or a monoester thereof in a stereoselective way to (+)-1-(3-dimethylaminopropyl)-1-(4'-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile which is isolated as such or as a non- toxic acid addition salt thereof

• **EXAMPLE 27**

Terfenadine

Patent number US 6509353

Publication date: 2003-01-21

Methods and pharmaceutical compositions employing a terfenadine metabolite and a leukotriene inhibitor for the treatment or prevention of inflammation or allergic disorders, such as asthma, or symptoms thereof. Also included are methods and compositions employing a terfenadine metabolite, a leukotriene inhibitor, and a decongestant for the treatment or prevention of inflammation or allergic disorders, such as asthma, or symptoms thereof.

Claims

1. A method for treating or preventing a condition responsive to leukotriene inhibition in a human which comprises administering to a human in need of such treatment or prevention a therapeutically effective amount of terfenadine metabolite, or a pharmaceutically acceptable salt thereof, and a therapeutically effective amount of a leukotriene inhibitor, or a pharmaceutically acceptable salt thereof.

• EXAMPLE 28

1-phenyl-2-dimethylaminomethyl cyclohexane compounds used for the therapy of depressive symptoms, pain, and incontinence

Patent number: WO2004009067

Publication date: 2004-01-29

The invention relates to metabolites of [2-(3-methoxyphenyl)-cyclohexylmethyl]-dimethylamine as free bases and/or in the form of physiologically acceptable salts, corresponding medicaments, the use of [2-(3-methoxyphenyl)-cyclohexylmethyl]-dimethylamine and the metabolites thereof for producing a medicament used for treating depressions, and methods for treating depressions.

Claims

1. Use of:

-3-(2-dimethylaminomethyl-ciclohexyl) – phenol(1R,2R)-3-(2-dimethylaminomethyl-cycloexyl) –phenol [...]

optionally in the form of their racemates, their pure stereoisomers, in particular enantiomers or diastereomers, or in the form of mixtures of the stereoisomers, in particular the enantiomers or diastereomers, in any desired mixture ratio; in the form shown or in the form of their acids or their bases or in the form of their salts, in particular the physiologically acceptable salts, or in the form of their solvates, in particular the hydrates; for the preparation of a medicament for treatment of depressions.

• EXAMPLE 29

N3 Alkylated Benzimidazole derivatives as MEK inhibitors

Patent number: WO03077855

Publication date: 2003-09-25

Disclosed are compounds of the formula (I) and pharmaceutically acceptable salts and prodrugs thereof, wherein W, t, R<1>, R<2>, R<7>, R<9>, R<10>, R<11> and R<12> are as defined in the specification. Such compounds are MEK inhibitors and useful in the treatment of hyperproliferative diseases, such as cancer and inflammation, in mammals. Also disclosed is a method of using such compounds in the treatment of hyperproliferative diseases in mammals, and pharmaceutical compositions containing such compounds.

Claims

1. A compound of the formula [Formula omitted]

and pharmaceutically accepted salts, prodrugs and solvates thereof, wherein: R1, R2, R9 and R10 are independently selected from hydrogen, halogen, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, azido, -[...].

• **EXAMPLE 30**

Prodrugs of carbonic anhydrase inhibitors

Patent number: US5095026

Publication date: 1992-03-10

Prodrugs are prepared of the carbonic anhydrase inhibitors 2-benzothiazolesulfonamide, hydroxymethazolamide, and dichlorphenamide. The prodrugs link a water soluble compound to the pharmacologically active carbonic anhydrase inhibitor through an enzymatically or hydrolytically degradable bond.

Claims

1. Prodrugs of 2-benzothiazolesulfonamide carbonic anhydrase inhibitors (CAI) having the formula:
wherein Z is a water soluble carrier, and A is a moiety which when attached to said 2-benzothiazolesulfonamide will still retain CAI activity and which can also form an enzymatically cleavable bond with Z .
2. The prodrugs of claim 1 wherein the water soluble carrier Z is selected from the group consisting of monosaccharides and 6-carboxylic acid derivatives of monosaccharides.

• **EXAMPLE 31**

Controlled release pharmaceutical composition containing midodrine and/or desglymidodrine

Patent number: WO0174334A1

Publication date: 2001-10-11

Novel controlled release pharmaceutical compositions for oral use containing midodrine and/or its active metabolite desglymidodrine. The novel compositions are designed to release midodrine and/or desglymidodrine after oral intake in a manner which enables absorption to take place in the gastrointestinal tract so that a relatively fast peak plasma concentration of the active metabolite desglymidodrine is obtained followed by a prolonged and relatively constant plasma concentration of desglymidodrine. Also disclosed is a method for treating orthostatic hypotension and/or urinary incontinence, the method comprising administration to a patient in need thereof of an effective amount of midodrine and/or desglymidodrine in a composition according to the invention.

Claims

1. A controlled release pharmaceutical composition for oral use comprising midodrine (ST 1085) or a pharmaceutically acceptable salt thereof and/or its active metabolite desglymidodrine (ST 1059) or a pharmaceutically acceptable salt thereof, the composition

being adapted to release midodrine and/or desglymidodrine in such a manner that a relatively fast peak plasma concentration of desglymidodrine is obtained and that a therapeutically effective plasma concentration of desglymidodrine is maintained for at least about 9 hours such as, e.g. at least about 10 hours, at least about 11 hours, at least about 12 hours, at least about 13 hours, or at least about 14 hours.

• **EXAMPLE 32**

Pharmaceutically active morpholinol

Patent number: US6274579

Publication date: 2001-08-14

New active isomer of bupropion morpholinol metabolite.

Claims

1. (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol or pharmaceutically acceptable salts and solvates thereof.
2. Pharmaceutical compositions comprising a compound according to claim 1 or pharmaceutically acceptable salts and solvates thereof together with one or more pharmaceutically acceptable carriers, diluents or excipients.

• **EXAMPLE 33**

Antihistaminic 11-(4-piperidylidene)-5H-benzo-[5,6]-cyclohepta-[1,2-b]-pyridines

[**Loratadine**] Patent number: US4282233

Publication date: 1981-08-04

11-(4-piperidylidene)-5H-benzo-[5,6]-cyclohepta-[1,2-b]-pyridines and their 5,6-dihydro derivatives are disclosed. The compounds are useful as antihistamines with little or no sedative effects.

Claims

1. A compound of the formula wherein the dotted line represents an optional double bond; X is hydrogen or halo; and wherein Y is --COOR or SO₂ R; with the proviso that when Y is --COOR, R is C₁ to C₁₂ alkyl, substituted C₁ to C₁₂ alkyl, Phenyl, substituted phenyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ phenylalkyl wherein the phenyl moiety is substituted or R is -2, -3, or -4 piperidyl or N-substituted piperidyl wherein the substituents on said substituted C₁ to C₁₂ alkyl are selected from amino or substituted amino and the substituents on said substituted amino are selected from C₁ to C₆ alkyl, the substituents on said substituted phenyl and on said substituted phenyl moiety of the C₇ to C₁₂ phenylalkyl are selected from C₁ to C₆ alkyl and halo, and the substituent on said N-substituted piperidyl is C₁ to C₄ alkyl; and with the proviso that when Y is SO₂ R, R is C₁ to C₁₂ alkyl, phenyl, substituted phenyl, C₇ to C₁₂ phenylalkyl, C₇ to C₁₂ phenylalkyl wherein the phenyl moiety is substituted, wherein the substituents on said substituted phenyl and said

substituted phenyl moiety of the C₇ to C₁₂ phenylalkyl are selected from C₁ to C₆ alkyl and halo.

7. 11-(N-carboethoxy-4-piperidylidene)-8-chloro-6, 11-dihydro-5H-benzo-[5,6]-cyclohepta-[1,2-b]-pyridine [The active metabolite of loratadine is descarboethoxyloratadine (DCL)]

• **EXAMPLE 34**

Antihistaminic 8-(halo)-substituted 6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridines

Patent number: US4659716

Publication date: 1987-04-21

Disclosed are 7- and/or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridines and the pharmaceutically acceptable salts thereof, which possess antihistaminic properties with substantially no sedative properties. Methods for preparing and using the compounds and salts are described.

Claims

1. A compound of the formula or a pharmaceutically acceptable salt thereof, wherein X represents Cl or F.

• **EXAMPLE 35**

Methods of treating HIV infection

Patent number: WO2005058237

Publication date: 2005-06-30

The invention includes methods of treating HIV infection in a patient where the method includes administration of an antibody to TNF-alpha and an antibody to interferon-gamma to the patient and administering antiretroviral therapy to a patient. The invention further includes methods of treating HIV infection in a patient where the method comprises administration of an antibody to TNF-alpha and an antibody to alpha interferon to the patient and administering antiretroviral therapy to a patient. The invention further includes a method of treating HIV infection in a patient where the method includes administering an antibody to alpha interferon and antiretroviral therapy to a patient. The invention further includes a method of treating an HIV infection in a patient where the method comprises administering a chimeric TNF-alpha receptor and antiretroviral therapy to a patient.

Claims

1. A method of treating an HIV infection in a treatment experienced patient, the method comprising administering an effective amount of a chimeric tumour necrosis factor alpha receptor.
2. The method of claim 1, wherein the chimeric tumour necrosis factor alpha receptor is administered by the route selected from the group consisting of intramuscularly,

- intravenously, intradermally, cutaneously, subcutaneously, ionophoretically, topically, locally, orally, rectally and inhalation.
3. The method of claim 1, wherein the chimeric tumour necrosis factor alpha receptor is selected from the group consisting of a chimeric tumour necrosis factor alpha receptor comprising a 55 kDa tumour necrosis factor alpha receptor and a chimeric tumour necrosis factor alpha receptor comprising a 75 kDa tumour necrosis factor alpha receptor.
 4. The method of claim 1, wherein the treatment experienced patient is further administered an effective amount of an antiretroviral therapy.

• **EXAMPLE 36**

Intraoral dosing method of administering trifluorobenzodiazepines, propoxyphene, and nefazodone

Patent number: US5504086

Publication date: 1996-04-02

A method of therapeutically administering certain BZ1 specific trifluorobenzodiazepines in order to maximize the BZ1 effects and minimize the BZ2 effects on the human central nervous system in order to maximize the anti-anxiety, anticonvulsant and hypnotic effects and minimize the ataxic and incoordination effects of the drug. Also, a method of sublingual administration of trifluorobenzodiazepines and certain other compounds, such as propoxyphene and nefazodone, in order to decrease unwanted metabolites.

Claims

1. A method for administering nefazodone compound to the human central nervous system wherein a therapeutically effective amount of said compound is sublingually or buccally administered to a human, the improvement comprising the steps of: a. selecting a lipid soluble compound comprising 2-(3-(4-(3-chlorophenyl)-1-piperazinyl)propyl)-5-ethyl-2,4-dihydro-4-(2-phenoxyethyl)-3H-1,2,4-triazol-3-one hydrochloride that has one or more unwanted or aversive metabolites comprising m-chlorophenylpiperazine that are increased by portal vein entry to the liver; b. placing said compound in a suitable sublingual or buccal formulation; c. sublingually or buccally administering a therapeutically effective amount of said sublingual or buccal formulation so as to bypass the portal vein entry to the liver and thereby to decrease the formation of the unwanted metabolites; d. increasing the ratio of nefazodone to the unwanted metabolite m-chlorophenylpiperazine made available to the central nervous system; and e. utilizing this sublingual or buccal method over a period of one or more doses to achieve sustained high levels of the nefazodone relative to the unwanted metabolite m- chlorophenylpiperazine.

• **EXAMPLE 37**

Method for inhibiting bone resorption

Patent number: EP0998292B1

Publication date: 2001-11-21

Disclosed are methods for inhibiting bone resorption in mammals while minimizing the occurrence of or potential for adverse gastrointestinal effects. Also disclosed are pharmaceutical compositions and kits for carrying out the therapeutic methods disclosed herein.

Claims

1. Use of alendronic acid or a pharmaceutically acceptable salt thereof, or a mixture thereof, for the manufacture of a medicament for inhibiting bone resorption in a human wherein said medicament is adapted for oral administration, in a unit dosage form which comprises from about 8.75 mg to 140 mg of alendronic acid or a pharmaceutically acceptable salt thereof, on an alendronic acid active weight basis, according to a continuous schedule having a periodicity from about once every 3 days to about once every 16 days.

• **EXAMPLE 38**

Ibandronic acid for the promotion of the osseointegration of endoprostheses

Patent number: EP1135140B1

Publication date: 2005-08-31

The invention relates to use of ibandronic acid (1-hydroxy-3-(N-methyl-N-pentyl)aminopropyl-1,1-diphosphonic acid) or physiologically compatible salts or esters thereof for improving the osseointegration of cement-free anchored endoprostheses. Ibandronate or salts thereof is applied for a short time immediately after insertion of an endoprosthesis, with the surprising result that secondary stability of the implant is obtained in only 5 weeks or less after the operation.

Claims

1. Use of ibandronic acid or physiologically compatible salts or esters thereof for the manufacture of medicaments for improving the osseointegration of cement-free anchored endoprostheses by short term application directly after the operation and for a period of two to four weeks.
2. Use according to claim 1 **characterized in that** ibandronate is in a form for application at a dosage of 1 to 100 µg/kg body weight.
3. Use according to claim 1 or 2, **characterized in that** ibandronate in solution form is in a form for parental application with a content of active substance of 0.01 to 20 mg.

• **EXAMPLE 39**

Terfenadine metabolites and their optically pure isomers for treating allergic disorders

Patent number: WO9403170A1

Publication date: 1994-02-17

A pharmaceutical composition comprising a compound of formula (I): wherein Z is COOH, COOCH₃ or CH₂OH, or a pharmaceutically acceptable salt thereof, for use in an anti-

histaminic treatment which does not induce any significant cardiac arrhythmia, comprising administering a therapeutically effective amount of a compound of formula (I) to a human patient.

Claims

1. A pharmaceutical composition comprising a compound of formula I wherein Z is COOH, COOCH₃ or CH₂OH, or a pharmaceutically acceptable salt thereof, for use in an anti-histaminic treatment which does not induce any significant cardiac arrhythmia, comprising administering a therapeutically effective amount of a compound of formula I to a human patient.

• **EXAMPLE 40**

Methods for the treatment of mental disorders

Patent number: WO0113905A2

Publication date: 2001-03-01

The anti-allergic medication comprising loratadine or a metabolite of loratadine.

Claims

1. A method for treating a patient suffering from a mental disorder, comprising administering an effective amount of an anti-allergic medication to said patient to diminish the symptoms of said mental disorder.
2. The method of Claim 1, wherein said mental disorder is selected from the group consisting of depression, alcoholism, weight management disorders, social disorder, impotence/sexual dysfunction, panic and obsessive/compulsive disorder.
3. The method of Claim 2, wherein said anti-allergic medication is loratadine or a metabolite of loratadine.
9. The method of Claim 5, wherein said metabolite of loratadine is desloratadine.

• **EXAMPLE 41**

Treating premenstrual or late luteal phase syndrome

Patent number: EP0386117

Publication date: 1990-09-12

Abstract (as contained in application WO8903692)

Compositions useful in the treatment of disturbances of appetite, disturbances of mood, or both, associated with premenstrual syndrome, as well as methods of use therefor. The compositions include serotonergic drugs, such as d-fenfluramine and fluoxetine.

Claims

1. Use of one or more serotonin-mediated neurotransmission enhancing drugs for the manufacture of a medicament for treating disturbances of mood, disturbances of appetite, or both, associated with premenstrual syndrome in women.
6. Use of a drug selected from the group consisting of a monoamine oxidase inhibitor, lithium and tryptophan and a drug selected from the group consisting of d- fenfluramine, d,l-fenfluramine, chlorimipramine, cyanimipramine, fluoxetine, paroxetine, fluvoxamine, citalopram, femoxetine, cianopramine, ORG 6582, RU 25591 and LM 5008, IS-4S-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthylamine, DU 24565, indalpine, CGP 6085/A, WY 25093, alaprociate, zimelidine, trazodone, amitriptyline imipramine, trimipramine, doxepin, protriptyline, nortriptyline and dibenzoxazepine; b. tryptophan and a drug selected from the group consisting of: metergoline, methysergide, cyproheptadine, deprenyl, isocarboazide, phenelzine, tranlycypromine, furazolidone, procarbazine, moclobemide and brofaromine; c. a drug selected from the group consisting of fluoxetine, paroxetine, cyanimipramine, fluvoxamine, citalopram, femoxetine, cianopramine, ORG 6582, RU 25591, LM 5008, IS-4S-N-methyl-4-(3,4- dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthylamine, DU 24565, indapline, CGP 6085/A, WY 25093, alaprociate, zimelidine, trazodone, amitriptyline, imipramine, trimipramine, doxepin, protriptyline, nortriptyline, dibenzoxazepine, and a drug selected from the group consisting of metergoline, methysergide, and cyproheptadine; or d. d-fenfluramine, d,l-fenfluramine or chlorimipramine and a drug selected from the group consisting of fluoxetine, fluvoxamine, citalopram, femoxetine, paroxetine, cianopramine, ORG 6582, RU 25591, LM 5008, IS-4S-N- methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthylamine, DU 24565, indalpine, CGP 6085/A, WY 25093, alaprociate, zimelidine, trazodone cyanimipramine, amitriptyline, imipramine, trimipramine, doxepin, protriptyline, and dibenzoxazepine; all for the manufacture of a medicament for treating disturbances of mood, disturbances of appetite, or both, associated with premenstrual syndrome, in a woman having premenstrual syndrome.

• **EXAMPLE 42**

Use of carbazole compounds for the treatment of congestive heart failure

Patent number: EP0808162

Publication date: 1997-11-26

Abstract (as contained in application WO9624348)

A method of treatment using a compound of formula (I), wherein R1 is hydrogen, lower alkanoyl of up to 6 carbon atoms or aroyl selected from benzoyl and naphthoyl; R2 is hydrogen, lower alkyl of up to 6 carbon atoms or arylalkyl selected from benzyl, phenylethyl and phenylpropyl; R3 is hydrogen or lower alkyl of up to 6 carbon atoms; R4 is hydrogen or lower alkyl of up to 6 carbon atoms, or when X is oxygen, R4 together with R5 can represent –CH₂-O-; X is a valency bond, -CH₂, oxygen or sulfur; Ar is selected from phenyl, naphthyl, indanyl and tetrahydronaphthyl; R5 and R6 are individually selected from hydrogen, fluorine, chlorine, bromine, hydroxyl, lower alkyl of up to 6 carbon atoms, a -CONH₂- group, lower alkoxy of up to 6 carbon atoms, benzyloxy, lower alkylthio of up to 6 carbon atoms, lower alkylsulphonyl of up to 6 carbon atoms and lower alkylsulphonyl of up to 6 carbon atoms; or R5

and R6 together represent methylenedioxy; or a pharmaceutically acceptable salt thereof, preferably carvedilol, alone or in conjunction with one or more other therapeutic agents, said agents being selected from the group consisting of ACE inhibitors, diuretics, and cardiac glycosides for decreasing mortality resulting from congestive heart failure (CHF) in mammals, particularly humans.

Claims

10. The use of carvedilol for the manufacture of a medicament for decreasing mortality resulting from congestive heart failure in mammals according to the following regimen:
 - (a) administering a pharmaceutical formulation which contains either 3.125 or 6.25 mg carvedilol per single unit for a period of 7-28 days, given once or twice daily,
 - (b) administering thereafter a pharmaceutical formulation which contains 12.5 mg carvedilol per single unit for a period of additional 7-28 days, given once or twice daily, and
 - (c) administering finally a pharmaceutical formulation which contains either 25.0 or 50.0 mg carvedilol per single unit, given once or twice daily as a maintenance dose.
12. Use of a compound according to claim 1 for the preparation of a medicament for the treatment of CHF to be administered in a daily maintenance dose of 10-100 mg, said medicament being administered in incremental dosage schemes comprising three dose regimens, the first regimen comprising administering an amount of 10-30 per cent of the daily maintenance dose of the compound for a period of 7-28 days.

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CHAPTER VII

GUIDE FOR THE APPLICATION AND GRANTING OF COMPULSORY LICENCES AND AUTHORIZATION OF GOVERNMENT USE OF PHARMACEUTICAL PATENTS

INTRODUCTION

Patents – as well as other intellectual property rights – confer exclusive rights. This means that the title-holder may exclude competition in the manufacture and sale of the protected products and, therefore, control the production and distribution of such products and their prices.

The existence of patents on products or processes¹ may prevent in some cases the acquisition of pharmaceutical products at low prices² or in sufficient quantities, such as when the products are offered at prices that are not affordable to patients or government purchasing agencies, or the patent owner has no capacity to timely deliver the needed products. In these cases, patent owners may exercise their exclusive rights and prevent supplies from alternative sources.

Like other rights, however, patent rights are not absolute. There are situations in which their exercise can be limited to protect public interests. Such situations may arise, in particular, in the area of public health, when access to needed pharmaceutical products must be ensured. "Compulsory licences" and "government use for non-commercial purposes" (hereinafter referred to as "government use") are mechanisms provided for in most laws worldwide to limit the exercise of exclusive patent rights – under the circumstances specified in the respective laws – which can specifically be used to address public health needs.

For the purposes of this document:

"Compulsory licence"³ is an authorization given by a national authority to a natural or legal person for the exploitation, without the consent of the title-holder, of the subject matter protected by a patent in order to attain certain public policy objectives.

"Government use"⁴ is an act by the government authorizing a government department to exploit by itself or through a contractor a patented invention without the consent of the title-holder.

The right of States to limit the use of patents through compulsory licences has been recognized since the end of the 19th century. They were incorporated into the Paris Convention for the Protection of Industrial Property (Paris Convention) in 1925, and thereafter in most

¹ In some countries, patents on the therapeutic *indication* or *use* of products are also allowed by the national law.

² Of course, there are other factors that affect prices of pharmaceutical products. See, e.g. WHO/WTO Workshop on Differential Pricing and Financing of Essential Drugs, available at http://www.wto.org/english/tratop_e/TRIPs_e/tn_hosbjor_e.htm.

³ Often also called a "non-voluntary licence".

⁴ Also called "Crown use" under British and Commonwealth legislation.

national laws. Compulsory licences and government use have become regular features in patent laws all over the world⁵. The right to use such mechanisms was recognized in the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) in 1994⁶.

The concerns of developing countries about the possible impact of patents in the pharmaceutical sector led the WTO to adopt, in November 2001, the Doha Declaration on the TRIPS Agreement and Public Health⁷. The Declaration confirmed, *inter alia*, that the granting of compulsory licences (and government use) was one of the clearly admitted flexibilities under the TRIPS Agreement⁸, and that WTO Members were free to determine the reasons for the granting of such licences (see Box).

Doha Declaration on the TRIPS Agreement and Public Health: Sub-paragraph 5 (b)

5. Accordingly and in the light of paragraph 4 above, while maintaining our commitments in the TRIPS Agreement, we recognize that these flexibilities include: ...

b. Each Member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted.

Compulsory licences and government use can be utilized in relation to any of the rights conferred by a patent, including the manufacture, importation or exportation (subject to the limitation imposed in Article 31(f) of the TRIPS Agreement⁹) of patent-protected products¹⁰, and with regard to all kinds of products, including medicines, vaccines and diagnostic kits.

The present Guide aims to provide practical advice to governments, purchasing and funding entities and NGOs about the modalities for the application of compulsory licences and the utilization of government use provisions. It focuses on the utilization of such mechanisms for the *purchase* and *importation* of patent-protected pharmaceutical products¹¹. It contains two

⁵ See, e.g. Correa C. *Intellectual property rights and the use of compulsory licenses: options for developing countries*. Trade-Related Agenda, Development and Equity, Working Papers. Geneva, South Centre, 1999; Reichman J. and Hasenzahl C. *Non-voluntary Licensing of Patented Inventions: historical perspective, legal framework under TRIPS and an Overview of the Practice in Canada and the USA*. UNCTAD-ICTSD Issue Paper No. 5, Geneva, 2003; *Battling HIV/AIDS. A Decision Maker's Guide to the Procurement of Medicines and Related Supplies*. Washington, DC, The World Bank, 2004.

⁶ Article 31 of the TRIPS Agreement, however, does not refer to "compulsory licences" but to "other use without authorization of the right holder". This provision applies to both compulsory licences and government use.

⁷ WT/MIN(01)/DEC/W/2, 14 November 2001, available at www.wto.org (full text in Annex 1).

⁸ On TRIPS flexibilities, see *Globalization and Access to Drugs: Perspectives on the WTO/TRIPS Agreement*. Health Economics and Drugs Series No. 7, Revised. Geneva, World Health Organization, 1999 (WHO/DAP/98.9); Musungu S, Oh C. *The use of flexibilities in TRIPS by developing countries: can they promote access to medicines?* Study commissioned by the WHO Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH). 2006. Available from www.intellectualpropertyandpublichealth.org/en/index.html.

⁹ Article 31(f): "any such use shall be authorized predominantly for the supply of the domestic market of the Member authorizing such use".

¹⁰ The expression "patent-protected products" includes patents on products as such, as well as products directly obtained by a patented process. See Article 28.1(b) of the TRIPS Agreement.

¹¹ As a result, this Guide does not consider aspects that would be particularly important for the use of such mechanisms for the production of pharmaceutical products.

sections: in the first section, the application for and granting of a compulsory licence is dealt with; and the second section considers the case of government use, subject to the general conditions established by domestic legislation. The special requirements that may arise in cases where a compulsory licence is granted in the *importing country* in accordance with the waivers approved by the Decision of 30 August 2003 (which address situations of lack of or insufficient manufacturing capacity in pharmaceuticals)¹² are mentioned in the text, wherever appropriate.

It is important to note that *the concrete application and grant will necessarily be subject to the provisions of the applicable national law*. Therefore, knowledge and understanding of the national law and regulations will be unavoidable in order to efficiently undertake the proceedings for obtaining and putting into practice such authorizations.

As already mentioned, the first section deals with compulsory licences and the second with government use. This sequence has been chosen only for presentation purposes: it does not mean that governments or agencies wishing to purchase medicines should consider granting a compulsory licence as the first option. As explained below, government use may in many cases be the simplest and fastest way of purchasing patented medicines, notably because it can be decided by the government *ex officio* without the need for a third party's request and, if issued for a public non-commercial purpose, without prior negotiation with the patent holder.

COMPULSORY LICENCES

Establishing the Need to Apply for a Compulsory Licence

The essential precondition for the application of a compulsory licence is that the required product (or the process for its manufacture) is patented and the purchasing party is seeking to obtain the product from a source different from the patent owner, his licensees or other authorized parties. This will occur, for instance, when the potential supplier is a generic company that has not obtained a licence, in the importing country, to use the relevant patent(s).

If the product is not patent-protected in the country where the importation will take place, there is no limitation (stemming from the patent law) to import the required medicine.

Notes:

1. *The need to apply for a compulsory licence would normally arise when there are relevant patents in force on the **products** to be purchased. In some situations, there may be no patents on the products themselves but on the **process** for their manufacture¹³. In accordance with the TRIPS Agreement, the protection conferred on a process extends to the product directly obtained with it (Article 28.1(b)). This means that, even if a product patent does not exist in the importing country, a process patent may be used to prevent the importation of a product directly obtained abroad with the same process. It is a matter of proof whether a given product has been directly obtained with the patented process. Article 34 of the Agreement provides, under certain circumstances, the reversal of the burden of proof in cases of infringement of a process patent.*

¹² Article 31*bis* of the TRIPS Agreement incorporates the WTO Decision of 30 August 2003 (WT/L/540, available at www.wto.org). This article is not yet in force, pending acceptance by WTO Members.

¹³ Often patents are hybrid, that is, they include claims on both products and processes (and, where allowed, therapeutic uses of the product).

2. *In countries where patents on second pharmaceutical indications are admitted, a compulsory licence may also be necessary if the intended use of the product is covered by the patent.*

3. *If the product to be purchased has been commercialized by the patent owner or his licensee(s) in a foreign country, a compulsory licence is not needed if the national legislation admits "parallel imports", that is, if it considers that the rights of the patent owner have been exhausted with the sale of the product in a foreign country¹⁴. Depending also on the national law (of the importing country), parallel imports may also take place when the supplier is authorized to commercialize or distribute the product under a compulsory licence in the exporting country¹⁵.*

4. *It should be noted that patents are territorial, that is, they are only valid in the specific countries where they have been applied for and granted. Therefore, there is no need to apply for a compulsory licence if the patent is not in force in the country of importation, irrespective of the existence of such patent in other countries.*

5. *Irrespective of whether or not patents are in force in the relevant country, compliance with health regulations (such as those requiring the marketing approval of medicines) would normally be necessary for the importation and distribution of pharmaceutical products. The facilities provided by the WHO Prequalification Project, established in 2001, can be used by countries and procurement agencies to acquire products that have been tested and found to meet high quality standards and speed up access to required products¹⁶.*

Special Situation of Least Developed Countries

Least developed countries (LDCs) need not implement the obligations under the TRIPS Agreement relating to patents (and data protection) for pharmaceutical products until 2016, by virtue of Paragraph 7 of the Doha Declaration on the TRIPS Agreement and Public Health¹⁷. This means that LDCs that make use of this transitional period, need neither grant nor enforce (if granted) pharmaceutical patents and, therefore, the purchase and importation of such products can be made without compulsory licences.

LDCs interested in the support of international and other organizations in the purchase of pharmaceutical products, may possibly be required by these organizations to state that, in accordance with paragraph 7 of the Doha Declaration and the Decision of the Council for TRIPS of 27 June 2002, they do not grant or enforce patents on such products. WHO and UNICEF have collaborated in the drafting of a "Paragraph 7 Model Letter" (see Annex 2) which LDCs may consider using in order to confirm that pharmaceutical patents are not recognized or enforceable in their country. The letter may be signed by any competent authority, as appropriate according to domestic legislation.

¹⁴ On parallel imports see, e.g. Correa C. "The TRIPS Agreement: how much room for maneuver?" *Journal of Human Development*, UNDP, CARFAX Publishing, 2001, vol. 2, no. 1.

¹⁵ While there are opposing views on the consistency of this possibility with the TRIPS Agreement, such imports may in some cases be important to secure the supply of low-priced pharmaceutical products.

¹⁶ For more information about this Project, see www.who.int.

¹⁷ See Decision of the Council for TRIPS of 27 June 2002 on "Extension of the Transition Period under Article 66.1 of the TRIPS Agreement for Least-Developed Country Members for Certain Obligations with respect to Pharmaceutical Products", IP/C/25, available at www.wto.org.

Determining the Patent Status of Required Products

Although it would seem simple to determine when a compulsory licence is needed, because there is patent protection, and which patents would be involved, this is not often the case. It may be difficult to establish the patent status of pharmaceutical products in developing countries. In these cases, and where prior negotiation with the patent holder is not required, an application for a compulsory licence could be made with regard to all patents that may be infringed by the importation and use of the required product(s). Although this approach has not been discussed at the WTO, some countries have already applied it.

Notes:

1. *There are various reasons why the identification of patents may be difficult. Pharmaceutical companies tend to apply for (and generally obtain) more than one patent for the same product¹⁸. Even for products that have been on the market for a long time, it is possible to find a multiplicity of patents on variations thereof, such as different salts, ethers, polymorphs, etc., or new therapeutic indications. Although in some countries (e.g. India) legislation has been adopted to limit the patenting of such variants (often called “evergreening” patents) the possibility of finding more than one patent for a given product is considerable.*
2. *Sometimes patent information available at the patent offices is incomplete or difficult to access (particularly where computerized records do not exist).*
3. *Moreover, data contained in published abstracts of patent applications or grants, often do not provide sufficient information to identify the drug they refer to, especially when they do not include the International Nonproprietary Names for Pharmaceutical Substances (INN).*
4. *It should be noted that when patents on specific formulations exist, but the active ingredients are off-patent, there will be no need to apply for a compulsory licence if a different formulation can be purchased.*
5. *If the existence of a patent relevant for a given product has been identified, a question that may be raised is whether such a patent was validly granted or not. In some cases, patents are granted without fulfilling the patentability requirements (novelty, inventive step or non-obviousness and industrial applicability or utility) and may be invalidated upon request. However, a process for the invalidation of a patent may take several years, unless a faster post-grant examination by an administrative authority (such as the patent office) is permitted under national law.*
6. *In applying for a compulsory licence for a particular patent, the applicant might be deemed as implicitly endorsing its validity. When there are doubts in this respect, a reservation could be made by the applicant regarding a possible challenge of the validity of the patent, if needed.*
7. *In some cases, there may be pending patent applications with regard to products to be purchased. In these cases, it would not be necessary to apply for a compulsory licence (nor possible in fact since no patent exists yet). It should be noted, however, that according to some laws the applicant may exercise the rights ordinarily conferred on a patent owner after the publication of the application¹⁹, while under other laws the patentee may, after the grant of the*

¹⁸ For instance, of 403 patented medicines registered in Canada in 2004, 42 had an average of nearly six patents; 361 medicines had from one to three patents. The highest number of patents on a single medicine was 13. See *Therapeutic Products Directorate Statistical Report 2003*. Health Canada, 27 October 2004 (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/docs/.patmedbrev/patmrep_mbrevrap_2003_e.html), accessed May 2008.

¹⁹ See, e.g. Section 46 of the Patent Act of Philippines – *Rights Conferred by a Patent Application After Publication*: “The applicant shall have all the rights of a patentee under Section 76 against any person who,

patent, claim for a compensation with regard to acts conducted by a third party before the grant.

8. *One of the reasons, admitted in most national laws, for the invalidation of a patent is the lack of payment of maintenance fees (that is, fees that must be paid by the patent owner to keep a patent in force). In many countries, patents automatically lapse if such fees have not been paid²⁰. A quick investigation with the national patent office is therefore recommended, to establish if the maintenance fees have been paid for the identified patents and, therefore, whether or not they remain in force.*

9. *It is also of note that under many laws a third party can file an opposition to or make observations on a patent application, indicating reasons why the patent should not be granted.*

Searching Patent Data

The key issue for the purpose of applying for a compulsory licence is to determine, as mentioned, the existence of valid and enforceable patents in the importing country.

The most straightforward way to determine whether a relevant and valid patent exists and whether a compulsory licence is needed is to consult the patent office about existing patents on a given product. Patent offices may take, however, from a few weeks to several months to undertake the search and, in many cases; the results may not be conclusive due to the lack of appropriate records.

The fact that a patent on a given product or process has been applied for or granted in another jurisdiction (e.g. by the US Patent and Trade Mark Office or the European Patent Office) may provide an indication that an equivalent patent may be found in the potential country of importation. However, patents are territorial in nature, and there should be no automatic assumption that a patent applied for or granted in a foreign country has been applied for or granted domestically.

Notes:

1. *There are several databases that can be accessed in order to search data on patents in particular jurisdictions, such as esp@cenet for the European Patent Office, <http://www.uspto.gov> for US patents, and many web pages of other national patent offices. There are also a number of private databases that can be accessed, normally for a fee.*

2. *The Patent Cooperation Treaty (PCT) allows for "international applications" for patents in which the countries (which must be PCT members) where the applicant intends to file a patent are designated. The PCT offers an Online File Inspection System that permits interested parties to search more than one million international patent applications (<http://www.wipo.int/pctdb/en/search-adv.jsp>).*

3. *Information regarding the patent status of medicines in developing countries is often neither readily accessible nor available in an easily-understood form. In the interest of facilitating the availability of up-to-date and accurate information on the patent status of essential medicines in developing countries, WHO, in conjunction with Médecins Sans Frontières (MSF) and UNAIDS, has published a patent table which lists the patent status of a*

without his authorization, exercised any of the rights conferred under Section 71 of this Act in relation to the invention claimed in the published patent application, as if a patent had been granted for that invention".

²⁰ In some countries, however, national laws allow for a grace period; if payment of the fee takes place within that period, the validity of a patent may be restored.

*number of essential medicines, including antiretrovirals, in selected developing countries*²¹. WHO is undertaking work to expand the patent table, so as to increase the number of medicines and the list of countries.

Establishing Whether the Acts to Be Performed Are Subject to Patent Rights

Another important consideration to establish the need for a compulsory licence is whether or not the intended acts will constitute an infringement of a patent, if it exists. Most patent laws provide exceptions to the patentee's exclusive rights with regard to certain acts, such as

- research or experimentation;
- acts done for private use and with non-commercial purpose;
- submission of information (and samples) to obtain the marketing approval of a pharmaceutical product before the expiry of the patent²².

Note:

Except if admissible as parallel imports, the importation of a large number of products would fall under the exclusive rights conferred by a patent. Before applying for a compulsory licence, however, the national law should be checked to determine whether the importation of products made for non-profit could be deemed an act exempted from patent rights.

Articulating the Grounds for Compulsory Licences

As mentioned, most patent laws in the world provide for the granting of compulsory licences (and government use). However, the grounds under which such licences may be conferred vary from country to country. The Doha Declaration confirmed the right of WTO Members to determine such grounds. They may include, for instance, some or all of the following:

- national emergency or situation of extreme urgency;
- dependency of patents;
- licences to remedy anti-competitive practices;
- lack of or insufficient working of the patent;
- refusal to deal;
- public interest;
- public health.

Not only may the grounds for granting a compulsory licence vary, but also the way in which such grounds are applied. For instance, the lack of or insufficient working is deemed to refer, in some jurisdictions (e.g. Brazil) to the industrial exploitation of the patent in the national territory, while in others working may be justified merely through importation²³.

As a result of these variations, before applying for a compulsory licence the specific grounds that may support its grant under the applicable national law should be carefully examined.

²¹ See *Determining the patent status of essential medicines in developing countries*. Health Economics and Drugs Series No. 17. Geneva, World Health Organization, 2004 (WHO/EDM/PAR/2004.6).

²² This exception is generally known as "early working", regulatory review or "Bolar exception".

²³ The interpretation of Article 27.1 of the TRIPS Agreement in this regard is, however, controversial. See, e.g. the WTO document *Brazil - Measures Affecting Patent Protection*, WT/DS 199/1 and 4.

Notes:

1. *The grounds invoked for granting a compulsory licence should normally be indicated in the application. In some cases, more than one ground may apply.*
2. *In some countries, the situations of "emergency" may need to be formally declared by a competent authority, while in others its existence can be determined by the authority granting the compulsory licence.*

Compulsory Licence Solely for Importation

The text of the TRIPS Agreement is open with respect to the rights that can be exercised by the beneficiary of a compulsory licence. It may be granted only for importation²⁴.

WTO Members with insufficient or no manufacturing capacity in the pharmaceutical sector that have notified their intention to use the mechanism established by Article 31*bis* of the TRIPS Agreement, are bound to notify the Council for TRIPS of the following:

- (i) the names and expected quantities of the product(s) needed;
- (ii) confirmation that the importing Member in question, other than a least developed country Member, has established that it has insufficient or no manufacturing capacities in the pharmaceutical sector for the product(s) in question in one of the ways set out in the Appendix to the Annex to Article 31*bis* of the Agreement; and
- (iii) confirmation that, where a pharmaceutical product is patented in its territory, it has granted or intends to grant a compulsory licence in accordance with Articles 31 and 31*bis* of the Agreement and the provisions of its Annex.

Notes:

1. *The possibility of granting compulsory licences solely for importation has been confirmed beyond any doubt by paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health and the subsequent WTO Decision of 30 August 2003²⁵, incorporated on 6 December 2005 into the TRIPS Agreement as Article 31*bis*.²⁶*
2. *It is important to note that, in the case of application of Article 31*bis* of the TRIPS Agreement, the "expected quantities of the product(s) needed" have to be indicated in the notification to the Council for TRIPS, but this is not a requirement for the granting of the compulsory licence itself.*

Applying for a Compulsory Licence

Who can apply?

In principle, any interested party may request the granting of a compulsory licence. However, some national laws impose specific requirements on applicants, such as proof of technical or economic capacity to utilize the licence.

²⁴ Some national laws seem to require local production of the protected product but, as mentioned, this is not required by the TRIPS Agreement.

²⁵ See WT/L/540, available at www.wto.org and Correa C. *Implementation of the WHO General Council Decision on paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health*. Health Economics and Drugs Series No. 16. Geneva, World Health Organization, 2004 (WHO/EDM/PAR/2004.4).

²⁶ As noted, this amendment is still subject to acceptance by Members in accordance with WTO rules.

Compulsory licences for the production or importation of pharmaceuticals may be applied for by commercial entities, as well as by any other natural or legal person that complies with the requirements established by the national law. NGOs and international organizations may apply for such licences, if allowed under their respective bylaws or statutes, subject to the applicable national law.

Notes:

1. *A compulsory licence may be applied for by any natural or legal person with an interest in the execution of the licence.*
2. *International organizations that are active in the purchasing and distribution of pharmaceutical products may apply for a compulsory licence. They may also act on behalf of the government or other parties. As mentioned below, they may act as contractors or agents of governments in the case of government use²⁷.*

When can a compulsory licence be applied for?

In many cases, such as when UN and other purchasing agencies intervene, the acquisition of pharmaceutical products is done through bidding procedures. In these cases an apparent dilemma may be faced by potential suppliers: an offer for sale may be deemed a patent infringement²⁸, although it would be extremely costly and cumbersome, and in the last instance a wasteful exercise, to apply for a compulsory licence just to make an offer that may be accepted or not.

This problem may be addressed by including in all offers under bidding procedures a disclaimer indicating that the offer is conditional and subject to the granting of a compulsory licence, if the offer were accepted by the purchasing party. Such a disclaimer would make clear that the supplier does not intend to supply a patent-protected product unless the respective authorization is given.

How should the application be made?

The procedures to obtain a compulsory licence are governed by national laws. The application must comply with the required formalities and procedures. Important issues to consider include:

- which is the competent authority to grant a compulsory licence?;
- requirements about domicile;
- documentation about the applicant;
- justification of the application;
- proof of economic or technical capacity, where required;
- identification of products(s) and of the patents involved, if known;
- identification of the title-holder(s);
- unsuccessful prior request, where necessary, to the patent owner for a voluntary licence on reasonable commercial terms;
- scope and duration of the compulsory licence.

²⁷ See the section on government use below.

²⁸ See Article 28.1 of the TRIPS Agreement, which includes "offering for sale" as one of the acts that can be prevented by the patent owner.

Which is the competent authority to grant a compulsory licence?

A compulsory licence must be granted by a national authority with legal competence to that effect. The institutional models vary considerably in this regard.

In most countries, compulsory licences are granted by a department of the executive branch. There are cases, however, where such competence lies with judicial courts.

In the case of a grant by the executive branch, there may be one or more offices or departments involved. Thus, in some cases, the grant is made by the patent office. Often, however, other departments need to be consulted or intervene, such as the departments of health or trade.

Notes:

1. *The institutional setting for the granting of a compulsory licence must be properly examined. In some cases, the intervention of the Ministry of Health is required, when the compulsory licence is grounded on public health considerations.*
2. *In administrative procedures the services of legal professionals are not generally required, and a certain degree of informality is admitted. If judicial courts intervene, however, the support of an attorney will normally be required.*

Domicile or establishment

Unless otherwise determined by the national law, a compulsory licence can be requested by an applicant with or without domicile or establishment in the country where the compulsory licence is sought. However, the national law may require the designation of an address for service or the appointment of an agent to act before the administration or court.

Identification of the applicant

Under most legal systems, the applicant, if not a natural person, will have to submit copies of the statutes or bylaws. In addition, the person acting as an agent of the applicant will have to demonstrate his capacity to do so.

Note:

It should be recalled that, according to the TRIPS Agreement, a compulsory licence is non-assignable (that is, it cannot be used by a person other than the applicant). It can only be assigned with that part of the enterprise or goodwill which enjoys such use (Article 31(e) of the TRIPS Agreement).

Justification of the application

The application for a compulsory licence should, to the extent possible

- indicate the specific legal provisions on which its grant is sought;
- provide a brief justification of the reasons for the request.

The justification needs to show the extent to which the application falls under the applicable provisions of the law. It should also briefly explain the motivation for the granting

of the licence. These elements in the application may help the competent national authority to speed up the granting procedures.

Notes:

1. *Since compulsory licences are a legitimate means to achieve public policy objectives, governments should act according to the prescriptions of the national law, in conformity with the standards set out by the TRIPS Agreement.*

2. *The granting of a compulsory licence should be seen as an ordinary administrative or judicial act, and be considered only in the light of the relevant legal requirements. However, the issue is politically sensitive. Although not a party in the procedures, governments of the companies eventually affected by a compulsory licence may involve themselves in discussions and other actions regarding the licence. In a rule-based system, the granting government should decide on the basis of the applicable legal requirements and the merits of the case.*

Proof of economic or technical capacity, where required

Some national laws require that the applicants for compulsory licences demonstrate a technical or economic capacity to execute the compulsory licences they have applied for. The evidence to be provided will vary depending on whether the purpose of the licence is to manufacture or to import the protected product. While in the former case the availability of manufacturing facilities (owned or not by the applicant) may have to be shown, in the latter it may be sufficient to indicate that the applicant is a legally established entity with a credible capacity to finance and undertake the acquisition and distribution of the relevant products.

Identification of products(s) and of the patents involved, if known

As discussed above²⁹, it is frequently difficult to identify the patent or patents in force in a given country with regard to certain products. This should not be a deterrent for the application for and granting of a compulsory licence, as the proper identification of the product (by its generic name) would be sufficient to establish the scope of the licence.

A compulsory licence may be applied for with regard to the whole subject matter covered by a patent (e.g. all forms of administration of a drug) or be limited to a sub-set of modalities in which the patented product may be presented (e.g. oral formulations). This will depend on the evaluation of the applicant in the light of the health needs to be addressed.

Identification of title-holder(s)

An application for a compulsory licence should ideally identify the owners of all the relevant patents. The lack of a precise identification of such patents, however, should not be a deterrent for the application for, and granting of, the compulsory licence.

Notes:

1. *In the absence of identification of the title-holders, the prior request for a voluntary licence (where applicable, as discussed below) may not take place. Negotiation (where provided for under national laws) between the applicant and the title-holder(s) on a mutually agreeable remuneration for the use of the patent, may not be possible either.*

²⁹ See page 6.

2. *If the title-holders are not identified at the time of the granting of the compulsory licence and when payments of the remuneration are due (see below), the compulsory licensee may have to deposit (judicially or otherwise) the corresponding amounts. Payment may be calculated on the basis of the product supplied under the compulsory licence*³⁰.

Prior request for a voluntary licence

In conformity with Article 31(b) of the TRIPS Agreement, in some cases there is a need to request a voluntary licence from the patent owner before a compulsory licence is applied for. Wherever this requirement applies, the applicant may need to prove that: (a) the patent owner has refused to grant a voluntary licence on reasonable commercial terms within a reasonable period, or (b) the patent owner has not replied to such a request after the expiry of a reasonable period.

The request to the patent owner for a voluntary licence may include:

- identification of the product(s);
- purpose of the licence (e.g. manufacture, importation, non-profit distribution);
- designation under which the product(s) will be distributed;
- remuneration to be paid;
- duration of the licence (for instance, until the expiry of the relevant patent(s)).

The evaluation of whether a voluntary licence has been requested or offered on reasonable commercial terms will lie with the competent authority for the granting of the compulsory licence. Any decision in this regard should be taken in line with commercial practice while taking into account the public health objectives that could be attained with the compulsory licence³¹. The critical criterion will generally be the level of offered remuneration, which may be determined according to the methods described below.

Some national laws establish the period within which the patent owner is bound to indicate its acceptance or refusal to grant a voluntary licence on reasonable commercial terms³².

It is important to note that the prior negotiation of a voluntary licence is not required, in accordance with the TRIPS Agreement (and, most probably, the applicable national law), when a compulsory licence is applied for in order to:

- address a national emergency or other circumstances of extreme urgency;
- remedy anti-competitive practices.

³⁰ For methods that may be used to determine the remuneration to be paid, see Love J. *Remuneration guidelines for non-voluntary use of a patent on medical technologies*. Health Economics and Drugs Series No. 18. Geneva, World Health Organization, 2005 (WHO/TCM/2005.1), 83-85.

³¹ See paragraph 4 of the Doha Declaration on the TRIPS Agreement and Public Health, which states: "We agree that the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all".

³² In Argentina, for instance, the period to accept or refuse a request for a voluntary licence is 150 days (Law 24.481, as amended by Law 24.572, Article 42).

However, in these cases the right holder shall be notified as soon as reasonably practicable about the granting of a compulsory licence.

Notes:

1. *A request to obtain a voluntary licence should always be made in a written form, ensuring that the reception of the request by the addressee can be proven, if necessary.*
2. *In the case of government use for non-commercial purposes, there is no need to previously request a voluntary licence justification of the application (see section on government use below).*

Scope and duration of a compulsory licence

Depending on national law, the act granting a compulsory licence may be conceived in broad terms and allow for the exercise of the rights of making, using, offering for sale, selling, or importing for these purposes the covered product(s) for the full term of the patent. It may also limit the licence to some of such rights or to a period shorter than the life of the patent, or to some claims or fields of use of the patent.

Beneficiaries of a compulsory licence can also export, provided that they predominantly supply the domestic market of the country where the licence has been granted (Article 31(f) of the TRIPS Agreement)³³. This limitation, however, does not apply in cases where the compulsory licence is granted to remedy anti-competitive practices (Article 31(k) of the TRIPS Agreement).

In filing an application for a compulsory licence, the applicant may either request it without any limitation with regard to the scope of use of the patent or duration of the licence, or deliberately limit the application to certain acts and duration.

In cases, for instance, where the only intended purpose of the compulsory licence is to import and distribute medicines, this can be explicitly stated in the application. It is likely that the broader the potential scope of a compulsory licence, the stronger will be the opposition of the patent owner (and of the host country's government).

With regard to duration, it is advisable to request the compulsory licence for the full remaining period of the patent, in order to avoid having to request extensions or start procedures anew for the granting of a licence.

Notes:

1. *It should be recalled that, in all cases, a compulsory licence shall be non-exclusive (Article 31(d) of the TRIPS Agreement), that is, the patent owner or other licensees (voluntary or compulsory) may compete with the beneficiary of the compulsory licence.*
2. *It should also be borne in mind that, according to some national laws, a compulsory licence may be revoked if not utilized within a certain period.*
3. *Moreover, a compulsory licence is liable, subject to adequate protection of the legitimate interests of the compulsory licensee, to be terminated if and when the circumstances which led to it cease to exist and are unlikely to recur. The competent national authority shall have the authority to review, upon motivated request, the continued existence of these circumstances (Article 31(g) of the TRIPS Agreement) and can, hence, determine in certain cases the termination of the licence.*

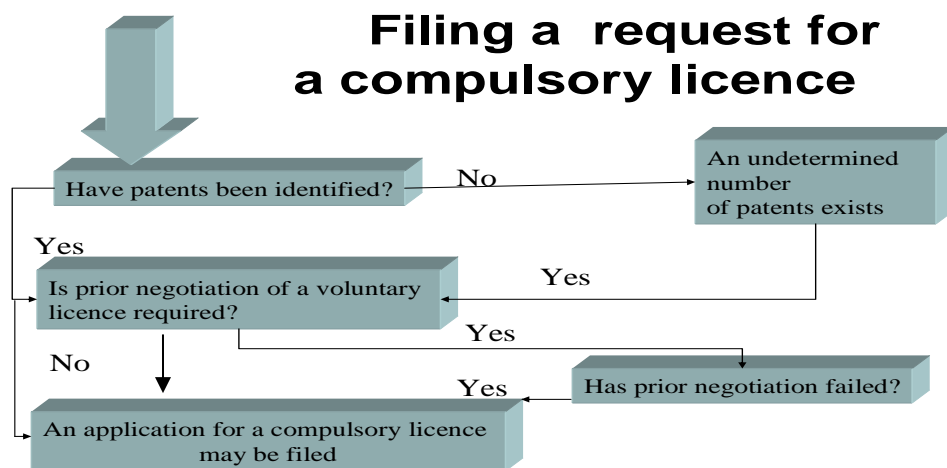
³³ This limitation may be waived in accordance with the system adopted by the afore-mentioned Decision of 30 August 2003, pending the acceptance of the proposed new Article 31bis of the TRIPS Agreement.

4. *Compulsory licences create an exception to patent rights. The applicant should not be required to specify the value or quantity of the product(s) to be produced or imported, or the time or other conditions under which production or importation may occur*³⁴.

Summary

Some of the aspects of the previous analysis on the application for a compulsory licence are schematically presented in Figure 1.

Figure 1



Procedures for Granting a Compulsory Licence

The procedures for processing an application for a compulsory licence are exclusively determined by the applicable national legislation. They are subject, however, to the general obligations relating to the procedures for the enforcement, acquisition and maintenance of intellectual property rights set out in Parts III and IV of the TRIPS Agreement. Such procedures shall be "fair and equitable"³⁵.

In accordance with some national laws, once an application for a compulsory licence is filed, the competent authority should notify the patent owner and seek an agreement with the applicant about the level of remuneration to be paid. Since the requested licence is compulsory, the patent owner – who is not a party to such procedures – should not be allowed to make other submissions that interfere with the procedures.

In some cases, decisions about the granting of compulsory licences should be made within periods specifically provided for by the national law or regulations. If such periods are

³⁴ It is to be noted, however, that the Decision of 30 August 2003 requires the exporting country and the supplier to provide certain information about the products to be exported. See, e.g. Correa C. *Implementation of the WHO General Council Decision on paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health*. Op.cit.

³⁵ See Articles 62.4 and 41.2 of the TRIPS Agreement.

not provided for, the general administrative (or judicial) procedural rules will apply. In any case, it is of note that Article 41.2 of the TRIPS Agreement requires that "Procedures concerning the enforcement of intellectual property rights shall ... not be unnecessarily complicated or costly, or entail unreasonable time-limits or unwarranted delays". Although conceived to protect right-holders, the same treatment should be accorded, in a non-discriminatory way, to all parties in procedures involving intellectual property rights.

Degree of discretion left to grant or refuse a licence

When the requirements for the granting of a compulsory licence have been complied with, the competent authority should grant it. While some laws clearly mandate the granting of a licence in such circumstances³⁶, in other cases the laws leave more room for the exercise of discretion by said authority. While the TRIPS Agreement is merely permissive, from a public health perspective, such discretion may be deemed limited by the State's obligation to protect public health and respect patients' human right to have access to affordable medicines³⁷.

Validity of the act granting a compulsory licence

The administrative (or judicial) act granting a compulsory licence should generally contain:

- legal background and justification for the granting of a compulsory licence;
- identification of the product(s) and of the patents involved, if known;
- remuneration to be paid to the patent owner;
- scope (e.g. production, importation) and duration of the licence.

Like any other administrative (or judicial) act, the validity of an act conferring a compulsory licence may be subject to challenges by the patent owner or other interested parties, in accordance with the general rules applicable to administrative or judicial procedures. The TRIPS Agreement specifically provides that "the legal validity of any decision relating to the authorization of such use shall be subject to judicial review or other independent review by a distinct higher authority in that Member" (Article 31(i)).

An appeal questioning the validity of the act granting the compulsory licence may delay for a long time the execution of the licence and frustrate the purpose for which it has been sought. Some laws have attempted to avoid this possibility and only allow for an appeal against the grant of a compulsory licence that does not suspend its effects³⁸, that is, the appeal would not impede the immediate execution of the licence, at the option of the compulsory licensee.

Note:

The compulsory licence does not need to specify a determined quantity or value of the product to be produced or imported, including in the case where a licence is granted in an eligible

³⁶ See, e.g. Section 21.04 of Canadian Bill C-9 ("An Act to amend the Patent Act and the Food and Drugs Act") which implements the WTO Decision of 30 August 2003.

³⁷ The International Covenant on Economic, Social and Cultural Rights recognizes "the right of everyone to the enjoyment of the highest attainable standard of physical and mental health" (Article 12.1). In General Comment No. 14 on Article 12, the Committee on Economic, Social and Cultural Rights enumerates basic obligations that include the provision of essential biomedical innovations, General Comment E/C.12/2000/4, 11 August 2000.

³⁸ The TRIPS Agreement does not regulate the effects of judicial or administrative appeals.

importing country under the mechanism of the Decision of 30 August 2003 (proposed Article 31bis of the TRIPS Agreement), where applicable.

Remuneration

A key aspect in the granting of a compulsory licence is the determination of the remuneration to be paid to the patent owner, and the modalities of payment. Governments have considerable discretion in defining the level and mode of payment, subject to the general rule that the remuneration is adequate in the circumstances of each case, taking into account the economic value of the authorization in conformity with Article 31(h) of the TRIPS Agreement. The level of remuneration, however, should be reasonable and not frustrate the purpose of a compulsory licence that is intended to address a public health need, such as ensuring access to pharmaceutical products at the lowest possible price.

According to the already quoted "*Remuneration guidelines for non-voluntary use of a patent on medical technologies*", the following are some of the methods of calculation that may be reasonably applied to determine the level of remuneration:

- a) The 1998 Japan Patent Office (JPO) Guidelines (applicable to government-owned patents) allow for normal royalties of 2 to 4 per cent of the price of the generic product, and can be increased or decreased by as much as 2 per cent for a range of 0 to 6 per cent.
- b) The 2001 United Nations Development Programme (UNDP) Human Development Report proposed a base royalty rate of 4 per cent of the price of the generic product. This can be increased or decreased by 2 per cent, depending upon such factors as the degree to which a medicine is particularly innovative or the role of governments in paying for research and development.
- c) The 2005 Canadian Government royalty guidelines for compulsory licensing of patents for export to countries that lack the capacity to manufacture medicines, in accordance with the WTO Decision of 30 August 2003, establish a sliding scale of 0.02 to 4 per cent of the price of the generic product, based upon the country rank in the UN Human Development Index. For most developing countries, the royalty rate is less than 3 per cent. For most countries in Africa, the rate is less than 1 per cent.
- d) The Tiered Royalty Method is different from the 2001/UNDP, 1998/JPO or 2005/Canadian methods in that the royalty rate is not based upon the price of the generic product. Instead, the royalty is based upon the price of the patented product in the high-income country. The base royalty is 4 per cent of the high-income country price, which is then adjusted to account for relative income per capita or, for countries facing a particularly high burden of disease, relative income per person with the disease.

In addition to establishing the level of remuneration, the act granting a compulsory licence should specify how the payment will be made, notably:

- time of payment;
- base for the calculation of royalties (the net sales value should normally be considered);
- currency of payment;
- bank account where the payment will be deposited.

The patent owner can appeal a decision granting a compulsory licence with regard to the remuneration to be paid by the applicant³⁹.

Note:

The methods and guidelines summarized above may also be used by a would-be applicant to calculate a reasonable remuneration to be offered where prior negotiation with the patent owner is required.

Waiver of the obligation to pay remuneration

In the case of a compulsory licence granted under the Decision of 30 August 2003 (or, if accepted, the proposed Article 31bis of the TRIPS Agreement) the obligation to pay a remuneration is waived in the importing country when adequate remuneration pursuant to Article 31(h) is paid in the exporting country.

Data Exclusivity

Article 39.3 of the TRIPS Agreement requires protection of undisclosed test data against unfair commercial use. It does not mandate the granting of exclusive rights; on the contrary, it is firmly based on the discipline of unfair competition⁴⁰, which neither confers property nor exclusive rights⁴¹, but protects against dishonest commercial practices as defined under national laws. Under this interpretation, generic competition – which pushes prices down and increases access to medicines – is not unduly delayed when the products are off-patent and, hence, freely available for manufacturing and sale.

In some countries, such as the United States, countries of the European Union and Japan, as well as those that have signed free trade agreements (FTAs) with the United States, test data relating to pharmaceutical products may be subject to exclusive rights (data exclusivity). This may mean that, unless clinical trials are repeated, a third party may not be able to obtain marketing approval for a product without the authorization of the originator of the data.

In countries where data exclusivity is enforced, the very purpose of granting a compulsory licence may be frustrated until the period of data exclusivity ends (generally after five years counted from the date of approval of the product), since the beneficiary would not be able to commercialize the product under the licence without the respective marketing approval. In order to avoid this situation, an application for a compulsory licence should include, where necessary, a petition for a waiver of any restrictions that may stem from data exclusivity.⁴²

³⁹ Article 31(j) of the TRIPS Agreement: "any decision relating to the remuneration provided in respect of such use shall be subject to judicial review or other independent review by a distinct higher authority in that Member".

⁴⁰ See Article 39.1 of the TRIPS Agreement. For an analysis of this subject, see Correa C. *Protection of data submitted for the registration of pharmaceuticals: implementing the standards of the TRIPS Agreement*. Geneva, South Centre, 2004.

⁴¹ Note that there are diverging views on the interpretation of Article 39.3 among WTO Members. Thus, the USA and the European Union have argued that it obliges to confer exclusive rights. See, e.g., WTO documents IP/C/W/296 and IP/C/M/31.

⁴² Such a waiver is explicitly provided for in Article 18 of the Regulation (EC) 816/2006 adopted by the European Parliament on "compulsory licensing of patents relating to the manufacture of pharmaceutical products for export to countries with public health problems". This Regulation implements the WTO Decision of 30 August 2003 in the European Union.

GOVERNMENT USE

In the case of government use, similar steps and conditions to those described above for compulsory licences apply. The main difference between compulsory licences and government use is that the former is conferred, upon request, to a third party, while the latter permits the use of a patent by the government itself or by a contractor or agent appointed by it.

There is no need for a formal request to the government, as it can act *ex officio* to address identified public health needs. Government use may be utilized, for instance, for distribution of medicines in dispensaries, hospitals and other medical institutions owned by or on behalf of the Government.

Government use may have distinct advantages *vis-à-vis* compulsory licences in cases where the purchase of pharmaceutical products is made with non-commercial purposes, since:

- the government can act *ex officio*
- a contractor or agent can be appointed
- there is no need to engage in previous negotiations with the title-holder, thereby speeding up the process
- national laws can limit the remedies available against government use to payment of remuneration in accordance with subparagraph (h) of Article 31 of the TRIPS Agreement, that is, no injunctions may be admitted⁴³.

Who Can Authorize the Use of a Patent?

Depending on national laws, government use can be decided in a decentralized form by different departments or government bodies, or by a particular authority designated by law. Certainty about competence to give the authorization may avoid possible challenges to the validity of the act.

Content of an Administrative Act Authorizing Government Use

The use of a patent by the government requires an administrative act indicating, at least:

- department or government body that authorizes the government use;
- legal background;
- justification of the need to use the patent(s);
- identification of product(s);
- identification of the patents involved and of the title-holders, if known;
- remuneration to be paid to the patent owner;
- scope and duration of the intended use;
- persons or entities authorized to act as contractor or on behalf of the government.

Note:

An administrative act authorizing government use of a patent does not need to specify a determined quantity or value of the product to be produced or imported thereunder.

⁴³ See Article 44.2 of the TRIPS Agreement.

Who Can Use the Patent(s)?

The TRIPS Agreement (Article 31(b)) suggests that, in cases of government use, the relevant patent(s) may be used by a *contractor*, as is common practice, for instance, in the United States⁴⁴. Moreover, actual use of the patent(s) may be made by a natural or legal person on behalf of the government authorizing the use.

Notes:

1. *Any natural or legal person designated by the government may act on its behalf to execute an authorization of government use.*
2. *In particular, UN agencies, such as WHO and UNICEF, and NGOs, may act on behalf of the government in the purchase and distribution of pharmaceutical products.*
3. *The fact that a commercial entity is involved as a contractor or acts on behalf of the government does not prevent government use from being qualified as "non-commercial", to the extent that the patented invention is used for a public purpose.*

Notification of the Patent Owner

As in the case of compulsory licences, the government may authorize the use of any patents relating to a particular product. As mentioned above, a patent search to establish which patents are relevant may take a long time and face practical difficulties.

In accordance with Article 31(b) of the TRIPS Agreement, "in the case of public non-commercial use, where the government or contractor, without making a patent search, knows or has demonstrable grounds to know that a valid patent is or will be used by or for the government, the right holder shall be informed promptly". This provision suggests that the patent owner can be notified before or after the use of the patent has commenced, and that this notification should take place when the right holder has been identified through a patent search or by other means.

Notes:

1. *Patents may be assigned and they often are. Patent laws require that any assignment be registered in order to be valid. Therefore, it would not be sufficient to check the original title of a patent to determine who the right holder is, but the complete files relating to the patent must be examined.*
2. *The notification of patent owners does not mean that they may become a party to whatever procedures have been initiated. As in the case of compulsory licences, they would have the right to appeal against the authorization to use a patent on grounds of validity of the authorization or the remuneration determined for its use.*

⁴⁴ See Reichman J. op. cit.

ANNEX 1

**WORLD TRADE
ORGANIZATION**

WT/MIN(01)/DEC/W/2
14 November 2001
(01-5770)

MINISTERIAL CONFERENCE
Fourth Session
Doha, 9-14 November 2001

DECLARATION ON THE TRIPS AGREEMENT AND PUBLIC HEALTH

Adopted on 14 November 2001

1. We recognize the gravity of the public health problems afflicting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics.
2. We stress the need for the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) to be part of the wider national and international action to address these problems.
3. We recognize that intellectual property protection is important for the development of new medicines. We also recognize the concerns about its effects on prices.
4. We agree that the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all.

In this connection, we reaffirm the right of WTO Members to use, to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose.

5. Accordingly and in the light of paragraph 4 above, while maintaining our commitments in the TRIPS Agreement, we recognize that these flexibilities include:
 - (a) In applying the customary rules of interpretation of public international law, each provision of the TRIPS Agreement shall be read in the light of the object and purpose of the Agreement as expressed, in particular, in its objectives and principles.
 - (b) Each Member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted.
 - (c) Each Member has the right to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health

crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.

- (d) The effect of the provisions in the TRIPS Agreement that are relevant to the exhaustion of intellectual property rights is to leave each Member free to establish its own regime for such exhaustion without challenge, subject to the MFN and national treatment provisions of Articles 3 and 4.

6. We recognize that WTO Members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement. We instruct the Council for TRIPS to find an expeditious solution to this problem and to report to the General Council before the end of 2002.

7. We reaffirm the commitment of developed-country Members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country Members pursuant to Article 66.2. We also agree that the least-developed country Members will not be obliged, with respect to pharmaceutical products, to implement or apply Sections 5 and 7 of Part II of the TRIPS Agreement or to enforce rights provided for under these Sections until 1 January 2016, without prejudice to the right of least-developed country Members to seek other extensions of the transition periods as provided for in Article 66.1 of the TRIPS Agreement. We instruct the Council for TRIPS to take the necessary action to give effect to this pursuant to Article 66.1 of the TRIPS Agreement.

ANNEX 2⁴⁵

Certification of Non-Recognition and Non-Enforceability of Patents and Data Protection in Respect of Pharmaceutical Products

Whereas

Further to Paragraph 7 of the Declaration on the TRIPS Agreement and Public Health adopted by the WTO Ministerial Conference on 14 November 2001 (WT/MIN(01)/DEC/W/2), the WTO Council for TRIPS decided on 27 June 2002 (IP/C/25) that least developed country Members of the WTO need not enforce patents and data protection with respect to pharmaceutical products at least until 1 January 2016.

The 30 August 2003 Decision by the WTO General Council on the Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health (WT/L/540) acknowledged that the system established by the Decision is without prejudice to the exemption granted to least developed country Members pursuant to Article 66.1 of the TRIPS Agreement.

The [insert title of government official] hereby confirms that:

- (a) patents and data protection with respect to pharmaceutical products shall not be recognized or deemed enforceable within and with respect to [insert country name] at least until 1 January 2016;
- (b) importation, manufacturing, use, sale, and offering for sale of pharmaceutical products is authorized notwithstanding any patents which may have been granted or data protection rules which may be applicable with respect to those products; and
- (c) patents and data protection rights may not be enforced by holders thereof within and with respect to [insert country name] with regard to any actions by the government or third parties undertaken during the period extending at least until 1 January 2016.

⁴⁵ There is no guidance from WTO regarding the certification of the non-recognition or enforceability of patents and data protection pursuant to paragraph 7 of the Declaration on the TRIPS Agreement and Public Health. This Annex provides a model for such certification, on the understanding that the legal situation in each country should be assessed in the light of its domestic legislation and constitution.

The purpose of this book is to facilitate the elaboration of national health policies and strategies to improve access to medicines, using fully the flexibilities allowed by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) of the World Trade Organization (WTO). It includes documents of the World Health Organization (WHO) written by Professor Carlos Correa and published between 1997 and 2009. As consultant to WHO, Professor Correa helped to initiate and formulate WHO policy perspectives and to provide advice to Member States on intellectual property issues relating to the production, distribution and use of medicines. The content of this book illustrates the pioneer role that WHO played in identifying the public health implications of the binding rules introduced by the TRIPS Agreement.



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