Bio-business in brief: The challenges of clinical trials

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Many individuals and institutions doing many things over long periods, often with significant pressures and not necessarily in ideal settings. All working to answer a single question. That is the world of CLINICAL TRIALS†. It is therefore not possible to start thinking about this issue without a sense of inadequacy. Nevertheless, clinical trials are currently a growth industry in India, and hence it is worth learning about them.

Keywords: Bio-business, clinical trial, ethics.

The complexity of clinical trials

AS lay people, we think of a trial as something done by a large (usually foreign) pharma company, in which a new drug is tested on humans. This is an incomplete picture.

Who conducts these clinical trials? Trials can indeed be conducted by a drug company, foreign or Indian. Or a company could outsource the work to a specialist Clinical Research Organization (CRO). Aside from trials done by or on behalf of the drug industry, public institutions (such as ICMR institutions in India and the NIH in the US) may also conduct trials. These trials could be, for instance, for reasons of public health or for conditions that are not of particular interest to the drug companies. Finally, a clinician – at a for-profit or not-for-profit hospital – may also initiate a trial on his or her own.

Furthermore, if a person is willing to be a part of a clinical study or a trial, it is assumed that a new drug candidate is being tested. However, there are several kinds – such as preventive, diagnostic, screening and quality of life trials – that may not involve any intervention. In fact, about three decades ago, a survey of the performance of American Institutional Review Boards (IRBs) reported that 60% of the studies were biomedical, of which only half involved administering a drug candidate or blood product to the RESEARCH SUBJECT and the other half involved studying blood or tissue samples; about 33% involved behavioural studies, about 1% involved surgery and the final 6% undertook secondary analysis of pre-existing data[1]. Although these figures may have changed, the point is that a variety of studies take place, with different levels of attendant risk.

Thus, there are a variety of SPONSORS and several types of trials. To add to the complexity of the story, the locations for conducting trials also vary. The trials follow the patients, so to speak. A specialty hospital or a big clinic would be a good site because of the number of patients being treated. It is also easier to monitor urban patients more regularly than if a patient has to periodically travel from a rural area to the urban hospital. However, studies can also take place in academic settings or in other not-for-profit ones.

The clinical trial process

We provide a brief outline of the clinical trial process in Figure 1. In order to ensure that the risk to any person taking part in a trial is minimal, several checks and balances are built into the process as follows:

- The PROTOCOL committee (put together by the sponsor), and sometimes editors of journals, review proposed protocols and recommend changes if required.
- The national drug regulatory body – the Drugs Controller General of India (DCGI) in India and The Food and Drug Administration (FDA) in the US – needs to give approval to start a trial.
- The ethics board – including medical doctors and other biomedical researchers and also people with completely different expertise, such as lawyers or lay people – of an institution hosting a trial also needs to pass the protocol before the trial is initiated. A point to note is that the names and contact information of the subjects are kept strictly confidential and are not conveyed to the sponsors at any time.
- The research subject needs to give INFORMED CONSENT.

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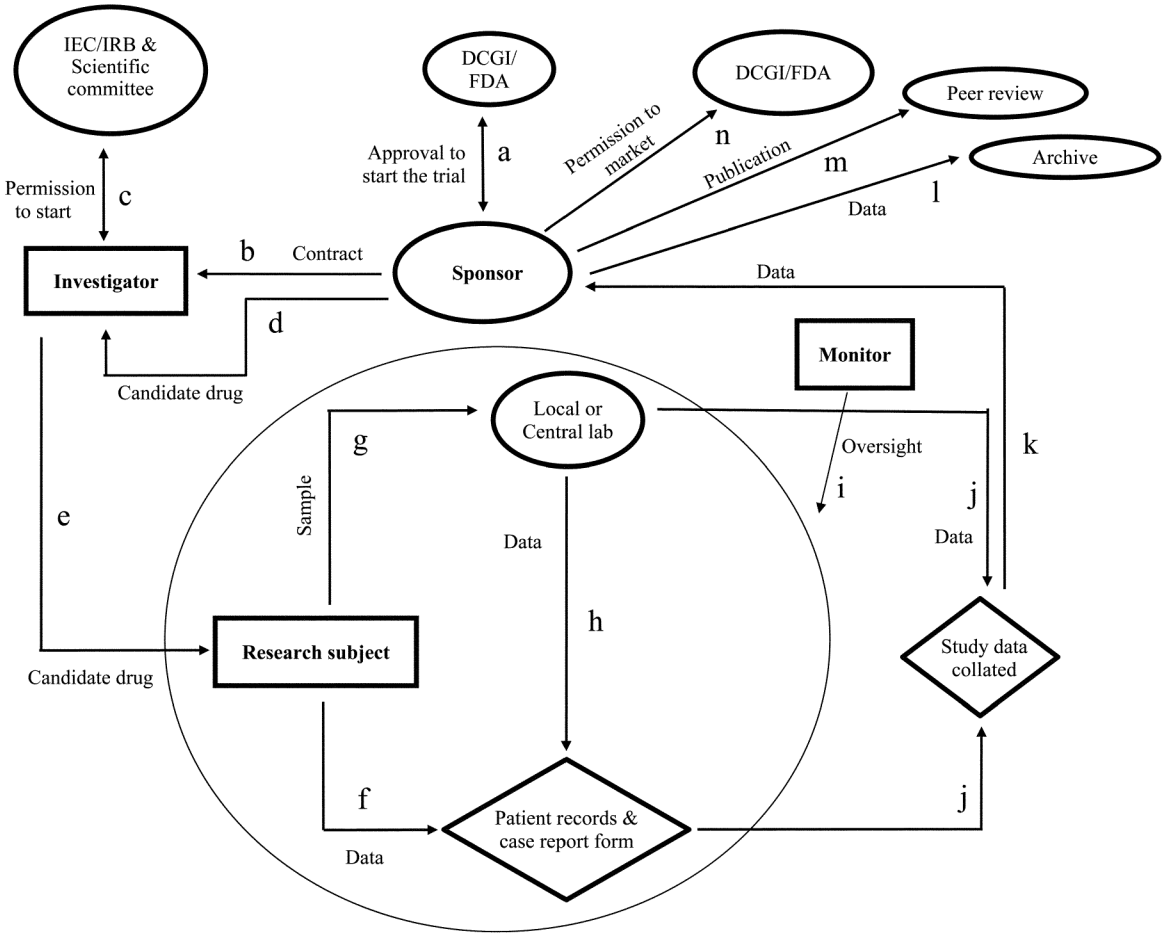


Figure 1. A broad outline of the clinical trial process (largely based on a figure provided by Dr Girish Nair). After *in vitro* and animal studies, the company files for an INDA, for first-time-in-human use that is based on pre-clinical data (a). The sponsor pays doctors (investigators) to perform the trial (b). In parallel to the sponsor filing an INDA (with the DCGI, FDA, or both) a doctor (investigator) approaches the institutional ethics review board for approval of the protocol and permission to start the trial (c). Each hospital/institution has its own ethics board that approves the protocol to be tested on research subjects (who enroll themselves for any one phase of a trial). Alternatively, an investigator may work with an independent ethics review board in case the institution does not have such a board. Assuming that both (a) and (b) have positive outcomes, the investigational drug is supplied to the investigator (d). The research subjects receive the investigational treatment (e). Clinical data are entered into PATIENT RECORDS and CASE REPORT FORMS (f). Samples of fluids or tissues taken from research subjects are analysed at either a local or a central laboratory (g). Some of the laboratory data so obtained are entered into the patient records and case report forms (h). A data MONITOR appointed by the sponsor oversees all the steps of the trial (i). All the information is collated in the requisite format (j). Finally, the collated data are sent to the sponsor (k). Trial data are filed in archives of the sponsor for several years (l). If the sponsor does not have any objection, then the physicians running the study may publish their results (m). If the trial data are significant, the company approaches the regulatory authorities again, this time for approval to market the drug (n).

- ADVERSE EVENTS get reported to a number of people: to all other INVESTIGATORS doing the same trial, to all the ethics boards, the steering committee, the DATA SAFETY AND MONITORING BOARD, the local PHARMACOVIGILANCE committee, the pharmacovigilance centre of WHO in Sweden, the local drug authority and the international one in case it has given permission for the trial. If there is a pattern to the adverse events over several sites, these will be detected and the trial halted.
- The Steering Committee is authorized to 'unblind' a study before it is over, and look for evidence that the drug is safely and effectively working. This may be done, say, when 30% of the trial is completed. If the drug is obviously ineffective, it would be unethical to continue to administer it, and the trial is halted. Likewise, if a positive effect of the trial treatment is detected, the trial is halted so that those who are receiving a placebo, or the best current treatment, may be put on the new treatment regimen. Either way, doing anything less would be unethical.

Clinical trials in India

In 2004, *BioSpectrum* listed about 20 leading CROs that do at least some of their trials in India[2]. There are over

100 CROs in the country today (supplementary material 1). The DCGI is receiving more than 20 applications a month for conducting trials, including those for which permission to test has already been received in highly regulated markets such as the US. By way of an introduction to the local scene, we have done an analysis of 50 trials being conducted in India today (Box 1).

The pull factors

What is causing the large interest in clinical trials? This is primarily due to policy changes of the Indian Government. Earlier, the rule was that a Phase I would only be permitted if the candidate drug had been developed by an Indian company or, in case of other companies, if phase I data had already been generated outside India. This was to guard against the Indian population being exploited as 'guinea pigs' by the international pharma industry. This has changed: a phase I trial may now be conducted for a drug candidate developed elsewhere, if it is relevant to the health problems of India. However, it is not generally encouraged[3].

The second major recent policy change concerns the phase of a trial in India vis-à-vis elsewhere in the world. Until recently, trials were allowed in India only if they were a phase behind trials elsewhere. Thus, if a phase III trial was on in the US, a phase II could be run in India. A phase lag is no longer needed and today a phase II could take place simultaneously in India and the rest of the world, if phase I data (from other countries) are submitted[3].

Several other factors bolster the momentum created by these policy changes. As mentioned often in the popular press, we have a large population with probably every disease imaginable, many patients are 'treatment-naïve' (that is, they have not been treated for this condition before) and our medical system transacts much of its work in English. Increasingly, the population suffers not merely from infectious diseases more common in tropical countries, but also from maladies that are common in the West – diabetes, cardiovascular problems, cancer – which the drug companies are interested in treating. India's new patent regime, where, in addition to process patents, product patents are also now recognized, and the increasing number of good clinical practice (GCP) facilities are further adding to the attraction of India as a location for conducting trials[4]. According to the industry, high patient enrollment rates, good patient compliance and retention, ability to meet International Conference on Hormonization for Good Clinical Practices (ICH–GCP) requirements, good hospital facilities and strong IT capabilities are other factors that make it attractive to be in this business (http://www.igatecorp.com/icri/html/aboutus/tia.htm). Last but not least, the FDA has started accepting NEW DRUG APPLICATIONS that include data from Indian trial sites[5].

These are the 'pull factors' that are attracting clinical research to India. What are the 'push factors'? That is, what is making it less attractive to doing this work in the West?

The push factors

There are several reasons why it is harder to do clinical trials in, say, the US[6]. The first concerns who is conducting the trials. Until the 1980s, trials were mainly conducted in academic settings. At that time, drug companies were at liberty to charge what they wished for their drugs and this helped them not merely to survive but also post handsome returns. In the early 1990s health management organizations (HMOs) came into existence, putting a sealing on drug prices. In order to keep up the steady stream of revenues expected by investors, the pharma industry had to now put more effort into both selling existing drugs and creating new ones. The latter was difficult with clinical trials in academic institutions, where there was no particular emphasis on speed, and where issues deriving from a tradition of academic rigour and ethical research 'slowed down' trials. The drug companies turned to private doctors and in due course to specialist companies called CROs to conduct clinical trials. Private players were more likely to see the need for speed and its relationship to cost cutting in drug development. They were also more in a position to achieve a higher speed. Companies have found that for reasons of both cost and speed, it is worth working in India.

The second issue concerns public perception. Stories in the press about problems with how trials are conducted, leading in some cases to fatalities, have caused the Western public to be disillusioned with clinical research, except in situations where the patient is in the terminal stage of a disease. In the latter case a patient would want to be on a trial that tests a new drug and therefore offers some hope. It is becoming harder to recruit subjects for trials in the West[3].

The third major issue concerns regulations. Over the years there have been a number of studies and calls for higher levels of scrutiny by the Institutional Review Boards (IRBs) and also of their functioning itself. Overall, the regulations for conducting clinical research have become more stringent in the West[7], adding to the time and cost involved.

And the fourth major issue concerns the possibility that a given drug has differential efficacy in different groups of people. This was shown to be the case with BiDil – with a stronger effect in Afro-Americans – which is the first drug approved by the FDA for a particular race. As a result, the Agency has called for increased testing on different groups of people (http://www.fda.gov/cber/gdlns/racethclin.htm).

This brings us back to the present scenario in India. A large fraction of the corporate pharma R&D budget re-

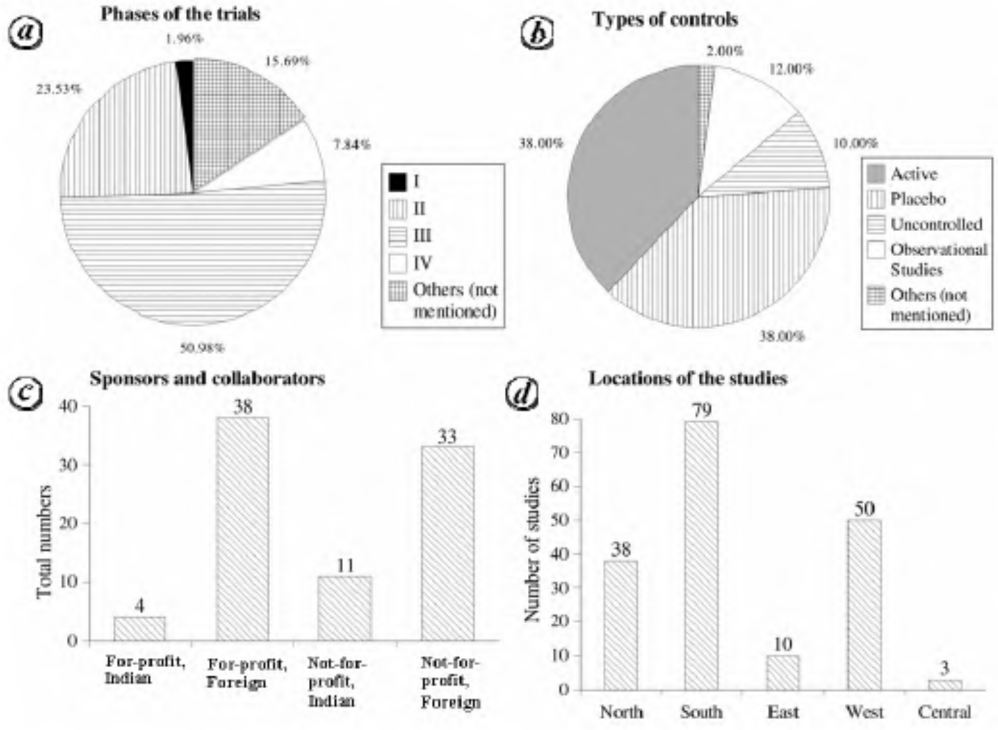
Box 1. Analysis of 50 clinical trials being conducted in India.

Clinicaltrials.gov is a REGISTRY sponsored by NIH. Although there are many such registries, this one is easier to search than many others. To identify some of the trials going on in India, we browsed the section entitled 'Search clinical trials' and entered 'India'. A list of clinical trials being conducted in the country – and registered with this registry – appeared. These numbered 238 studies when the registry was accessed on 20.02.2007. We analysed a random sample of 50 trials. The titles and unique identifier numbers of these trials are provided in supplementary material 2).

Our findings are as follows.

- Among the 50 trials, 88% (44) are INTERVENTIONAL and 12% (6) are OBSERVATIONAL.
- The studies cover the following conditions: cancer (22%), diabetes (18%), CNS disorders, including Alzheimer's and Parkinson's (14%), viral infections including HIV and HPV (8%), and other infections (8%). The remaining 30% is for interventions ranging from treatment of pain to folic acid as a nutritional supplement. Not more than 4% of the latter group of trials is for any one condition.
- In terms of the phase of the trial, 51% of the studies is for phase III, 24% for phase II, 2% for phase I and 8% for phase IV. 12% are observational studies and for 3% the phase is not mentioned (Figure *a*).
- There are few studies for phases I and IV. Thus, there is only one phase I study, with targetted enrollment of 1000, a rather large number for a phase I trial. There are four phase IV studies, with an average of 529 patients.
- More studies are for phases II and III: There are 12 studies in phase II. Two studies had rather large targetted enrollment, that of 920 and 1000 patients. Other than these two outliers, the average over 10 studies is 180 patients. This falls within the usual range of 100–300 for phase II trials. There were 24 studies in phase III for which enrollment is listed. Other than one outlier, with 110,000 targetted enrollment, the average of 23 studies is 607. This is significantly lower than the usual range of 1000–3000 for phase III trials and implies that India is only a minor centre for what must be multi-location trials.
- ACTIVE and PLACEBO controls are each being used in 38% of the trials with 10% of the trials uncontrolled and 2% not declared (Figure *b*).
- We grouped the sponsors and collaborators into four categories: for-profit (Indian and foreign) and not-for-profit (Indian and foreign). Each trial can be sponsored by more than one sponsor and so we counted the total number of occurrences of each type of sponsor. We found that the two highest occurrences were for foreign for-profit (38 times) and foreign not-for-profit (33 times) sponsors. Indian not-for-profits occurred 11 times and for-profits occurred 4 times (Figure *c*). A list of all sponsors and collaborators, and their number of occurrences is provided in supplementary material 3.
- In terms of trial locations, 79 (44%) are taking place in the south, 50 (28%) in the west and 38 (21%) in the north of the country. The minor locations are east with 10 (6%) and central with 3 (2%) studies. Due to multiple locations of specific trials, a given trial may be happening in more than one region (Figure *d*).

These data are represented graphically in the following figure. Although it is a small sample, it provides a window on the trials in progress. Currently, there is no publicly available definitive source of information on all ongoing trials in the country.



Box 2. Recommendations to improve the safety and quality of clinical trials in India

We summarize below some of the major recommendations from an interactive workshop organized by ICMR at Hyderabad held in October 2005 entitled 'Building and managing clinical trial capacity in India: challenges in ethics, equity and efficiency'. The entire report is available with Sen and Muthuswamy[25,26].

Prioritizing clinical trials:

- Priority in approval for a clinical trial should be on the basis of (a) the potential benefit of the candidate drug and its relevance to a large fraction of the Indian population; (b) drugs which are of relevance to Indian populations, but are not of high interest in the West and so on. Criteria for denying permission for a trial in India need to be spelled out. Thus, a drug banned in other countries should not be tested here.
- Different kinds of trials could have different types of accelerated review and also different levels of review.
- The specific roles of different parts of the Government in the trial process need to be spelled out unambiguously.

The ethical review of trials:

- Training of ethics committee members is required to ensure that ethical guidelines – relevant both nationally and internationally – are followed.
- To improve the quality of the review process, an accreditation system for the ethics committees should be created.

Capacity building:

- There should be regulations requiring intense monitoring, reporting and reviewing of clinical data, especially if a placebo is used.
- There is an acute need for a Government department to oversee the protection of vulnerable populations. Also, a special set of precautions for phase I trials are required.
- In order to conduct need-based trials, a public sector CRO should be set up. This CRO could also be involved in training professionals in the area of clinical research.
- Medical college curricula should include GCP, with a focus on clinical research and ethics.
- Principal investigators need to be certified.
- Research subjects need to be insured.
- There is need to develop expertise in approving and monitoring a trial, and also in the enforcement of regulations. Furthermore, there is a need to train people in research design, data management and analysis of clinical trial data.

Registries and database management:

- Registration of trials should be compulsory. Some portions of the registry should be accessible to the public, and others should be held in confidence by the regulatory authorities. The registry should be made along the lines proposed by WHO and IEMJ (International Editors of Medical Journals).

Other suggestions include the need for a mechanism to ensure that research subjects receive life-long care. In addition, the feasibility of the following needs to be looked into: (1) Restricting phase I trials to the urban population as it is educated enough to understand the risks involved. (2) Permitting only such investigators to take up trial work as would not, in the process, earn more than one-third their annual salary.

lates to clinical development, and in the year 2004 the US industry spent about $33 billion on R&D. Of this, about $33 million was spent in India on clinical research[3]. That is, of the order of 0.1% of the amount spent in the US. McKinsey has forecast that Western companies will spend $1.5 billion annually in India[8] by the year 2010. Clearly, even at that amount and also accounting for lower costs for several aspects of the trials in India, it is actually a small percentage of the global industry and therefore probably readily achievable. The potential for growth of this industry locally is therefore apparently enormous. The critical factor now is the readiness of the Indian ecosystem to handle this growth responsibly. We are told by those in the know that one of the chief bottlenecks is the number of tertiary care doctors. India simply does not have enough of them to enable the relentless growth of trials.

In October 2005, there was an interactive workshop on clinical trials in Hyderabad. This involved all stakeholders in this industry: pharma and clinical research organizations, ethics board members, the Government, social scientists, doctors, media, etc. The recommendations of this workshop are summarized in Box 2. It is clear that various procedural issues for approving trials in India are still being debated (see also http://cdsco.nic.in/Global_Clinical_Trials.htm).

Why was this meeting necessary? The meeting highlighted the major concerns related to the clinical trial

industry in India. Its aim was to help the various stakeholders and policy makers analyse the gaps in expertise, policy, infrastructure and so on, and to come up with possible solutions. We consider only one of these major issues here, that of the ethical conduct of trials.

Ethical issues

Clinical trials have been running in the US for several decades now. Over time, several problems, including ethical ones, have been identified. Some have come to light as a result of painstaking efforts by investigators examining different facets of the clinical trial process. Others are in response to experiences of individuals (or institutions) who have faced problems while conducting trials. Some issues are isolated instances, others more systemic. All of these have arisen even after the infamous Tuskegee experiments, where medication was deliberately denied so that the experiment could proceed and subjects were enrolled in a trial from which no useful conclusion could be drawn (http://www.infoplease.com/spot/bhmtuskegee1.html).

Some of the most serious and widely known cases that have come to light in the last couple of decades include: the death of 18-year-old Jesse Gelsinger who died during a trial for gene therapy in 1999 (http://www.newsweekly.com.au/articles/2000aug12_bio.html), that of 24-year-old Ellen Roche who died during a trial for asthma in 2001 (http://www.aafp.org/fpr/20011000/2.html), children put on anti-depressants who became more suicidal (http://www.usatoday.com/news/health/2004-09-08-drug-warning-usat_x.htm), children who developed leukaemia during a gene therapy trial in 2002 (http://www.unifr.ch/nfp37/adverse.html), the discovery in 2004 that patients on Rofecoxib (Vioxx) for over 18 months had a higher risk of heart attack and stroke (http://www.adrugrecall.com/vioxx/heart-attack.html) and the six volunteers of TeGenero's phase I trial for a novel monoclonal antibody in 2006 who suffered multiple organ failure (http://www.nature.com/news/2006/060313/full/060313-17.html). Each of these was a tragedy. Nevertheless, one must also note the overall responsiveness of the Western regulatory system that moves quickly to prevent the recurrence of a similar problem. This is illustrated by the recent case of TeGenero, where a committee has recommended 22 steps to be taken for future phase I trials in the UK (http://www.gnn.gov.uk/environment/fullDetail.asp?ReleaseID=248673&NewsAreaID=2&NavigatedFromDepartment=False) and by the recent proposals to radically overhaul the FDA in response to the Vioxx case[9]. Although there has been much criticism about the regulatory system in the West, the fact that relatively few cases occur for so many thousands of trials each year indicates that the system works to fairly effectively safeguard patient safety.

Other issues that have come to light include the following:

- Fraud, including fabrication of subject data[10].
- Inability of CLINICAL INVESTIGATORS to speak out in case they detect problems with a trial[11].
- Institutions having too much of a financial incentive to conduct clinical research[12].
- Large payments to doctors and other staff for recruiting subjects for trials and bonus payments – up to US $1 million – for speedy recruitment of subjects[6].
- Lack of disclosure to patients, and sometimes IRBs, about potential conflicts of interest[13].
- Trials conducted by doctors inexperienced in clinical research, or by doctors in areas outside their expertise[6].
- Competitive recruitment for trials wherein a site needs to recruit a certain number of trial subjects (sometimes by a certain date) or risk being dropped as a site[14].
- NIH's failure to systematically AUDIT its trials[10].
- Consent forms drafted in a highly academic style of writing, making them difficult to understand by a lay person[1].
- The issue of too many regulatory bodies and inadequate clarity on various aspects of conducting trials[15].
- For multi-centre trials, inconsistencies in how different IRBs view the same proposal[16].
- Too broad a remit of the IRBs, including the examination of issues that pose very low risk such as interviews and secondary analysis of data[17].
- The proper functioning of the IRBs hindered by too much paperwork leading to 'overregulation and underprotection' of research subjects[17].

These are general concerns, aside from special situations such as studies on tissue samples already collected by hospitals, on minors, the mentally infirm, etc.

In addition to these problems in studies within the US, problems with trials conducted abroad have also come to light.

- In China, HIV-positive subjects were injected with living malarial parasites[18].
- 'Best local treatment' instead of 'best current care' was offered to mothers taking part in a mother–child HIV transmission study in the Third World[7].
- In 2000, estimates that organizations conducting trials overseas do not – in 33% of the cases – subsequently market the drug in the area from which subjects for the trial had been recruited[19].
- In Africa, a trial drug was administered to patients by the African collaborator of a US investigator without Investigational New Drug (IND) approval from the FDA and without IRB permission[20].

- In India, a one-person clinic was found to be conducting clinical trials[3].

Ethics in the Indian setting is particularly complex. On the one hand, there are general issues such as vast socio-economic disparities, various levels of literacy and education, and a multitude of languages. On the other, trial-related issues such as the fact that patients often revere the doctor and assume that the latter has his/her interest at heart, and that it may be a family, and not an individual, that takes the decision on whether or not to participate in a trial[21]. Some of these issues were discussed by Balaram[22] more than five years ago. With the rapid push to have more clinical trials – by or on behalf of foreign companies – conducted locally, matters have got even more complicated.

Two issues are critical to the proper conduct of trials. One, the need for impeccable functioning of the ethics committees. Two, that research subjects' consent is truly informed. The joke that informed consent means that the doctor informs and the patient consents, does not give much confidence for regular patients, let alone individuals participating in trials. Furthermore, there must be social issues such as whether a woman freely decides on whether participate or not in a trial where counselling would be valuable. Perhaps it would help to train a special cadre of people who specialize in the issue of informed consent in the Indian context[23].

The issue of placebo controls is also a difficult one, which many people are uncomfortable with. The Declaration of Helsinki, which is often referred to for its ethical guidelines, does allow placebo use under specific conditions (http://www.wma.net/e/policy/b3.htm). And the FDA, for instance, often mandates placebo controls[24].

Conclusion

As discussed above, clinical trials are complex. Despite the challenges, however, the clinical trial industry is growing in India and will perhaps be an economic success story. If it is to be so, it must also be an ethical success story. We have an active enough civil society that the former will – and should – be prevented from happening without the latter. On the one hand, NGOs, the media and others with 'watchdog' interest in clinical research must ensure that they have the right facts and figures, and also a good understanding of the issues they take up. On the other hand, clinical investigators and trial sponsors must guard against taking ethical short cuts. India has perhaps not been prepared to handle the sudden influx of trials, and a lot of learning in a variety of settings is taking place. Even as this learning is taking place, ethics must be kept at the forefront. Only then will medical benefits accrue to individuals and communities, and economic and 'capacity building' benefits accrue to participating institutions and the country as a whole.

Note added in proof: In October 2007, it was estimated that between 2000 and 2005, there were 350,000 trial sites in the US. Of these, less than 1% had been monitored by the FDA (http://www.biopharma-reporter.com/news/ng.asp?n=80241&m=2BPRO26&c=ugbhfeyctaievyh).

Glossary

- Active control: Subjects who are given a known effective treatment.
- Adverse event: Any medical issue that arises while the subject is a part of a clinical trial. Thus, fever, nausea or diarrhoea would each be considered an adverse event. It may or may not be due to the trial.
- Audit (and auditor): The cross-checking of a patient's record with his/her case report form, for the purpose of ensuring fidelity in the data that is collated for analysis. An auditor conducts the audit.
- Case report form: The form in which data about a subject in a clinical trail are recorded, to be forwarded to the sponsor for analysis.
- Clinical investigator: A medical doctor who conducts a clinical trial in his/her area of specialization.
- Clinical trial: The testing of a candidate drug before it is launched in the market as a new drug. There are four stages of a trial: phase I (testing the safety of the molecule on a small group of, say, ten people), phase II (studies done on a larger group of around 200–300 people), phase III (in which more than 1000 people are enrolled) and phase IV (performed after the drug is approved and has reached the market; also called post-marketing surveillance). There are different types of trials:
- Treatment trials: to test new drugs, new combinations of known drugs, new approaches and new therapies.
- Prevention trials: to reduce occurrence of disease in people who are prone to certain conditions or to prevent a disease from returning. These test medicines, vitamins, vaccines, minerals or lifestyle changes.
- Diagnostic trials: to find better ways to diagnose certain diseases or conditions.
- Screening trials: to detect particular diseases or health conditions.
- Quality of life/Supportive care trials: to improve the quality of life of patients with a chronic illness.
- CRO: A clinical research organization is an independent organization that conducts clinical trials on a contract basis for multiple sponsors.
- Data Safety Monitoring Board: A board that periodically unblinds and analyses data from an ongoing trial.
- DCGI: The Drugs Controller General of India is the regulatory authority for granting approval for conducting a trial in India.

- FDA: The Food and Drug Administration is part of the US Department of Health and Human Services that regulates the use of drugs, vaccines, medical devices and blood transfusions in USA.
- GCP: Good Clinical Practice, a body of rules and regulations on how clinical trials should be conducted.
- ICH–GCP: International Conference on Harmonization for Good Clinical Practices, an international body that regulates clinical trials.
- HMO: Health Maintenance Organization, a form of managed healthcare that enables healthcare providers to negotiate lower prices with pharma companies.
- ICMR: The Indian Council of Medical Research is the apex body in India for the advancement of biomedical research. It is funded by the Government of India and its research priorities include communicable diseases, fertility control and maternal and child health.
- IEC: The Institutional Ethics Committee (called IRB or Institutional Review Board in the US) is an independent committee that comprises individuals with a variety of expertise and points of view. It is likely to include medical doctors, biomedical scientists and perhaps a lawyer or any other member of the public. Its job is to review each proposal for clinical research in a given institution from the ethical and scientific angle. It does this by reviewing, approving and providing continuing review of trials, of protocols and of the material and methods to be used in obtaining and documenting informed consent of the trial subjects.
- IND: An Investigational New Drug is a new candidate drug that is used in a clinical investigation for the first time.
- INDA: An Investigational New Drug Application is filed when a company is seeking permission from the DCGI or FDA, for instance, to put a candidate drug into humans for the first time, in a phase I trial.
- Informed consent: The process by which a subject, after evaluating the pros and cons, confirms his/her willingness to participate in a particular trial.
- Interventional study: A study in which the research subject receives a candidate drug as part of the study. See also 'Observational study'.
- Investigator: See 'Clinical investigator'.
- IRB: See 'IEC'.
- Monitor: This is a person employed by the sponsor who is responsible for monitoring an ongoing trial. He/she assesses the conduct of the trial, and sees to it that all data collection and documentation are ethically done.
- NDA: A New Drug Application is filed with the FDA or DCGI when a company has completed all requisite clinical trials and is seeking permission to market the molecule as a new drug for a specific condition.
- NIH: The National Institutes of Health. This is one of the world's largest groups of medical research centres having 27 research institutes. It conducts intra-mural research and also funds research at other institutions.
- Observational study: A study in which the research subject does not receive a candidate drug, and is merely under observation during the trial. See also 'Interventional study'.
- Patient records: The data about a patient in the hospital, as recorded in regular hospital records.
- Pharmacovigilance: Studies done to see if there are any side effects of medicines already on the market or currently in trials.
- Phase I trial: See 'Clinical trial'.
- Placebo: An inert substance, also known as a sugar pill which ought not to have any effect on the patient but may do so. The 'placebo effect' is not well understood.
- Protocol: A document that describes the guidelines for and methodology of a given trial.
- Registry: A site where a sponsor discloses certain basic information of a trial. Guidelines for what information should be disclosed have been set by international bodies such as WHO and IEMJ. An example of a registry is Clinicaltrials.gov.
- Research subject: A person taking part in a trial. The person may be a healthy volunteer or a patient whose condition is a prerequisite for being enrolled in the trial.
- Sponsor: A person or an organization that funds a trial. For example, a pharma company is a sponsor when it funds clinical trials for its candidate drug.
- Trial: See 'Clinical trial'.

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