Patent Oppositions & Strict Patentability Criteria: What it Means for Access to Treatment?

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RIGHT TO HEALTH AND ACCESS TO MEDICINES

- Access to medicines is an integral part of the right to health.
- Nearly two billion people lack access to essential medicines. [“WHO Medicines Strategy: Countries at the Core, 2004-2007”, (2004).]
- In the case of HIV, it is presently estimated that around 15 million people living with HIV (PLHIV) need ARV treatment (based on revised WHO Guidelines). However, as of end-2010, only 6.65 million PLHIV are receiving treatment.
- Cost of medicines is one of the key factors that affect the access to medicines. In low and middle-income countries, medicines account for 60% of the healthcare cost. [The World Medicines Situation, WHO, 2004].
- Millions will be pushed into poverty by purchasing high cost medicines, especially branded medicines. [Niëns LM, et al, “*Quantifying the Impoverishing Effects of Purchasing Medicines: A Cross-Country Comparison of the Affordability of Medicines in the Developing World*”, PLoS Med 7(8) e1000333 (2010)].

PATENTS → HIGH COSTS OF MEDICINES

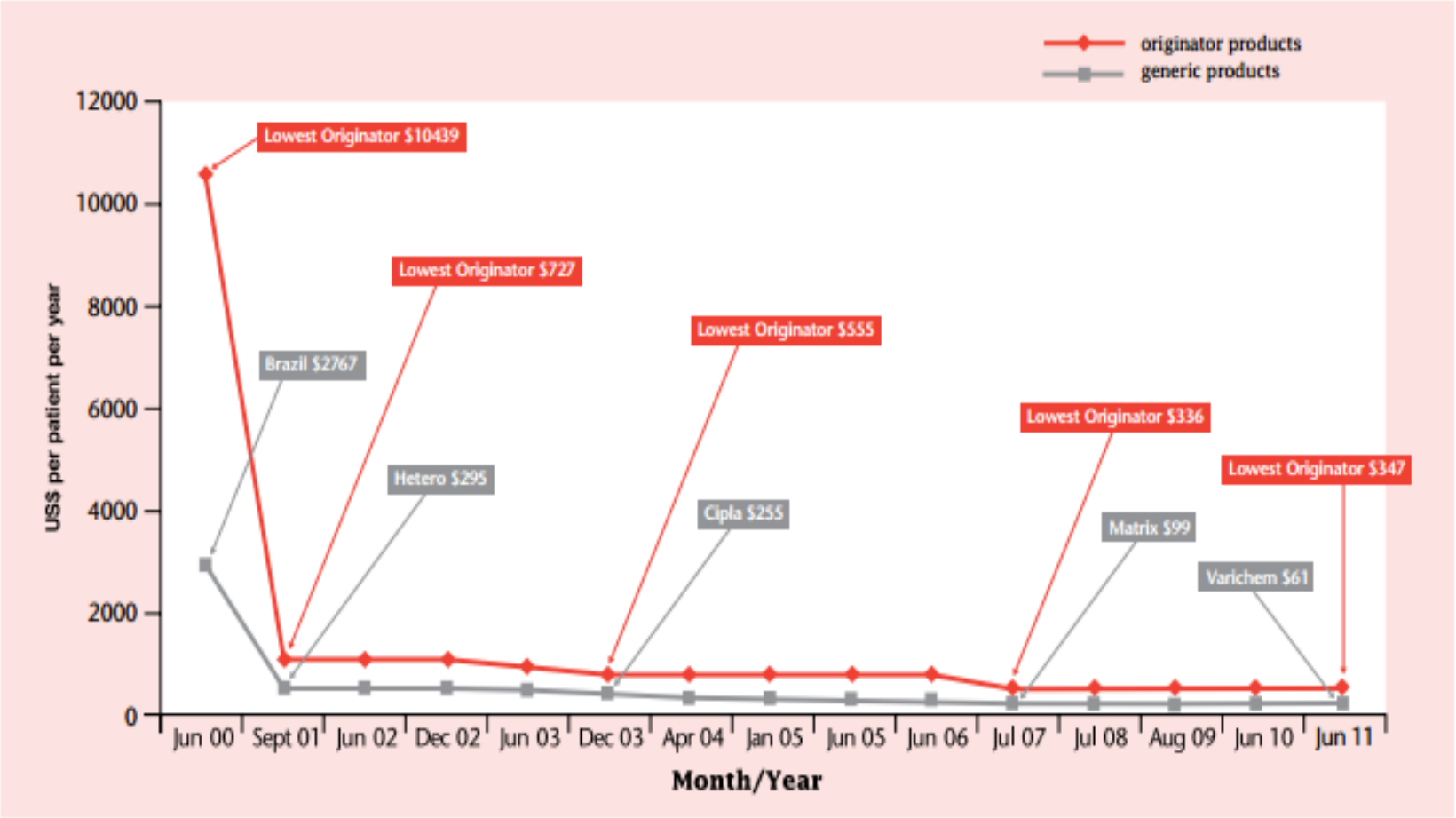
- Patent barriers: one of the factors for high cost of medicines.

- Patents → monopolies → monopolistic prices → high costs for medicines

- Examples of prices of patented medicines:
  - Anti-retrovirals (mid-1990s to 2000): USD 15,000 per patient per year
  - *Imatinib mesylate* (*Gleevec*) – Anti-cancer medicine to treat chronic myeloid leukemia:
    - Novartis' price = 2400 USD per patient per month
    - Generic version price = 160 to 200 USD per patient per month
  - Tenofovir + Lamivudine / emtricitabine + Efavirenz (*Atripla*):
    - Gilead's price = 1800USD per patient per month
    - Generic version = 15 USD per patient per month

NO PATENTS → COMPETITION → DROP IN PRICES

Graph 3: Fall in the prices of first line combination of stavudine(d4T)+ lamivudine (3TC), Nevirapine (NVP). Lowest world price per patient per year since 2000



Source: Untangling Web of Price Reductions, 14 Edn, 2010, Médecins Sans Frontières

COMPETITION REDUCES PRICES: INDIA EXPERIENCE

- Eg: Indian Patent law and Impact
  - *1911 : Patents and Designs Act, 1911*
    - Product and process patent protection
    - Term of patent: 16 years
  - *Patents Act, 1970* (For pharmaceuticals and agrochemicals):
    - No product patent protection, only process patent
    - Process patent for best process known to inventor
    - Maximum term of patent: 7 years
- Consequence:
  - No monopoly on pharmaceutical products
  - Indian pharmaceutical companies used alternate, non-infringing processes to manufacture drugs
  - > 1 manufacturer of drug → competition → lower prices
  - Prices of medicines in India are the lowest in the world.
  - Indian companies supply generic drugs to other countries

2005: PROBLEMS BEFORE INDIA

- 2005: Deadline for India under TRIPS to change its law to grant product patents for medicines.
- Problem 1: Multiple patents for single medicine → patent thickets and evergreening

  2010 study shows that, in the US, the average was nearly 3.5 patents per drug in 2005, with over five patents per drug for the best-selling pharmaceuticals. [Lisa Larrimore Ouellette, 17 Mich. Telecomm. Tech. L. Rev. 299 (2010)].

- Problem 2: Decline in drug approvals despite patent protection

  *While patents were supposed to provide an incentive for R&D, data from other countries also showed that such *robust* patent protection did not yield the supposed R&D results. Number of NMEs being approved was on the decline.*

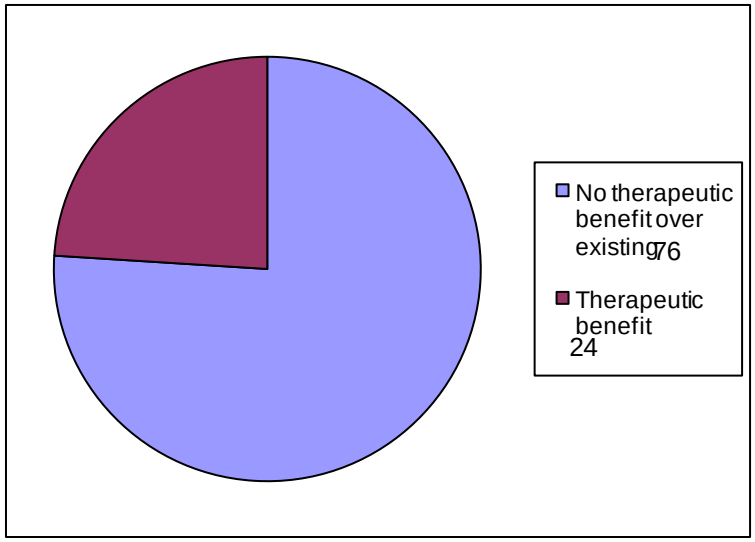
PATENTS: PROBLEMS BEFORE INDIA – I

1964	Thereafter	1984-85	1985
• Zidovudine discovered and patented.	• Explored as anti-cancer treatment and shelved	• Discovered to work against HIV	• Patent granted on **NEW USE**

1964	1985	1989	1992
• Zidovudine patented.	• Zidovudine (new use) patented	• Lamivudine patented	• **COMBINATION** of Zidovudine + Lamivudine patented

1993 + 20	1995-96	1997 + 20
• Imatinib and all pharmaceutical salts patented.	• Mesylate salt of imatinib published	• Application for different crystal **FORMS** of mesylate salt of imatinib

PATENTS: PROBLEMS BEFORE INDIA – II



- 1035 new drugs approved by US FDA (1989-2000)
- Only 15% of new drugs approved between 1989-2000 were highly innovative priority new molecular entities (NMEs).

Source: "Changing Patterns of Pharmaceutical Innovation", National Institute for Health Care, Management Research and Educational Foundation, May 2002

- Multiple patents → Same protection for all "inventions" → me-too drugs → Decline in new molecular entities being approved

- An estimated 12,000 pharmaceutical applications had been filed mostly relating to <u>incremental</u> improvement over existing old drugs.

INDIAN PATENT LAW – HIGHER STANDARDS

- 2005:
  - India required to comply with TRIPS and provide patent protection for pharmaceuticals
  - Parliament deliberated issue of pharmaceutical patents and problem of evergreening
  - Patents (Amendment) Act, 2005: Safeguards introduced to prevent "evergreening"
    - Higher patentability criteria set (SECTION 3(d): no patents on new forms of known substances unless there is a significant enhancement of efficacy)
    - Definition of "inventive step" introduced
    - Patent oppositions (pre-grant retained; post-grant introduced; revocation)
  - Objective of Section 3(d):
    - To prevent frivolous patenting
    - To prevent evergreening
    - To promote access to essential life saving medicines

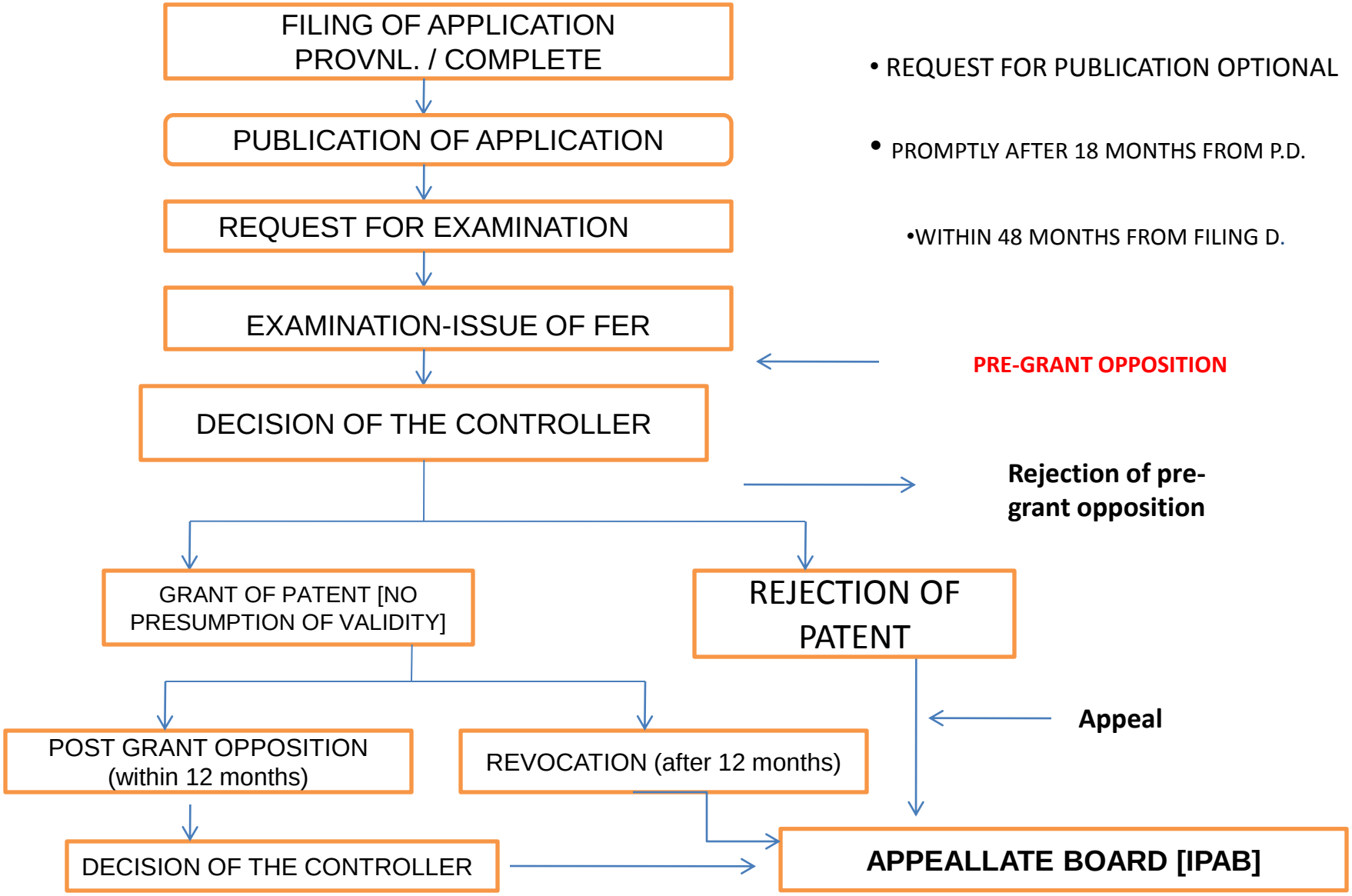
SECTION 3(d): Higher Patent Standards

SECTION 3 (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 of a known substance …

  Explanation: "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.**

STAGES OF GRANT OF PATENT



EXAMPLE I: COMBIVIR

- Combivir is a fixed-dose combination of ARVs
  - Zidovudine (known substance) +
  - Lamivudine (known substance) +
  - “glidant,” an inactive substance (e.g. silicon dioxide (sand), calcium carbonate (chalk), talc, etc) (known substances)
- GlaxoSmithKline (GSK) filed a patent application for combivir.
- Generic version of Combivir is priced at Rs 1,100 per patient per month.
- GSK's Combivir was not available in the local market.
- 31 March 2006: Manipur Network of Positive People (MNP+) and the Indian Network of People Living with HIV/AIDS (INP+) filed an opposition.
- 7 August 2006: Protests against GSK for exorbitant price and frivolous patenting by patients groups in India and Thailand
- To avoid a precedent of patent rejection, GSK decided to withdraw its patent application for Combivir in India and Thailand.

EXAMPLE II: GLEEVEC NOVARTIS CASE … not over yet

- Imatinib mesylate:
  - 1998: Patent application filed in India claiming beta-crystal form
  - 2005: Pre-grant oppositions filed
  - 2006: Patent Office rejects on grounds of novelty, inventive step and section 3(d); increase in bioavailability ≠ efficacy
- Challenge to section 3(d)
  - 2006-2007: Constitutional validity of section 3(d) upheld; efficacy = therapeutic efficacy
- Appeal
  - 2007-2009: Novartis' appeal against patent rejection heard and rejected.
    - Novartis failed to satisfy section 3(d); efficacy = therapeutic efficacy
    - Novelty, inventive step recognised
- Present status
  - Appeal filed by Novartis in Supreme Court
  - Asking for a re-interpretation of "efficacy"

USE OF SECTION 3(d) IN OPPOSITIONS

Patent applications rejected	Patent application s Withdrawn/ Abandoned
- Imatinib mesylate - Valganciclovir - Nevirapine HH - Lopinavir/ritonavir tablet	- Combivir - Lopinavir/ritonavir soft gels capsules - Abacavir sulphate - Atazanavir - Amprenavir agenerase

STATUS OF CIVIL SOCIETY OPPOSITIONS

Drug	*Opponent*	*Status*
Gleevec	Cancer Patients Aid Association	Application rejected. Appeal filed.
Combivir	MNP+	Application withdrawn
Atazanavir	INP+ and KNP+	Application deemed abandoned
Amprenavir agenerase	INP+ and UPNP+	Application deemed abandoned

STATUS OF CIVIL SOCIETY OPPOSITIONS

Drug	*Opponent*	*Status*
Valganciclovir	INP+ and TNNP+	Patent granted without hearing. Set aside. Patent revoked yet again on merits.
Tenofovir (3 Oppositions)	INP+ and DNP+	1 opposition withdrawn 1 Rejected. 1 Pending
Kaletra (soft gel)	INP+	Application deemed abandoned
Lopinavir	INP+, DNP+ and NMP+	Pending

STATUS OF CIVIL SOCIETY OPPOSITIONS

Drug	*Opponent*	*Status*
Ritonavir	INP+ and DNP+	Pending
Abacavir sulfate	INP+	Application deemed abandoned
Efavirenz	DNP+	Post-grant opposition rejected
Nevirapine hemihydrate	PWN+	Application rejected
Pegasys	Sankalp Rehabilitation Trust	Post-grant opposition rejected – Appeal pending