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Clinical Trials in India: Emerging Legal and Ethical Issues

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I. INTRODUCTION

Science and technology have brought qualitative changes in almost every aspect of human life, bringing with them problems which were otherwise unheard of. The development of Bio-technology, Nano-Technology coupled with growth and development of Pharmaceutical industries has brought about situations not previously contemplated. At present in India we have 40 million asthmatic patients[1], about 40 million diabetic patients[2], 2.4 million people with HIV[3], 5-6 million epileptic patients[4], 2.5 million cancer patients[5], more than 2 million cardiac-related deaths[6], 1.5 million people

with Alzheimer's disease[7]; 140 million is hypertensive[8], and 8.7 million suffers from schizophrenia[9] In order to give best treatment to above diseases research on humans and trials thereon are necessary and desirable. A clinical trial is defined as "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes[10]." Interventions include not only drugs but also cells and other biological products, surgical procedures, radiological procedures, devices, behavioral treatments, process-of-care changes, preventive care, etc.[11]

A huge patient population, genetically distinct groups, specialty hospitals with state-of-the-art facilities, nearly 700,000 hospital beds and 330 teaching medical colleges, and skilled, English-speaking investigators, have facilitated the conduct of clinical trials in India.[12] Inspite of such an infrastructure the Central Government has conceded before the Supreme Court of India[13] that as many as 2,644 people died during the clinical trials of 475 new drugs on human beings in last seven years, others suffering 'serious

adverse effects'.[14] Only 17 of the medicines were approved for marketing in India.[15]

Responding to a query in Parliament in March, the Minister for Health and Family Welfare informed that as per the information given in the Clinical Trials Registry maintained by the Indian Council of Medical Research (ICMR), the target Indian sample size in clinical trials had shown an upward trend in 2009 and 2010 but had declined in 2011.[16] The number of clinical trials permitted by the Drugs Controller General of India (DCGI), in the past three years were 453 (2009), 505 (2010) and 271 (2011). The number of serious adverse events (SAE) of deaths in all clinical trials in the past three years stood at 637, 668 and 438 respectively. He also informed that two clinical trials had been conducted without the DCGI's permission in the past two years. But as no adverse event of death was reported, no compensation was paid.[17] The experiences of the human papilloma virus (HPV) vaccine projects in Andhra Pradesh and Gujarat had brought to light a number of issues and problems relating to the execution of clinical trials. Despite common ICMR guidelines, there were differences in the performance of projects across different States.[18]

Is law responding adequately to the scientific and technological developments? If so, how far it can control and has handled the scientists and technologists in the best and ultimate interests of the community? To what extent can the society exert itself to enable the law and the government to be more effective in meeting squarely the challenges posed by developments

and solving problems created by scientific and technological developments?[19] These are some of the questions which need answers.

This paper highlights misuse/abuse of clinical trials in India. It explores regulatory frame work related to clinical trials in India and ethical issues in clinical research. The present work deals with initiatives concerning law reforms related to clinical trials in India. It takes into account reports of Parliamentary Standing Committees related to clinical trials. It also examines the role of Supreme Court of India to propel the Central Government and State Governments for enacting/framing regulatory framework for protecting the Indian citizens from being used as guinea pig for clinical trials. The present paper makes a strong case for stringent standards and legislations for future medical research on human subjects. So, an humble attempt is made in the present exercise to research in an area though very fertile yet remaining unexplored. It examines the core areas in clinical trials in India which needs legal control. It further explores the success and failure of the judicial approach.

II. Existing Laws/Guidelines Related to Clinical Trials in India

A. Agencies

Public Health is the State subject largely in the domain of State Governments but a lot of guidelines/directions for health comes from the Centre. Institutionally, Union Ministry of Health and Family Welfare (MOHFW) is in charge of prevention and control of health related hazards in India. The MOHFW has a large mandate that includes inter alia drug regulation administered under the Directorate General of Health Services (DGHS). Directorate General of Health Services (DGHS) is the agency overseeing the implementation of the various health programmes and schemes and provides technical inputs to the Ministry on various aspects of their functioning and implementation and serves as a coordinating agency for all the specialized health related matters including drug regulation and standard setting. The Central Drugs Standards Control Organization (CDSCO) is the apex central authority that is responsible for new drugs approval, overseeing clinical trials, laying down standards for drugs and quality control for imported drugs. The CDSCO in the Directorate General of Health Services, is a division in Union Ministry of Health and Family welfare, Government of India, headed by Drug Controller General of India (DCGI). It has four zonal, three sub-zonal and seven port/airport offices and

six laboratories to carry out its activities.[20] Further it also provides expert advice to the state authorities (State Drug Controllers) on the other hand have the primary responsibility of overseeing the regulation, manufacture, sale and distribution (including licensing) of Drugs. The approval of new drugs entails examination of the clinical trial reports and checking them for bioequivalence, etc before granting marketing approval.

There is a basic problem to un-uniformity in the interpretation of the provisions of the related legislations amongst the various state drugs controllers. This is squarely the failure of CDSCO to provide for adequate coordination between state units. There is a disconnection between and among the number of manufacturing and selling establishments licensed within the state territory and the number of drug inspectors overseeing such establishments.[21] The CDSCO is also the implementing agency for the National Pharmacovigilance Program. CDSCO, although a separate organisation, works within the structure of DGHS and its mandate, activities, infrastructure etc. fall under the purview of the Directorate.[22] Pharmacovigilance refers to the monitoring systems that are put into place to oversee the safety of new pharmaceutical entities (NCEs) or even generics manufactured by domestic pharmaceutical companies. Indian regulators have previously had a dependence on data generated in other countries. However since the last decade, it has been recognized and largely accepted that the Indian population is distinctive in both its physiological composition and genetics makeup and therefore populations' effects data generated in other countries cannot be taken as a correct index of the effect of those drugs on

the Indian population. All these reasons were paramount to the government decision to incorporate and launch a National Pharmacovigilance Program (NPP) in 2004.

B. The Laws

(a) The Drugs & Cosmetics Act, 1940

The Drugs and Cosmetics Act, 1940 regulates all aspects of drugs and cosmetics pertaining to their import, manufacture, distribution and sale. Any manufacture of sale of drugs has to be in compliance with the standards laid down in the schedule of the Act.[23] A patent or proprietary medicine cannot be sold, unless the true formula or list of active

ingredients contained in it along with the quantities thereof is displayed in the prescribed manner on the label or container. The inspector is empowered to collect sample, inspect and seize drugs. Further, the central government is also empowered even to prohibit manufacture, etc., of drug and cosmetic in public interest. Such a prohibition can be imposed on import of drugs as well where such import is likely to involve any risk to human beings or animals or it does not have therapeutic value. The Act also empowers the central government to prohibit import and manufacture of drugs and cosmetics in public interest. Risk to human beings/animals has been mentioned as one of the circumstances under which the government can activate it self. The Act also enables the government to specify a quality standard. The Act provides for detailed penalties in case of adulterated drugs and cosmetics, which include cases where the container is composed of composed of any poisonous or deleterious substance which may render the contents injurious to health or where it contains any harmful or toxic substance which may render it injurious to health. It also contains enabling provisions for regulating and ensuring quality, safety and efficacy of drugs and, therefore, contains inherent enabling powers for regulating the clinical trials.[24]

Under the inherent plenary powers vested in the Act, necessary rules, procedures and guidelines have been framed under the Drugs and Cosmetics Rules, 1945. Schedule Y of the Drugs and Cosmetics Act, 1940 was amended in the year 2005. Thus National Pharmacovigilance Program (NPP) was first launched as a voluntary initiative and then later incorporated into the legal regime through the review and amendment of Schedule, Y, under the Drugs Control Act in 2005.[25] The relevant provisions of Schedule Y can be classified in three categories. The first category deals with application procedures, responsibili-ties 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.[26] On submission of the relevant Phase I data on drugs discovered outside the Indian territory,[27] 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.

Rule 2(5) of the aforesaid rule 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.[28] The pre-requisites for obtaining permission to conduct Phase III trials are expounded in Rule 2(8).[29] Informed consent provided for in Schedule Y contemplates a free, informed and written consent.[30] For those lacking legal capacity, the consent of their legal representa-tives or proxies is sought.[31] 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.[32] Rule 3 deals with studies conducted on special groups, such groups comprising in the Schedule of ageing people, children, and pregnant women.[33] It defines the cir-cumstances under which recruiting subjects from vulnerable or special groups is justified,[34]

additionally also contemplating the requirement of assent in the case of paediatric subjects.[35] It may be noted that in case of non-compliance to the provisions of clinical trials by any Sponsor including the representative, investigators conducting clinical trial and clinical trial sites, the DCG (I) can take following actions: reject or discontinue the study; suspend or cancel the clinical trial permission; debar the Investigator(s), sponsor including his representative to conduct any clinical trial in future.[36]

Regulatory provisions for conducting clinical trials in the country are prescribed under the Schedule Y to the Drug and Cosmetics Rules, 1945. Unfortunately, till some time back, the provisions of compensation to the vulnerable subjects who suffer injury or death during participation in clinical trial[37] of a new drug which targeted to be launch in the market by Pharma companies were silent and not covered under the Drug and Cosmetics Rule, 1945.[38] However, the insertion of the new Rules 122-DAB, Rule 122-DAC and Rule 122 DD (vide first, second and third amendments) respectively have been able to fulfill the lacuna of the need of such compensatory provisions.[39] Rule 122-DAB (1) lays down the requirement of

providing free medical management as long as required, in the case of an injury occurring to a clinical trial subject. Further if the injury suffered by the trail subject is related to the clinical trial conducted on such subject, he or she shall also be entitled for financial compensation as per order of the Licensing Authority. In case the clinical trial results in the death of the subject, financial compensation, as per the order of the Licensing authority, has to be compensated to the nominee of the deceased subject. Rule 122 DAC specifies the prerequisites required for a clinical trial to be considered as adequate so as to grant permission by the Licensing Authority to be conducted on any human body. Further the rule lays down the power of the Licensing Authority to impose any additional conditions to be fulfilled in case of grant of permission in respect of any specific clinical trial, as it is deem fit.[40] Rule 122-DD deals with mandatory registration of the Ethics Committee and specifies that no Ethics Committee shall review and accord its approval to a clinical trial protocol without prior registration with the Licensing Authority as defined in clause (b) of Rule 21 and describes the procedure of such registration to be made by filling an application to be made to the Licensing Authority in accordance with the requirements as specified in the Appendix VIII of Schedule Y of the Rule and the procedure thereof.[41]

The new regulations, the Drugs and Cosmetics (First Amendment) Rules, 2013, for clinical trials have some controversial clauses.[42] One clause states that for an injury/illness occurring to a clinical trial subject, he or she shall be given free medical management as long as required. It may be noted that this does not specify what type or cause of injury. Thus a trial participant may be involved in a traffic accident or assaulted by someone. Under this clause the trial sponsor has to cover all costs in an open ended fashion. Another clause calls for financial compensation to be paid over and above costs of any medical management in the case of an event occurring that is considered trial related. This is certainly justified. However the key question is what constitutes a trial related injury. These are defined in subsequent

clauses most of which are unexceptional. There are however some which creates confusion. One such is "failure of investigational product to provide intended therapeutic effect". It has been claimed that this is counterintuitive. Regulatory authorities require a trial to be carried out to prove that the medication works. Earlier phases of clinical trials give a fairly good idea of the medication being likely to be effective but it is the large phase three trial that has to prove this. Some medications may not meet the required standard. Again, even if a medication works it may not work 100 per cent all the time. A person whose cancer was not stopped from progressing may claim compensation under this clause even though in the trial as a whole the treatment was effective.[43]

A second definition of a trial related injury in the regulations is use of placebo in a placebo-controlled trial. A placebo controlled trial is usually a requirement by regulatory agencies to ensure lack of bias in a trial being done to prove effectiveness of a new medication. It should be made clear that in any condition in which treatment already exists, all subjects in the trial should get this treatment. The new treatment or placebo is given in addition as an add — on. Thus no group should be denied best available treatment especially in a potentially serious condition. The use of a placebo cannot be considered as equivalent to a trial related injury unless it is shown that the subject was denied existing standard treatment. It has been mentioned that compensation for an "adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol". This clause seems to imply that if the patient has a reaction or complication not due to the trial medication but to one of the other medicines that he/she is taking or advised to take, the trial sponsor is responsible not only to pay for any treatment but also to pay compensation in addition. How can the trial sponsor take responsibility for drugs that the patient has been taking all of which have been approved for marketing and are in common use? Dr. Prem Pais argues that often trial protocols advise investigators to make sure that trial participants are taking the best available treatment for their illness apart from the trial medication. These are all approved marketed medication. As such this clause may discourage such steps to ensure best treatment for study participants.[44]

It has been advocated that the Ministry of Health to have a re-look at its notified revised regulations and consult people with the knowledge and experience in the ethics as well as the science of clinical trials both from India and abroad. It is most important that the rights of trial participants be protected while at the same time ensuring that the greater good of our

people is not harmed by killing off clinical trials. Other countries have found the right balance. There is no reason we should not be able to do the same.[45] Thus the recent amendment to the Drug and Cosmetic Rules, 1945 has ignited debates related to implementation of rules concerning clinical trials in India.

(b) Indian Medical Council Act, 1956

Indian Medical Council Act, 1956 was passed to uniformly regulate the medical education/profession in India. The Council is empowered to withdraw recognition in cases where it finds the lowering of standards of proficiency, knowledge of skill.[46] The rule making power is conferred upon the Government while regulation making power conferred upon the council.[47]

It may be noted that all clinical trials in India should follow the ICMR guidelines of 2000. The ICMR has a mechanism of review for its own institutions. Every doctor is governed by the MCI Act. Any doctor having committed wrong in a trial or in practice can be prosecuted and the hospital can be closed. The Medical Council of India has the power to take punitive measures.

The Ethical Guidelines for Biomedical Research on Human Participants ('the Guidelines') were issued by the ICMR,[48] with the same ob-jective as that of the Council for International Organizations of Medical Sciences (CIOMS) guidelines. ICMR sought to customize the univer-sal principles in order to make them better suited for application to the Indian front. The Guidelines were issued in 2006.[49] The introductory chapter of

the Guidelines deals with the twelve general principles of biomedical ethics.[50] 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[51] In the event that human subjects are used, other principles such as those of free informed consent, non-exploita-tion, accountability and transparency gain prominence.[52]

The Clinical trial can be initiated only (i) after permission from the Drugs Controller General (India) [DCG(I)], (ii) approval from respective Ethics Committee and (iii) mandatory registration on website[53] being maintained by ICMR before the enrolment of the first trial participant for the clinical trial.[54] The Clinical Trial Registry of India (CTRI), maintained

by Indian Council of Medical Research (ICMR), will create a database of prospective clinical trials in India after their registration. The data and reports of these clinical trials and their status will be available to the public and professionals free of cost after formal registration on their website. Currently, the registration of clinical trials is only voluntary and not mandatory.[55] With increased awareness about this initiative and wide acceptance of the purpose of CT registration, it is likely that it may become mandatory in the future for initiation of clinical trials in India. It has been affirmed that CT registration should be done before the actual enrollment of study subjects in the trial. The principal investigator or sponsor should share the responsibility of CT registration. In the case of multi-centric studies, the lead investigator or sponsor should ensure that the CT is registered. For the registration of a CT, it is essential to declare 20 items relevant to the CT as determined by the International Clinical Trial Registration Platform (ICTRP) of the World Health Organization (ICRTP-WHO). For registration with the CTRI, additional items related to the EC or IRB's permission and that of Director Controller General of India (DCGI) are included. At the end of a successful registration, each CT is assigned a unique WHO identification number called the Unique Trial Reference Number (UTRN).[56]

(c) The Proposed Reforms

(i) The First Committee

In January, 2003, the Central Government constituted an Expert Committee under the Chairmanship of Dr. R.A. Mashelker, Director General of the Council of Scientific and Industrial Research (CSIR) to undertake a comprehensive examination of drug regulatory issues, including the menace of spurious drugs and to suggest measures to improve the drug administration in the country. The Committee noted that the problems in the drug regulatory system in the country are primarily due to inadequate or weak drug control infrastructure at the State and Central level and therefore, recommended centralised licensing of manufacture of drugs. The Committee further recommended for a strong, well equipped, empowered, independent and professionally managed Central Drugs Standard Control

Organisation (CDSCO) which may be given the status of Central Drug Administration reporting directly to the Central Government. With a view to give effect to the recommendations of the Mashelkar Committee, the Central Government brought in a new proposed law.

(ii) The Second Committee

The Fifty-ninth Report of the Parliamentary Standing Committee on Health and Family Welfare, May 8, 2012 essentially dealt with the functioning of the Central Drugs Standard Control Organisation (CDSCO).[57] In its Status Report on CDSCO, the Ministry of Health and Family Welfare stated that the mission of CDSCO was to "meet the aspirations…. demands and requirements of the pharmaceutical industry."[58]

The Parliamentary Committee discovered that the opinions submitted by the experts on various drugs were actually written by the invisible hands of drug manufacturers and experts merely obliged by putting their signatures'.[59] The committee also makes a case for unambiguous and clear guidelines for a range of issues related to clinical research particularly related to approval of new drugs and the selection processes of 'outside experts' for this purpose; highlighting the importance of identification of all possible biases and potential conflicts of interest. The Committee pointed out that for approving the new drugs, too much is left to the

absolute discretion of the CDSCO officials. There are no well laid down guidelines for determining whether consultation with experts is required. Thus the decision to seek or not to seek expert opinion on new drugs lies exclusively with the non-medical functionaries of CDSCO, leaving the doors wide open to the risk of irrational and incorrect decisions.

The Committee, therefore, strongly recommended that there should be non-discretionary, well laid down, written guidelines on the selection

process of outside experts[60] with emphasis on expertise including published research, in the specific therapeutic area or drug or class of drugs'.[61] All experts must be made to file the conflict of Interest declaration outlining all past and present pecuniary relationships with entities that may benefit from the recommendations given by such experts. The DCGI must take action against those CDSCO functionaries who colluded with private interests and got the drug approved in violation of laws.[62] The Committee further recommended that Section 26-A of Drug and Cosmetic Act, 1940 empowering the Central Government to ban any drug to protect public health which was not activised, be made operative. On the whole the Parliamentary Committee expressed its deep concern, extreme displeasure and disappointment at the state of affairs related to clinical trials in India.[63]

(iii) The Third Committee

The Sixty - Sixth Report[64] of the Parliamentary Standing Committee on Health[65] and Family Welfare, April 23, 2012 dealt with the action taken by the Department of Health and Family Welfare on the "Functioning of Central Drugs Standards Control Organization (CDSCO)". The Committee examined these actions taken replies of the Government in-depth. Most of them were evasive, inconclusive, dilatory and vague. The Parliamentary Committee took note of inaction of the government and condemned the

continued inaction of the Ministry. It recommended immediate and conclusive action.[66]

Coming to clinical trials, the Committee pointed out that DCGI clears sites of pre-approval trials without application of mind to ensure that major ethnic groups are enrolled in trials to have any meaningful data. Thus such trials did not produce any useful data and merely served to complete the formality of documentation.[67] The Committee recommended that while approving Phase III clinical trials, the DCGI should ensure that subject to availability of facilities, such trials are spread across the country so as to cover patients from major ethnic backgrounds and ensure a truly representative sample. Besides this, trials should be conducted in well equipped medical colleges and large hospitals with round the clock emergency services to handle unexpected serious side effects and with expertise in research and not in private clinics given the presence of well equipped medical colleges and hospitals in most parts of the country in present times.[68] The Committee pleaded that there was an urgent need to increase the minimum number of subjects that ought to be included in Phase III pre-approval clinical trials to determine safety and efficacy of New Drugs before marketing permission was granted. In most western countries the required numbers run into thousands'[69]. The Committee added that this could be easily achieved by changes in the Good Clinical Practice (GCP) guidelines.[70] The Committee exhorted that the Government, therefore, was morally bound to heed to the advice of the Parliamentary Committees in the national interest. On the analysis of the action taken by the Government on the Recommendations of Committee it showed that out of 69 Recommendations that were actionable only 19 had been implemented by the Government in varying degrees. In case of 46 Recommendations the action taken by Government was only with the intent to delay, obfuscate, stagger implementation or not implement at all with a view to delay/negate action in proven cases of wrongdoing.[71] The Committee therefore, desired the Ministry to

make expeditious efforts to sew up the proposed Scheme and start its implementation proper at least from the Second Fiscal of the Twelfth Plan.[72]

(iv) The Fourth Committee

To formulate policy, guidelines and standard operating procedures for approval of new drugs including biologicals, clinical trials and banning of drugs, Ministry of Health Family Welfare constituted one more Committee on 6th February 2013.[73] The Committee was to recommend changes and introduce measures which would result in a drug regulatory system for India which was to be robust, transparent and built on the foundations of science and ethics.[74] The major recommendations of Committee is enumerated as under: included, for example, firstly, the Clinical trials can only be carried out at centres which have been accredited for such purpose. The principal investigator of the trial should be an accredited clinical investigator. The ethics committee of the institute must also have been accredited. Only those trials conducted at centres meeting these stipulations will be accepted by the Drugs Controller General of India (DCGI). Secondly, a Central Accreditation Council should be set up to oversee the accreditation of institutes, clinical investigators and institute ethics committees. Thirdly the Selection experts to review new drug applications and other purposes will be made by a blind randomized procedure from a Roster of Experts. This Roster will be prepared after a nationwide search of appropriate

experts and approval by the Technical Review Committee. The selection will have built-in safeguards for gender sensitivity and geographical representation. Fourthly, a broad expertise-based Technical Review Committee may be constituted to ensure speedy clearance of applications without compromising on quality of data and rules and regulations. The Committee would be assisted as required by appropriate subject experts selected from the Roster of Experts. Fifthly, an informed consent from each participant.

Coming to the informed consent the Committee, fifthly recommended that it was is a mandatory prerequisite for a clinical trial. In circumstances where informed consent has to be obtained from special groups of people who have diminished capacity to protect their interests or give consent for themselves, the consent given by the guardian should be witnessed by an independent person who also has to sign the informed consent document. Audiovisual recording of the informed consent process should be undertaken and the documentation preserved, adhering to the principles of confidentiality. Sixthly, If any adverse effect (AE) or serious adverse effect (SAE) occurs during a clinical trial, the sponsor investigator will be responsible for providing medical treatment and care to the patient at his/their cost till the resolution of the *AE/SAE.* This is to be given irrespective of whether the patient is in the control group, placebo group, standard drug treatment group or the test drug administered group. A compensation will be paid to the trial participant if any drug-related anomaly is discerned at a later stage and accepted to be drug related by a competent authority whether in India or abroad. Seventhly, the Government of India, State governments and institutions should create a fund in order to encourage academic and clinical research. The fund may be raised by imposing a cess if needed. This fund will be available to the institution for paying compensation. And last but not the least, information technology will be used at all steps of a clinical trial to ensure total transparency in the system. And a Special Expert Committee should be set up to review all drug formulations in the market and identify drugs which are potentially hazardous and/or of doubtful therapeutic efficacy.[75]

(d) The New Proposed Law

On the recommendation of the Mashlekar Committee, the Central Government drafted an Amendment Bill, the Drugs and Cosmetics (Amendment) Bill, 2007 in the Rajya Sabha on 21st August, 2007, which, *inter alia*, provided for centralised licensing of manufacture of drugs, regulatory provisions for clinical trials and export of drugs and cosmetics, creation of strong, well

equipped, empowered, self managed and independent

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Central Drugs Authority in place of the existing central drugs regulatory body i.e. the CDSCO and do away with the Drugs Technical Advisory Board. The said Bill was referred to the Department-related Parliamentary Standing Committee on Health and Family Welfare for examination and Report. The Committee in its 30th Report made several recommendations, including for creation of a separate Chapter for regulating medical devices. The provisions relating to regulation of clinical trials and exports in the Bill also needed to be made more comprehensive and therefore, the Central Government decided to withdraw the Bill of 2007 and introduce a new Bill, namely, the Drugs and Cosmetics (Amendment) Bill, 2013[76] excluding the provisions relating to AYUSH drugs for which it was suggested that a separate Bill will be brought before Parliament.

The new Bill contains, a revised approach to the centralised licensing, in respect of seventeen categories of very critical drugs included in the proposed Third Schedule to the Act, a separate Chapter containing regulatory provisions for Medical Devices, more comprehensive provisions for regulating clinical trials and exports and a revised composition of the Central Drugs Authority consisting of, *inter alia*, Secretaries of seven Ministries and Departments of the Central Government, four State Drugs Controllers and four experts, with the Drugs Controller General (India) as its Member-Secretary. The proposed new Section 4-A provides for the constitution of the Central Drugs Authority[77]; Section 4-B provides for composition of the Central Drugs Authority; 4-G empowers the Central Government to appoint the Drugs Controller General of India; 4-H empowers the Central Government to create posts in the Central Drugs Authority; 4-I enumerates the powers and functions of the Central Drugs Authority power to issue directions to ensure compliance of guidelines, norms, etc., to review, suspend or cancel permission, licence or certificate issued by the Central or State Licensing Authority; to specify the fees, or charges for issue or renewal of licenses; coordinate, mediate and decide upon the disputes arising out of the implementation of the provisions of the Act, rules, etc., recommend to the Central Government the measures as regards the standards of Drugs, cosmetics, etc. Section 4-J provides for the powers and functions of the Drugs Controller General of India.[78] The Bill also contains Penal

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action include imprisonment of maximum 10 years and penalty of up to Rs. 30 lakh.[79]

The proposed new Section 4-Q empowers the Drugs Controller General of India or any other prescribed authority to decide the cause of injury or death of person which may occur in course of or due to clinical trial. The proposed new Section 4-R provides for the person conducting clinical trial to give medical treatment and compensation in case of an injury or death of a person as a result of his participation in clinical trial. The proposed new Section 4-S empowers the Central Licensing Authority in public interest to abbreviate, defer or omit the pre-clinical and clinical data requirements for approval of clinical trial indicated in life threatening or serious diseases or diseases of special relevance to the country. The proposed Section 4-T provides for the registration of Ethics Committee the period of its validity and its renewal; 4-U provides for the composition of the Ethics Committee; Section 4-V provides for the functions and responsibilities of the Ethics Committee; Section 4-W empowers the Central Licensing Authority to suspend or cancel the registration of Ethics Committee and disqualification of its members on such cancellation, in case the Ethics Committee fails to discharge its functions and responsibility under the Act. The proposed Section 4-X empowers the Central Licensing Authority to carry out inspections of clinical trials; Section 4-Y provides for the person, sponsor and organization conducting clinical trial to disclose name, address and other particulars of the persons involved in conducting the clinical trials, including the trial participants; Section 4-Z provides for the person, sponsor and organisation to maintain of data, records, registers and other documents and furnishing of information related to clinical trials to the Central Drugs Authority. Section 4-ZA

provides for penalty for conducting clinical trials in respect of any drug; Section 4-ZB provides for penalty for repeat offence for conducting clinical trials; Section 4-ZD provides for penalty for repeat offence for conducting clinical trial of cosmetics without permission.

Section 4-ZE provides for penalty for violation of conditions of permission for clinical trials in respect of any drug or investigational new drug or any medical device or investigational medical device or cosmetic. It further provides enhancement of penalty for resulting grievous hurt or death during clinical trial. Section 4-ZF provides for penalty for repeat offence for contravention of conditions of permission for clinical trials in respect of any drug or investigational new drug or any medical device or investigational medical device or cosmetics. Section 4-ZG provides for penalty for failure to provide compensation for clinical trial related injury or death. Section 33-Q empowers the Central Drugs Authority to suspend or cancel any permission, licence or certificate issued by the Central Licensing Authority

or the State Licensing Authority, in the public interest if such permission, licence or certificate is found not to have been issued in accordance with the provisions of the Act; Section 33-R provides for preferring appeal to the Central Drugs Authority against any action or decision of any State Licensing Authority or the Central Licensing Authority and to the Central Government against any action or decision of the Central Drugs Authority. Looking to the above amendments one can say that if Drug and Cosmetic (Amendment) Bill, 2013 is passed by Parliament, it would facilitate the proper and effective implementation of laws related to clinical trials in India.

III. Ethics in Clinical Research

Most basic and complex principle of clinical research ethics is informed consent. An ethically valid informed consent has four key components: disclosure, understanding, voluntariness, and competence. This creates challenges for researchers in pediatrics, psychiatry, emergency and critical care medicine. One can take surrogate consent or waived consent in the following circumstances they are for example where a study of people at risk for Alzheimer's disease, more than 90% thought that surrogate consent was acceptable for minimal risk studies as well as randomized trials of new medications. Whereas in case of intensive care and surgery patients their consent is also informed consent, but in reality people are not aware of the fact that they are in clinical trials.

The ICMR has a Central Ethics Committee on Human Research (CECHR). This committee audits the functioning of the Institutional Ethics Committees (IEC). No Ethics Committee shall review and accord its approval to a clinical trial protocol without prior registration with DCG (I). An application for registration of Ethics Committee is required to be made to DCG (I) along with detailed information about the committee as per Appendix VIII of Schedule Y, which include the Authority under which the committee has been constituted, details of qualification, etc of chairman and the members, procedures for replacement or removal of members, maintenance of records, Standard Operating Procedures (SOPs) to be followed by the committee for various activities like policy regarding training of members, prevention of conflict of interest, procedures for vulnerable population etc.[80] The Ethics Committee shall review and accord its approval to a clinical trial and also carry ongoing review of the trial at appropriate intervals. The Ethics Committee shall allow inspectors of officials authorized by the DCG (I) to inspect their facilities, records, documents etc. The registration of an Ethics Committee shall be valid for a period of three years from the date of issue. If the Ethics Committee fails to comply with any of the

conditions of registration, DCG (I) may suspend or cancel the registration of the Ethics Committee.

Coming to the informed consent the general rule is that consent for most treatments must be an informed consent. This means that the treating provider is required to give to the decision-

maker several elements of information before the consent decision.[81] Patients ordinarily expect physicians to use the drugs and procedures customarily used for their condition. When experimental methods are used or when established procedures are used for research purposes, the investigator must disclose this to the subject and obtain the consent of the subject or the subject's representative.

In November 1999, 25 people with oral cancer who went to the government-run Regional Cancer Centre in Thiruvananthapuram were given an experimental drug, the chemical tetra-O-methyl nor-dihydro-guaiaretic acid (M4N) or tetraglycinyl nor-dihydro-guaiaretic acid (G4N), though there was an established treatment for their condition. They were not told that they were taking part in an experiment or that they were being denied an established treatment. Only later did it become known that the trial had not been approved by the Drugs Controller of India (approval was obtained retroactively). Further, the sponsor institution, the Johns Hopkins University in the United States, had not given ethical clearance to the study, but managed to release the money for research anyway.

Drawing attention to gross violation of ethics during the conduct of trials, it has been pointed out that in Andhra Pradesh out of 9,543 consent forms, 1,948 had thumb impressions while hostel wardens signed 2, 763 others. In Gujarat, out of 6,217 forms, 3,944 had thumb impressions. The data revealed that a very large number of parents/guardians were illiterate and could not even write in their local language, Telugu or Gujarati.[82] How can it be treated as informed consent, it is interesting to note, In Mumbai, a small firm that used to translate legal documents is making a fortune translating informed consent forms into a dozen local languages. Contract research organizations (CROs), which compete with each other to provide clinical trial services for pharmaceutical companies, are mushrooming across India. US companies are acquiring Indian CROs and turning them into hubs of their clinical research activities.[83]

It may be recalled that of the 78 doctors who were found conducting these trials, the State government penalised only 12, with a fine of Rs.

5,000 each. While replying to a question in Parliament about these trials, the Health Minister said that while Schedule Y of the rules and Good Clinical Practice (GCP) guidelines recognised that mentally challenged and mentally differently abled persons, who were incapable of personally giving consent, were considered vulnerable subjects, there was no prohibition under the said rules and guidelines that clinical trials could not be conducted on such patients. For enrolling such patients, informed consent was required from a legally acceptable representative of the patient. The Minister did not specify whether this was done in all the cases or that whether economic compulsions were behind the cases of informed consent. In any event, this was a loophole that needed to be corrected.[84] It was shocking to find from one of the reports that out of 100 consent forms for Andhra Pradesh, project signatures of witnesses were missing in 69 forms. In many forms there were no dates. One particular person had signed seven forms. In fact, the legality of the State government directing headmasters in all private/government/ashram/schools to sign the consent forms on behalf of parents/guardians was highly questionable. The absence of photographs of parents/guardians/wardens on consent forms and of signatures of investigators, the fact that signatures of parents/guardians did not match with their names; and the date of vaccination being much earlier than the date of signature of parents/guardian in the consent forms spoke of grave irregularities.[85]

IV. The *Swasthya Adhikar Manch* Case

Coming to Judicial response, a Public Interest Petition was filed by an Indore based non-profit, organization seeking the court's intervention to put a stop to unethical clinical trials. The petition also highlighted irregularities in drug trials like the principal investigator of a clinical trial also being a member of ethical committee in violation of the ethics guidelines, the inactive role played by ethics committees and no compensation being paid to patients for adverse effects. The petition filed by Swasthya Adhikar Manch was admitted by the Court on February 6, 2012.[86] The Bench comprising Justice R.M. Lodha and Justice H.L. Gokhale issued notices to the Ministry

of Health and Family Welfare, the Indian Council of Medical Research (ICMR), the Drugs Controller General of India (DCGI), the Medical Council of India (MCI) and the State of Madhya Pradesh. They had been asked to review and file replies on the existing rules governing drug trials and the desired amendments within six weeks. The writ petition filed by Swasthya Adhikar Manch[87] came up for hearing on 8th Oct. 2012 before Bench of Supreme Court consisting of Justice R.M Lodha and Justice A.R Dave.[88] Taking a serious view of alleged use of human beings as guinea pigs for *clinical trials* by drug companies, the *Supreme Court* asked the Centre and various *States Governments* to reply to the allegation.[89] A Bench also directed the *Union government* to come out with details of the deaths, if any, and the side effects and compensation, if any, paid to the victims or their family members.[90] The bench while expressing its serious concern, however, refrained from passing any blanket ban on the trials and instead sought a comprehensive reply from the Centre on the four issues.

In the instant case, the petitioner, Swasthya Adhikar Manch filed application for directions regarding investigations of clinical trials of New Chemical Entities (NCEs) without approval as drugs for human use anywhere in the world. Advocate Sanjay Parikh appearing for the petitioner, Swasthya Adhikar Manch drew attention of the court to the illustrative list of all NCEs and 59th report of Parliament Standing Committee dated 8th May 2012, which was submitted to the Court. It was pointed out that the Parliamentary Committee has observed in its report that Indian citizens are being treated as guinea pigs by multinational pharmaceutical industries and the report questioned the role of central and state governments in this matter.[91]

The learned counsel Mr. Parikh also pointed out that the New Chemical Entities (NCEs) of which the foreign pharmaceutical companies hold the patents conduct trials in different countries but the soft targets are developing countries such as India. The data on the side effects and efficacy is generated by Multinational Companies (MNCs) in a country like India at very low cost and without fear of any liability/responsibility. Lured by easy money, free trips to foreign countries, free equipments, hefty payments

to doctors and collusion of drug controlling authorities are some of the apparent causes for continuing trials illegally. The constitution of Ethical Committees as private bodies or within a private hospital or a clinic, is another factor which permits unethical risky clinical trials. Therefore, the drug companies mostly multinational, purely for profits, use the people of our country in clinical trials which have of no benefit to our country'.[92] It was also pointed out that, apart from Madhya Pradesh, there are other States i.e. Maharastra, Andhra Pradesh, Gujarat & all UTs, where illegal & unethical trials are being conducted and they don't have rules related to clinical trials.[93] The Court directed all the States and UTs to provide information related to status of clinical trials in their States. The Court also asked for independent investigation reports, if any, carried out by the State within 8 weeks.[94]

In the *Swasthya Adhikar Manch case*[95], an Intervention application in Writ Petition (Civil) No. 33 of 2012 was filed on behalf of the victims of the Bhopal gas leak disaster by the Bhopal Gas Peedith Mahila Udyog Sanghathan (BGPMUS) and the Bhopal Gas Peedith Sangharsh Sahayog Samiti (BGPSSS), whose members are Indian citizens. The clinical trials which were carried out in the Bhopal Memorial Hospital and Research Centre (BMHRC) on the gas-victims were exposed in January, 2010. The BGPMUS and BGPSSS are deeply concerned with the wholly unethical manner in which many Bhopal gas-victims were used as guinea pigs in several clinical trials and, therefore, sought to intervene in the instant case in support of the Writ Petition.[96]

In the hearing of the matter on the 3rd January 2013, the Supreme Court directed that the clinical trials of new chemical entity shall be conducted strictly in accordance with the procedure prescribed in Schedule 'Y' of Drugs & Cosmetics Act, 1940 under the supervision of the Secretary, Health & Family Welfare. Accordingly, an Apex Committee under the chairmanship of the

Secretary, Health & Family Welfare, with Secretary, Health Research-cum-Director General, Indian Council of Medical Research, and the Director General Health Services, was constituted to monitor the approval and conduct of clinical trials. In this connection,

another Expert Committee under the chairmanship of Director General Health Services had been constituted to assist the Apex Committee.

The Court accepted the statement of Mr. Siddharth Luthra, learned Additional Solicitor General that until further order by this Court, clinical trials of new chemical entity shall be conducted strictly in accord with the procedure prescribed in Schedule 'Y' of Drugs & Cosmetics Act, 1940 under the direct supervision of the Secretary, Ministry of Health & Family Welfare, Government of India.

It was submitted that a certified copy of the above Order was sent to Ministry of Health and Family Welfare (Union of India), Drug Controller General of India and Respondents[97] for information and compliance.

The writ petition filed by Swasthya Adhikar Manch came up for hearing on 26 July 2013 before the bench of the Supreme Court consisting of Justice R.M Lodha and Justice Madan B. Lokur. The present case was filed in February, 2012 and this was the sixth hearing of the case[98], last hearing was held on 3rd January, 2013[99].

In the last hearing, the Hon'ble Supreme Court had directed the Director General, Health Services or the Secretary Ministry of Health to file an affidavit on different aspects concerning the Clinical trials of New Chemical Entities, in particular the deaths and adverse impacts that have taken place from 2005 to June, 2012. The Court had also issued notices to all States and UT's for filing status report on the ongoing clinical trials. Accordingly, reply from 16 States/UTs were filed. All the States/UTs stated that they have no role to play in the clinical trials or their approvals. The additional affidavit was filed by the Secretary, Ministry of Health and Family Welfare on the four issues raised by the Hon'ble court in its order dated 8th October, 2013.

The Additional Solicitor General appearing for the Ministry admitted that the said data was provided by the Companies and that DGC(I) has no data of its own. Therefore, it cannot be said that how many out of 2644 died because of clinical trial and out of 19772 how many suffered SAEs because

out of clinical trials. Therefore, it is obvious that the companies have fudged the data to escape the liability. More shocking fact related to the table given by the Ministry regarding deaths attributable to clinical trials and the compensation paid from 2008 to upto June, 2012.

The Petitioners in their rejoinder affidavit pointed out that though the Ministry of Health and Family Welfare had mentioned 164 deaths in the year 2012, out of which 125 died on account of clinical trial of Rivoroxaben by Bayer, in the letter which was written by Ministry of Health and Family Welfare dated 26.04.2011 to the Lok Sabha Secretariat as many as 671 cases of death in the Year, 2010 alone were reported.[100]

Counsel for Swasthya Adhikar Manch-Mr. Sanjay Parikh mentioned that the reason for so many deaths was because NCEs ware being tested on Indian citizens without following the regulations and taking necessary precautions. It was also urged by the Counsel that the clinical trial of NCEs was not at all beneficial to the Country and therefore, should not be allowed. Mr. Sanjay Parikh also represented the Bhopal Gas Peedith Mahila Udyog Sangathan (BGPMUS) and the Bhopal Gas Peedith Sangarsh Sahayog Samiti (BGPSSS) who are interveners in the instant case.[101]

The Hon'ble Court while passing the order noted the contention that one of the problematic areas is that the NCEs and its regulation and other one is proper monitoring. The petitioner had also pointed out that `during the entire process of clinical trial there was no check by the Drug

Authorities and the entire process of clinical trial is given in hands of Sponsor, Investigator appointed by Sponsor, Expert Committee. As such there was no independent person who gets any information about causes of death and causes of SAEs. Because of this serious lacuna, manipulation of data takes place. After the deaths/SAEs are caused the Drug Company without paying any compensation goes away with the data. Therefore, neither the country nor the citizens are benefited. Even if the medicine is ultimately approved,

citizens have to pay at the same cost as others have to pay in any other country in Asia'.[102]

Advocate Parikh also drew attention of the Court to the fact that after 3 January, 2013 onwards i.e. last six months there had been no improvement as regards clinical trial of NCEs/NMEs and protection of patients. The Rules have not resulted in any enhanced benefit to patients. It was also stated that in cases of death where no investigation/inquiry had been conducted, post mortem are not being done by the Authorities, even when the existing rules provide that.[103] NHRC also intervened in the instant case and stated that the NHRC has also formulated some suggestions regarding strengthening regulations for the conduct of Clinical trials in the interest of patients and wishes to submit its report.

In continuation of the aforesaid orders, the Apex court again expressed concerns about drug trials being permitted on humans without comprehensive rules to regulate the approval process. Records submitted in the court showed that the Health Ministry approved these trials between 3 July and 31 August 2013. A total of 1,122 applications for clinical trials were received this year till 31 August, according to documents submitted in court.[104] The Apex Court directed the Health Ministry to justify its approval for 162 global clinical trials in India, increasing the uncertainty faced by the nation's $500 million clinical research industry.

The approvals for clinical trials are usually given by India's drug regulator, Central Drugs Standard Control Organization, but in a 3rd January ruling[105], the Supreme Court revoked the powers of the regulator to approve trials for new chemical entities (or molecules) because of irregularities in the process. It banned clinical trials for new chemical entities unless these were personally vetted and cleared by the Union Health Secretary. While several amendments had been recommended to the Drugs and Cosmetics Act, no decision had been taking to frame new laws for regulation and ethical supervision of trials; compensation of trial subjects, and mandatory

accreditation of all stakeholders—institutional review boards, research institutions and sponsors. "We are nowhere close to having a comprehensive set of norms governing the clinical trial industry in India at state and central level," said *Sanjay Parikh*, advocate for Indore-based petitioner Swasthya Adhikar Manch, a non-governmental organization. "In less than two months, the government has approved so many clinical trials. There is currently no regulatory regime in place. Rules regarding compensation mechanism are being contested…Even a properly approved clinical trial would take weeks. This sort of approval process is why deaths take place."[106] The proponents of clinical trials argued that clinical research industry has come to a halt with top agencies like the US National Institutes of Health, cancelling nearly 40 clinical trials in the country due to the uncertain regulatory environment. "This has eroded the confidence of Indian and global Biopharma Companies, research and teaching institutions and not-for-profit organizations in doing clinical research in India, a significant decline can be seen in the number of clinical trials done in India."[107]

It is said that neutral experts, court appointed experts, expert panels, special juries and science courts all draw upon prevalent belief in the possibility of locating and employing 'neutral' expert' and 'neutral' or consensual knowledge to resolve disagreement and uncertainty located within the legal system.[108] It appears that policy makers are more concerned with the withdrawal

of multinational companies rather than life liberty of their own citizens. It is high time that State must wake up from long slumber to protect helpless, weaker/oppressed section of Indian Society from being used as guinea pig for clinical trials.

V. Concluding Observations

The clinical trials are conducted for establishing safety and efficacy of new drug before its introduction in the market for the human use. The Committee after Committees have instead of giving a clear direction, confused the position of legal control of clinical trials. It is time that the important role players and stake holders must evolve clear direction to regulate illegal and unethical clinical trials. Further more, their recommendations remained in many cases unattended and uncared for, a national colossal waste.

In our present constitutional set up, Parliament is mandated with the sacrosanct responsibility of monitoring the executive. The Parliamentary Committees taking a leaf out from this mandate carry out their responsibility of oversight/guidance through their Reports presented to the Parliament from time to time. Their advice in the form of Recommendations though not mandatory, is invaluable in the sense that they guide the Government to take remedial measures, were invaluable requiring the government to take remedial measures to solve the problems.

There are fundamental obligation of the State which includes, for example, the health and strength of people are not abused; to develop in a healthy manner and in conditions of freedom and dignity; to improve public health, and what not. On the other hand, the permissible and non-permissible clinical trials have resulted in irrepairable health problems including large number of deaths. The people of India should not allow such silent death. Parliament has baked half-justice. It is time that it must now rise to the occasion and face seriously the newly emerging challenges. It should rigidly control undesirable and injurious activities under the umbrella of clinical trials.

India, as an emerging economy needs to continue to promote a strong culture of research and development, including in the health sector. However, attention needs to be paid for framing stringent rules and regulation to check misuse/abuse of clinical trials in India. It is also necessary that ethical committee should grant permission by taking in to account the conduct of investigator/sponsoring agency and make them accountable for not conducting research in fair and transparent manner.

Coming to judicial response, though the Supreme Court of India has yet to finally rule in this matter. However it has raised a voice to protect helpless citizens from being used as guinea pig for clinical trials. The Supreme Court has expressed its dismay, frustration and disappointment by saying that India is becoming heaven for MNCs Pharma Industries to conduct clinical trials but are proving hell to the Country. The Court's important contribution has been that it has tried to awaken the role players who had gone in hibernation. It is time the Central Government and State Governments must come out with appropriate measures for ensuring safety and security of the helpless and hapless citizen of India from being used as guinea pig for clinical trials for the benefit, in many cases, of other countries. This has to be stopped immediately or else the pious hopes of the great men of India to make every Indian healthy, wealthy and happy, will remain a dream of distant future.

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[1] The ICMR conducted an extensive asthma prevalence survey in four big cities of the country, including New Delhi, Bangalore, Chandigarh and Kanpur. The survey report was based on door-to-door contact in almost every nook and corner of these cities and included a wide and intensive questionnaire. *Ishita Mishra*, 'Industrial City has third highest number of asthma patients' Times of India, Kanpur, May 8, 2013. available at http://articles.timesofindia.indiatimes.com/2013-05-08/kanpur/39115771_1_asthma-patients-bronchial-asthma-survey-report, visited on 15-09-2013.

[2] Diabetes in India available at http://www.diabetes.co.uk/global-diabetes/diabetes-in-india.html.

[3] Available at http://www.indexmundi.com/g/r.aspx?t=100&v=35.

[4] www.who.int/mediacentre/factsheets/fs999/.

[5] Archana Jyoti, 'Despite rise, ministry is in no mood to notify cancer', available at http://www.dailypioneer.com/nation/despite-rise-ministry-is-in-no-mood-to-notify-cancer.html 11 September, 2013, New Delhi.

[6] Heart related disorders will kill about 20 million people by 2015, available at http://www.indiaprwire.com/pressrelease/health-care/20120925132054.htm, http://sathiyam.tv/english/science/heart-diseases-causes-most-deaths-in-india; see also http://articles.timesofindia.indiatimes.com/2013-07-22/chandigarh/40727030_1_heart-attack-primary-angioplasty-dr-jaswal.

[7] B.M. Gupta and Adarsh Bala, "Alzheimer's Disease Research in India: A Scientometric Analysis of Publications Output during 2002-11," Research in *Neurology: An International Journal*, Vol. 2013 (2013), available at http://www.ibimapublishing.com/journals/RNIJ/2013/204542/204542.pdf, See also http://www.worldlifeexpectancy.com/world-health-rankings.

[8] Hypertension major contributor to avoidable deaths in India: WHO, The Hindu 16 March 2013 available at http://www.thehindu.com/sci-tech/health/hypertension-major-contributor-to-avoidable-deaths-in-india-who/article4513904.ece visited on 15-09-2013.

[9] Available at http://www.schizophrenia.com/szfacts.htm#; See also; Sandhya Srinivasan, 'Indian Guinea Pigs for Sale: Outsourcing Clinical Trials', September 8, 2004 available at http://www.indiaresource.org/issues/globalization/2004/indianguineapigs.html visited on 15-09-2013.

[10] Available at http://www.who.int/topics/clinical_trials/en/.

[11] The basic difference between clinical research and Clinical Trials is as under; Clinical research is research that directly involves a particular person or group of people, or that uses materials from humans, such as their behavior or samples of their tissue and a Clinical Trial is one type of clinical research that follows a pre-defined plan or protocol. By taking part in clinical trials, participants can not only play a more active role in their own health care, but they can also access new treatments and help others by contributing to medical research. Available at http://www.nichd.nih.gov/health/clinicalresearch/Pages/index.aspx.

[12] It has been claimed that in the US, trials for a single drug can cost about $150 million. Early estimates are that drugs could be tested in India at 60% of that price. K.S. Jayaraman, Outsourcing clinical trials to India rash and risky, critics warn, available at http://www.nature.com/nm/journal/v10/n5/full/nm0504-440a.html.

[13] *Swasthya Adhikar Manch* v. *Union of India Bhopal Gas Peedith Mahila Udyog Sanghathan (BGPMUS)*...Intervener-Organizations in the Supreme Court of India extra ordinary writ jurisdiction of 2012 in writ petition (civil) no. 33 of 2012. See also, www.unethicalclinicaltrial.org/visited on 02.10.2013.

[14] Responding to allegations by NGO, Swasthya Adhikar Manch, that Indians were used as guinea pigs by foreign pharmaceutical majors for human trial of their new drugs, the Union health and family welfare ministry said of the 57,303 enrolled subjects, 39,022 completed the clinical trials. "Serious adverse events of deaths during the clinical trials during the said period were 2,644, out of which 80 deaths were found to be attributable to the clinical trials," health secretary Keshav Desiraju said in an affidavit on behalf of the ministry of health and family welfare. "Around 11,972 serious adverse events (excluding death) were reported during the period from January 1, 2005 to June 30, 2012, out of which 506 events were found to be related to clinical trials," he said. Clinical trial of two drugs - *Bayer's Rivaroxaban and Novartis's Aliskiren* v. *Enalapril* - accounted for maximum number of deaths.

[15] Available at http://gmandchemicalindustry.wordpress.com/2013/05/08/human-trials-by pharmaceutical-multinationals-have-serious-consequences/visited on 08.09.2013.

[16] As on 20-03-2013, as per the information of National Institute of Health, United States of America (USA), a total number of 1,42,239 clinical trials of different countries worldwide were registered. Out of these, 67,881 are from USA, 38,473 from Europe, 10,702 from Canada, 2,645 from Japan. Only 2,178 clinical trials were registered from India available at www.clinicaltrials.gov.

[17] T. Vijaya Kumar, Women who underwent clinical trials speak to district officials at the Government General Hospital in Guntur in Andhra Pradesh, Available at http://www.flonnet.com/f12913/stories/20120713291302600.htm.

[18] T.K. Rajalakshmi, 'The Parliamentary Committee's report touches upon some important aspects of unethical drug trials, but health activists say that is not enough', available at http://www.flonnet.com/f12913/stories/20120713291302600.htm.

[19] R.P. Dhokalia, "Interaction of Science, Technology & Law in India", 15 *The Banaras Law Journal*, 10, 1979.

[20] Central Drugs Standards Control organization. Ministry of Health and Family Welfare. Available at http://cdsco.nic.in/html/organisationalchart.htm.

[21] As per the Government of India, 'Report of the National Commission on Macroeconomics and Health, Ministry of Health and Family Welfare' (2005), only 17 of the State drug controlling agencies had access to drug testing facilities.

[22] *See* generally; available at http://cdsco.nic.in/CDSCO-GuidanceForIndustry.pdf.

[23] Available at http://www.rajswasthya.nic.in visited on 08-09-2013.

[24] The Drug and Cosmetic Act, 1940 and The Drugs and Cosmetic Rules, 1945 as amended from time to time. Ministry of Health and Family Welfare, Government of India. Available at http://www.cdsco.nic.in/Drugs&CosmeticAct.pdf.

[25] The primary aim of the of the programme is to create and manage a database of reports of Adverse Drug Reactions (ADRs) that would form the basis for regulatory decisions for market authorizations of drugs in India.

[26] The Drugs and Cosmetics Rules, 1945, Schedule Y, Rule 1.

[27] *Id.*, Schedule Y, Rule 1. Regulation of Clinical Trials.

[28] *Id.*, Schedule Y, Rule (2)(5).

[29] *Id.*, Schedule Y, Rule 2(8).

[30] *Id.*, Schedule Y, Rule 2(4)(*i*).

[31] *Id.*, Schedule Y, Rule 2(4)(*ii*).

[32] *Id.*, Schedule Y, Appendix V.

[33] *Id.*, Schedule Y, Rule 3.

[34] *Id.*, Schedule Y, Rule 3.

[35] *Id.*, Schedule Y, Rule 3.

[36] Amendments vide Gazette Notification G.S.R No. 72(E) dated 08-02-2013 specifying requirements and guidelines for registration of Ethics Committee.

[37] *See* generally K.P. Singh Mahalwar, "Experimentation on Human Subjects and the Emerging Law", 27-28 *The Banaras Law Journal*, 26-39, 1992; R.H. Singh and Mrs. Bharti, "Legal and Ethical Implications of therapeutic Trials with special reference to Ayurvedic Drugs and Remedies", 27-28 *The Banaras Law Journal*, 174-177, 1992.

[38] Available at http://cdsco.nic.in/html/D&C_Rules_Schedule_Y.pdf

[39] Mrinali Mudoi, 'India: Latest Amendments in 2013 To The Drugs And Cosmetics Rule, 1945', available at http://www.mondaq.com/india/x/244304/Healthcare/Latest+Amendments+In+2013+To+The+Drugs+And+Cosmetics+Rule+1945.

[40] Insertion of Rule 122 DAC in the Drugs and Cosmetics Rule, 1945 (called as The Drugs and Cosmetics (Second Amendment) Rules, 2013, G.S.R. 364 (E), The Gazette of India Part II-Section 3— Sub-Section (i) June 7, 2013, New Delhi. The Principal rules were published in the Official Gazette vide notification No. F. 28-10/45-H (1) dated 21st December 1945 and last amended vide notification number G.S.R. 72 (E) dated the 8th February, 2013.

[41] Insertion of Rule 122-DD in the Drugs and Cosmetics Rule, 1945 (called as The Drugs and Cosmetics (Third Amendment) Rules, 2013, G.S.R. 72 (E), The Gazette of India Part II-Section 3— Sub-Section (i) February 8, 2013, New Delhi. The Principal rules were published in the Official Gazette vide notification No. F. 28-10/45-H (1) dated 21st December 1945 and last amended vide notification number G.S.R. 63 (E) dated the Ist February, 2013.

[42] Dr. Prem Pais, Clinical trials in India in a crisis: Does it matter? 01 August 2013 available at http://pharma.financialexpress.com/sections/res/2451-clinical-trials-in-india-in-a-crisis-does-it-matter.

[43] Dr. Prem Pais, Clinical trials in India in a crisis: Does it matter? 01 August 2013 available at http://pharma.financialexpress.com/sections/res/2451-clinical-trials-in-india-in-a-crisis-does-it-matter.

[44] *Ibid.*

[45] *Ibid*.

[46] Section 19-A of Indian Medical Council Act, 1956 (as amended in 2001). See also Section 20-A.

[47] The Indian Medical Council (Amendment) Act, 1993, Ministry of Law, Justice and Company Affairs (Legislative Department), 3rd April, 1993 New Delhi, the Gazette of India — Part II, Section 1 No. 54 Dated April, 3 1993; The Indian Medical Council (Amendment) Act, 2001, Act No. 34 of 2001. 3rd September, 2001. The Gazette of India Extraordinary PART II — Section 1 No. 41 New Delhi. Ministry of Law, Justice and Company affairs (Legislative Department), New Delhi, http://www.mciindia.org/acts/Amendments-1.pdf. See also The Indian Medical Council (Amendment) Bill, 2013; On August 19, 2013 the Indian Medical Council (Amendment) Bill, 2013 was introduced in the Rajya Sabha. The Bill was brought in to replace an Ordinance notified on May 23, 2013, to amend the Indian Medical Council Act, 1956. Available at http://www.prsindia.org/billtrack/the-indian-medical-council-amendment-bill-2013-2866/.

[48] CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, available at http://www.cioms.ch/publications/layout_guide2002.pdf (see also; CIOMS & WHO, See also CIOMS & WHO, Council for International Organisations of Medical Sciences, available at http://www.cioms.ch/.

[49] Ethical guidelines for Biomedical Research on Human Participants, Indian Council of Medical Research New Delhi 2006, available at http://icmr.nic.in/ethical_guidelines.pdf. See also; 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).

[50] CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, available at http://www.cioms.ch/publications/layout_guide2002.pdf (see also; CIOMS & WHO, See also CIOMS & WHO, Council for International Organisations of Medical Sciences, available at http://www.cioms.ch/.

[51] *Supra* Note 58.

[52] To ensure transparency in approval of proposals for conduct of clinical trials for drugs by the DCG(I), twelve New Drug Advisory Committees (NDAC) consisting of experts from the government medical colleges and eminent institutions from all over the country have been constituted. Fresh applications of clinical trial proposals of new drug substances excluding investigational new drugs (INDs) are being evaluated by these Committees. For INDs, two separate expert committees have similarly been constituted.

[53] Available at www.ctri.in.

[54] The Pharmacovigilance protocol is a post-marketing tool in ensuring the safety of pharmaceutical and related health products. The protocol is designed for the collation and analysis of data, and the use of the inferences to recommend informed regulatory interventions as well as communicating risks to healthcare professionals and the public. There is provision for monitoring adverse drug reactions of medicines in order to identify previously unexpected adverse drug reactions or to indicate that certain reactions occur more commonly than previously believed (National Pharmacovigilance Protocol (NPP), para 6.1). All pharmaceutical companies are required to submit the Periodic Safety Update Reports (PSURs) every 6 monthly for the first 2 years of marketing in India, and annually for the subsequent 2 years (NPP, para 6.2.); The Advisory Committee shall assess the regulatory information relating to safety in order to determine what action, if necessary, needs to be taken to improve safe use. Based on the available data, the Advisory Committee shall make recommendations on product label amendments, product withdrawals and suspension (NPP, para 6.4. The National Pharmacovigilance Programme shall encourage reporting of all suspected drug related adverse events, including those suspected to have been caused by herbal, traditional or alternative remedies. The reporting of seemingly insignificant or common adverse reactions would be important since it may highlight a widespread prescribing problem; The NPP is a voluntary instrument and there is no framework under which the reports of adverse drug reactions can be addressed in a comprehensive manner. Regulatory assessment has been missing in the past studies of drug reactions. Another area in which the protocol might be lacking is in terms of a clear conflict of interest. The duty to report adverse drug reactions is on the companies, which are developing and promoting those very drugs. The reporting should be done by a permanent and independent body, rather than being left to the companies earning profit out of the sale of drugs. See also; Manish Anand, Nidhi Srivastava and Shilpanjali Deshpande Sarma, SD Sarma, Governance and Nano -Technology Developments: A focus On The Health Sector In India, Volume 9, Issue 1, April 2012).

[55] The clinical trial registry of India (CTRI) is the online registry of prospective clinical trials in India. This is the initiative started by the National Institute of Medical Statistics (NIMS) of the Indian Council of Medical Research and is supported by the Department of Science and Technology (DST) and the World Health Organization (WHO).

[56] The Objective behind registration of Clinical trials is transparency and accountability of clinical research; Internal validity of clinical trials; To oversee the ethical conduct of clinical trials; Reporting of results of clinical trials.

[57] T.K. Rajalakshmi, 'The Parliamentary Committee's report touches upon some important aspects of unethical drug trials, but health activists say that is not enough', http://www.flonnet.com/f12913/stories/20120713291302600.htm.

[58] As against this, the stated missions of Drug Regulatory Authorities of Developed Countries are as follows: United States: The Food and Drugs Administration (USFDA) mission is, "protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs."; United Kingdom: The Medicine and Healthcare Regulatory Authority's (MHRA) mission is "to enhance and safeguard the health of the public by ensuring that medicines and medical devices work, and are acceptably safe."; Australia: The mission statement of Therapeutic Goods Administration (TGA) states: "Safeguarding public health & safety in Australia by regulating medicines…."

[59] Available at http://164.100.47.5/newcommittee/reports/englishcommittees/committee%20on%20health%20and%20family%20welfare/59.pdf for detail, See annexure 6 & 8 of 59th Report of Parliamentary Standing Committee.

[60] In most cases, most of these experts whether appointed by CDSCO or DTAB are from Delhi. The following facts reveal this pattern: Rimonabant was referred to a committee of six experts, all from Delhi; Levonorgestrel: Four out of five from Delhi; Letrozole: Four out of five from Delhi; Sibutramine: All five from Delhi.

[61] Currently, the experts are arbitrarily chosen mainly based on their hierarchical position which does not necessarily correspond to the area or level of expertise.

[62] *See* Para 7.42 of 59th *Report of Parliamentary Standing Committee*, available at http://164.100.47.5/newcommittee/reports/englishcommittees/committee%20on%20health%20and%20family%20welfare/59.pdf.

[63] See Para 7.52 of 59th *Report of Parliamentary Standing Committee*, available at http://164.100.47.5/newcommittee/reports/englishcommittees/committee%20on%20health%20and%20family%20welfare/59.pdf.

[64] Parliamentary Standing Committee on health and family welfare sixty sixth report action taken by the government on the recommendations/observations contained in the fifty ninth report on the functioning of central drugs standards control organisation (cdsco) (ministry of health and family welfare) (presented to the Rajya Sabha on 26th april, 2013) (laid on the

table of lok sabha 26th april, 2013) available at xa.yimg.com/kq/groups/14696929/1081882008/name/66.pdf.

[65] Department-Related Parliamentary Standing Committee On Health And Family Welfare Sixty Sixth Report Action Taken By The Government On The Recommendations/Observations Contained In The Fifty Ninth Report On The Functioning Of Central Drugs Standards Control Organisation (Cdsco) (Ministry Of Health And Family Welfare) (Presented To The Rajya Sabha On 26th, 2013) (Laid On The Table Of Lok Sabha 26th 2013).

[66] *See*, para 3.39 of 66th *Report of Parliamentary Standing Committee on Health and Family Welfare*, available at xa.yimg.com/kq/groups/14696929/1081882008/name/66.pdf.

[67] *See*, 3.43, para 7.27 of 66th *Report of Parliamentary Standing Committee on Health and Family Welfare*, available at xa.yimg.com/kq/groups/14696929/1081882008/name/66.pdf.

[68] *See*, 3.44, para 7.28 of 66th *Report of Parliamentary Standing Committee on Health and Family Welfare*, available at xa.yimg.com/kq/groups/14696929/1081882008/name/66.pdf.

[69] The major objective in India is to determine the applicability or otherwise of the data generated overseas to Indian population, the requirement should be re-assessed and revised as per principles of medical statistics so that major ethnic groups are covered. A corresponding increase in the number of sites so as to ensure a truly representative sample spread should also be laid down in black and white. Furthermore, it should be ensured that sites selected for clinical trials are able to enroll diverse ethnic groups. For domestically discovered drugs, the number of subjects should be revised as well.

[70] *See*, 3.45, para 7.29 of 66th *Report of Parliamentary Standing Committee on Health and Family Welfare*, available at xa.yimg.com/kq/groups/14696929/1081882008/name/66.pdf.

[71] *See*, Para 3.200 of 66th *Report of Parliamentary Standing Committee on Health and Family Welfare*, available at xa.yimg.com/kq/groups/14696929/1081882008/name/66.pdf.

[72] *See*, Para 4.4 of 66th *Report of Parliamentary Standing Committee on Health and Family Welfare*, available at xa.yimg.com/kq/groups/14696929/1081882008/name/66.pdf.

[73] Terms of reference of the committee was; 1. To formulate policy, guidelines and standard operating procedures (SOPs) for approval of new drugs including biologicals, with special emphasis on the following: a) Planning a transparent and equitable system of clinical evaluation of new drugs; b) Requirements of a local clinical trial on the Indian population for drugs approved in other countries; c) Specific circumstances, if any, under which a local clinical trial can be abbreviated, relaxed or omitted; d) Types of local clinical trial, their design, sample size, sites and their distribution, inclusion of ethnic population, etc. in the local clinical trial; e) Requirements of post-marketing (Phase IV) trials to assess safety of new drugs in the post-marketing scenario. 2. To formulate policy, guidelines and SOPs for approval of clinical trials including global clinical trials of new drug substances discovered abroad and bioavailability and bioequivalence study for export, with special emphasis on the following: a) Monitoring the functions of ethics committees; b) Accreditation of clinical trial sites and investigators; c) Clinical trial inspections; d) Participation of state authorities in monitoring of clinical trials. 3. To formulate policy, guidelines and procedures for examination of issues related to continued marketing of drugs, not only due to safety or other reasons, but also due to launch/availability of safer and more efficacious alternative drugs in the country. 4. To formulate guidelines and SOPs on the functioning of new drug advisory committees (NDACs). 5. To formulate policy and procedures for identification of experts for advising Central Drugs Standard Control Organization (CDSCO) in various matters. 6. To advise CDSCO in other matters referred to it for advice. Available at http://www.cdsco.nic.in/Report_of_Dr_Ranjit_Roy.pdf.

[74] *The Report of the Prof. Ranjit Roy Chaudhury expert committee to formulate policy and guidelines for approval of new drugs*, clinical trials and banning of drugs July 2013 available at http://www.cdsco.nic.in/Report_of_Dr_Ranjit_Roy.pdf.

[75] Arti Dhar "Panel recommends sweeping changes in clinical trials", *The Hindu*, Allahabad, September, 18, 2013 p-2.

[76] The *Gazette of India Extraordinary*, Part II — Section 2, August 29, 2013/New Delhi, available at http://www.drugscontrol.org/Bill%20No.%20LVIII%20of%202013.pdf.

[77] *Ibid.*

[78] 4-J(*3*) empowers the Drugs and Controller General of India to delegate his powers with the prior approval of Central Drugs Authority; 4-J(*4*) provides that the Drugs Controller General of India shall be the legal representative of the Central Drugs Authority and 4-J(5) provides that the Drugs Controller General of India shall have administrative control over the officers and employees of the Central Drugs Authority. The proposed new Section 4-K provides for financial grants to be made by the Central Government to the Central Drugs Authority.

[79] 4-ZB of Drug and Cosmetic (Amendment) Bill 2013 available at http://www.drugscontrol.org/Bill%20No.%20LVIII%20of%202013.pdf.

[80] *Ibid.*

[81] The Robber D. Miller, "Decision-making Concerning Individuals", in *Problems in Health Care Law*, (Ninth Edition), 339, 2006.

[82] *Ibid*, See Para 6.12.

[83] K.S. Jayaraman, Outsourcing clinical trials to India rash and risky, critics warn available at http://www.nature.com/nm/journal/v10/n5/full/nm0504-440a.html.

[84] T.K. Rajalakshmi, 'The Parliamentary Committee's report touches upon some important aspects of unethical drug trials, but health activists say that is not enough', http://www.flonnet.com/f12913/stories/20120713291302600.htm.

[85] *See* Para 1.2 of Department-related Parliamentary Standing Committee on Health and Family Welfare Seventy-Second Report on Alleged Irregularities in the Conduct of Studies Using Human Papilloma Virus (HPV) Vaccine by Path in India (Department of Health Research, Ministry of Health and Family Welfare) Presented to the Rajya Sabha on 30th August, 2013, Laid on the Table of Lok Sabha on 30th August, 2013, Available at http://164.100.47.5/newcommittee/reports/EnglishCommittees/Committee%20on%20Health%20and%20 Family %20Welfare/72.pdf, See Para 6.14.

[86] *Swasthya Adhikar Manch, Indore etc.* v. *Ministry of Health & Family Welfare etc.*; The Supreme Court of India Civil Original Jurisdiction. http://courtnic.nic.in/supremecourt/temp/wc%2033rpt.txt.

See also, Ankur Paliwal, 'Supreme Court issues notices on unethical drug trials', Feb, 2012 http://www.downtoearth.org.in/content/supreme-court-issues-notices-unethical-drug-trials.

[87] Unethicalclinicaltrial.org/…/Bhopal%20Gas%20peedit%20Mahila%20Ud…

[88] http://napm-india.org/node/799.

[89] Supreme Court seeks governments' replies on human trial of drugs Oct 8, 2012, http://articles.economictimes.indiatimes.com/2012-10-08/news/34322898_1_clinical-trials-swasthya-adhikar-manch-side-effects.

[90] Supreme Court seeks governments' replies on human trial of drugs Oct 8, 2012, http://articles.economictimes.indiatimes.com/2012-10-08/news/34322898_1_clinical-trials-swasthya-adhikar-manch-side-effects.

[91] *Supra* note 134.

[92] Vide Order dated 09.08.2012.

[93] *Supra* note 139.

[94] The Supreme Court directed the Ministry of health and Family welfare & CDSCO to provide status of number of New Chemical Entities experimented between Jan. 2005 to 30th June 2012; Besides this number of deaths and instances of serious adverse impacts due to these trials should be provided too; To provide the list of persons to whom compensation was given to those who died during the process and also those who suffered severe adverse impacts in the course of Clinical trials.

[95] *Swasthya Adhikar Manch* v. *Union of India*, Bhopal Gas Peedith Mahila Udyog Sanghathan (BGPMUS) & Anr.…Intervener-Organizations in the Supreme Court of India extra ordinary writ jurisdiction in writ petition (civil) no. 33 of 2012.

[96] *Bhopal Gas Peedith Mahila Udyog Sangathan* v. *Union of India*, (2012) 8 SCC 326.

[97] Vide Registry's letter dated 05.01.2013.

[98] Supreme Court's Orders dated 6th February 2012, (Hon'ble Mr. Justice R.M. Lodha hon'ble Mr. Justice H.L. Gokhale); dated 26th March 2012 (Hon'ble Mr. Justice R.M. Lodha Hon'ble Mr. Justice H.L. Gokhale); dated 16th August 2012 (Hon'ble Mr. Justice R.M. Lodha Hon'ble Mr. Justice Anil R. Dave); dated 8th October 2012 (Hon'ble Mr. Justice R.M. Lodha Hon'ble Mr. Justice Anil R. Dave) WP(C) No. 33/2012 with WP(C) No. 79/2012.

[99] The matter is still pending (WP(C) No. 33/2012 with WP(C) No. 79/2012) in the Supreme Court of India. Available at http://napm-india.org/content/pharma-mncs-india-heaven-clinical-trials-hell-country-supreme-court.

[100] According, to the list provided in Annexure B to the said letter, in case of deaths which had taken place due to trial of Rivoraxaban the reason mentioned was cardiac arrest and the said reason was said to be not related to clinical trial. Out of 125 deaths which had taken place due to Rivoraxaban, Bayer paid compensation to only 5. From the said annexure B it also came out that other companies also participated in clinical trials of new chemical entities but their names have not been mentioned by the Ministry in the additional affidavit. The drug company-Sanofi did clinical trials because of which 135 persons died whereas in the additional affidavit only 5 deaths have been mentioned in the additional affidavit. As per Annexure B, 89 deaths took place in 2010 alone due to clinical trials as against 80 which Ministry of Health and Family Welfare claimed from year 2005 to 2012. The list of drug companies that conducted the trials included several pharmaceutical companies such Bayer, Eli Lilly, Pfizer, Sanofi Intas, Merck, Boahringer, Astrazeneca etc. The name of one of the pharmaceutical company-Novartis was missing from the list.

[101] *Swasthya Adhikar Manch* v. *Union of India*, Bhopal Gas Peedith Mahila Udyog Sanghathan (BGPMUS) & Anr.…Intervener-Organizations in the Supreme Court of India extra ordinary writ jurisdiction in writ petition (civil) no. 33 of 2012.

[102] Vidya Krishnan, 'SC asks why govt approved 162 global clinical trials in India', Sep 30 2013.

[103] As per the letter dated 26.04.2011 written by the Ministry to Lok Sabha Secretariat, from the year, 2005 to 2010 alone 1243 global clinical trials have been permitted. In the year, 2006 alone 671 death have occurred. The list annexed with the letter accepts that 89 deaths were related to clinical trials in the year, 2011. Out of 26 cases entitled for compensation details of only 19 persons were given. Out of the 19 persons only three have peen paid compensation. In the other letter dated 06.06.2011 it has been mentioned that out of 645 cases of death response has been received only in 300 cases and out of 300 in only 2 cases compensation and treatment expenses have been paid.

[104] Vidya Krishnan, 'SC asks why govt approved 162 global clinical trials in India', Sep 30 2013.

[105] *Swasthya Adhikar Manch* v. *Union of India*, WP (C) No. 33 of 2012, order dated 3-1-2013 (SC).

[106] Vidya Krishnan, 'SC asks why govt approved 162 global clinical trials in India', Sep 30 2013.

[107] Industry analysts estimate a loss of $150-200 million this year alone on account of the regulatory uncertainty. Research firm Frost and Sullivan puts the size of the clinical trials business in India at $500 million currently and expects it to grow to $1 billion by 2016. Vidya Krishnan, 'SC asks why govt approved 162 global clinical trials in India', Sep 30 2013.

[108] Gary Edmond, "Judicial Representation of Scientific Evidence", 63 *Modern Law Review*, 216, 242, (2000).