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Clinical Trial in India: a Boon or Bane

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ABSTRACT

The study of Pharmacodynamic and Pharmacokinetic characteristics of new chemical entity (NCE), device on a specific kind of patient, different dose treatments, therapies and surgical procedures to observe behavioral changes due to drug, before making it publicly available. It also examines safety and efficacy of already marketed medication or device for a new indication. These studies help in ensuring the effectiveness of new medicine or device in comparison with the old ones. India emerged as the most suitable country in the world for clinical trial during 2006 and 2010. Many reasons and facilities attracted outsiders for clinical trial in India. Those were mainly big population, availability of new patients for diverse treatment, low cost of drug experimentation and speedy approval. This was a big advantage for our country in terms of financial and scientific gain especially for individual who could not afford for medicines because of poverty. However, unethical practices, noncompliance of regulatory guidelines and protocol, conduction of trials without the approval of ethics committee were some of the discrepancies which converted it from boon to bane. There were several reports of exploitation of the poor and illiterate Indians. It was assumed that they were treated as guinea pigs for clinical trials. Increasing reports of trial participant fatalities aroused the need of robust vigilance. In 2013, the Supreme Court of India took serious cognizance on the PIL filed by Non-Government Organizations. All trials of new drugs were subsequently put on hold and passed strict regulation of three tier screening of their clinical trial documents before supplying drugs to the market. DCGI and ethics committee are the supervisory body of clinical trial to ensure safety, efficacy and quality of trial.

Keywords: *Pharmacokinetics; Pharmacodynamics; Clinical Trial; Safety and Efficacy; Public Interest Litigation (PIL); Ethics Ommittee; DCGI.*

1.0 Introduction

Clinical trial is similar to any other standard scientific and research activity since it is passed through specific objective and well framed procedure in ethical way. This research plays key role to ensure the safety and efficacy of new drugs, new dosages, therapies, surgical procedures and new medical devices on a specific kind of patients to monitor their behavioral and physical state. Moreover, the research is also important to confirm safety and efficacy of already marketed medication or device for a new indication. It compares effectiveness of two drugs for the same disease to set a standard therapy1. There should be a balance between medical research and patient safety. Hence, there are some regulations regarding clinical trials which help to ensure this balance. In India, we have enough regulations for import, manufacture, clinical research, sale and adverse drug reaction monitoring after independence. However, a no. of fraudulent foreign manufacturers came to India in early decades of 20th century to expand their business and enterprises in medical field. Indian market was over flooded with their spurious and adulterated drugs. Chopra Drug Inquiry Committee was constituted to inquire about big fraud of quinine drug. Chopra Committee recommended amendment to Drug and Cosmetics Act of 1940 which is known as Drug Bill to import drugs from abroad. Afterwards, central legislation also established Central Drug Standard Control Organization (CDSCO) under the chairmanship of Drug Controller General of India (DCGI)2.

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The Ethical impact of clinical trials became progressively significant since 1945. It resulted in robust regulation of medical experiments for safety and well being of subjects. These regulations have been justified in documents such as the Nuremburg Codex (1947), Declaration of Helsinki (1964, amended in 1975, 1983, 1989, 1996, 2000 and 2001), Good Clinical Practices (GCP) and EU regulations.

The concept of Good Clinical Practices (GCP) has created awareness among Indians regarding an ethical and a scientific quality standard for designing, conducting and recording trials that involve the participation of human subjects. But So far, all these practices have not been implemented fully.

Foreign companies were fearful in introducing their new innovative product in Indian market after getting process patent approval in 1970 in India. It was easier to conduct trial in India than in North America or Europe due to strict legislation and patient's awareness of their rights.

There was no compulsory registration system for clinical trials in India until 2006 then in order to ensure accountability, transparency and information sharing to make clinical trials a public subject. CDSCO has launched online Clinical Trial Registry (CTRI). CTRI saves time and money of pharmaceutical Company though it is freely accessible and provides risk, benefits, limitations and other outcomes of registered trial. 3-4

2.0 Discussion

Large population with ethnic varieties, speedy regulatory approval, quick recruitment process, good medical and IT infrastructure at low cost and trained English speaking man power made Clinical trial a boon in India. In terms of cost minimization, India was followed by Russia, Argentina, and China.

However, low labour cost in India made it vibrant place for clinical trial. Tax incentives to clinical research organization (CROs) and no data exclusivity in clinical trial made additional advantage for foreigner to attract for such a trial in India.5

Initially, foreign company was keenly interested in clinical trial in Indian pharmaceutical industry through outsourcing pre- clinical and clinical bio-medical research due to above mentioned facilities. The total numbers of clinical trials conducted in India were 221 in 2007 and had reached over 700 trials in 2008. It was estimated that it would grow exponentially at annual growth rate of 30%. In India, Clinical research increased by 84% during 2006-2008. Clinical research industry in India touched US$ 320 million in 2009, up from US$ 140 million in 2006, making the subcontinent one of the world's most preferred destinations for clinical trials.

The Indian Patent Act's was amended in March 2005 gave assurance to the foreign companies that data collected during and after the trials would not be used by local companies to manufacture and market cheap generic versions. India emerged as the second most preferred country in the world to conduct clinical trials next to the USA in 2009. Presently, Phase II and phase III clinical trial in India Constitute more than 80%. More than 100 pharmaceutical industries like Pfizer, Glaxo Smith Kline, Aventis, Novartis, Astra Zenica, Eli Lilly were conducting clinical trial in India during its booming period.

Apart from those foreign companies, some Indian companies like Dr. Reddys, Nicholas Piramal, Cipla and Lupin were also engaged in clinical trial.

The Indian government agreed to the demands of drug industries and announced the time limits for the approval of drug by DCGI i.e 90 days for Phase I trials, 45 days for Phase II trials and 45 days for Phase III trials. 6

The application is considered as approved beyond the time limits without having any reply from DCGI. Nevertheless, a decline in number of trials has been marked in recent years in India. It reduced from 500 in 2010 to 107 in 2013. In the same vein, availability of drug in Indian market had been subsequently reduced

The number of drugs decreased 270 in 2008 to 140 in 2011. Similarly, the number of drugs was counted less than half from 44 in 2012 to 25 in 2013.7

Table 1: Clinical Trial Approved by DCGI (Source- CDSCO Website)

Year	Approved trial by DCGI
2007	3
2008	65
2009	391
2010	500
2011	321
2012	262
2013	107
2014	150
2015 (Jan – April)	19
Total	1818

Several factors are found to be responsible for such a decrease in supply of drugs:

Investigators are not as skilled and aware in India as they are in the west. They have casual approach in obtaining consent from patients and also do not abide by robust guidelines to set standard. Around 70% of the total cost of developing molecule as a drug is incurred for clinical trial in fatal diseases.

Moreover, pharmaceutical company has to submit several reports for approval within the stipulated time. Therefore, they work under anxiety and may produce false data with inadequate documentation. Sometimes, the pharmaceutical companies do not show compliance to protocol due to limiting factor like rare diseases. Seasonal variation also becomes obstacle while conducting infectious diseases clinical trial, e.g. Influenza.

Indian regulatory body is understaffed and lacking expertise professionals to evaluate clinical trial protocols which cause delay in approval. There are some examples of approval of drug without clinical trial. Central Drugs Standard Control Organization approved 33 new drugs between January, 2008 and October, 2010 without testing them through trials on Indian patients because these drugs were for serious diseases and could cause death to patients during trial. In India, patient's illiteracy, poverty and unawareness of their rights subjected to exploitation in the hands of sponsors and investigators. Restrictions were necessary to overcome such exploitation of participants of clinical trial to ensure safety and well being of the trial subjects.

Seven girls died in 2009-2010 in Andhra Pradesh and Vadodra (Gujarat) during unethical trial of HPV Vaccine that was conducted by Indian and International pharmaceutical companies. According to The Times of India report - 2,644 died during clinical trial of drugs in 7 years, It raised grave concerns on clinical trial, even though the dependent of few families did not get any compensation. According to report of social activist to BMJ, 162 applications regarding global clinical trials including new chemical entities and new molecular entities were approved by the DCGI between July 3, 2013 and August 31, 2013. 8

It is a cumbersome task to approve such a big number of clinical trials in a short period. Thus it is clear that the Indian government has not monitored clinical trials as per prescribed norms.

The court made the stringent decision and held the trial of new drugs for a period, till the government would submit all documents of investigations and monitoring, after a petition filed by an Indore and Pune based health activist group on 30 September 2013. It was a revolutionary step of the court to strengthen the regulatory framework of clinical trials in the country. In addition to that the Supreme Court also assessed risk vs benefits to the patients, innovation vs prevailing medical options and current needs of medical science. The bench of court advised the government to take a balanced approach in order to save the patient from unsafe drug and continue the development in the areas of research.

Those decisions of the Supreme Court's are considered in favor of Indian patients but that adversely affect clinical trial of foreign pharmaceutical companies. In this way, India has lost opportunity and attraction of clinical trials by foreign companies.

CDSCO has issued a number of guidelines to make changes in the policy of the governing body to regulate clinical trial in India.

They are as follows:

- Sponsors, investigators, the regulator and Ethics Committees are responsible for ensuring that the design of placebo-controlled trials is appropriate, efficient and ethical;

- Investigators are limited to working on a maximum of three trials simultaneously;
- If a new chemical entity is approved in the innovator or "well-regulated" country for a disease prevalent in India, and the clinical trial included Indian participants, CDSCO advises that "approval should be sought from CDSCO" and "these NCEs should be marketed in India speedily." CDSCO also specifies that if a foreign trial included Indian participants, the number would have to be "adequate" for considering approval of the drug in India;
- Waiver of clinical trials in Indian populations with drugs already approved outside India will only be considered in cases of national emergency, extreme urgency and epidemic, and for orphan drugs for rare diseases and drugs for conditions/diseases for which there is no therapy;
- Generics and biosimilars marketing "in other countries like USA" for over four years and have a "satisfactory report" can be approved in India after abbreviated trials;
- Consideration of new drug applications will take into account ethnic differences in metabolism etc.;
- If two or more countries remove a drug from their market on the grounds of safety and efficacy, the continued marketing of the drug in India "will be considered for examination and appropriate action" by CDSCO; and Manufacturers, sponsors and CROs are advised to provide compensation for any drug-related anomaly detected at a later stage. 9

Moreover, recent amendments in Schedule Y in 2013 were the steps taken for further strengthening of clinical trial regulations for generating authentic bio medical data.

These regulations can be briefly summarized as:

1. *GSR 53 E; 30th Jan. 2013*: Serious Adverse Event (SAE) Reporting and Compensation for study Related Injury.
2. *GSR 63E; 1st Feb. 2013*: Conditions to be fulfilled by Sponsor to conduct clinical trial in India
3. *DCGI order dated 19th Nov. 2013*: Audio visual Recording of Informed Consent Process.
4. Expert committees have been constituted for examination of Serious Adverse Events other than death related to clinical trials.
5. *GSR 889E; 12th Dec. 2014*: Notification about specific provisions in respect of compensation for ineffectiveness and placebo controlled trials.
6. The National Accreditation Board for Hospitals and Healthcare Providers (NABH) has finalized the report on Accreditation Standards for Clinical Trials for Ethics Committee, Investigator and Clinical. 10

3.0 Conclusion

India has witnessed several ups and downs in various phases of clinical trial due to flexibility of its policies, rules and regulations. In the very beginning period of clinical trial from 2007- 2010 was a booming time in India. A good number of foreign companies rushed to India for conducting clinical trial. It also left a remarkable impact on GDP of our country. Owing to various reasons, a sharp declination was noticed in clinical trial by foreign pharmaceutical industries from 2011-2015. The supreme court of India took cognizance of irregularity and practices leading to several deaths during clinical trial.

The Supreme Court made firm decision and stopped all trials for a time being and suggested the governing body to supervise and monitor clinical trial thoroughly from safety and ethical point of view. Afterward, DCGI amended the guidelines of Schedule Y. Through this long discussion it is obvious that clinical trial in India is a boon if it is conducted in accordance with the given rules, regulations and guidelines.

There is a need of practically understanding of amendments so that changes can be done according to requirement and situations. They should also be transparent and in the interest of patients and pharmaceutical companies as well.

References

[1] Susan Devine, CCRP, Ramzi N. Dagher, MD, Karen D. Weiss, MD, and Victor M. Santana, MD. Good Clinical Practice and the Conduct of Clinical Studies in Pediatric Oncology: Pediatr Clin North Am. 2008 Feb; 55(1): 187–xii.

[2] *Imran* M, Najmi *AK*, *Rashid* MF, Tabrez S, Shah MA. Clinical research regulation in India-history, development, initiatives, challenges and controversies: Still long way to go: Journal of Pharmacy & BioAllied Sciences. 2013 January –March; 5 (1): 2-9.

[3] Shetty Y. C, Marathe. P.A, et.all. A study to assess completeness of project application forms submitted to Institutional Ethics Committees (IEC) of a tertiary care hospital: Perspect Clin Res. 2012 Oct-Dec; 3(4): 133–138.

[4] http://ctri.nic.in/Clinicaltrials/login.php

[5] http://mohfw.nic.in/WriteReadData/l892s/3683263752ENGLISH_ANNUAL_REPORT_2010-11.Cited on 10/2/16

[6] http://www.kppub.com/articles/sep2010/present_status_of_clinical_trials_in_india/present_status_of_clinical_trials_in_India.html. cited on 11/2/16

[7] http://www.cdsco.nic.in/forms/Default.aspx cited on 7/2/16.

[8] http://timesofindia.indiatimes.com/india/2644-died-during-clinical-trial-of-drugs-in-7-years-Govt-to-SC/articleshow/19719175.cms.

[9] http://www.raps.org/regulatory-focus/news/2014/07/19675/India-Releases-New-Clinical-Trial-Rules/

[10] Vihang S. Chawan, Kalpesh V. Gawand, Abhishek M. Phatak. Impact of new regulations on clinical trials in India: International Journal of Clinical Trials. 2015 Aug; 2(3):56-58.