

Presentation on **Optimal policy for biopharma drugs innovation and access in India**

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Objective of the thesis

Article-27.1 of the TRIPs agreement

Patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.

- Article 7: Protection and enforcement of Intellectual Property Rights should contribute to the promotion of Technological innovation and transfer and dissemination of technology to the mutual advantage of producer and user of the technological knowledge, in a manner conducive to social and economic welfare and balance of rights and obligations.

So the relationship of two very Articles (Article 7 and 27) in the context of Indian biopharma Industry to know the impact of TRIPs agreement on developing country like India.

Background

Why biopharma technology is needed for India?

1. Advances in the recombinant DNA technology, study of the cell growth, gene therapy proteomics, and bioinformatics contribute to the development of proteins can provide cures for many chronicle and hereditary disease as Alzheimer disease HIV AIDs, Malaria tuberculosis.

2. important for a country like India where there is widespread of these diseases.

3. investment for these drugs innovations is negligible, therefore availability through technology transfer from the multinational innovator companies are desired.

Such necessary technology needs to be developed by putting more and more investment into R&D and transferred to developing countries to reduce the spread and impact of disease which improves socio economic standing of the improvised populations.

If the potential is so great of biotechnology research, then what is all the opposition and controversy for?

patenting of DNA sequence is related with the blueprint of life.

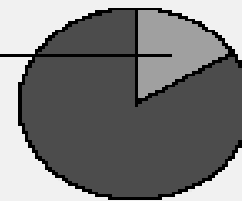
- several moral and ethical issues are attached with the patenting of the same.

- accessibility – due to the impact of the higher patent standards and data exclusivity on access to drugs.

Background

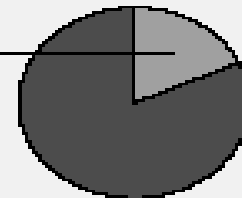
Disease Burden in India

16% of worldwide
population

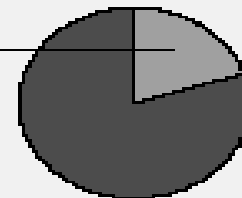


India
Rest of world

18% of worldwide
mortality

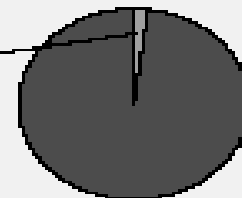


20% of worldwide
morbidity

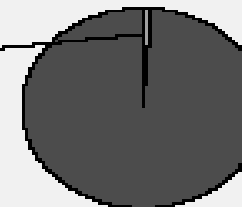


- but only -

2% of world GDP



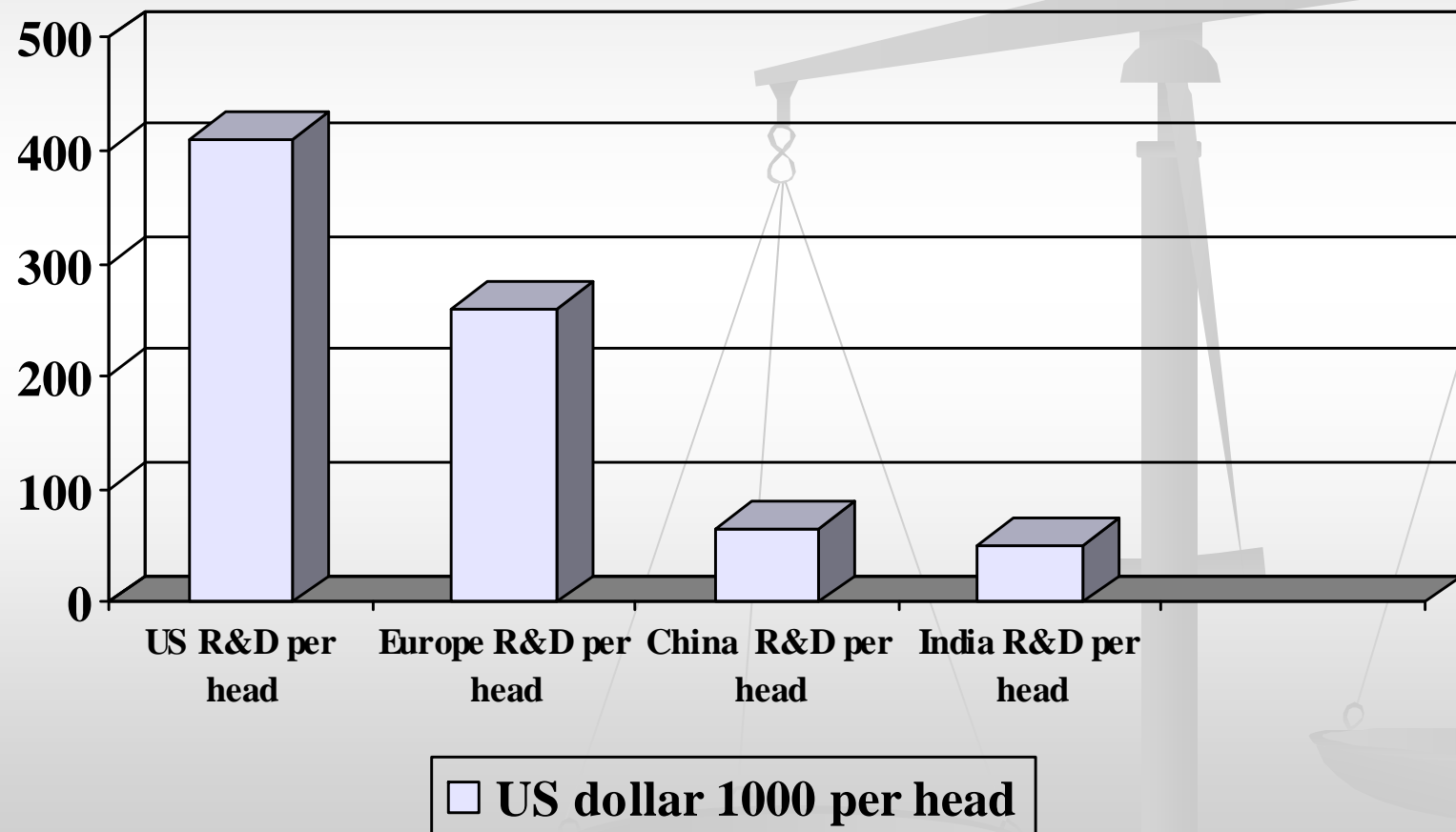
**1% of world healthcare
investment**



Biopharma R&D expenditure in different countries

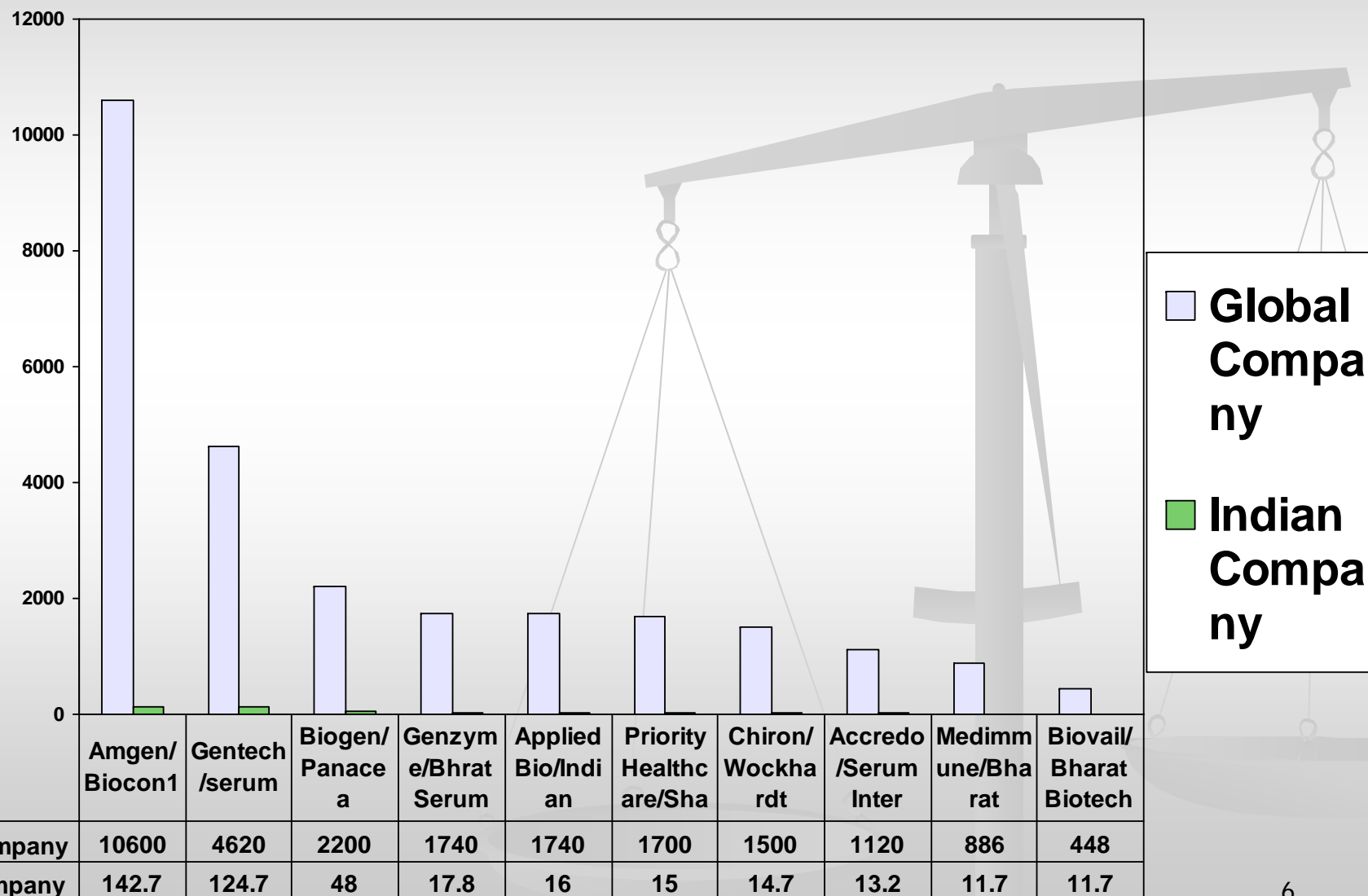
(Expenditure in US

Dollars)



Indian biopharmaceutical industry: Where does it stand in Globe?

Revenue comparison of top 10 companies -2004-05



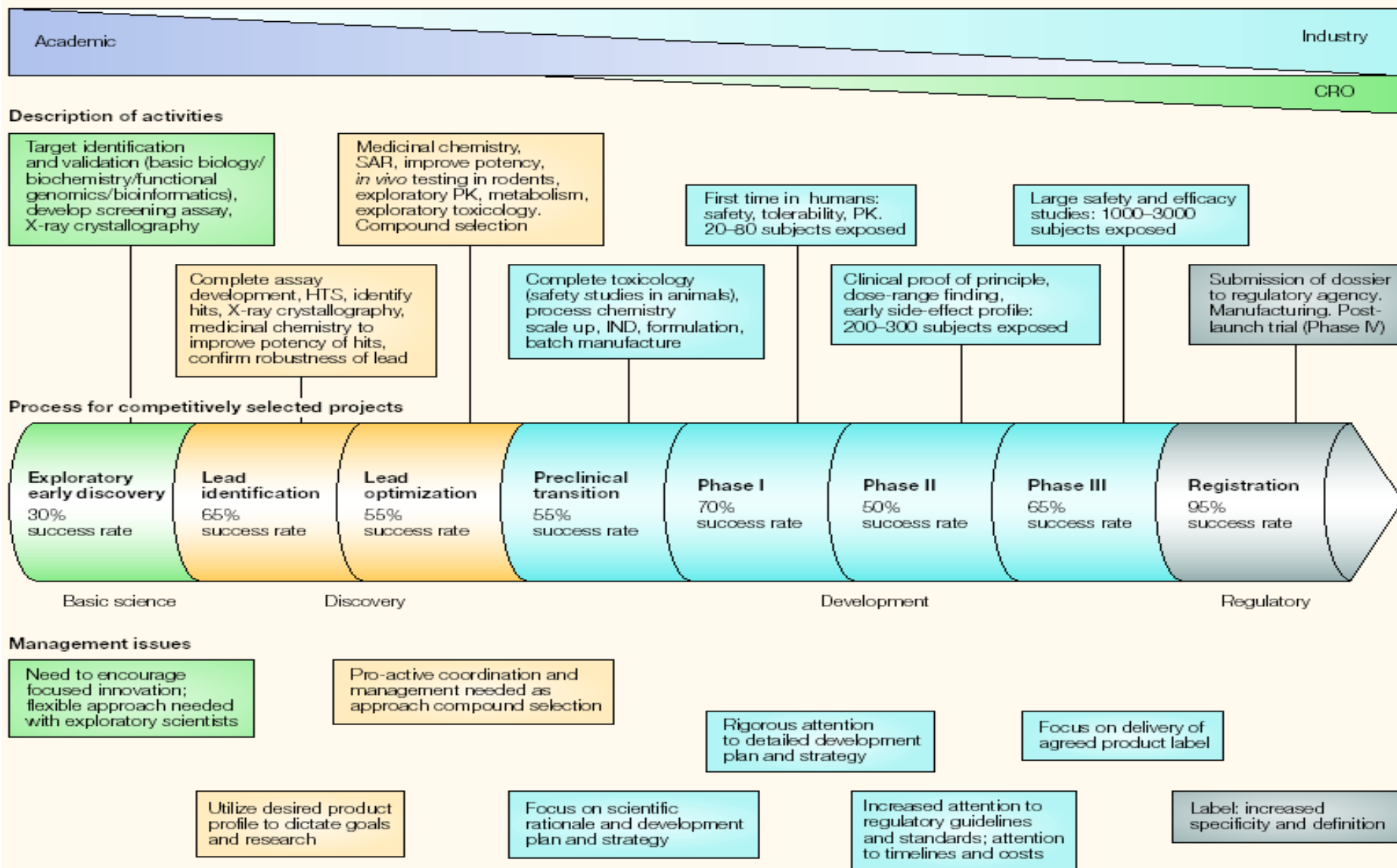


Figure 1 | Managerial aspects of drug R&D process. The figure focuses on partnership evolution and experience of public-private partnerships (PPPs) in key tasks performed in academia, pharma (big, small or biotech) and contract research organizations (CROs; top of figure). Success rates and managerial focus as projects progress from discovery to development are shown based on Medicines for Malaria (MMV) analysis for competitively selected malaria projects^{31,37}. Partnerships usually begin with academia for exploratory research, and move on to partnerships involving academia and industry once there is a need for chemistry at the drug discovery phase. Especially in cases in which small pharma companies are involved, there is frequently a need to involve CROs as projects move into the development phases. Success rates vary from phase to phase, and from project to project. However, an approximate average success rate from phase to phase in infectious disease is presented on the basis of MMV analysis for malaria^{31,37}. Some observed differences in management needs between discovery and development projects are highlighted. HTS, high-throughput screening; IND, Investigational New Drug application; PK, pharmacokinetics; SAR, structure-activity relationships.

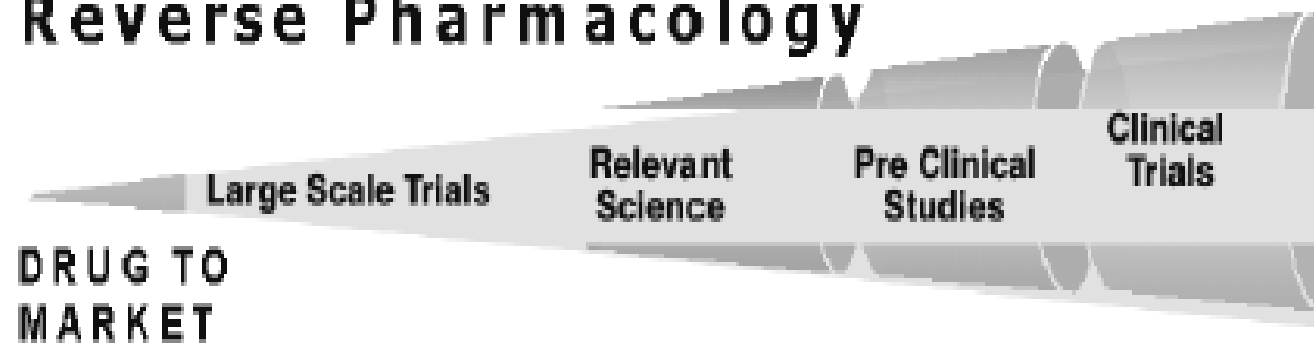
Figure 5: Drug Discovery and Development Process

Expensive, time consuming, numerous bottlenecks



Economical, time sparing, least bottlenecks

Reverse Pharmacology



Methodology used for the thesis

Industry level data

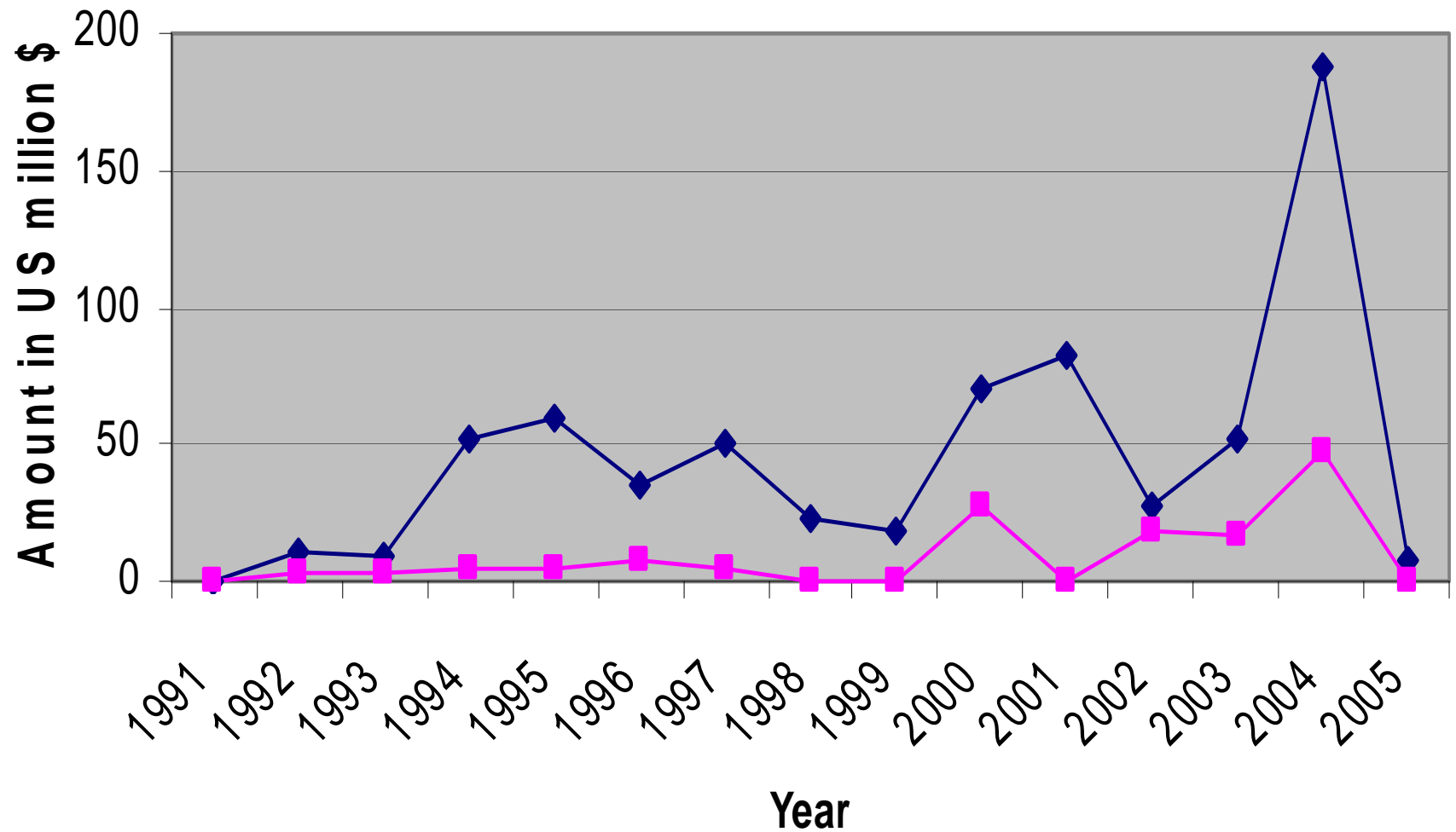
■ Firm level data

- Interview data- 45 Indian biopharmaceutical CEO, 10 MNC biopharmaceutical CEOs based in India,
- 10 NGOs working on public health in India, 5 states biotech department secretaries, Director General of CSIR, Science and technology Minister, Government of India.

Scrutinizing legal text

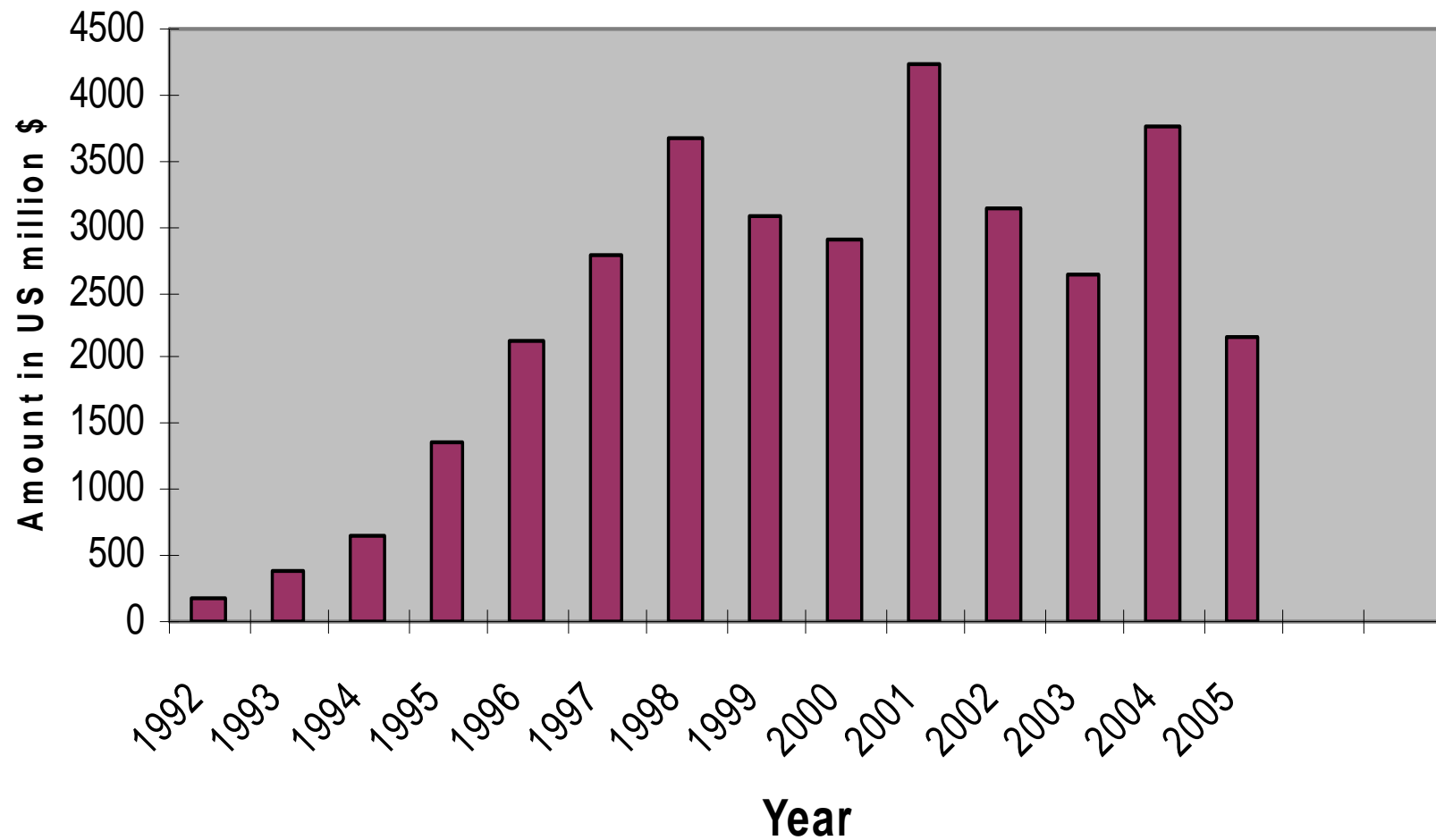
- TRIPs agreement text
- Doha Declaration
- 30th Aug
- Indian Patent Act 1970(with all three amendments- 1999,2002, 2005)
- Drug policy
- Fiscal policy

FDI flow in Indian pharma and Biopharma sector



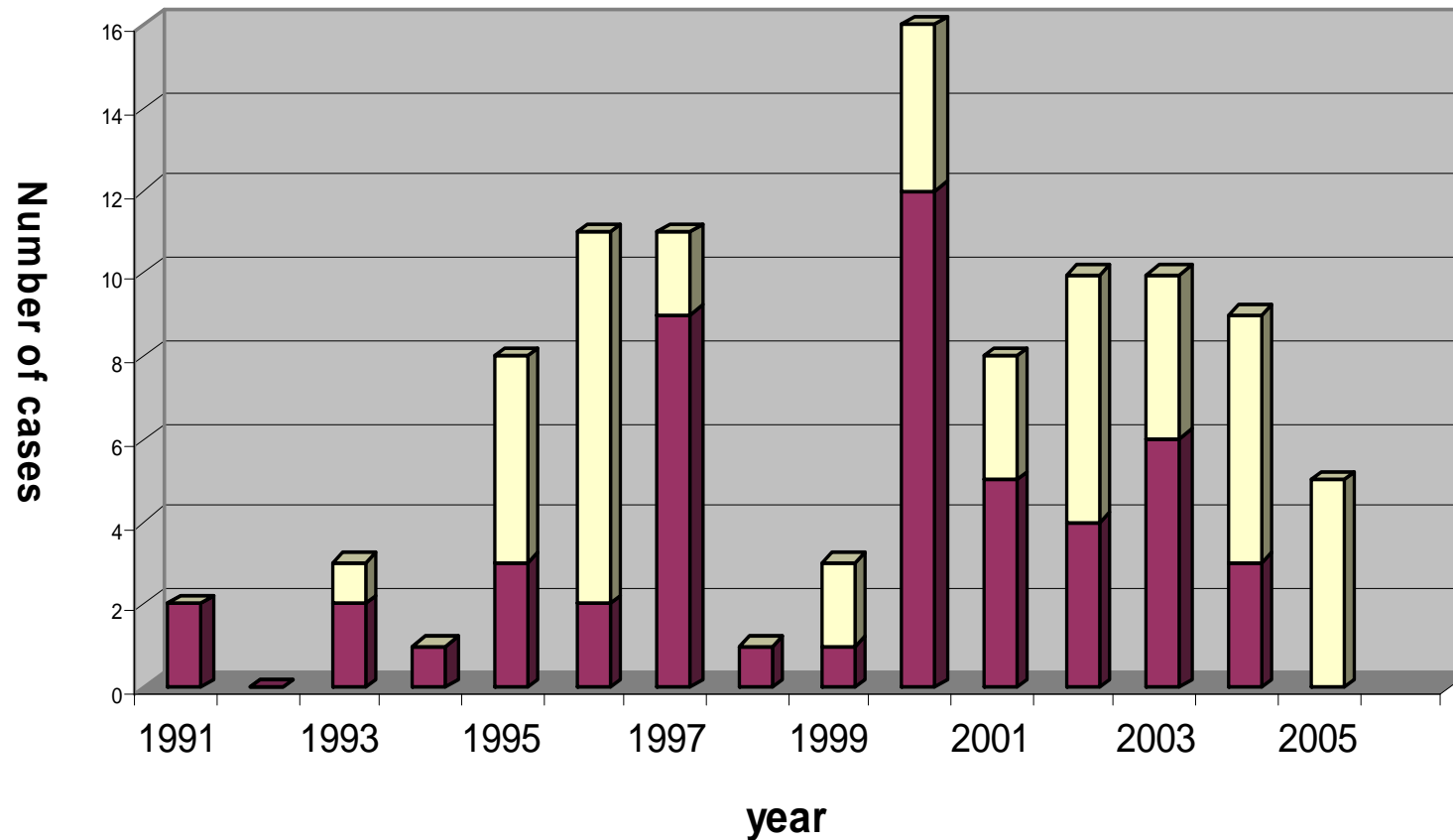
—◆— FDI in Pharma —■— FDI in Biopharma

Amount of FDI approved in all sectors (in US \$ million)



■ Amount of FDI approved in all sectors (in US \$ million)

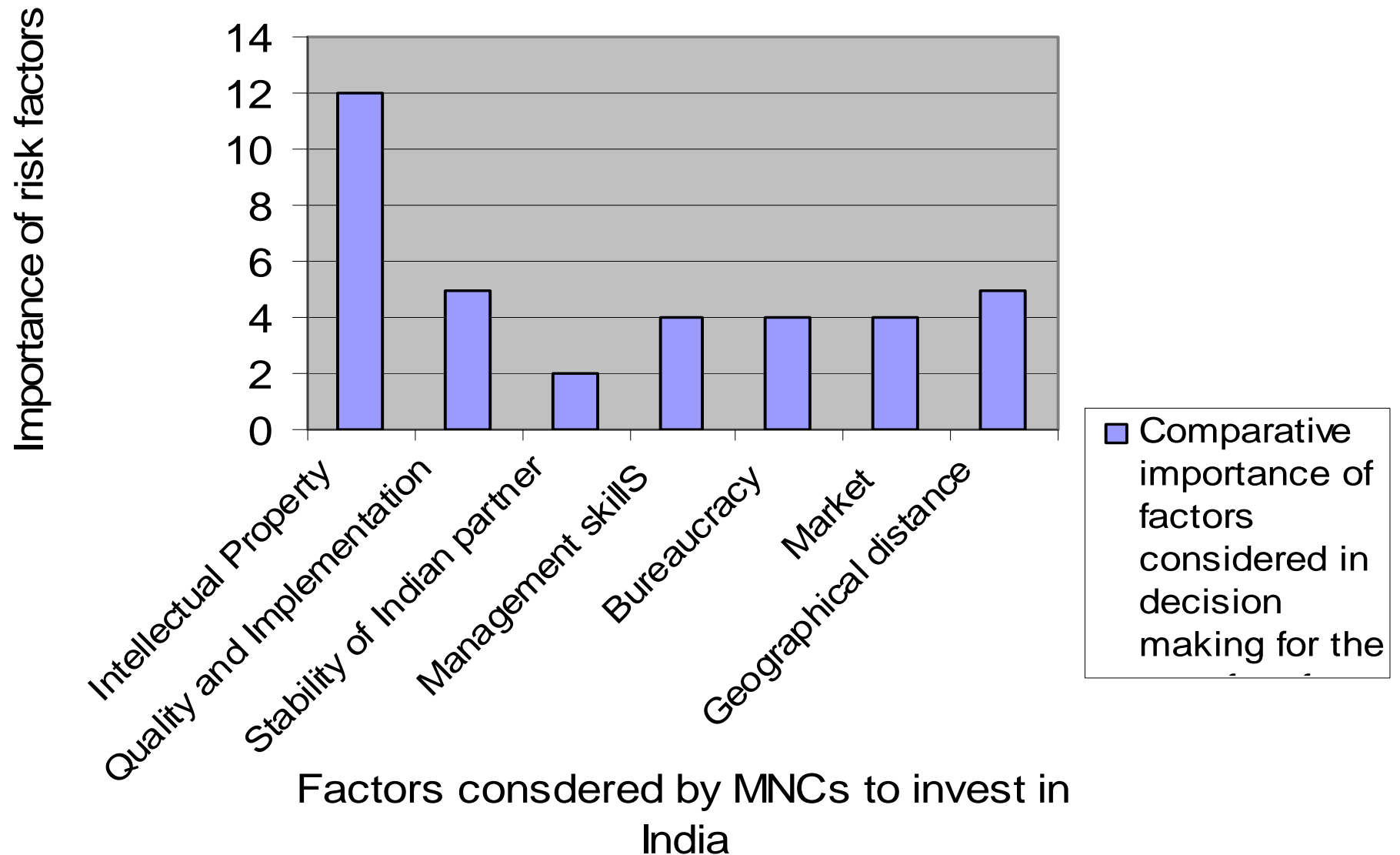
Foreign technology transfer in Indian biopharma sector



■ Number of Financial (FDI) cases approved in Biopharmaceutical sector

■ Number of Technical (Technology collaborations, licensing and joint ventures) cases approved in Biopharmaceutical sector

Comparative importance of factors considered in decision making for the transfer of technology in Indian bipharma sector (on 15 scale value)



Findings:

After the introduction of product patents in India has enhanced the innovator's incentive to innovate but still multinational biopharmaceutical companies demands higher patent standards and data exclusivity etc

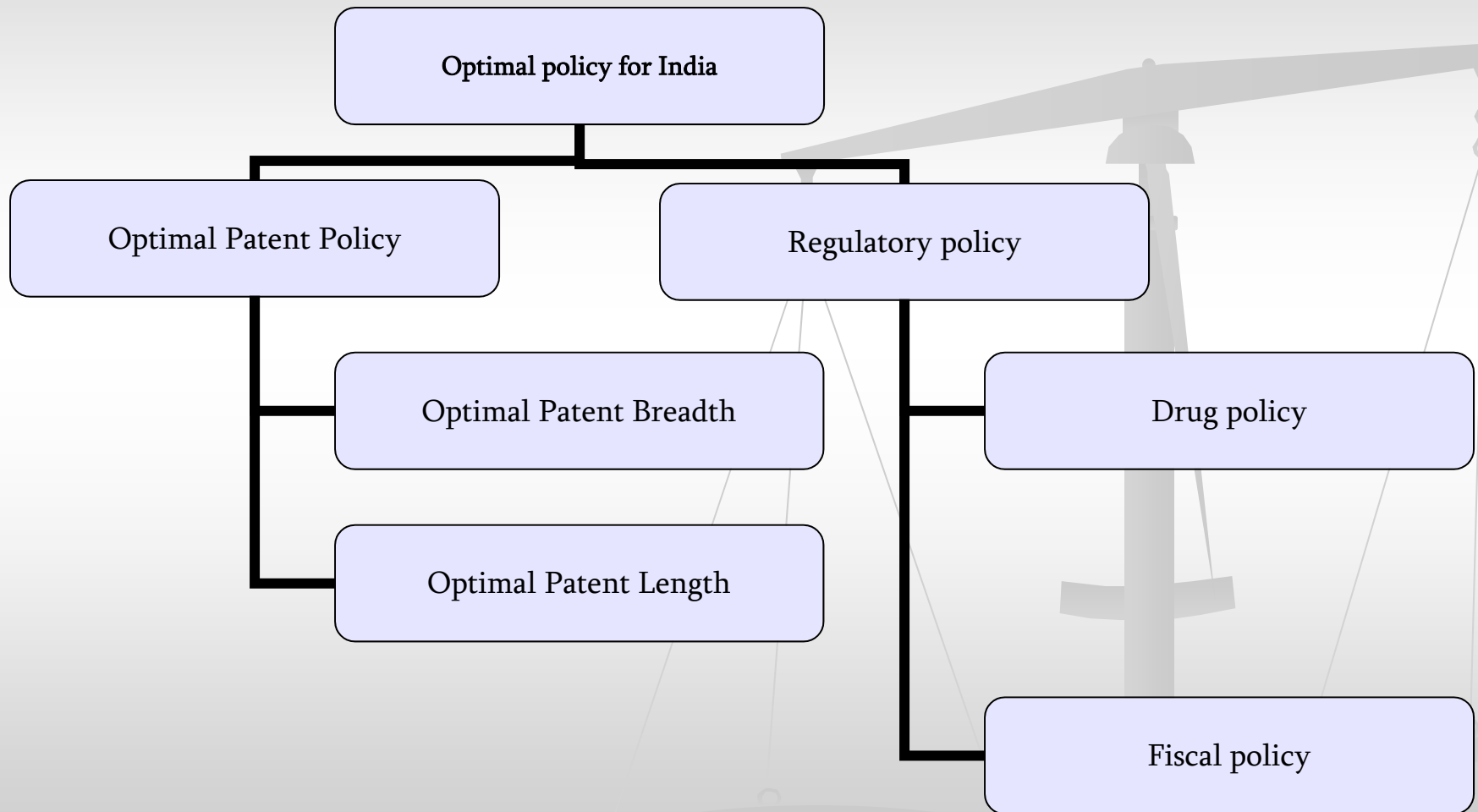
On the demand of the MNCs there are three issue which have been Raised:

1. Access to drugs- Higher price
2. Moral and ethical issue due to higher life form patenting
3. Access to genetic resource
4. Death knell for domestic generic industry

Aim of the presentation

Suggest optimal policy (Patent and other regulations) to have a balance between biopharma drugs innovation and their access in India while complying with the provisions of the TRIPs agreement.

Optimal policy design



Part A

Optimal Patent breadth

Indian position on higher life form patenting

"higher life form"

- not defined in law.

In common usage

plants and nonhuman animals other than single-celled organisms.

India: Current position

The landmark judgment of **Dimminiaco AG vs. Controller of patents (2001)** Kolkata high court held the biotech matter as patentable even if the end product of a process is a living virus/microorganism / living entity.

Section 3 of the Patent Amendment Act 2002

excluded from patentability, plants, animals in whole or any part thereof other than microorganisms but includes seeds varieties of seeds varieties species and essentially biological processes for production or propagation of plants and animals.

- Patent amendment Act 2005 has accepted living entities of artificial origin such as microorganism and vaccines which fulfills the cardinal principle of patentability and not harmful to human, animal or plant health or unethical.
- **controversy : Current controversy:**

Presently there is controversy with regard to the definition of microorganisms as there is absence of a working definition of microorganism in the TRIPs text.

Question

whether India should adopt a very narrow and limited definition of microorganism to exclude everything other than microscopic organisms including algae, bacteria, fungi, protozoa and viruses or whether it should expand the scope as in the Europe where all biological material containing genetic information and capable of reproducing itself or being reproduced in a biological system?

TRIPs Requirement: Art 27(3)- Members may also exclude from patentability:

- (a) diagnostic, therapeutic and surgical methods for the treatment of humans or animals;**
- (b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes.**

**US practice - Diamond Vs Chakrabarty, United States Supreme Court, June 16, 1980,
447 U.S. 303, [206 USPQ 193](#)**

- isolated and purified gene sequences are awarded patent protection in accordance with the novelty standard as per USC 102
- utility requirement under 35 USC 101
- for ascertaining the obviousness of an invention - *Duel case* re Thomas F. DEUEL; No. 94-1202; March 28, 1995; USFDA

EU practice:

Article 4 of the Biotech Directive (98/44/EC) animals and plant variety is not permitted for patenting but Article 4.2 -

- Article 5 of EC directive (98/44/EC)
- *Biogen vs. Medeva*, 1997; RPC; 1
- The European Directive on Biotechnological Inventions (No. 96/9/EC of March 11, 1996)
- European Directive (98/44/EC) provides broader definition of "Biological material"
- Directive 98/44/EC – moral doctrine
- Article 6 of the EPC
- Article 53(a) of the EPC prohibits patents for inventions that are contrary to the morals of society.
- *Harvard oncomouse case* – US
- *Florey/relaxin case* 1995; O.J.E.P.O, 388

■ **Higher life form patenting: benefits for India**

- financial incentive to industry to invent,
- Away from international patenting standard
- Important for newer innovation in field of biotechnology

■ **Problem related with the higher life form patenting**

- broader scope of biotech patentability currently, there are two problems:
- Access to basic platform technology such as DNA sequences, cell lines, plants and animals at reasonable costs which are crucial to the research.
- patents on plants and animals or any biological material (DNA sequences, genes, cells) – not ethical and moral.

Recommendation: Human Beings Not Patentable - however, prevent patent claims from being granted with respect to DNA sequences, cell lines or stem cells of human origin.

Balancing Act

Laws such as the *Competition Act*, the *Criminal Code*, prohibit certain types of behaviour such as unfair economic practices, cruelty to animals, or the cloning of human beings.

before many products can be sold in India, compliance with regulations designed to protect human and environmental health, to ensure product safety and to meet other requirements. Compliance with voluntary standards, such as Good Laboratory Practices is necessary to maintain public confidence in the product and its maker.

social and ethical considerations raised specifically by biotechnology should continue to be addressed primarily outside the *Patent Act*.

Access to Genetic material: Bolar provision

Controversy:

Novartis AG in 2007 filed writ petition challenging Section 3 (d)

denies Article 27 of the TRIPS Agreement, which obligates WTO member states to provide patent protection to all fields of technology without discrimination.

in the absence of a definition or guideline, phrases like 'enhancement of the known efficacy' or 'differ significantly in properties with regard to efficacy' give uncontrolled as well as unguided powers to the Controller of Patents.

violates the right to equality under Article 14 of the Constitution of India.

§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 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.

' 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.'

Argument of the other interest group:- 1 Ever greening, 2 frivolous patents, 3. generic drugs adversely affected, 4. prices will be high.

Decision

- Rejected Glivec patent application on the ground that a patent cannot be granted for "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."

Analysis

Difference between incremental innovation and ever greening

Benefit of incremental innovation for India

- improving therapeutic efficacy, but also in providing significant benefits in terms of drug delivery, patient safety and compliance
- Newer drugs innovation to combat diseases
- More foreign investment

Recommendation

Patents on Salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance should be granted if they fulfil the cardinal principal of patentability

Part B

Optimal Patent length for India

- The length of the patent protection characterizes the duration of monopoly power.

- **Controversy:**

MNC- Data Exclusivity- Article 39.3 of TRIPs text and Indian Patent Act 2005, advocating a definition to mean a new pharma product which has been introduced for the first time in a country irrespective of the fact whether it is patented or not. Another controversial matter is that what constitutes 'unfair commercial use' under Article 39.3.

Health Advocates and scholars:

- death knell for the Indian biopharma industry,
- Prices of the drugs will be high

Data-

Data exclusivity-

Data protection and data exclusivity-

Article 39.3 of the TRIPS Agreement:

*Members when requiring as a condition of approving marketing of pharmaceutical or of agricultural chemical product which utilize **new chemical entities**, the submission of undisclosed test or other data, the originator of which involves considerable efforts shall **protect such data against disclosure**, except where necessary to protect the public or unless steps are taken to ensure that the data are protected against **unfair commercial use**"*

Article 39.1 provides- *In the course of **ensuring effective protection against unfair competition** as provided in Article 10bis of the Paris Convention (1967), Members shall protect undisclosed information in accordance with paragraph 2 below with data submitted to governments or governmental agencies in accordance with paragraph below.*

- *Article 10bis of the Paris Convention:*
- *Article 6 of the WIPO model: Any act or practice, in the course of industrial or commercial activities, that results in the disclosure, acquisition or use by others of secret information **without the consent of the person lawfully in control of that information** (hereinafter referred to as "**the rightful holder**") and in a manner contrary to honest commercial practices shall constitute an act of unfair competition.*

- Satwant Reddy Committee constituted by Government of India has also recognized that not providing data exclusivity for pharmaceuticals could adversely impact FDI and discourage the launch of new products in India.

Recommendation

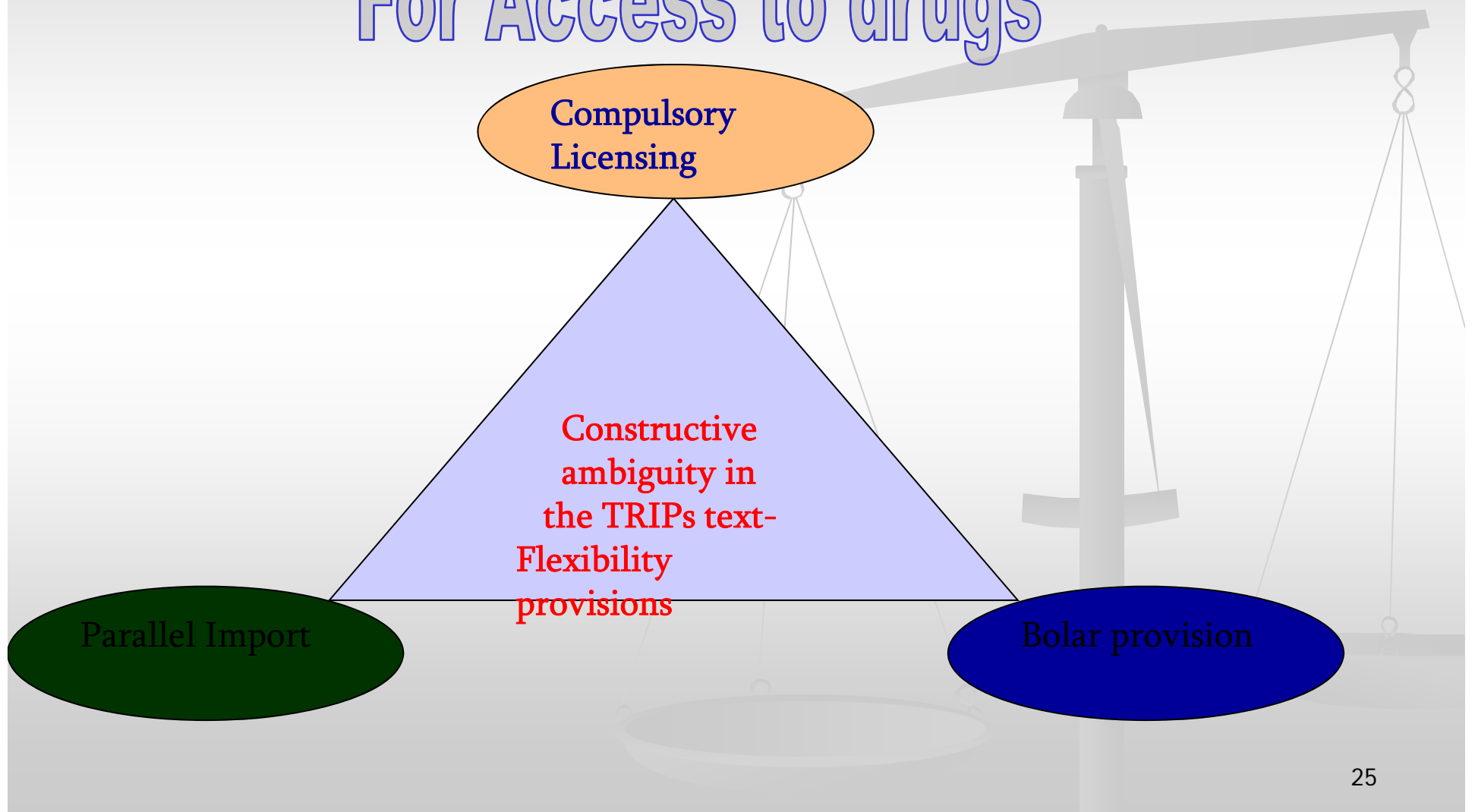
Five years of data exclusivity either starting from the date on which the company markets its product or ending with the expiry of patents whichever is earlier provided that company must have filed a patent in India.

Reason

- India has a well-developed Pharmaceutical industry,
- Around \$ 72 billion worth drugs will go off patented between 2006
- China competition

balance between access and innovation

For Access to drugs



Effectiveness of Compulsory License (CL)

- Compulsory license
- TRIPS
- Indian Patent Act 2005-
- Experience in India



Thailand and CL

In January 2007, compulsory license for Kaletra Patented by Abbott, and Plavix patented by Sanofi Aventis.

Abbott laboratories cut the price of second line drug lopinavir / ritanivir, to \$ 1,000 /month from \$ 2, 200 / Month for 45 lower and middle income countries.

Merck immediately cut the price of first line antiretroviral clavirez from 1400 baht /bottle to 767 baht/bottle in Thailand

Brazil-

Threat of compulsory license pressured pharmaceuticals trail companies like Abbott Merck and Roche manufacturer of Lopinavir, indinavir, melfinavir and saquinavir respectively) to substantially reduce the price, thus enabling 100,000 people to receive free treatment.

whether the same thing can happen in India?

- Hoffman La Roche Ltd Vs. Cipla Ltd
- Novartis case (the famous glivec case)

On the other hand at the same time, the drug companies worry that countries will abuse compulsory business,

■ Optimal patent policy for India

The arguments

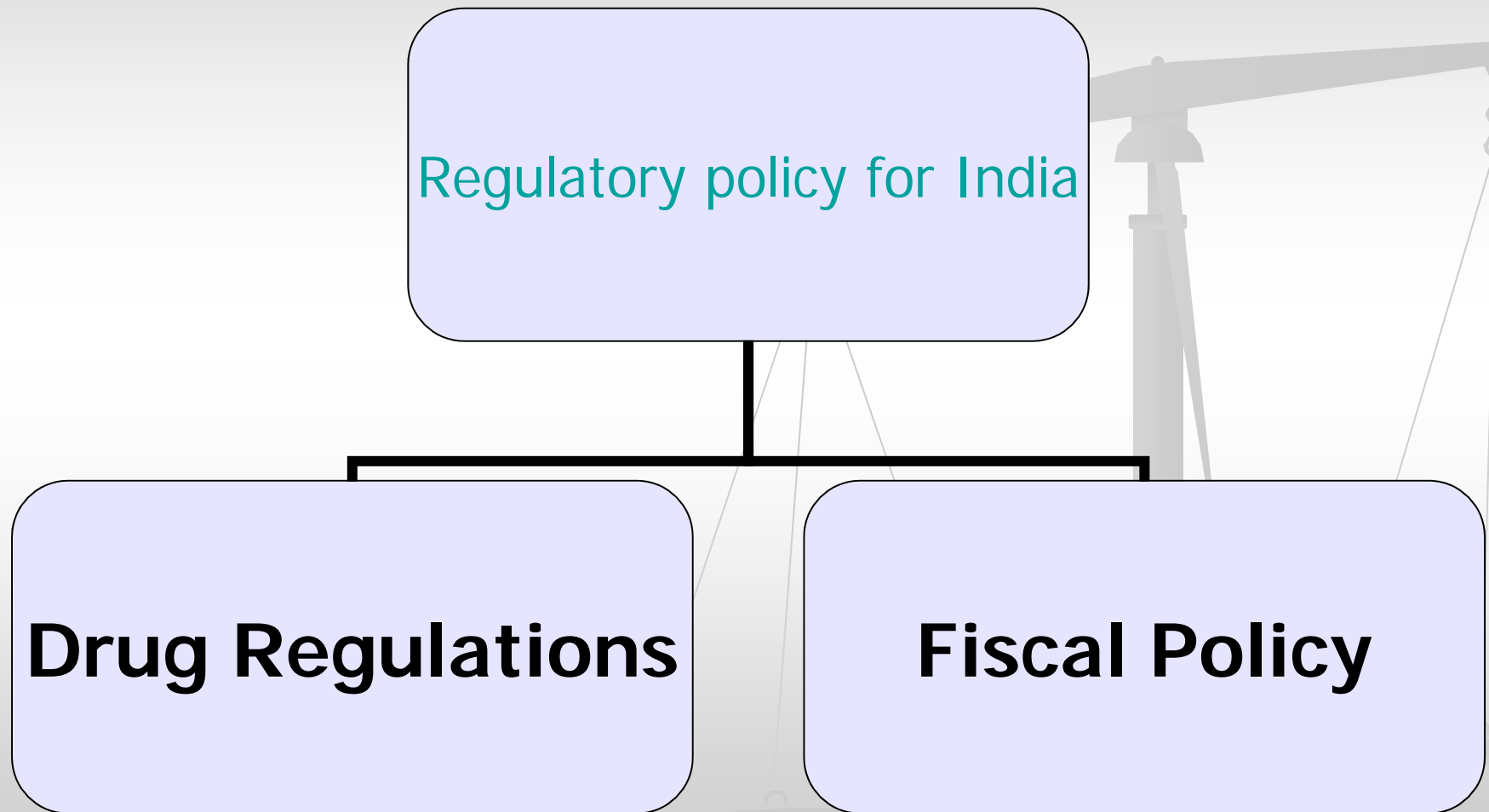
in India the combined taxes and tariffs on imported medicines are 55 percent. (Wilson Tim, 2008) To control the drugs prices, there is proper drug price control mechanism of Drug Price Control Order (DPCO).

compulsory licensing undermine IP in case of national emergency or other circumstances of extreme urgency or in case of public non commercial use. As there is need to balance between innovation and access.

■ Suggestion

Broader with higher life form patentability, incremental innovation and 5 years of data exclusivity with a balanced flexibility provisions and implementation of compulsory license mechanism, other regulatory and fiscal policies.

Part 2 optimal Regulatory policy for India



■ Factors

According to the report of the Investment Commission 2006, the major impediments to investment have been identified as

- investment restrictions and/ or entry route barriers,
- absence of long-term policies,
- inflexible labour laws,
- bureaucratic delays,
- discretionary interpretation,
- vested interest, bias and subjective practices,
- high cost of entry, transactions and exit; ineffective dispute resolution,
- poor infrastructure.

These impediments can be categorized in two groups, tariff barriers and non tariff barriers.

Tariff Barriers : higher rate of taxation, royalty, interest, gains from sale of capital assets located in India higher fees for technical services etc.

Non-tariff barriers : attitudes and bias toward foreign products, a rigid distribution system, and Government bureaucracy.

Access to drugs are affected : pricing policy, pharmaceutical procurement policy, Government subsidy policy, drug distribution policy, Administrative efficiency.

- - We find some common factors which can influence both investment and access such as pricing policy which needs careful framework to balance both
- - On the other hand there are factors which individually affect each proper framework of the same can balance the negative generated by the policy which affect both in common³¹

Government initiative in framing regulations:

Establish Central Drug regulatory authority (CDA) with a single, central, FDA-style agency.

- All facility-inspection, manufacturing-license, and data-evaluation functions concerning drugs in India.
 - Separate, semi-autonomous Departments for regulation, enforcement, legal, and consumer affairs; biotechnology products; pharmacovigilance and drugs safety; medical devices and diagnostics; imports; quality control; and traditional Indian medicines. It will set up offices throughout India for inspection, registration, and license.
-
- biotech Parks promotion policies: The DBT - 10 biotech parks by 2010.
 - In the biotech parks, concession like tax holiday U/S 10B of Income Tax Act 1961, duty free or import of equipments, instruments etc.
-
- The National biotechnology strategy 2007 provides many fiscal and non fiscal benefits to the industry.
 - 100 percent FDI approved in biotech

■ Government initiative to procure access

The Drug Policy Control Order 2006 declared that bulk drugs developed by Indian companies would be exempt from price control for five years or, in the case of new drugs, 10 years. Goods developed in India and patented in the U.S., Japan or E.U. enjoy a three-year waiver from excise duty, and companies get a 10-year tax holidays for income stemming from qualifying R&D.

- Better drug procurement and distribution policy

Fiscal policies

Government initiative

An 8 percent reduction in export duties along with export duties exemption for indigenous life saving drugs and 5 percent customs duty reduction for imported life saving drugs by the budget of 2008-09 will definitely make the drugs price lower. In fact this is a better way to address drugs costs rather than drugs price control. Given the current international political climate, systemic, Government driven reform of intellectual property protection seems unlikely in the near term.

Suggestion and Conclusion

optimal design of patent for biopharma innovation in India should confine to trade off between patent length and breadth taking into account the flexibility provisions of TRIPs. Larger breadth makes it more difficult to imitate, whereas increasing the duration of patent protection enhances the incentives to improve the invention by increasing R&D investment for the innovation of biopharmaceutical drugs in general and neglected diseases drugs through foreign investment in particular carrot in terms of data exclusivity and higher form of patent protection should be given along with the stick of properly framed compulsory licensing provision and parallel importation to balance the need of the access. Government subsidies promote the development of biopharma technologies.