World Health Organization

South-East Asia Region Western Pacific Region

How to conduct **patent** searches for medicines

A step-by-step guide

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Screen captures of patent data made available to the public through the Internet have been accessed from:

- Health Canada (http://www.patentregister.ca/);
- Indian Patent Office (http://ipindia.nic.in/ipirs/patentsearch.htm);
- Intellectual Property Organisation Pakistan (http://www.ipo.gov.pk/Patent/);
- Philippines Patent Office (http://patents.ipophil.gov.ph/PatSearch/);
- United States Food and Drug Administration (http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm);
- European Patent Office (http://ep.espacenet.com/); and
- World Intellectual Property Organization (http://www.wipo.int/pctdb/en/).

These screen captures are current as of 13 May 2010. Patent websites are subject to change and redesign, and may depart from the form represented here.

List of abbreviations and acronyms

ARV	antiretroviral
EPO	European Patent Office
INN	international non-proprietary name
INPADOC	international patent documentation centre collection
IPC	International Patent Classification
LDCs	least developed countries
NDA	new drug application
NDS	new drug submission
PCT	Patent Cooperation Treaty
SNDS	supplement to a new drug submission
TRIPS	Agreement on Trade-Related Aspects of Intellectual Property
US FDA	United States Food and Drug Administration
USPTO	United States Patent and Trademark Office
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

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Introduction

The globalization of intellectual property protection on medical products changes how developing country health authorities and procurement bodies make their decisions with respect to purchasing medicines. Whereas previously the decision to procure more cost-effective generic versions of medicines may not have required the consideration of intellectual property protection, that is no longer the case.

Under the Agreement on Trade-Related Aspects of Intellectual Property (TRIPS), Member States of the World Trade Organization (WTO) with developing country status were required to start examining patent applications and providing patent protection on medicines[1] either by 1 January 2000 or by 1 January 2005.[2] Many developing countries implemented patent protection on medicines much earlier than the required deadline. Today, patents on medicines are being granted in developing countries, and medicines under patent are entering the market.

This change in the patent laws of developing countries now requires local health authorities and procurement bodies to establish in advance of purchasing decisions whether patent(s) on a particular medicine have been filed, granted, lapsed or expired. Having such information in hand can help to decide whether more cost-effective medicines can be procured from alternative sources without the risk of patent infringement.

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1 A number of developing countries also introduced data exclusivity into their regulatory systems. This means that data submitted by a pharmaceutical company to national regulatory authorities for obtaining marketing approval of a medicine could not be used to approve generic versions of the same drug for at least a period of five years. This guide does not address how to determine whether data exclusivity impacts the procurement of generic medicines. In order to determine whether data exclusivity applies, the reader should refer to national legislation and the relevant national regulatory authority.

2 Least developed countries (LDCs) are not required to implement patents for pharmaceuticals until 2016. However, some LDCs may have already implemented TRIPS standards for pharmaceuticals within their patent laws.

Equally significant, access to patent information can also help ensure that countries engage with patent owners at a much earlier stage to explore possibilities for making medicines that are or could come under patent protection more affordable. Moreover, such information can help countries decide whether they should exercise the flexibilities available under TRIPS and the Doha Declaration (i.e. compulsory licensing and government use) to procure or produce local lower-priced generic versions.

In practice, obtaining relevant and accurate patent information on medicines, particularly in developing countries, is not without difficulties. This is due to a number of reasons:

- the technical language of patent specifications;
- the lack of reference to international non-proprietary names (INNs) or the commercial name of the product in patent specifications;
- the information is not up to date or is inaccurate;
- a drug may be covered by more than one patent;
- the information is not easily obtainable from the national patent office; and
- even where information is accessible, patent searches are subject to the frequent disclaimer that they may not reveal all the relevant patents.

Despite these constraints, patent information is increasingly being made available electronically. Freely accessible resources and methods that are not overly technical are available to help identify if relevant patents exist on medicines. Such methods, while not exhaustive, can nevertheless help health authorities and procurement agencies to identify pharmaceutical patents at the national level.

The purpose of this guide is to provide a starting point for health authorities, procurement bodies and others to identify whether patents relating to a pharmaceutical product exist in the country of interest.

The methods detailed in this guide use free resources that are available on the Internet. As patent searching is not an exact art, it is impossible for any guide to cover all the potential variables that a search may involve. The mechanics and effectiveness of a patent search are mainly determined by the depth of the user's knowledge of the subject matter, continuous iteration, and trial and error. This guide is therefore by no means intended to be a comprehensive guide; it merely is a starting point.

It is important to note that this guide does not discuss how to assess the claims of a patent in order to determine whether the purchase or production of a generic version of a medicine is prevented. Such an assessment would

require the services of a patent lawyer and a person with the relevant scientific background.

The intended purpose of this guide is to provide health authorities, procurement bodies and other interested parties with the basic tools to start obtaining critical information on patents covering a particular medicine in the country of interest. By doing so, decision-making on procurement issues could be made more effective and accurate.

1.1 Format of the guide

This guide is arranged into the following chapters.

Chapter 2 provides a basic introduction to the patent system and patent information. This chapter introduces the various treaties covering patents, the different types of patents (i.e. national and regional patents, and international patent applications) and key concepts (e.g. priority periods). It also explains how to read a patent document and how patent information is administered, including the arrangement of equivalent and corresponding patents in databases (patent families).

The purpose of this chapter is to provide readers who have little or no understanding of the patent system and related concepts with the necessary background information to carry out a meaningful search. Readers who fall into this category are advised to review this chapter first before moving to the practical parts of the guide.

As most medicines are protected by more than one patent, Chapter 3 of the guide familiarizes readers with the different types of patents that may exist in relation to a particular product.

Chapter 4 describes the various practical steps for conducting a search. Given the difficulties in identifying and matching patents to relevant products, the method adopted in this guide starts from the information about patents on medicines provided through the United States Food and Drug Administration (US FDA) Orange Book and the Health Canada Patent Register. Providing step-by-step examples, this chapter demonstrates how to extract patent information on medicines from the Orange Book and Health Canada.

As the Orange Book and Health Canada registers do not provide listings of all patents relating to marketed medicines, Chapter 4 also provides techniques for expanding a search using keywords, patent classifications, assignee/applicant and inventor name, citations and date ranges.

Applying the techniques discussed in Chapter 4, Chapter 5 explains how to find equivalent and corresponding patents in other countries using

available databases, or other methods when information is not available electronically.

Chapter 6 concludes by briefly discussing the steps that need to be taken following a search to determine whether there is freedom to procure or manufacture generic medicines.

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The patent system and patent information

Before commencing a patent search, it is necessary to have a grasp of:

- the various multilateral agreements governing the modern patent system and the concept of priority;
- the different ways of filing and obtaining patent protection;
- how patent information is administered; and
- how patent documents are structured.

Readers not familiar with the above should read this chapter first before proceeding through the remaining chapters of the guide.

2.1 Multilateral treaties on patents

Contrary to popular belief, there is no single global patent that provides protection in all countries. Patents are territorial rights that are granted in accordance with the national patent laws of a particular country. There are, however, various multilateral agreements that attempt to provide a degree of harmonization within the patent system. These are discussed briefly below.

2.1.1 The TRIPS Agreement

The most comprehensive of these frameworks is the TRIPS Agreement. TRIPS requires Member States of the WTO to implement minimum levels of intellectual property protection[1]. This includes providing for product and process patents in all fields of technology, and a minimum patent term of 20 years. However, countries are permitted some flexibility in determining what amounts to an invention and in deciding their own standards of patentability. Therefore, an invention that has been patented under the laws of one country may not be considered patentable in another country.

1 Least developed countries (LDCs) are not required to implement patents for pharmaceuticals until 2016.

It should be noted that granted patents might subsequently be invalidated in part or in full. Alternatively, granted patents may lapse due to failure to pay maintenance fees. The renewal period varies from country to country.

Aside from TRIPS, two other key international agreements that create a degree of harmonization within the patent system are the Paris Convention and the Patent Cooperation Treaty. The key elements of these legal frameworks for the purpose of this guide are discussed below.

2.1.2 The Paris Convention and priority period

In 1883, the Paris Convention created the first multilateral framework for intellectual property rights. As of 15 October 2009, 173 countries are signatories to the Convention (see Appendix I). One of the principal concepts introduced by the Convention is the priority system.

Under the priority system, an inventor may, within 12 months of the first patent application (the *priority application*) disclosing an invention in a member country, apply for protection for the same invention in other member countries.[2] This 12-month period is known as the *priority period*. Subsequent applications filed within the 12-month priority period will enjoy the same filing date (known as the *priority date*) as the first application. These later applications will also enjoy priority status over all other applications, acts and disclosures relating to the same invention that are filed after the priority date. The withdrawal or abandonment of the first application (the priority application), or the revocation of the first patent (the priority patent) does not affect the priority status of the subsequent applications that rely on the earlier patent.

The Convention permits applicants to claim "multiple priorities" or "partial priorities". Therefore, later applications filed within the priority period may claim priority from more than one earlier application, which cover different features of the invention. Partial priority exists where the later applications combine subject matter for which priority is claimed with elements of the invention for which there is no priority application.

2.1.3 The Patent Cooperation Treaty

The Patent Cooperation Treaty (PCT) came into being in 1970 and is open to states that are party to the Paris Convention. As of 15 May 2010, there were 142 contracting parties to the PCT (see Appendix II).

The PCT (also commonly referred to as the international patent system) makes it possible for an applicant who is a national or resident of a contracting

2 See Article 4 of the Paris Convention.

state to apply for patent protection for an invention in more than one country through a single application. The PCT filing system is discussed in more detail below (see Section 2.2.3).

2.2 Types of patent filing and protection

As already indicated above, patent rights are territorial. There are different routes to filing and obtaining patent protection in a country.

2.2.1 National patent filings

A patent application that is filed with the national patent office is typically referred to as a national filing. It will be examined and granted according to the patent law of that country. The patent will only be enforceable in the country(ies) where it was filed and granted.

The initial application (the priority application) may be followed by further patent applications for the same invention in other countries within the 12-month priority period.

2.2.2 Regional patent filings

In some regions, countries have come together and created regional patent conventions that harmonize the administration of patents. These regional conventions allow applicants to file a single application with a regional patent office, designating the contracting states that they wish to seek protection in. The regional patent office will administer, and in some cases (the European Patent Office (EPO) and the African Intellectual Property Organization (OAPI)), conduct the examination and issuing of the patent.

Regional patents have the same effect as national patent rights in the designated Member States. In some cases, for example a European patent, the patent is granted as a bundle of national rights.

The current regional patent conventions and their respective regional patent offices are: the European Patent Convention and the EPO; the Harare Protocol on Patents and Industrial Design (Harare Protocol) and the African Regional Industrial Property Organization (ARIPO); the Bangui Agreement relating to OAPI; the Eurasia Patent Convention and the Eurasian Patent Office (EAPO). The Member States of each of these regional patent conventions can be found on the relevant organizational websites.

2.2.3 International patent applications

Under the PCT system, an international application makes it possible for an applicant who is a national or resident of a contracting state to apply

for patent protection for an invention in more than one country through a single application.

The application can be filed through either the national patent office of the contracting state where the applicant is resident or through the International Bureau of the World Intellectual Property Organization (WIPO). Applicants resident in a contracting state that is party to a regional patent convention may file the international application at the respective regional patent office.

If the applicant does not withdraw an international application it will be published under an international publication number by WIPO's International Bureau 18 months from the date of filing or from the priority date, if any. The applicant then has up to 30 months (31 months in some countries) from the date of the priority application upon which the international application is based to decide whether to pursue national protection for the invention in each of the countries designated, or only in a few. By selecting to pursue the international application in a particular country, the application enters what is termed the national phase. The single international application thus becomes a national application in each of the designated states and is published as such in each country's patent office journal. Each of those national applications will then be examined by the respective national patent office.

2.3 Patent information

An applicant must describe the invention and the subject matter for which patent protection is sought in the patent specification.

Once the specification has been filed through one of the filing systems discussed above, the receiving patent office will administer the application. Unless the applicant withdraws the application, in most countries the first time that the patent specification and its filing details become public is 18 months after the priority date of the first application (the priority application).

Thereafter, the application is given a substantive examination[3] to determine whether the invention meets the requirements of patentability as defined under the country's national law. During the examination of an application or due to a pre-grant opposition by a third party, the subject matter claims and description in the specification may be revised. Therefore, it is necessary to track an application through examination to grant (or refusal) in order to obtain the final subject matter that a patent covers.

3 However, not all countries undertake a substantive examination.

2.3.1 Understanding information in a patent specification

A patent specification consists of various pieces of information that can be used for the purpose of searching.

The format of patent documents (the specifications) and the information contained therein are largely the same from one patent office to another. This information generally falls into three categories:

- bibliographic data, which usually appears on the front page of a patent specification;
- technical information, which includes the description of the invention; and
- legal information, referred to as the claims, which define the scope of protection sought.

Bibliographic data

With the exception of a few differences between patent authorities, the fields of information appearing on the cover page of a patent document will generally be the same. Below is a summary of the most common fields of information that appear in the bibliographic data.

- **Application number:** A unique number given to each patent application filed.

  In the case of US patents, there may be additional numbers that reveal earlier related applications from which the current application derives. These earlier applications are known as “continuation applications”, “continuation-in-part applications” or “provisional applications”. It is worth noting that the numbers of continuation applications, continuation-in-part applications and provisional applications will often form the priority data for subsequent filings in other countries.

- **Patent number:** A unique number given to each granted patent.

- **Document kind codes:** An alphanumeric code used to distinguish the particular status of a published application or patent. The code will follow a publication number or patent number (e.g. A1 or B1). See Box 1 below for further information on kind codes.

- **Filing date:** The date the application was filed and accepted by the relevant patent office. This is the date that the 20 years of patent protection will run from, if the patent is granted.

- **Priority data:** Includes the application number(s), date(s) and two-letter code of the country where the first application(s) filed for the invention from which priority is claimed were made. The priority date(s) given is also the date from which the invention will be protected, if the patent is granted.

- **Publication number:** This is the number given to an application when it is first published in an official patent office journal (usually 18 months after the priority date). In some countries the publication number will remain the same as the original application number.

- **Publication date:** The date the application/specification was first published (usually 18 months after the priority date).

- **Date of patent/Date of publication of the grant of the patent:** The date that the patent was published as granted.

- **International Patent Classification:** Code that represents the field of technology to which the subject matter of the patent relates. All published patents will be classified using a standard classification system, the International Patent Classification (IPC) system. For further information on patent classification systems, see Box 2 below.

- **Applicant/Proprietor/Assignee:** The name of the individual or company that is applying for protection of an invention. In the United States, if there has been a legal assignment of the invention prior to a patent application being filed, the field "Assignee" in a US patent document represents the applicant. This field also provides the business address or city where the applicant is based.

- **Inventor(s):** The name of the person(s) who invented the subject matter claimed in the patent application and their address.

- **Representative/Agent:** The name and address of the patent attorney or lawyer that is on record as handling the application on behalf of the applicant.

- **Designated States:** For PCT and European patents, this field displays the designated countries where protection may be sought. The designated countries are displayed using two-letter codes created by WIPO.

  The list of designated states provided at the time of the 18-month publication will reflect the states that the applicant included at the

time of filing the application. However, as discussed above, it is possible that an applicant may not proceed to pursue the application in every designated country.

- **Divisional application:** Refers to related application(s) that are descended from (or "divided out" from) a previous application, which is known as a parent application. A divisional application will usually be filed where the parent application claims more than one invention. Also, where the parent application has been refused by a patent office during examination or opposition, an applicant may file one or more divisional applications covering the same or virtually the same subject matter as the parent application in order to have another chance at obtaining a patent. An example of a granted European patent with two related divisional patent applications is shown in Figure 2. By searching for the divisional application numbers provided in the bibliographic data of the parent patent document, users can obtain information about these additional patents.

  In some countries, e.g. India, the bibliographic data of a parent application will not provide details of any related divisional applications. However, the bibliographic data of the divisional application (which would have to be found through conducting searches as described in Chapter 4) will show the details of the related parent application.

- **References cited:** These relate to prior patent documents or non-patent literature relating to the subject matter of the application disclosed by the applicant or identified by the patent office examiner during examination of the application.

- **Title:** Provides a brief indication of the nature of the subject matter of the patent.

- **Abstract:** Provides a summary of the subject matter of the patent application or patent. Some abstracts may include a diagram.

Figures 1 to 3 illustrate how bibliographic data is presented on the front page of a US, European and PCT patent specification.

In some countries, the bibliographic data for a patent specification may not appear on the front page of a patent specification. Instead, the data is provided in the official patent office journal when the application is published after 18 months. Figure 4 illustrates how bibliographic data is presented in the Official Journal of the Indian Patent Office.

Figure 1: Example of bibliographic data as presented on the front page of a US patent specification

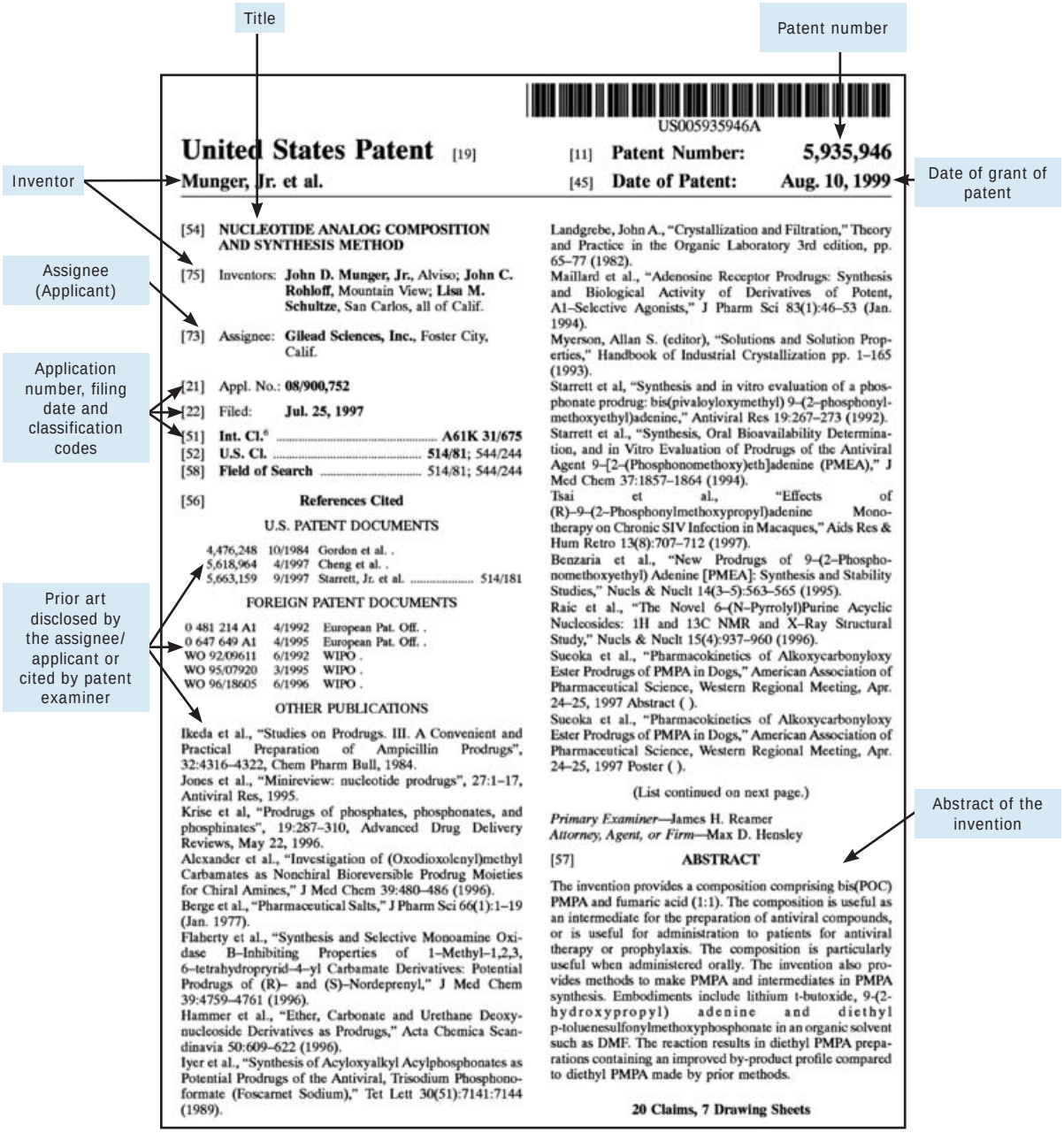


Figure 2: Example of bibliographic data as presented on the front page of a European patent specification filed through the PCT

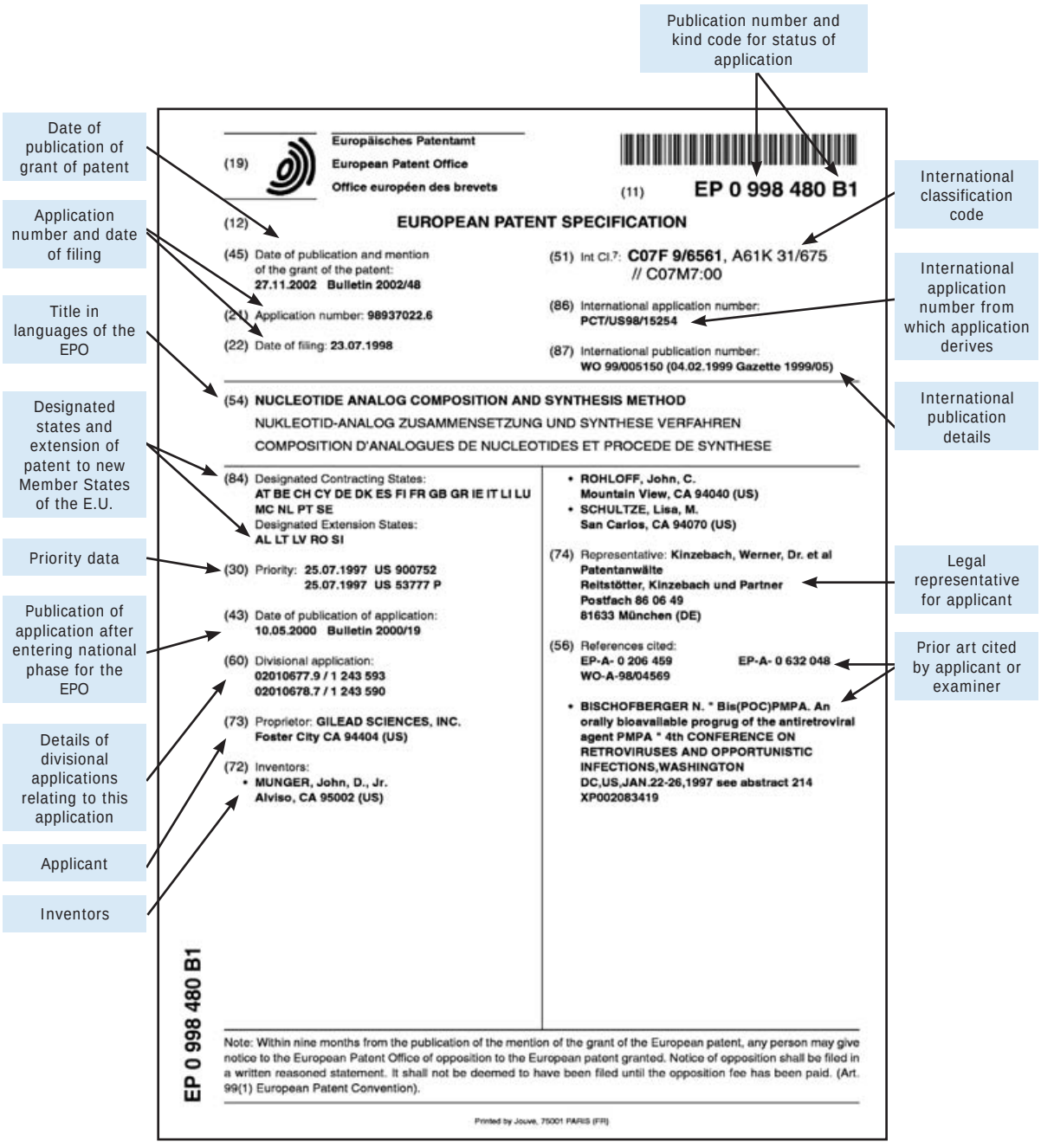


Figure 3: Example of bibliographic data as presented on the front page of a PCT patent specification

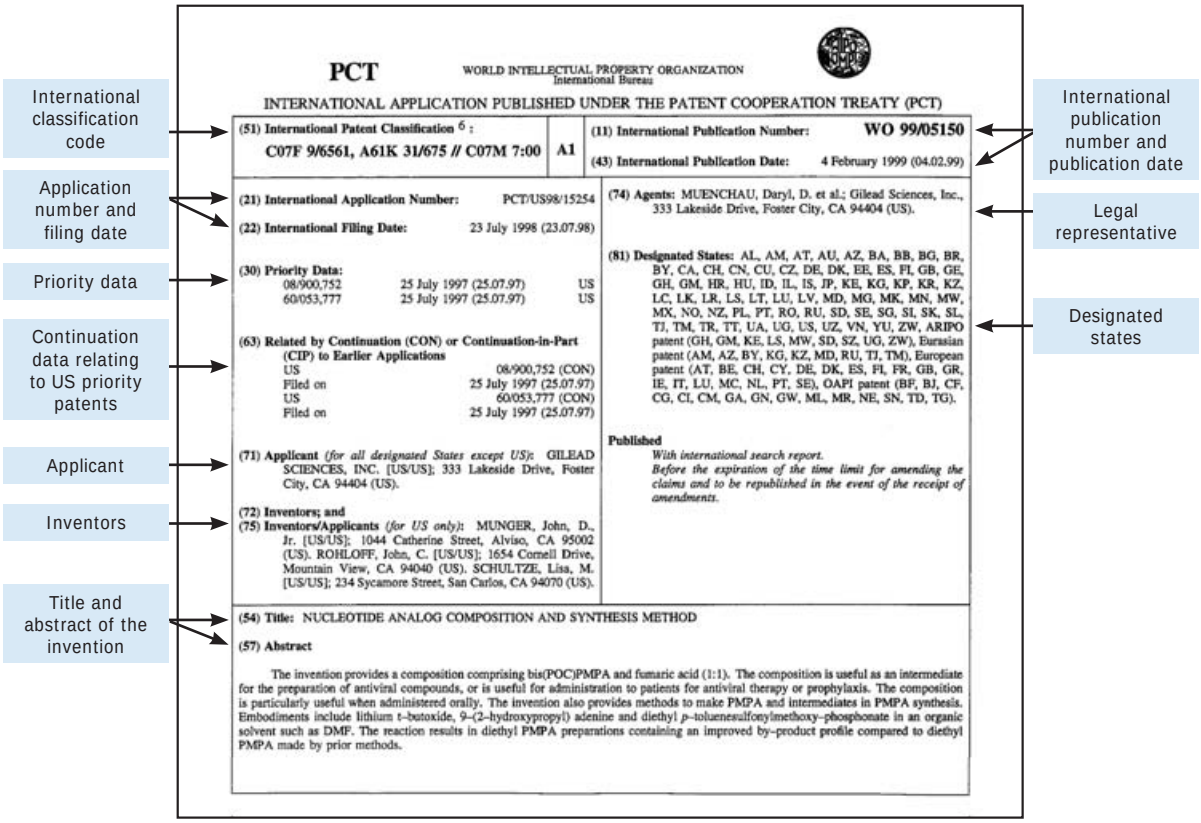


Figure 4: Example of bibliographic data as presented in the Official Journal of the Indian Patent Office

9. Application No. 896/DEL/2002 A ***(22)Date of filing of Application :04/Sep/2002***

(54)Title of the invention :Nucleotide Analog Composition.

(51)International classification:C 07 D 473/00; C 12 P 17/00	***(71)Name of the Applicant.:***
(30)Priority Date:	***GILEAD SCIENCES, INC.***
(31)Document No. :60/053,777;08/900,752	***Address of the Applicant.:***
(32)Date :25/Jul/1997;25/Jul/1997	***333 LAKESIDE DRIVE, FOSTER CITY, CALIFORNIA 94404***
(33)Country :UNITED STATES OF AMERICA; UNITED STATES OF AMERICA	***UNITED STATES OF AMERICA***
(62)Divisional to Application No 2174/DEL/1998 filed on 24/Jul/1998	***(72)Name of the Inventor.:*** ***JOHN DUCAN MUNGER, JR.,*** ***JOHN CHRISTIAN ROHLOFF*** ***LISA MARIE SCHULTZE***

Abstract :

The invention provides a composition comprising bis(POC)PMPA and fumaric acid (1:1). The composition is useful as an intermediate for the preparation of antiviral compounds, or is useful for administration to patients for antiviral therapy or prophylaxis. The composition is particularly useful when administered orally. The invention also provides methods to make PMPA and intermediates in PMPA synthesis. Embodiments include lithium t-butoxide, 9-(2-hydroxypropyl) adenine and diethyl p-toluenesulfonylmethoxyphosphonate in an

Box 1. Kind Codes

As patent documents change in their content between publication and grant, patent authorities classify the different versions using kind codes. Kind codes will follow the application or granted patent number e.g. EP 0996622 (A1) or EP 0996622 (B1). Although there is some harmonization in the document kind codes used by the different patent authorities, they can vary.

For example, most patent offices will use the document kind code "A" to indicate that a patent application is published for the first time and is either unexamined or under examination. The document kind code "A" may be followed by a numeral, e.g. "A1", "A2" or "A3".

A1 indicates the publication of a PCT or European patent (referred to as an EP patent) with a search report through the International Search Authority (under the auspices of WIPO).

A2 indicates the publication of a PCT or EP patent without an International Search Authority search report.

A3 indicates the publication of a PCT or EP with an International Search Authority search report for a patent previously documented as A2.

B1 indicates a granted EP patent. B2 indicates a granted EP patent with revisions. To obtain the final granted patent claims for an EP, one needs to download the patent that is suffixed with letters "B1" or "B2".

The United States also uses the kind code B for granted patents. Other countries using the kind code B for a granted patent include Indonesia and Viet Nam. China and a number of other countries use the letter "C".

NB: Published PCT applications only appear as applications—thus, they will never be referenced by the kind codes "B" or "C" (which signify that a patent has been granted). However, when a PCT application enters into the national phase and matures into a granted patent in a designated country, that country's patent database or publication will indicate its status by either the kind code "B" or "C".

For specific details on country kind codes, see: http://www.delphion.com/help/kindcodes or http://www.cas.org/expertise/cascontent/caplus/patcoverage/patkind.html

Box 2. The Patent Classification System

Although the different patent authorities maintain their own classification schemes, the most widely used system is the IPC administered by WIPO. The IPC contains about 70 000 entries (classification symbols) that can be used to classify patent documents. The different classifications are arranged into the following eight sections with a hierarchical structure:

Section A – Human Necessities

Section B – Performing Operations; Transporting

Section C – Chemistry; Metallurgy

Section D – Textiles; Paper

Section E – Fixed Constructions

Section F – Mechanical Engineering; Lighting; Heating; Weapons; Blasting

Section G – Physics

Section H – Electricity

Each of the above sections contains subsections. For example, Section A (Human Necessities) contains the following subsections: Agriculture; Foodstuffs; Tobacco; Personal or Domestic Articles; Health; Life Saving; Amusement.

Each section/subsection is divided into classes, represented by the letter of the section followed by a two-digit number. Example: A61 includes technologies relating to "Medicine or Veterinary Science; Hygiene".

Classes are further divided into subclasses, represented by a capital letter. Examples: A61K for "Preparations for Medical, Dental, or Toilet Purposes" and A61P for "Therapeutic Activity of Chemical Compounds or Medicinal Preparations".

The subclass is further broken down into subdivisions called "groups", also known as the "main group" within the hierarchical structure. The main group can be identified by a two-digit-number. Example: A61P 31 for "Antiinfectives i.e. antibiotics, antiseptics, chemotherapeutics".

The main group is further divided into subgroups. The subgroup is separated from the main group number by a forward oblique stroke followed by a one- to three-digit number. Example: A61P 31/18 for "HIV" and A31P 33/06 for "Antimalarials".

Pharmaceutical products are usually classified under A61K, A61P and/or C07.

The IPC system can also be searched electronically online at: http://www.wipo.int/classifications/ipc/ipc8/?lang=en

Although the IPC is widely used, different patent authorities may have their own classification systems. The European and US Patent Offices are two such examples. They are useful to know for the purpose of this guide, given that many pharmaceutical product patents originate from these regions.

The European Classification (ECLA) system builds on the IPC system and contains some 134 000 groups. The ECLA system can be searched online at: http://v3.espacenet.com/eclasrch.

The US Patent and Trademark Office (USPTO) classification guide has its own format. The US classification guide is available at: http://www.uspto.gov/go/classification/selectnumwithtitle.htm.

Technical information

Following the bibliographic data, a patent specification will provide the technical information relating to the subject matter of the invention. This section, often referred to as the body of the patent specification, consists of a written and diagrammatic description of the invention.

The technical section of a patent specification will usually include the following subsections:

- **Field of the invention**: Describes in one or two sentences the subject matter of the invention and its benefits.
- **Background of the invention:** Sets out any previous disclosures known to the applicant/patentee at the time of filing the patent that may be relevant to the subject matter of the invention. Depending on the particular requirements of the patent office in question, the applicant provides information about earlier related patent(s) or literature(s). The section will then usually describe the object of the invention and the problem it seeks to solve, and how it represents an advance over what was previously known.
- **Summary of the invention:** Briefly explains the main subject matter of the invention. The summary may also make reference to related embodiments—i.e. a particular implementation or method of carrying out the invention—of the main claim.
- **Brief description of the drawing/figures:** Any figures or drawings needed to explain the invention will be briefly described under this subsection. In most cases any figures/drawings will appear at the end of the patent document after the claims section (see page 20).
- **Detailed description of the invention:** Provides the technical details of the invention and how it may be used. The description should be detailed enough to allow a third party to be able to carry out the invention.
- **Examples:** Demonstrate various workings of the invention. They can range from examples explaining which process to use to make the invention, to data showing how the invention provides improvements (such as stability or bioavailability) over other or earlier known forms of the subject matter for which a patent is being claimed.

Figures 5 and 6 illustrate how the technical information in a patent specification may be presented.

Depending on the user's knowledge of the subject matter to be searched and the type of database used, it may be possible to search for terms that only appear in the body of the specification. Using such a search method may provide a more comprehensive set of results than searching only the bibliographic data, title or abstract of a patent document. Such search techniques will be discussed further in Chapter 4.

Figure 5: Example of technical information in a patent specification

Description

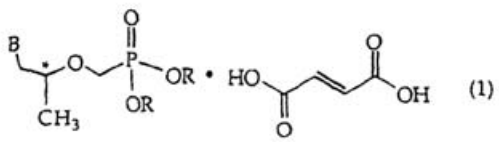
BACKGROUND OF THE INVENTION

[0001] The present invention relates to 9-[2-(*R*)-[[Bis[[(isopropoxycarbonyl)oxy]methoxy]phosphinoyl]methoxy]propyl]adenine• fumaric acid ("bis(POC)PMPA fumarate"), and compositions suitable for oral delivery of (*R*)-9-[2-(phosphonomethoxy) propyl]adenine ("PMPA") to a human or animal for use as an antiviral agent which contain said compound.

[0002] Phosphonomethoxy nucleotide analogs are known and various technologies for oral delivery are known. See, e.g., U.S. Application serial No. 08/686,838, U.S. 5,208,221, 5,124,051, WO 91/19721, WO 94/03467, WO 94/03466, WO 92/13869, DE 41 38 584 A1, WO 94/10539, WO 94/10467, WO 96/18605, WO 95/07920, WO 95 79/07919, WO 92/09611, WO 92/01698, WO 91/19721, WO 88/05438, EP 0 632 048, EP 0 481 214, EP 0 369 409, EP 0 269 947, U.S. Patent Nos. 3,524,846 and 5,386,030, Engel *Chem. Rev.* 77:349-367 1977, Farquhar et al., J. *Pharm. Sci.* 72: 324-325 1983, Starrett et al., *Antiviral Res.* 19:267-273 1992, Safadi et al., *Pharmaceutical Research* 10(9):1350-1355 1993, Sakamoto et al., *Chem. Pharm. Bull.* 32(6):2241-2248 1984, and Davidsen et al., *J. Med. Chem.* 37(26): 4423-4429 1994. bis(POC)PMPA is disclosed in WO 98/04569.

SUMMARY OF THE INVENTION

[0003] The invention provides a compound of formula (1), which includes 9-[2-(*R*)-[[bis[[(isopropoxycarbonyl)oxy] methoxy] phosphinoyl]methoxy]propyl]-adenine•fumaric acid (1:1) ("bis(POC)PMPA fumarate" or "BPPF"),



(1)

wherein B is adenin-9-yl and R independently is -H or $-CH_2-O-C(O)-O-CH(CH_3)_2$, but at least one R is $-CH_2-O-C(O)-O-CH(CH_3)_2$.

[0004] Another embodiment of the invention comprises the use of a compound of formula (1) for preparing a composition for prophylactically or therapeutically treating viral infections.

[0005] In another embodiment, a method for preparing a compound of formula (1) comprises contacting fumaric acid with bis(POC)PMPA.

Brief Description of Figures

[0006] Figure 1 shows a BPPF crystal X-ray powder diffraction pattern. Figure 2 shows a thermogram obtained by differential scanning calorimetry of BPPF crystals. Figure 3 shows a Fourier transform infrared absorption spectrum of BPPF crystals. Figure 4 is a picture of a photograph showing embodiments of BPPF crystals at 100X magnification by light microscopy. Figure 5 is a picture of a photograph showing embodiments of BPPF crystals at 100X magnification by light microscopy. Figure 6 is a picture of a photograph showing embodiments of BPPF crystals at 200X magnification by light microscopy. Figure 7 is a picture of a photograph showing embodiments of BPPF crystals at 40X magnification by light microscopy. Figures 4-7 are copies of the photographs made at a 132% enlargement.

DETAILED DESCRIPTION OF THE INVENTION

[0007] "Alkyl" as used herein, unless stated to the contrary, is a hydrocarbon containing 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 normal, secondary, tertiary or cyclic structures. Examples are $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)CH_2CH_3$, $-C(CH_3)_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_2CH_3$, $-CH(CH_2CH_3)_2$, $-C(CH_3)_2CH_2CH_3$, $-CH(CH_3)CH(CH_3)_2$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH(CH_3)CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH(CH_3)CH_2CH_2CH_2CH_3$, $-CH(CH_2CH_3)(CH_2CH_2CH_3)$, $-C(CH_3)_2CH_2CH_2CH_3$, $-CH(CH_3)CH(CH_3)CH_2CH_3$, $-CH(CH_3)CH_2CH(CH_3)_2$, $-C(CH_3)(CH_2CH_3)_2$, $-CH(CH_2CH_3)CH(CH_3)_2$, $-C(CH_3)_2CH(CH_3)_2$, $-CH(CH_3)C(CH_3)_3$, cyclopropyl, cyclobutyl, cyclopropylmethyl, cyclopentyl, cyclobutylmethyl, 1-cyclopropyl-1-ethyl, 2-cyclopropyl-1-ethyl, cyclohexyl, cyclopentylmethyl, 1-cyclobutyl-1-ethyl, 2-cyclobutyl-1-ethyl, 1-cyclopropyl-1-propyl, 2-cyclopropyl-1-propyl, 3-cyclopropyl-1-propyl, 2-cyclopropyl-2-propyl, and 1-cyclopropyl-2-propyl.

Figure 6: Examples given in a patent specification explaining the invention

Rockville, MD) and manufacturer's Coulometer instructions. The amount of BPPF used in the assay, about 50-100 mg, was measured using a five place analytical balance (Sartorius, Model RC210D, or equivalent). A typical batch contained less than 1.0% w/w water.

[0068] BPPF crystals were analyzed by infrared spectrophotometry using a Perkin-Elmer model 1650 FT-IR spectrophotometer according the manufacturer's instructions. KBr (Aldrich, IR grade) was dried overnight at 60°C under vacuum before use. A translucent pellet containing about 10% by weight (about 5 mg) of BPPF crystals and about 90% by weight (50 mg) of dried KBr was prepared by grinding the two powders together to obtain a fine powder. IR spectroscopy has been described (see, e.g., U.S. Pharmacopoeia, vol. 22, 1994 method 197, U.S.P. Pharmacopeial Convention, Inc, Rockville, MD; Morrison, R.T. et al, *Organic Chemistry*, 3rd ed., Allyn and Bacon, Inc., Boston, p 405-412, 1973). The spectrophotometer sample chamber was purged for at least 5 minutes with high purity nitrogen gas at about 6 p.s.i. to reduce carbon dioxide absorbance interference to ≤ 3% in a background scan prior to scanning with the sample. BPPF crystals exhibited an infrared absorption spectrum in potassium bromide with characteristic bands expressed in reciprocal centimeters at approximately 3224 (O-H), 3107-3052 (N-H, C=C-H), 2986-2939 (aliphatic C-H), 1759 (alkyl ester C=O), 1678 (aromatic C=N), 1620 (aromatic C=C), 1269 (phosphonate P=O) and 1102 (C-O-C).

[0069] The solubility of BPPF in different solvents was examined. BPPF was found to be generally most soluble in polar solvents, which are typically used in the invention methods and embodiments. BPPF solubility in dimethylformamide was 428 mg/mL and BPPF solubility in isopropyl acetate:water (1:1 v/v), methanol, ethanol, isopropanol, 0.1 N HCl and acetone was about 15-100 mg/mL. BPPF solubility in acetonitrile, isopropyl acetate and deionized water (pH 3.3) was about 3-15 mg/mL. BPPF had a low solubility in CH_2CL_2, diethyl ether and hexane.

[0070] BPPF crystals were analyzed by ultraviolet spectrophotometry using a Hewlett-Packard model 8425A diode array spectrophotometer according the manufacturer's instructions. The amount of BPPF used in the assay, about 25 mg, was measured using a five place analytical balance (Sartorius, Model RC210D, or equivalent) and HPLC or spectrophotometric grade solutions. The molar absorptivity of 10 µg/mL BPPF at pH 6.0 in 0.01 M potassium phosphate buffer was 14930 M^{-1} cm^{-1} and 15010 M^{-1} cm^{-1} at pH 2.0 in 0.01 N HCl for 15 µg/mL BPPF. BPPF (10 µg/mL) in methanol had a λmax at about 260 nm.

[0071] BPPF crystals were not hygroscopic when kept at 92% relative humidity and at room temperature for up to 37 days. BPPF has a pKa of 3.8 as determined by potentiometric titration.

Example 2

[0072] Chiral enrichment of (*R*)-PMPA. (*R,S*)-PMPA•H_2O (2.5 g, about 93% *R* isomer) was suspended in a flask containing water (100 mL) and the pH was adjusted to 7.12 using HCl or NaOH as needed. The solution was warmed to 40 °C and the pH was adjusted to about 5.0. The pH was then adjusted to 3.1, and the solution was seeded with (*R*)-PMPA. The solution was allowed to cool to room temperature and left for about 2 hours. The solids were collected on a coarse glass frit sintered glass funnel, washed with ice cold water (10 mL) and then washed with acetone (10 mL). The resulting PMPA consisted of 98.3% of the (*R*) isomer. No chiral enrichment of the (*R*) isomer was observed when similar protocols were performed using 2.5 g of (*R,S*)-PMPA (about 93% (*R*)-isomer) and 25 mL of water. Chiral enrichment of the (*R*) isomer to 99.6% (*R*)-isomer was observed when a similar protocol was performed using 0.766 g of (*R,S*)-PMPA (about 93% (*R*)-isomer) and 10 mL of water.

Example 3

[0073] The solid state chemical stability of cBPPF and bis(POC)PMPA•citrate salt was compared by analyzing each compound after storage under different conditions. The results showed that BPPF powder was unexpectedly more stable to storage at elevated temperature and relative humidity.

Conditions	time*	BPPF%	mono(POC) PMPA fumarate%	bis(POC) PMPA citrate%	mono(POC) PMPA citrate%
40°C, 75%**	0	99.0	1.0	99.0	1.0
	14	98.3	1.7	96.9	3.1
	30	98.1	1.9	92.9	7.1
	60	97.1	2.9	77.6	22.4

* days,
** relative humidity.

Legal information

The claims defining the legal rights over the invention will be found at the end of the patent specification (see Figure. 7). Understanding the scope of the claims and the subject matter it covers is necessary to assess whether there is freedom to procure or manufacture generic versions of a particular medicine.

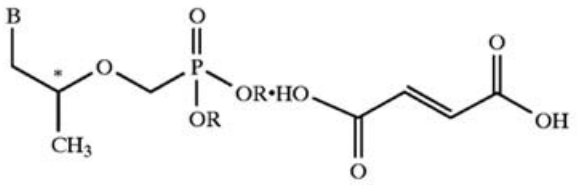
As the laws regarding claim construction may differ from country to country, the topic of claims analysis is beyond the scope of this guide. It is suggested that once a particular patent(s) has been identified, a patent lawyer/attorney and/or a pharmaceutical chemist who is familiar with construing the claims of a patent in accordance with national laws should be engaged, in order to determine the exact scope of the claims.

Figure 7: Example of patent claims

We claim:

1. A composition of formula (1)

(1)



wherein B is adenin-9-yl and R independently is —H or —CH_2—O—C(O)—O—$CH(CH_3)_2$, but at least one R is —CH_2—O—C(O)—O—$CH(CH_3)_2$.

2. The composition of claim **1** wherein both R are —CH_2—O—C(O)—O—$CH(CH_3)_2$.

3. The composition of claim **1** wherein the composition is a crystalline solid.

4. The composition of claim **1** wherein the compound is enriched or resolved at the carbon atom chiral center (*).

5. The composition of claim **1** having an X-ray powder diffraction spectrum peak using Cu-Kα radiation, expressed in degrees 2θ at about 25.0.

6. A composition comprising the composition of claim **1** and an acceptable excipient.

7. A composition comprising a lithium alkoxide and a 9-(2-hydroxypropyl)adenine solution.

8. A composition comprising an (R,S)-PMPA solution at a pH of about 2.7–3.5 wherein the solution has less than about 0.1 g/mL (R,S)-PMPA and wherein about 90–94% of the PMPA is in the (R) configuration.

2.4 Where to obtain patent information

How patent data and specifications are obtained varies from country to country. A number of developed country patent offices provide free online access to patent information, including both bibliographic data and related patent documents. Although most of the free online databases only cover information relating to patents in developed countries, there are exceptions.

The EPO's online database (esp@cenet) provides access to selected patent information and specifications from other national patent offices.[4] WIPO's patent database (Patentscope) provides access to international patent documents (PCT applications) as well as selected information on whether those applications have entered the national phase.[5]

There are a growing number of developing country patent offices that now have patent databases that can be searched freely. However, many if not all of these databases only provide limited data with no online access to the full patent specification. In some countries, there may be separate databases that have to be searched and cross-referenced in order to obtain complete information. For example, the Indian Patent Office has two separate databases, one for published patent applications and one for granted patents. Also, many of these databases are only searchable in the national language. Once the details of a particular patent are found from a search of one of these databases, a request has to be made to the patent office itself to obtain a copy of the full patent document. In some cases, such as in India, payment of an official fee will be necessary.

Where a national patent office does not provide an online searchable database, it is possible to obtain information on patents by manually searching the official journal (or gazette) of the relevant patent office. Unlike online searching, manually searching patent office journals/gazettes is a laborious and time-consuming task. Patent offices normally have an official journal/gazette in one form or another within which details of all patent applications[6] and granted patents will be presented. The journal/gazette may either be available for download from the particular national patent office website or can be purchased for an official fee. In some cases, it may be necessary to visit the patent office to search the records on-site. As journals/gazettes will not include the full patent document, it will be necessary to request this from patent office once the relevant application or granted patent has been found.

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4 http://ep.espacenet.com/

5 http://www.wipo.int/pctdb/en/

6 As explained above, patent applications usually will be published 18 months after the priority date.

For a list of free online databases or journals provided by national/ regional patent offices and the type of patent information they offer, see **Appendix III.**

In addition to patent office databases, there are a number of commercial and non-profit databases that provide patent information online.

The commercial databases offer a subscription-based service and tend to provide more comprehensive coverage. For example, Thompson Reuters' Derwent World Patent Index provides patent information from 41 patent offices around the world. However, even though such databases provide information that may not be available from the databases of the EPO and WIPO, they still lack data from most developing countries.

The non-profit databases are usually limited to patent information from Europe, Japan, the United States and WIPO. Nevertheless, as explained in Chapters 4 and 5, these databases can be useful to obtain full electronic copies of EPO, PCT and US patent documents that are not available from the national patent office databases.

Box 3. Examples of non-profit patent databases

- BigPatents India: http://india.bigpatents.org/
- Freepatentsonline: http://www.freepatentsonline.com/
- Google Patents: http://www.google.com/patents
- IP.com: http://ip.com/
- Patent Lens: http://www.patentlens.net/patentlens/structured.html
- PriorSmart: http://www.priorsmart.com/

2.5 How patent information is arranged

With the ever-increasing volume of patent information and improvements in patent search technology, various concepts have been developed to make searching more thorough. One such concept is the *patent family*. A patent family can be defined in various ways.

Broadly, a patent family arises when several patent documents around the world claim the same priority or priorities from the first patent application(s) filed for an individual invention. As a result, all the patents sharing the same priority or priorities become related *family members*. Therefore, depending on the database used, a search against one member of a patent family can reveal other members of the family from around the world.

Although a patent family may reveal a list of patents that share the same priority patent(s), it does not mean that the patent documents and their claims will be the same. The narrowest definition of a patent family is one including documents that have exactly the same priorities and claims. Patent documents that have the exact same priorities are usually referred to as *equivalents*. The feature *Also published as* in the esp@cenet database will highlight patents that are considered to be equivalent.

A broader and more comprehensive patent family is where the patents will be directly or indirectly linked by the priority, but the body of all listed patent documents and their claims will not be the same. For example, such a patent family would include patents that cover different aspects of the invention deriving from one or more of the priority claims, as well as ones that have been divided out from other applications. The EPO's database esp@cenet uses this more comprehensive patent family system, called the International Patent Documentation Centre Collection (INPADOC).

The information provided in patent families will likely have missing or incorrect information; this is due to delays in receiving information from the participating national patent offices. Therefore, to make sure of the actual status of a patent in a particular country, users should double check with the relevant national patent office.

For the purpose of demonstrating examples in this guide, the INPADOC patent family system will be used.

3

Types of patents on medicines

The patent system is designed to provide one patent for one invention. Therefore, if Company X invents a new chemical compound, Company X may be entitled to a single patent to protect the newly invented compound and how it is manufactured. If Company X then also discovers new forms of the compound, invents new ways to deliver or manufacture the compound, in each case Company X may be entitled to a separate patent for each claimed invention.

Most of today's marketed pharmaceutical products consist of relatively small chemical molecules. Others derive from biological material (i.e. biotechnology drugs or biologicals). Whether the medicine in question is a chemical or biological product, several patents are likely to have been filed and/or granted to protect it.

In the case of non-biological pharmaceutical products, a single medicine may be covered by separate patents claiming:

- the chemical compound (the active ingredient or base compound);
- polymorphic forms of the compound;
- salts, esters, ethers, enantiomers, metabolites and other derivative compounds;
- formulations and compositions of the compound, e.g. capsule, tablet and oral solutions;
- different dosage forms;
- one or more indications (uses) for the medicine;
- a combination of the compound with other active ingredients;
- processes and methods for manufacturing the active ingredient, polymorphic forms, derivative compounds and formulations/ compositions.[1]

1 For a more detailed discussion of the different types of chemical based pharmaceutical patents, see Carlos Correa, Guidelines for the Examination of Pharmaceutical Patents: Developing a Public Health Perspective; WHO, ICTSD and UNCTAD, January 2007, available at http://www.iprsonline.org/resources/docs/Correa_Patentability%20Guidelines.pdf.

Biological medicinal products, such as vaccines, are also usually covered by more than one patent. Typically there will be separate patents covering the protein sequence and/or combinations of proteins of a virus-like particle, followed by subsequent patents covering compositions and formulations (i.e. adjuvants and excipients).

It is worth noting here, that while it is important to identify as many of the different patents as possible that may relate to a particular medicine, some patents are more important than others in terms of whether they will block the procurement or local manufacture of more affordable generic versions.

In the case of non-biological pharmaceutical products, for example, a patent claiming the base chemical compound will likely prevent any use of the same compound. Such a patent would, most likely, prevent any production, importation or sale of formulations or dosage forms that include that base compound. Where there exists only a patent claiming a particular salt or polymorph of the base compound, then it is possible that a local manufacturer may be able to use an alternative salt or polymorph of the compound (provided it meets regulatory requirements). Similarly, if the patent covering the base compound has expired or was never filed in a country, but patents covering formulations of the compound exist, it may still be possible to procure or manufacture alternative formulations. However, only by consulting a local patent lawyer/attorney and/or pharmaceutical chemist and analysing the scope of the claims of a patent will it be possible to determine whether more affordable generic versions can be procured or manufactured without infringing the patent(s).

Chapters 4 and 5 discuss some basic search techniques for identifying the different patents that may exist in relation to a pharmaceutical product.

4

How to find patents on medicines

The remaining chapters of this guide focus on basic tools and techniques for finding patents on pharmaceutical products.

As mentioned in the introduction, obtaining relevant and accurate patent information on medicines, in particular in developing countries, is not without its difficulties. To help overcome some of these difficulties, this guide uses a stepwise approach. The steps, which are summarized in Box 4, will be explained in more detail in this chapter and in Chapter 5. Although this method may not always yield results, it should in most cases help users get a broad sense of the patents that exist in relation to a particular product, and ideally, obtain key information.

Box 4: Summary of steps illustrated in this guide to search for patents on medicines

Step 1

The first step is to identify patents that relate to marketed medicines. One efficient way of obtaining this information is through public databases made available online by the US FDA (the Orange Book) and Health Canada (Patent Register). These databases match some key US and Canadian patent numbers to medicines that are marketed in these countries, but that may also be sold in other countries (see Sections 4.1 and 4.2 and 4.4).

Step 2

Once US and/or Canadian patent(s) number(s) relating to a medicine have been identified, the next step is to obtain the bibliographic details of the patent(s). It is also recommended to obtain the specification(s) of the US and/or Canadian patent(s) found. Having access to the bibliographic data and full details of the identified patents is not only useful for identifying priority data relevant to equivalent patents filed in other countries, but also for finding keywords that may be used to expand the search to other related patents. Section 4.3 describes the steps for obtaining bibliographic data and specifications of US and/or Canadian patents using the EPO's esp@cenet database.

Step 3

As the Orange Book and Health Canada Patent Register do not provide information on all relevant patents relating to a particular medicine, further searches are necessary. Section 4.5 explains how to expand patent searches using various techniques including keywords, applicant/assignee name, patent classification, citations and date range information. This section also introduces readers to the WIPO public database, Patentscope, which offers more search fields than other public databases and provides information on international patent applications, as well as national phase data. The techniques discussed are demonstrated using different national patent office databases.

Step 4

Taking the techniques and information obtained through steps 1 to 3, the next step is to apply them to finding patents in the country of interest. Chapter 5 provides various examples of how to search for patents in other countries that are equivalent to those filed or granted in the United States, Canada or through the PCT. This chapter also provides examples of keyword and applicant/assignee name searching using patent databases of different countries. Finally, as many countries do not provide searchable online databases, Chapter 5 discusses methods for finding patent information from patent office journals.

4.1 Sources linking medicines and patent information

Despite the growing number of databases providing online patent information, one of the major problems when searching for patents on medicines is matching the relevant patent(s) to a particular product.

When inventors/companies discover a new compound or derivative that forms the basis of a medicine, a patent will be filed immediately to protect the invention. This means that the initial patent covering the basic active ingredient will be filed well before the World Health Organization has provided it with an INN or modified INN (INN(M)), which becomes the generic name of the new molecule. As a result, searches using the generic name of a medicine will normally not retrieve the basic patent protecting the active ingredient of a product. It is also not possible to search using a brand name of a product, as patents covering active ingredients are filed before medicines are commercialized and brand names are assigned.

A similar problem usually exists in relation to subsequent patents covering the final formulation of a product. It is common for patent applicants not to include the INN, INN(M) or brand name in the specification, even when it is available.

A useful method and first step for overcoming the problem of identifying which patents may relate to a particular medicine is to use the US FDA's Orange Book and the Health Canada Patent Register. Both the United States and Canada operate a system linking patent data to regulatory approval. As a result the United States and Canadian regulatory agencies maintain public databases providing lists of approved drugs and their related patents.[1]

The workings of the Orange Book and Health Canada Patent Register, and the types of patents listed, are discussed in more detail below.

4.1.2 Introduction of the US FDA Orange Book

As required under US regulatory law (commonly known as the Hatch-Waxman Act), all new drugs that are approved for marketing in the United States have to be listed in the Orange Book. In addition, the company seeking to market a new drug must provide information regarding any relevant patent (including patents owned by third parties) that might be used to protect the medicine for listing in the Orange Book.[2] This information should include the expiry date of those patents. The data must be submitted either with the new drug application (NDA) if the patent has already been issued, within 30 days of the approval of the NDA, or if the concerned patent application is still pending, within 30 days of the issuance of the patent.[3]

The Orange Book requires that patents covering the following subject matter be listed by applicants of a new drug/NDA[4]:

- Active ingredient (the active drug substance, including the polymorphic form used in the NDA)
- Formulation and compositions (the end product for the purpose of human use)
- Method of approved use and treatment
- Product-by-process if the end product is novel and is the subject matter of the NDA

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1 The linking of patents to the regulatory approval of medicines means that regulatory agencies are prevented from granting approval to generic versions of medicines where the originator company has a valid patent listed. Although such linkage systems may aid the transparency of patent information relating to medicines, they can be the subject of misuse and litigation and lead to delays in generic versions entering the market. Countries may want to consider these drawbacks when deciding whether to introduce such linkage. It should be noted that linking patents to regulatory approval of generic medicines is not mandated by TRIPS or any other multilateral agreement.

2 Federal Food, Drug and Cosmetic Act 21 USC §355(b)(1)

3 Federal Food, Drug and Cosmetic Act 21 USC §355(c)(2)

4 Federal Food, Drug and Cosmetic Act 21 C.F.R §314.53(b)(1)

By contrast, patents covering the following subject matter are not permitted to be listed:

- Processes for making the product
- Metabolites
- Intermediate compounds used during the process of making the active ingredient
- Product-by-process patents covering an end product that is not novel and is not the subject matter of the NDA

While regulatory requirements do not prevent the listing of biologicals and their patents (i.e. vaccines), they are rarely entered into the Orange Book.

An electronic version of the Orange Book is available at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm

4.1.3 Introduction of the Health Canada Patent Register

The Patented Medicines (Notice of Compliance) Regulations (PM(NOC) Regulations) govern the types of pharmaceutical patents originator manufacturers may file with a New Drug Submission (NDS) or Supplement to a New Drug Submission (SNDS). It is worth noting here that the regulations stress that originator manufacturers *may* file patents relating to a NDS or SNDS, thereby making patent listing optional.

Relevant patents that the originator would like to have listed should be submitted at the time of filing an NDS or SNDS or within 30 days of issuance of the patent.[5] The patents submitted with an NDS or SNDS are reviewed by the Minister of Health and added to the Health Canada Patent Register if considered relevant. The types of patents that are relevant for listing with an NDA or SNDS are ones claiming:

- An approved medicinal ingredient.[6]

  A medicinal ingredient can be chemical or biological in nature, including the ingredient's chemical equivalents. Therefore, the definition includes claims for different polymorphs of the medicinal ingredient. However, different chemical forms of a medicinal ingredient (e.g. salts, esters, isomers/enantiomers, hydrates or solvates) are not eligible for listing.[7]

5 PM(NOC) Regulations s4(5) and s4(6)

6 PM(NOC) Regulations s4(2)(a)

7 PM(NOC) Regulations s2

- A formulation or dosage form.[8]

  A claim for a formulation means a claim for a substance that is a mixture of medicinal and non-medicinal ingredients in a drug, and which is administered in a particular dosage form.[9]

  A claim for the dosage form means a claim for a delivery system for administering a medicinal ingredient in a drug or a formulation of a drug that includes within its scope that medicinal ingredient of the formulation.[10]

- An approved use of a medical ingredient.[11]

  A claim for the use of a medicinal ingredient means a claim for the use of the medicinal ingredient for the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms.[12]

Patents covering the following subject matter are not eligible for listing on the Health Canada Patent Register:

- Processes for making the product
- Metabolites
- Intermediate compounds used during the process of making the active ingredient
- Different chemical forms of a medicinal ingredient (e.g. salts, esters, isomers/enantiomers, and hydrates or solvates)

Health Canada allows for the listing of biologicals, and unlike the Orange Book, patents relating to some biotech drugs and vaccines are included in the register.

The Health Canada Patent Register can be accessed online at: http://www.patentregister.ca/

8 PM(NOC) Regulations s4(2)(b) and (c)

9 *Supra* n.11

10 *Supra* n.12

11 PM(NOC) Regulations s4(d)

12 *Supra* n.13

4.2 How to find patents listed in the Orange Book and Health Canada Patent Register

4.2.1 Using the Orange Book

Step 1

Enter the URL: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm to access the electronic Orange Book search options as shown in Figure 8.

The electronic Orange Book allows users to search for listed drugs and their related patents through five different options. Unless the relevant NDA application number or patent number is already known, for specific queries, it is suggested users search under the option *Active Ingredient* or *Proprietary Name*.

Step 2

By clicking on one of the search options (shown in Figure 8), the user will be directed to a new page where the relevant term can be entered in the search box. For illustration, the option *Active Ingredient* and the generic name "abacavir" is used in Figure 9. Ensure that the option Rx (Prescription Drug Products) is selected.

Step 3

The search for the active ingredient abacavir should retrieve information relating to marketed forms of the drug (see Figure 10).

Figure 8: US FDA Electronic Orange Book search options

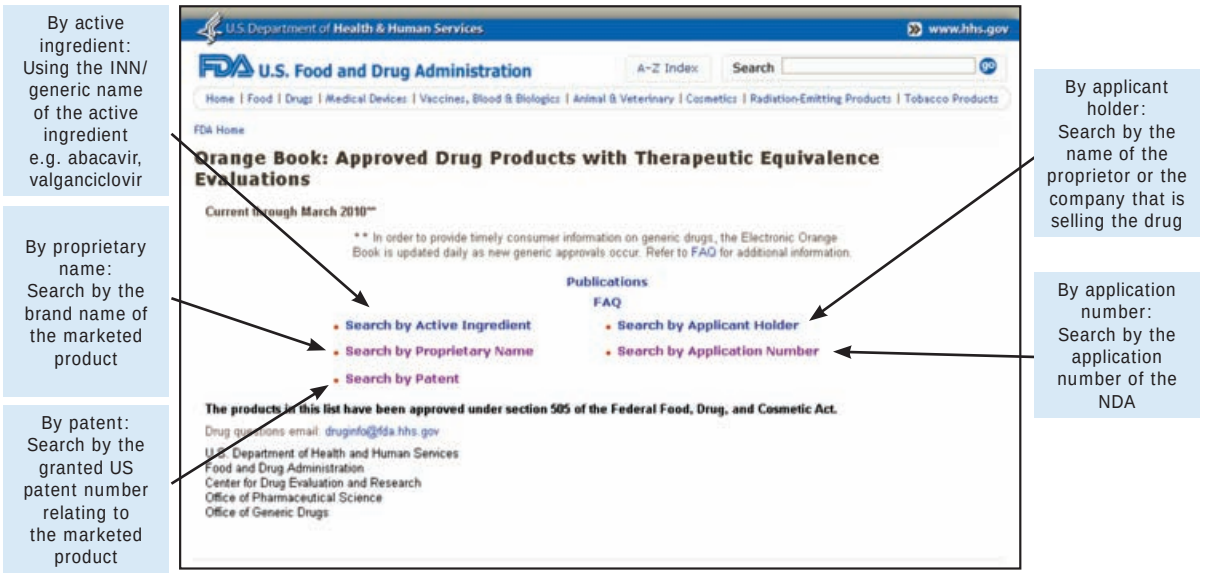


Figure 9: US FDA Electronic Orange Book active ingredient search

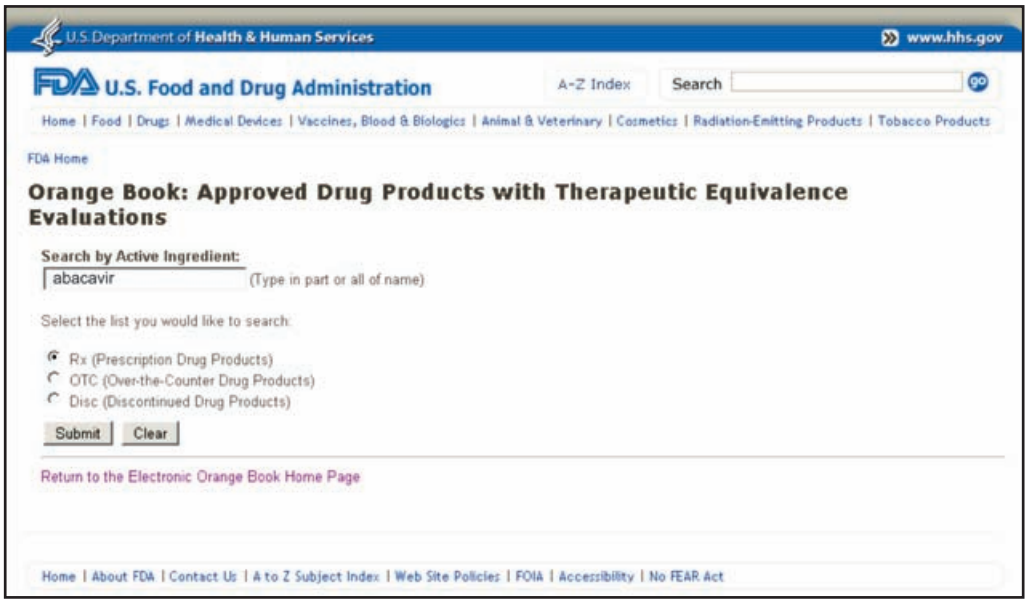


Figure 10: US FDA Electronic Orange Book active ingredient search results

Click on any one of these numbers to access the page linking to patent data for the relevant product

Active Ingredient Search Results from "OB_Rx" table for query on "abacavir."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
N020978		Yes	ABACAVIR SULFATE	SOLUTION; ORAL	EQ 20MG BASE/ML	ZIAGEN	VIIV HLTHCARE
N020977		Yes	ABACAVIR SULFATE	TABLET; ORAL	EQ 300MG BASE	ZIAGEN	VIIV HLTHCARE
N021652		Yes	ABACAVIR SULFATE; LAMIVUDINE	TABLET; ORAL	EQ 600MG BASE;300MG	EPZICOM	VIIV HLTHCARE
N021205		Yes	ABACAVIR SULFATE; LAMIVUDINE; ZIDOVUDINE	TABLET; ORAL	EQ 300MG BASE;150MG;300MG	TRIZIVIR	VIIV HLTHCARE

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through March, 2010
Patent and Generic Drug Product Data Last Updated: May 07, 2010

The information provided includes:

- Appl No: the NDA application number for marketing approval.
- Active ingredient: the active ingredient(s) of the marketed product.
- Dosage form/Route: the route for administering the drug.
- Strength: the amount of active ingredient in the dosage form.
- Proprietary name: the brand name of the product as sold in the United States.
- Applicant: the proprietor of the marketed product.

To access the page that links to the patent data relating to the marketed product(s), click on any one of the numbers provided under the column Appl No.

Note: Although the example shown in Figure 10 lists products combining more than one active ingredient, the patent listings (shown in Figure 12) are likely to only include patents covering each individual active ingredient.

Example: For the product Epzicom® (abacavir sulfate and lamivudine), only individual patents for the two active ingredients will likely be provided, and not any patents covering the combination of the two ingredients. (For discussion and examples of how to conduct further searches for other patents including patents on combinations, see Section 4.5 and Chapter 5.)

Step 4

Having clicked on a link under the column Appl No, as shown in Figure 10, a page repeating information relating to the marketed product will appear.

In addition to the marketing approval information, a link is provided to view patent and exclusivity data for the drug (see Figure 11). Click on the link *View* to proceed to the page containing patent listings.

Step 5

The next page should provide the patent(s) listed by the proprietor in relation to the marketed product.

The key items of information provided are the patent number (US) and the patent expiration date (US) (see Figure 12).

All the patent numbers obtained (see list in Figure 12) should be noted down, as it will be necessary to obtain the patent specification for each one (see Section 4.3) in order to identify its subject matter and relevance.

Figure 11: US FDA Electronic Orange Book patent information link

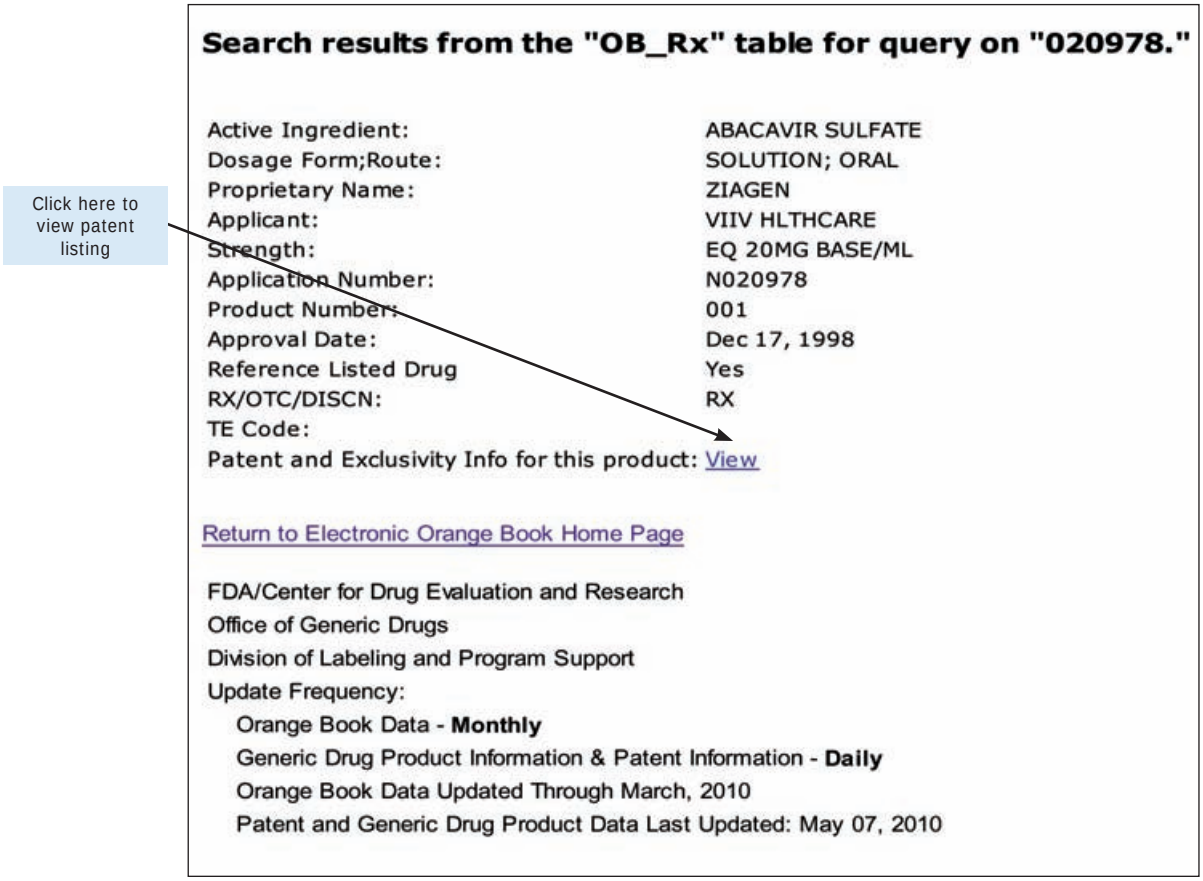
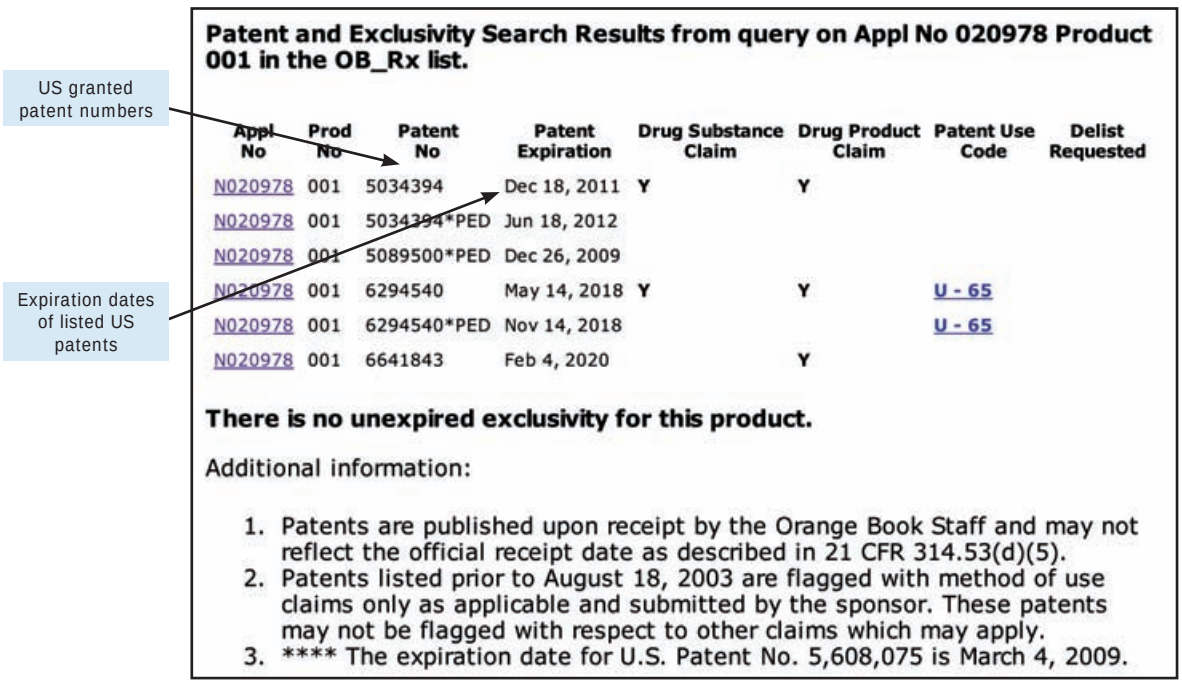


Figure 12: US FDA Electronic Orange Book patent listings for abacavir



4.2.2 Using the Health Canada Patent Register

Step 1

Enter the URL: http://www.patentregister.ca/ to access the Health Canada Patent Register. The front page of the Health Canada website provides users the choice of two languages to work in, English and French. Click on the preferred choice. (For illustration, the examples provided here are in English.)

The user will then access the patent register search page as shown in Figure 13.

Health Canada provides three main search options:

- By medicine (i.e. the generic name of the active ingredient in the drug)
- By brand name
- By patent number

Unlike the Orange Book, the Health Canada Patent Register provides a drop-down menu list of medicines and brand names on the register, from which users can choose the product of interest. Searches may only be conducted using one option at a time (i.e. by *Medicine* or *Brand Name*).

Step 2

The search results will display the brand name, strength of the dosage used in the marketed product, dosage form, DIN (drug identification number) and patent number(s) related to the product (see Figure 14).

All the patent numbers thus obtained (see list in Figure 14) should be noted down, as it will be necessary to obtain the patent specification for each one (see Section 4.3) in order to identify its subject matter and relevance.

To obtain more detailed information such as the filing and expiry date(s) of the listed Canadian patents, users can click on the links provided under the column-heading *DIN* (see Figure 15).

Figure 13: Health Canada Patent Register search page

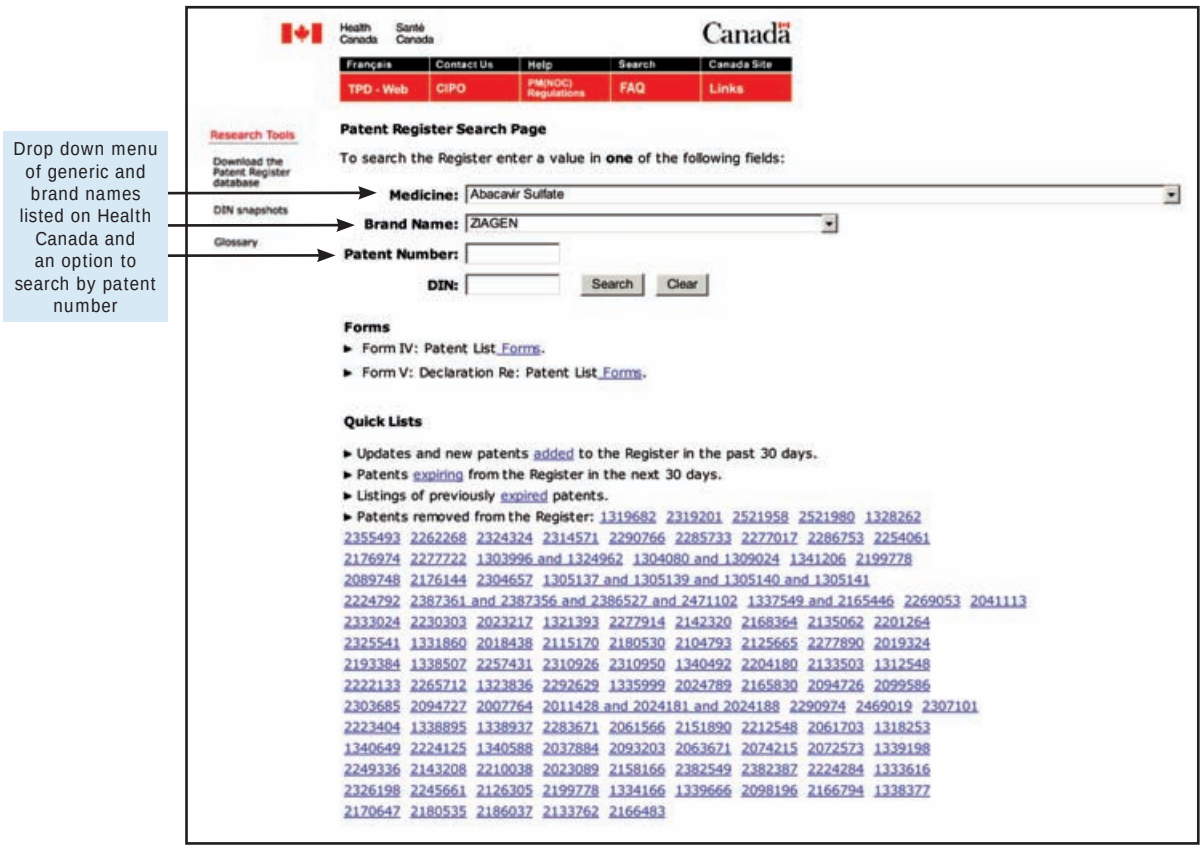


Figure 14: Health Canada Patent Register search results for abacavir

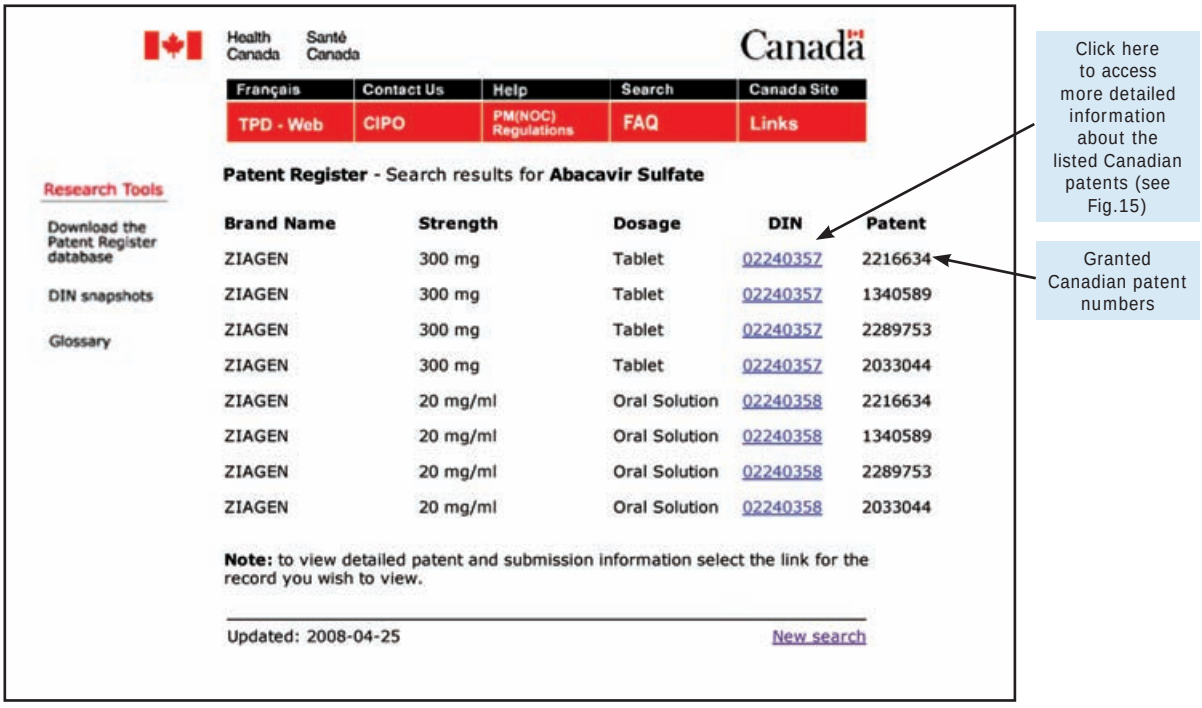
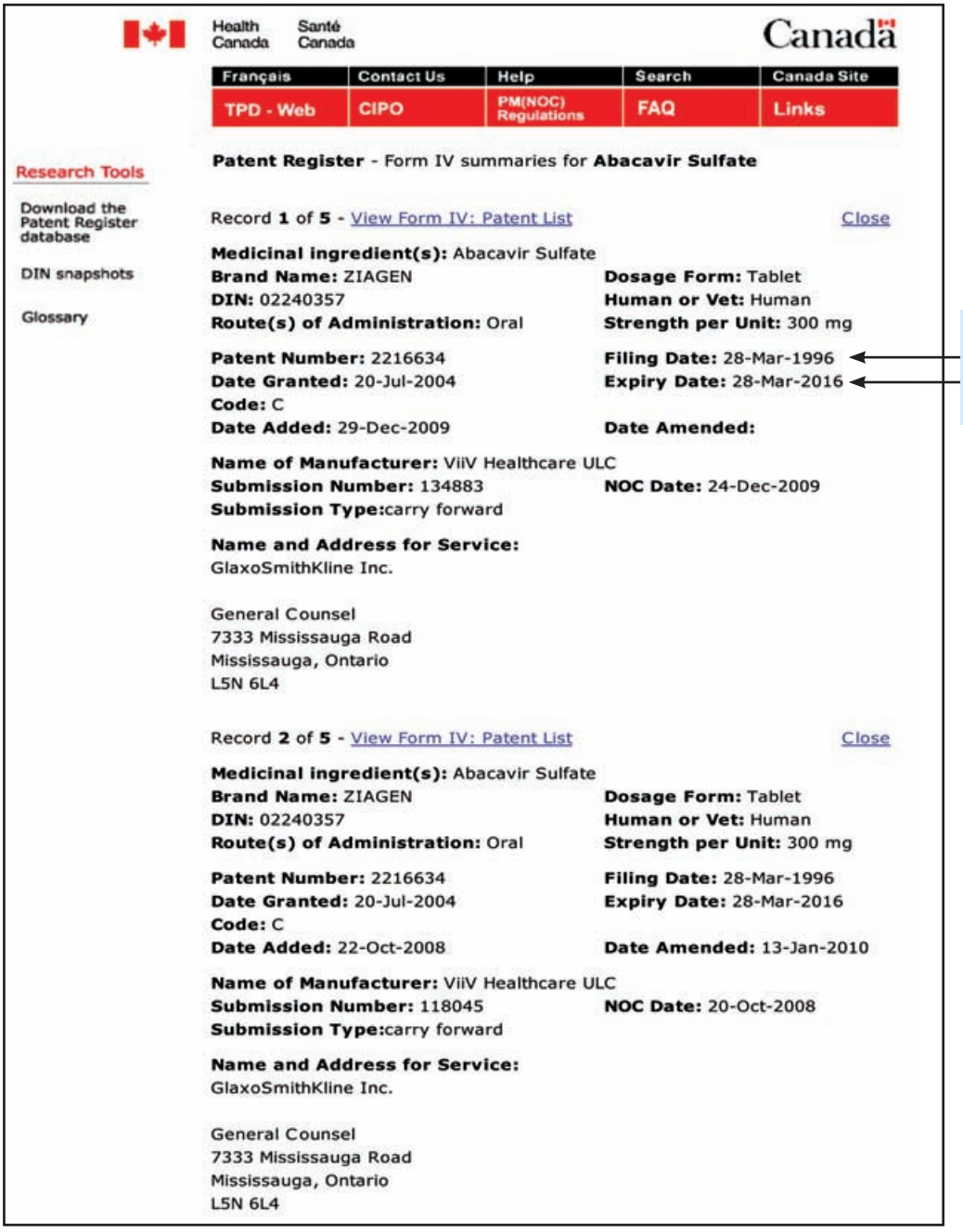


Figure 15: Health Canada Patent Register detailed patent information for abacavir



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TPD - Web | CIPO | PM(NOC) Regulations | FAQ | Links

Research Tools

Download the Patent Register database

DIN snapshots

Glossary

Patent Register - Form IV summaries for **Abacavir Sulfate**

Record **1** of **5** - View Form IV: Patent List Close

Medicinal ingredient(s): Abacavir Sulfate
Brand Name: ZIAGEN
DIN: 02240357
Route(s) of Administration: Oral
Dosage Form: Tablet
Human or Vet: Human
Strength per Unit: 300 mg

Patent Number: 2216634
Date Granted: 20-Jul-2004
Code: C
Date Added: 29-Dec-2009
Filing Date: 28-Mar-1996
Expiry Date: 28-Mar-2016
Date Amended:

Name of Manufacturer: ViiV Healthcare ULC
Submission Number: 134883
Submission Type:carry forward
NOC Date: 24-Dec-2009

Name and Address for Service:
GlaxoSmithKline Inc.

General Counsel
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4

Record **2** of **5** - View Form IV: Patent List Close

Medicinal ingredient(s): Abacavir Sulfate
Brand Name: ZIAGEN
DIN: 02240357
Route(s) of Administration: Oral
Dosage Form: Tablet
Human or Vet: Human
Strength per Unit: 300 mg

Patent Number: 2216634
Date Granted: 20-Jul-2004
Code: C
Date Added: 22-Oct-2008
Filing Date: 28-Mar-1996
Expiry Date: 28-Mar-2016
Date Amended: 13-Jan-2010

Name of Manufacturer: ViiV Healthcare ULC
Submission Number: 118045
Submission Type:carry forward
NOC Date: 20-Oct-2008

Name and Address for Service:
GlaxoSmithKline Inc.

General Counsel
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4

Filing and expiration dates of Canadian patent for abacavir

4.3 Obtaining copies of patent documents listed in the Orange Book and Health Canada Patent Register

Once the patent numbers from the Orange Book and/or Health Canada have been obtained, it is recommended that a full copy of the US and/or Canadian patent document be retrieved. This is so that the subject matter covered by each listed patent can be identified.

Two other key reasons for obtaining copies of the relevant US or Canadian patent(s) before embarking on more expansive searches and locating related patent(s) in other countries are:

- A significant number of patents on medicines claim priority from filings first made in the United States. As will be discussed in Chapter 5, in some cases, matching patents from other countries with those in the Orange Book is made easier when the priority number is known.

  Matching priority data from Canadian patent documents can sometimes be a much simpler process than from US patent documents. This is because priority claims are often based on a continuation, continuation-in-part or provisional application number made in the United States, and not on the actual US patent application number. As continuation, continuation-in-part or provisional application numbers are usually found in the main text of a US patent document, rather than in the bibliographic data on the front page, it can be more time efficient to view the front page of a Canadian patent for the priority data.
- Despite their technical nature, reviewing the body of a patent document and claims of the US and/or Canadian patent can be useful for learning about the product and the science behind it. Adopting this practice can also help in identifying key terms or specific chemical names used by applicants that might be helpful when trying to conduct further patent searches related to the product. This will be discussed in more detail below (see Section 4.5).

The most straightforward way to obtain US and Canadian patent information is through the respective online patent office databases:

- United States Patent and Trademark Office (USPTO): http://patft.uspto.gov/
- Canadian Intellectual Property Office (CIPO): http://brevets-patents.ic.gc.ca/opic-cipo/cpd/eng/introduction.html

Both databases provide a basic search option whereby users can insert the relevant patent number into a field. However, neither allows users to download complete PDF versions of patent documents.

4.3.1 Using esp@cenet to obtain US and Canadian patent documents

To obtain complete PDF versions of patent documents, the patent database of the European Patent Office (EPO), esp@cenet, can be used. Esp@cenet maintains bibliographic data for patents from over 90 countries and regions, including Canada and the United States. The esp@cenet database also allows users to download complete PDF versions of patent documents from a number of countries, including Canada and the United States.

The following steps demonstrate how to download a PDF version of US or Canadian patent document from esp@cenet:

Step 1

Enter the URL: http://ep.espacenet.com/ to access the main page of esp@cenet (see Figure 16).

Click on the option *Number Search* to be directed to the databases and search options.

Step 2

The *Number Search* page is divided into two parts (see Figure 17).

Database

Under the heading *Database*, the user is provided with the option *Select a Patent Database*. The drop-down menu provides the following database options:

- EP esp@cenet—this database enables users to search European patents published by the EPO over the last 24 months. European patent publications older than 24 months should be searched using the Worldwide database.
- Worldwide—allows users to search for published patent information from over 90 countries.
- WIPO—provides access to patent applications published by WIPO in the last 24 months.

For the purpose of searching Canadian and US patents, select the *Worldwide* database.

Figure 16: Front page of esp@cenet

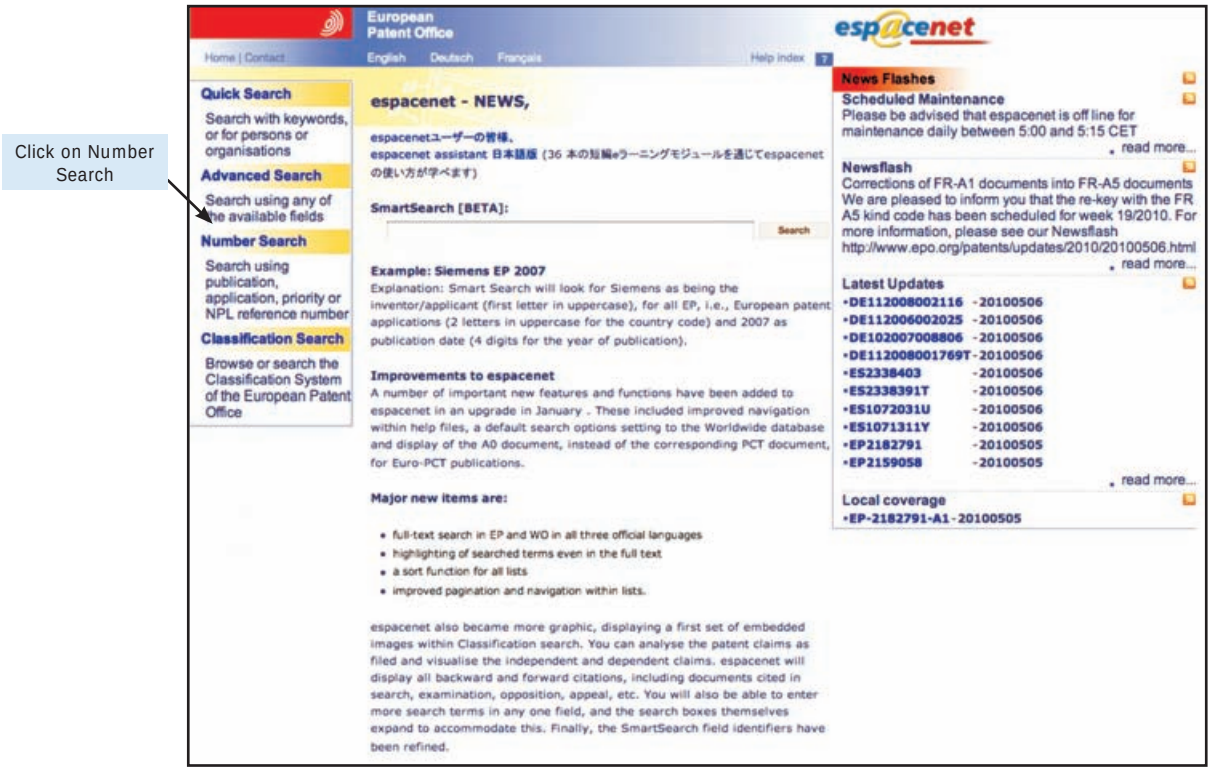
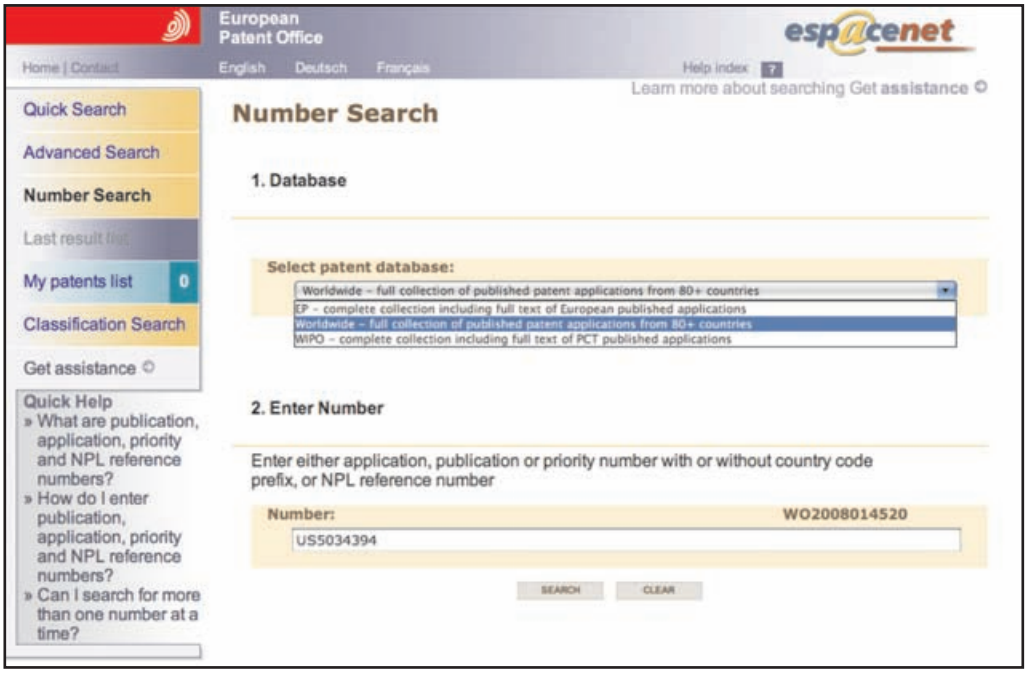


Figure 17: Esp@cenet number search



Enter number

Beneath the option *Select a Patent Database* is a search field marked *Number*. This is the field for entering the number of the patent to be searched.

Insert the patent number(s) obtained through the Orange Book and/or Health Canada in the search field. Ensure there is no space between the country code and patent number. For illustration, the first patent number (US patent No. 5034394) from the Orange Book listing for abacavir shown in Figure 12 is used. This patent number should be entered as US5034394.

The search field accepts application, publication (including granted published patents) or priority numbers, with or without a country code prefix. To retrieve more precise results, it is suggested that users include a country code prefix. It is possible to search up to four publication numbers at a time.

Step 3

The search should return a list of results comprising basic bibliographic data and a link for US patent No.5034394 (see Figure 18).

Click on the title of the patent (in this example *Therapeutic nucleosides)* to access more detailed data and the option for downloading a complete copy of the specification and claims.

Step 4

Esp@cenet should then display a page comprising bibliographic data and a number of other information options relating to US patent No. 5034394 (see Figure 19).

To download the complete patent document for US patent No. 5034394, click on the tab *Original document.*

A prompt may appear asking the user to save the file. However, as this option only downloads the first page of the patent document, press *Cancel* and then click on the link *Save Full Document* as shown in Figure 20. Another prompt will appear requesting a number code to be entered. Enter the number code provided and another window will appear asking the user to *Open* or *Save* the file. Press either option and the complete version of the patent document will be opened/saved (see Figure 21).

Figure 18: Esp@cenet number search result list for US patent No. 5034394

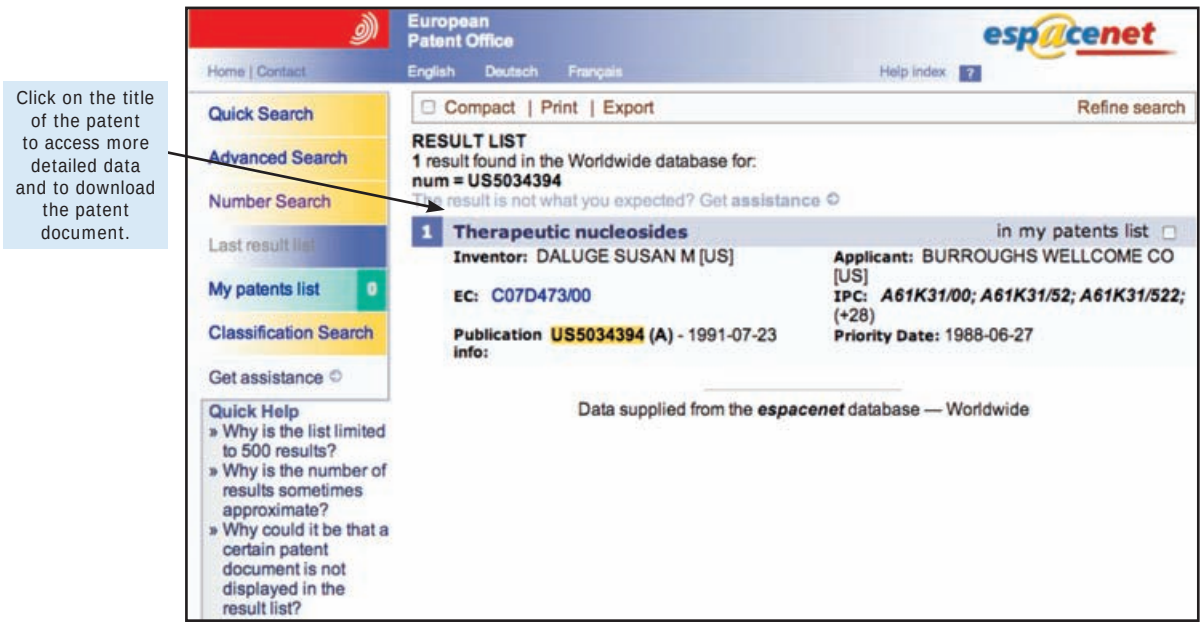


Figure 19: Esp@cenet bibliographic data and patent document download option for US patent No. 5034394

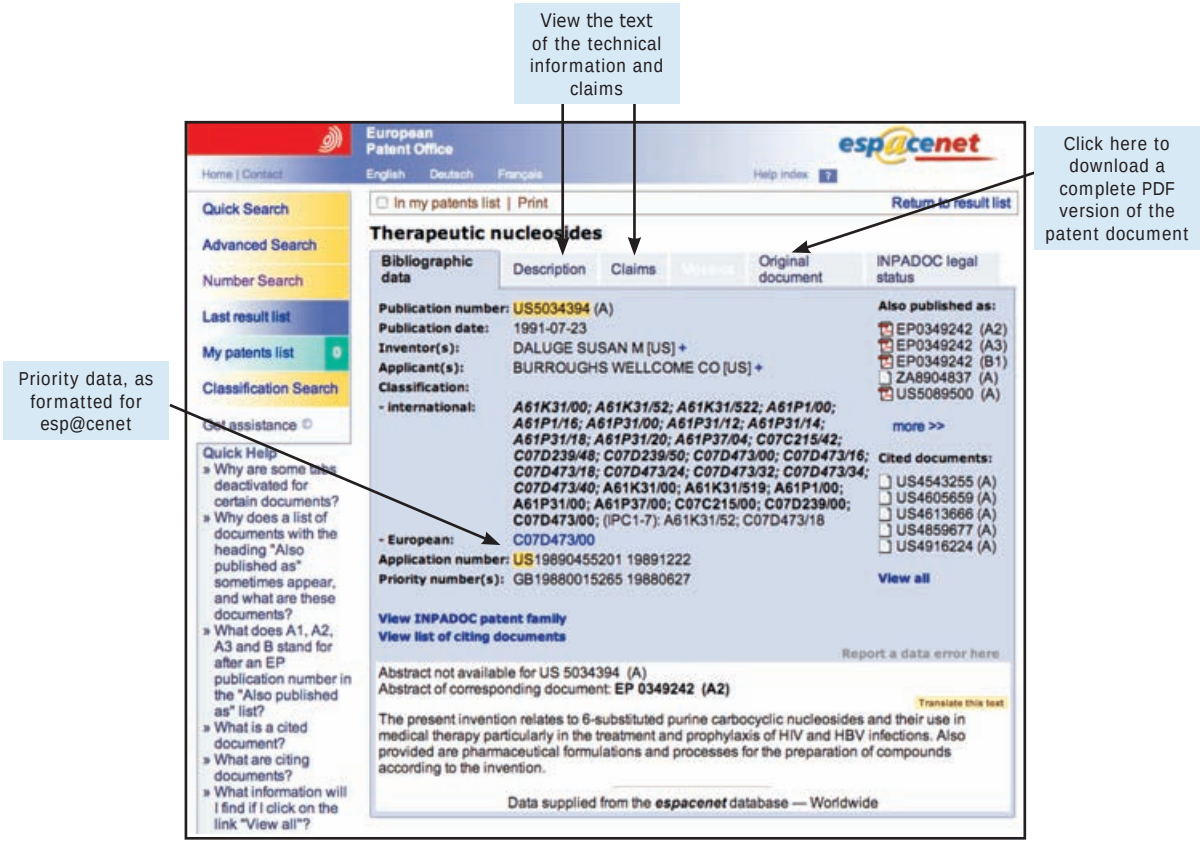
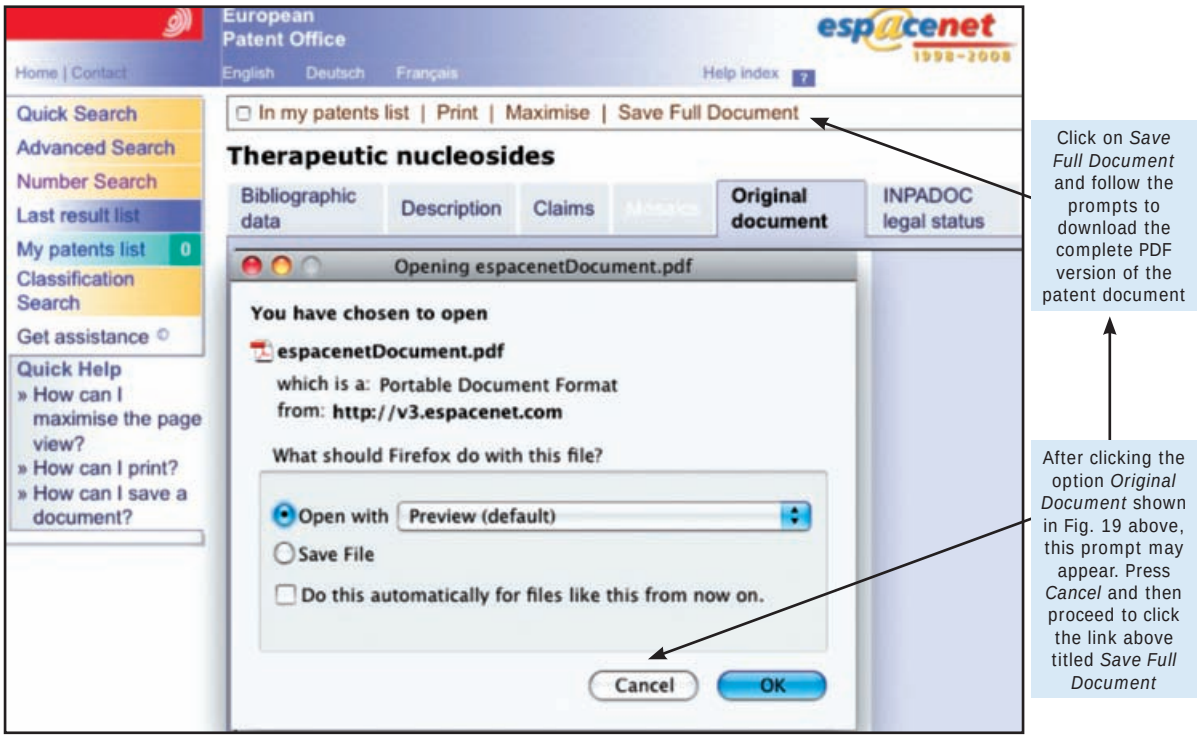


Figure 20: Esp@cenet link to download full PDF version of a patent document



Note: As shown in Figure 19, it is possible to obtain priority information for the patent in view from the bibliographic data.

However, the format of the priority numbering in esp@cenet's bibliographic data is often different from how it is recorded by other national patent offices. As a result, it may be difficult to make a direct match when using other patent office databases or reviewing patent office journals.

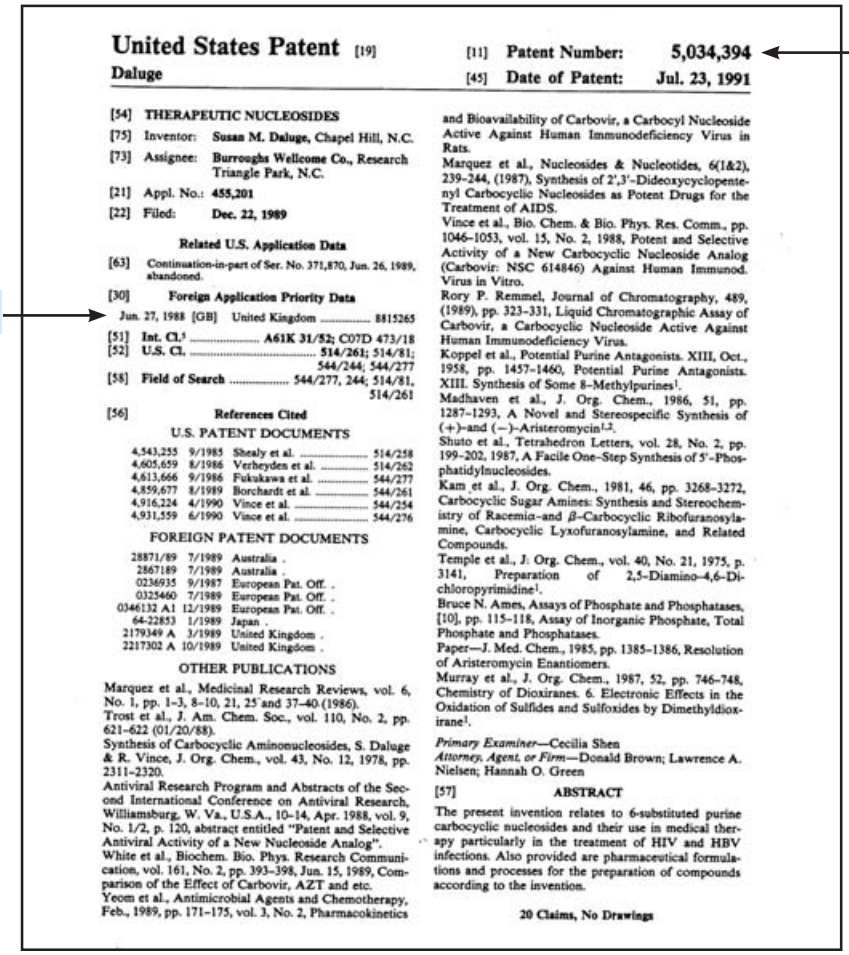
Example: the priority number for US patent No. 5034394 is presented as GB19880015265 in esp@cenet, but is referenced as GB8815265 in other databases. Downloading the original patent document is usually helpful to overcome such differences.

The tabs *Description* and *Claim*, as shown in Figure 19, allow users to review the text of the technical information and claims of the patent in view without having to download the complete document. Where the text and claims are not available in English, esp@cenet will either provide the text of an equivalent patent that is in English, or provide users the option to translate the text.

Once the patent data and complete specification have been obtained, through esp@cenet, for a patent listed in the Orange Book and/or Health Canada, the user should have sufficient information to find related patents in other countries. Methods and techniques for locating equivalent and related patents in other countries are discussed in Chapter 5.

However, before proceeding to Chapter 5 it is important to note that there are limitations to relying solely on the Orange Book and Health Canada to find all potential patents that may impact procurement or local manufacturing decisions. The following sections discuss these limitations and suggest additional search techniques that may be used to fill those gaps.

Figure 21: Front page of the complete patent document for US patent No. 5034394 as downloaded from esp@cenet



United States Patent [19]
Daluge

[11] **Patent Number: 5,034,394**
[45] **Date of Patent: Jul. 23, 1991**

Patent number

[54] **THERAPEUTIC NUCLEOSIDES**

[75] Inventor: **Susan M. Daluge**, Chapel Hill, N.C.

[73] Assignee: **Burroughs Wellcome Co.**, Research Triangle Park, N.C.

[21] Appl. No.: **455,201**

[22] Filed: **Dec. 22, 1989**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 371,870, Jun. 26, 1989, abandoned.

[30] **Foreign Application Priority Data**

Priority data

Jun. 27, 1988 [GB] United Kingdom 8815265

[51] **Int. Cl.**[5] **A61K 31/52; C07D 473/18**
[52] **U.S. Cl.** **514/261; 514/81; 544/244; 544/277**
[58] **Field of Search** 544/277, 244; 514/81, 514/261

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Primary Examiner—Cecilia Shen
Attorney, Agent, or Firm—Donald Brown; Lawrence A. Nielsen; Hannah O. Green

[57] **ABSTRACT**

The present invention relates to 6-substituted purine carbocyclic nucleosides and their use in medical therapy particularly in the treatment of HIV and HBV infections. Also provided are pharmaceutical formulations and processes for the preparation of compounds according to the invention.

20 Claims, No Drawings

4.4 Limitations of relying on the Orange Book and Health Canada Patent Register to identify patents

The Orange Book and the Health Canada Patent Register do not cover all medicines marketed globally, but only products approved and sold in the United States and Canada. As a result a number of medicines and their related patents may be missing. For example, many if not all drugs for neglected diseases such as malaria, sleeping sickness and Chagas disease are unlikely to appear given that there is no commercial market for such products in Canada and the United States. Many fixed-dose combinations of antiretrovirals (ARVs) may also be missing. Although products that fall under the category of biologicals (i.e. vaccines and biotech drugs) are largely missing from the Orange Book, they do appear to be listed on Health Canada. However, there is no certainty that all such products will be included.

Second, only granted patents can be listed on the Orange Book and Health Canada. Therefore, there will be situations where an NDA, NDS or SNDS has been approved, but the related patent is still pending. Such patents will not be included in the Orange Book or Health Canada Patent Register until they are granted. Indeed, it may be the case that the relevant patent will not be granted in the United States or Canada, but nevertheless it may have been filed and granted in another country. An example of such a scenario may be a patent for a new formulation for an already marketed drug.

Third, the FDA's maintenance of the Orange Book is only administrative and does not include ensuring that listings are accurate. Also, there is no obligation on companies to provide information on process patents or on patents for intermediates of a product. As for Health Canada, originators are not under any obligation to list patents with an NDS or SNDS. Even where companies list relevant patents on Health Canada, as for the Orange Book, they are not permitted to list patents covering processes, metabolites and intermediate compounds. Therefore, interested parties seeking information on such patents will need to conduct further searches (see Section 4.5 and Chapter 5). Such information will be particularly important for local manufacturers who may need to identify the relevant process and intermediate patents in order to be sure the processes used do not infringe any patent.

4.5. Search techniques for expanding on Orange Book and Health Canada patent listings

As more and more patent information is becoming digitized in online databases with different data fields, there are a number of techniques that may used to conduct more expansive searches. These techniques can be particularly important for identifying patents covering new formulations and combinations

of existing medicines whose key patents (as identified in the Orange Book or Health Canada) may not have been filed in other countries.

The search techniques discussed here are using:

- Keywords (text queries)
- Applicant(s)/Assignee(s) and inventor name(s)
- Patent classification
- Citations and reference to earlier patents
- Date ranges

It is worth mentioning again, because patent searching is a continually iterative process, the search techniques described here have to be refined throughout the search process for the best results. This means using any one or more of the techniques at a time in different data fields to obtain a broad or narrow set of results. Through this process, the searcher should be able to retrieve patents that may be relevant to a particular medicinal product. However, unlike patents listed in the Orange Book or Health Canada, the patents identified through the above techniques will ultimately have to be evaluated for relevance through an expert analysis of the claims.

4.5.1 Keyword searching

Keyword/text queries are searches using words that may appear in a patent document describing the subject matter, technology or problem that the claimed invention is designed to solve.

A keyword could for example be:

- the initial code name given to a drug during the research stage (e.g. TMC 278 for rilpiverine)
- the INN of an active ingredient (e.g. abacavir)
- a technology used in formulation (e.g. melt-extrusion)
- a disease the invention works against (e.g. malaria or HIV)

Most online patent databases allow for some form of keyword searching. However, databases may vary in terms of the word search operators (Boolean operators) and truncation limiters (wildcards) available for use. Tables 1 and 2 provide examples of the more common operators available in patent databases. However, not all databases offer all these operators. There may also be differences in whether the database permits users to search only the bibliographic data or also the technical information and claims of a patent specification. As many developing country patent office databases do not yet provide online access to the text of complete patent documents, in such cases it will only be possible to search the bibliographic data.

Table 1: Word/Boolean operators found in patent databases

Boolean Operator	Function
AND	Retrieves records containing both the words searched. The use of *AND* provides a narrow search. *Example:* ritonavir AND lopinavir would capture all data/ specifications including both these terms.
ANDNOT (or NOT)	Retrieves records containing only one of the words searched. The use of ANDNOT or NOT serves to provide a narrow search. *Example:* ritonavir ANDNOT lopinavir would capture all data/ specifications including only the term ritonavir but not lopinavir.
OR	Retrieves records containing either of the words searched, or both. The use of *OR* serves to broaden a search. *Example:* ritonavir OR lopinavir would capture all data/ specifications including either ritonavir, or lopinavir, or both ritonavir and lopinavir.
XOR	Retrieves records containing either of the words searched, but not both. Provides for a narrow search. *Example:* ritonavir XOR lopinavir would capture all data/ specifications including either ritonavir or lopinavir, but not both ritonavir and lopinavir.
NEAR	Retrieves records containing all words searched, within a certain number of words of each other. In most databases, *NEAR* is equivalent to *within 10 words*. *Example:* artemisinin NEAR malaria would capture data/ specifications containing both words within a given number of words from each other.
ADJ	Retrieves all words searched that appear next to one another in the order specified or within a prescribed number of words.
WITH	Retrieves all words searched that appear within the same sentence.
SAME	Retrieves all words searched that appear in the same paragraph.

Table 2: Truncation symbols found in patent databases

Truncation symbols	Function
*	Truncation symbols serve to shorten the principal root (or stem) of a word. This technique captures an unlimited or prescribed number of characters in front (left truncation) or behind (right truncation) of the principal root of a word, enabling the user to expand the scope of a search. *Example*: **arte*** would capture all data/documents including artemisinin, artemisinic acid, artemether, artesunate, arteether, artemotil.
?	
$	
%	

In addition to Boolean operators, some databases also permit the use of *Nested Queries or Nesting.* Nested queries use parentheses to specify the order in which the search terms in conjunction with Boolean operators should be interpreted. Words appearing within the parentheses will be read first followed by the terms outside of the parentheses.

Example: (ritonavir OR lopinavir) AND HIV will capture all data/specifications with the words ritonavir and/or lopinavir plus HIV.

Example: artemisinin AND (malaria OR protozoan) will capture all data/specifications with the word artemisinin and either the word malaria or protozoan.

It may also be possible to search for phrases within data/documents by surrounding a group of words in quotation marks. This technique allows users to search for multi-word phrases without having to specify each word separately.

Example: "ritonavir lopinavir"

The effectiveness of a keyword search is often dependent on how much knowledge the searcher has of the relevant subject matter. For example, reviewing the specifications of patents listed on the Orange Book and/or Health Canada, or scientific literature about a particular product, can help improve keyword searches. This is because patents or literature written by the applicant often use particular keywords that may also appear in subsequent patents. Therefore, it is advisable to do as much background reading as possible about a particular medicine before embarking on a keyword search.

As will be shown in the examples at the end of this section and in Chapter 5, carrying out keyword searches is extremely useful and important for two reasons. First, as already mentioned, they can be used to locate patents not listed in the Orange Book or Health Canada. Additionally, such searches can be useful to locate patents equivalent to those listed in the Orange Book or Health Canada in a third country's online patent office database that does not provide an option to search by priority data.

4.5.2 Searching by applicant/assignee and inventor name(s)

Most developing country online patent office databases allow users to search by applicant/assignee or inventor name(s).

This option can be useful when little prior information is available about a particular medicine. For example, searching by applicant/assignee can provide a broad set of results from which a searcher may be able to locate

some relevant patents. Such searches can also provide an understanding of the patenting activities of a specific company.

Alternatively, combining a keyword search with an applicant/assignee or inventor name can narrow a set of results (see examples below).

It is important to note that a single applicant may appear under different names as a result of abbreviation or a misspelling. To help avoid missing important data/specifications, additional searches should make use of the keyword searching techniques discussed above.

4.5.3 Searching by patent classification

As already discussed in Chapter 2 (see Box 2, page 16) all patent documents and claimed inventions are individually classified into technology groups and hierarchical sub-groups according to a standardized system.

Most patent databases allow users to search by classification. However, searching by classification is only useful if accompanied by a keyword, an applicant/assignee or inventor name. Simply searching using a classification code for pharmaceutical products alone would retrieve too many records.

4.5.4 Citation searching

Patent documents will often contain references (citations) to earlier patents or literature disclosed by an applicant as known prior art or found by a patent examiner during examination. For example, patent Y claiming a new formulation of the drug abacavir might cite patent X, which first disclosed the base compound for the drug.

Databases that allow the text of specifications to be searched will usually allow for what are known as *backward* and *forward* citation searching. Using the example above, if patent X is cited by patent Y, this would be known as a backward citation. Patent Y would be considered a forward citation of patent X.

Citation searching can be invaluable for demonstrating the evolving patent landscape of a particular drug. As mentioned above, there are likely to be several patents filed on one medicine and chances are they will cite some of the related patents. Using patent information from the Orange Book (most citations for pharmaceutical patents will be to either US or EU patents) and patent families, it may be possible to conduct citation searches to locate subsequent patents that may claim an improvement. Coupled with keywords and applicant/assignee details, citation searches can be narrowed to meet a desired result. This particular search technique can also help identify alternative terms about a technology for conducting further searches.

One note of caution with citations in patent documents; applicants and examiners may not cite all relevant patents or may cite earlier patents that are irrelevant.

References to earlier patents and literature usually appear in the section of the patent document titled *Background to the Invention* or *Description*. As a result, backward citation searching is only possible if the patent database allows the complete patent document to be searched. For an illustration of citation searching, see example 4.4 on page 63.

4.5.5 Searching by date ranges

As patent documents contain filing dates, publication dates and priority dates, it is possible to search using a range of dates in some databases.

Databases that offer the ability to search by a range of dates may use different operators. Typical operators are: greater than (>), less than (<), greater than or equal to (>=), less than or equal to (<=) and unequal to (<>). WIPO's Patentscope database uses the operator -> to specify a range of dates, e.g. 20000101->20090101 (between 1 January 2000 and 1 January 2009).

Combining a date range alongside another data field, such as applicant name or a keyword, can be helpful when trying to narrow a set of records to a particular period.

The following examples illustrate some of the above techniques using the Patentscope, esp@cenet and the Indian Patent Office databases. These databases have been selected because they allow users to search by one or more of the techniques discussed. WIPO's Patentscope database holds records of PCT applications dating back to 1978 and allows for searches using several search fields. Patentscope also allows users to search the text of PCT patent specifications, download PCT patent specifications, and access useful information concerning national phase data of PCT applications. Esp@cenet offers similar search features to Patentscope, but is not limited only to PCT applications. See also Box 3 (page 22) and **Appendix III** for other online databases that offer free access.

Example 4.1 – Search for "abacavir" using WIPO's Patentscope database

Step 1

To access the structured search page of Patenscope, enter the URL: http://www.wipo.int/pctdb/en/search-struct.jsp

The structured search page provides a choice of 33 data fields that a user can select to form the basis of a search. Patentscope also provides 11 search fields that can be used for any one search.

In the search field next to the data field *Description* (which allows users to search the main body of patent specifications in the database), enter the term *abacavir* (see Figure 22).

As of the time of writing, the search returns a list of 2068 records (see Figure 23).

Figure 22: Patentscope search for "abacavir" using description data field

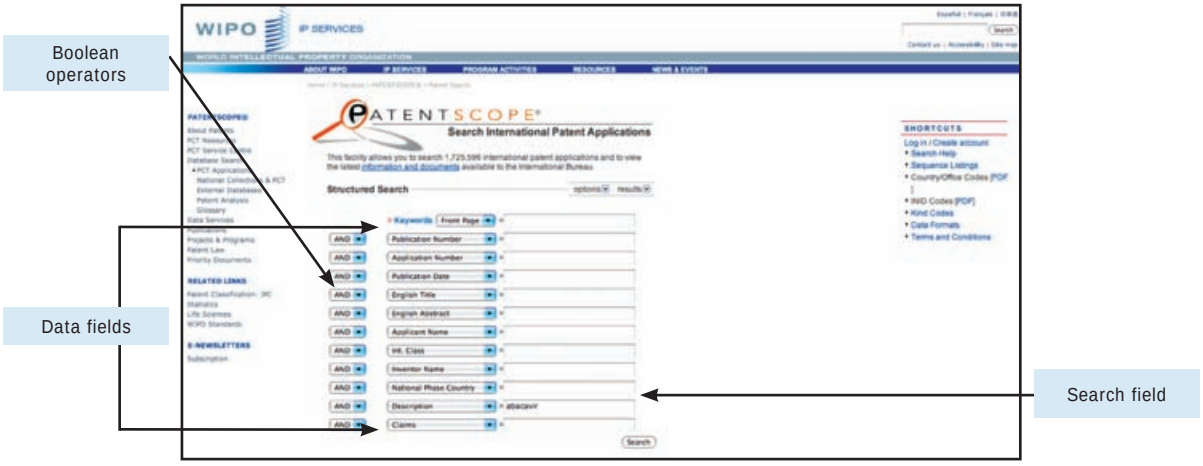
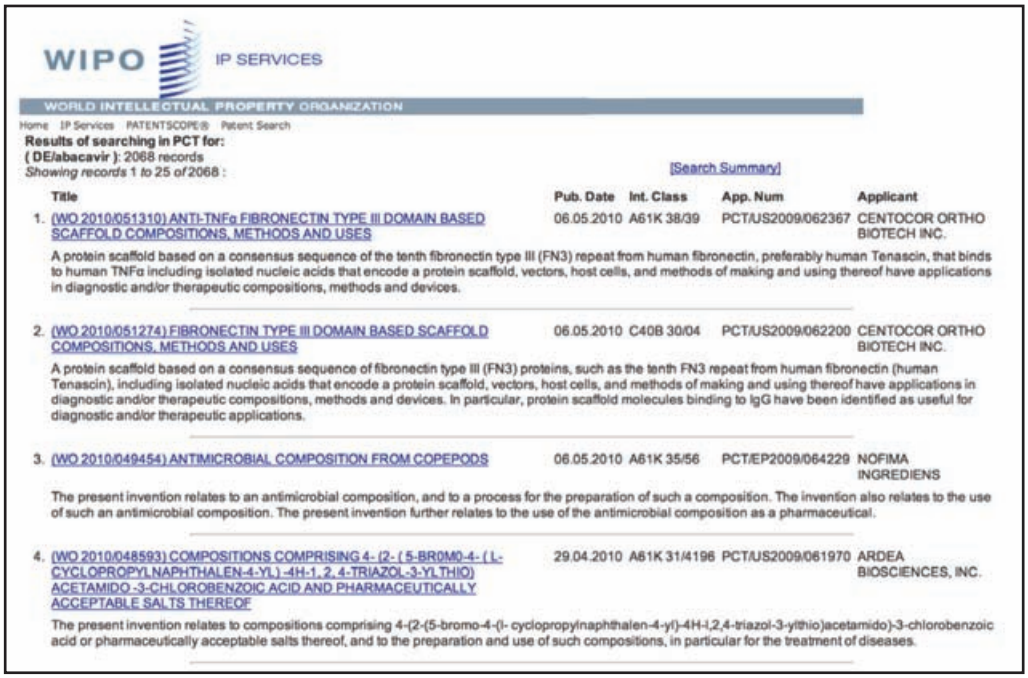


Figure 23: Patentscope search results for "abacavir" using description data field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Results of searching in PCT for:
(DE/abacavir): 2068 records
Showing records 1 to 25 of 2068 :

[Search Summary]

	Title	Pub. Date	Int. Class	App. Num	Applicant
1.	(WO 2010/051310) ANTI-TNFα FIBRONECTIN TYPE III DOMAIN BASED SCAFFOLD COMPOSITIONS, METHODS AND USES	06.05.2010	A61K 38/39	PCT/US2009/062367	CENTOCOR ORTHO BIOTECH INC.
	A protein scaffold based on a consensus sequence of the tenth fibronectin type III (FN3) repeat from human fibronectin, preferably human Tenascin, that binds to human TNFα including isolated nucleic acids that encode a protein scaffold, vectors, host cells, and methods of making and using thereof have applications in diagnostic and/or therapeutic compositions, methods and devices.				
2.	(WO 2010/051274) FIBRONECTIN TYPE III DOMAIN BASED SCAFFOLD COMPOSITIONS, METHODS AND USES	06.05.2010	C40B 30/04	PCT/US2009/062200	CENTOCOR ORTHO BIOTECH INC.
	A protein scaffold based on a consensus sequence of fibronectin type III (FN3) proteins, such as the tenth FN3 repeat from human fibronectin (human Tenascin), including isolated nucleic acids that encode a protein scaffold, vectors, host cells, and methods of making and using thereof have applications in diagnostic and/or therapeutic compositions, methods and devices. In particular, protein scaffold molecules binding to IgG have been identified as useful for diagnostic and/or therapeutic applications.				
3.	(WO 2010/049454) ANTIMICROBIAL COMPOSITION FROM COPEPODS	06.05.2010	A61K 35/56	PCT/EP2009/064229	NOFIMA INGREDIENS
	The present invention relates to an antimicrobial composition, and to a process for the preparation of such a composition. The invention also relates to the use of such an antimicrobial composition. The present invention further relates to the use of the antimicrobial composition as a pharmaceutical.				
4.	(WO 2010/048593) COMPOSITIONS COMPRISING 4- (2- (5-BROMO-4- (L-CYCLOPROPYLNAPHTHALEN-4-YL) -4H-1, 2, 4-TRIAZOL-3-YLTHIO) ACETAMIDO -3-CHLOROBENZOIC ACID AND PHARMACEUTICALLY ACCEPTABLE SALTS THEREOF	29.04.2010	A61K 31/4196	PCT/US2009/061970	ARDEA BIOSCIENCES, INC.
	The present invention relates to compositions comprising 4-(2-(5-bromo-4-(l- cyclopropylnaphthalen-4-yl)-4H-l,2,4-triazol-3-ylthio)acetamido)-3-chlorobenzoic acid or pharmaceutically acceptable salts thereof, and to the preparation and use of such compositions, in particular for the treatment of diseases.				

Step 2

The initial search results provide a broad set of results, but can be narrowed as desired.

For example, by adding an applicant name (e.g. Glaxo), to the original search for the term abacavir (see Figure 24), the search (at the time of writing) returns only 28 results (see Figure 25).

Figure 24: Patentscope search for "abacavir" using description field and applicant name

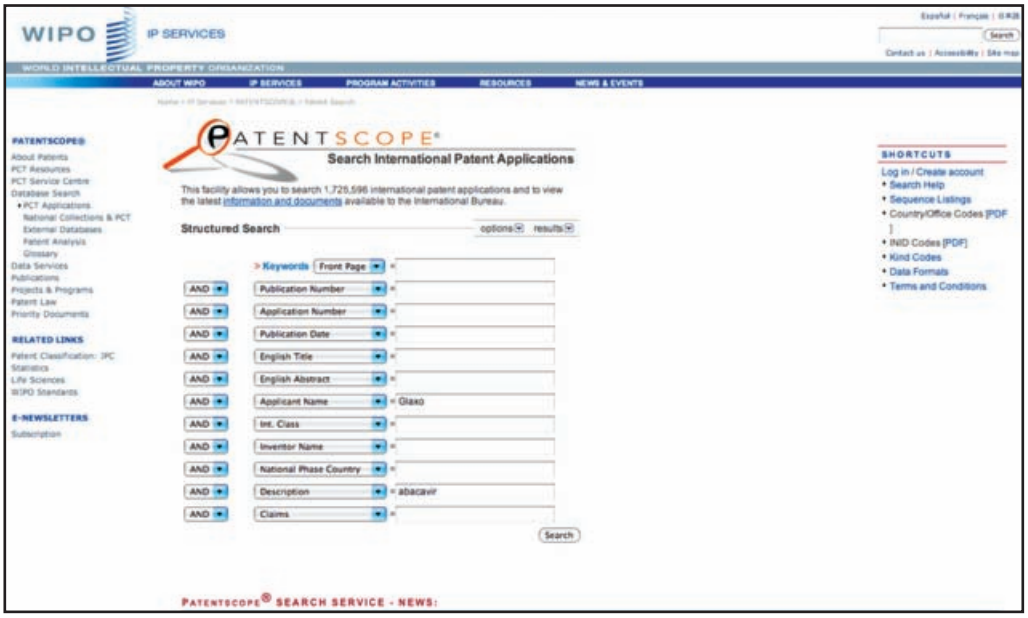
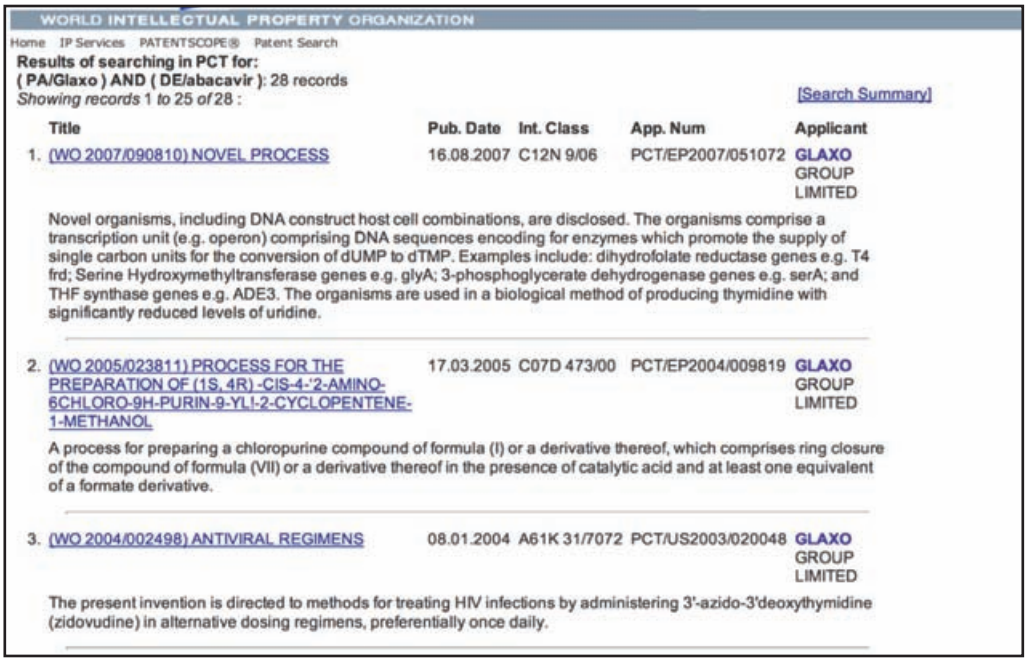


Figure 25: Patentscope search results for "abacavir" using description field and applicant name



Alternatively, it is possible to narrow the results further to target patent documents that include the term abacavir in the claims. This can be done by selecting the data field *Claims* and adding the term abacavir in the associated search field (see Figure 26). The results of the search then narrow to seven hits (see Figure 27).

Figure 26: Patentscope search for "abacavir" using description, claim data fields and applicant name

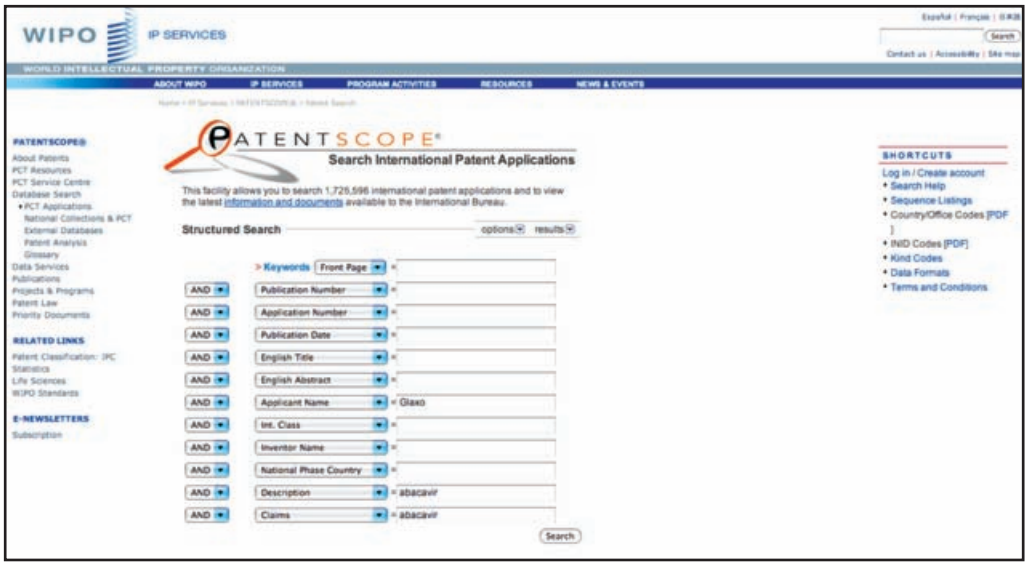
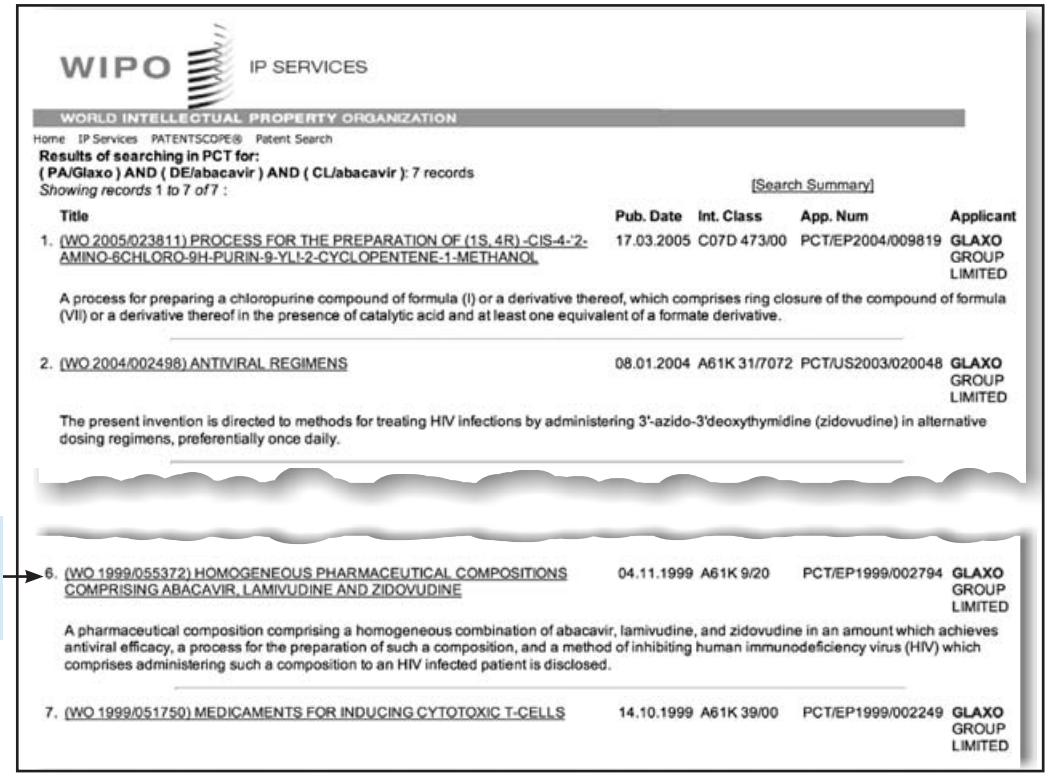


Figure 27: Patentscope search results for "abacavir" using description, claim data fields and applicant name



Click on the link for the application of interest to view further details.

Step 3

After one has clicked on the link for the application of interest, Patentscope takes the user to a page providing the bibliographic data of the patent (see Figure 28). In addition to the bibliographic data, Patentscope provides various tabs where users can access the following information:

- Description—provides access to the text of the patent document, which includes the technical information, examples and other descriptions relating to the claimed invention (see Figure 29).
- Claims—provides access to the original claims filed for the application (see Figure 30). As international applications will be examined by the national patent offices of the countries designated in the application, these claims may be amended or refused entirely.
- National phase—provides details of selected countries where the international application has entered the national phase, and the current status (see Figure 31).

  If the listed country has an online patent database, WIPO may provide a direct link to the national phase application. As will be discussed further in Chapter 5, this can be a useful way to identify if a patent exists in one of the designated states of an international application. However, **only information from countries that make their data available to WIPO will be listed.** Also, as with all databases, the information may not always be up to date.

  Note: Although not mentioned in Patentscope, it is worth noting that the US national phase application of this PCT application was abandoned. As a result, this patent will not be granted in the United States and will not appear in the Orange Book. Also, the national phase application in Canada (application No. 2330391) does not appear among the patents listed for abacavir in Health Canada as shown in Figure 14 above. Furthermore, the application for a European Patent was withdrawn, whereas in New Zealand it was granted as patent No. 507745.
- Notices—provides information on any amendments made to the application after publication.
- Documents—provides access to PDF versions of the international patent document and the related International Search Authority report.

Figure 28: Patentscope bibliographic data for PCT application No. WO/1999/055372

Tabs to view Description, Claims, etc.

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Search result: 6 of 7

(WO/1999/055372) HOMOGENEOUS PHARMACEUTICAL COMPOSITIONS COMPRISING ABACAVIR, LAMIVUDINE AND ZIDOVUDINE

Biblio. Data | Description | Claims | National Phase | Notices | Documents

Latest bibliographic data on file with the International Bureau

Pub. No.: WO/1999/055372
Publication Date: 04.11.1999
Chapter 2 Demand Filed: 02.11.1999
International Application No.: PCT/EP1999/002794
International Filing Date: 26.04.1999

IPC: ***A61K 45/06*** (2006.01), ***A61K 9/20*** (2006.01)

Applicants: **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB) *(All Except US)*.
CURRIE, Robin [US/US]; (US) *(US Only)*.
JAIN, Sunil [IN/US]; (US) *(US Only)*.
WOOD, Allen, Wayne [US/US]; (US) *(US Only)*.

Inventors: **CURRIE, Robin**; (US).
JAIN, Sunil; (US).
WOOD, Allen, Wayne; (US).

Agent: **CRAWLEY, Karen**; Glaxo Wellcome plc, Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB) .

Priority Data: 9809213.3 29.04.1998 GB

Title: HOMOGENEOUS PHARMACEUTICAL COMPOSITIONS COMPRISING ABACAVIR, LAMIVUDINE AND ZIDOVUDINE

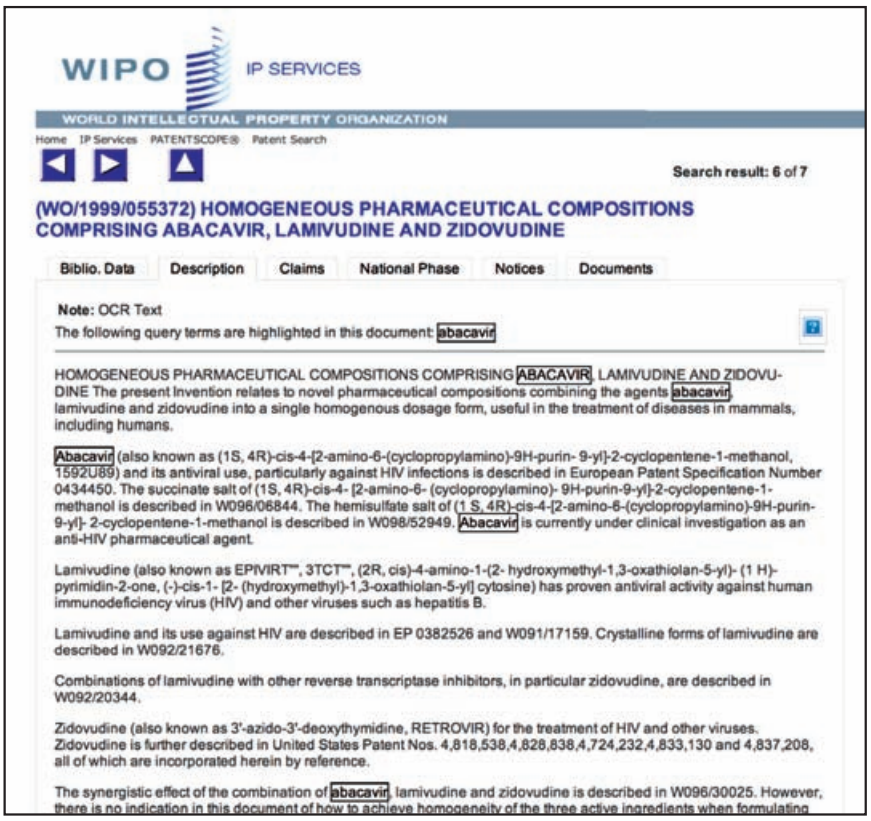
Abstract: A pharmaceutical composition comprising a homogeneous combination of abacavir, lamivudine, and zidovudine in an amount which achieves antiviral efficacy, a process for the preparation of such a composition, and a method of inhibiting human immunodeficiency virus (HIV) which comprises administering such a composition to an HIV infected patient is disclosed.

Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW.
African Regional Intellectual Property Org. (ARIPO) (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW)
Eurasian Patent Organization (EAPO) (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)
European Patent Office (EPO) (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE)
African Intellectual Property Organization (OAPI) (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Publication Language: English (EN)

Filing Language: English (EN)

Figure 29: Patentscope description for PCT application No. WO/1999/055372



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Search result: 6 of 7

(WO/1999/055372) HOMOGENEOUS PHARMACEUTICAL COMPOSITIONS COMPRISING ABACAVIR, LAMIVUDINE AND ZIDOVUDINE

Biblio. Data | Description | Claims | National Phase | Notices | Documents

Note: OCR Text

The following query terms are highlighted in this document: abacavir

HOMOGENEOUS PHARMACEUTICAL COMPOSITIONS COMPRISING ABACAVIR, LAMIVUDINE AND ZIDOVUDINE The present Invention relates to novel pharmaceutical compositions combining the agents abacavir, lamivudine and zidovudine into a single homogenous dosage form, useful in the treatment of diseases in mammals, including humans.

Abacavir (also known as (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin- 9-yl]-2-cyclopentene-1-methanol, 1592U89) and its antiviral use, particularly against HIV infections is described in European Patent Specification Number 0434450. The succinate salt of (1S, 4R)-cis-4- [2-amino-6- (cyclopropylamino)- 9H-purin-9-yl]-2-cyclopentene-1-methanol is described in W096/06844. The hemisulfate salt of (1 S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]- 2-cyclopentene-1-methanol is described in W098/52949. Abacavir is currently under clinical investigation as an anti-HIV pharmaceutical agent.

Lamivudine (also known as EPIVIRT™, 3TCT™, (2R, cis)-4-amino-1-(2- hydroxymethyl-1,3-oxathiolan-5-yl)- (1 H)-pyrimidin-2-one, (-)-cis-1- [2- (hydroxymethyl)-1,3-oxathiolan-5-yl] cytosine) has proven antiviral activity against human immunodeficiency virus (HIV) and other viruses such as hepatitis B.

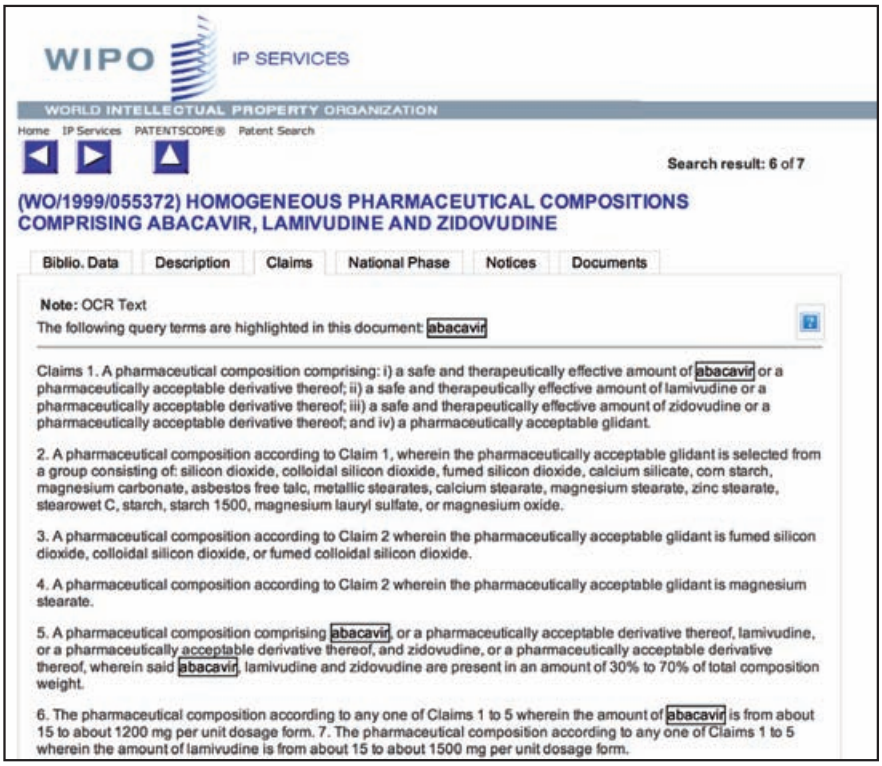
Lamivudine and its use against HIV are described in EP 0382526 and W091/17159. Crystalline forms of lamivudine are described in W092/21676.

Combinations of lamivudine with other reverse transcriptase inhibitors, in particular zidovudine, are described in W092/20344.

Zidovudine (also known as 3'-azido-3'-deoxythymidine, RETROVIR) for the treatment of HIV and other viruses. Zidovudine is further described in United States Patent Nos. 4,818,538,4,828,838,4,724,232,4,833,130 and 4,837,208, all of which are incorporated herein by reference.

The synergistic effect of the combination of abacavir, lamivudine and zidovudine is described in W096/30025. However, there is no indication in this document of how to achieve homogeneity of the three active ingredients when formulating

Figure 30: Patentscope claims for PCT application No. WO/1999/055372



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Search result: 6 of 7

(WO/1999/055372) HOMOGENEOUS PHARMACEUTICAL COMPOSITIONS COMPRISING ABACAVIR, LAMIVUDINE AND ZIDOVUDINE

Biblio. Data | Description | Claims | National Phase | Notices | Documents

Note: OCR Text

The following query terms are highlighted in this document: abacavir

Claims 1. A pharmaceutical composition comprising: i) a safe and therapeutically effective amount of abacavir or a pharmaceutically acceptable derivative thereof; ii) a safe and therapeutically effective amount of lamivudine or a pharmaceutically acceptable derivative thereof; iii) a safe and therapeutically effective amount of zidovudine or a pharmaceutically acceptable derivative thereof; and iv) a pharmaceutically acceptable glidant.

2. A pharmaceutical composition according to Claim 1, wherein the pharmaceutically acceptable glidant is selected from a group consisting of: silicon dioxide, colloidal silicon dioxide, fumed silicon dioxide, calcium silicate, corn starch, magnesium carbonate, asbestos free talc, metallic stearates, calcium stearate, magnesium stearate, zinc stearate, stearowet C, starch, starch 1500, magnesium lauryl sulfate, or magnesium oxide.

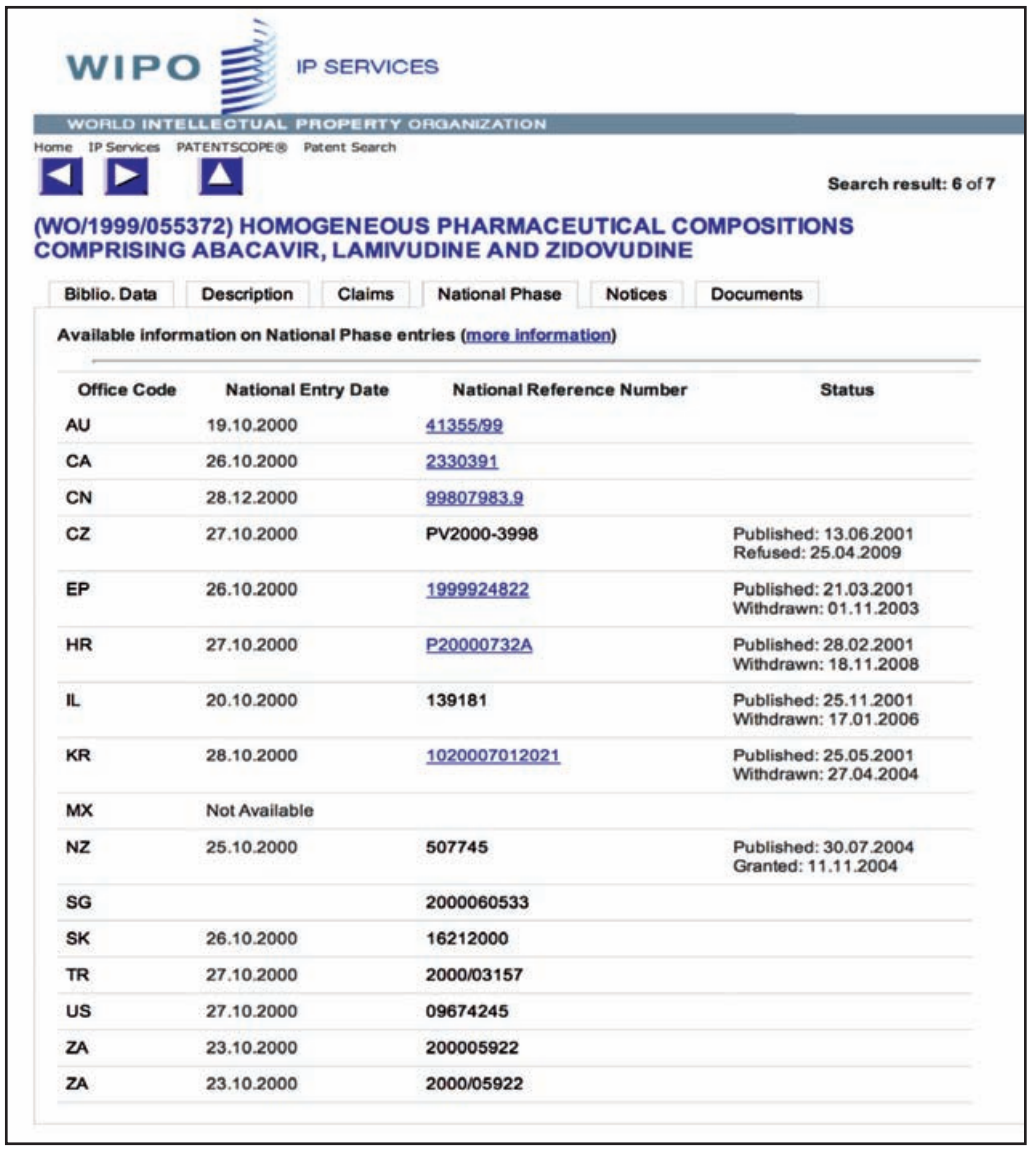
3. A pharmaceutical composition according to Claim 2 wherein the pharmaceutically acceptable glidant is fumed silicon dioxide, colloidal silicon dioxide, or fumed colloidal silicon dioxide.

4. A pharmaceutical composition according to Claim 2 wherein the pharmaceutically acceptable glidant is magnesium stearate.

5. A pharmaceutical composition comprising abacavir, or a pharmaceutically acceptable derivative thereof, lamivudine, or a pharmaceutically acceptable derivative thereof, and zidovudine, or a pharmaceutically acceptable derivative thereof, wherein said abacavir, lamivudine and zidovudine are present in an amount of 30% to 70% of total composition weight.

6. The pharmaceutical composition according to any one of Claims 1 to 5 wherein the amount of abacavir is from about 15 to about 1200 mg per unit dosage form. 7. The pharmaceutical composition according to any one of Claims 1 to 5 wherein the amount of lamivudine is from about 15 to about 1500 mg per unit dosage form.

Figure 31: Patentscope national phase data for PCT application No. WO/1999/055372



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Search result: 6 of 7

(WO/1999/055372) HOMOGENEOUS PHARMACEUTICAL COMPOSITIONS COMPRISING ABACAVIR, LAMIVUDINE AND ZIDOVUDINE

Biblio. Data | Description | Claims | National Phase | Notices | Documents

Available information on National Phase entries (more information)

Office Code	National Entry Date	National Reference Number	Status
AU	19.10.2000	41355/99	
CA	26.10.2000	2330391	
CN	28.12.2000	99807983.9	
CZ	27.10.2000	PV2000-3998	Published: 13.06.2001 Refused: 25.04.2009
EP	26.10.2000	1999924822	Published: 21.03.2001 Withdrawn: 01.11.2003
HR	27.10.2000	P20000732A	Published: 28.02.2001 Withdrawn: 18.11.2008
IL	20.10.2000	139181	Published: 25.11.2001 Withdrawn: 17.01.2006
KR	28.10.2000	1020007012021	Published: 25.05.2001 Withdrawn: 27.04.2004
MX	Not Available		
NZ	25.10.2000	507745	Published: 30.07.2004 Granted: 11.11.2004
SG		2000060533	
SK	26.10.2000	16212000	
TR	27.10.2000	2000/03157	
US	27.10.2000	09674245	
ZA	23.10.2000	200005922	
ZA	23.10.2000	2000/05922	

Example 4.2 – Search for patent applications using "HIV protease" or applicant name "Abbott" in the Indian Patent Office online database

Step 1

Enter the following URL to access the Indian Patent Office online database: http://ipindia.nic.in/ipirs/patentsearch.htm

Select the option *Published Patent Applications* which appears in the left-hand side of the screen. (NB: The Indian Patent Office provides a separate option for searching granted patents. For a discussion on how to search for granted patents in India, see Chapter 5).

After clicking the option *Published Patent Applications,* two further options will appear, one for a *Quick Search*, the other for an *Advanced Search*.

The *Quick Search* only allows users to search one search field at a time, e.g. either *Applicant Name* or *Abstract* or *Journal Number*.

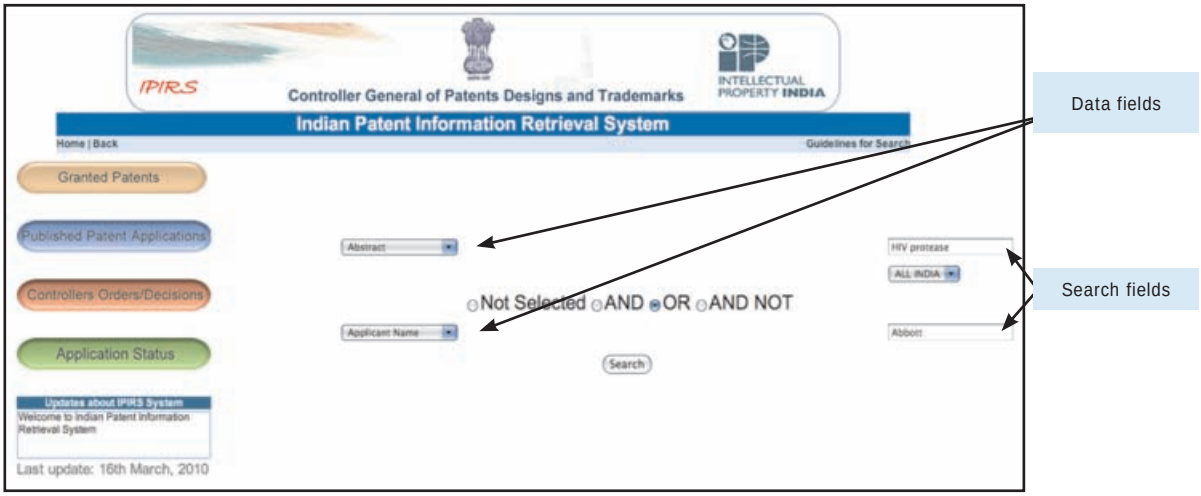
For this example, the option *Advanced Search* is used. The Advanced Search option provides eight data fields and two search fields for searching. The Boolean operators available are *AND*, *OR* and *AND NOT*. Under the option *Location* users have the option to search applications filed with the four branches of the IPO or by a specific branch (i.e. Chennai, Delhi, Kolkata and Mumbai).

Select one of the data fields from the drop-down menu. For this example the data field *Abstract* is chosen. Enter the words *HIV Protease* in the opposite search field.

To conduct a broad search, select the Boolean operator *OR*.

From the second of the two data fields, select the option *Applicant Name.* Insert the name *Abbott* in the search field (see Figure 32).

Figure 32: Indian Patent Office search for "HIV protease" or applicant name "Abbott"



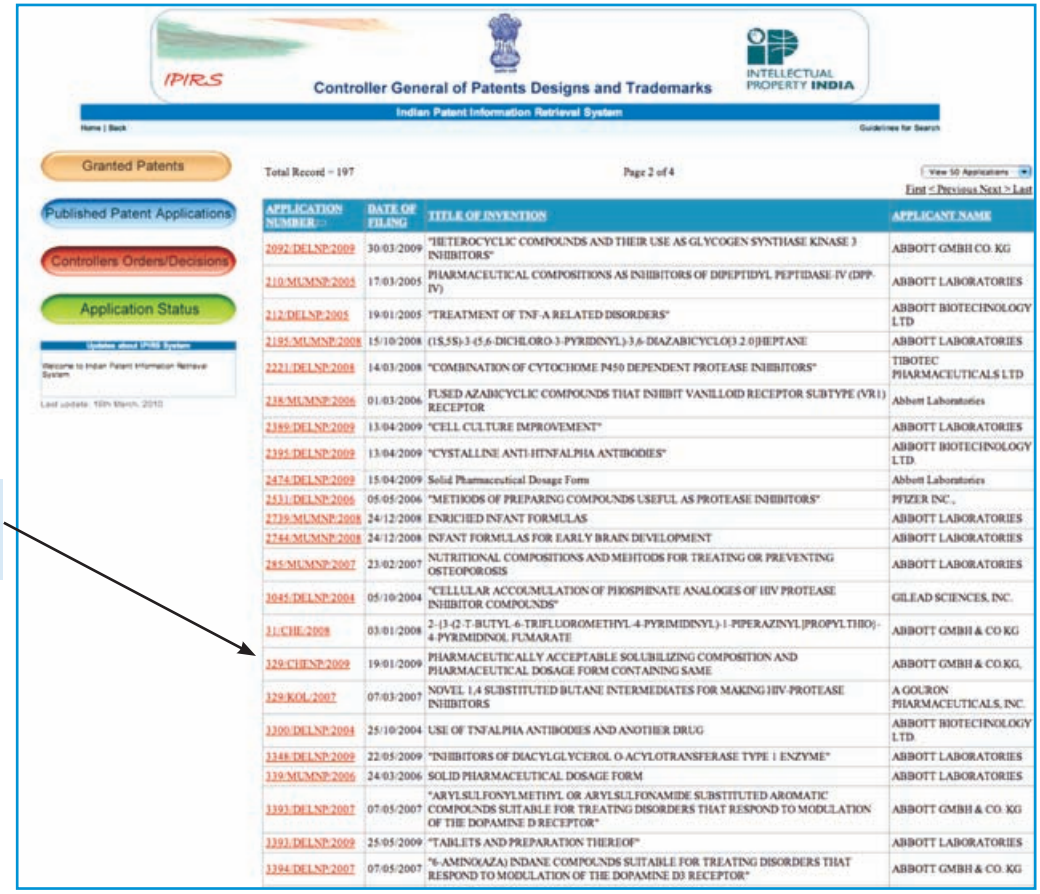
Step 2

The search should return all patent publications that contain the words *HIV Protease* within the abstract or the applicant name Abbott (see Figure 33).

Given the general nature of the words *HIV Protease* and use of the Boolean operator *OR*, the search returns a broad set of results—197 in this case (see Figure 33). As the Indian Patent Office database only provides a relatively limited number of search and data fields, conducting broad searches may be necessary to capture the patents of interest.

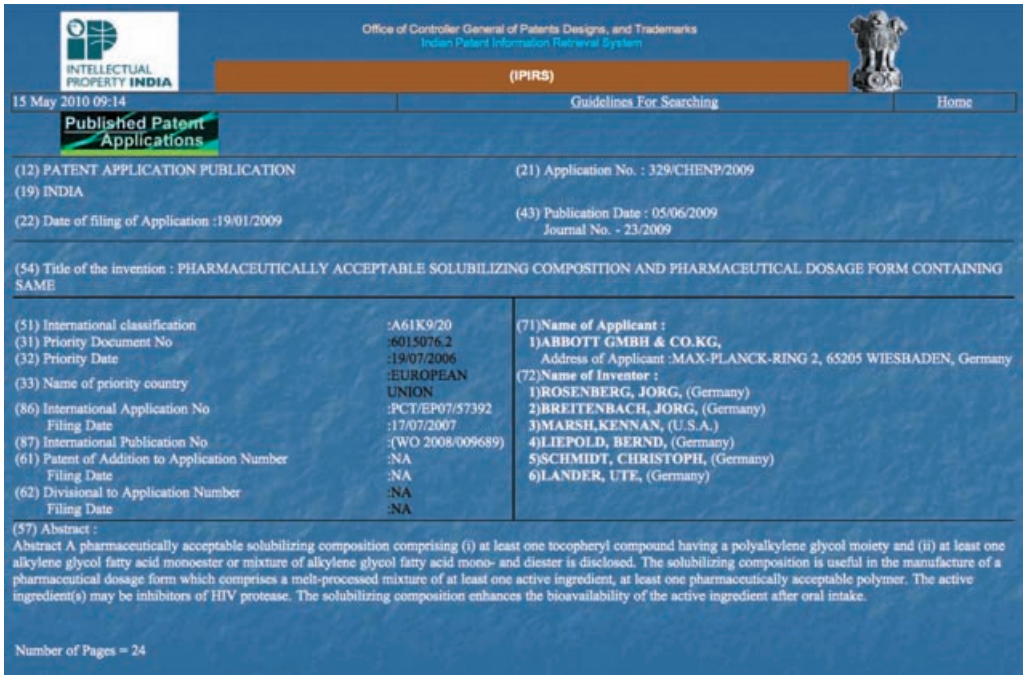
To view the bibliographic details of the patents listed, click on the application number, as shown in Figure 33. The bibliographic details of the application will be presented as shown in Figure 34.[13]

Figure 33: Indian Patent Office search results for "HIV Protease" or applicant "Abbott"



13 As of this writing, the Indian Patent Office database does not provide the option to view the full specification of a published application. Copies of patent applications, published 18 months after the priority date, can be requested from the relevant patent office branch where the application was filed, on payment of an official fee. In the case of the example provided in Figure 34, as the application was filed with the Chennai branch, any request for the specification must be made to that office.

Figure 34: Indian Patent Office publication of application No. 329/CHENP/2009



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Indian Patent Information Retrieval System

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Published Patent Applications

(12) PATENT APPLICATION PUBLICATION
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Journal No. - 23/2009

(54) Title of the invention : PHARMACEUTICALLY ACCEPTABLE SOLUBILIZING COMPOSITION AND PHARMACEUTICAL DOSAGE FORM CONTAINING SAME

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Filing Date	:NA
(62) Divisional to Application Number	:NA
Filing Date	:NA

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(57) Abstract :
Abstract A pharmaceutically acceptable solubilizing composition comprising (i) at least one tocopheryl compound having a polyalkylene glycol moiety and (ii) at least one alkylene glycol fatty acid monoester or mixture of alkylene glycol fatty acid mono- and diester is disclosed. The solubilizing composition is useful in the manufacture of a pharmaceutical dosage form which comprises a melt-processed mixture of at least one active ingredient, at least one pharmaceutically acceptable polymer. The active ingredient(s) may be inhibitors of HIV protease. The solubilizing composition enhances the bioavailability of the active ingredient after oral intake.

Number of Pages = 24

Example 4.3 – Search using IPC classification code A61P 33/18 for HIV and applicant name "Tibotec" using esp@cenet database

Step 1

Enter the URL: http://ep.espacenet.com/ to access the front page of esp@cenet.

Click on the option *Advanced Search* to access the database search options (see Figure 35).

Select *Worldwide* for the patent database. Enter the applicant name (i.e. Tibotec) in the search field next to the data field marked *Applicant(s)*. In the search field next to the data field *International Patent Classification (IPC)*, insert the IPC code A61P33/18 for HIV (see Figure 36).

Figure 35: Front page of esp@cenet database

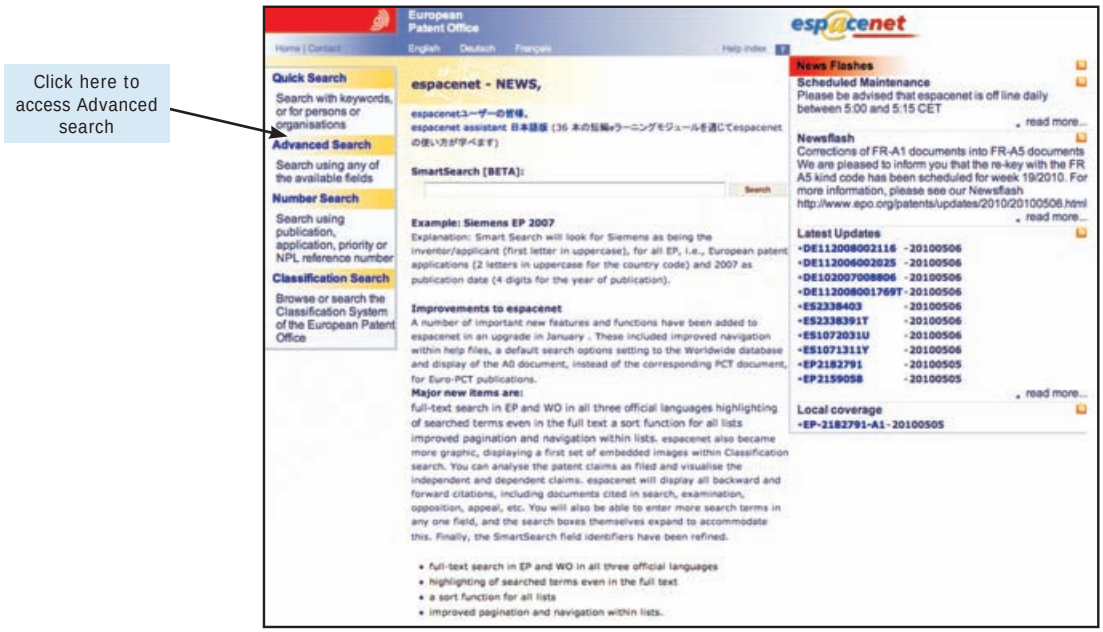
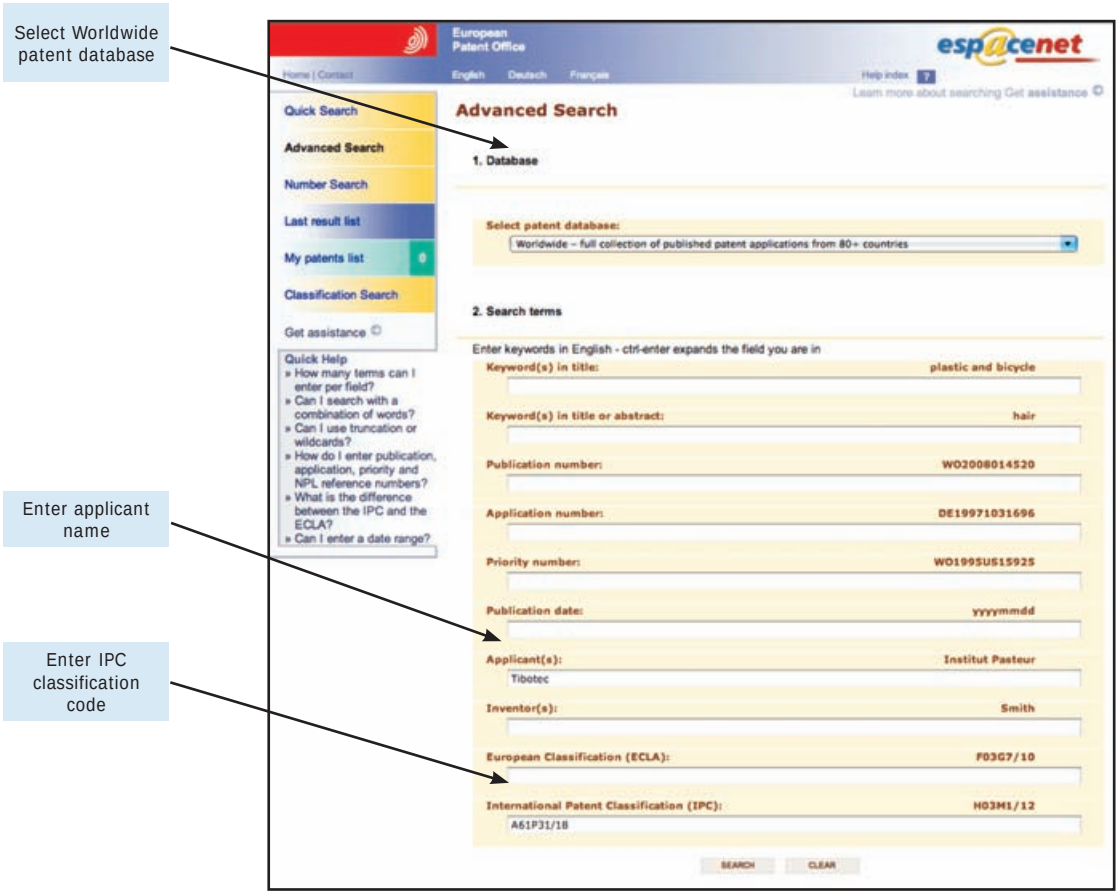


Figure 36: Esp@cenet advanced search for IPC classification code "A61P31/18" and applicant name "Tibotec"



Step 2

The search will retrieve all patents available in esp@cenet in the name of Tibotec with the IPC classification code for chemical compounds with therapeutic activity relating to HIV (see Figure 37).

The bibliographic data, complete patent documents (where available) and patent family data can be viewed by clicking on the title of a particular patent (using the steps described in Section 4.3 of this guide).

Searching by *sub-class* and *Applicant name* is useful for obtaining broad coverage of a company's patent portfolio in a particular therapeutic class.

Example 4.4 – Citation search using WIPO's Patentscope database

Step 1

Select a patent number for a product from the Orange Book, using the steps described in Section 4.2.1 (Figures 8-12).

For the purpose of this example, US patent No. 5935946 for the active ingredient tenofovir disoproxil fumarate is used (see Figure 38).

Proceed to the structured search page of WIPO's Patentscope database, as demonstrated in example 4.1 (Figure 22).

Insert the number 5935946 in the search field next to the data field *Description* (see Figure 39). As mentioned above, citations to earlier patents appear only in the patent document itself. For this reason, the search has to be conducted using the data field *Description*.

Step 2

Figure 40 shows international patent applications citing US patent No. 5935946.

Results 3 and 4 of the search show two applications by Gilead Sciences that appear to cover a combination of products. Neither of these patents features in the Orange Book listings shown in Figure 38.

By clicking on the title and selecting the tab *Description,* users can review the body of the specification and the earlier cited patents, which will be highlighted in the text. As Figure 41 shows, PCT application No. WO 2004/064845 cites US patent No. 5935946 and other relevant patents that may not be listed in the Orange Book (e.g. US patent No. 6069249).

As will be discussed further in Chapter 5, once the information from an international patent has been found there are various methods for identifying whether similar or related patents exist in a country of interest.

Figure 37: Esp@cenet advanced search results for IPC classification code "A61P31/18" and applicant name "Tibotec"

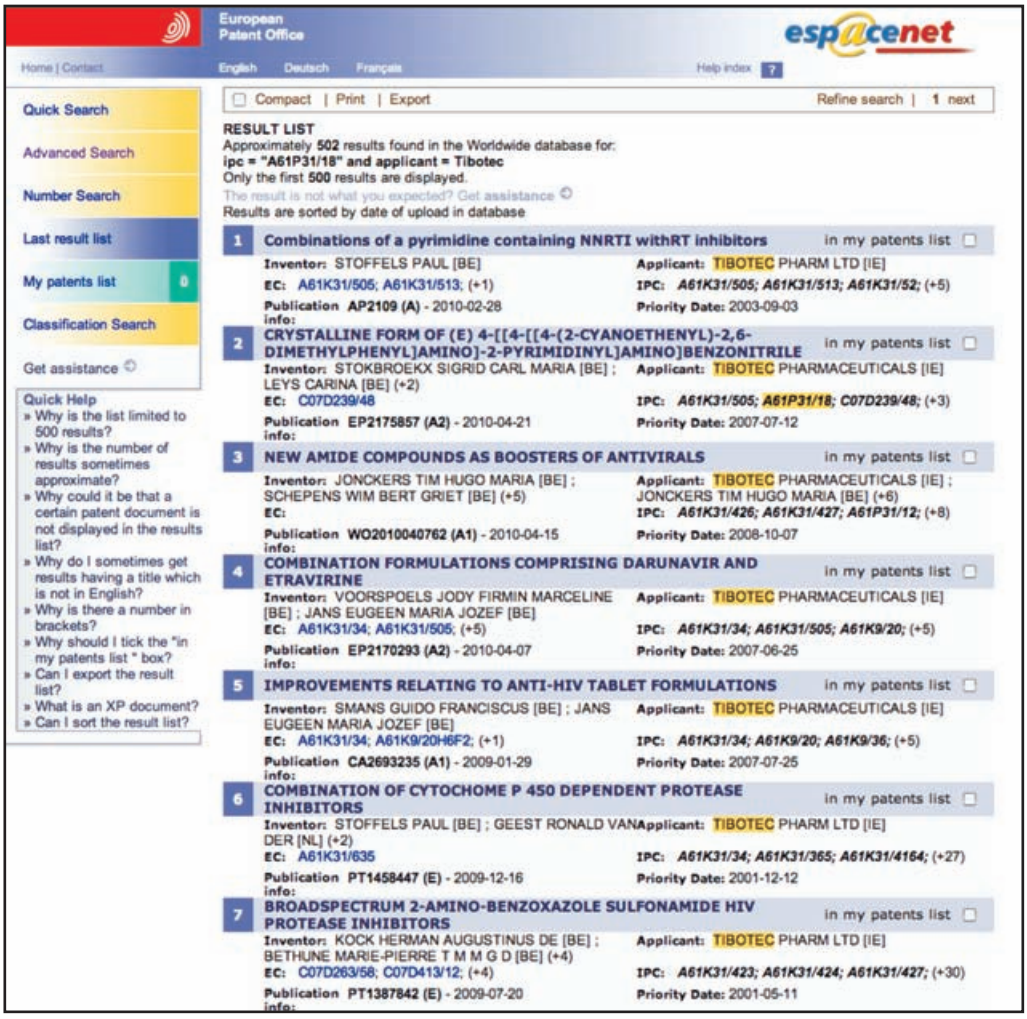


Figure 38: Orange Book patent listings for tenofovir disoproxil fumarate

Figure 39: Patentscope citation search for US patent No. 5935946

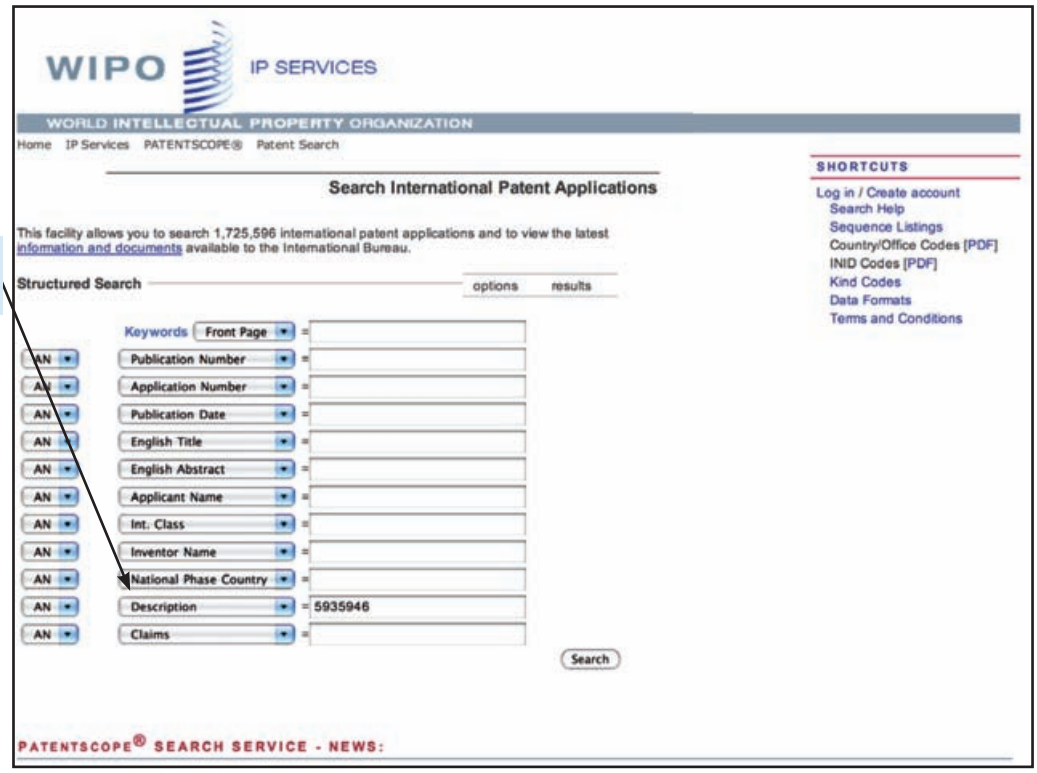
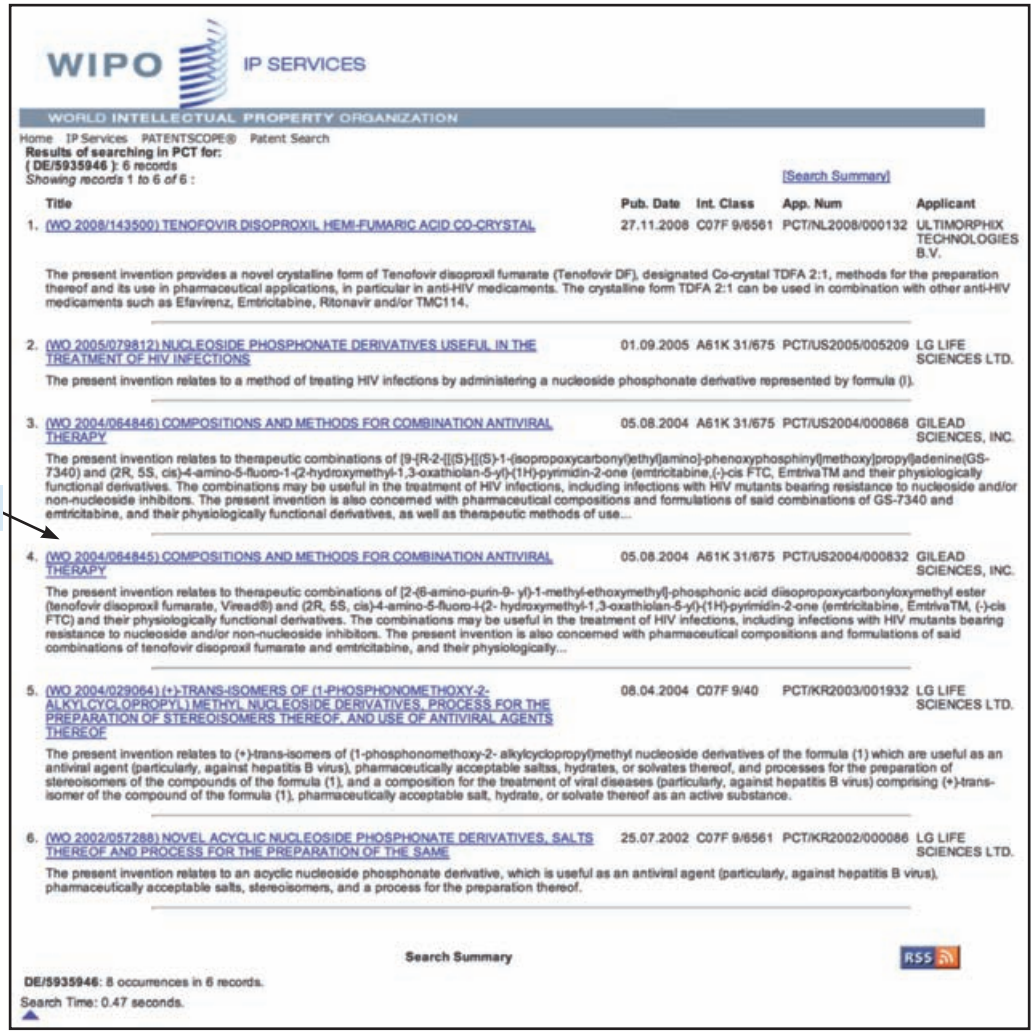


Figure 40: Patentscope search results for international patents citing US patent No. 5935946



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Results of searching in PCT for:
(DE/5935946): 6 records
Showing records 1 to 6 of 6 :

[Search Summary]

	Title	Pub. Date	Int. Class	App. Num	Applicant
1.	(WO 2008/143500) TENOFOVIR DISOPROXIL HEMI-FUMARIC ACID CO-CRYSTAL	27.11.2008	C07F 9/6561	PCT/NL2008/000132	ULTIMORPHIX TECHNOLOGIES B.V.

The present invention provides a novel crystalline form of Tenofovir disoproxil fumarate (Tenofovir DF), designated Co-crystal TDFA 2:1, methods for the preparation thereof and its use in pharmaceutical applications, in particular in anti-HIV medicaments. The crystalline form TDFA 2:1 can be used in combination with other anti-HIV medicaments such as Efavirenz, Emtricitabine, Ritonavir and/or TMC114.

2.	(WO 2005/079812) NUCLEOSIDE PHOSPHONATE DERIVATIVES USEFUL IN THE TREATMENT OF HIV INFECTIONS	01.09.2005	A61K 31/675	PCT/US2005/005209	LG LIFE SCIENCES LTD.

The present invention relates to a method of treating HIV infections by administering a nucleoside phosphonate derivative represented by formula (I).

3.	(WO 2004/064846) COMPOSITIONS AND METHODS FOR COMBINATION ANTIVIRAL THERAPY	05.08.2004	A61K 31/675	PCT/US2004/000868	GILEAD SCIENCES, INC.

The present invention relates to therapeutic combinations of [9-{R-2-[[(S)-[[(S)-1-(isopropoxycarbonyl)ethyl]amino]-phenoxyphosphinyl]methoxy]propyl}adenine(GS-7340) and (2R, 5S, cis)-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one (emtricitabine,(-)-cis FTC, EmtrivaTM and their physiologically functional derivatives. The combinations may be useful in the treatment of HIV infections, including infections with HIV mutants bearing resistance to nucleoside and/or non-nucleoside inhibitors. The present invention is also concerned with pharmaceutical compositions and formulations of said combinations of GS-7340 and emtricitabine, and their physiologically functional derivatives, as well as therapeutic methods of use...

WO 2004/064845

4.	(WO 2004/064845) COMPOSITIONS AND METHODS FOR COMBINATION ANTIVIRAL THERAPY	05.08.2004	A61K 31/675	PCT/US2004/000832	GILEAD SCIENCES, INC.

The present invention relates to therapeutic combinations of [2-(6-amino-purin-9- yl)-1-methyl-ethoxymethyl]-phosphonic acid diisopropoxycarbonyloxymethyl ester (tenofovir disoproxil fumarate, Viread®) and (2R, 5S, cis)-4-amino-5-fluoro-1-(2- hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one (emtricitabine, EmtrivaTM, (-)-cis FTC) and their physiologically functional derivatives. The combinations may be useful in the treatment of HIV infections, including infections with HIV mutants bearing resistance to nucleoside and/or non-nucleoside inhibitors. The present invention is also concerned with pharmaceutical compositions and formulations of said combinations of tenofovir disoproxil fumarate and emtricitabine, and their physiologically...

5.	(WO 2004/029064) (+)-TRANS-ISOMERS OF (1-PHOSPHONOMETHOXY-2-ALKYLCYCLOPROPYL) METHYL NUCLEOSIDE DERIVATIVES, PROCESS FOR THE PREPARATION OF STEREOISOMERS THEREOF, AND USE OF ANTIVIRAL AGENTS THEREOF	08.04.2004	C07F 9/40	PCT/KR2003/001932	LG LIFE SCIENCES LTD.

The present invention relates to (+)-trans-isomers of (1-phosphonomethoxy-2- alkylcyclopropyl)methyl nucleoside derivatives of the formula (1) which are useful as an antiviral agent (particularly, against hepatitis B virus), pharmaceutically acceptable saltss, hydrates, or solvates thereof, and processes for the preparation of stereoisomers of the compounds of the formula (1), and a composition for the treatment of viral diseases (particularly, against hepatitis B virus) comprising (+)-trans-isomer of the compound of the formula (1), pharmaceutically acceptable salt, hydrate, or solvate thereof as an active substance.

6.	(WO 2002/057288) NOVEL ACYCLIC NUCLEOSIDE PHOSPHONATE DERIVATIVES, SALTS THEREOF AND PROCESS FOR THE PREPARATION OF THE SAME	25.07.2002	C07F 9/6561	PCT/KR2002/000086	LG LIFE SCIENCES LTD.

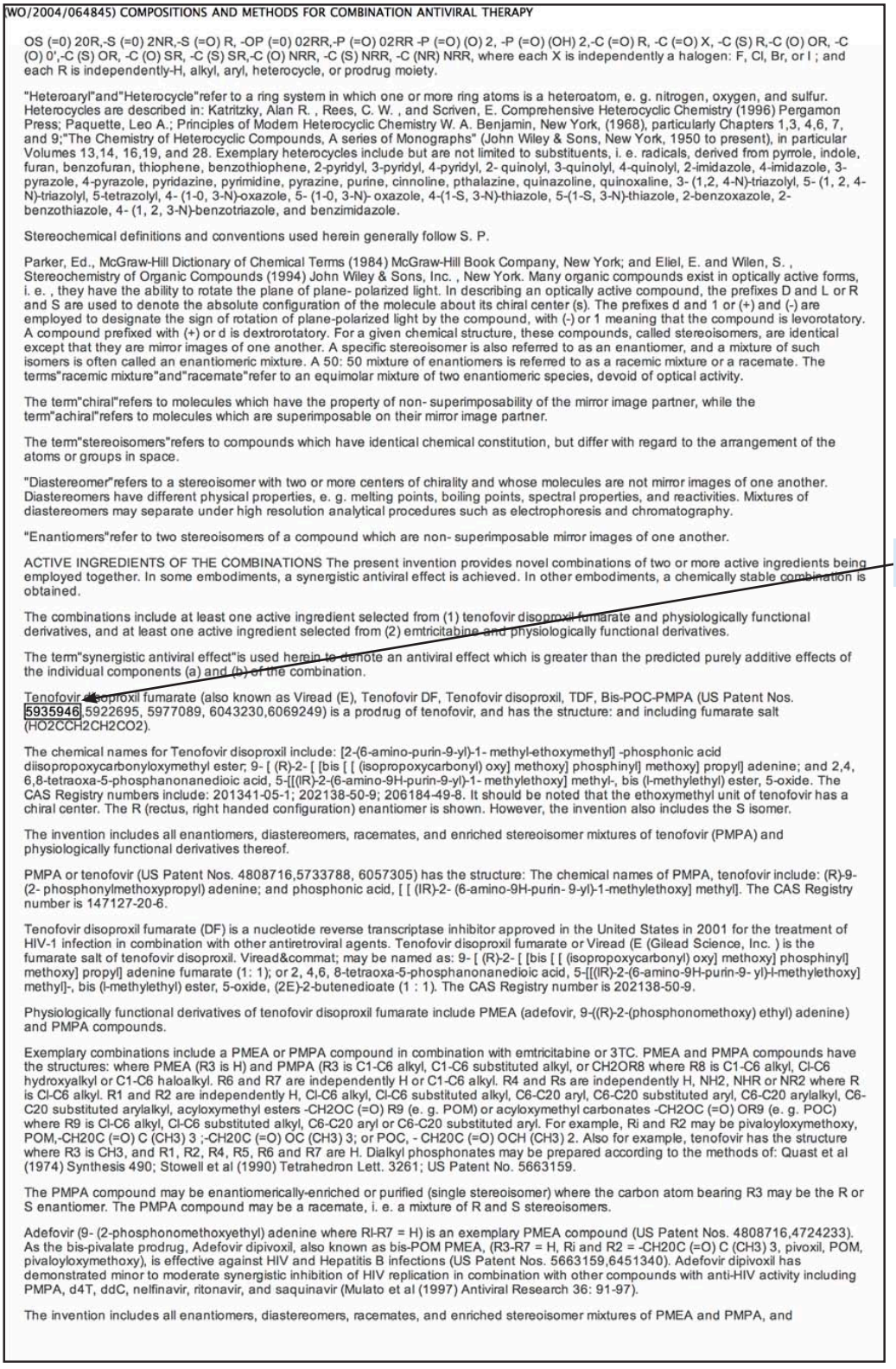
The present invention relates to an acyclic nucleoside phosphonate derivative, which is useful as an antiviral agent (particularly, against hepatitis B virus), pharmaceutically acceptable salts, stereoisomers, and a process for the preparation thereof.

Search Summary

RSS

DE/5935946: 8 occurrences in 6 records.
Search Time: 0.47 seconds.

Figure 41: Patentscope description for international publication No. WO 2004/06484



WO/2004/064845) COMPOSITIONS AND METHODS FOR COMBINATION ANTIVIRAL THERAPY

OS (=0) 20R,-S (=0) 2NR,-S (=O) R, -OP (=0) 02RR,-P (=O) 02RR -P (=O) (O) 2, -P (=O) (OH) 2,-C (=O) R, -C (=O) X, -C (S) R,-C (O) OR, -C (O) 0',-C (S) OR, -C (O) SR, -C (S) SR,-C (O) NRR, -C (S) NRR, -C (NR) NRR, where each X is independently a halogen: F, Cl, Br, or I ; and each R is independently-H, alkyl, aryl, heterocycle, or prodrug moiety.

"Heteroaryl"and"Heterocycle"refer to a ring system in which one or more ring atoms is a heteroatom, e. g. nitrogen, oxygen, and sulfur. Heterocycles are described in: Katritzky, Alan R. , Rees, C. W. , and Scriven, E. Comprehensive Heterocyclic Chemistry (1996) Pergamon Press; Paquette, Leo A.; Principles of Modem Heterocyclic Chemistry W. A. Benjamin, New York, (1968), particularly Chapters 1,3, 4,6, 7, and 9;"The Chemistry of Heterocyclic Compounds, A series of Monographs" (John Wiley & Sons, New York, 1950 to present), in particular Volumes 13,14, 16,19, and 28. Exemplary heterocycles include but are not limited to substituents, i. e. radicals, derived from pyrrole, indole, furan, benzofuran, thiophene, benzothiophene, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2- quinolyl, 3-quinolyl, 4-quinolyl, 2-imidazole, 4-imidazole, 3-pyrazole, 4-pyrazole, pyridazine, pyrimidine, pyrazine, purine, cinnoline, pthalazine, quinazoline, quinoxaline, 3- (1,2, 4-N)-triazolyl, 5- (1, 2, 4-N)-triazolyl, 5-tetrazolyl, 4- (1-0, 3-N)-oxazole, 5- (1-0, 3-N)- oxazole, 4-(1-S, 3-N)-thiazole, 5-(1-S, 3-N)-thiazole, 2-benzoxazole, 2-benzothiazole, 4- (1, 2, 3-N)-benzotriazole, and benzimidazole.

Stereochemical definitions and conventions used herein generally follow S. P.

Parker, Ed., McGraw-Hill Dictionary of Chemical Terms (1984) McGraw-Hill Book Company, New York; and Eliel, E. and Wilen, S. , Stereochemistry of Organic Compounds (1994) John Wiley & Sons, Inc. , New York. Many organic compounds exist in optically active forms, i. e. , they have the ability to rotate the plane of plane- polarized light. In describing an optically active compound, the prefixes D and L or R and S are used to denote the absolute configuration of the molecule about its chiral center (s). The prefixes d and 1 or (+) and (-) are employed to designate the sign of rotation of plane-polarized light by the compound, with (-) or 1 meaning that the compound is levorotatory. A compound prefixed with (+) or d is dextrorotatory. For a given chemical structure, these compounds, called stereoisomers, are identical except that they are mirror images of one another. A specific stereoisomer is also referred to as an enantiomer, and a mixture of such isomers is often called an enantiomeric mixture. A 50: 50 mixture of enantiomers is referred to as a racemic mixture or a racemate. The terms"racemic mixture"and"racemate"refer to an equimolar mixture of two enantiomeric species, devoid of optical activity.

The term"chiral"refers to molecules which have the property of non- superimposability of the mirror image partner, while the term"achiral"refers to molecules which are superimposable on their mirror image partner.

The term"stereoisomers"refers to compounds which have identical chemical constitution, but differ with regard to the arrangement of the atoms or groups in space.

"Diastereomer"refers to a stereoisomer with two or more centers of chirality and whose molecules are not mirror images of one another. Diastereomers have different physical properties, e. g. melting points, boiling points, spectral properties, and reactivities. Mixtures of diastereomers may separate under high resolution analytical procedures such as electrophoresis and chromatography.

"Enantiomers"refer to two stereoisomers of a compound which are non- superimposable mirror images of one another.

ACTIVE INGREDIENTS OF THE COMBINATIONS The present invention provides novel combinations of two or more active ingredients being employed together. In some embodiments, a synergistic antiviral effect is achieved. In other embodiments, a chemically stable combination is obtained.

The combinations include at least one active ingredient selected from (1) tenofovir disoproxil fumarate and physiologically functional derivatives, and at least one active ingredient selected from (2) emtricitabine and physiologically functional derivatives.

The term"synergistic antiviral effect"is used herein to denote an antiviral effect which is greater than the predicted purely additive effects of the individual components (a) and (b) of the combination.

Tenofovir disoproxil fumarate (also known as Viread (E), Tenofovir DF, Tenofovir disoproxil, TDF, Bis-POC-PMPA (US Patent Nos. 5935946,5922695, 5977089, 6043230,6069249) is a prodrug of tenofovir, and has the structure: and including fumarate salt (HO2CCH2CH2CO2).

The chemical names for Tenofovir disoproxil include: [2-(6-amino-purin-9-yl)-1- methyl-ethoxymethyl] -phosphonic acid diisopropoxycarbonyloxymethyl ester; 9- [(R)-2- [[bis [[(isopropoxycarbonyl) oxy] methoxy] phosphinyl] methoxy] propyl] adenine; and 2,4, 6,8-tetraoxa-5-phosphananonedioic acid, 5-[[(IR)-2-(6-amino-9H-purin-9-yl)-1- methylethoxy] methyl-, bis (I-methylethyl) ester, 5-oxide. The CAS Registry numbers include: 201341-05-1; 202138-50-9; 206184-49-8. It should be noted that the ethoxymethyl unit of tenofovir has a chiral center. The R (rectus, right handed configuration) enantiomer is shown. However, the invention also includes the S isomer.

The invention includes all enantiomers, diastereomers, racemates, and enriched stereoisomer mixtures of tenofovir (PMPA) and physiologically functional derivatives thereof.

PMPA or tenofovir (US Patent Nos. 4808716,5733788, 6057305) has the structure: The chemical names of PMPA, tenofovir include: (R)-9-(2- phosphonylmethoxypropyl) adenine; and phosphonic acid, [[(IR)-2- (6-amino-9H-purin- 9-yl)-1-methylethoxy] methyl]. The CAS Registry number is 147127-20-6.

Tenofovir disoproxil fumarate (DF) is a nucleotide reverse transcriptase inhibitor approved in the United States in 2001 for the treatment of HIV-1 infection in combination with other antiretroviral agents. Tenofovir disoproxil fumarate or Viread (E (Gilead Science, Inc.) is the fumarate salt of tenofovir disoproxil. Viread@ may be named as: 9- [(R)-2- [[bis [[(isopropoxycarbonyl) oxy] methoxy] phosphinyl] methoxy] propyl] adenine fumarate (1: 1); or 2, 4,6, 8-tetraoxa-5-phosphananonedioic acid, 5-[[(IR)-2-(6-amino-9H-purin-9- yl)-I-methylethoxy] methyl]-, bis (I-methylethyl) ester, 5-oxide, (2E)-2-butenedioate (1 : 1). The CAS Registry number is 202138-50-9.

Physiologically functional derivatives of tenofovir disoproxil fumarate include PMEA (adefovir, 9-((R)-2-(phosphonomethoxy) ethyl) adenine) and PMPA compounds.

Exemplary combinations include a PMEA or PMPA compound in combination with emtricitabine or 3TC. PMEA and PMPA compounds have the structures: where PMEA (R3 is H) and PMPA (R3 is C1-C6 alkyl, C1-C6 substituted alkyl, or CH2OR8 where R8 is C1-C6 alkyl, Cl-C6 hydroxyalkyl or C1-C6 haloalkyl. R6 and R7 are independently H or C1-C6 alkyl. R4 and Rs are independently H, NH2, NHR or NR2 where R is Cl-C6 alkyl. R1 and R2 are independently H, Cl-C6 alkyl, Cl-C6 substituted alkyl, C6-C20 aryl, C6-C20 substituted aryl, C6-C20 arylalkyl, C6-C20 substituted arylalkyl, acyloxymethyl esters -CH2OC (=O) R9 (e. g. POM) or acyloxymethyl carbonates -CH2OC (=O) OR9 (e. g. POC) where R9 is Cl-C6 alkyl, Cl-C6 substituted alkyl, C6-C20 aryl or C6-C20 substituted aryl. For example, Ri and R2 may be pivaloyloxymethoxy, POM,-CH20C (=O) C (CH3) 3 ;-CH20C (=O) OC (CH3) 3; or POC, - CH20C (=O) OCH (CH3) 2. Also for example, tenofovir has the structure where R3 is CH3, and R1, R2, R4, R5, R6 and R7 are H. Dialkyl phosphonates may be prepared according to the methods of: Quast et al (1974) Synthesis 490; Stowell et al (1990) Tetrahedron Lett. 3261; US Patent No. 5663159.

The PMPA compound may be enantiomerically-enriched or purified (single stereoisomer) where the carbon atom bearing R3 may be the R or S enantiomer. The PMPA compound may be a racemate, i. e. a mixture of R and S stereoisomers.

Adefovir (9- (2-phosphonomethoxyethyl) adenine where RI-R7 = H) is an exemplary PMEA compound (US Patent Nos. 4808716,4724233). As the bis-pivalate prodrug, Adefovir dipivoxil, also known as bis-POM PMEA, (R3-R7 = H, Ri and R2 = -CH20C (=O) C (CH3) 3, pivoxil, POM, pivaloyloxymethoxy), is effective against HIV and Hepatitis B infections (US Patent Nos. 5663159,6451340). Adefovir dipivoxil has demonstrated minor to moderate synergistic inhibition of HIV replication in combination with other compounds with anti-HIV activity including PMPA, d4T, ddC, nelfinavir, ritonavir, and saquinavir (Mulato et al (1997) Antiviral Research 36: 91-97).

The invention includes all enantiomers, diastereomers, racemates, and enriched stereoisomer mixtures of PMEA and PMPA, and

Citation of earlier patents

5

How to find patents in developing countries

Locating patents in developing countries that are equivalent or related to those found in the Orange Book, the Health Canada Patent Register or through the extended searches described in Chapter 4 is not a straightforward process.

One reason is that the patent family and national phase data available in esp@cenet and Patentscope do not cover all countries where the patent may have been filed. Only information that the EPO or WIPO has been able to obtain from countries will be available. Also, there are only a handful of online searchable databases or patent journals provided by developing country patent offices (see **Appendix III**). Even where developing country patent offices offer an online searchable database, the data fields that are available to be searched are not as extensive as in esp@cenet or Patentscope. For example, there may not be a search field whereby the user can search by priority number. Key data may be omitted, incorrectly inputted or out of date, all of which can lead to an unsuccessful search. Finally, as complete specifications and claims for patents filed or granted in developing countries are rarely available online, in many cases they will have to be requested directly from the concerned national or regional patent office.

Ultimately, even if patent information for a particular developing country is available online, in most cases the search process will inevitably end with having to request a patent document from the relevant national or regional patent office.

Despite these limitations, in a number of developing countries it may still be possible to identify whether a patent exists using information available on the Internet. Having such information in hand can make the step of obtaining the relevant patent document from the national or regional patent office a much simpler process.

5.1 Using online patent databases

The following examples illustrate how to use patent information identified in Chapter 4 to check for equivalent or related patents in other countries.

Example 5.1: Using esp@cenet to find patents in other countries

For this example, refer to Figures 8-12 (Section 4.2.1) and Figures 16-21 (Section 4.3.1), which demonstrated how to locate patent listings for abacavir in the Orange Book and to obtain the patent document for US patent No. 5034394 using esp@cenet. Continuing from that example, the following steps set out some techniques for searching for patents in other countries that are equivalent or related to US patent No. 5034394.

Step 1

Having located US patent No. 5034394 on esp@cenet, it is now possible to view patents that are considered equivalent or which share the same priority application in other countries.

To view patents that are considered to be equivalent to US patent No. 5034394, esp@cenet provides a list under the heading *Also published as* (see Figure 42). For some records that have a large number of equivalent patents available, esp@cenet provides a link titled *more>>* which allows users to expand the list of equivalent patents available in esp@cenet (see Figure 42). By clicking on the thumbnail of the PDF logo, the user can download the patent document for a particular patent, if available, by following the steps shown in Figures 19 and 20.

As explained in Section 2.5, to view a broader and more comprehensive patent family for U.S patent No. 5034394, users should click on the option *View INPADOC patent family* (see Figures 43 and 44). Developing countries and regional patent organizations included in the INPADOC patent family may include Argentina, ARIPO (AP), Brazil (BR), China (CN), Colombia (CO), Indonesia (IN), Mexico (MX), OAPI (OA) and South Africa (ZA). However, the country information available in esp@cenet varies from patent to patent. Also, users should remember that the specifications and claims of the patents listed in the INPADOC patent family might not be exactly the same as for US patent No. 5034394.

Repeating steps 3 and 4 of section 4.3.1 (Figures 18–20), click on the link of the country of interest to view the bibliographic data and related patent document for each patent. By way of example, Figure 45 provides the bibliographic data for ARIPO patent number AP196A, Figure 46 the front page of the patent document for AP196A, and Figure 47 an extract of the claims from AP196A.

Figure 42: Esp@cenet equivalent patent and INPADOC patent family links for US patent No. 5034394

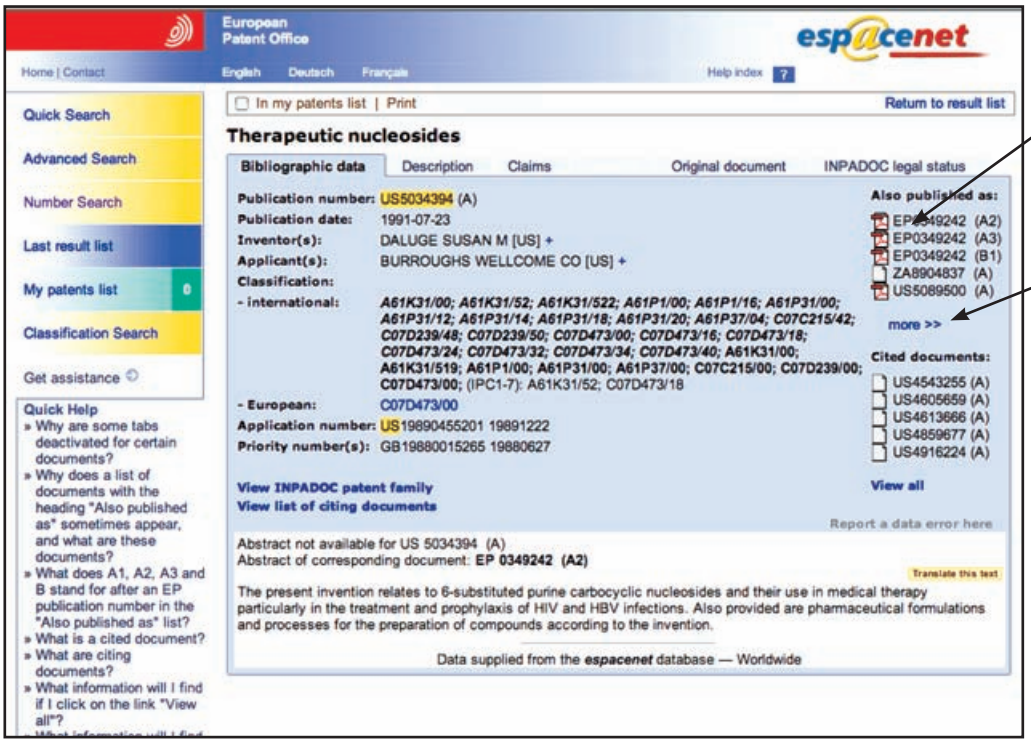


Figure 43: Esp@cenet equivalent patent list for US patent No. 5034394

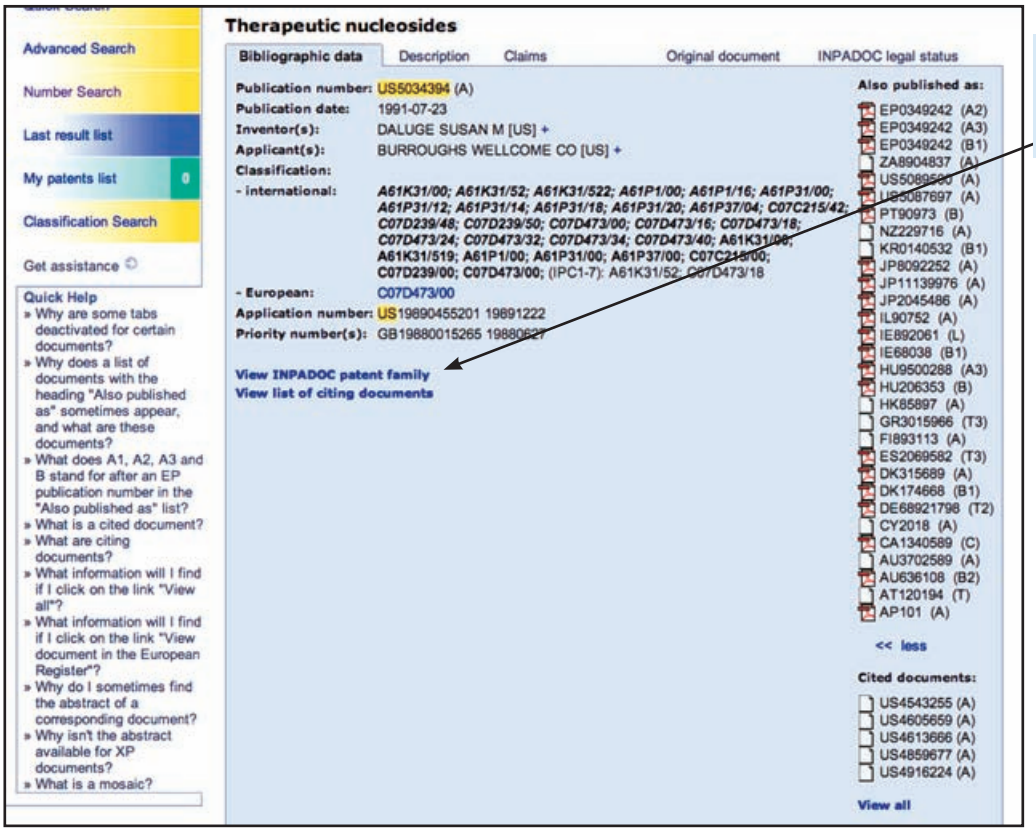
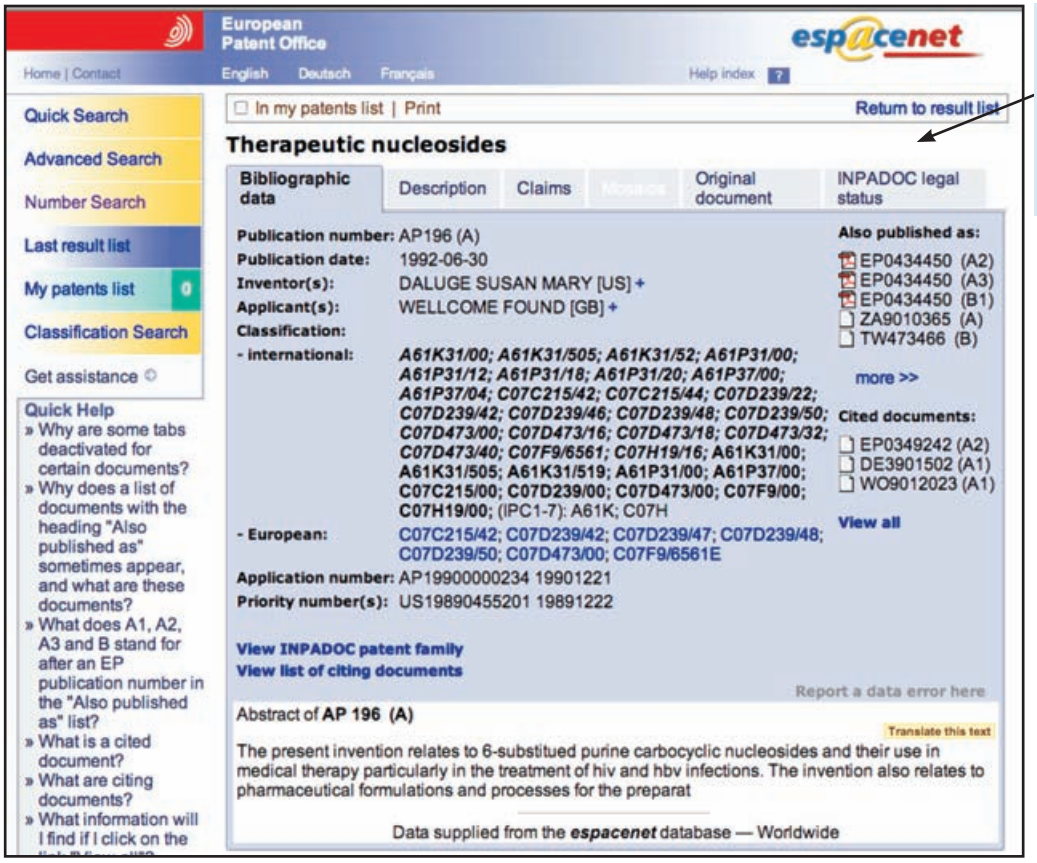


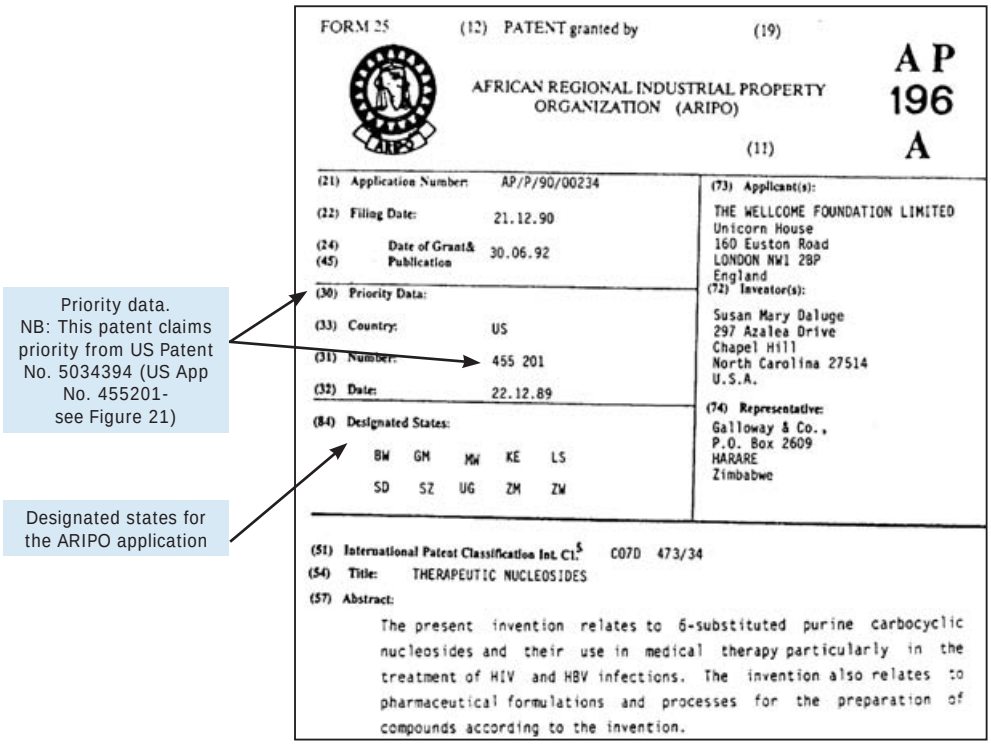
Figure 44: Esp@cenet INPADOC patent family for US patent family No. 5034394

Figure 45: Esp@cenet bibliographic data page for ARIPO patent No. AP196A



Click here to obtain legal status of AP196A. NB: The legal status of applicaitons may not always be available.

Figure 46: Front page of ARIPO patent No. A196A as downloaded from esp@cenet



FORM 25 (12) PATENT granted by (19)

AFRICAN REGIONAL INDUSTRIAL PROPERTY ORGANIZATION (ARIPO)

AP 196 A

(11)

(21) Application Number: AP/P/90/00234

(22) Filing Date: 21.12.90

(24) (45) Date of Grant & Publication: 30.06.92

(30) Priority Data:

(33) Country: US

(31) Number: 455 201

(32) Date: 22.12.89

(84) Designated States:

BW GM MW KE LS

SD SZ UG ZM ZW

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(74) Representative:

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(51) International Patent Classification Int. Cl.[5] C07D 473/34

(54) Title: THERAPEUTIC NUCLEOSIDES

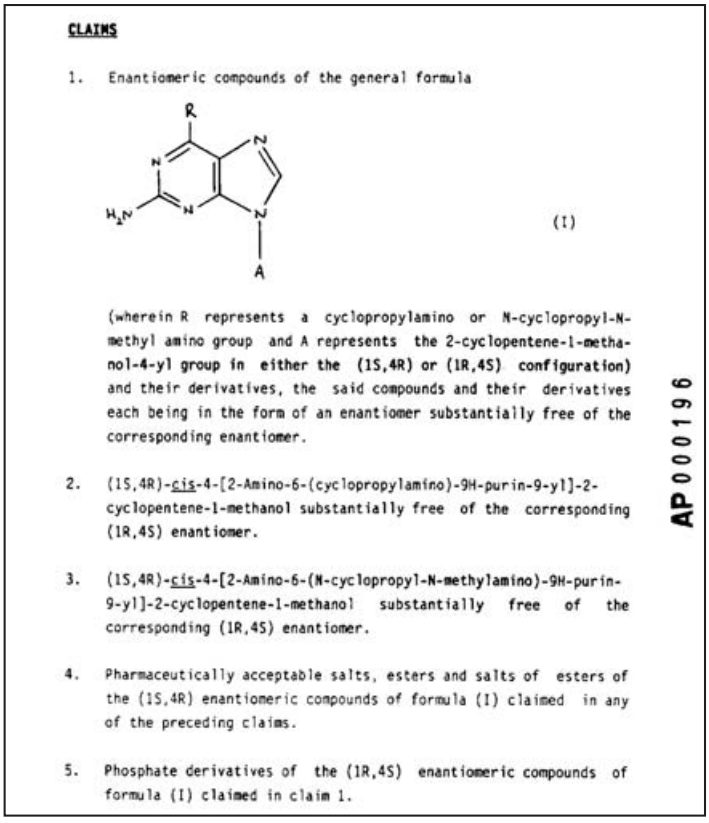
(57) Abstract:

The present invention relates to 6-substituted purine carbocyclic nucleosides and their use in medical therapy particularly in the treatment of HIV and HBV infections. The invention also relates to pharmaceutical formulations and processes for the preparation of compounds according to the invention.

Priority data. NB: This patent claims priority from US Patent No. 5034394 (US App No. 455201- see Figure 21)

Designated states for the ARIPO application

Figure 47: Extract of claims from ARIPO patent No. AP196A as downloaded from esp@cenet



CLAIMS

1. Enantiomeric compounds of the general formula

(I)

(wherein R represents a cyclopropylamino or N-cyclopropyl-N-methyl amino group and A represents the 2-cyclopentene-1-methanol-4-yl group in either the (1S,4R) or (1R,4S) configuration) and their derivatives, the said compounds and their derivatives each being in the form of an enantiomer substantially free of the corresponding enantiomer.

2. (1S,4R)-cis-4-[2-Amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol substantially free of the corresponding (1R,4S) enantiomer.

3. (1S,4R)-cis-4-[2-Amino-6-(N-cyclopropyl-N-methylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol substantially free of the corresponding (1R,4S) enantiomer.

4. Pharmaceutically acceptable salts, esters and salts of esters of the (1S,4R) enantiomeric compounds of formula (I) claimed in any of the preceding claims.

5. Phosphate derivatives of the (1R,4S) enantiomeric compounds of formula (I) claimed in claim 1.

AP 000196

Step 2

If the relevant patent information is located in esp@cenet's INPADOC patent family, it is necessary to check its legal status. This can be done by clicking on the tab *INPADOC Legal Status* as shown in Figure 45. The status of a patent will usually be indicated by one or more of the following terms depending on the country and stage of examination:

- Assignment—indicates the patent has been assigned and provides the current and previous proprietor.
- Publication—indicates that the application has been published (18 months after the priority or filing date).
- Request of examination as to substance—indicates that the applicant has requested examination of the application.
- Granted—indicates that the patent has been granted.
- Certificate of Correction—applies to US patents, indicating that an error in the patent specification has been rectified.
- Supplementary Patent Certificate (SPC) Filed/Granted—applies to European patents, indicating the application or grant of extension of the patent term.[1]
- Extension of Patent Term—applies to US patents, indicating that the term of the patent has been extended beyond 20 years.[2]

However, for other countries the legal status of a patent application may not always be available or may not be up to date. It is recommended that the legal status and/or final claims as granted and shown in esp@cenet always be checked with the relevant national or regional patent office.

Example 5.2: Using national databases to locate patents-Philippines

Where esp@cenet INPADOC does not list the country of interest, it may be possible to locate the patent using a national patent office database (see **Appendix III** for online databases made available by national patent offices).

---

1 Supplementary Patent Certificates (SPC) are available for products that have a basic patent in force that constitutes the active ingredient or a combination of active ingredients of a medicinal product (Articles 1 and 3 of Regulation (EC) No 469/2009). SPCs take effect at the end of the lawful term of the basic patent (20 years) and may not exceed a period of five years unless an extension is granted—in which case the extension of the SPC will be for an additional six months (Article 13). Extensions are granted when an authorized medicinal product that is protected by a patent has completed all the studies required in compliance with an agreed paediatric investigation plan (Article 36 of Regulation (EC) No 1901/2006). The INPADOC Legal Status screen provides information on SPCs of European patents using PRS (patent register service) codes. The current PRS codes can be obtained by entering the URL: http://www.epo.org/patents/patent-information/raw-data/useful-tables.html and clicking on the link *Table of all PRS codes available for SPCs.*

2 Extensions of patent terms relate to patents that claim a product, a method of using a product or a method of manufacturing (USC 35 s156).

For example, the Intellectual Property Office of the Philippines provides an online searchable database called PhilPAT.

Step 1

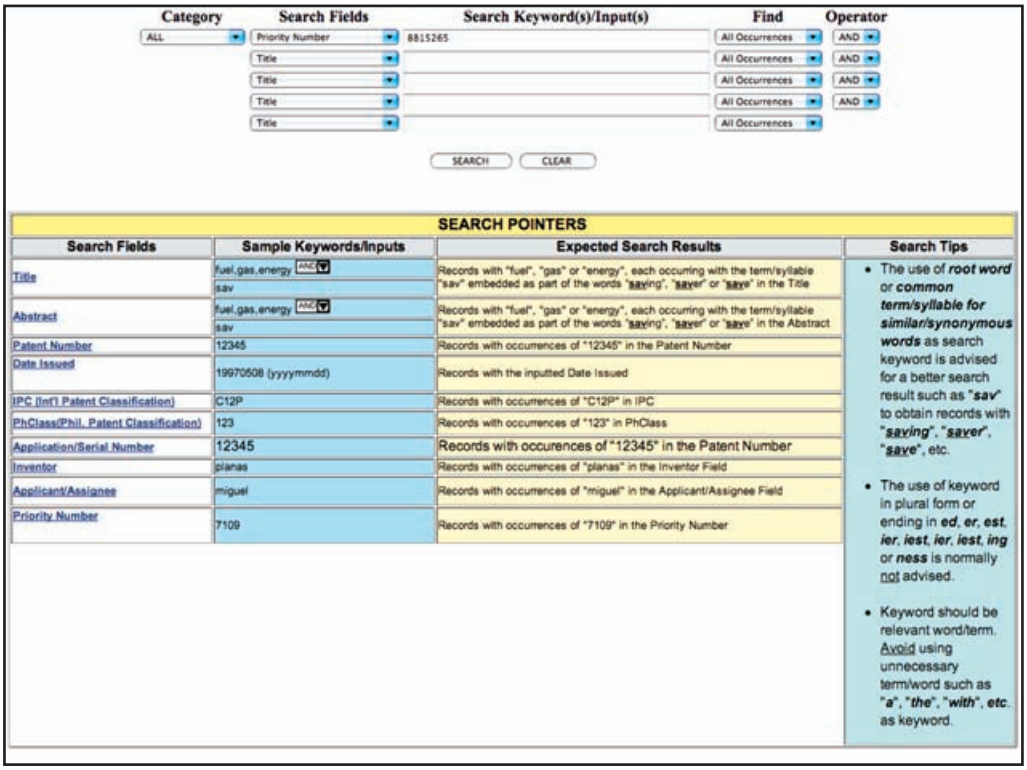
Enter the URL: http://patents.ipophil.gov.ph/PatSearch/ and select the *Advanced Search* option.

The Advanced Search page provides five search and data fields (see Figure 48). The Boolean operators used by PhilPAT are *AND* and *OR*. PhilPAT also allows users to choose between searching for *All Occurences* of a word or *As Separate Word*. As there are different types of patents (i.e. inventions and utility models), PhilPAT provides a drop-down menu under the heading *Category* from which the searcher can select the relevant type of patent. For pharmaceutical/biotech patents, the relevant option would be *Invention.* Alternatively the setting can be left as *All*, but this may return a wider set of results depending on the terms searched.

PhilPAT is one of the national patent office databases that enables users to search by priority data. When searching by priority number it may be necessary to input the priority number in various formats to obtain a result.

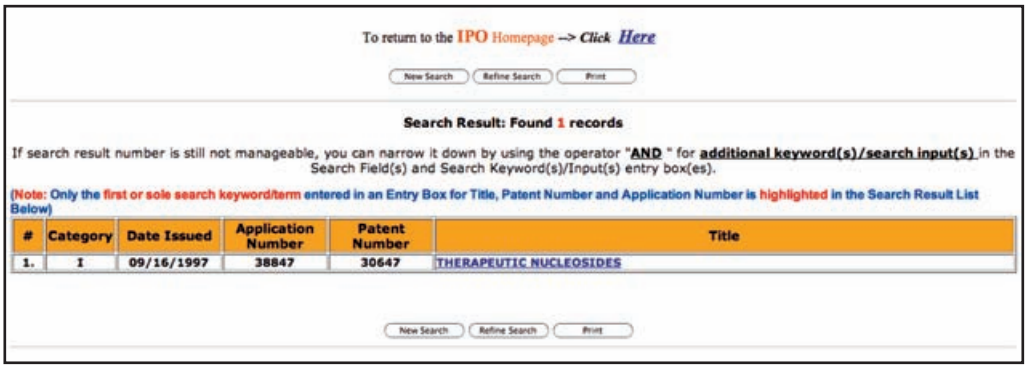
Select the option *Priority Number* and enter the priority number for US patent No. 5034394, e.g. 8815265 (see Figure 48).

Figure 48: PhilPAT database search by priority number 8815265



The search retrieves one result with the priority number 8815265 (see Figure 49). Click on the title of the patent *Therapeutic Nucleosides* to review the patent information (see Figure 50). Note that PhilPAT only provides access to the bibliographic data. To view the patent specification and claims, and to know whether the patent has been renewed, a request would have to be made to the Intellectual Property Office of the Philippines.

Figure 49: PhilPAT database search results for priority number 8815265



To return to the IPO Homepage --> Click Here

New Search | Refine Search | Print

Search Result: Found 1 records

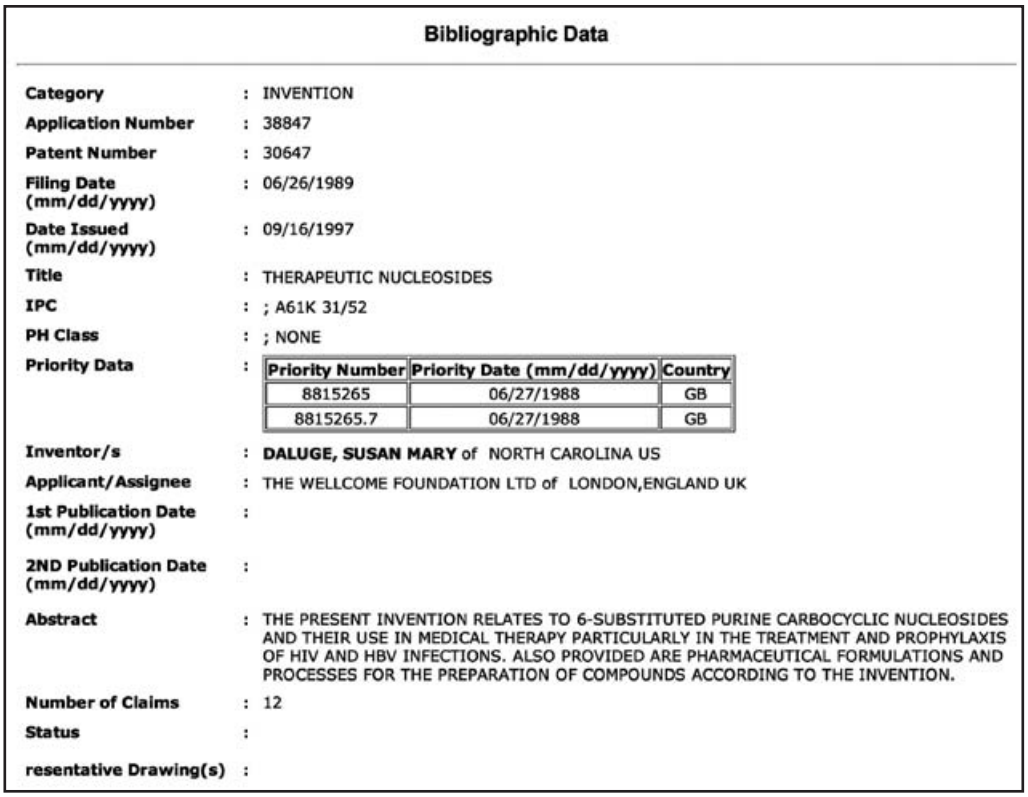
If search result number is still not manageable, you can narrow it down by using the operator "**AND** " for **additional keyword(s)/search input(s)** in the Search Field(s) and Search Keyword(s)/Input(s) entry box(es).

(Note: Only the first or sole search keyword/term entered in an Entry Box for Title, Patent Number and Application Number is highlighted in the Search Result List Below)

#	Category	Date Issued	Application Number	Patent Number	Title
1.	I	09/16/1997	38847	30647	THERAPEUTIC NUCLEOSIDES

New Search | Refine Search | Print

Figure 50: PhilPAT bibliographic data for Philippines patent No. 30647



Bibliographic Data

Category	:	INVENTION
Application Number	:	38847
Patent Number	:	30647
Filing Date (mm/dd/yyyy)	:	06/26/1989
Date Issued (mm/dd/yyyy)	:	09/16/1997
Title	:	THERAPEUTIC NUCLEOSIDES
IPC	:	; A61K 31/52
PH Class	:	; NONE
Priority Data	:	Priority Number: 8815265, Priority Date (mm/dd/yyyy): 06/27/1988, Country: GB; Priority Number: 8815265.7, Priority Date (mm/dd/yyyy): 06/27/1988, Country: GB
Inventor/s	:	**DALUGE, SUSAN MARY** of NORTH CAROLINA US
Applicant/Assignee	:	THE WELLCOME FOUNDATION LTD of LONDON,ENGLAND UK
1st Publication Date (mm/dd/yyyy)	:	
2ND Publication Date (mm/dd/yyyy)	:	
Abstract	:	THE PRESENT INVENTION RELATES TO 6-SUBSTITUTED PURINE CARBOCYCLIC NUCLEOSIDES AND THEIR USE IN MEDICAL THERAPY PARTICULARLY IN THE TREATMENT AND PROPHYLAXIS OF HIV AND HBV INFECTIONS. ALSO PROVIDED ARE PHARMACEUTICAL FORMULATIONS AND PROCESSES FOR THE PREPARATION OF COMPOUNDS ACCORDING TO THE INVENTION.
Number of Claims	:	12
Status	:	
resentative Drawing(s)	:	

Step 2

Patent databases may not always retrieve all records for a particular search. There can be many reasons for this. For example, the priority number that is being searched may have been entered incorrectly or the database's search function is not accurate. To obtain a more complete set of results, additional searches should always be conducted.

In the case of this example, searching the PhilPAT database using the title of the US patent No. 5034394 (i.e. *Therapeutic Nucleosides*) returns a number of other patents (see Figures 51 and 52).

Figure 51: PhilPAT database search for "Therapeutic Nucleosides"

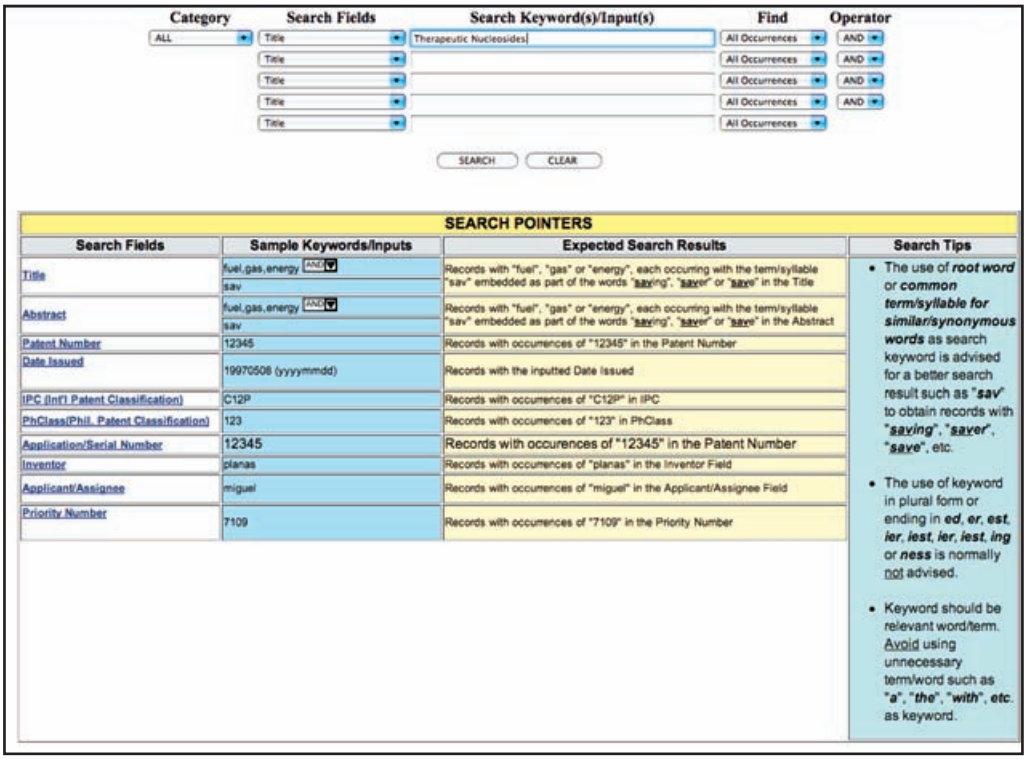
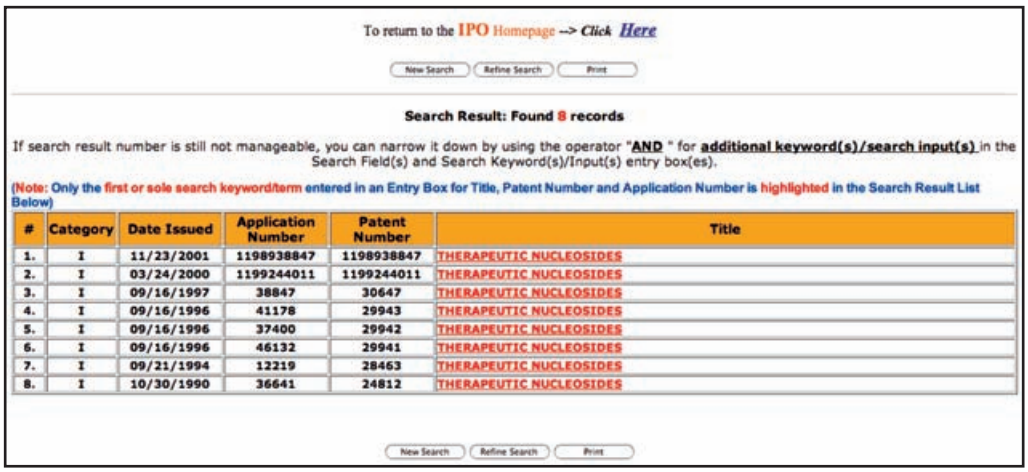


Figure 52: PhilPAT database search results for "Therapeutic Nucleosides"



To return to the IPO Homepage --> Click Here

New Search | Refine Search | Print

Search Result: Found 8 records

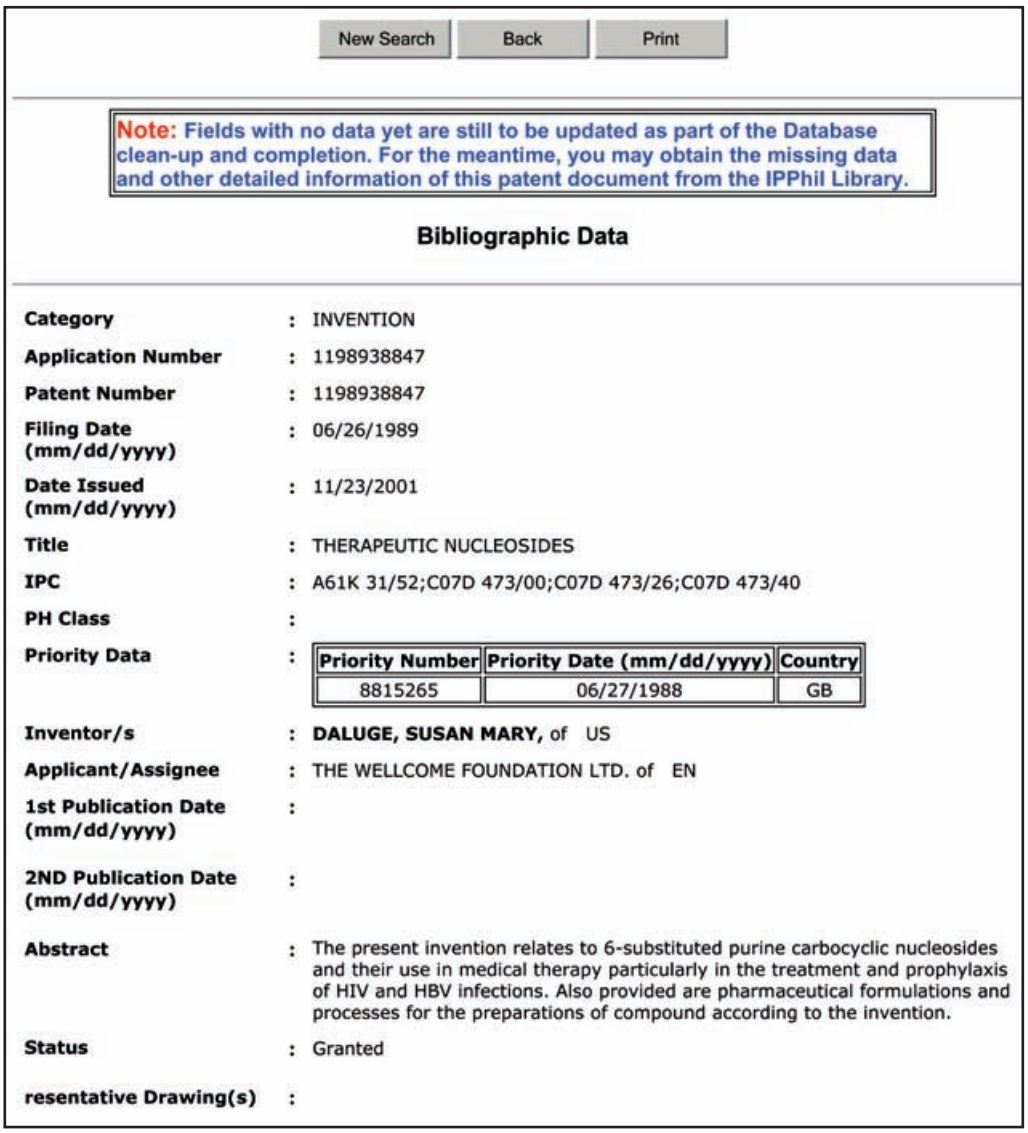
If search result number is still not manageable, you can narrow it down by using the operator "**AND** " for **additional keyword(s)/search input(s)** in the Search Field(s) and Search Keyword(s)/Input(s) entry box(es).

(Note: Only the first or sole search keyword/term entered in an Entry Box for Title, Patent Number and Application Number is highlighted in the Search Result List Below)

#	Category	Date Issued	Application Number	Patent Number	Title
1.	I	11/23/2001	1198938847	1198938847	THERAPEUTIC NUCLEOSIDES
2.	I	03/24/2000	1199244011	1199244011	THERAPEUTIC NUCLEOSIDES
3.	I	09/16/1997	38847	30647	THERAPEUTIC NUCLEOSIDES
4.	I	09/16/1996	41178	29943	THERAPEUTIC NUCLEOSIDES
5.	I	09/16/1996	37400	29942	THERAPEUTIC NUCLEOSIDES
6.	I	09/16/1996	46132	29941	THERAPEUTIC NUCLEOSIDES
7.	I	09/21/1994	12219	28463	THERAPEUTIC NUCLEOSIDES
8.	I	10/30/1990	36641	24812	THERAPEUTIC NUCLEOSIDES

New Search | Refine Search | Print

Figure 53: PhilPAT bibliographic data for Philippines patent No. 1198938847



New Search | Back | Print

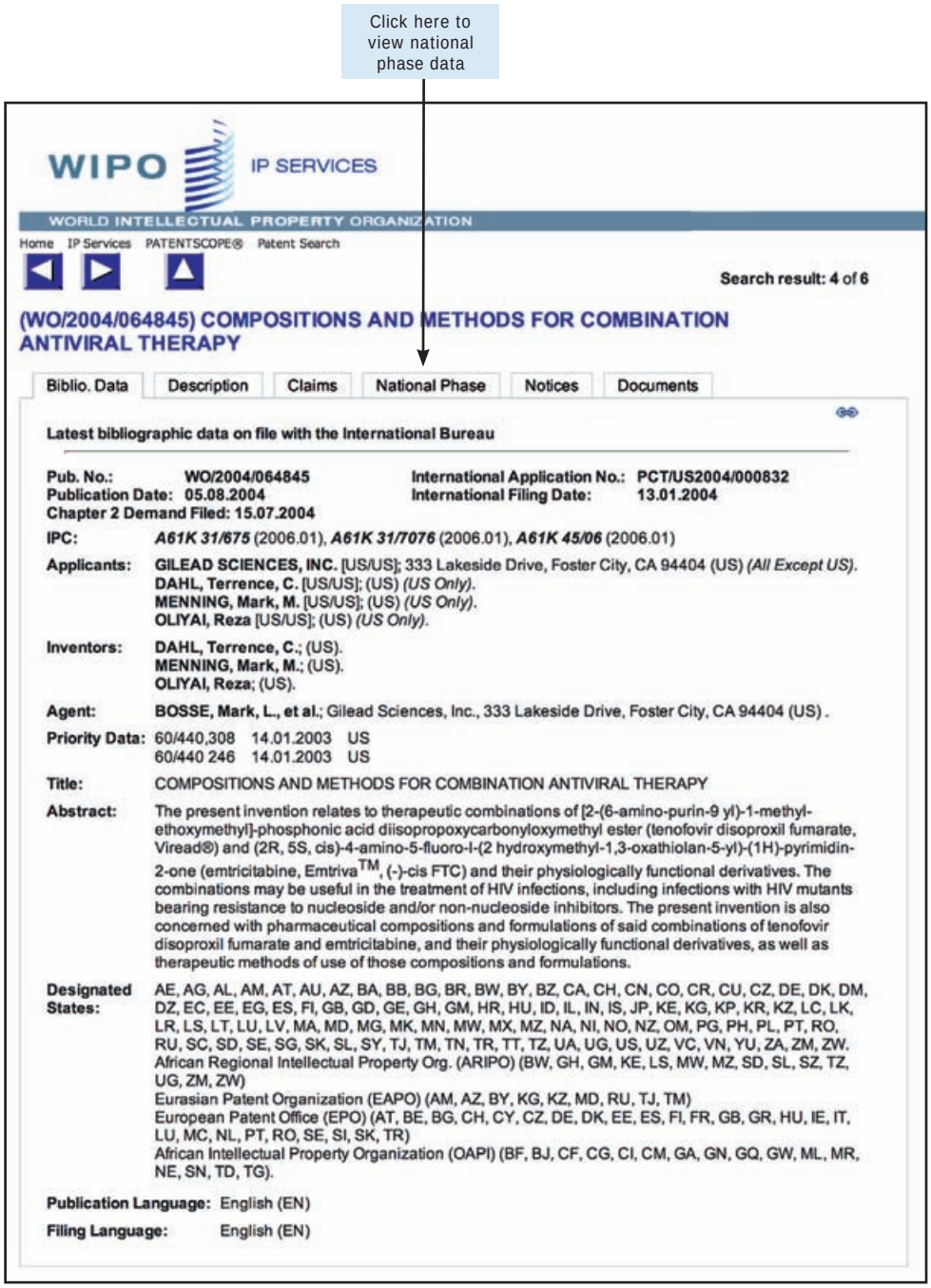
Note: Fields with no data yet are still to be updated as part of the Database clean-up and completion. For the meantime, you may obtain the missing data and other detailed information of this patent document from the IPPhil Library.

Bibliographic Data

Category	:	INVENTION
Application Number	:	1198938847
Patent Number	:	1198938847
Filing Date (mm/dd/yyyy)	:	06/26/1989
Date Issued (mm/dd/yyyy)	:	11/23/2001
Title	:	THERAPEUTIC NUCLEOSIDES
IPC	:	A61K 31/52;C07D 473/00;C07D 473/26;C07D 473/40
PH Class	:	
Priority Data	:	Priority Number: 8815265; Priority Date (mm/dd/yyyy): 06/27/1988; Country: GB
Inventor/s	:	**DALUGE, SUSAN MARY,** of US
Applicant/Assignee	:	THE WELLCOME FOUNDATION LTD. of EN
1st Publication Date (mm/dd/yyyy)	:	
2ND Publication Date (mm/dd/yyyy)	:	
Abstract	:	The present invention relates to 6-substituted purine carbocyclic nucleosides and their use in medical therapy particularly in the treatment and prophylaxis of HIV and HBV infections. Also provided are pharmaceutical formulations and processes for the preparations of compound according to the invention.
Status	:	Granted
resentative Drawing(s)	:	

By reviewing each patent it transpires that Philippines patent No. 1198938847 also claims priority from 8815265 (see Figure 53). Notably, patent No. 1198938847 has the same filing date but a different date of grant than patent No. 30647 (see Figure 50). In this case, as the filing dates are identical, these patents should expire at the same time.

Figure 54: Patentscope bibliographic data for international patent publication No. WO 2004/064845



Example 5.3: Checking for PCT national phase data in esp@cenet

This example continues from Example 4.4 on pages 63-67.

Step 1

Figure 40 on page 66 displays the Patentscope search results for international applications citing US patent No. 5935946.

Using international publication number WO 2004/064845 as an example, click on the title of the patent as shown in Figure 40 to access the bibliographic data and patent information (see Figure 54).

As mentioned above (Example 4.1, step 3), Patentscope provides national phase data for those countries that make their patent information available to WIPO. Click on the tab *National Phase* to view the national phase data for WO 2004/064845. Figure 55 shows that WO 2004/064845 has entered the national phase in the following designated developing countries: China, Mexico, Viet Nam and South Africa.

Figure 55: Patentscope national phase data for international patent publication No. WO 2004/064845

Office Code	National Entry Date	National Reference Number	Status
AP	24.06.2005	AP/P/2005/003348	
AU	28.06.2005	2004206821	Published: 21.07.2005
CN	14.07.2005	200480002190.5	
EP	01.07.2005	2004701819	Published: 12.10.2005 Granted: 18.06.2008
HR	06.07.2005	P20050619A	Published: 31.10.2005
IL	16.06.2005	169243	Published: 21.02.2006
JP	12.07.2005	2006500939	
KR	14.07.2005	1020057013069	Published: 22.09.2005
KR		1020087007002	Withdrawn: 02.06.2009
KR	06.05.2009	1020097009376	Published: 27.05.2009 Refused: 16.02.2010
MX	27.06.2005	PA/a/2005/007016	
NZ	14.06.2005	540728	Published: 29.08.2008 Granted: 11.12.2008
PL	Not Available		
US	20.03.2006	10540794	Published: 02.11.2006
US	20.03.2006	2006246130	
VN	15.06.2005	1200500812	
ZA	21.07.2005	200505852	
ZA	21.07.2005	2005/05852	

Using the reference numbers provided in Patentscope, users can contact the respective national patent office to obtain further information.

Step 2

Patentscope only provides limited national phase data. If the country of interest is not listed but was designated in the international patent application, it will be necessary to conduct further searches using other tools.

One way to do this is through esp@cenet's INPADOC patent family, which may provide information about additional countries where WO 2004/064845 may have entered into the national phase.

Select the option *Number Search* from esp@cenet's main page (see Figures 16 and 17). Using the Worldwide patent database, enter publication number WO2004064845, without any spaces or special characters (as shown in Figure 56).

The search yields one result. As shown in Figures 18 and 42-44, click on the title of the patent to access the bibliographic data and INPADOC patent family link. Click on the INPADOC patent family link to view the patent family.

The only additional information provided by esp@cenet in relation to a developing country is that W2004/064845 may have entered the national phase in Brazil (see Figure 57). However, on reviewing the bibliographic data (see Figure 58), it is apparent that the Brazilian national phase application may stem from a related international patent WO2004/064846, which shares the same priority numbers as WO2004/064845.

Figure 56: Esp@cenet number search for WO 2004/064845

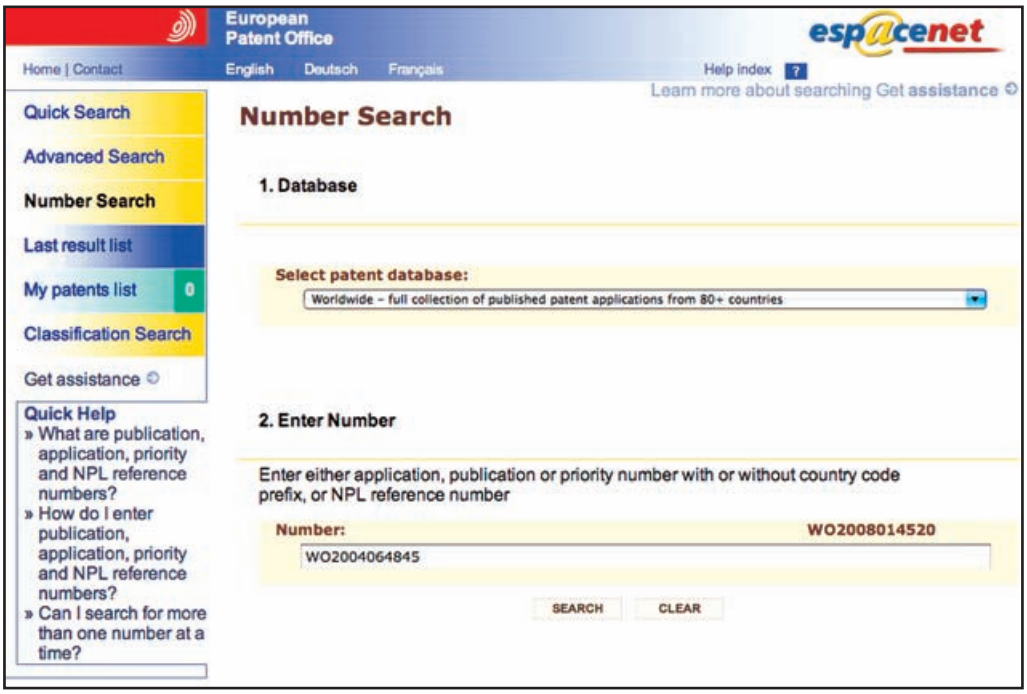
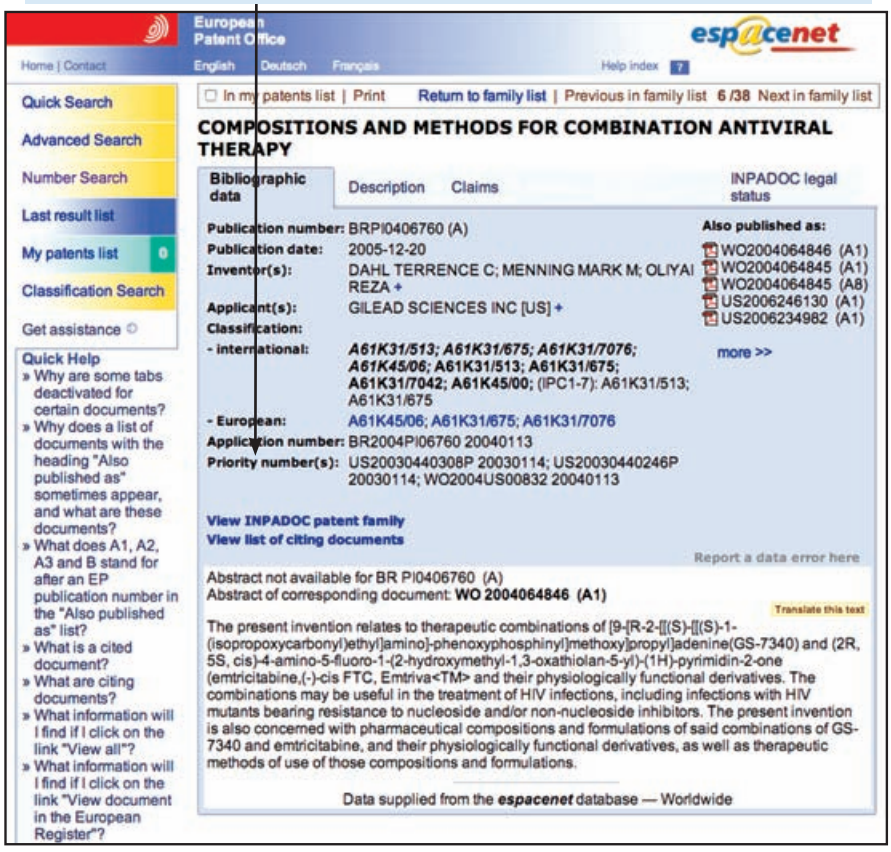


Figure 57: Esp@cenet INPADOC patent family results for international patent number WO 2004/064845

Figure 58: Esp@cenet bibliographic data for Brazilian national phase application No. PI 0406760



Example 5.4: Using national databases to locate PCT national phase applications - India

Step 1

An alternative method for identifying whether an international patent has entered the national phase and/or has been granted in a designated country is by using an online database provided by a national/regional patent office.

Using India as an example, the first step is to search the Indian Patent Office database of published patent applications (see Example 4.2 on page 59 for details on how to access the database). Select the data field *Applicant Name* and insert the applicant details (i.e. *Gilead*) as provided in the Patentscope record shown in Figure 54. Then select the Boolean operator *AND*, and the data field *Abstract*. In the search field, enter a distinctive term from the abstract of WO 2004/064845 as provided in Patentscope. For this example, the word *tenofovir* has been selected (see Figure 59).

As of this writing, the search retrieved four results (see Figure 60). The first two results share the same title as WO 2004/064845, i.e. *Compositions and Methods for Combination Antiviral Therapy.* Reviewing the bibliographic data of the two applications informs the searcher that Application No. 3383/DELNP/2005 derives from international publication number WO 2004/064845 (see Figure 61).

Figure 59: Indian Patent Office search for national phase application relating to WO 2004/064845

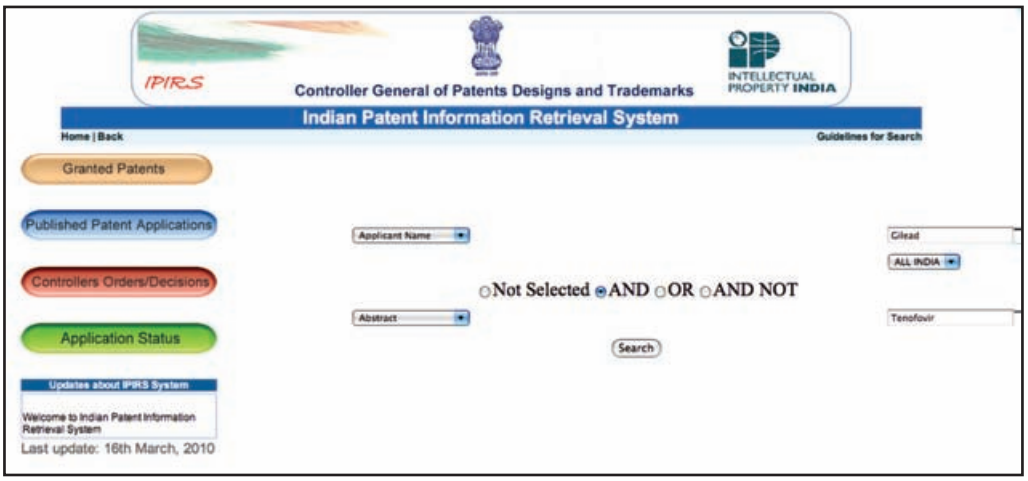
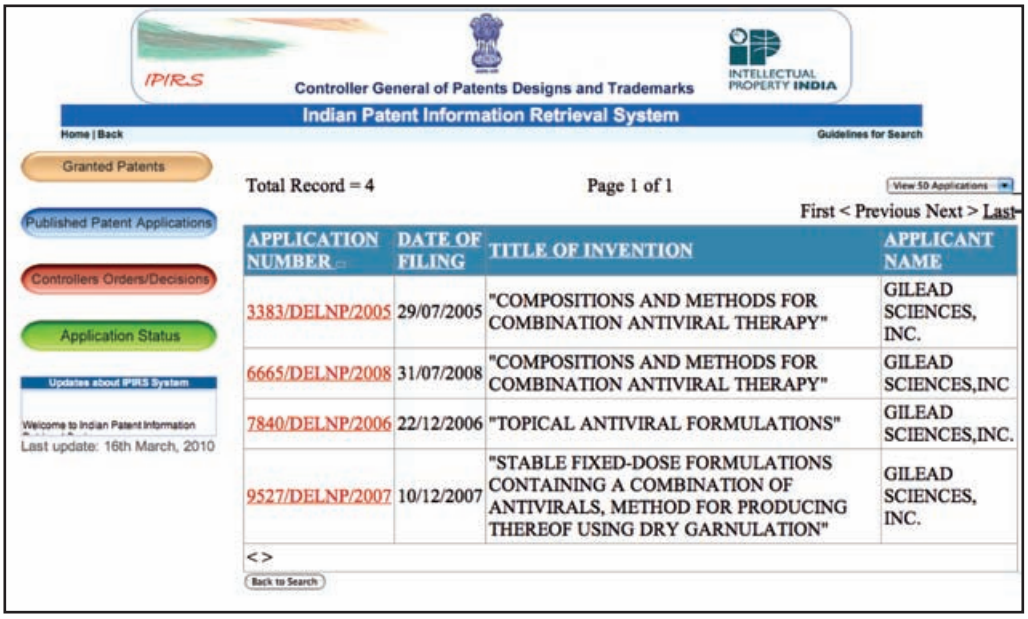


Figure 60: Indian Patent Office search results for national phase application relating to WO 2004/064845



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Application Status

Updates about IPIRS System

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Last update: 16th March, 2010

Total Record = 4

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View 50 Applications

First < Previous Next > Last

APPLICATION NUMBER	DATE OF FILING	TITLE OF INVENTION	APPLICANT NAME
3383/DELNP/2005	29/07/2005	"COMPOSITIONS AND METHODS FOR COMBINATION ANTIVIRAL THERAPY"	GILEAD SCIENCES, INC.
6665/DELNP/2008	31/07/2008	"COMPOSITIONS AND METHODS FOR COMBINATION ANTIVIRAL THERAPY"	GILEAD SCIENCES,INC
7840/DELNP/2006	22/12/2006	"TOPICAL ANTIVIRAL FORMULATIONS"	GILEAD SCIENCES,INC.
9527/DELNP/2007	10/12/2007	"STABLE FIXED-DOSE FORMULATIONS CONTAINING A COMBINATION OF ANTIVIRALS, METHOD FOR PRODUCING THEREOF USING DRY GARNULATION"	GILEAD SCIENCES, INC.

<>

Back to Search

Figure 61: Indian Patent Office bibliographic data for national phase application No. 3383/DELNP/2005 (deriving from WO 2004/064845)

International patent application and publication data confirms that this application derives from WO 2004/064845

INTELLECTUAL PROPERTY INDIA

Office of Controller General of Patents Designs, and Trademarks

Indian Patent Information Retrieval System

(IPIRS)

15 May 2010 09:32 | Guidelines For Searching | Home

Published Patent Applications

(12) PATENT APPLICATION PUBLICATION

(19) INDIA

(22) Date of filing of Application :29/07/2005

(21) Application No. : 3383/DELNP/2005

(43) Publication Date : 20/04/2007
Journal No. - 16/2007

(54) Title of the invention : "COMPOSITIONS AND METHODS FOR COMBINATION ANTIVIRAL THERAPY"

(51) International classification	:A61K 31/675
(31) Priority Document No	:60/440,308
(32) Priority Date	:14/01/2003
(33) Name of priority country	:U.S.A.
(86) International Application No	:PCT/US2004/000832
Filing Date	:13/01/2004
(87) International Publication No	:WO 2004/064845
(61) Patent of Addition to Application Number	:NA
Filing Date	:NA
(62) Divisional to Application Number	:NA
Filing Date	:NA

(71)**Name of Applicant :**
1)GILEAD SCIENCES, INC.
Address of Applicant :333 LAKESIDE DRIVE, FOSTER CITY, CA 94404, U.S.A. U.S.A.

(72)**Name of Inventor :**
1)DAHL, TERRENCE, C (U.S.A.)
2)MENNING, MARK, M (U.S.A.)
3)OLIYAI, REZA (U.S.A.)

(57) Abstract :
The present invention relates to therapeutic combination of [2-(6-amino-purin-9 yl)-l-methyl-ethoxymethyl]-phosphonic acid diisopropoxycarbonyloxymethyl ester (tenofovir disoproxil fumarate, Viread ®) and (2R, 5S, cis)-4-amino-5-fluoro-l-(2 hydroxymethyl-l,3-oxathiolan-5-yl)- (lH)-pyrimidin-2-one (emtricitabine, Emtriva™, (-)-Cis FTC) and their physiologically functional derivatives. The combinations may be useful in the treatment of HIV infections, including infections with HIV mutants bearing resistance to nucleoside and/or non-nucleoside inhibitors. The present invention is also concerned with pharmaceutical compositions and formulations of said combinations of tenofovir disoproxil fumarate and emtricitabine, and their physiologically functional derivatives, as well as therapeutic methods of use of those compositions and formulations.

Step 2

To establish whether a patent has been granted in India, return to the home page of the Indian Patent Office's website (URL: http://ipindia.nic.in/ipirs/patentsearch.htm). Click on the option *Application Status*. Enter the national phase application number 3383/DELNP/2005 as shown in Figure 62. The search reveals that application No. 3383/DELNP/2005 has been abandoned under Section 21(1) of the Indian Patents Act (see Figure 63). It is important to note, when checking the status of an application, that there may be errors in the database. Hence, negative results are not conclusive. To be prudent, it is always worth requesting in writing confirmation of the status of an application from the patent office.

Figure 62: Indian Patent Office search for application status of application No. 3383/DELNP/2005 (deriving from WO 2004/064845)

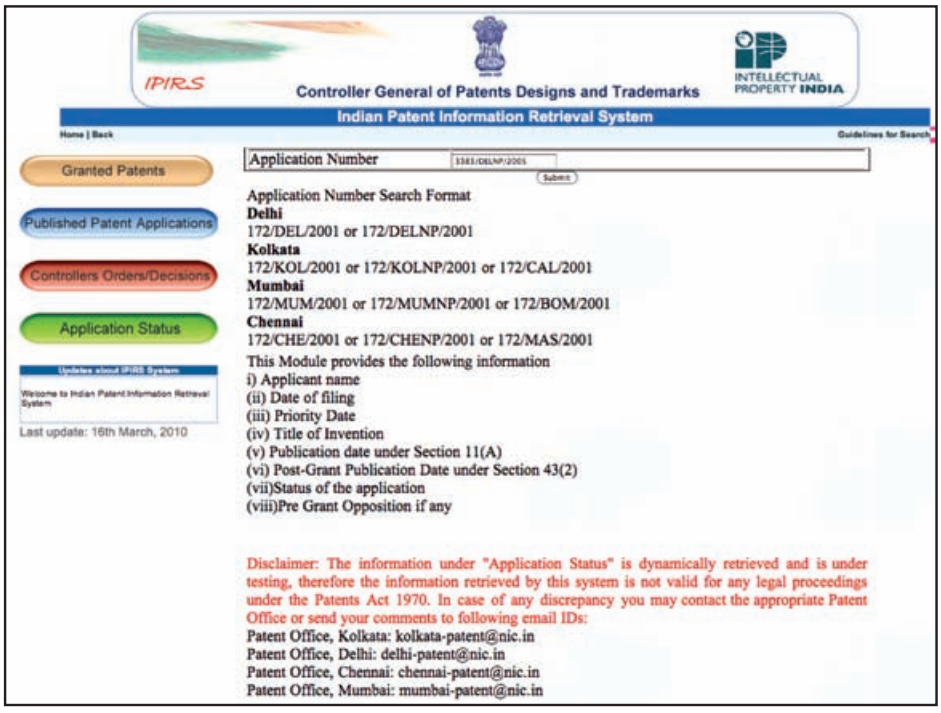
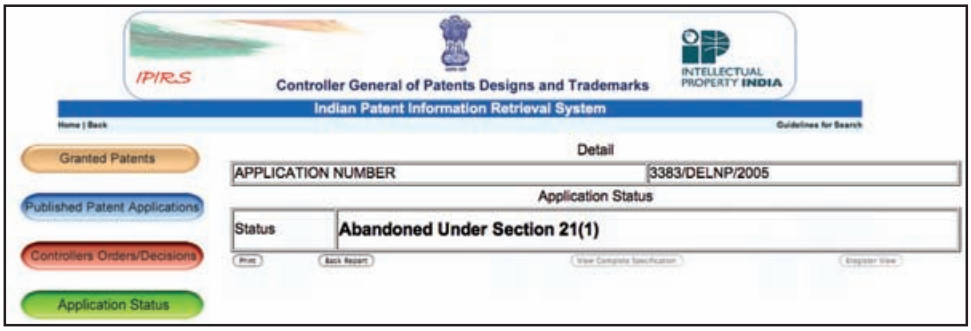


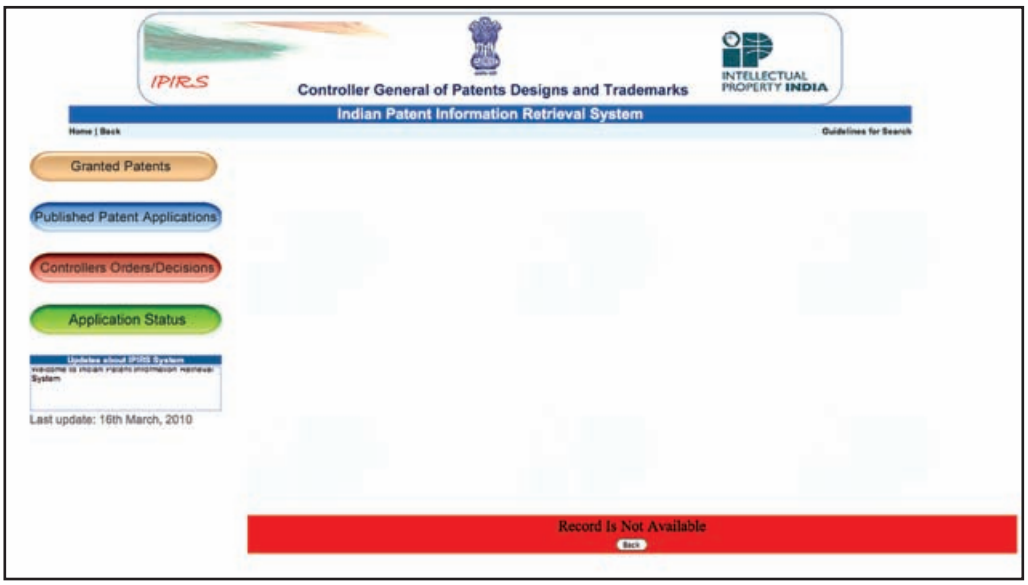
Figure 63: Indian Patent Office search results for application status of application No. 3383/DELNP/2005 (deriving from WO 2004/064845)



It is also recommended to check in the granted patent database. This is done to double check in case of errors in the *Application Status* database and to verify whether the patent has been granted.

To search for patents granted in India, at the URL mentioned above, click on the option *Granted Patents*. Select the option *Advanced Search*. A new page will appear providing data and search field options mirroring the search options for published patent applications discussed in Example 4.2 on page 59. Following the process described in Example 4.2, select the data field *Application Number* and enter the application number 3383/DELNP/2005 in the text box. If the patent is granted, the granted patent number and other bibliographic data will be displayed.[3] In this case, the search confirms that the patent has not been granted (see Figure 64).

Figure 64: Indian Patent Office granted patents search result for application No. 3383/DELNP/2005 (deriving from WO 2004/064845)



5.2 Using official patent office journals

Where patent information for the country of interest is not available in an online searchable database, an alternative but time-consuming method for locating patents is to review the official patent office journal (also referred to as gazette or bulletin) of the relevant national (or regional) patent office.

3 It is possible to view the entire specification and claims of granted patents in India, in HTML format.

All national and regional patent offices should provide some form of official office journal where applications and granted patents are published for public viewing. Official patent office journals are usually made available in hard copies or on a CD, and released at intervals. For example, the Intellectual Property Organisation of Pakistan usually releases its journal for published patent applications every seven days. Publication details of patents will typically be in the local language of the country or in the language in which legal proceedings are conducted.

Official patent journals can be obtained by mail from a patent office following payment of a subscription fee. Alternatively, it is possible to visit a patent office and search hard copies of journals on-site.

However, there is a small but growing number of countries that provide access to their patent journals online in a PDF or Word format (see **Appendix III**). Although search options in PDFs and Word documents are extremely limited and each journal will have to be reviewed individually, their availability in an electronic format does make searching easier.

It should be noted, journals available in electronic form might only begin from a particular year. Therefore, it may still be necessary to contact the national (or regional) patent office directly for details of patents that were published prior to the start of the online availability of journals. Also, some journals will only provide a minimum amount of information, such as the applicant name and title of the patent. Despite the fact that some journals only offer limited information, it may be possible to obtain further details about the relevance of a patent using some of the techniques discussed in Chapter 4.

The following example demonstrates how searching online patent office journals may be useful for identifying patents of interest.

Example 5.5: Official Patent Gazette of the Intellectual Property Organisation of Pakistan

Step 1

Enter the following URL to access electronic versions of the official patent gazette for published applications by Intellectual Property Organisation of Pakistan: http://www.ipo.gov.pk/Patent/PatentGazzette.aspx

As it is not possible to identify in advance the specific issue of the journal/gazette in which a patent of interest may have been published, it will be necessary to go through each one. While this is a time-consuming exercise, for countries that do not provide a searchable online database, this is the only way to identify relevant patents on medicines.

Click on the gazette of interest to download the PDF file (see Figure 65). Once the PDF version of the gazette is downloaded, it is possible to review the new applications for patents published in Pakistan (see Figure 66).

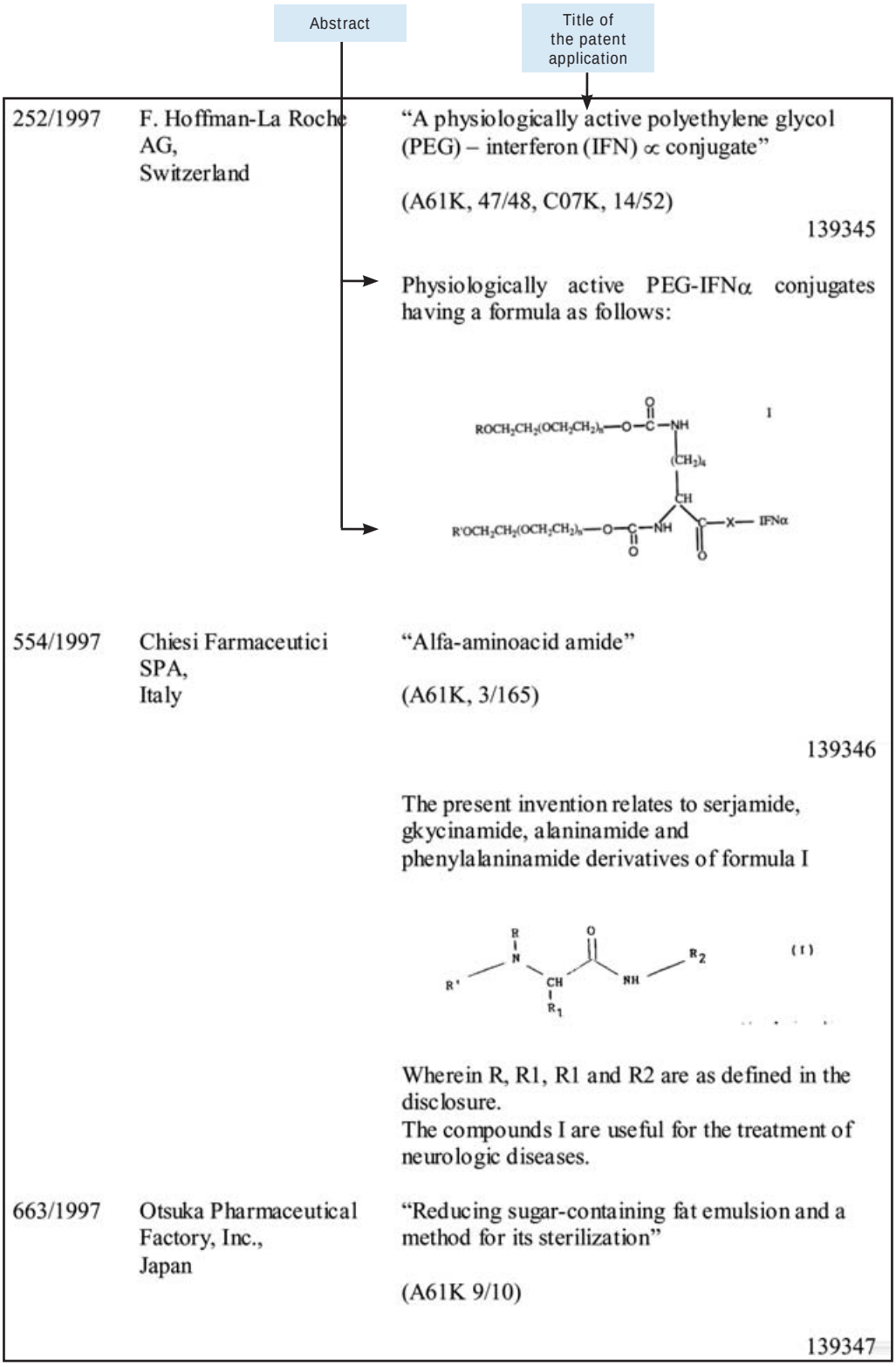
Figure 65: Intellectual Property Organisation of Pakistan Patents Gazette notifications

NB: The Intellectual Property Organisation of Pakistan also provides electronic documents, which list basic information for patents granted. The documents can be downloaded here: http://www.ipo.gov.pk/Patent/PatentGranted.aspx

Step 2

Figure 66 shows an extract from the official patent gazette of Pakistan published on 2 February 2008.

Figure 66: Extract from the Official Patents Gazette of Pakistan
2 February 2008



Using Application No. 139345 by F. Hoffmann La Roche for *A physiologically active polyethylene glycol (PEG) – interferon (IFN) conjugate* as an example, a person with knowledge of the field may be able to determine the subject matter of this patent by simply looking at the chemical structure provided.

If the information provided in the gazette is limited, further details that could help identify the subject matter of the patent may be obtained by searching for equivalent patent documents through esp@cenet or Patentscope. This would mean using the techniques discussed in Chapter 4, but now in inverse order--working back from the limited national data (gazette) to obtain the equivalent or related patents filed in other countries.

For this example, the esp@cenet database is used. Access the *Advanced Search* option for esp@cenet as shown in Figure 35.

Using the information provided for Pakistan application No. 139345, conduct a keyword search as shown in Figure 67. Note that the results of the search will depend on the terms selected. In the example shown here, a keyword search against the words *physiologically*, *conjugate* and the applicant name *Hoffmann* returns one result (see Figure 68).

Figure 67: Esp@cenet advanced search for keywords "Physiologically", "Conjugate" and Applicant Name "Hoffmann"

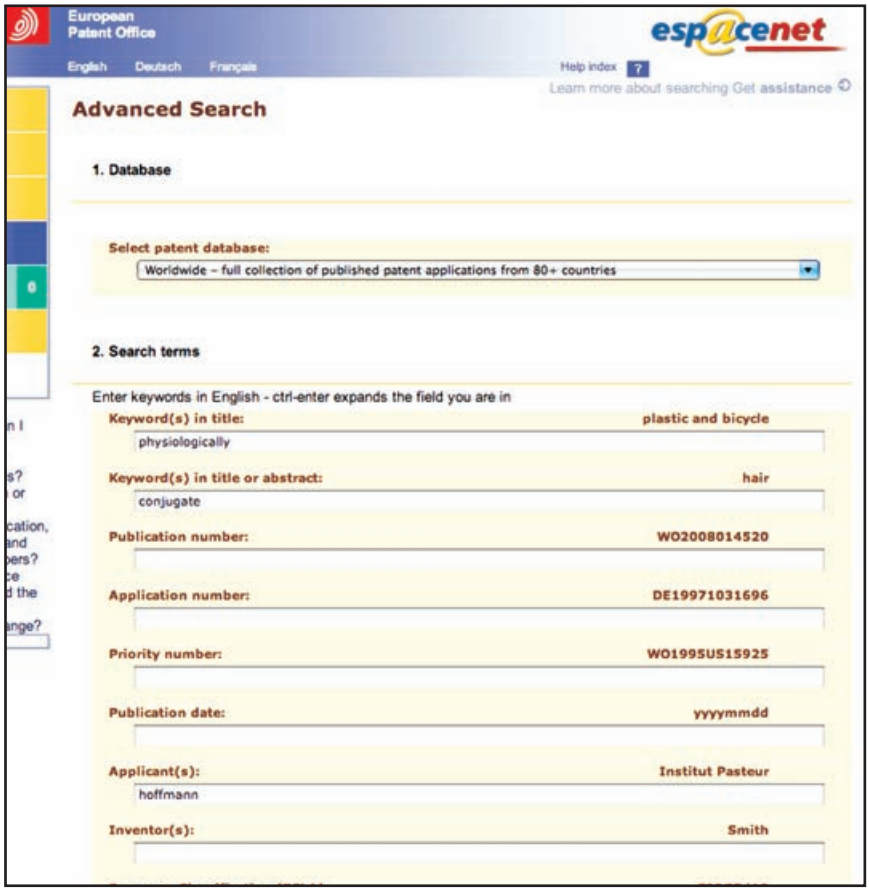
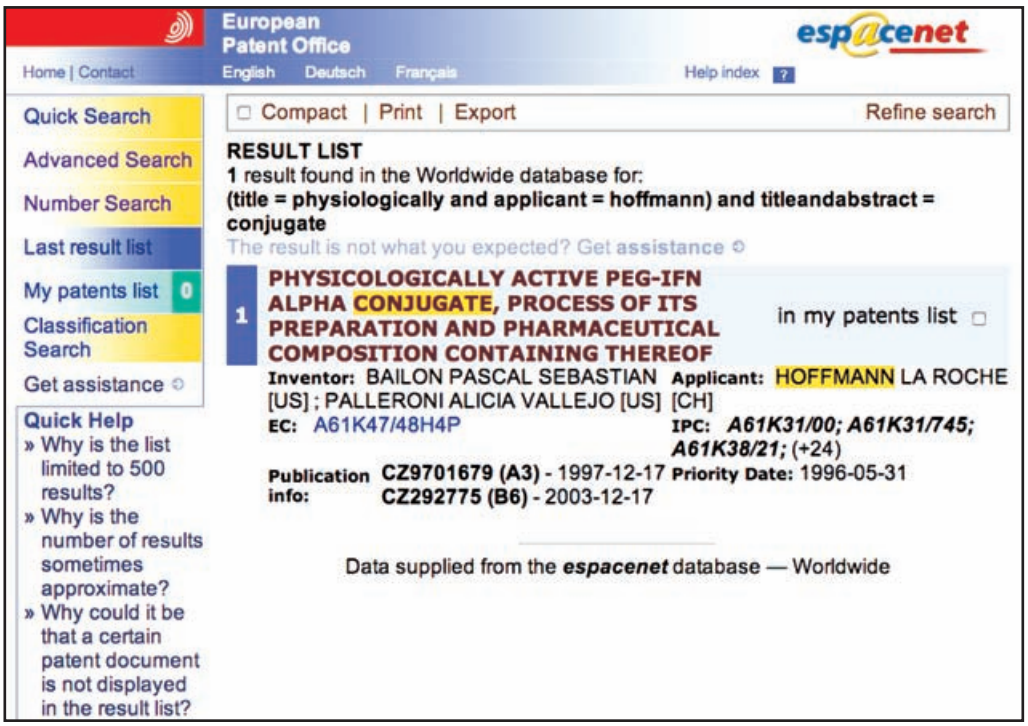


Figure 68: Esp@cenet advanced search results for keywords "Physiologically", "Conjugate" and Applicant Name "Hoffmann"



Click on the title of the patent retrieved to review the bibliographic details (see Figure 69). As can be seen from the bibliographic details of the patent retrieved, the English title and abstract appear to relate to Pakistan application No. 139345. As the patent retrieved is for the Czech Republic (CZ), to obtain access to a patent document in English, click on the INPADOC patent family link.

From the INPADOC patent family list click on the title of the patent for Canada as shown in Figure 70. Although the title of the Canadian patent is not identical to Pakistan application No. 139345, the abstract is. It would appear that Canadian patent No. 2203480 (shown in Figure 71) might cover identical or similar subject matter, though of course this can only be determined once the patent document for application No. 139345 is obtained. Nonetheless, this exercise can be a useful way to obtain an impression of the subject matter that the published application may cover. This process can also help one to decide whether it is necessary to obtain a copy of the complete specification for the patent.

Figure 69: Esp@cenet bibliographic data for Czech Republic patent publication No. 9701679

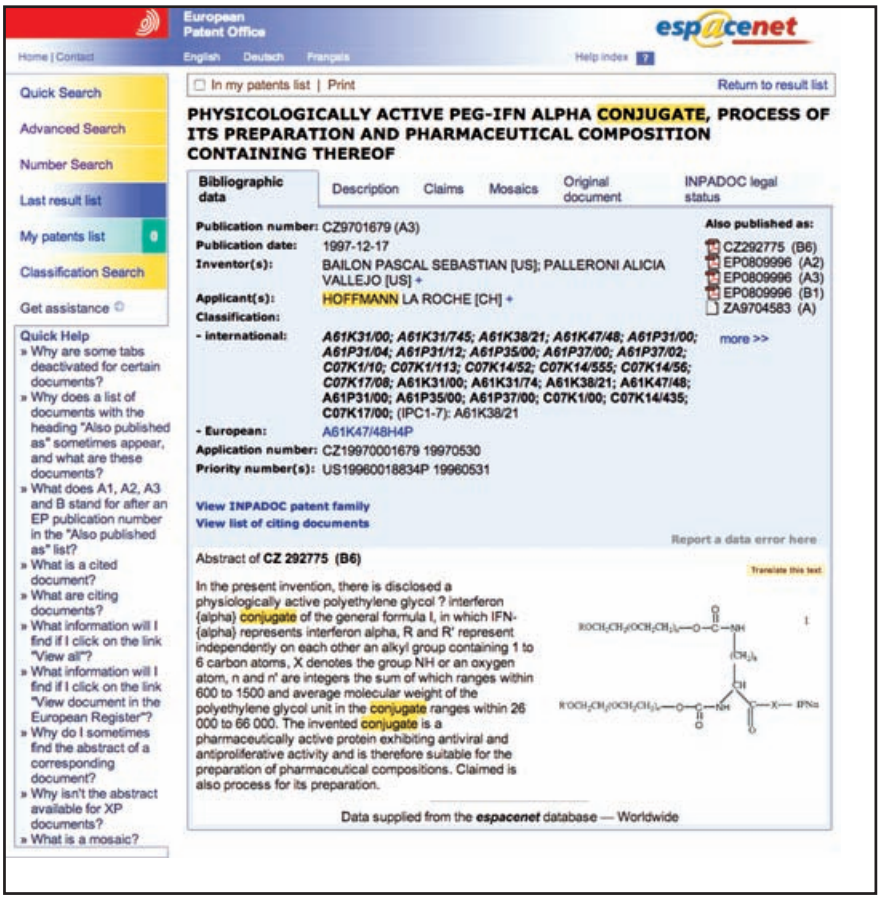


Figure 70: Esp@cenet INPADOC patent family for Czech Republic patent publication No. 9701679

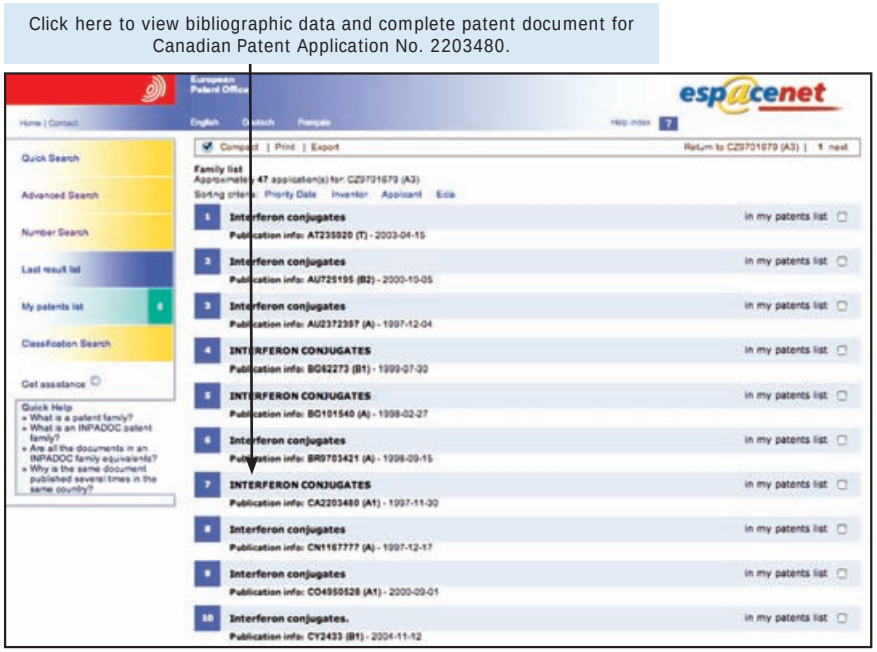
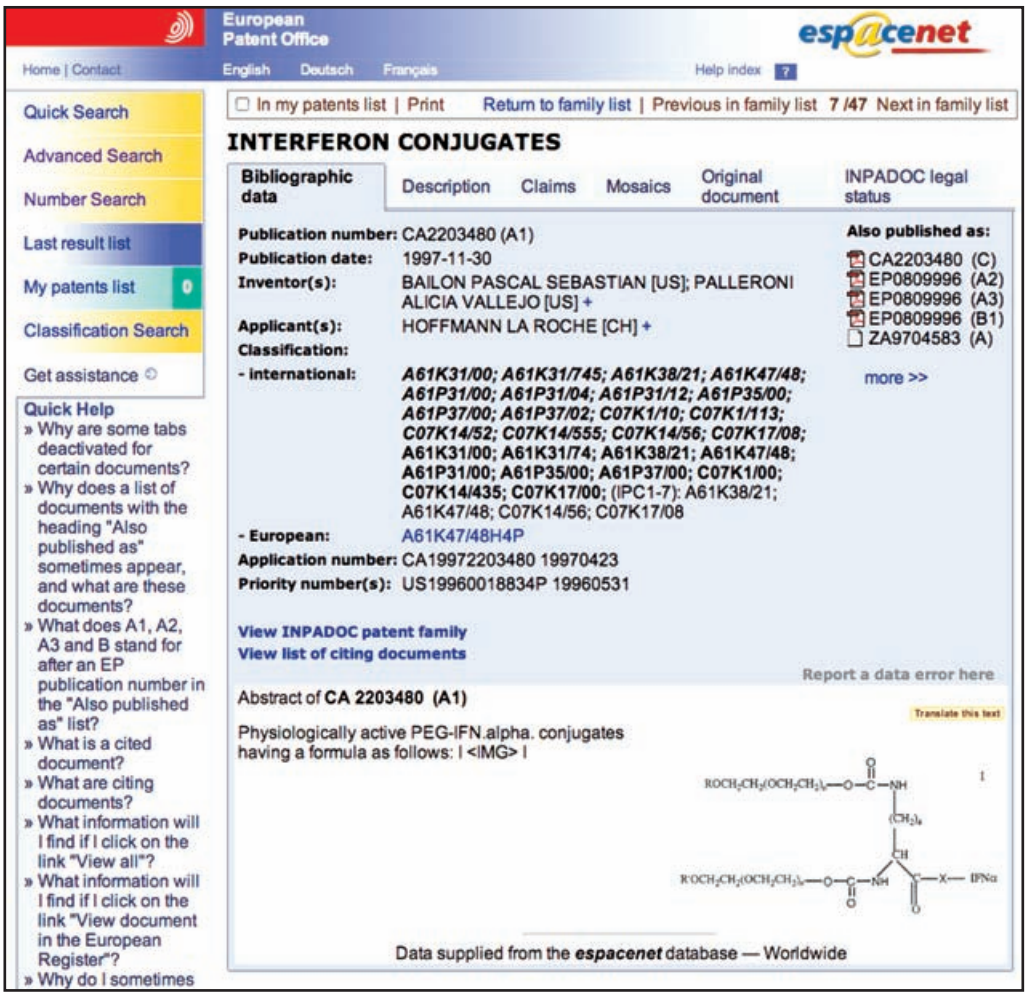


Figure 71: Esp@cenet bibliographic data for Canadian patent application No. 2203480



To access the full patent document for Canadian application No. 2203480, follow the steps discussed in Figures 19 and 20.

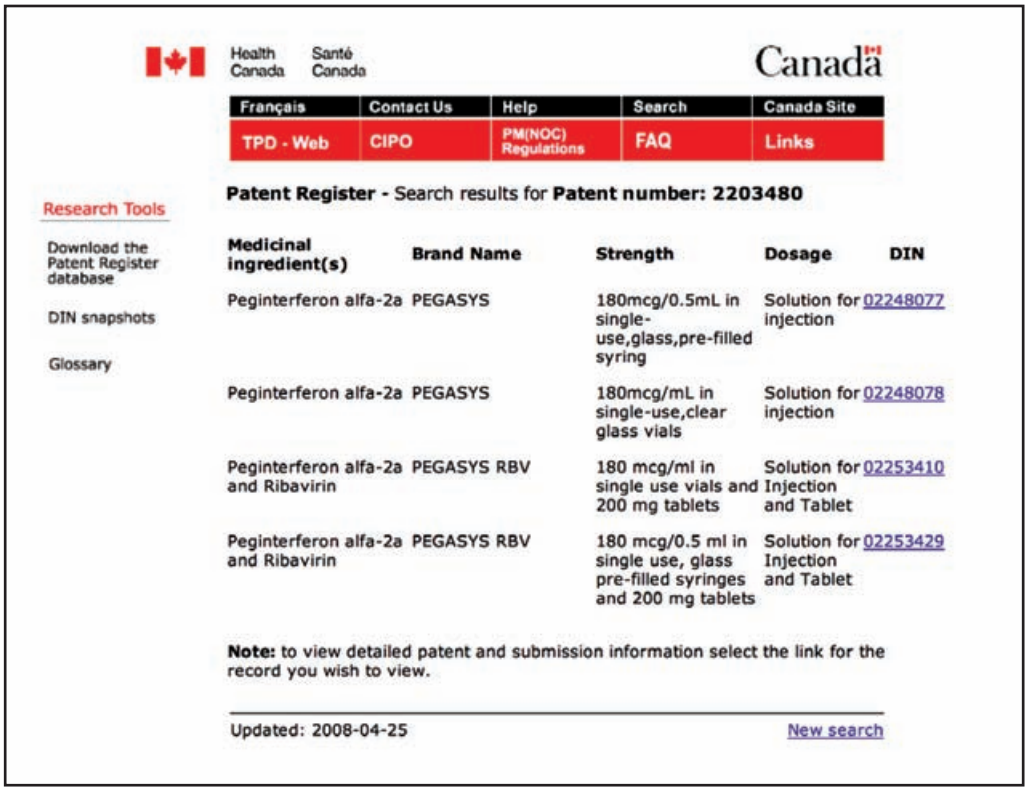
Step 3

Where the INPADOC patent family lists a Canadian patent (as in the example above), using this information to search the Health Canada Patent Register may help verify which marketed medicine the patent relates to.

To access the Health Canada Patent Register, follow step 1 described in Section 4.2.2. Enter Canadian patent No. 2203480 in the search field next to *Patent Number* (see Figure 13).

The search reveals that Canadian patent No. 2203480 is listed for the marketed product Pegasys® (pegintereferon alfa-2a injection), used to treat hepatitis C (see Figure 72). Click on the links under *DIN* to obtain further product and patent details.

Figure 72: Health Canada Patent Register search for Canadian patent application No. 2203480



Health Canada / Santé Canada — Canada

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TPD - Web | CIPO | PM(NOC) Regulations | FAQ | Links

Research Tools

Download the Patent Register database

DIN snapshots

Glossary

Patent Register - Search results for **Patent number: 2203480**

Medicinal ingredient(s)	Brand Name	Strength	Dosage	DIN
Peginterferon alfa-2a	PEGASYS	180mcg/0.5mL in single-use,glass,pre-filled syring	Solution for injection	02248077
Peginterferon alfa-2a	PEGASYS	180mcg/mL in single-use,clear glass vials	Solution for injection	02248078
Peginterferon alfa-2a and Ribavirin	PEGASYS RBV	180 mcg/ml in single use vials and 200 mg tablets	Solution for Injection and Tablet	02253410
Peginterferon alfa-2a and Ribavirin	PEGASYS RBV	180 mcg/0.5 ml in single use, glass pre-filled syringes and 200 mg tablets	Solution for Injection and Tablet	02253429

Note: to view detailed patent and submission information select the link for the record you wish to view.

Updated: 2008-04-25 New search

5.3 Obtaining patent information from national/regional patent offices using priority data

Where patent information for a developing country is not available using the techniques discussed above, it may be possible to locate patents using priority data. For example, by providing the priority number(s) for a patent relating to an Orange Book listing, a patent office may be able to match it to a patent filed locally.

It is worth noting that some developing country patent authorities may lack the resources to deal with specific requests or do not have systems in place to locate patents. For those countries where obtaining information is difficult, an alternative route is to use the service of a local patent lawyer. Although there is a cost involved, local patent lawyers can be helpful in retrieving patent information. However, it is important to check the credentials of local patent lawyers to ensure they are able to carry out the task required. A useful starting point is to search the Internet for legal services guides that rate law firms in the area of intellectual property around the world.

5.4 Obtaining patent specifications from national/ regional patent offices

Once a patent is located using one of the methods described above, the next step is to obtain a copy of the concerned patent document to review the claims as filed and granted in the country of interest. Although having the patent numbers and basic bibliographic data may imply that a patent on a particular medicine exists in a country, it is still necessary to review the actual content of the relevant national patent to determine its scope.

Given that only a limited number of developing country patent offices provide online access to the full text of patent documents, in many instances it will be necessary to make a request directly to the relevant patent office. As patent claims can be refused partially or entirely during examination, or even after grant (e.g. as a result of a revocation), it is important to track the status of a patent once located. In a number of countries, this may require paying separate official patent office fees for a copy of the patent application as filed as well as for a certified copy of the final granted patent.

5.5. Ensuring patent information is up to date

Patents holders are required to pay renewal fees to maintain a patent. The timing of the payment of renewal fees varies from country to country, ranging from once a year to every four years. In some countries a renewal fee will also be due during the application phase in order to keep the patent application alive on the register. Depending on the status of the patent and the laws governing renewal payments, failure to pay the required renewal fee could result in the patent becoming abandoned or revoked. Note that patent laws may allow applicants or patent holders a grace period of six or more months after the due date for renewal within which to make payment. As many of the online patent databases may not be accurate in terms of providing whether an applicant or patent holder has paid the required renewal fees, it is worth checking with the national or regional patent office on an annual basis.

The status of patents may also change as a result of an opposition or revocation action. Although a patent may have been granted and renewed, it can still be revoked if a third party successfully invalidates it (through legal proceedings).

Therefore, whichever method is used to obtain patent information, it is imperative that the information is kept up to date.

6

Evaluating patent information for public health needs

The mere existence of a patent application or granted patent should not be taken as blocking the path to procuring or manufacturing generic versions of a medicine. For example, a patent covering a particular formulation, dosage form or process may not be infringed when an alternative dosage form of the same medicine is procured, or when a different production process is used. Only after the claims of the relevant patent(s) have been analysed will it be possible to assess this.

This guide only looks at how to find patents on medicines. The subject of patent claim interpretation and construction goes beyond the scope of this guide, and involves specialist subject areas; it is especially complex given the fact that laws and practices vary from one country to the next. For this reason, when analysing a patent, a lawyer familiar with the patent law of the country in question should be consulted. It is also recommended that persons skilled in the specific subject matter of the patent be involved.

It is worth bearing in mind, even where a patent or patent application calls into question whether a generic version of a medicine can be manufactured or procured, a number of options may be available. When there is reason to believe that the patent does not meet patentability requirements, one option may be to file an opposition or revocation action to ensure patent is not granted or is invalidated if already granted. Many patent laws allow for such interventions by third parties where there is evidence to suggest that a patent should not be or should not have been granted. However, such proceedings can take considerable time and expertise, and are dependent on whether there is sufficient evidence for challenging a patent.

Another option is negotiating directly with the patent holder, either for a reduction in the price of the medicine, or for a voluntary license to enable local manufacturing of the product. Compulsory licenses and government use authorizations are also options that are permitted under the TRIPS Agreement and that are available in most national patent laws.

Numerous considerations come into play when making decisions on whether there is freedom to procure or manufacture generic versions of a particular medicine. However, a fundamental part of the decision-making process is knowing which medicines are covered by patents. It is hoped that this guide will provide a useful starting point for navigating the various databases and obtaining the required patent information.

Appendices

Appendix I

Paris Convention for the Protection of Industrial Property

Paris Convention (1883), revised at Brussels (1900), at Washington (1911), at The Hague (1925), at London (1934), at Lisbon (1958) and at Stockholm (1967), and amended in 19 79 (Paris Union)

Status on October 15, 2009

State	Date on which State became party to the Convention	Latest Act[1] of the Convention to which State is party and date on which State became party to that Act	
Albania	October 4, 1995	Stockholm:	October 4, 1995
Algeria	March 1, 1966	Stockholm:	April 20, 1975[2]
Andorra	June 2, 2004	Stockholm:	June 2, 2004
Angola	December 27, 2007	Stockholm:	December 27, 2007
Antigua and Barbuda	March 17, 2000	Stockholm:	March 17, 2000
Argentina	February 10, 1967	Lisbon:	February 10, 1967
		Stockholm,	Articles 13 to 30: October 8, 1980
Armenia	December 25, 1991	Stockholm:	December 25, 1991[2]
Australia	October 10, 1925	Stockholm,	Articles 1 to 12: September 27, 1975
		Stockholm,	Articles 13 to 30: August 25, 1972
Austria	January 1, 1909	Stockholm:	August 18, 1973
Azerbaijan	December 25, 1995	Stockholm:	December 25, 1995
Bahamas	July 10, 1973	Lisbon:	July 10, 1973
		Stockholm,	Articles 13 to 30: March 10, 1977
Bahrain	October 29, 1997	Stockholm:	October 29, 1997
Bangladesh	March 3, 1991	Stockholm:	March 3, 1991[2]
Barbados	March 12, 1985	Stockholm:	March 12, 1985
Belarus	December 25, 1991	Stockholm:	December 25, 1991[2]
Belgium	July 7, 1884	Stockholm:	February 12, 1975
Belize	June 17, 2000	Stockholm:	June 17, 2000
Benin	January 10, 1967	Stockholm:	March 12, 1975
Bhutan	August 4, 2000	Stockholm:	August 4, 2000
Bolivia (Plurinational State of)	November 4, 1993	Stockholm:	November 4, 1993
Bosnia and Herzegovina	March 1, 1992	Stockholm:	March 1, 1992
Botswana	April 15, 1998	Stockholm:	April 15, 1998
Brazil	July 7, 1884	Stockholm,	Articles 1 to 12: November 24, 1992
		Stockholm,	Articles 13 to 30: March 24, 1975[2]
Bulgaria	June 13, 1921	Stockholm,	Articles 1 to 12: May 19 or 27, 1970[3]
		Stockholm,	Articles 13 to 30: May 27, 1970

State	Date on which State became party to the Convention	Latest Act[1] of the Convention to which State is party and date on which State became party to that Act	
Burkina Faso	November 19, 1963	Stockholm:	September 2, 1975
Burundi	September 3, 1977	Stockholm:	September 3, 1977
Cambodia	September 22, 1998	Stockholm:	September 22, 1998
Cameroon	May 10, 1964	Stockholm:	April 20, 1975
Canada	June 12, 1925	Stockholm,	Articles 1 to 12: May 26, 1996
		Stockholm,	Articles 13 to 30: July 7, 1970
Central African Republic	November 19, 1963	Stockholm:	September 5, 1978
Chad	November 19, 1963	Stockholm:	September 26, 1970
Chile	June 14, 1991	Stockholm:	June 14, 1991
China[4]	March 19, 1985	Stockholm:	March 19, 1985[2]
Colombia	September 3, 1996	Stockholm:	September 3, 1996
Comoros	April 3, 2005	Stockholm:	April 3, 2005
Congo	September 2, 1963	Stockholm:	December 5, 1975
Costa Rica	October 31, 1995	Stockholm:	October 31, 1995
Côte d'Ivoire	October 23, 1963	Stockholm:	May 4, 1974
Croatia	October 8, 1991	Stockholm:	October 8, 1991
Cuba	November 17, 1904	Stockholm:	April 8, 1975[2]
Cyprus	January 17, 1966	Stockholm:	April 3, 1984
Czech Republic	January 1, 1993	Stockholm:	January 1, 1993
Democratic People's Republic of Korea	June 10, 1980	Stockholm:	June 10, 1980
Democratic Republic of the Congo	January 31, 1975	Stockholm:	January 31, 1975
Denmark[5]	October 1, 1894	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 1970
Djibouti	May 13, 2002	Stockholm:	May 13, 2002
Dominica	August 7, 1999	Stockholm:	August 7, 1999
Dominican Republic	July 11, 1890	The Hague:	April 6, 1951
Ecuador	June 22, 1999	Stockholm:	June 22, 1999[2]
Egypt	July 1, 1951	Stockholm:	March 6, 1975[2]
El Salvador	February 19, 1994	Stockholm:	February 19, 1994
Equatorial Guinea	June 26, 1997	Stockholm:	June 26, 1997
Estonia	August 24, 19946	Stockholm:	August 24, 1994
Finland	September 20, 1921	Stockholm,	Articles 1 to 12: October 21, 1975
		Stockholm,	Articles 13 to 30: September 15, 1970
France[7]	July 7, 1884	Stockholm:	August 12, 1975
Gabon	February 29, 1964	Stockholm:	June 10, 1975
Gambia	January 21, 1992	Stockholm:	January 21, 1992
Georgia	December 25, 1991	Stockholm:	December 25, 1991[2]
Germany	May 1, 1903	Stockholm:	September 19, 1970
Ghana	September 28, 1976	Stockholm:	September 28, 1976

State	Date on which State became party to the Convention	Latest Act[1] of the Convention to which State is party and date on which State became party to that Act	
Greece	October 2, 1924	Stockholm:	July 15, 1976
Grenada	September 22, 1998	Stockholm:	September 22, 1998
Guatemala	August 18, 1998	Stockholm:	August 18, 1998[2]
Guinea	February 5, 1982	Stockholm:	February 5, 1982
Guinea-Bissau	June 28, 1988	Stockholm:	June 28, 1988
Guyana	October 25, 1994	Stockholm:	October 25, 1994
Haiti	July 1, 1958	Stockholm:	November 3, 1983
Holy See	September 29, 1960	Stockholm:	April 24, 1975
Honduras	February 4, 1994	Stockholm:	February 4, 1994
Hungary	January 1, 1909	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 1970[2]
Iceland	May 5, 1962	Stockholm,	Articles 1 to 12: April 9, 1995
		Stockholm,	Articles 13 to 30: December 28, 1984
India	December 7, 1998	Stockholm:	December 7, 19982
Indonesia	December 24, 1950	Stockholm,	Articles 1 to 12: September 5, 1997
		Stockholm,	Articles 13 to 30: December 20, 1979[2]
Iran (Islamic Republic of)	December 16, 1959	Stockholm:	March 12, 1999[2]
Iraq	January 24, 1976	Stockholm:	January 24, 1976[2]
Ireland	December 4, 1925	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 1970
Israel	March 24, 1950	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 1970
Italy	July 7, 1884	Stockholm:	April 24, 1977
Jamaica	December 24, 1999	Stockholm:	December 24, 1999
Japan	July 15, 1899	Stockholm,	Articles 1 to 12: October 1, 1975
		Stockholm,	Articles 13 to 30: April 24, 1975
Jordan	July 17, 1972	Stockholm:	July 17, 1972
Kazakhstan	December 25, 1991	Stockholm:	December 25, 1991[2]
Kenya	June 14, 1965	Stockholm:	October 26, 1971
Kyrgyzstan	December 25, 1991	Stockholm:	December 25, 1991[2]
Lao People's Democratic Republic	October 8, 1998	Stockholm:	October 8, 1998[2]
Latvia	September 7, 1993[8]	Stockholm:	September 7, 1993
Lebanon	September 1, 1924	London:	September 30, 1947
		Stockholm,	Articles 13 to 30: December 30, 1986[2]
Lesotho	September 28, 1989	Stockholm:	September 28, 1989[2]
Liberia	August 27, 1994	Stockholm:	August 27, 1994
Libyan Arab Jamahiriya	September 28, 1976	Stockholm:	September 28, 1976[2]

State	Date on which State became party to the Convention	Latest Act[1] of the Convention to which State is party and date on which State became party to that Act	
Liechtenstein	July 14, 1933	Stockholm:	May 25, 1972
Lithuania	May 22, 1994	Stockholm:	May 22, 1994
Luxembourg	June 30, 1922	Stockholm:	March 24, 1975
Madagascar	December 21, 1963	Stockholm:	April 10, 1972
Malawi	July 6, 1964	Stockholm:	June 25, 1970
Malaysia	January 1, 1989	Stockholm:	January 1, 1989
Mali	March 1, 1983	Stockholm:	March 1, 1983
Malta	October 20, 1967	Lisbon:	October 20, 1967
		Stockholm,	Articles 13 to 30: December 12, 1977[2]
Mauritania	April 11, 1965	Stockholm:	September 21, 1976
Mauritius	September 24, 1976	Stockholm:	September 24, 1976
Mexico	September 7, 1903	Stockholm:	July 26, 1976
Monaco	April 29, 1956	Stockholm:	October 4, 1975
Mongolia	April 21, 1985	Stockholm:	April 21, 1985[2]
Montenegro	June 3, 2006	Stockholm:	June 3, 2006
Morocco	July 30, 1917	Stockholm:	August 6, 1971
Mozambique	July 9, 1998	Stockholm:	July 9, 1998
Namibia	January 1, 2004	Stockholm	January 1, 2004
Nepal	June 22, 2001	Stockholm:	June 22, 2001
Netherlands[9]	July 7, 1884	Stockholm:	January 10, 1975
New Zealand[10]	July 29, 1931	London:	July 14, 1946
		Stockholm,	Articles 13 to 30: June 20, 1984
Nicaragua	July 3, 1996	Stockholm:	July 3, 1996[2]
Niger	July 5, 1964	Stockholm:	March 6, 1975
Nigeria	September 2, 1963	Lisbon:	September 2, 1963
Norway	July 1, 1885	Stockholm:	June 13, 1974
Oman	July 14, 1999	Stockholm:	July 14, 1999[2]
Pakistan	July 22, 2004	Stockholm	July 22, 2004[2]
Panama	October 19, 1996	Stockholm:	October 19, 1996
Papua New Guinea	June 15, 1999	Stockholm:	June 15, 1999
Paraguay	May 28, 1994	Stockholm:	May 28, 1994
Peru	April 11, 1995	Stockholm:	April 11, 1995
Philippines	September 27, 1965	Lisbon:	September 27, 1965
		Stockholm,	Articles 13 to 30: July 16, 1980
Poland	November 10, 1919	Stockholm:	March 24, 1975
Portugal	July 7, 1884	Stockholm:	April 30, 1975
Qatar	July 5, 2000	Stockholm:	July 5, 2000
Republic of Korea	May 4, 1980	Stockholm:	May 4, 1980
Republic of Moldova	December 25, 1991	Stockholm:	December 25, 1991[2]
Romania	October 6, 1920	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 19702

State	Date on which State became party to the Convention	Latest Act[1] of the Convention to which State is party and date on which State became party to that Act	
Russian Federation	July 1, 1965[11]	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3,11]
		Stockholm,	Articles 13 to 30: April 26, 1970[2,11]
Rwanda	March 1, 1984	Stockholm:	March 1, 1984
Saint Kitts and Nevis	April 9, 1995	Stockholm:	April 9, 1995
Saint Lucia	June 9, 1995	Stockholm:	June 9, 1995[2]
Saint Vincent and the Grenadines	August 29, 1995	Stockholm:	August 29, 1995
San Marino	March 4, 1960	Stockholm:	June 26, 1991
Sao Tome and Principe	May 12, 1998	Stockholm:	May 12, 1998
Saudi Arabia	March 11, 2004	Stockholm:	March 11, 2004
Senegal	December 21, 1963	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 1970
Serbia[12]	April 27, 1992	Stockholm:	April 27, 1992
Seychelles	November 7, 2002	Stockholm:	November 7, 2002
Sierra Leone	June 17, 1997	Stockholm:	June 17, 1997
Singapore	February 23, 1995	Stockholm:	February 23, 1995
Slovakia	January 1, 1993	Stockholm:	January 1, 1993
Slovenia	June 25, 1991	Stockholm:	June 25, 1991
South Africa	December 1, 1947	Stockholm:	March 24, 1975[2]
Spain	July 7, 1884	Stockholm:	April 14, 1972
Sri Lanka	December 29, 1952	London:	December 29, 1952
		Stockholm,	Articles 13 to 30: September 23, 1978
Sudan	April 16, 1984	Stockholm:	April 16, 1984
Suriname	November 25, 1975	Stockholm:	November 25, 1975
Swaziland	May 12, 1991	Stockholm:	May 12, 1991
Sweden	July 1, 1885	Stockholm,	Articles 1 to 12: October 9, 1970
		Stockholm,	Articles 13 to 30: April 26, 1970
Switzerland	July 7, 1884	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 1970
Syrian Arab Republic	September 1, 1924	Stockholm:	December 13, 2002[2]
Tajikistan	December 25, 1991	Stockholm:	December 25, 1991[2]
Thailand	August 2, 2008	Stockholm:	August 2, 2008[2]
The former Yugoslav Republic of Macedonia	September 8, 1991	Stockholm:	September 8, 1991
Togo	September 10, 1967	Stockholm:	April 30, 1975
Tonga	June 14, 2001	Stockholm:	June 14, 2001
Trinidad and Tobago	August 1, 1964	Stockholm:	August 16, 1988
Tunisia	July 7, 1884	Stockholm:	April 12, 1976[2]
Turkey	October 10, 1925	Stockholm,	Articles 1 to 12: February 1, 1995
		Stockholm,	Articles 13 to 30: May 16, 1976

State	Date on which State became party to the Convention	Latest Act[1] of the Convention to which State is party and date on which State became party to that Act	
Turkmenistan	December 25, 1991	Stockholm:	December 25, 1991[2]
Uganda	June 14, 1965	Stockholm:	October 20, 1973
Ukraine	December 25, 1991	Stockholm:	December 25, 1991[2]
United Arab Emirates	September 19, 1996	Stockholm:	September 19, 1996
United Kingdom[13]	July 7, 1884	Stockholm,	Articles 1 to 12: April 26 or May 19, 1970[3]
		Stockholm,	Articles 13 to 30: April 26, 1970
United Republic of Tanzania	June 16, 1963	Lisbon:	June 16, 1963
		Stockholm,	Articles 13 to 30: December 30, 1983
United States of America[14]	May 30, 1887	Stockholm,	Articles 1 to 12: August 25, 1973
		Stockholm,	Articles 13 to 30: September 5, 1970
Uruguay	March 18, 1967	Stockholm:	December 28, 1979
Uzbekistan	December 25, 1991	Stockholm:	December 25, 1991[2]
Venezuela (Bolivarian Republic of)	September 12, 1995	Stockholm:	September 12, 1995
Viet Nam	March 8, 1949	Stockholm:	July 2, 1976[2]
Yemen[2]	February 15, 2007	Stockholm:	February 15, 2007
Zambia	April 6, 1965	Lisbon:	April 6, 1965
		Stockholm,	Articles 13 to 30: May 14, 1977
Zimbabwe	April 18, 1980	Stockholm:	December 30, 1981

(Total: 173 States)

1 "Stockholm" means the Paris Convention for the Protection of Industrial Property as revised at Stockholm on July 14, 1967 (Stockholm Act); "Lisbon" means the Paris Convention as revised at Lisbon on October 31, 1958 (Lisbon Act); "London" means the Paris Convention as revised at London on June 2, 1934 (London Act); "The Hague" means the Paris Convention as revised at The Hague on November 6, 1925 (Hague Act).

2 With the declaration provided for in Article 28(2) of the Stockholm Act relating to the International Court of Justice.

3 These are the alternative dates of entry into force which the Director General of WIPO communicated to the States concerned.

4 The Stockholm Act applies also to the Hong Kong Special Administrative Region with effect from July 1, 1997, and to the Macau Special Administrative Region with effect from December 20, 1999.

5 Denmark extended the application of the Stockholm Act to the Faroe Islands with effect from August 6, 1971.

6 Estonia acceded to the Paris Convention (Washington Act, 1911) with effect from February 12, 1924. It lost its independence on August 6, 1940, and regained it on August 20, 1991.

7 Including all Overseas Departments and Territories.

8 Latvia acceded to the Paris Convention (Washington Act, 1911) with effect from August 20, 1925. It lost its independence on July 21, 1940, and regained it on August 21, 1991.

9 Ratification for the Kingdom in Europe, the Netherlands Antilles and Aruba.

10 The accession of New Zealand to the Stockholm Act, with the exception of Articles 1 to 12, extends to the Cook Islands, Niue and Tokelau.

11 Date of adherence of the Soviet Union, continued by the Russian Federation as from December 25, 1991.

12 Serbia is the continuing State from Serbia and Montenegro as from June 3, 2006.

13 The United Kingdom extended the application of the Stockholm Act to the Isle of Man with effect from October 29, 1983.

14 The United States of America extended the application of the Stockholm Act to all territories and possessions of the United States of America, including the Commonwealth of Puerto Rico, as from August 25, 1973.

Appendix II

PCT Contracting States[1]

Name of State followed by the two-letter code	Date on which State became bound by the PCT[1]	Name of State followed by the two-letter code	Date on which State became bound by the PCT[1]
Albania AL	4 October 1995	Dominican Republic DO	28 May 2007
Algeria DZ[2]	8 March 2000	Ecuador EC	7 May 2001
Angola AO	27 December 2007	Egypt EG	6 September 2003
Antigua and Barbuda AG	17 March 2000	El Salvador SV	17 August 2006
Armenia AM[2]	25 December 1991	Equatorial Guinea GQ	17 July 2001
Australia AU	31 March 1980	Estonia EE	24 August 1994
Austria AT	23 April 1979	Finland FI[3]	1 October 1980
Azerbaijan AZ	25 December 1995	France FR[2, 4]	25 February 1978
Bahrain BH[2]	18 March 2007	Gabon GA	24 January 1978
Barbados BB	12 March 1985	Gambia GM	9 December 1997
Belarus BY[2]	25 December 1991	Georgia GE2	25 December 1991
Belgium BE	14 December 1981	Germany DE	24 January 1978
Belize BZ	17 June 2000	Ghana GH	26 February 1997
Benin BJ	26 February 1987	Greece GR	9 October 1990
Bosnia and Herzegovina BA	7 September 1996	Grenada GD	22 September 1998
Botswana BW	30 October 2003	Guatemala GT	14 October 2006
Brazil BR	9 April 1978	Guinea GN	27 May 1991
Bulgaria BG	21 May 1984	Guinea-Bissau GW	12 December 1997
Burkina Faso BF	21 March 1989	Honduras HN	20 June 2006
Cameroon CM	24 January 1978	Hungary HU[2]	27 June 1980
Canada CA	2 January 1990	Iceland IS	23 March 1995
Central African Republic CF	24 January 1978	India IN[2]	7 December 1998
Chad TD	24 January 1978	Indonesia ID[2]	5 September 1997
Chile CL2	2 June 2009	Ireland IE	1 August 1992
China CN	1 January 1994	Israel IL	1 June 1996
Colombia CO	28 February 2001	Italy IT	28 March 1985
Comoros KM	3 April 2005	Japan JP	1 October 1978
Congo CG	24 January 1978	Kazakhstan KZ[2]	25 December 1991
Costa Rica CR	3 August 1999	Kenya KE	8 June 1994
Côte d'Ivoire CI	30 April 1991	Kyrgyzstan KG[2]	25 December 1991
Croatia HR	1 July 1998	Lao People's Democratic Republic LA	14 June 2006
Cuba CU2	16 July 1996	Latvia LV	7 September 1993
Cyprus CY	1 April 1998	Lesotho LS	21 October 1995
Czech Republic CZ	1 January 1993	Liberia LR	27 August 1994
Democratic People's Republic of Korea KP	8 July 1980	Libyan Arab Jamahiriya LY	15 September 2005
Denmark DK	1 December 1978	Liechtenstein LI	19 March 1980
Dominica DM	7 August 1999	Lithuania LT	5 July 1994

Name of State followed by the two-letter code	Date on which State became bound by the PCT[1]	Name of State followed by the two-letter code	Date on which State became bound by the PCT[1]
Luxembourg LU	30 April 1978	Senegal SN	24 January 1978
Madagascar MG	24 January 1978	Serbia RS	1 February 1997
Malawi MW	24 January 1978	Seychelles SC	7 November 2002
Malaysia MY[2]	16 August 2006	Sierra Leone SL	17 June 1997
Mali ML	19 October 1984	Singapore SG	23 February 1995
Malta MT[2]	1 March 2007	Slovakia SK	1 January 1993
Mauritania MR	13 April 1983	Slovenia SI	1 March 1994
Mexico MX	1 January 1995	South Africa ZA[2]	16 March 1999
Monaco MC	22 June 1979	Spain ES	16 November 1989
Mongolia MN	27 May 1991	Sri Lanka LK	26 February 1982
Montenegro ME	3 June 2006	Sudan SD	16 April 1984
Morocco MA	8 October 1999	Swaziland SZ	20 September 1994
Mozambique MZ[2]	18 May 2000	Sweden SE[3]	17 May 1978
Namibia NA	1 January 2004	Switzerland CH	24 January 1978
Netherlands NL[5]	10 July 1979	Syrian Arab Republic SY	26 June 2003
New Zealand NZ	1 December 1992	Tajikistan TJ[2]	25 December 1991
Nicaragua NI	6 March 2003	Thailand TH[2]	24 December 2009
Niger NE	21 March 1993	The former Yugoslav Republic of Macedonia MK	10 August 1995
Nigeria NG	8 May 2005	Togo TG	24 January 1978
Norway NO[3]	1 January 1980	Trinidad and Tobago TT	10 March 1994
Oman OM[2]	26 October 2001	Tunisia TN[2]	10 December 2001
Papua New Guinea PG	14 June 2003	Turkey TR	1 January 1996
Peru PE	6 June 2009	Turkmenistan TM[2]	25 December 1991
Philippines PH	17 August 2001	Uganda UG	9 February 1995
Poland PL[3]	25 December 1990	Ukraine UA[2]	25 December 1991
Portugal PT	24 November 1992	United Arab Emirates AE	10 March 1999
Republic of Korea KR	10 August 1984	United Kingdom GB[6]	24 January 1978
Republic of Moldova MD[2]	25 December 1991	United Republic of Tanzania TZ	14 September 1999
Romania RO[2]	23 July 1979	United States of America US[7, 8]	24 January 1978
Russian Federation RU[2]	29 March 1978	Uzbekistan UZ[2]	25 December 1991
Saint Kitts and Nevis KN	27 October 2005	Viet Nam VN	10 March 1993
Saint Lucia LC[2]	30 August 1996	Zambia ZM	15 November 2001
Saint Vincent and the Grenadines VC[2]	6 August 2002	Zimbabwe ZW	11 June 1997
San Marino SM	14 December 2004		
Sao Tome and Principe ST	3 July 2008		

(Total: 142 States)

1 All PCT Contracting States are bound by Chapter II of the PCT relating to the international preliminary examination.
2 With the declaration provided for in PCT Article 64(5).
3 With the declaration provided for in PCT Article 64(2)(a)(ii).
4 Including all Overseas Departments and Territories.
5 Ratification for the Kingdom in Europe, the Netherlands Antilles and Aruba.
6 Extends to the Isle of Man.
7 With the declarations provided for in PCT Articles 64(3)(a) and 64(4)(a).
8 Extends to all areas for which the United States of America has international responsibility.

(15 May 2010)

Appendix III

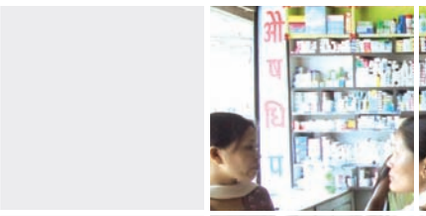
Patent Office Databases and Electronic Journals/ Gazettes

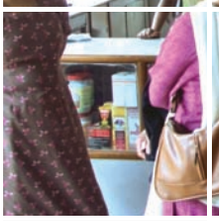
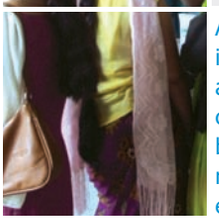
The following is a selection of patent office databases and electronic patent office journals/ gazettes available online

Patent Office	Database	Electronic Patent Office Journal/Gazette
IP Australia (Australia)	Provides quick, structured and advanced search options and status of applications. http://pericles.ipaustralia.gov.au/ols/auspat/welcome.do	http://pericles.ipaustralia.gov.au/ols/epublish/content/olsAOJPatentPDFs.jsp
Instituto Nacional Da Propriedade Industrial (Brazil)	To access database, enter code provided. Search fields include: application number, title of the patent, applicant and inventor. Each patent record also includes the status of the patent. The database is in Portuguese http://pesquisa.inpi.gov.br/MarcaPatente/jsp/servimg/servimg.jsp?BasePesquisa=Patentes	
Canadian Intellectual Property Office (Canada)	Provides basic, Boolean and advanced search options and PDF versions of the specifications. http://brevets-patents.ic.gc.ca/opic-cipo/cpd/eng/introduction.html	
State Intellectual Property Office of the Peoples Republic of China (China)	Search fields include: application number, title of the patent, applicant and inventor. The database is available to be searched in English. The database offers machine translation of patent specifications where available. http://www.chinatrademarkoffice.com/index.php/ptsearch/	
Industria y Comercio Superintendencia Republica de Colombia (Colombia)	Search fields include: application number, priority number, applicant and granted patent number. http://190.254.15.230/~oparra/externas/datospatente.php	
Cuba	Search fields include: application number, title of the patent, applicant and inventor. To access the database click on the links *Bases de Datos* and *Invenciones.* http://www.ocpi.cu/	Under the link *Publicaciones* click on the option *Boletin Official* to access the official journals.

Patent Office	Database	Electronic Patent Office Journal/Gazette
Egyptian Patent Office (Egypt)	Search fields include: application number, title of the patent, applicant and inventor. Searches can be conducted in Arabic or English. http://www.egypo.gov.eg/inner/english/Search_1.html	
European Patent Office	Options include basic, structured (Boolean) and advanced searching of bibliographic data and text of the specifications. Esp@cenet provides access to patent information from over 80 countries, including patent specifications and status where available. http://ep.espacenet.com/	
Intellectual Property India (India)	Options include basic and advanced search. Search fields include: abstract, application number, title of the patent, applicant and inventor. The site also offers the status of patent applications and HTML text of granted patents. http://ipindia.nic.in/ipirs/patentsearch.htm	Under the heading *Publications* click on the link *Patent Office Journal* to access the official journal of published patents. The Official Patent Office Journal is published every 7 days. http://ipindia.nic.in/ipr/patent/patents.htm
Korea Intellectual Property Rights Information Service (Republic of Korea)	Provides a general (basic) and advanced search. Search fields include: title, priority date and patentee. Searches can be conducted in English. http://patent2.kipris.or.kr/pateng/searchLogina.do?next=GeneralSearch	
Mexico	Options include basic *(Busqueda simple)*, structured (*Busqueda estructurada)* and advanced search *(Busqueda avanzada)*. Search fields include: abstract, application number, title of the patent, applicant and inventor. Searches can only be conducted in Spanish. http://siga.impi.gob.mx/wb/SIGA/SIGA_busqueda_simple	Patent Office Gazettes can be downloaded from the row titled *Solicitudes de Patente* under the column *Ejemplar*. To access past gazettes, click the drop down arrow under the column *Oficio de Puesta en Circulation*. Gazettes are published in Spanish. http://siga.impi.gob.mx/wb/SIGA/SIGA_avisos_puesta_en_circulacion (It is also possible to view the patent office gazette through the database under the link *Busqueda por ejemplar*).
Intellectual Property Organisation of Pakistan (Pakistan)		For patents published after 18 months: http://www.ipo.gov.pk/Patent/PatentGazzette.aspx For granted patents: http://www.ipo.gov.pk/Patent/PatentGranted.asp

Patent Office	Database	Electronic Patent Office Journal/Gazette
Intellectual Property Philippines (Philippines)	Provides quick and advance search options. Search fields include: title, abstract, priority number, classification and applicant and assignee. http://patents.ipophil.gov.ph/PatSearch/	Each patent office gazette can be viewed online but is not available in PDF format. http://patents.ipophil.gov.ph/PatGazette/
Department of Intellectual Property Thailand (Thailand)	Provides various search options including a quick search, simple search, by classification, patent number and a complex search allowing more than one search field. Searches can be conducted in with Thai or English. http://patentsearch.moc.go.th/DIPSearch/PatentSearch/SearchSimple.aspx	
United States Patent and Trade Mark Office (United States of America)	Provides quick and advance search options. Search fields include: title, abstract, priority number, description, claims, classification and assignee. http://patft.uspto.gov/	
World Intellectual Property Organization	Allows users to search over 1.6 million PCT applications. Options include basic, structured (Boolean) and advanced searching of bibliographic data and text of the specifications. The database allows the specifications of PCT applications to be downloaded as well as providing the national phase status of applications where available. http://www.wipo.int/pctdb/en/	



Agencies that procure medicines are increasingly faced with questions about the patent status of pharmaceutical products. This is important because these agencies have a responsibility to use their budgets efficiently (for example by procuring generic medicines), but do not want to infringe on intellectual property rights.

Many organizations involved in medicines procurement have limited knowledge of and little experience in establishing whether a particular medicine is under patent in a particular country. This guide describes a step-by-step approach to locating information about patents on medicines, which, though not easily found, is often available on the Internet. Concrete examples are given of how to trace, through the various online databases, whether a patent has been applied for, granted, refused or revoked. Suggestions are also provided for using Internet sources to obtain data (such as priority dates) that can facilitate efforts to identify relevant patents through more traditional means, such as patent office gazettes.

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World Health Organization

South-East Asia Region Western Pacific Region