

INADEQUACIES OF CLINICAL TRIAL REGULATIONS IN INDIA

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Madhya Pradesh has gained its fair share of media attention of late owing to the unethical drug trials being conducted on mentally challenged patients and children in the 'heart of Incredible India'. In the wake of these trials, the Swasthya Adhikar Manch, an Indore based NGO, has filed a public interest petition in the Supreme Court. The Court has issued notice to the Central Government and the Government of Madhya Pradesh and though the matter has been listed for hearing on a future date, the legal limbo surrounding clinical trials needs immediate and serious consideration. According to the public interest petitions, 1727 people have died during drug trials between 2007 and 2010. Art. 21 of the Constitution does not allow for the deprivation of life and personal liberty, except according to the procedure established by law. In the absence of any binding law to regulate clinical trials, one would question the safeguards conferred to protect the rights of the subjects of these clinical trials, who are more often than not, the impoverished strata of the Indian society.

I. BACKGROUND OF CLINICAL TRIALS IN INDIA

The process of clinical trials is charted out in four phases,¹ the most expensive among these being the third phase, which involves testing the drug in different stages and in combination with different medicines to ascertain the therapeutic benefits on the patient who is being tested.² It only stands to reason that profit-oriented pharmaceutical corporations would want to reduce this financial burden by outsourcing the third phase of trials to countries

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¹ See generally Ankur Paliwal, *Ethics on Trial*, DOWN TO EARTH (New Delhi) June 30, 2011, available at <http://www.downtoearth.org.in/content/ethics-trial> (Last visited on September 8, 2012). Phases of clinical trials- phase I: conducted on 8-10 healthy volunteers to estimate the safety and tolerability of the new drug; phase II: conducted on 100-200 patients to determine the efficacy and side effects of a new drug. It determines dose and regime for phase III trial; phase III: conducted on 1,000-3,000 patients to confirm the therapeutic benefits of a new drug. The drug is tested in different stages of diseases in combination with other medicines; phase IV: conducted for at least three years after the drug is approved by the Drug Controller General of India, and launched in the market. Feedback is taken from users to assess its efficacy.

² *Id.*

where regulations are less stringent and costs are low. According to the Drugs Controller General of India ('DCGI'), India will be a preferred site for clinical trials because, in addition to its medical infrastructure and trained English speaking human resource pool, it has a "large, diverse and treatment-naïve [untreated] population with six out of the seven genetic varieties of the human race".³ Diversity in a diseased gene pool is not the only factor that makes India a favourable destination. The impoverishment that characterizes a majority of the population that participates in these trials ensures that recruitment rates to such trials are high. A report by a Dutch non-profit organization SOMO goes so far as to say that India has "the highest recruitment rates for such trials internationally".⁴ The unconscionable terms of such recruitment are obvious, given that the recruiter is a multinational corporation wielding enormous clout whereas the recruitee, more often than not, an impoverished individual. At present Schedule Y of the Drugs and Cosmetic Rules, 1945 ('DCR') provides the regulatory framework for clinical trials, along with the Ethical Guidelines for Biomedical Research on Human Participants ('Guidelines') prescribed by the Indian Council of Medical Research ('ICMR'). Schedule Y, however, fails to offer a comprehensive framework for regulating trials.⁵ The Guidelines admittedly are very comprehensive, yet they do not enjoy a statutory status making compliance discretionary.⁶ As a result, clinical trials take place in a legal limbo, leaving recruitees with no substantively effectuated safeguards against the violation of their rights.

This paper seeks to analyse the regulatory framework for regulating clinical trials in India. Part II elucidates the international precepts that have emerged over a period of time to govern experimentation on human beings. Part III discusses the policy debates and judicial discourse centered on clinical trial regulations in India. Part IV expounds the existing regulatory framework in the country. Through the course of this part, we have analysed the relevant provisions of the constituent elements of the regulatory framework in order to ascertain the efficacy of the safety monitoring infrastructure in India. In addition to the exercise of locating loopholes in the present regulations, this part also examines the enforcement of these regulations. The constituent elements are contrasted with those of other jurisdictions to provide a more holistic understanding of the working of the safety mechanisms. Part V of the paper engages

³ Sandhya Srinivasan, *Ethical Concerns in Clinical Trials in India: an Investigation*, available at http://www.fairdrugs.org/uploads/files/Ethical_concerns_in_clinical_trials_in_India_An_investigation.pdf (Last visited on August 10, 2012) (cites the presentation by Surinder Singh, Drug Controller General of India, at the meeting of the Institute of Clinical Research, India, Mumbai, October 10-11, 2008).

⁴ *Id.*

⁵ SAMA, *Regulation of Drugs Trials: A National Consultation*, available at http://www.sama-womenshealth.org/ow_drugtrials_consult.html (Last visited on October 10, 2012).

⁶ Ankur Paliwal, *Ethics on Trial*, DOWN TO EARTH (New Delhi) June 30, 2011, available at <http://www.downtoearth.org.in/content/ethics-trial> (Last visited on September 8, 2012).

in a multidimensional analysis of the ramifications of unregulated clinical trials in India.

II. INTERNATIONAL CODES REGULATING MEDICAL EXPERIMENTATION

The Hippocratic ethical principle of *primum non nocere*⁷ is a time-tested principle that has governed the field of medicine,⁸ but an international discourse on the subject was wanting since before the Second World War.⁹ One would argue, given the extensive medical experimentation that occurred in that era, especially in the Nazi regime, that the existence of laws, guidelines or regulations should have been a condition precedent. The lack of any such legal or ethical regulation, however, led to disregard for the sanctity of human life with physicians advocating the idea of ‘State before the individual’,¹⁰ which is characteristic of the Nazi era. Human beings who served as clinical trial subjects were at the mercy of the physicians, who made no distinction in the treatment doled out to lab rats and humans. In responding to the ‘national threat’ of disease, physicians acted in contravention to their ethical obligations.¹¹

The divorce of ethics from the field of medicine spurred the international medical community into action. Various international declarations and codes emerged to regulate medical experimentation. The instrumental ones are discussed hereinafter.

A. THE NUREMBERG CODE

The Nuremberg Code (‘the Code’) was developed by the American judges who adjudicated the Nuremberg Trial.¹² It involved the convergence of Hippocratic ethics and the protection of human rights into a single code.¹³ The ten principles articulated were constructed with the research subject’s welfare as the focal point. This implied a change in perception with regard to the status of the research subject. While the Hippocratic ethics viewed the subject as

⁷ See generally Merriam-Webster Online Dictionary, *Primum non nocere*- The first thing is to do no harm, available at <http://www.merriam-webster.com/dictionary/primum%20non%20nocere> (Last visited on October 9, 2012).

⁸ Delon Human & Sev S. Fluss, *The World Medical Association’s Declaration of Helsinki: Historical and Contemporary Perspective*, available at http://www.wma.net/en/20activities/10ethics/10helsinki/draft_historical_contemporary_perspectives.pdf (Last visited on August 27, 2012).

⁹ *Id.*

¹⁰ Mustafa Khidir Mustafa Elnimeiri, *Nuremberg Code: A Landmark Document on Medical Research Ethics*, 3(2) SUDANESE JOURNAL OF PUBLIC HEALTH 94 (2008).

¹¹ *Id.*

¹² Evelyne Shuster, *Fifty Years Later: The Significance of the Nuremberg Code*, 337(20) N. ENGL. J. MED. 1436 (1997).

¹³ *Id.*

“passive and dutiful”¹⁴ and assumed that the physician knows best, they nevertheless imposed ethical obligations on the physician to prioritize the welfare of the subject. The Code recognized the autonomy of an individual, at the core of which is the codification of consent. In according positive rights to the subjects, it destabilized the notion of passivity.

In the Code, the principle reflecting the recognition of individual autonomy is that of voluntary consent. In order to effectuate individual autonomy, Principle 1 of the Code provides that consent is a non-negotiable precedent to an individual’s participation in a clinical trial.¹⁵ The implications of the same are threefold. Firstly, a participant should have the legal capacity to give consent. Secondly, such consent should be voluntary and free, and not a by-product of force, coercion, fraud, deceit, duress, etc. Thirdly, such consent should be an exercise of informed choice, involving “sufficient knowledge and comprehension about the subject-matter”.¹⁶ The individual conducting the experiment ought to discern the quality of the consent.¹⁷ The remainder of the provisions deal with facets of clinical trial, the design of the experiment, expected outcomes and risk mitigation,¹⁸ prohibiting an experiment wherever a strong likelihood of disability or death exists,¹⁹ adequacy of preparation, facilities, the quality of risk control equipment²⁰ and the obligation of the researcher to terminate the experiment if required.²¹

The Code has not acquired the status of binding international law but it has nevertheless been instrumental in shaping medical ethics and serves as a model law.²²

¹⁴ *Id.*

¹⁵ The Nuremberg Code, Principle 1: The voluntary consent of the human subject is absolutely essential.

¹⁶ See Elnimeiri, *supra* note 10.

¹⁷ *Id.*

¹⁸ *Id.*, Principle 2, “The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature”; Principle 3: “The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or other problem under study that the anticipated results justify the performance of the experiment”; *Id.*, Principle 4, “The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury”.

¹⁹ *Id.*

²⁰ *Id.*, Principle 7, “Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death”.

²¹ *Id.*, Principle 10, “During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject”.

²² See Shuster, *supra* note 12; *see generally* The United Nations International Convention on Civil and Political Rights (the ‘UN ICCPR’), Art. 7; the Declaration of Helsinki; The International Ethical Guidelines for Biomedical Research Involving Human Subjects.

Critics of the Code claim that it is a copy of the Guidelines for Human Experimentation, 1931, and that the lack of acknowledgment to that effect amounts to plagiarism.²³ Despite the divided schools of thought on the subject of the Code, even its critics cannot gainsay that this Code catalyzed the shift in approach with respect to the status of the research subjects, restoring the dignity they deserve and conforming to their autonomy.

B. THE DECLARATION OF HELSINKI

A document confirming the rights of the subject would be rendered ineffectual, if measures to check the excesses of the physician/researcher were not supplanted. The Declaration of Helsinki ('the Declaration') expounded on the obligations of the physician/researcher. A draft of the Declaration was tabled in 1961, and after subjecting it to intensive examination, it was adopted as the Declaration of Helsinki in 1964.²⁴ The Declaration went through six amendments,²⁵ and the version in use currently is the one amended in 2008.

The salient provisions of the Declaration are classified into three categories: the principles concerned with the obligation of the physician,²⁶ the principles of consent,²⁷ and the principles advocating transparency to bring about the effective regulation of clinical trials.²⁸

It is worth noting that the established concept of consent undergoes an evolution in the Declaration. It goes a step further by recognizing that groups lacking capacity to consent are vulnerable.²⁹ Principle 17 is one such medium for providing this protection. It excludes these vulnerable groups from being used as subjects unless the research is in furtherance of their interest, so that their lack of capacity is not exploited to further research *in rem*. As a further check against exploitation, it mandates that the consent of the subject's legal representative has to be supplanted by the assent of the subject wherever possible.³⁰

²³ Ravindra B. Ghooi, *The Nuremberg Code – A Critique, Perspectives in Clinical Research*, 2(2) PERSPECTIVES IN CLINICAL RESEARCH 75 (2011).

²⁴ World Medical Association, *Declaration of Helsinki*, available at <http://www.wma.net/en/30publications/10policies/b3/> (Last visited on September 12, 2012) (The Declaration of Helsinki was adopted at the 18th General Assembly in Helsinki, Finland).

²⁵ *Id.*

²⁶ *See generally* The Declaration of Helsinki, Principles 3, 4, 6, 23 and 24.

²⁷ *Id.*, Principles 9, 17, 26, 27 and 28.

²⁸ *Id.*, Principle 19.

²⁹ *Id.*, Principle 9.

³⁰ *See supra* note 24, Principle 28, "When a potential research subject who is deemed incompetent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected".

The principles of the Declaration have been emulated through implicit³¹ and explicit³² incorporation and are accepted as a uniform standard of ethics applicable to trials.³³

The Declaration finds place in national legislation, ordinances and references as well. A noteworthy example is that of Uganda, a country which in spite of being a developing country, has incorporated the Declaration as well as the Code in its 1997 Guidelines for the Conduct of Health Research Involving Human Subjects.³⁴

C. CIOMS GUIDELINES – INTERNATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

The challenge faced by the Declaration, despite the recognition of its authority, was its universal application in a culturally, socially, economically, and politically diversified world.³⁵ Clinical trials were increasingly acquiring an international character, with developed countries outsourcing them to less-developed countries. The principles set forth in the Declaration were rendered ineffectual when applied to outsourced clinical trials in less-developed countries. This was either because the developed countries would apply these principles with complete disregard to the culture, socio-economic scenario and legal infrastructure of the less-developed country, or would not apply the principles at all.³⁶

It was to prevent this that the Council for International Organizations of Medical Sciences ('CIOMS') in collaboration with the World Health Organisation prepared guidelines³⁷ to indicate how the ethical principles

³¹ See generally Delon Human & Sev S. Fluss, *The World Medical Association's Declaration of Helsinki, Historical and Contemporary Perspective*, available at http://www.wma.net/en/20activities/10ethics/10helsinki/draft_historical_contemporary_perspectives.pdf (Last visited on August 27, 2012) (The 1995 World Health Organization Guidelines, The New European Union Directive on Good Clinical Practices (GCP) for clinical trials of 2001, the Commonwealth Medical Association's 1993 Guiding Principles on Medical Ethics, the Ethical Guidelines for Biomedical Research on Human Subjects issued in 2000 by the Indian Council for Medical Research (the ICMR), are all illustrations of implicit incorporation of the Declaration).

³² *Id.* (For instance, Israel has incorporated the 1975 version of the Declaration in the Public Health (Medical Experiments Involving Human Beings) Regulations 1980. The Ordinance No. 28 issued on March 27, 1997 by the Ministry of Health and Welfare of Japan, which prescribes that all clinical trials are to be conducted in accordance with the principles set forth in the Declaration, is yet another illustration).

³³ Human & Fluss, *supra* note 31.

³⁴ *Id.*

³⁵ CIOMS & WHO, *Council for International Organisations of Medical Sciences*, available at <http://www.cioms.ch/> (Last visited on September 12, 2012).

³⁶ *Id.*

³⁷ *Id.*

to guide the conduct of biomedical research involving human subjects set forth in the Declaration could be effectively applied in developing countries.³⁸ The CIOMS guidelines thus served as the key to customize the Declaration as suited to different circumstances, while the basic structure remained untouched. These guidelines were the 1982 version of Proposed International Ethical Guidelines for Biomedical Research Involving Human Subjects.³⁹ In time, these were revised and bifurcated into the International Guidelines for Ethical Review of Epidemiological Studies, 1991,⁴⁰ and the International Ethical Guidelines for Biomedical Research Involving Human Subjects, 1993.⁴¹

This part examines the guidelines issued in 1993 and aims to cast light on certain relevant provisions of the 2002 amended version. The guidelines discussed are classified into two categories - those governing consent *i.e.*, Guidelines 4 and 5; and those governing vulnerable groups *i.e.*, Guideline 14, 15, 16 and 17.

Guideline 4 provides for the informed consent of competent individuals as well as consent in case of incapacitated individuals, reiterating the principles in the Declaration of Helsinki. In addition to reiterating the requirement of consent, the Guideline provides three essential components characterizing free consent. The first component states that the decision is made by an individual having the legal capacity after he/she has received the relevant information; the second being that such individual has understood the relevant information; and the third being that the individual, after considering the information received, has arrived at the decision of his own volition.⁴² Additionally it stresses on the fact that consent permeates the entire process of clinical trials.⁴³

It is interesting to note that while Guidelines 14, 15 and 17 are concerned with guarding the subject against exploitation,⁴⁴ Guideline 16 serves to prevent gender discrimination as well. Thus Guideline 16 confirms the right to self-determination of a woman. The biological fact that a woman can bear

³⁸ *Id.*

³⁹ *Id.*

⁴⁰ *Id.*

⁴¹ CIOMS, *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, available at http://www.cioms.ch/publications/layout_guide2002.pdf (Last visited on September 12, 2012); see CIOMS & WHO, *supra* note 35.

⁴² See CIOMS & WHO, *supra* note 35, Guideline 4, "For all biomedical research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee".

⁴³ See CIOMS, *supra* note 41.

⁴⁴ *Id.*, Principles 14, 15 and 17.

children has often been used to exclude her from participating in clinical trials.⁴⁵ Resultantly, little is known of the possible effects of drugs on women, which puts them at risk.⁴⁶ Contrary to popular belief that ignorance is bliss, ignorance in science often leads to potentially dangerous consequences for humankind. This guideline thus provides for the participation of women, albeit with the prerequisite of a risk analysis with regard to a woman's fertility and her health in general. Owing to the domination over women in patriarchal societies, the guideline does away with the need for authorization being obtained from the spouse or partner in order to guard them against such domination.⁴⁷

III. POLICY DEBATES AND JUDICIAL DISCOURSE WITH REGARD TO REGULATIONS OF CLINICAL TRIALS- THE INDIAN CONTEXT

While discussing the regulation of clinical trials in India, it is pertinent to look at important legal discourse in this context such as the judicial pronouncements and Lok Sabha debates dealing with the same. While very little jurisprudence exists in this regard, it is nevertheless important to analyse the discourse these authorities have engaged in so as to isolate the principles propounded so far with regard to regulations related to clinical trials.

The Supreme Court, in *A.I. Democratic Women Association v. Union of India*,⁴⁸ was dealing with a writ to ban the sale, production and manufacture of Quinacrine in the form of pellets.⁴⁹ It disposed the petition on the basis that the Government was already taking steps in that direction under

⁴⁵ *Id.*, Guideline 16: "Investigators, sponsors or ethical review committees should not exclude women of reproductive age from biomedical research. The potential for becoming pregnant during a study should not, in itself, be used as a reason for precluding or limiting participation. However, a thorough discussion of risks to the pregnant woman and to her foetus is a prerequisite for the woman's ability to make a rational decision to enrol in a clinical study. In this discussion, if participation in the research might be hazardous to a foetus or a woman if she becomes pregnant, the sponsors/investigators should guarantee the prospective subject a pregnancy test and access to effective contraceptive methods before the research commences. Where such access is not possible, for legal or religious reasons, investigators should not recruit for such possibly hazardous research women who might become pregnant".

⁴⁶ *Id.*

⁴⁷ *Id.*

⁴⁸ (1998) 5 SCC 214.

⁴⁹ *Id.*

§§10-A⁵⁰ and 26-A⁵¹ of the Drugs and Cosmetics Act, 1945.⁵² While the petition by itself was disposed of, the judgment is important because the Supreme Court took note of the fact that there was violation of the clinical trial guidelines and a symbolic acquiescence that the Courts would not tolerate such malpractices.

The Government, however, did not immediately notify such a change, and it was subsequently brought up in the Lok Sabha where the Government was urged to do so speedily.⁵³ Moreover, while courts did ban Quinacrine, there have been reports that there is continued use in parts of India even now,⁵⁴ which only strengthens the case for the school of thought which believes that a stronger regulatory framework is required.

In the 59th Report on the Functioning of the Central Drugs Standard Control Organisation (CDSCO) too, the Department Related Parliamentary Standing Committee on Health and Family Welfare, stated that it was “the skewed priorities and perceptions of the Central Drugs Standard Control Organisation”, which accorded excessive “propagation and facilitation” of the drugs industry, instead of assuring that the interests of the consumers be secured first.⁵⁵ It further went on to observe that the regulatory framework in India was not as stringent as that of the US, UK and Australia.⁵⁶ It also noted that India’s infrastructure and personnel fell short of the minimum required numbers, let alone the requirements at the post-licensing phase.⁵⁷

⁵⁰ The Drugs and Cosmetics Act 1945, §10-A, “Prohibition of import of certain drugs or cosmetics. - From such date as may be fixed by the Central Government by notification in the Official Gazette in this behalf, no person shall import – (a) any drug or cosmetic which is not of standard quality”.

⁵¹ *Id.*, §26-A, “Power of Central Government to prohibit manufacture, etc., of drug and cosmetic in public interest – Without prejudice to any other provision contained in this Chapter, if the Central Government is satisfied, that the use if any drug or cosmetic is likely to involve any risk to human beings or animals or that any drug does not have the therapeutic value claimed or purported to be claimed for it or contains ingredients and in such quantity for which there is no therapeutic justification and that in the public interest it is necessary or expedient so to do, then the Government may, by notification in the Official Gazette, prohibit the manufacture, sale or distribution of such drug or cosmetic”.

⁵² See Paliwal, *supra* note 1.

⁵³ Prof. A K Premajan (Badagara), Lok Sabha Debates, June 5, 1998.

⁵⁴ See generally Rajashri Dasgupta, *Quinacrine Sterilization in India: Women’s Health and Medical Ethics Still at Risk*, available at http://popdev.hampshire.edu/sites/popdev/files/uploads/dt/DifferenTakes_34.pdf (Last visited on September 4, 2012).

⁵⁵ The Department Related Parliamentary Standing Committee on Health and Family Welfare, *Fifty Ninth Report on the Functioning of the Central Drugs Standard Control Organisation (CDSCO)*, available at <http://164.100.47.5/newcommittee/reports/EnglishCommittees/Committee%20on%20Health%20and%20Family%20Welfare/59.pdf> (Last visited on September 4, 2012).

⁵⁶ *Id.*, 17.

⁵⁷ *Id.*, 9.

The Allahabad High Court, in a writ petition still pending before it took cognizance of the fact that illegal clinical trials were rampant in India.⁵⁸ It observed that there was a *prima facie* violation of the fundamental rights of human subjects, guaranteed under Art. 21 of the Constitution, and that based on individual cases, §§302, 304 and 304-A of the Indian Penal Code ('IPC') could be attracted.⁵⁹ Justice Umanath Singh and Justice Rituraj Awasthi also noted that the Court would consider awarding damages and came down hard on pharmaceutical companies for flouting the norms on informed consent and causing the death of subjects who were not even aware of the fact that they were being used as guinea pigs.⁶⁰

The view that the regulatory framework for clinical trials needs to be improved was reiterated by Shri B. Mahtab during the Lok Sabha debates of March 5, 2012.⁶¹ He argued that over the course of time, India has become a lucrative market for conducting clinical trials by pharmaceutical companies, and citing instances such as those of the deaths of 49 children in AIIMS,⁶² he said that a tighter regulatory mechanism was required.

Another case, which will hopefully change the dynamics of clinical trial regulations in India, is the case of *Swasthya Adhikar Manch v. Union of India*.⁶³ A bench, constituted by Justice R.M. Lodha and H.L. Gokhale criticized the government for its inaction in curbing illegal clinical trials wherein the poor and destitute, particularly juveniles, tribals and *dalits* were being used as guinea pigs.⁶⁴ While the matter is still being heard, one can only hope that the Supreme Court directs the government to take concrete measures in a stipulated time period to ensure that such events do not recur.

An analysis of the legal discourse reveals that the moot problem here is not the lack of cognizance of the inadequacy of clinical trial regulations in India. As can be inferred from the limited discussion on the subject, the inadequacy does not happen to be a bone of contention either. The problem is the passivity reflected by the courts and the legislature in dealing with this issue. Admittedly, the courts' hands are tied, so to speak, in terms of making new law

⁵⁸ Rahul Dutta v. Union of India, Misc. Bench No. 12280 of 2010.

⁵⁹ *Id.*

⁶⁰ *Id.*

⁶¹ Shri B Mahtab (Cuttack), Lok Sabha Debates, March 5, 2012.

⁶² Rema Nagarajan, *Indore Docs Flout Clinical Trial Norms, Earn Lakhs*, THE TIMES OF INDIA (Indore) June 3, 2011, available at http://articles.timesofindia.indiatimes.com/2011-06-03/india/29616513_1_clinical-trials-quintiles-research-doctors (Last visited on August 23, 2012); Mahim Pratap Singh, *In Indore Man Made Guinea Pig for Drug Trial without Consent*, THE HINDU (New Delhi), April 12, 2012, available at <http://www.thehindu.com/news/states/other-states/article3304445.ece> (Last visited on August 23, 2012).

⁶³ WP(C) No. 33 of 2012.

⁶⁴ PTI, *Supreme Court Pulls Up Centre, MP Govt for Illegal Drug Trials*, THE HINDU BUSINESS LINE (New Delhi) July 16, 2012, available at <http://www.thehindubusinessline.com/industry-and-economy/economy/article3645017.ece> (Last visited on September 4, 2012).

to fill the lacuna. The role of the judiciary after all is to interpret the law and not to legislate. Deference to the legislature is appreciated; however there exists a thin line between deference to the legislature's actions and indifference to them. The judiciary is also the bulwark of individual autonomy. It is the protector of fundamental rights- fundamental rights that are being dispensed with, by pharmaceutical corporations and clinical trial investigators. To say that in the absence of adequate laws, there is nothing that can be done to protect those participating in clinical trials would make us all complicit in the holocaust created by unregulated clinical trials. When it comes to enforcing unwritten rights, the judiciary has started reading in the directive principles into fundamental rights, in order to impose positive obligations on the State and make it accountable for not fulfilling these.⁶⁵ The directive principles, thus, by implicit reading have been rendered indirectly enforceable. This paper makes an analogous argument with regard to regulations for clinical trials. Till a new comprehensive legislation is developed, the judiciary can read in the basic ethical principles incorporated in the ICMR guidelines to supplant the provisions of Schedule Y wherever they are found to be inadequate.

While judicial passivity can still be justified by the argument of the lack of power to legislate, the inactivity of the legislature and the regulatory body is inexcusable. The ICMR drafted a comprehensive bill with regard to regulating clinical trials in 2002 and submitted it to the Ministry of Health. The Bill was approved by the Law Ministry in 2006.⁶⁶ Ever since, there has been no progress on the bill, save for a comment from the Health Minister as late as October 2010 to the effect that the bill has been "fast-tracked".⁶⁷ Any objective evidence of this fast-tracking is yet to appear.

IV. REGULATORY FRAMEWORK OF CLINICAL TRIALS IN INDIA

The regulatory framework of clinical trials is discussed within the broader rubric of pharmacovigilance herein.⁶⁸ Given that the clinical research industry in India is in its nascent stages, the mechanisms in place for

⁶⁵ *Grih Kalyan Kendra Workers' Union v. Union of India*, (1991) 1 SCC 619.

⁶⁶ Ramesh Shankar, *Modified Biomedical Research Bill to be Sent to Health Ministry Soon*, CHRONICLE SPECIALS January 14, 2010, available at <http://saffron.pharmabiz.com/article/det-news.asp?articleid=53961§ionid=50> (Last visited on October 7, 2012).

⁶⁷ P. T. Jyothi Datta, *Bill to Protect Humans in Research to Become Law Soon*, THE HINDU BUSINESS LINE (Mumbai) October 11, 2010, available at <http://www.thehindubusinessline.in/bline/2010/10/11/stories/2010101151160300.htm> (Last visited on September 27, 2012).

⁶⁸ See generally World Health Organization, *Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre* Pharmacovigilance is Concerned with the Detection, Assessment and Prevention of Adverse Reactions to Drugs, available at <http://apps.who.int/medicinedocs/en/d/Jh2934e/3.html> (Last visited October 7, 2012).

pharmacovigilance are also in the initial stages of development.⁶⁹ It is crucial at this point to familiarize oneself with the mechanics of the regulatory framework before proceeding further. The DCGI, which is the licensing and monitoring authority for clinical trials.⁷⁰ Subsequent to obtaining approval from the DCGI, the trial sponsor has to submit relevant information with regard to the trial.⁷¹ The approval structure is two tiered; meaning thereby that in addition to seeking approval at the central level, the trial sponsor must also seek approval of the local ethics committee at the site.⁷² The clinical trial commences at this juncture.

A. RULES AND GUIDELINES

The core of the regulatory framework of clinical trials in India is constituted by Schedule Y of the Drugs and Cosmetics Rules 1945 (amended 2005).⁷³ Schedule Y has been supplanted by the Ethical Guidelines for Biomedical Guidelines issued by the ICMR,⁷⁴ and the Good Clinical Practice ('GCP') guidelines issued by the Central Drugs Standard Control Organization ('CDSCO').⁷⁵ Before identifying the loopholes in the existing regulatory mechanisms, the part provides for a schematic layout of the abovementioned rules and regulations.

The relevant provisions of Schedule Y can be classified in three categories. The first category deals with application procedures, responsibilities of sponsors and ethics committees, and an explanation of Phase III trials; the second deals with consent; and the third deals with studies conducted on special groups. Rule 1 of Schedule Y provides the application procedure for obtaining permission to conduct clinical trials.⁷⁶ On submission of the relevant Phase I data on drugs discovered outside the Indian territory,⁷⁷ permission is granted to either repeat Phase I, and conduct the subsequent phases of the trials as well, or to carry out Phase II and Phase III trials in concurrence with other

⁶⁹ Ballari Brahmachari, Melanie Fernandes & Arun Bhatt, *Pharmacovigilance For Clinical Trials In India: Current Practice And Areas For Reform*, *PerspectClin Res.* 2011 Apr-Jun; 2(2): 49–53, available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3121263/?tool=pubmed> (Last visited on September 13, 2012).

⁷⁰ See Srinivasan, *supra* note 3.

⁷¹ *Id.*

⁷² *Id.*

⁷³ The Drugs and Cosmetics Rules, 1945.

⁷⁴ See *supra* note 41.

⁷⁵ Central Drugs Standard Control Organisation, *Good Clinical Practices for Clinical Research in India, 2001*, available at <http://cdsco.nic.in/html/GCP.htm> (Last visited August 24, 2012); Jayasheel B G, *Carrying Out Clinical Trials in India*, Raj Pharma, London, June 2010, available at http://www.acunovalife.com/pdf/whitepapers/RAJ_Pharma%20June%202010_Jayasheel%20final.pdf, (Last visited on September 13, 2012).

⁷⁶ The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 1.

⁷⁷ *Id.*, Schedule Y, Rule 1.

global trials for that particular drug.⁷⁸ In the contingency that serious adverse events ('SAE') arise from prior trials, a communication to that effect should take place between the sponsor and the licensing authority.⁷⁹ Rule 2(5) enlists the responsibilities of the Ethics Review Committee, entrusting them with the safety and protection of rights and well-being of subjects, more so where such subjects belong to vulnerable groups.⁸⁰ The pre-requisites for obtaining permission to conduct Phase III trials are expounded in Rule 2(8).⁸¹ Informed consent provided for in Schedule Y contemplates a free, informed and written consent.⁸² For those lacking legal capacity, the consent of their legal representatives or proxies is sought.⁸³ Rule 2(4) read in conjunction with Appendix V is the exhaustive source for consent under the present rules. Appendix V lays down the checklist for the elements of the informed consent document.⁸⁴ Rule 3 deals with studies conducted on special groups, such groups comprising in the Schedule of ageing people, children, and pregnant women.⁸⁵ It defines the circumstances under which recruiting subjects from vulnerable or special groups is justified,⁸⁶ additionally also contemplating the requirement of assent in the case of paediatric subjects.⁸⁷

The Ethical Guidelines for Biomedical Research on Human Participants ('the Guidelines') were issued by the ICMR,⁸⁸ with the same objective as that of the CIOMS guidelines. ICMR sought to customize the universal principles in order to make them better suited for application to the Indian front. The Guidelines were issued in 2006.⁸⁹ The introductory chapter of the Guidelines deals with the twelve general principles of biomedical ethics.⁹⁰ At the core of these principles is the principle of essentiality, which entails that only after having explored all other possible avenues in that area of research and after a due inspection of the research collected so far and establishing that the use of human subjects is absolutely essential to this area of research, shall the research use human participants.⁹¹ In the event that human subjects are used, other principles such as those of free informed consent, non-exploitation, accountability and transparency gain prominence. Subsequent to general

⁷⁸ *Id.*, Schedule Y, Rule 1(1)(iv).

⁷⁹ *Id.*, Schedule Y, Rule 2 (2)(iv).

⁸⁰ *Id.*, Schedule Y, Rule (2)(5).

⁸¹ *Id.*, Schedule Y, Rule 2 (8).

⁸² *Id.*, Schedule Y, Rule 2 (4)(i).

⁸³ *Id.*, Schedule Y, Rule 2(4)(ii).

⁸⁴ *Id.*, Schedule Y, Appendix V.

⁸⁵ *Id.*, Schedule Y, Rule 3.

⁸⁶ *Id.*, Schedule Y, Rule 3.

⁸⁷ *Id.*, Schedule Y, Rule 3.

⁸⁸ *See supra* note 41.

⁸⁹ N. Ananthakrishnan, Shanthi AK, *ICMR'S Ethical Guidelines for Biomedical Research on Human Participants: Need for Clarification*, 9(3) INDIAN J. MED. ETHICS 207-209 (2012).

⁹⁰ *See supra* note 41.

⁹¹ *Id.*

principles, the Guidelines deal with specific facets of the pharmacovigilance mechanism.

Chapter II of the Guidelines builds on the basic responsibilities of the Ethics Committee provided for in Schedule Y and stipulates criteria for the composition of such committee as well as their training, regulation, decision making process, monitoring, and review procedures. It is worth mentioning here that the Guidelines in providing for review recognize categories of review- periodic, continuing, and interim review. The significance of this is that at intermittent stages of the clinical trial, the EC will be apprised of any adverse events, the general progress of the trial and flouting of ethical principles. This will aid in making the pharmacovigilance system more efficient in ensuring the safety of subjects, in juxtaposition to a one time blanket review conducted only at the stage of inception of the clinical trial. Chapter III of the Guidelines deals with general ethical issues,⁹² the salient ones discussed herein are- informed consent, selection of vulnerable groups as participants, and compensation. With regard to informed consent, the Guidelines stress on the requirement for information, and as such require that the informed consent form is accompanied by a patient information sheet. This patient information sheet apprises the participant of information with regard to the methodology and procedure of the experiment, the cost benefit analysis, the compensation policy, alternative methods available, benefits arising from commercialization, and most importantly the voluntary nature of his or her participation.⁹³ In contrast to the corresponding provision in Schedule Y where the only acceptable form of consent is written, the Guidelines allow for non-written documentation of consent,⁹⁴ if the participant is willing to or is unable to communicate his consent in writing.

While most of the requirements for conducting research on vulnerable groups in the Guidelines are in tandem with the corresponding provisions of the CIOMS Guidelines, there is an additional noteworthy provision. The Guidelines recognise groups having reduced autonomy, i.e. people whose liberty or autonomy is curtailed either lawfully due to their incarceration as is in the case of prisoners, or informally through relationships such as employer-employee.⁹⁵ They further provide that adequate justification needs to be provided if these people are recruited so as to refute the presumption of undue influence or coercion.⁹⁶ The compensation provisions are applicable in the event of participation and also for accidental injury. In the first scenario the Guidelines contemplate that while remuneration and reimbursement are to be provided to participants, the amount should not be so exorbitant as to operate

⁹² *Id.*, Chapter III.

⁹³ *Id.*, Chapter III, Guideline 1.

⁹⁴ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 2(4)(i).

⁹⁵ See *supra* note 41, Chapter III, Guideline I and IV(d).

⁹⁶ *Id.*

as a factor of undue influence.⁹⁷ In the latter, the Guidelines provide that it is the obligation of the sponsor to pay the participant, and that the amount of compensation due would be decided by an arbitration or an appellate body on a case- by-case basis.⁹⁸ Thus the Guidelines, albeit devoid of recognition as binding law, entail integral ethical principles that should inform the decisions of each investigator through the various stages of clinical trials.

The GCP were issued by the CDSCO in the year 2001.⁹⁹ Following an amendment to Schedule Y in January 2005, the GCP has now acquired the status of law.¹⁰⁰ The underlying principle of the GCP is that sanctity of human life must not be violated on the justification that such violation is for the greater good of science and society.¹⁰¹ It has been stated that “the GCP seeks to establish two cardinal principles: protection of the rights of human subjects and authenticity of biomedical data generated”.¹⁰² By and large, the GCP is a reiteration of the ICMR guidelines, as well as an acknowledgment to internal declarations such as the Declaration of Helsinki, which served as its parent code.¹⁰³

B. COMPARATIVE ANALYSIS – CONTRASTING THE INDIAN LEGAL FRAMEWORK WITH THE FRAMEWORK OF THE UNITED KINGDOM

India, as opposed to countries like the UK and US, lacks adequate legislation that regulates clinical trials. The only body of law lies in Schedule Y of the DCR and the GCP. The ICMR Guidelines, for want of statutory force, merely serve as non-binding guidelines.

Moreover, even the regulations that do exist have a rather questionable enforcement mechanism. Constant reminders from the media about flouting of the rules regulating clinical trials,¹⁰⁴ such as reports of over 211 people dying in the period between January to June 2012 as a result of clinical trials¹⁰⁵ make it evident that the enforcement mechanism is not stringent enough. In that light, it is pertinent for India to broaden its horizons, and look to foreign

⁹⁷ *Id.*, Chapter III, Guideline II.

⁹⁸ *Id.*, Chapter III, Guideline VI.

⁹⁹ *Id.*

¹⁰⁰ Dr. Arun Bhat, *From Guidelines to Law*, available at <http://www.clininvent.com/clininvent/Publications/From%20guidelines%20to%20law%20-%20Editorial%20-%20Express%20Pharma%20Pulse.htm> (Last visited on September 13, 2012).

¹⁰¹ See Jayasheel BG, *supra* note 75.

¹⁰² *Id.*

¹⁰³ *Id.*

¹⁰⁴ See Nagarajan, *supra* note 62 and Singh, *supra* note 62.

¹⁰⁵ Kounteya Sinha, *211 People Died in Six Months during Clinical Trials in India*, THE TIMES OF INDIA (New Delhi) August 18, 2012, available at http://articles.timesofindia.indiatimes.com/2012-08-18/india/33261237_1_ppd-and-pfizer-bristol-mayer-clinical-trials (Last visited on August 23, 2012).

shores for much needed inspiration to create a strong regulatory framework with ‘teeth’ to avoid such deviations from the law.

The UK and India are both advocates of the GCP as was evident from their participation in the International Conference for Harmonisation (‘ICH’). Since India derives the bulk of its legal-justice mechanism from the common law jurisdiction of the UK, it serves as a suitable illustrative model for India, in terms of what constitutes an ideal regulatory framework.

The pharmaceutical industry is the most regulated industry in Europe.¹⁰⁶ In 2001, the European Commission adopted the Directive on the approximation of laws, regulations and administrative provisions of the Member States relating to the implementation of the GCP in the conduct of clinical trials on medicinal products for human use.¹⁰⁷ The purpose of this Directive was to introduce a uniform regulatory process for Member States, to be read in conjunction with their municipal laws.¹⁰⁸ The Use of Medicines for Human Use (Clinical Trials) Regulations, 2004 (‘UK Regulations’)¹⁰⁹ are the primary body of laws regulating clinical trials in the UK. They were adopted in 2004 to transpose the provisions of the 2001 Directive into British law¹¹⁰ and to be read in conjunction with the Medicines Act, 1968.

Akin to the framework in India,¹¹¹ clinical trials in the UK can only be started after obtaining approval of the licensing authority¹¹² and the ethics committee’s favorable opinion.¹¹³ The U.K. Regulations, however, differ from the Indian Rules in so far as medicinal products in the UK are categorised into general medicinal products, medicinal products for gene therapy

¹⁰⁶ European Federation for Pharmaceutical Industries and Associations, *Clinical Trials in Europe*, available at http://www.zdrave.net/DOCUMENT/INSTITUTE/e-library/EFPIA//10_Kniga/clinical.pdf (Last visited on August 19, 2012).

¹⁰⁷ EC 2001/20 L 121/34 (‘2001 Directive’).

¹⁰⁸ A. J. Baeyens, *Implementation of the Clinical Trials Directive: Pitfalls and Benefits*, 9 EUR. J. HEALTH L. 31 (2002).

¹⁰⁹ The Use of Medicines for Human Use (Clinical Trials) Regulations, 2004 (UK).

¹¹⁰ Regulatory Compliance Section of the Imperial College London, *Summary of the Medicines for Human Use Regulations*, available at <http://www3.imperial.ac.uk/clinicalresearchgovernanceoffice/researchgovernance/medicinesforhumanuseregulations> (Last visited on August 19, 2012); Medicines and Healthcare Products Regulatory Agency, *Description of the Use of Medicines for Human Use (Clinical Trials) Regulations 2004*, available at http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2022633&RevisionSelectionMethod=Latest (Last visited on August 19, 2012).

¹¹¹ See *supra* note 73, Schedule Y, Rule 2(1)(i) (The trial may only begin once the Licensing Authority has granted permission and a favourable opinion has been given by the respective ethics committee).

¹¹² Medicines and Healthcare Products Regulatory Agency, *Description of the Use of Medicines for Human Use (Clinical Trials) Regulations 2004*, available at http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2022633&RevisionSelectionMethod=Latest (Last visited on August 19, 2012) (The Ministers acting through the Medicines and Healthcare Products Regulatory Authority (‘MHRA’) constitute the licensing authority).

¹¹³ See Use of Medicines for Human Use (Clinical Trials) Regulations, 2004 (UK), Reg. 12.

and medicinal products with special characteristics, and a separate procedure for application has been prescribed to conduct clinical trials for each of these types.¹¹⁴ No such distinction exists in Schedule Y of India's Rules, except Item 1(3) of Schedule Y, which gives the licensing authority the power to grant the applicant wishing to import or manufacture new drugs or start clinical trials for drugs of 'special relevance' to India, exemption from providing toxicological and clinical data. The term 'drugs of special relevance' has, however, been left ambiguous.

Incorporating such a change would streamline the clinical trial authorization process making it more efficient and less time consuming. Clearly, an analgesic and a drug for cancer cannot be placed on the same footing, and require their own unique application procedures. Further, the lack of differentiation creates a safety hazard as the parameters for checking whether clinical trials are compliant with the prescribed guidelines remain the same for all kinds of drugs.¹¹⁵ The minimum threshold requirements in terms of a compliance check would remain the same, thus relieving drug manufactures and researchers of the obligation of complying with the stringent safety requirements for high-risk drugs.

Another area that may be examined is the Indian and British licensing authorities, ethics committees, sponsors and investigators by juxtaposing the two. While on paper these institutions share similar roles, what lacks in India is enforcement of the same.¹¹⁶

The UK Regulations strive to give powers to the licensing authority to inspect or delegate the powers to inspect clinical trial sites in cases where the trials are being conducted in 'third world countries' so as to ensure that the trials adhere to the GCP.¹¹⁷ Under Reg. 21,¹¹⁸ it is stipulated that if the licensing authority deems fit, it may ask for an undertaking from either the sponsor or

¹¹⁴ *Id.*, Regs. 18; 19 and 20.

¹¹⁵ See generally The Central Drugs Control Organisation, *Guidance on Clinical Trial Inspection*, available at <http://www.cdsc.nic.in/CT%20Inspection%20-11-2-2011.pdf> (Last visited on October 4, 2012).

¹¹⁶ See generally Srinivasan, *supra* note 3 (The fact that such deviations from the law occur are evidence that rules are oft flouted and that the enforcement mechanism is not strong enough).

¹¹⁷ See The Use of Medicines for Human Use (Clinical Trials) Regulations, 2004 (UK), Regulation 21; see *supra* note 112.

¹¹⁸ See The Use of Medicines for Human Use (Clinical Trials) Regulations, 2004 (UK), Regulation 21:

“(1) If the licensing authority receives a valid request for authorisation relating to a clinical trial which is or is to be conducted in a third country as well as the United Kingdom, the licensing authority may, if they think fit, require the production by the sponsor of any one or more of the following—

(a) an undertaking, given by the sponsor, to permit their premises in that country to be inspected by or on behalf of the licensing authority for the purpose of establishing whether the conditions and principles of good clinical practice are satisfied or adhered to in relation to that trial; or

the owner of the foreign clinical trial premises to allow the licensing authority or those authorized by it to conduct inspections, and refusing to give such an undertaking is valid justification for the licensing authority not to give authorization for clinical trials as required under Regs. 18,¹¹⁹ 19¹²⁰ and 20.¹²¹

Not only do the UK Regulations have an exemplary pre-licensing framework, they also have a noteworthy post-licensing one. Part V of the U.K. Regulations deal with Pharmacovigilance and stipulate that an investigator is required to report cases of adverse events¹²² to the sponsors,¹²³ and file a detailed report.¹²⁴ Moreover, the sponsor is required, in cases of suspected unexpected adverse reactions in the course of the trials, to inform the licensing authorities, the competent authorities of the EEA and the ethics committees.¹²⁵

The Indian Rules do not empower the licensing authorities to make similar inspections at foreign clinical trial sites. At best, at the time of making an application for importing, manufacturing or starting clinical trials, information about the regulatory frameworks in those countries in addition to other data is required for drugs being produced domestically as well.¹²⁶ India provides for inspectors who are authorized to examine the clinical trial sites and interview the ethics committees, sponsors, investigators and check whether the trials are in accordance with the GCP. Critics, however, point out

(b) an undertaking, given by the owner or occupier of any premises in that country at which the clinical trial is or is to be conducted, to permit those premises to be inspected by or on behalf of the licensing authority for the purpose of establishing whether the conditions and principles of good clinical practice are satisfied or adhered to in relation to that trial.

(2) If a sponsor fails to produce an undertaking required by the licensing authority in accordance with paragraph (1), that failure constitutes a ground for not accepting the request for authorisation, for the purposes of regulations 18 to 20”.

¹¹⁹ See The Use of Medicines for Human Use (Clinical Trials) Regulations, 2004 (UK), Regulation 18.

¹²⁰ *Id.*, Reg. 19.

¹²¹ *Id.*, Reg. 20.

¹²² *Id.*, Reg. 2(1), “In these Regulations— “adverse event” means any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product”.

¹²³ *Id.*, Reg. 3(1), “In these Regulations, subject to the following paragraphs, “sponsor” means, in relation to a clinical trial, the person who takes responsibility for the initiation, management and financing (or arranging the financing) of that trial”.

¹²⁴ *Id.*, Reg. 32.

¹²⁵ *Id.*, Reg. 33.

¹²⁶ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 1(v):

“Regulatory status in other countries as prescribed in item 9.2 of Appendix I, including Information in respect of restrictions imposed, if any, on the use of the drug in other countries, e.g. dosage limits, exclusion of certain age groups, warning about adverse drug reactions, etc. (item 9.2 of Appendix I). Likewise, if the drug has been withdrawn in any country by the manufacturer or by regulatory authorities, such information should also be furnished along with the reasons and their relevance, if any, to India. This information must continue to be submitted by the sponsor to the Licensing Authority during the course of marketing of the drug in India”.

that Indian authorities do not even have the capability to make inspections in the Indian sites, let alone foreign ones. This is buttressed by the fact that as of 2009, India had only five to six professionals for the job.¹²⁷

The role and constitution of ethics committees in India and the UK are largely similar. Both include persons who are from the medical profession in addition to laypersons.¹²⁸ It also assigns them the role of protecting the rights of human subjects in clinical trials. The Indian Rules take a step forward by making the ethics committees responsible for the protection of the rights of vulnerable social groups like the impoverished, refugees, nomads, prisoners etc.,¹²⁹ the prescribed norms are not followed. An instance reported by the media, was that of Indore's M.Y. Hospital, where in several instances "instead of obtaining permission from the on-site ethics committee of the medical college, permission was obtained from strange non-verifiable entities claiming to be ethics committees located thousands of kilometers away".¹³⁰

Further, the Indian Rules fall short of accepted standards as they leave scope for ambiguity by stating that the ethics committee must document 'standard operating procedures' ('SOPs').¹³¹ The Indian Rules do not go on to clarify what these SOPs are, and to whom these SOPs would apply.

In light of the case of *Swasthya Adhikar Manch v. Union of India* ('*Swasthya Adhikar Manch*'),¹³² it is important to draw lessons from the guidelines of informed consent in the UK. The Indian Rules provide for the requirement of informed consent wherein the information provided to the human subjects has to be in a non-technical and understandable form; and the provisions to obtain informed consent from the legal representatives of those unable to provide consent.¹³³ The Indian Rules, however, in all of their noble intentions, fail to match up to the foresight of their legislative counterpart in the UK.

¹²⁷ See Srinivasan, *supra* note 3.

¹²⁸ The Use of Medicines for Human Use (Clinical Trials) Regulations 2004 (United Kingdom), Schedule 2, Reg. 3(1):

"An ethics committee shall consist of—

(a) expert members; and

(b) lay members."; See *supra* note 73, Appendix VIII, Item 1, "The number of persons in an Ethics Committee should have at least seven members. Ethics Committee should appoint, from among its members, a Chairperson (who is from outside the institution) and a Member Secretary. Other members should be a mix of medical/non-medical, scientific and non-scientific persons, including lay public, to reflect the different viewpoints".

¹²⁹ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 3.

¹³⁰ See Nagarajan, Pratap, *supra* note 62.

¹³¹ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 2(5)(i) "Ethics committees(s) should get document 'standard operating procedures' and should maintain a record of its proceedings".

¹³² WP(C) No. 33 of 2012.

¹³³ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 2(4)(i) "The Investigator must provide information about the study verbally as well as using patient information sheet, in a language that is non-technical and understandable by the study subject".

In the UK, incapacitated adults are divided into three categories; those who gave informed consent to take part in the clinical trial prior to the onset of incapacity, those who neither gave consent nor refused to take part in the clinical trial prior to the onset of incapacity, and those who refused to give consent prior to the onset of incapacity.¹³⁴ Different provisions apply to each of these classes.¹³⁵ In the first case, the subjects have a right to revoke their own consent.¹³⁶ In the second, the consent may be obtained from the legal representative subject to considerations and provisions like interview with the investigator, means to contact for future reference and giving consent only if the possible benefits outweigh the risks¹³⁷ and in the third case the persons may not be used as subjects at all.¹³⁸

India does not follow the same distinction as the UK. It uses the blanket term ‘people unable to give consent’, which includes, but is not limited to, minors, unconscious persons and persons with disabilities and allows for them to be included in clinical trials by obtaining the consent of their legal representatives.¹³⁹ Incapacitated people in India are viewed as one homogenized group incapable of giving consent, as opposed to the three sub-groups in the UK. Thus, in the UK, if the incapacitated person refuses to be involved in the trial before the onset of incapacity his autonomy is respected albeit to a limited extent. In India, however, it is possible to include them by obtaining consent of the legal representative. Moreover, where there is a stipulation to conduct studies on special populations, incapacitated adults are not included in that list.¹⁴⁰

While in the UK, legal representatives are prohibited from giving consent on behalf of prospective subjects who are incapacitated, in lieu of financial incentive, in India no such explicit prohibition exists. This discrepancy is susceptible to be abused in the Indian context where the poor and impoverished, driven by financial motives, may consent for disabled persons to be used as subjects in clinical trials. There are instances where families of such subjects

¹³⁴ See generally *The Use of Medicines for Human Use (Clinical Trials) Regulations 2004* (United Kingdom), Schedule 1, Part I, Reg. 1.

¹³⁵ *Id.*

¹³⁶ See *The Use of Medicines for Human Use (Clinical Trials) Regulations, 2004* (U.K.), Schedule 1, Part III, Reg. 4.

¹³⁷ *Id.*, Schedule 1, Part V, Reg. 5.

¹³⁸ *Id.*, Schedule 1, Part I, Reg. 1(5).

¹³⁹ See *The Drugs and Cosmetics Rules, 1945*, Schedule Y, Rule 2(4)(ii):

“Where a subject is not able to give informed consent (e.g. an unconscious person or a minor or those suffering from severe mental illness or disability), the same may be obtained from a legally acceptable representative (a legally acceptable representative is a person who is able to give consent for or authorize an intervention in the patient as provided by the law(s) of India). If the Subject or his/her legally acceptable representative is unable to read/write – an impartial witness should be present during the entire informed consent process who must append his/her signatures to the consent form”.

¹⁴⁰ *Id.*, Schedule Y, Rule 3 (The Rule restricts its stipulation for special studies on pediatrics, geriatrics and pregnant or nursing women).

have been provided the promise of free daily check-ups.¹⁴¹ Such incentives appear as “healthcare windfalls” to the legal representatives and hence consent to their incapacitated relatives to be used as subjects.¹⁴²

C. LOOPHOLES IN THE EXISTING REGULATIONS

The inadequacy of the present regulatory framework is a by-product of two factors - loopholes in the existing law and lackadaisical implementation of that law. Before elucidating on the structural flaws of the enforcement mechanism, this section will deal with the loopholes in the existing regulations, i.e. Schedule Y.

The only form of consent that Schedule Y provides for is a written one.¹⁴³ Such a provision would render well for a country with high literacy rates. In a country some of whose districts admittedly have a lower adult literacy rate than the three worst performing countries of sub-Saharan Africa,¹⁴⁴ however, that would not be the case. Admittedly the ICMR guidelines provide for other forms of documenting consent.¹⁴⁵ Since they do not have the binding force of law, however, they can be easily circumvented by investigators.

As stated above, in the UK the incapacitated are divided into three categories under the law.¹⁴⁶ Schedule Y does not even contemplate the incapacitated in its provision for studies on special groups, which are limited to the ageing, children and pregnant or nursing women. It has rendered invisible a segment of the population of the vulnerable group. The ramification is that the incapacitated are being used as research subjects for studies, which are in no remote way beneficial to them,¹⁴⁷ and owing to the lacuna in the legal system, are left without recourse.

¹⁴¹ See Srinivasan, *supra* note 3.

¹⁴² James Cekola, *Outsourcing Drug Investigations to India: A Comment on U.S., Indian, and International Regulation of Clinical Trials in Cross-Border Pharmaceutical Research*, 28 Nw. J. INT'L L. & BUS. 125 (2007-08).

¹⁴³ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 2(4)(i).

¹⁴⁴ AMARTYA SEN, DEVELOPMENT AS FREEDOM 101 (1999).

¹⁴⁵ Indian Council of Medical Research, *Ethical Guidelines for Biomedical Research On Human Participants, 2006*, available at http://icmr.nic.in/ethical_guidelines.pdf (Last visited at September 8, 2012). Guideline 2 (v) states that one must take verbal consent when the participant refuses to sign or give thumb impression or cannot do so. This can then be documented through audio or video means.

¹⁴⁶ See generally The Use of Medicines for Human Use (Clinical Trials) Regulations 2004 (United Kingdom), Schedule 1, Part I, Reg. 1.

¹⁴⁷ Gyanant Singh, *Illegal Drug Trials: Supreme Court Issues Notice to Government*, INDIA TODAY (New Delhi) February 7, 2012, available at <http://indiatoday.intoday.in/story/supreme-court-glare-on-illegal-clinical-trials/1/172417.html> (Last visited on September 13, 2012).

The CIOMS guidelines in dealing with special groups provides for studies with women as participants¹⁴⁸ and studies with pregnant women as research participants¹⁴⁹ separately. The logic as was aforementioned is that provision for women as research subjects is seen as a measure of emancipation from the patriarchal societal constructs prevalent in most less developed countries. It reinforces their right to self-determination, ruling out the possibility of gender discrimination, which is usually justified on the grounds of ‘shielding’ women from experimental methodology so as to not jeopardize their fertility. Schedule Y provides for no such provision which is surprising in a country like India where patriarchal constructs are not just perpetuated by society, but reinforced by law.¹⁵⁰ The silence of the law implicitly allows discrimination based on gender, and indirectly aids the prevention of participation of women in clinical trials. In juxtaposition where women are used as subjects, in the absence of such a provision, there is a strong likelihood that in the lower strata of society their partners or spouses who usually dominate them will enroll them for monetary benefit. If there was a provision, however, providing that women can participate in clinical trials and their participation should be a function of their own volition, this exploitation could be ruled out even if to a limited extent.

In what can be called an all time low for humanity, the sphere of clinical trials is witness to the commoditization of ethics. Ethics Committee (‘EC’) forum shopping is now a common phenomenon.¹⁵¹ In the absence of any stringent regulation with regard to the functioning of Ethics Committees, independent committees are sprouting up.¹⁵² These independent committees are guided not by a non-negotiable set of ethics but purely by financial motives.¹⁵³ Albeit the ICMR Guidelines expound on the functions of ethics committees providing for intermittent reviews through the clinical trial process,¹⁵⁴ the absence of a binding legal status makes such periodic review optional. The law in this regard, *i.e.* Schedule Y merely provides that there shall be an ethics committee and enlists the responsibilities of the committee.¹⁵⁵ While the Guidelines meticulously provide for periodic as well as intermittent review, all Schedule Y contemplates is that the “EC(s) should make, at appropriate intervals, an ongoing review of the trials for which they review the protocol(s)”.¹⁵⁶ What constitutes an ‘appropriate’ interval is, however, left unspecified and open to interpretation. Schedule Y is also silent on the issue of conflict of interest. Resultantly, in hospitals the members of the ethics committee are the investigators themselves. What qualifies as an unethical practice is thus decided in

¹⁴⁸ See *supra* note 145, Chapter III, Guideline IV.

¹⁴⁹ See *supra* note 145, Guideline IV (i).

¹⁵⁰ Indian Penal Code, §377.

¹⁵¹ See Paliwal, *supra* note 6.

¹⁵² *Id.*

¹⁵³ *Id.*

¹⁵⁴ See *supra* note 145, Chapter II.

¹⁵⁵ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rules 2(1) and 2(5).

¹⁵⁶ *Id.*, Schedule Y, Rule 2(5)(ii).

accordance with the convenience of the investigators, whose sole aim is to fast track the trial. Other than the very likely possibility of bias, the issue here is how this loophole is used to make a mockery of the EC.

One would think that given how ineffective the Schedule is for providing stringent ethical and legal regulation of clinical trials, at least a nominal provision for compensation would be provided as a remedy to all the violations that evidently occur in such legal limbo. The only mention of compensation, however, is in the Appendix V of Schedule Y, and even here it is only an element on the checklist of the informed consent sheet.¹⁵⁷ The law is silent on the mechanism of providing and computing such compensation. The paltry compensation paid in the absence of a legal mandate tries to affix a cheap price tag on the life lost thereby further degrading the violations perpetrated during the trial. Currently, a life is worth a minimum of fifty thousand rupees.¹⁵⁸ Furthermore there is no punitive provision stipulated in Schedule Y. The result is that clinical trials take place in legal vacuum and when violations occur, offenders go scot free. An illustration of this is the Tadalafil drug trial conducted in MGM Memorial College and Maharaja Yashwantrao Hospital. This trial was undertaken by two doctors without the prior permission of the DCGI and when the drug had not been approved for the indication of pulmonary arterial hypertension in the country.¹⁵⁹ Following an investigation of the matter, the only action taken against the doctors was a Ministry issued ban on conducting any further experimentation for a period of six months.¹⁶⁰ Thus, the only punitive measure resorted to, if it can be called that at all, was the suspension of permission to conduct clinical trials.¹⁶¹ The irony of suspending a permission that never existed to begin with is of course lost on the Ministry, as is the need for stringent action.

In contravention of global practice, which requires that the occurrence of any SAE be reported to the EC within seven days of the calendar, Schedule Y provides that the reporting time should be seven working days.¹⁶² The timeline provided is inordinately lenient in circumstances where a speedy reporting mechanism is crucial.¹⁶³ In what serves to compound such leniency, Schedule Y fails to provide for any expedited reporting of SAE to the CDSCO. As per Schedule Y reporting of such events to the CDSCO must be carried out

¹⁵⁷ *Id.*, Schedule Y, Appendix V.

¹⁵⁸ Khomba Singh, *Drugs Cos Use Guinea Pigs, But Play With Their Pennies*, THE ECONOMIC TIMES (New Delhi) August 21, 2012, available at <http://www.indiaenvironmentportal.org.in/news/drug-cos-use-guinea-pigs-play-their-pennies> (Last visited on September 13, 2012).

¹⁵⁹ T.K. Rajalakshmi, *Criminal Trials*, FRONTLINE January 28, 2012, available at <http://www.frontlineonnet.com/fl2902/stories/20120210290203300.htm> (Last visited on September 8, 2012).

¹⁶⁰ *Id.*

¹⁶¹ *Id.*

¹⁶² See The Drugs and Cosmetics Rules, 1954, Schedule Y, Appendix VII; See Brahmachari *et al.*, *supra* note 69.

¹⁶³ *Id.*

within fourteen calendar days.¹⁶⁴ There is, however, no requirement to differentiate between the reporting period for events having a causal association and events that are life threatening or resulting in unexpected deaths.¹⁶⁵

Admittedly, the amendment to Schedule Y in 2005 has aimed to streamline the regulations,¹⁶⁶ but the amended version is not without its fair share of shortcomings either, shortcomings that make its beneficial intentions rather questionable. To begin with, the amendment has resulted in a removal of the phase lag.¹⁶⁷ The concept of phase lag entailed that Phase II trials could not be conducted in India unless such trials had been conducted elsewhere before, the underlying idea being that of preventing the usage of Indian citizens as guinea pigs.¹⁶⁸ As a consequence of the amendment, however, Phase II and Phase III trials can now be conducted concurrently,¹⁶⁹ thus doing away with the protective provision.

There exists a disparity between Schedule Y and the trial approval letter issued by the CDSCO. While the amended Schedule Y mandates the reporting of SAE,¹⁷⁰ the trial letter contemplates the reporting of Serious Adverse Reaction ('SADR')¹⁷¹. The difference between SAE and SADR is that of the element of causality.¹⁷² While an adverse event does not necessarily have linkage with the drug study, an adverse reaction is indicative of being a function of causality.¹⁷³ This discrepancy in terminology raises a doubt as to whether the element of causality is to be accounted for in reporting or not.¹⁷⁴ In addition to this while providing for the reporting of serious and unexpected events, Schedule Y leaves the term 'unexpected' undefined, illustrating yet another lacuna in the law.¹⁷⁵ It points us in the direction of the GCP for such definition,¹⁷⁶ which constitutes on the part of the legislators a complete oversight of the fact that the definition of 'unexpected' is wanting in the GCP as well. Consequently, there is ambiguity with regard to what would constitute an unexpected event, and this ambiguity introduces an element of subjectivity in terms of reporting of such events.

¹⁶⁴ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 2(2).

¹⁶⁵ See Brahmachari, Fernandes & Bhatt, *supra* note 69.

¹⁶⁶ Dr. Riddhi Godambe & Dr. Arun Bhatt, *2005 and Beyond: Renaissance of the Indian Regulatory System*, available at <http://saffron.pharmabiz.com/article/detnews.asp?articleid=47948§ionid=50> (Last visited on September 12, 2012).

¹⁶⁷ See Srinivasan, *supra* note 3.

¹⁶⁸ See Cekola, *supra* note 142.

¹⁶⁹ See Srinivasan, *supra* note 3.

¹⁷⁰ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 2(2)(iv).

¹⁷¹ See Brahmachari, Fernandes & Bhatt, *supra* note 69.

¹⁷² *Id.*

¹⁷³ *Id.*

¹⁷⁴ *Id.*

¹⁷⁵ *Id.*

¹⁷⁶ See The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 2(2)(iv).

A progressive step that the amendment took despite all its shortcomings was eliciting the statutory support of the GCP thus conferring on the guidelines the status of binding law. The question of the status of trials that commenced before 2005 with regard to laws applicable, however, is still unanswered as is the larger question of the ground reality with regard to the implementation of such law.

D. STRUCTURAL FLAWS IN THE IMPLEMENTATION MECHANISM

While a systemized implementation mechanism is wanting, the failure of implementation follows a remarkably chronological pattern that is reflected at every stage of the clinical trial, right from the approval to its culmination.

The law mandates approval for all clinical trials. When such law is put in practice, however, a different picture emerges. For instance a protocol submitted by Panacea Biotech to the DCGI was wanting not only in the adverse consequences of the drug and its elementary requirements, but also in something as basic and important as the phase of trial.¹⁷⁷ This protocol received DCGI clearance without any hitches whatsoever.¹⁷⁸ The state of affairs is aptly summarized by C.M. Gulhati when he says, "...the DCGI approves clinical trials in the same way as ration cards were issued by food inspectors".¹⁷⁹

In the absence of an independent monitoring body, keeping track of the exponentially growing clinical trials is a logistical nightmare. The silence of the law on this matter promotes the flourishing of unethical practices that go unchecked. The medical community and the subjects are thus blindsided with regard to the risks arising from such trials. This jeopardizes not just the welfare of the subjects but also the veracity of the biological data.

In the event that the adverse consequences of a trial become visible to public eye in the nick of time, the lack of implementation of the compensatory provision in the ICMR guidelines, ensures that no punitive measures are undertaken. Contrary to ICMR requirements of inbuilt compensation mechanisms that cover all foreseeable and unforeseeable risks in trial,¹⁸⁰ the DCGI approves clinical trials where no undertaking is provided for by the sponsors.¹⁸¹

An overall analysis of the situation reveals that the underlying reason behind the loopholes and the lack of implementation is the phenomenon

¹⁷⁷ C. M. Gulhati, *Needed: Closer Scrutiny of Clinical Trials*, 1(1) INDIAN J. MED. ETHICS 4-5(2004).

¹⁷⁸ *Id.*

¹⁷⁹ *Id.*

¹⁸⁰ *Id.*

¹⁸¹ *Id.*

of “regulatory capture”.¹⁸² This phenomenon, which forms the central thesis of George Stigler’s paper essentially entails that “...regulation is acquired by the industry and is designed and operated primarily for its benefit”.¹⁸³ Applying this thesis to the clinical trial industry, it becomes evident how the regulations are exploited for the benefit of the industry, even though they were purportedly designed to protect the public. In the absence of regulatory authorities seeking any conflict of interest information from the investigators, such investigators continue to reap the “benefits of largesse”¹⁸⁴ from the pharmaceutical corporations.¹⁸⁵ As a consequence, investigators and other regulatory authorities incentivized by the benefits they receive from the pharmaceutical corporations prioritize profit over safety of subjects. In a situation that is both tragic and ironic, these officials now are servants of the very industry they were appointed to regulate.¹⁸⁶

V. EFFECTS ON CLINICAL TRIAL SUBJECTS - TRIAL OR ERROR?

Globalisation has permeated the field of science and technology significantly. Clinical trials are no longer confined to domestic territorial boundaries and are increasingly being outsourced to various countries. The acquisition of a transnational character by clinical trials is accompanied with emerging global actors such as transnational pharmaceutical corporations that are instrumental in the outsourcing and conducting of such trials. As stated above, the underlying rationale behind outsourcing trials to developing countries is the cost effectiveness of conducting trials in these countries.¹⁸⁷ In the outsourcing relationship corporations are not the only beneficiaries as developing countries are dependent on these corporations too. In fact the degree of dependence of the latter is higher as these corporations being part of the private sector are seen as a source of growth for the country in terms of investment, value addition and as a consequence, greater fiscal stability.¹⁸⁸ This can be attributed to one primary reason- the competition promoted among nation states as a result of globalisation. Economic globalisation is characterised by a phenomenon of “golden straitjacket”¹⁸⁹ in developing countries.¹⁹⁰ This phenomenon is connotative of the restructuring of economy that pressurized developing

¹⁸² George J. Stigler, *The Theory of Economic Regulation, The Bell Journal of Economics and Management Science*, 2(1) THE BELL JOURNAL OF ECONOMICS AND MANAGEMENT SCIENCE 3-21 (1971).

¹⁸³ *Id.*

¹⁸⁴ See Gulhati, *supra* note 177.

¹⁸⁵ *Id.*

¹⁸⁶ *Id.*

¹⁸⁷ See Srinivasan, *supra* note 3.

¹⁸⁸ Timothy K. Kuhner, *International Poverty Law: A response to Economic Globalisation*, 22 BUFFALO PUB. INT. L. J., 85 (2003-04).

¹⁸⁹ *Id.*

¹⁹⁰ *Id.*

countries undertake, so as to align them with international market trends. An analogous illustration of this phenomenon can be located in the globalised clinical trial market as well. Clinical trials in India take place in a setting of abject poverty and poor access to healthcare.¹⁹¹ Clinical trials are thus viewed as a mechanism to obtain medical treatment affordably, and the government is only too eager to ensure that India is a favourable destination for clinical trials.¹⁹² As stated above, the Government has removed the ‘impediment’ created by the phase lag provision by an amendment to Schedule Y in 2005. This removal is characteristic of the international pressure faced by the Government to make regulations more ‘investment friendly’. In the event that they fail to do this, the country will lose out not just on investment, but also on access to the drug for its own citizens. Consequently, two phases of clinical trials can now be carried out concurrently, resulting in exploitation. The inference drawn is that “the regulatory function of the government and its social obligations take a backseat in the face of international integration”.¹⁹³ The goal of international integration in the clinical trial market is the utilitarian notion of benefit of a better health-care system. The orchestrators of these trials often adopt the populist line of argument, that the sacrifice of a few is justified given that the outcome will be beneficial in terms of greater good. They further mandate participation in the name of “beneficence”.¹⁹⁴ The question however is who reaps the benefit. The trickle-down effect of globalisation is limited.¹⁹⁵ The poor are still dominated by “...the forces of extortion, arbitrariness and uncertainty”.¹⁹⁶ Why this part focuses on the poor, is because a majority of the recruitees to clinical trials in less developed countries are the poor. In fact agents of the contract research organisations (‘CRO’) that conduct these clinical trials, are specifically asked to target the poor as potential subjects because they are in dire need of the money that comes as a result of their participation.¹⁹⁷ Having established that, the question that needs be reiterated is how beneficial these trials are to the poor in terms that are more holistic than pure financial gain. It is this question that this part attempts to answer by analysing the effects of clinical trial on these subjects.

¹⁹¹ S. Srinivasan, *Trial by Fire*, available at <http://infochangeindia.org/public-health/analysis/trial-by-fire.html> (Last visited on October 7, 2012).

¹⁹² *Id.*

¹⁹³ See Kuhner, *supra* note 188, 86.

¹⁹⁴ See Schaefer, Emanuel & Wertheimer, *The Obligation to Participate in Biomedical Research*, 302(1) JAMA 68 (2009):

“According to the beneficence argument, if a person can prevent something bad or produce some good then that person has a duty to perform that action. Any action that is beneficial to society overall would be obligatory. Participation in many clinical trials is therefore obligatory merely because it helps society at large”.

¹⁹⁵ Antonia Juhasz, *The Failure of Globalisation*, 15(3) CAMBRIDGE REVIEW OF INTERNATIONAL AFFAIRS 407 (2002).

¹⁹⁶ PARTH J. SHAH & NAVIN MANDAVA, LAW LIBERTY AND LIVELIHOOD: MAKING A LIVING ON THE STREET 20 (2009).

¹⁹⁷ See Paliwal, *supra* note 6.

The increasing number of deaths caused by unregulated clinical trial¹⁹⁸ constitutes a violation the right to life under Art. 21¹⁹⁹ of the Indian Constitution. To limit the effects of clinical trials only to death, however, would result in an oversight of other annihilating effects which admittedly, do not cost them their life, but their dignity with which they are entitled to live. In fact, “any form of torture or cruel, inhuman or degrading treatment would be offensive to human dignity”.²⁰⁰ The right to life does not merely mean the absence of death.²⁰¹ There are various implicit nuances that contribute in attributing dignity to life.²⁰² Comprehending the effects in their entirety would entail the factoring in of ramifications on these nuances. The illustrations given subsequently will demonstrate how clinical trials do not necessarily have to spell out a death sentence in order to be detrimental to the poor.

One of the causal factors of the effects is the terminology attributed to those participating in clinical trials- subjects. The use of the term ‘subject’, very strategically dehumanises those participating in clinical trials, rendering them as passive objects as opposed to active bearers of rights. The term ‘subject’ literally connotes someone placed under authority or control.²⁰³ The Hippocratic notion of the term is that of a dutiful, obedient being.²⁰⁴ The terminology has thus resulted in the indoctrination of the idea that the subject is essentially submissive. It is this indoctrination that has validated the infringement of individual autonomy, making it acceptable for physicians to prioritize the interest of science over the autonomy of the subject. This choice of terminology thus naturalises what is centrally problematic. What is required is a change in terminology from ‘subject’ to ‘participant’.²⁰⁵ Admittedly, the change in terminology by itself is not enough, but at least it catalyses the de-schooling process and does away with the historical baggage associated with the term ‘subject’.

In spite of the legal requirement of informed consent, in the absence of an independent monitoring body, the ground reality is starkly different. Physicians in furtherance of their own vested interests routinely recruit patients to clinical trials without their consent. The ‘treatment naïve population’, unsuspectingly submits itself to trial and error. In Hyderabad, for example, a research firm subjected the poor to a trial for an anti-cancer drug without

¹⁹⁸ See Nagarajan, *supra* note 62.

¹⁹⁹ Constitution of India, Art. 21, “Protection of life and personal liberty: No person shall be deprived of his life or personal liberty except according to procedure established by law”.

²⁰⁰ Francis Coralie Mullin v. Administrator, Union Territory of Delhi, (1981) 1 SCC 608.

²⁰¹ Bandhua Mukti Morcha v. Union of India, (1984) 3 SCC 161.

²⁰² *Id.*

²⁰³ Merriam-Webster Online Dictionary, available at <http://www.merriam-webster.com/dictionary/subject> (Last visited on October 9, 2012).

²⁰⁴ See Elnimeiri, *supra* note 10.

²⁰⁵ N. M. TRIPATHI, LAW AND POVERTY CRITICAL ESSAYS vi-viii (Upendra Baxi ed., 1988) (The authors have relied on the shift in terminology from poverty to impoverishment advocated by Upendra Baxi).

their consent.²⁰⁶ In another incident, self-proclaimed researchers illegally carried out a trial where 400 women were tested without their consent to determine if an anti-cancer drug Letrozole could induce ovulation.²⁰⁷ One would hope that the depravity would stop there, but that is not the case. Documents submitted by Novartis, the inventor of this drug, revealed that “both the US Food and Drug Administration (‘USFDA’) and the British Authority (MHRA) have labelled Letrozole as embryotoxic, foetotoxic, as well as teratogenic at miniscule doses”.²⁰⁸ The idea of informed consent is reflective of a decision that is the product of an informed choice. The lack of consent can be used to establish claims for battery and assault.²⁰⁹ While such claims would account for the corporeal violation, they do not factor in the violation of the intangible, sacrosanct concepts of human dignity and autonomy. Negation of informed consent amounts to the negation of individual autonomy.²¹⁰ It further serves to contravene the Kantian notion of autonomy wherein a person is an end in himself and he should not be used as means for the welfare of others.²¹¹ An illustration of such contravention is the aforementioned *Swasthya Adhikar Manch* case wherein, the mentally disabled were recruited to a trial that was not even catering to the needs specific to their population.²¹² They were essentially mere instruments that were subjected to trial and error, to ‘serve the greater good’. Bioethicists do not subscribe to the Kantian notion of a physician’s obligation to respect autonomy in the event that the autonomous choice made is to the detriment of the patient.²¹³ They do, however, recognize that the integrity and autonomy of an individual needs to be respected, even if at a very basic minimal level,²¹⁴ a fact that physicians carrying out clinical trials in India seem to be blissfully ignorant of.

It could be argued that a majority of the recruitees willingly sign up for these trials for monetary gain. The question is how meaningful is this consent? To equate this ‘willingness’ to earn money - which the authors would like to point out is more a need than a willful fancy- with consent, would be analogous to arguing that since the poor willingly sell off their organs for financial gain, the black market of organ trade should be legitimised. Furthermore, an argument that puts forth the proposition that the willingness of the recruitees to earn money ascribes legitimacy to these trials is not only fallacious but also hypocritical. Beggary is often opted for as a means to earn money. The State refuses to legalize this act on the grounds of it being violative of human dignity. Botched medical procedures, however, do not seem to make

²⁰⁶ See Rajalakshmi, *supra* note 159.

²⁰⁷ See Gulhati, *supra* note 177.

²⁰⁸ *Id.*

²⁰⁹ Nir Eyal, Stanford Encyclopedia of Philosophy, *Informed Consent*, available at <http://plato.stanford.edu/entries/informed-consent/> (Last visited at September 8, 2012).

²¹⁰ *Id.*

²¹¹ MICHAEL J SANDEL, JUSTICE 103, 110 (2010).

²¹² *Swasthya Adhikar Manch v. Union of India*, WP(C) No. 33 of 2012.

²¹³ See Eyal, *supra* note 209.

²¹⁴ *Id.*

the cut. What investigators try to pass off as consent is more often than not “economic coercion”.²¹⁵ Economic coercion as is described in *People’s Union for Democratic Rights v. Union of India* includes, “...not only physical or legal force but also force arising from the compulsion of economic circumstance which leaves no choice of alternatives to a person in want and compels him to provide labour or service”.²¹⁶ For people who lack the resources to make ends meet, participation in clinical trials is represented as an attractive way of making money. The consent given by them is tainted by their economic compulsion, and their lack of requisite knowledge. It would be pertinent to note the characteristics of the service offered by the recruitee at this juncture. The work does not require any skill, it lacks autonomy as the recruitee is the ‘subject’ of the physician/investigator, and it pays an amount in most cases paltry enough to be able to afford nothing more than two meals a day. The three attributes discussed also happen to be the attributes Iris Young ascribes to menial labour.²¹⁷ In Young’s elucidation on exploitation as a tool of oppression, she observes that, “the central insight expressed in the concept of exploitation, then, is that this oppression occurs through a steady process of transfer of the results of the labour of one social group to benefit another”.²¹⁸ Thus, according to her, what is centrally problematic is not the paltry remuneration *per se*, but the fact that the work a menial labour does is controlled by someone else, and for the benefit of someone else. Applying this analogy to the sphere of unethical, unregulated clinical trials, it becomes clear that the fundamental question is not of financial gain but of the loss of control that the recruitees suffer in this entire process. The recruitment of the vulnerable section of society has little to do with consent, and more to do with the undue influence that the investigators and pharmaceutical corporations exert over them. It is to protect the vulnerable section of society from such forces of coercion and undue influence that the ICMR Guidelines explicitly state that “people who are economically or socially disadvantaged should not be used to benefit those who are better off than them”.²¹⁹ The catch here is that this statement being part of a guideline is non-binding, and the silence of the law *i.e.*, Schedule Y only serves to aid the contravention of this provision. This lacuna in the law serves as a perfect niche for the exploitation and thus oppression of the powerless.²²⁰

What exacerbates the oppression is the violence that unethical, unregulated clinical trials perpetrate. The general understanding of violence is centered on random acts of corporeal violation. The nature of violence perpetrated by clinical trials however is not limited to mere corporeal facets. It

²¹⁵ *People’s Union for Democratic Rights v. Union of India*, (1982) 3 SCC 235, ¶13.

²¹⁶ *Id.*

²¹⁷ IRIS MARION YOUNG, *JUSTICE AND THE POLITICS OF DIFFERENCE* 52 (1990).

²¹⁸ *Id.*

²¹⁹ See *supra* note 145, Chapter III, Guideline IV(iii).

²²⁰ Staff Reporter, *Clinical Trials of HPV Vaccine Conducted on Tribal Girls*, THE HINDU (Andhra Pradesh) June 29, 2011, available at <http://www.hindu.com/2011/06/29/stories/2011062965081000.htm> (Last visited on September 12, 2012).

factors in the infringing of individual integrity and is a product of deliberate systemized acts as opposed to random acts of violence. The perverse nature of this violence is further accentuated by the fact that it is a rationalized, conscious decision to prioritize high profit margins over the life and integrity of the recruitees. The trials conducted in 2004 by the Bhopal Memorial Hospital serve as an apt illustration here. It should come as no surprise that the consent of the recruitees was not sought; or that this trial was not designed to cater to recruitee specific needs; or that out of the cocktail of drugs tested, only one had been approved for human use. Here the unimaginable depravity was the choice of subjects: they were the victims of the Bhopal Gas Tragedy. The Nazis used the Jews; the Soviets used prisoners from their labour camps, people they considered non-citizens. In the largest democracy in the world, we subjected our so called citizens, the victims of a tragedy no less, to patently unsafe trials to quell our perverse curiosity. What possible justification can the doctors of a democratic welfare state offer for using the victims of a gas tragedy as guinea pigs?

In the contingency that they offer development of science and technology as a justification, this paper contends that there needs to be a shift in approach from this skewed perception that development not only validates but also legitimizes violation of basic inalienable rights of vulnerable groups or for that matter any human being. The new paradigm should aim to synthesize the currently conflicting claims of development and human rights and establish that any form of development has to be located within the non-negotiable framework of human rights. Locating clinical trials within this framework by enforcing proper regulations will not just ensure against violation of human rights, but also ensure to a great extent the veracity of biological data gathered in such trials. It only stands to reason then that accurate data has a higher likelihood of actually contributing to the development of science than data that is falsified for furtherance of pure financial motives.

VI. CONCLUSION

As of 2011, 483 people died in India in the course of clinical trials. Compensation was, however, paid to only 16 volunteers.²²¹ The ledger sheets of pharmaceutical corporations, hardly if ever reflect the human costs. Recently the DCGI has issued draft guidelines for the purpose of allocation of compensation to victims and their families in cases of injury or death in the course of clinical trials.²²² The irony of using the binding force of law for issuing a license to kill on one hand and issuing sketchy guidelines that have no binding value in any court of law to deal with compensation, on the other hand, is seemingly lost on the regulatory authorities. To advocate development of science and technology is one thing, to prioritize it over the sacrosanct notions of autonomy and life in furtherance of commercial interests, quite another. The only business

²²¹ See Singh, *supra* note 158.

²²² *Id.*

that field of medicine and healthcare should be invested in, is that of saving lives. The assumed intendment with regard to clinical trials is that they were designed to liberate people and eliminate diseases. Somewhere down the line, they have taken to eliminating people themselves.

Through the course of this paper, we have sought to establish the inadequacy of the clinical trial regulations in India. The argument that establishes the inadequacy is two pronged- the first is with regard to the existing regulations being replete with loopholes; the second with regard to the ineffective implementation of the regulations, owing to regulatory capture. The comparative analysis with analogous legislation in the UK, serves to illustrate how glaring these inadequacies are. The absence of a comprehensive legal framework has led to the creation of a legal limbo – a perfect niche for unregulated clinical trials. Resultantly, recruitees are not only left remediless at the end of a clinical trial gone wrong, but also completely unprotected during the course of such unregulated clinical trials. For-profit corporations put a pittance of a dollar figure on their suffering and investigators forsake the Hippocratic oath to make quick money off it. In the face of all of this, the government of a welfare state is content with having enacted what is best described as a mockery in the name of regulation. In light of the annihilating effects of clinical trials as discussed above, it is imperative that a comprehensive law, which integrates scientific development with medical ethics, is enforced immediately.

The current development paradigm, be it in the sphere of economics or science, views human rights as an impediment in the developmental process.²²³ Human rights, however, are not antithetical to development. If anything, they only serve to aid the developmental process making it more sustainable suffusing it with notions of equitability. The current paradigm thus needs to be remodeled to incorporate human rights and recognize that they are non-negotiable. Supporters of the current paradigm would no doubt oppose this proposition, employing the utilitarian argument of prosperity and welfare of the majority. The inherent flaw in this utilitarian argument is best displayed in an excerpt from Michal Sandel's Justice- "In ancient Rome, they threw Christians to the lions in the Coliseum for the amusement of the crowd. Imagine how the utilitarian calculus would go: Yes, the Christian suffers excruciating pain as the lion mauls and devours him. But think of the collective ecstasy of the cheering spectators packing the Coliseum".²²⁴ Admittedly clinical trials are not for sheer amusement, the point that this paper makes, however, is that the inherent flaw in this approach is that it views individuals as expendable, be it for amusement or the 'greater good'. The new law should seek to rectify this flaw and focus on protecting recruitees from systemic violations. It should adopt the language of entitlement, according to these recruitees the status of dignified human beings, as opposed to their present status of collateral damage.

²²³ Upendra Baxi, *Human Rights, Accountability and Development*, 18 IJIL 279 (1978).

²²⁴ See Sandel, *supra* note 211, 37.