

Making the Patent System More Democratic: The Role of Public Participation

Examination of Pharmaceutical Patents: Arguing from a Pro-Public
Health Perspective

Associação Brasileira Interdisciplinar de AIDS - ABIA

Rio de Janeiro, Brasil

18 November 2008

Tahir Amin

Director of Intellectual Property, I-MAK, Inc
tahirmamin@gmail.com

 I-MAK INITIATIVE FOR MEDICINES ACCESS & KNOWLEDGE

www.i-mak.org

India- The Story so Far

- 1856 - first exclusive rights on inventions under British rule
- 1911 - Indian Patents & Designs Act
- 1970 - Patents Act
- 1972-2005 - No pharmaceutical product patents
- 1995 - TRIPS comes into force - patent application mailbox opened for pharmaceutical product patents
- 1 January 2005 - As required under TRIPS, India begins examining and granting pharmaceutical product patents



India- The Story so Far

- Civil society, local generic companies and left parties in Government coalition fight to implement TRIPS flexibilities into new patent law.
- Two important provisions implemented:
 - i) A new standard of patentability
 - ii) Pre-grant Opposition



India- The Story so Far

*Section 3(d) The following are **not inventions** within the meaning of this Act, –*

*(d) – the mere discovery of a **new form of a known substance** which **does not** result in the **enhancement of the known efficacy** of that substance or the mere discovery of **any new property** or **new use for a known substance** or the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.*

*Explanation – For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the **same substance**, unless they differ significantly in properties with regard to efficacy.*



India-The Story so Far

- Novartis drug for myleoid leukemia, imatinib mesylate (Glivec) - \$US 2,500 per month under exclusive marketing rights between 1995-2005
- Generic versions \$200 per month
- Cancer patient group and generic companies file separate challenges to remove exclusive marketing rights.
- 2005 - New Patent Act - cancer patient group and generic companies file separate pre-grant oppositions against patent application for Glivec.
- January 2006 -Indian patent office rejects Glivec patent
- Novartis challenge constitutional validity of s3d - High Court of Madras dismisses case
- Case on appeal at the patent office appellate board - starting this week!



India-The Story so Far

Drug	Status
Abacavir Sulfate	Withdrawn
Amprenavir	Pending
Atazanavir	Application divided/abandoned - status unclear
Combivir	Withdrawn
Efavirenz	Pending (Post grant opposition)
Lopinavir/Ritonavir	LPV Polymorph - Pending RTV Polymorph - Pending Heat Stable Tablet combination - Pending Soft-gel capsule combination - Withdrawn
Nevirapine	Refused



India-The Story so Far

Drug	Status
Pegasys	Pending (Post grant opposition)
Tenofovir DF	Ester - Pending Salt - Pending
Valganciclovir	Pre-grant Opposition rejected Post-grant opposition filed



Brazil - The Right to Participate in the Patent System

Lei 9279/96:

Article 31 - *Documents and information for aiding examination may be filed by interested parties between the publication of the application and the termination of examination.*



How to Oppose a Patent

Important questions before starting:

- What resources do I need?
- How do you decide which drug to oppose?
- How do I find the correct patent to oppose?
- How can we involve patient groups?



Building the Right Team and Resources

- Lawyers
- Organic, medicinal and bio-chemists (preferably ex-industry)
- Pharmacists
- Researchers (students)
- Science databases, textbooks and journals
- Patent databases



Know Your Patent Law

Article 8:

*To be patentable an invention must meet the requirements of novelty, inventive activity and **industrial application**.*

Article 9:

*An object of **practical use**, or part thereof, is patentable as a Utility model, when it is susceptible of industrial application, presents anew shape or arrangement and involves an inventive act that results in a **functional improvement** in its use or manufacture.*



Know Your Patent Law

- Implementing rules and procedure - need to learn rules/formalities for filing a patent application and general procedure of patenting
- Patent office practice guidelines?
- Brazilian patent case law?
- Are Brazilian patent office decisions public? If so they should be reviewed
- European Patent Office and U.S and U.K patent decisions

<http://www.epo.org/patents/appeals/case-law.html>

<http://www.cafc.uscourts.gov/dailylog.html>

http://www.bailii.org/form/search_cases.html



Choosing a Drug to Oppose

- Brazilian essential medicines list
- MSF knowledge of drugs needed in the field
- Drug prices list - those that are out of reach are good test cases
- Procurement agencies e.g WHO/Clinton Foundation/GFTAM



How Do I Find the Patent?

- Good starting point - US FDA electronic Orange Book

<http://www.fda.gov/cder/ob/>

- Sometimes patent may not be listed on Orange Book - then need to do broader search

<http://www.wipo.int/pctdb/en/> or see INPI patent site (below).

- Use Orange Book patent to broaden search and pull U.S specification and related patents families:

http://oa.espacenet.com/search97cgi/s97_cgi.exe?Action=FormGen&Template=/oa/en/home.fts

- Search INPI and check for priority number from patent listed in Orange Book.

<http://pesquisa.inpi.gov.br/MarcaPatente/jsp/servimg/servimg.jsp?BasePesquisa=Patentes>

- Check with industry chemist (e.g Farmaguinhos) to see if this is the patent used to produce the marketed drug



Reading the Patent

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
6 May 2005 (06.05.2005)

PCT

(10) International Publication Number
WO 2005/039551 A2

- (51) International Patent Classification: **A61K 31/00**
- (21) International Application Number:
PCT/US2004/097401
- (22) International Filing Date: 23 August 2004 (23.08.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
10550.178 28 August 2003 (28.08.2003) US
- (71) Applicant for all designated States except US: **ABBOTT LABORATORIES** [US/US]; Dept. 377 Bldg AP5A-1, 100 Abbott Park Road, Abbott Park, IL 60094-6008 (US).
- (72) Inventors; and
(75) Inventors/Applicants for US only: **ROSENBERG, Jiery** [DE/DE]; Bruchstrasse 29, 67158 Hirstand (DE); **REINHOLD, Ulrich** [DE/DE]; Heiga Y-strasse 13, 67546 Speyer (DE); **LIEPOLD, Bernd** [DE/DE]; U1, 8; Mannsirt, 68151 Mannheim (DE); **BERNDT, Gunther** [DE/DE]; Am Kirrling 7, 67273 Hirschheim (DE); **BREITENBACH, Jörg** [DE/DE]; Hans Sachs Ring 95a, 68199 Mannheim (DE); **ALANI, Laman** [US/US]; 4612 Merchant Square, Lansdale, PA 19646 (US); **GHOSH, Soumyajit** [IN/US]; 48826 Central Park Drive, Canton, VT 06188 (US).
- (74) Agents: **FUZALL, Kalim, S. et al.**, Dept. 377 Bldg AP5A-1, 100 Abbott Park Road, Abbott Park, IL 60094-6008 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AT, AG, AT, AM, AU, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NL, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TH, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, UJ, UZ), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BI, CT, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— without international search report and to be established upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



Reading the Patent

- Note priority data and publication date of application
- What is priority?
- Two ways to read patent - start with claims first/read the body of specification first.
- Claims define what the patent covers - what is its scope
- Body of the patent (specification/description) describes the invention
- Examples given in the body of the specification is important information to understand how the invention is made



Reading the Patent

- What are the key embodiments ('buzz words') and claimed benefits of the patent? E.g:
 - Solid pharmaceutical dosage form
 - Bioavailability (aqueous solubility)
 - Water-soluble polymer and acceptable surfactant (note the ones used e.g pages 6-9)
 - Matrix
 - Melt extrusion
- Extract and read any prior art listed by the applicant to understand the background to the invention claimed. Patents can be retrieved from:

http://oa.espacenet.com/search97cgi/s97_cgi.exe?Action=FormGen&Template=/oa/en/home.hts

See also <http://www.i-mak.org/patent-databases/> for free patent databases to extract patent specifications



Building Your Case

- Can you request the INPI examination report to see what examiner has said?
- Brazil patent office tends to follow practices of EPO. Check the EPO examination file says. (Need to know the corresponding European patent)

<http://www.epoline.org/portal/public>

- Can also check what the USPTO examination report says, if application is pending there.

<http://www.uspto.gov/ebc/index.html>



Building Your Case

- Extract and review prior art cited by INPI/EPO/USPTO - prosecution history gives you focus of key validity issues.
- Conduct broad prior art search using some of buzz words and inventor names. **There is no magic formula here!** Useful sites:

Google - www.google.com

Sciencedirect - <http://www.sciencedirect.com/>

PubMed - <http://www.pubmedcentral.nih.gov/>

WIPO Patentscope - <http://www.wipo.int/pctdb/en/>



Some Useful Textbooks

- Pharmaceutical Salts: Properties, Selection and Use, P Heinrich Stahl
(Useful to look at all previous literature cited in this book on history of salt selection and techniques)
- Encyclopedia of Pharmaceutical Technology, Edited by James Swarbrick (20 Volumes of various pharmaceutical industry techniques)
- The Organic Chemistry of Drug Design and Drug Action, Silverman
- Polymorphism, Rolf Hilfiker
- Solid state chemistry of Drugs, Stephen Byrn
- Handbook of Pharmaceutical Excipients, Raymond Rowe et al



Constructing Your Case

- Working with a chemist - ask the right questions based on research and prior art:
 - What are the properties of PVP polymers?
 - What benefits are derived from PVPs?
 - Are such properties expected to work with the compound in question?

BASF, *ExAct – Excipients and Actives for Pharma*, No. 2, July 1999 (BASF).

*“Due to their chemical structure, namely the amide bond, PVP forms a variety of complexes with other chemical compounds including pharmacological actives. For these compounds, complexation results in either **enhanced solubility, improved bioavailability or increased stability.**”*

*Due to its thermoplasticity and balanced aqueous solubility properties, Kolidon(PVP) grades have been found to provide a **comprehensive and universal base for various types of drugs.** After melt extrusion, the active drug can present in the extrudate in one or two forms: as a crystal suspended in the hardened Kollidon matrix, or as a molecule dissolved in the polymer during the melting phase and remaining dissolved in the finished product a solid solution. Melt extrusion paves the way for benefits in therapy.*

*“the benefits of polymer/drug melt extrusion, namely: formulation with **controlled release** (instant and sustained release) and **improved bioavailability for compounds with low aqueous solubility** (as Ritonavir/Lopinavir are known to be).”*



Constructing Your Case

- Benefits of surfactants:

Polyoxyethylene alkyl esters are widely used for oral pharmaceutical formulations that need to enhance the aqueous solubility and dissolution of poorly soluble compounds such as Ritonavir/Lopinavir. They are known to be stable, hydrophilic, water-soluble and offer physical stability for storage purposes. Abbott has already disclosed the surfactant polyoxyl 35 castor oil, sorbitan mono laurate and many of the other surfactants listed formulating Ritonavir/Lopinavir in a soft-gel capsule (see pages 24 and 25 of **WO 2000/74677**).

Useful reference: *Handbook of Pharmaceutical Excipients, Raymond Rowe et al, APhA Publications, 4th Edition, 29 May 2003*



Constructing Your Case

- Companies will always argue that a commonly used technique described in prior literature does not reveal the information for the compound in question and therefore it is inventive.
- Science may not be an exact art, but there are common techniques often repeated in new formulations.
- The ability to combine prior art literature, knowledge of patent law and various sub-criteria of novelty/anticipation and inventive step is useful to counter these arguments. Eg inventive step many different criteria:
 - common general knowledge
 - obvious to try
 - reasonable expectation of success.



Role of Civil Society/Patient Groups

- Most diseases have a patent and access issue - so combining different patient group needs can be effective. E.g Cancer groups in India used its case to support HIV patients
- Build public awareness/legitimacy - makes patents a public issue.
- Media strategy using patient groups e.g opinion/editorials in papers - make the issue relevant to everyone
- MAKE THE MESSAGE SIMPLE



Thank you

