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Analysis Of Legal Remedies
Available To Subjects Of
Clinical Trials

Agenda

Scope and limitations of the Paper

Remedies – Drug Laws in India

Secondary Remedies

Amendments to the Drugs Act

Clinical Trial on Patients Bill, 2006

Conclusion & Suggestions

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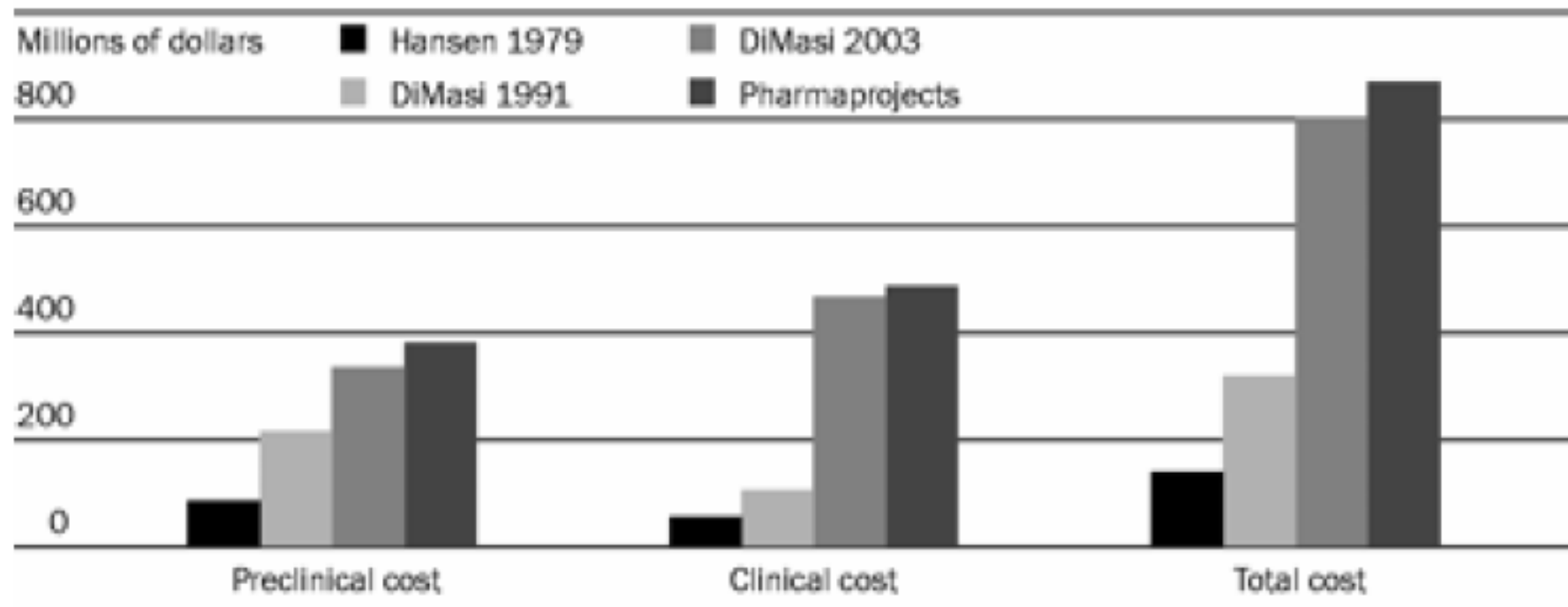
Globalization of pharmaceutical development

Two powerful dynamics are at the forefront of contemporary pharmaceutical development:

- *global outsourcing of clinical trials*
- pharmacogenomics

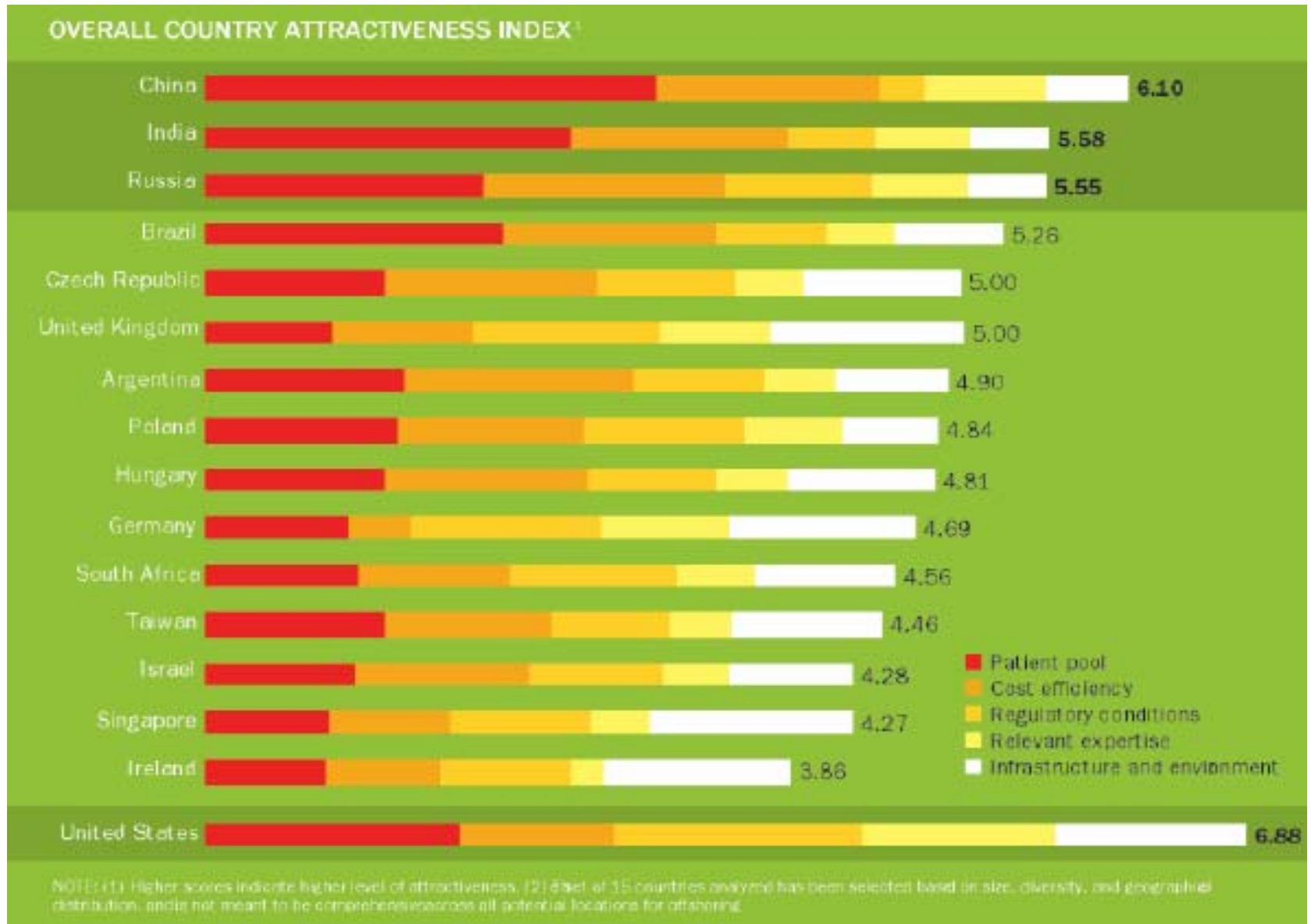
The Price of Innovation

Capitalized Preclinical, Clinical, And Total Cost Per New Drug, In Millions Of 2000 Dollars



SOURCES: R.W. Hansen, "The Pharmaceutical Development Process: Estimates of Current Development Costs and Times and the Effects of Regulatory Changes," in *Issues in Pharmaceutical Economics*, ed. R.I. Chien (Lexington, Mass.: Lexington Books, 1979), 151-187; J.A. DiMasi et al., "Cost of Innovation in the Pharmaceutical Industry," *Journal of Health Economics* 10, no. 2 (1991): 107-142; J.A. DiMasi, R.W. Hansen, and H.G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22, no. 2 (2003): 151-185; and data from Pharmaprojects.

States of Attraction



Why India?

Large pool of naïve patients, a larger spectrum of diseases profiles & a genetically distinct group

Accountability to whom?

Phases of trials		
The four phases of trials, what they mean, and how many are taking place in India		
Stage	No. of subjects usually required	No. of trials being done in India*
One: Safety and toxicity studies and the side effects associated with increasing doses	20-80	7
Two: To gauge a drug's efficacy in a disease and to see the common short-term side-effects and risks	100-300	55
Three: Study done on a large number of patients to assess the overall risk-benefit of the drug	1,000-3,000	156
Four: Post-marketing studies to get additional information on the drug's risk, benefit and its optimal use	No specific no.	23

*Registered with the US FDA Source : www.clinicaltrials.gov, BW research

Trial of Trials

- Patients Enrolling - Those who are most vulnerable, who have little resources, those who do not have proper social security systems
- As the number of clinical trials increases, the rights, safety etc., of the patients participating in the trials will become a growing concern
- "There's still a long way to go to ensure & assure subject protection in biomedical research" – N.K. Ganguly (Director General, ICMR)

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Primary Remedies

- The Drugs and Cosmetics Act, 1940 (the "**Act**") regulates the manufacture and sale of drugs and chemicals in India
- Rule 122 DA of the Rules stipulates ***that clinical trial for a new drug shall be conducted only with the written permission of the Licensing Authority***
- Information and data as required under Schedule Y shall also be provided. Schedule Y of the Rules deals with the requirements and guidelines to obtain permission:
 - (a) to import and/or manufacture new drugs for sale;
 - (b) ***to undertake clinical trails in India***

Primary Remedies

- In 2005 the government amended Schedule Y and incorporated significant changes. Amongst other things, newly revised Schedule Y –
 - (a) Permits multi centre drug trials to be conducted in India;
 - (b) It requires the sponsor, investigator and other concerned parties **to comply with** GCP Guidelines, ICMR Guidelines etc.
- As the revised Schedule Y requires **mandatory compliance** with the GCP and Ethical Guidelines (the “Guidelines”), the stakeholders are under an obligation to provide for **far-reaching victim compensation package** as expected under the Guidelines.

Responsibilities under Schedule Y

- **Sponsor** - The sponsor is ***responsible*** for implementing & maintaining quality assurance systems to ensure that the clinical trial is conducted & data generated, documented & reported ***in compliance with the protocol & GCP Guidelines*** [Schedule Y, Item 2 (2) (i)]
- **Investigator** - Investigator(s) shall be responsible for the conduct of the trial according to the protocol and the GCP Guidelines and also for the compliance as per the undertaking given in Appendix VII. He is also the person who is responsible for the rights, health and welfare of the study subjects[Sch. Y, Item 2 (3) (i)]

Responsibilities under GCP Guidelines

- The Guidelines seek to establish ***two cardinal principles: protection of the rights of human subjects*** and authenticity of biomedical data generated
- The GCP Guidelines also sets out that Study Subjects ***should be satisfactorily insured*** against any injury ***caused by the study*** [Chapter 2]
- It stipulates that all research involving human subjects should be conducted in accordance with the ethical principles contained in the current revision of Declaration of Helsinki [Chapter 2]

Compensation under GCP Guidelines

- The Sponsor *should agree* to provide compensation for *any injury* for which subjects are entitled. Also agree to provide insurance coverage *for unforeseen injury* [Ch. 2]
- For participation– Subjects *may* be paid for the inconvenience & time present; should be reimbursed for expenses. They may also receive free medical services
- For accidental injury– Subjects *are entitled* to financial or other assistance for any temporary or permanent impairment
- In case of death- Dependents of Subjects *are entitled* to material compensation

Ethics Committee

- The Committee is required to grant approval and permit the company to undertake clinical trials
- It has the power to revoke the approval granted to a trial protocol [Sch. Y, Item 2 (5) (i)]
- More importantly it is the responsibility of the Committee to verify the protection of the rights, safety, and well being of human subjects involved in a study by carefully monitoring the different phases involved in the clinical trial

Action against Ethics Committee

- To my knowledge no such action has ever been brought in the Indian Courts
- **Canadian Case** – *Weiss v. Solomon*, the SC of Quebec had held that the Ethics Committee was negligent because it had failed to ensure that prospective participants were given adequate information about the risks
- Notwithstanding whether it is persuasive, in the Indian context, it can be argued that such an assumption of responsibility can be found on the members of the ethics committee

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Secondary Remedies – Professional Misconduct

- Chapter VII of the Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002 mandates that clinical trials can be undertaken as per the ICMR Guidelines
- As the Code of Ethics is binding on the physicians, all those who are involved in the clinical trial process are under an ***obligation to comply*** with the same
- In the event they ***fail*** to comply, such doctors might have to subject themselves for disciplinary action of the Indian Medical Council as it amounts to ***professional misconduct***

Secondary Remedies – Criminal Liability

- **Section 336** of the Indian Penal Code states that whoever does any act so ***rashly or negligently*** as to ***endanger human life*** or the ***personal safety*** of others shall be punished with imprisonment of either description for a term which may extend to ***three (3) months*** or with fine which may extend to Rs.250 or with both
- Rash and negligent acts that endanger human life, or the personal safety of others are punishable under section 336 of the Penal Code ***even though no harm follows to the victim***
- This section applies only to acts done rashly or negligently ***but without any criminal intent***

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Drugs & Cosmetics (Amendment) Bill, 2007 – What does it propose

- Shifts the approval mechanism from the Rules to the Act
- Proposes to insert Chapter IB (Clinical Trials) into the Act to provide for grant of permission for clinical trials, punishment for conducting clinical trials without permission, trial of offences etc.,
- Section 5 (O) of the new Chapter imposes a fine of **Rs. 10 Lakhs** & prescribes imprisonment for **5 years** in case trials are conducted without procuring permission from the Central Drugs Authority

Drugs & Cosmetics (Amendment) Bill, 2007 - Drawbacks

- It's a mere eyewash as it simply introduces punishment and ***fails to contemplate the consequences*** of incorporating the proposed amendments
- It's a half-hearted effort as it fails to indicate what will happen to ***Schedule Y subsequent*** to amending the Act
- The Statement & Objects of the Bill fails to identify any guideline which must be considered while framing the Rules

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Clinical Trial of Drugs on Patients (Regulation) Bill, 2006 - Objectives

- Regulation of clinical trials, to determine safety and efficacy of new drugs & ***to protect the interests of patients*** undergoing these clinical trials
- Makes it ***mandatory*** to register clinical trials with the Clinical Trial of Drugs Registry [Sec. 5]
- Proposes that every patient undergoing the clinical trial ***shall be paid Rs. 50,000*** by the pharmaceutical companies or the CROs [Sec. 6]
- Imposes an ***obligation*** on the Government to establish ***Clinical Trial Fund*** [Sec. 7]
- **Penalty** – Imprisonment for ***3 years*** & fine which may extend to ***Rs. 20 Lakhs***

Clinical Trial of Drugs on Patients (Regulation) Bill, 2006 - Drawbacks

- **Legislative blunder** - Assumes that all participants are and will be *patients*
- **Fraught with uncertainties** - How to reconcile this Bill with a Proposal to amend the Drugs & Cosmetics Act, 2007?
- **Commercialize the process** – By prescribing payment of *Rs. 50,000* to all the participants irrespective of the nature of involvement

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- Question is not of imposing penalty, but that of revoking permission granted to undertake clinical trials
- One must also acknowledge the fact that not every company would want to portray itself as being LAWLESS
- Participants should give serious consideration before deciding to volunteer

Suggestions – The Trial of Trials

Instead of introducing new chapters or enacting new Acts, it will be worthwhile if the government endeavours

- to amend the Drugs & Cosmetics Act to **introduce penalty** in cases of non compliance with Schedule Y & the GCP Guidelines;
- to **withdraw or revoke** the granted permission to undertake clinical trials for defaulting companies
- to **impose obligations** on the IEC to regularly monitor the drug development process and to **empower** the IEC to withdraw or revoke the approval granted to conduct clinical trials
- to categorically state that ICMR and GCP Guidelines **are law of the land** just as Schedule Y of the Act

Suggestions

- Provide for **arbitration** to resolve any disputes during the trial for any claims based on trial related injury

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Thank you

