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## **Clinical trials in India – Changing regulatory environment**

According to a recent report published by the Tufts Center for the Study of Drug Development, the average cost of developing a new drug – from identifying a potential candidate to its discovery, development and commercialisation, is approximately US\$ 2.6 billion. It is estimated that of the total drug development cost, only about 30 per cent cost goes into drug discovery and development. The balance 70 per cent is spent on conducting clinical testing.

### **Early years**

After becoming fully TRIPS compliant in 2005, India emerged as a favourable destination for conducting clinical trials. Various factors were in favour of India such as large pool of patients, highly skilled medical investigators and related professionals like physicians, nurses, clinical research assistants and clinical practitioners well qualified in fields like mathematics and computer science and timely completion of trials. It is estimated that India offers 35 to 60 per cent cost advantage compared to the western markets. All these factors gave India a favourable edge over other competing nations like China, Russia and Argentina and its share in the global clinical trials increased from 0.9 per cent in 2008 to 5 per cent in 2013.

### **Set back**

However, in 2013, the Supreme Court of India stopped approval of new clinical trial applications following a public interest litigation filed by an NGO due to alleged trials related deaths and Serious Adverse Events and directed the government to amend the regulatory mechanism to ensure patient safety. The objective was to improve patient safety, reporting timeliness of serious adverse events, including deaths, during clinical trials and to ensure that patients get their due compensation.

In response, the government introduced new measures which required that compensation had to be paid to affected patients irrespective of whether the damage was caused as a result of the trial or not. The government also made it mandatory that all companies engaging in clinical trials must maintain audio-visual recording of 'informed consent' of the patients participating in the trial. Both these new policies shook the entire pharmaceutical industry and caused them irreparable damage. Clinical trials in India reduced drastically and the progress of the existing trials were very slow. These changes in the regulatory framework forced many multinational pharmaceutical companies to withdraw their clinical studies from India resulting in a standstill for the entire clinical research industry in the country.

## **Revival**

Subsequently, the Ministry of Health, convened an Advisory Council to formulate more practical policies related to the approval of clinical trials and new drugs. Following extensive input from various stakeholders - sponsors, CROs, investigators, pharma industry - the committee recommended changes to the regulatory framework with an objective to revive the industry while ensuring that they are based on sound science and the highest ethical standards.

According to the new regulations, all clinical trial applications (CTA) have to be submitted online and shall be reviewed by a Subject Expert Committee (SEC), Technical Committee and an Apex Committee. The major criteria for review are assessment of risk versus benefit to the patients, innovation vis-a-vis existing therapeutic choice and fulfilling the unmet medical needs of the country. The SEC has replaced the earlier NDAC and approximately 25 other subcommittees thus speeding up the approval process.

One big improvement is that regulators have provided a pre-trial checklist to help sponsors ensure that their CTA dossier meets all the information requirements from the outset, avoiding potential delays down the road. Another improvement is that the CTA submission can include an application for an import and export "No Objection Certificate" (NOC) license. Previously, sponsors could not apply for an import/export license until after their CTA was approved. This has brought predictability and defined the timelines for the process. If all documents in the dossier are in order, one could expect to commence the studies in about six months of submitting the application.

According to the revised regulations, compensation had to be paid to the patients only if there is definitive proof that the damage caused to them was because of the experimental drug. This is in line with global practice. A clear formula has also been defined to determine compensation for fatal and non-fatal injuries. Initial medical care however needs to be provided to the patient regardless of causal relationship to study participation by the patient.

Requirement of audio-video recording of consent procedure also has been clarified. It is mandatory only for health human volunteer studies and only the vulnerable patients as identified by CDSCO and EC during the approval process.

Independently functioning Ethical Committees (EC) at hospitals and investigator sites were accredited by the Central Drugs Standard Control Organization/Drugs Controller General of India (CDSCO/DCGI). The main aim of these committees was to scrutinize clinical trials and to ensure that they are conducted fairly and in an unbiased manner. The restriction on the number of trials an Investigator can undertake has also been removed and the EC has been empowered to approve the involvement of an Investigator in a trial based on the risk and complexities involved.

The 50-bed restriction for conducting clinical trials has also been done away with and the EC can decide the suitability of a site for conducting clinical trials irrespective of the number of beds. The EC can also approve the addition of a new site or investigator to a trial in the normal course without obtaining an NOC from DCGI.

Currently, the DCGI also requires a confirmatory phase 3 study that includes a portion of local patients, although if Indians are included in multinational trials then this policy can be avoided and decisions can be made on a case-by-case basis. The CDSCO handles the approval process for all clinical trials and apart from this, DCGI has given rights to each state's drug control authority to regulate the manufacture, sale and distribution of drugs.

In a major relief for the industry, the requirement for getting the approval of the Indian Council of Medical Research (ICMR) for importing or exporting biological samples has been removed. All such shipments can now be directly cleared at the port of entry or exit based on a self-declaration by the applicant that all applicable rules and regulations will be complied with. Also all import license applications now need to be submitted electronically and Zonal Centres have been authorized to provide approvals thereby reducing the approval time to 1-2 weeks.

The Indian clinical trials industry has been on a roller-coaster ride over the past decade; peaking in 2011-12 significantly losing out over the next two–three years and now once again slowly showing signs of revival. The recent regulatory and policy changes announced by the government has once again made clinical trials in India lucrative for the global healthcare industry.

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**Source:**

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