Using TRIPS-flexibilities to prevent barriers to access to medicines in India: Current challenges and changing landscape

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LAWYERS COLLECTIVE

ORGANIZATIONAL PROFILE

Lawyers Collective(LC): oldest *pro bono* legal service provider in India (registered in 1981)-to meet the unmet legal needs of the poor

1998: legal aid to persons living with and affected by HIV; advocacy and research and policy work around issues pertaining to legal and ethical issues

1999: lack of access to medicines due to exorbitant price faced by clients

2001: Aware of the impending patent regime change in India and its likely impact on access to medicines, LC commenced work on issues pertaining to intellectual property barriers

2005: advocating for introduction / retention of public health safeguards in the amendments to the Indian patent law (TRIPS compliant)

2006: The Unit had represented Cancer Patients' Aid Association (CPAA) in the litigation against Novartis in the Supreme Court

INDIAN PATENT REGIME

1911

- Product and process patent protection
- 16 yrs protection

1970

- Only process patents were granted
- 7 yrs protection

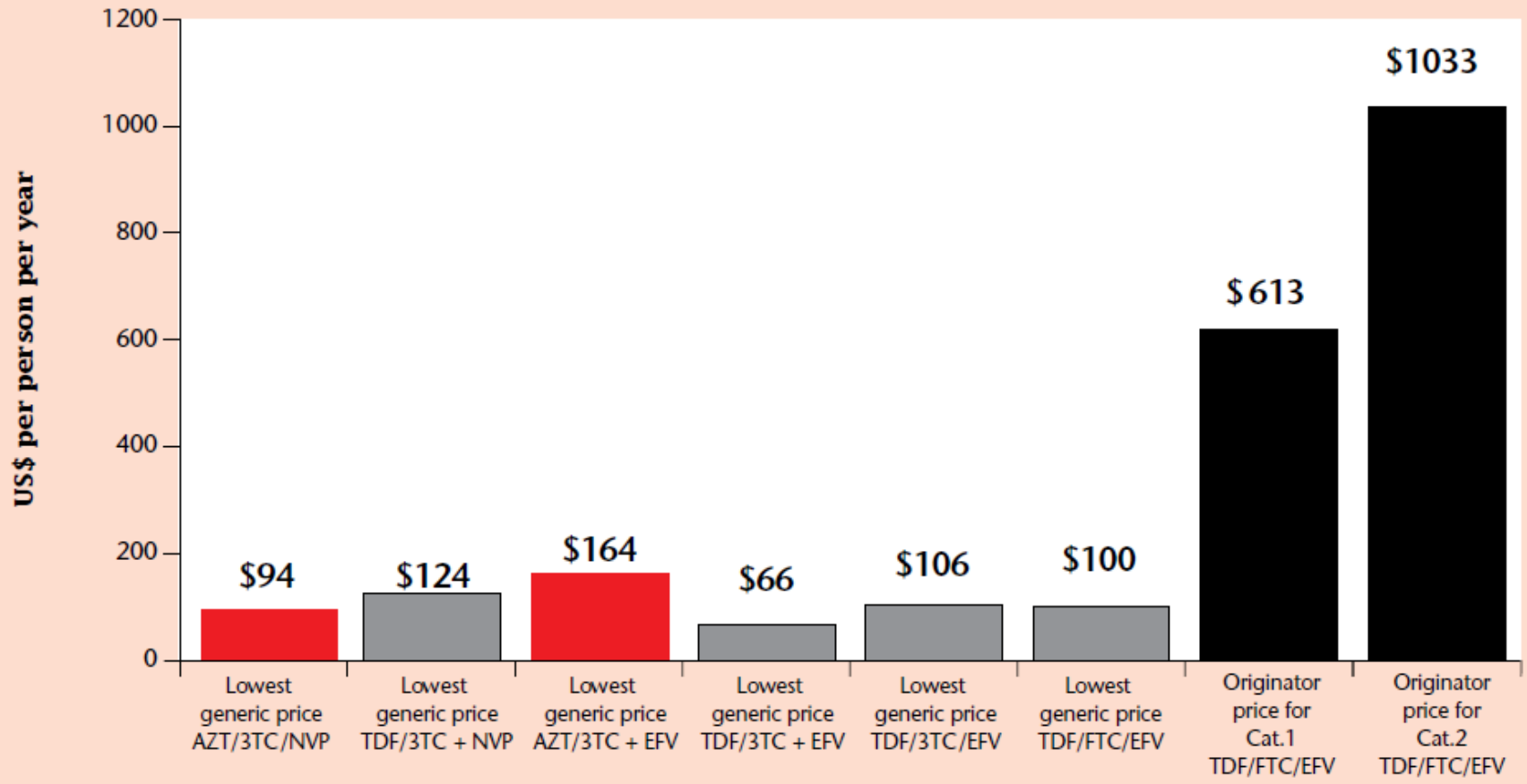
1995

- India signed the TRIPS agreement
- had to amend its Patent law by 2005;mailbox provision and EMR (5years)

2005

- Product patent on pharmaceutical compounds incorporated in the Law; 20 years protection

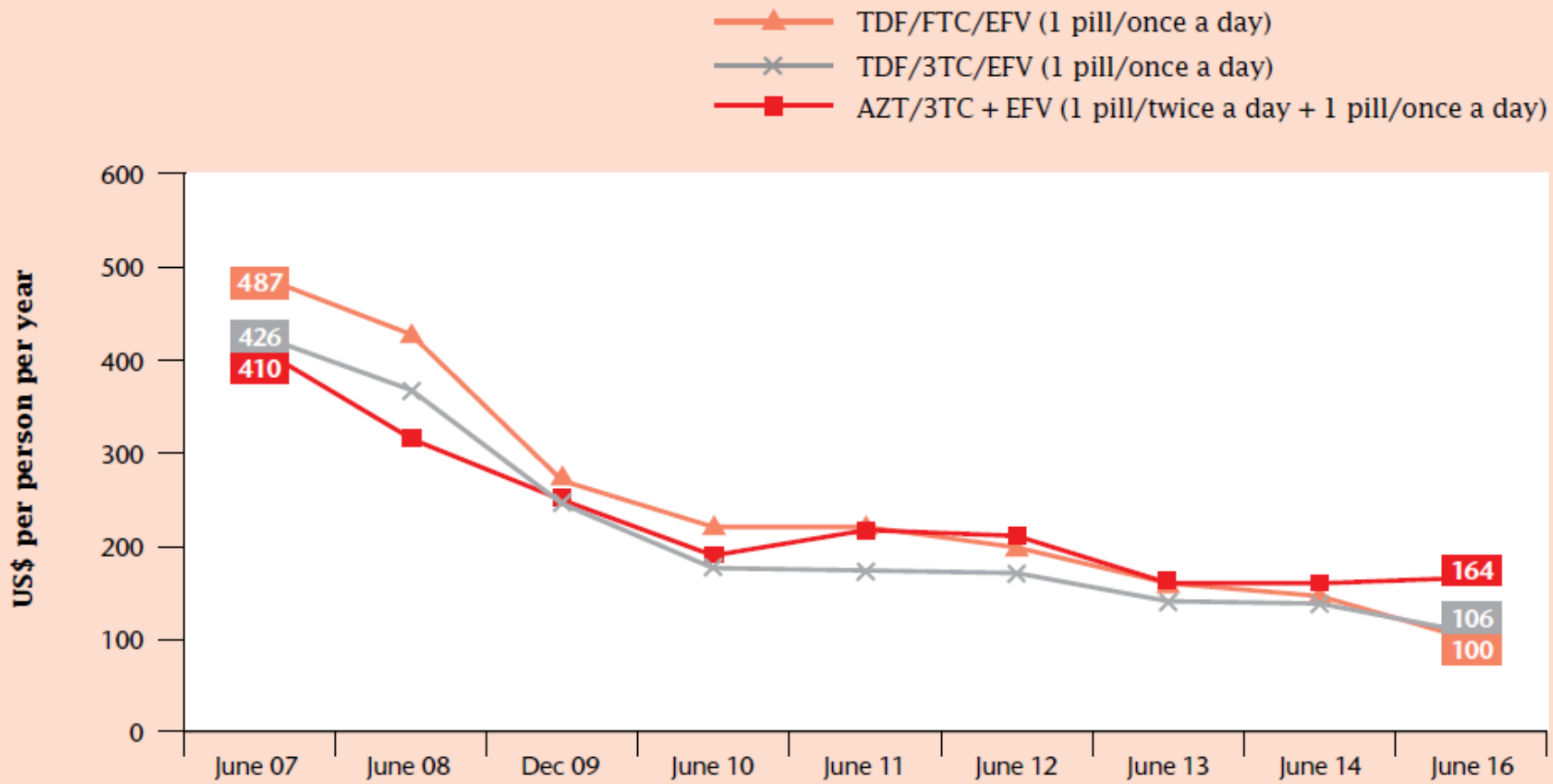
GENERICS vs. ORIGINATOR PRICES FOR FIRST LINE REGIMEN



Source: Untangling the Web of Antiretroviral Price Reductions, 18 Edn, July 2016, Médecins Sans Frontières

EFFECT OF COMPETITION ON PRICES (GENERICS)

THE EVOLUTION IN PRICE OF DIFFERENT FIRST-LINE REGIMENS



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PUBLIC HEALTH SAFEGUARDS-INDIAN PATENT ACT, 2005

1. Pre-grant and Post grant Patent opposition
2. Section 3(d) – Restricts the scope of patentability & limits patenting to real innovations
3. Compulsory licensing for drugs patented in India but not yet produced by generic manufacturers

PATENT OPPOSITIONS

- Structured to restrain wrongful obtaining of patents and claiming of the frivolous or petty inventions.
- This is separate from and independent of the extensive examination conducted by the Patent Office. The examination takes place before the grant of hearing in an opposition.

Pre-grant opposition

Post-grant opposition

PRE-GRANT OPPOSITION: any person may challenge the application of grant of patent and inform the controller of Patents, in writing against the grant of a patent after the application for a patent has been published but before the grant of a patent; free of cost

Pre-grant opposition acts as a defensive shield to confirm the validity of the patent applications before a patent is granted

POST-GRANT OPPOSITION: may be filed at any time after the grant of patent but before the expiry of a period of one year from the date of publication of grant of the patent.

Grounds under both pre and post grant opposition are similar but certain procedural differences exist.

Can be filed only by "person interested" and has a prescribed fee.

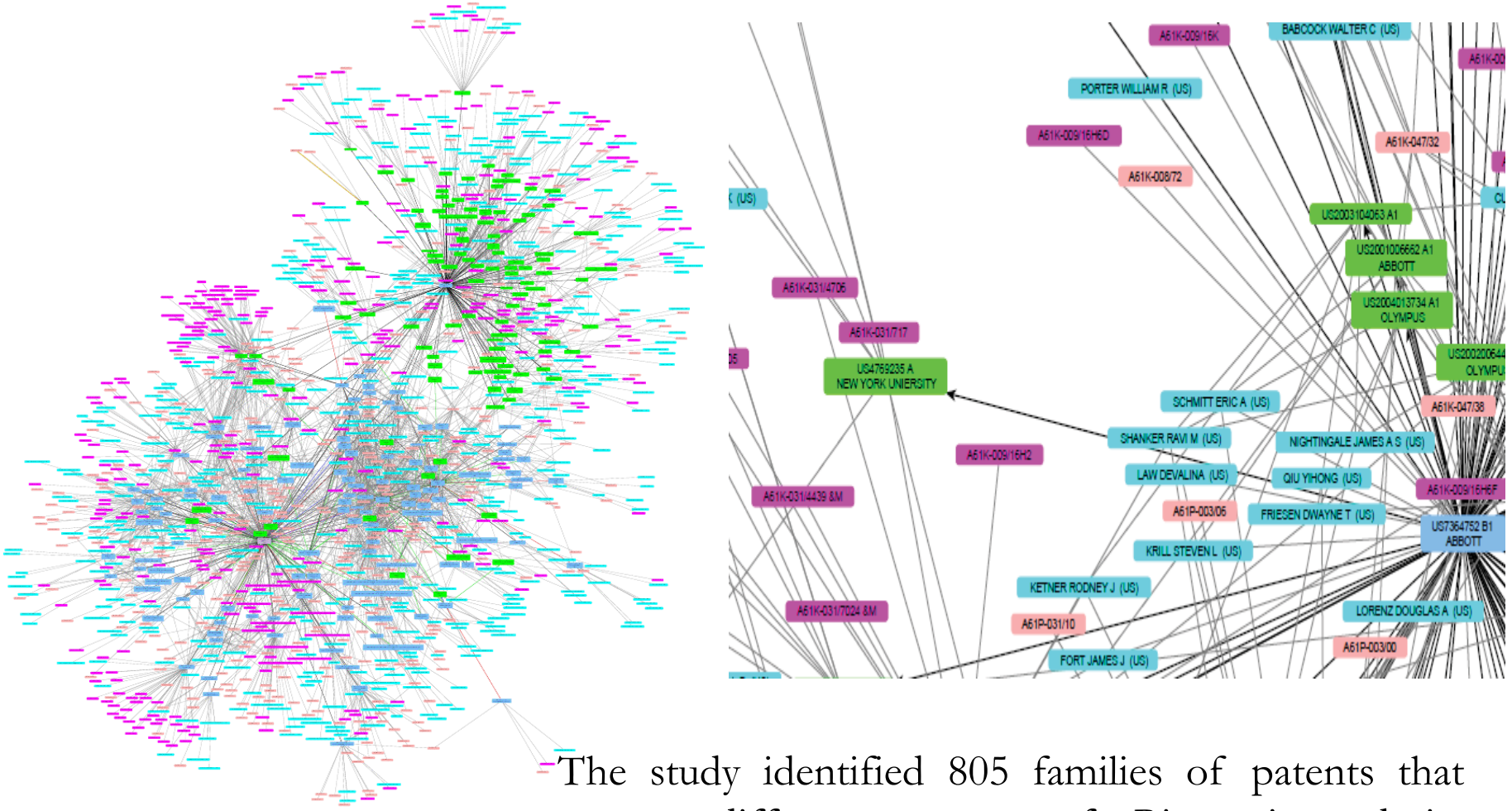
OPPOSITION GROUNDS FREQUENTLY USED IN PHARMACEUTICAL OPPOSITION

1. • **NOVELTY**
2. • **OBVIOUSNESS**
3. • **SECTION 3(d)**
3. • **PRIOR CLAIMING**
4. • **INSUFFICIENT DESCRIPTION**
5. • **FAILURE TO DISCLOSE INFORMATION U/S 8**
6. • **WRONGFULLY OBTAINED INVENTION/PATENT MAINTAINABILITY U/S SECTION 16 (DIVISIONAL PATENT STATUS)**

ONE DRUG! MULTIPLE PATENTS!

- pharmaceutical ingredient (API) of a drug, i.e. its basic active chemical compound;
- intermediate -a salt or crystalline, polymorph form
- delivery mechanisms or formulations for an API
- Metabolites, pro-drugs
- a process for making or formulating the API
- combinations of an API, or an intermediate or a different form of it, with another drug
- second or subsequent medical uses of the drug

PATENT FAMILY MEMBERS-RITONAVIR



The study identified 805 families of patents that protect different aspects of Ritonavir and its methods of use.

Source: WIPO landscape report, 2011

SOFOSBUVIR- PATENT APPLICATIONS

DESCRIPTION	Publishing date
Patent No. 1: Base compound (4 applications filed in India)	13 Jan 2005
Patent No. 2 Structural formula and pro-drugs of nucleoside derivatives + processes (ex: salts, hydrates, solvates, steroisomers, and crystalline forms)	9 Oct 2008
Patent No. 3:Process	6 Oct 2011
Patent No.4:Process for preparation of active compound	6 Oct 2011
Patent No. 5:Product by process	25 Nov 2010
Patent No. 6:Specific derivative in crystalline or crystal-like form	6 Oct 2011
Patent No. 7:Combinations exhibiting synergistic effects + methods of use	21 Mar 2013
Patent No. 8:Composition of sofosbuvir + at least one excipient	6 Jun 2013

Base patent expires in 2025 whereas secondary patents will expire 2033 or later!

PATENT EVERGREENING AND IMPORTANCE OF SECTION 3(d)

- Not all patent applications are valid.
- Many patent applications are for a new use of an old drug, or simply for derivatives of old drugs or combinations of old drugs.
- Evergreening is where a company extends its patent monopoly on a drug by re-patenting slightly modified versions of the drug without any therapeutic improvement.
- Under section 3(d) of the Indian patent act, drugs cannot be patented if they result from "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."
- This has allowed the continued production of cheap generic versions of drugs by Indian companies.

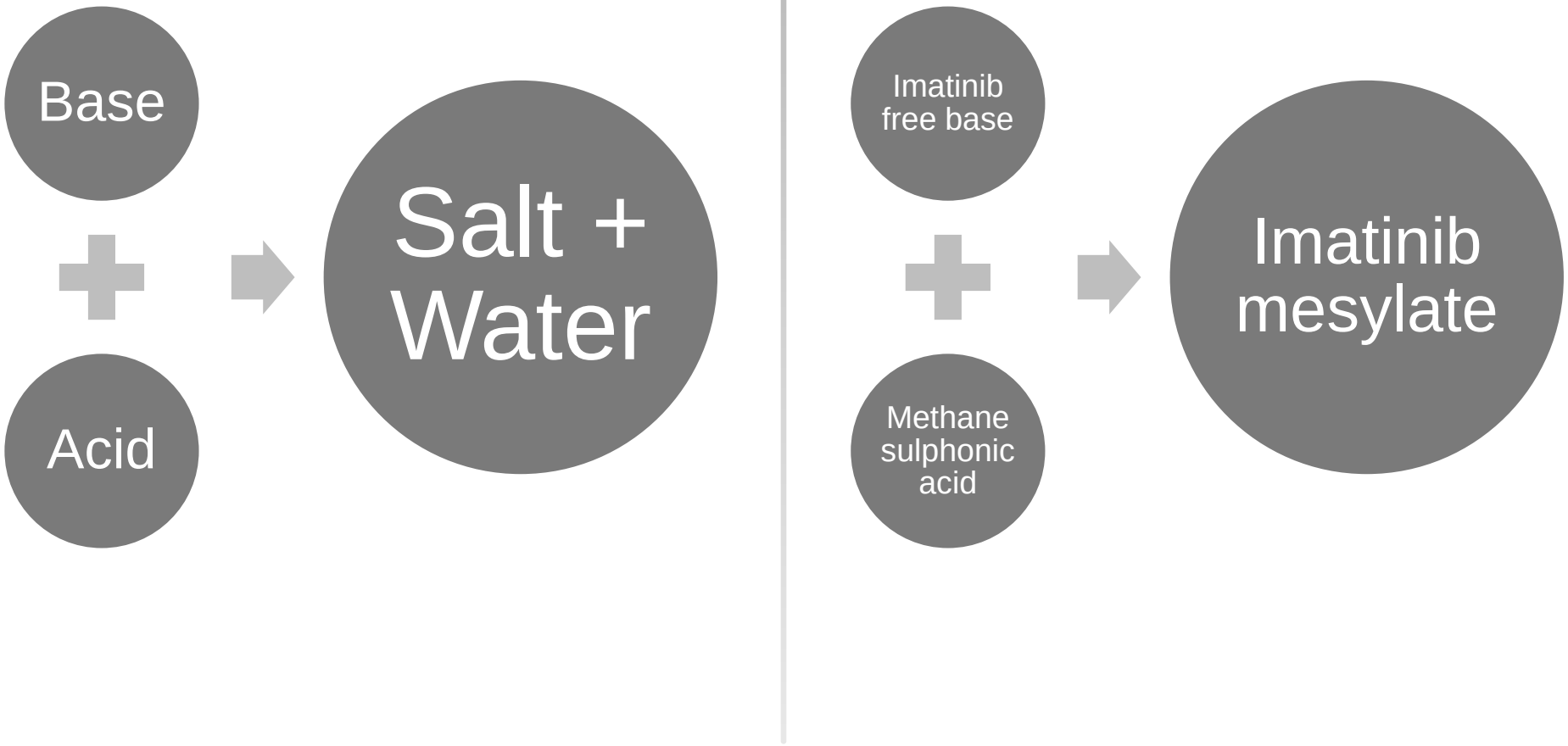
SECTION 3(d)

S. 3 What are not inventions.—The following are not inventions within the meaning of this Act,—

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

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

GLEEVEC-CLAIMED 'INVENTION'



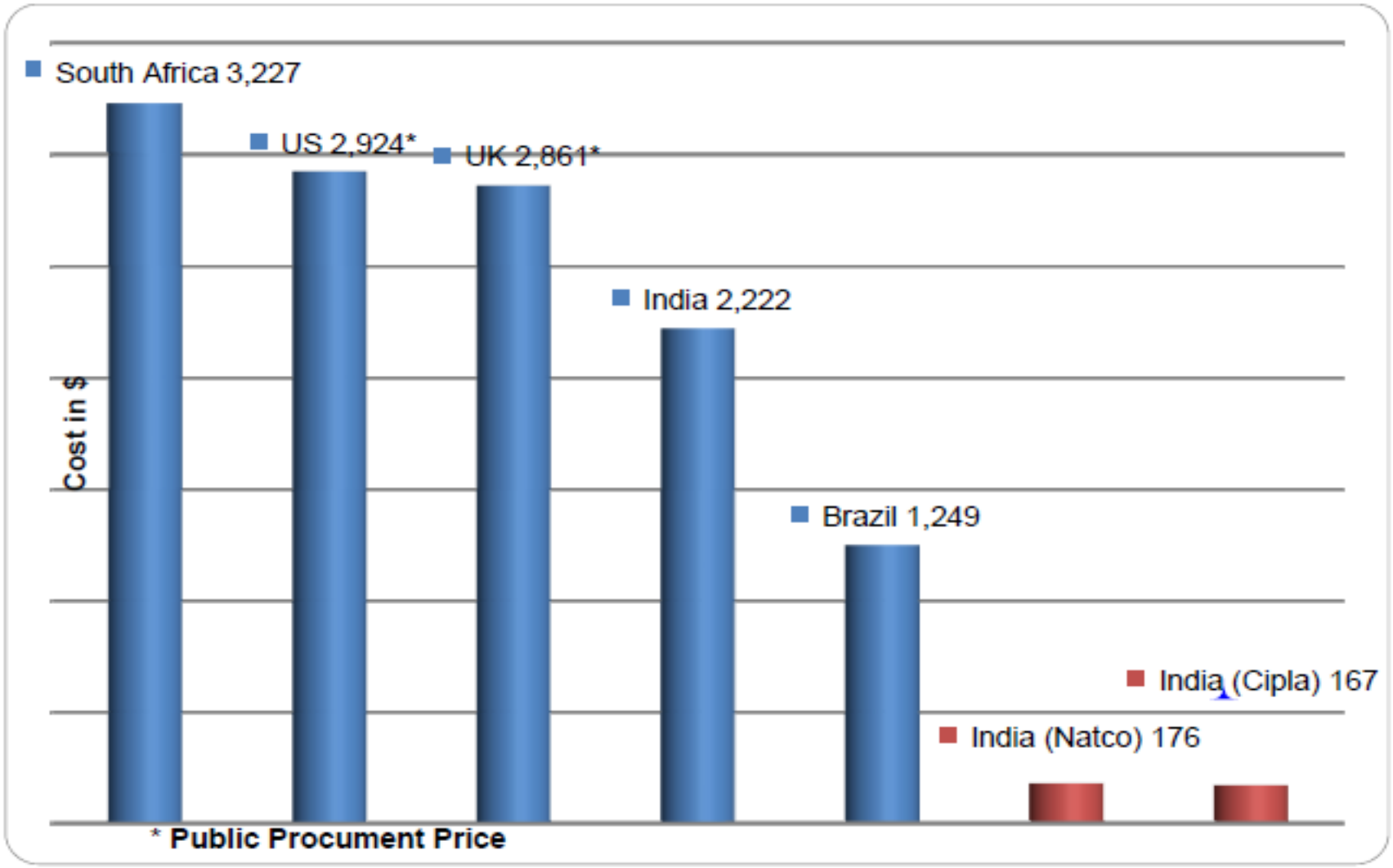
MADRAS HIGH COURT ON SECTION 3(d)

"We have borne in mind the object which the Amending Act wanted to achieve, namely…to provide easy access to the citizens of this country to life saving drugs and to discharge their Constitutional obligation of providing good health care to its citizens."

NOVARTIS AND SECTION 3(D)

- Need to strike balance between R&D in science and technology and to keep private monopoly at the minimum
- Invention and patentability are two distinct concepts and was the heart of 2005 amendment
- 3(d) sets up second tier of qualifying standards for chemical substances
- Novartis was obliged to show enhanced efficacy of Beta-crystalline form over Imatinib mesylate but it has compared solubility of beta crystalline form with Imatinib free base.
- More beneficial flow properties, thermodynamic stability and lower hygroscopicity may be otherwise beneficial but cannot be considered as therapeutic efficacy
- The test of efficacy would depend upon the function, utility or the purpose of the product under consideration which in case of medicine can only be therapeutic efficacy.

Cost of imatinib brand Gleevec (blue bars) and cost of generic imatinib per patient per month (red bars)



Source: MSF-India 2013

STATUS OF CIVIL SOCIETY PREGRANT OPPOSITIONS

Drug	Application Number	Opponent	Status
Combivir	2044/CAL/1997	MNP+	Application withdrawn
Atazanavir	805/MAS/1997	INP+ and KNP+	Application abandoned
Amprenair agenerase	727/DEL/1997	INP+ and UPNP+	Application abandoned
Kaletra (soft gel)	IN/PCT/2002/00936/MUM	INP+	Application abandoned
Abacavir sulfate	872/CAL/1998	INP+	Application abandoned
Ritonavir	IN/PCT/2001/00018/MUM	INP+ and DNP+	Application rejected
Nevirapine hemihydrate	2485/DEL/1998	PWN+	Application rejected
Gleevec		CPAA	Application rejected

STATUS OF CIVIL SOCIETY PREGRANT OPPOSITIONS

Drug	Application Number	Opponent	Status
Lopinavir	IN/PCT/2002/1243 /MUM	INP+, DNP+ and NMP+	Patent application rejected
Tenofovir Disoproxil	2076/DEL/1997	DNP+ , INP+ and ABIA	Patent application rejected
Tenofovir Fumarate	896/DEL/2002	DNP+ and INP+	Patent application rejected. Appeal filed – presently pending.
Tenofovir Disoproxil Fumarate	2256/DEL/2009	DNP+	Patent application rejected.
Tenofovir Disoproxil Fumarate	1135/DEL/2007	DNP+	Patent application rejected
Atazanavir	310/CHE/2007 (divisional application of 805/MAS/1997)	INP+	Pending

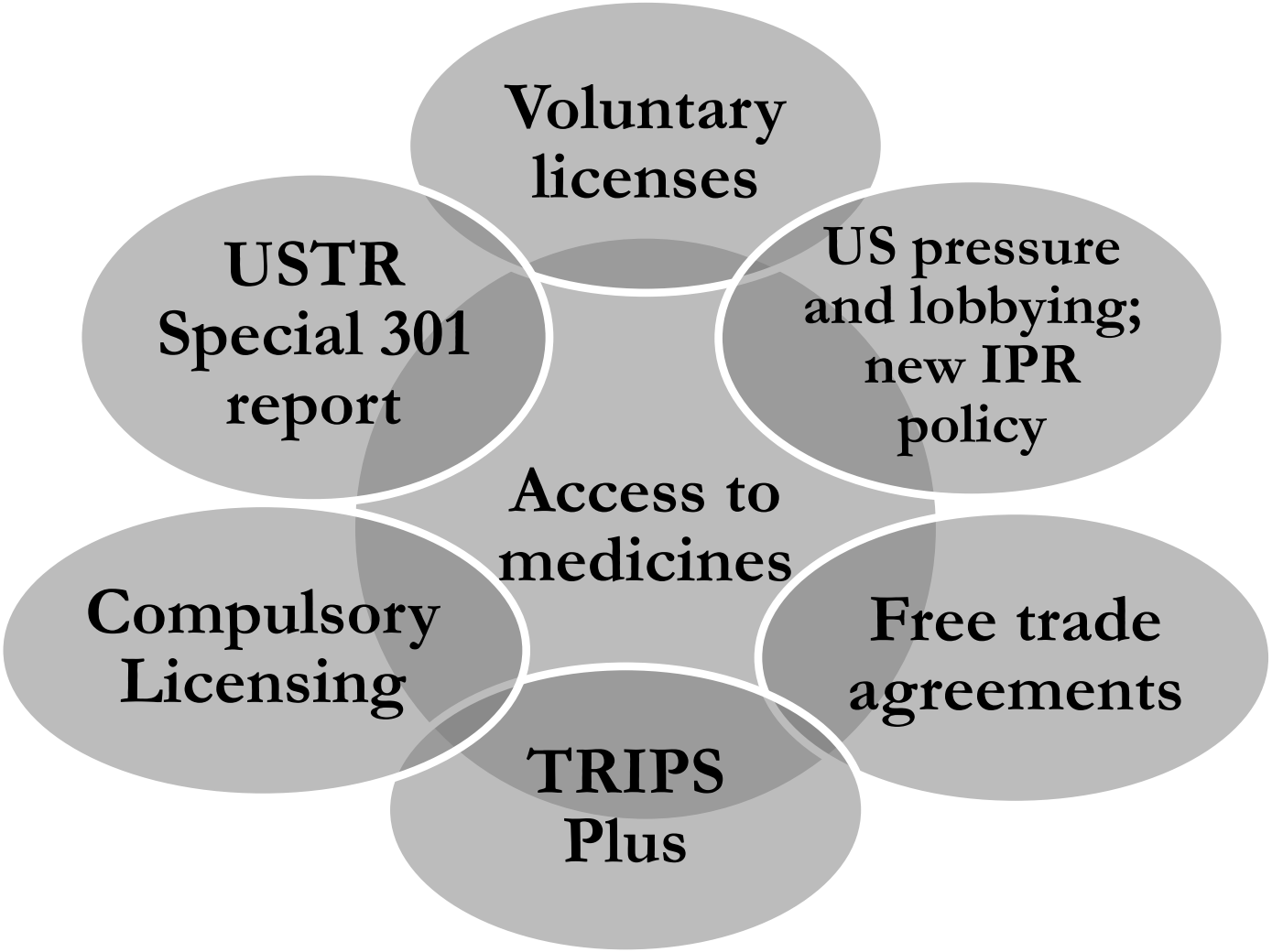
STATUS OF CIVIL SOCIETY PREGRANT OPPOSITIONS

Drug	Application Number	Opponent	Status
Kaletra	6733/DELNP/2007	INP+	Application abandoned.
Raltegravir	4187/DELNP/2007	DNP+	Pending
Pegasys (Patent Number:198952)	1032/MAS/1997	Sankalp Rehabilitation Trust	Revocation stayed by madras High court
Valganciclovir (Patent Number: 207232)	959/MAS/1995	INP+ and TNNP+	Arguments concluded in January 2015 before patent controller. Order awaited.
Efavirenz (Patent Number: 195367)	IN/PCT/2000/553/ MUM	DNP+	Post grant opposition rejected.
Peg-intron (powder)	IN 207233	Sankalp Rehabilitation filed on 01/04/2014	Pending
Peg- intron (aqueous)	IN 234103	Sankalp Rehabilitation	Pending

RECENTLY FILED OPPOSITIONS AND REVOCATIONS

Drug	Patent Number	Petitioner/opponent	Status
Abacavir hemisulphate	IN 212734	DNP+	Pending
Sofosbuvir prodrug	3658/kolnp/2009	APN+, HepCon & sankalp	Pending ; Hearing scheduled in December 2016
Sofosbuvir base	6087/delnp/2005	Sankalp rehabilitation trust	Granted; writ petition challenging the order pending at the Delhi High Court
Elvitegravir	5576/delnp/2008	Nayi Umang Positive Welfare Society	Pending
Cobicistat	10487/DELNP/2008	UPNP plus	Pending
Dolutegravir	3865/KOLNP/2007	BNP+ and Feroz Khan	Matter was heard on 16 May, 2016. Controller allowed the Opponent's request to cross-examine the Applicant's expert.
Daclastasvir	853/DELNP/2009	Sankalp Rehabilitation, HepCon & APN+	Pending

CURRENT CHALLENGES AND CHANGING LANDSCAPE



VOLUNTARY LICENSES- *INCREASING ACCESS TO MEDICINE OR ENSURING MARKET CONTROL??*

- Within the context of pharmaceutical industry, voluntary license (VL) is a permission granted by the originator drug company to the generic manufacture(s) *in lieu* of royalty payments, permitting them to manufacture market and distribute the drugs.
- VLs has recently picked up pace → generic players view it as a cost-effective solution, giving them easy access to markets
- Mainly issued for blockbuster drugs.

Gilead has signed restrictive license agreements with eleven Indian companies on three HCV medicines – sofosbuvir, ledipasvir and velpatasvir. **Generic versions cannot be sold in 50 middle-income countries.**	There are approximately **49 million people living with HCV in excluded middle-income countries –** 30 million in China alone. Gilead is planning to charge thousands of dollars for its new HCV drugs in these countries.	The generic price of a three-month DAA regimen is expected to eventually be less than US $200 with fierce generic competition, but Gilead is working to make excluded middle-income countries dependent on tiered pricing, **resulting in much higher prices,** which could range from over $2,000 to $15,000.

- Source: MSF fact sheet on Gilead license 2015

KEY TERMS AND CONDITIONS-VLs

- Geographical Scope Of VL's
- Number of licensees
- Provisions relating to API manufacturing
- Provisions related to royalty
- Freedom to co-formulate into fixed dose combinations
- Technology Transfer
- Provisions related to data exclusivity and anti-diversion
- No-challenge clauses
- Provisions of compulsory license

FREE TRADE AGREEMENTS AND TRIPS PLUS PROVISIONS

- FTAs are international agreements that are legally binding
- Developing countries will have to change laws and government will have to change policies based on international legal commitments in FTAs
- FTAs cover a broad range of subjects: trade in goods, investment, competition, tariffs…
- They also include Intellectual Property Chapters that feature demands far in excess of the TRIPS Agreement.
- TRIPS-plus provisions undermine or even remove TRIPS flexibilities re-affirmed by the Doha Declaration
- Patent Term Extension: Patent term to be greater than 20 years
- Data Exclusivity: Monopoly on off-patent medicines
- Enforcement measures: Public money used to enforce private rights; hampering judges ability to protect public health
- Investment provisions: Allows MNCs to sue Indian government over health policies and laws

OTHER CHALLENGES

The United States government has been using the Special 301 Review Process and other trade tools to force developing countries to implement data protection provisions with a data exclusivity regime; also to change patentability standards.

New IPR policy and private assurance to the US-India Business Council (USIBC) and other lobby groups that India would not invoke compulsory licensing for commercial purposes → diluting TRIPS flexibilities.

Due to VLs, the generics are no more interested in challenging patents → diluting TRIPS flexibility. Burden now shifts entirely on the Civil society .

VLs have also ruled out the possibility for filing compulsory licenses-again diluting the TRIPS flexibilities.

74% foreign direct investment in brownfield pharma

Source: wikileaks,2015

THANK YOU!