



***BUILDING AND MANAGING CLINICAL TRIAL
CAPACITY IN
INDIA: CHALLENGES
IN ETHICS, EQUITY AND EFFICIENCY***

Report

**Interactive workshop (ICMR-ASCI-FORDHAM)
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**By
Dr. Vasantha Muthuswamy (ICMR) and Dr. Falguni
Sen
(Fordham University)**

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FOREWORD

Tropical diseases like malaria, filarial, dysentery, hepatitis, dengue fever, yellow fever are a significant cause of mortality and morbidity in the country. Lack of new drugs, problem of drug resistance, lack of infrastructure, inadequate financial resources etc. are some of the important issues that need consideration. Science of clinical pharmacology has emerged as a systematic scientific study of new drugs contributing to actual patient care through individualization of drug therapy that can be achieved by developing proper sensitive procedures with prioritization. ICMR-ASCI-Fordham University held workshop on some thought provoking topics in the area of clinical trials that are of interest to the national and international community especially for the scientists working in the area.

With India becoming a global hub for the clinical trials, the workshop held at ASCI, Hyderabad analyzed some very important aspects of clinical trial research in the country which are required to be managed well for the better future of the country in the global market.

Clinical trials are powerful tools; like all-powerful tools they need to be used with care as with this investigators test biological hypothesis in living patients which has potential to change the standards of care. Economic impact of such changes is substantial when new drugs come to the market after properly conducted clinical trials leading to enormous financial gains. The trials have become more sophisticated for untreated disease which would be harder to reach, there has been great increase in size of trials and consequently in the cost of developing new drugs. The control of the costs has been tried by various industrial organization private / public, non-academic research groups through contract research organization and hence for the last few years these CRO's have received major share of clinical trial revenue. But the integrity of clinical trials essentially for the development of new drugs is increasingly under threat from commercial influence, resulting in an urgent need for guidelines to safeguard the reliability of such trials due to conflicts of interest, inappropriate involvement of research sponsors in their design and management and publication bias in disseminating their results. In

the recent years a stunning output has been seen in the area of new medicines and vaccines. Continued progress depends critically upon the quality of the clinical trials. As it is in the interest of stakeholders that a proper document covering different areas related to clinical trials like prioritization, capacity building, expertise building, clinical trial registries etc. for necessary implementation through networking is prepared for the use of key persons from the regulatory set up and necessary implementation. This workshop has resulted in such type of document for submission to the Secretary, Ministry of Health and Family Welfare for arranging the implementation process.

(N. K. Ganguly)
D.G.,ICMR

PURPOSE OF THE REPORT

This report aims to provide policy makers with a roadmap to the issues surrounding the conduct of clinical trials in India, which is edging towards becoming a booming industry. It is meant to provide perspective, so that any future legislative, voluntary or other policy decision strikes an appropriate balance between two critical needs: the need for transparency and accountability of the bio-pharmaceutical research enterprise to advance public health, patient safety and restore public trust, and the need to ethically build capacity to enable the sponsors and investigators of clinical trials so that they remain active players in an innovative, sustainable health product industry and healthcare delivery system. This report is based on an interactive stakeholder workshop hosted in October 2005 as a joint enterprise of the Indian Council of Medical Research (ICMR), the Administrative Staff College of India (ASCI) and Fordham University of New York. Sixty participants representing a wide cross-section of stakeholders including industry, government, patient advocacy, medical practice, ethics review boards, clinical research organizations, media and independent investigators attended the workshop. The objective of the workshop was to discuss and debate the existing provisions, gaps and the policy guidelines that need to be developed and the actions to be taken by the different stakeholders in the clinical trials industry to make it grow in an efficient and ethical way. A summary of the main issues and a set of recommendations from each panel are being included here. This will highlight concerns across the spectrum of stakeholders and will provide policy makers and other stakeholders with a roadmap of issues to consider in fashioning any future approach. The workshop did not vote on the recommendations. However, a number of issues did have broad agreement and are presented here as recommendations for further action. Patient/subject safety was the underlying theme in all the topics discussed. The following topics were covered in formal panels:

- Prioritization of Clinical Trials
- Creating a review mechanism for clinical trials
- Building ethical capacity
- Need for transparency and monitoring

INTRODUCTION

Rapid advances in the clinical research have been witnessed since the last decade or so world over. India with its cultural diversity, myriad of communicable and non communicable diseases , english speaking people, cheap labor, low infrastructure cost etc is the fast emerging as clinical trials outsourcing opportunity for many multinational companies,. Regulatory guidelines in India have been laid down and are required to be given wider publicity for necessary acceptance with sustained efforts from all the stakeholders so as to initiate a stronger emphasis on quality mechanisms in the area of clinical research in the country.

In view of above, a selected group of stakeholders (65 participants) including Government of India officials and the private industry and the various CRO's, NGO's journalists and also some of the international experts in this area to highlight the relevant recommendations to the public, the industry, and policy makers on issues of national import involving the conduct of clinical trials in India, was chosen as the participant of this conference.

INAUGURAL SESSION

Dr. Vasantha Muthuswamy, Sr. Deputy Director General, ICMR and Dr. Falguni Sen , Professor , Fordam University, USA and Dr S.K. Rao ASCI, Hyderabad welcomed the participants and gave a brief introduction about the workshop. This was followed by the inaugural address by Dr P. Hota, Secretary, MOH&FW who welcomed everybody and said that he will look forward towards the concrete deliberation of the meeting and assured the support from the ministry. He said about the various regulatory activities that are being looked into in the drug and food sector and it is planned to make clinical trials an integral part of the same. There is need to scale up our abilities and the support of the scientists in the area is essentially required. remain in rear with our fears nor we can throw open our doors without preparations and that is why These kind of assemblies are essential to throw open the doors for outsourcing the trials with proper preparations . The right intuitions with

the right balance, the legislations, the protocols, the institutional arrangements the humans skill available in the country how to regroup them and what sort of budgetary and the other supports the administrative supports are needed need to be identified quickly as being late there is chance of missing the bus. While talking about the trial opportunities in neighboring countries he said if China would have had English as their lingua francium, in India it is there historically. So, it is an opportunity but it is not as Neo-commercial opportunity, to see it like that would be a dangerous proposition. In fact, there would be a backlash. India is a very alive democracy and hence the concerns of the human rights group and citizen group who would frown upon any unethical practice has to kept uppermost in the mind while making the recommendations. There is a very complex legislative thought system and I would say that it is good for the professionals in the field to quickly sit together and device legislative and regulatory backdrop for this eminently important field of activity. Being facilitators, it is expected from the scientists dedication and initiative to not know the current trends so as to integrate this knowledge and concerns into an operational framework..It is a multitasking situation and the idea is to strike and appropriate balance and see this balance in a dynamic context so as tackle several issues in a comprehensive manner. How to strike that balance and if we really think that India is going to provide a major global platform for this important area a process cannot be made which will be too centralized and too delayed. This important opportunity should not be buried on the red tapes. So, there is need to see what sort of self regulatory mechanism, decentralized mechanisms can be created in the country, which institution of the country can be listed to play regional and sub-regional roles, to scale what sort of facilitation is needed from Government as well as from the user group. While speaking on financial issues he said for good work, there should be resources available, it would be more convincing if right from the beginning that the beneficiary user groups are seen, particularly those who scale it to commercial levels and benefit. So the brunt of cost of the regulations could be borne through fees and such of the levies. He said about the visit of the members of US Pharmacopoeia about two three months back when they advocated for a more stronger regulatory regime as a pre-condition for attracting quality investment in pharma sector to India. They did not mean by the strong regulatory regime a proliferation and

expansion of the Inspectors etc, but for technical competence, labs, skills, faster process, global processes so on and so forth. Only strong regulatory regime would keep off spurious drug manufacturing which is also part of the Asiatic reality and similarly in clinical trials sector also a strong competent regulatory regime is in the interest of all concerned and instead of looking the universal budgetary process to fund it, the user groups should be ready from the beginning, they should infact come forward and volunteer a fee structure where by these cost are met. To achieve this there should be proper representation of the user industries in the decentralized committees etc in the regulatory set up. This should be seen as professional activity right in the beginning. Indians cannot be treated as guinea pigs, this sector is much more sensitive to moral issues. If there would be 99 clinical trials giving tremendous benefit to deducing the mode the disease etc. yet if there would be one wrong doing that one will really occupy most of the media and intellectual space, so the clinical trials experimentation can't be fool-proof. As long as bonafide are established and any mistakes are quickly rectified through a structural framework and there are auditing of the process these kind of issue have to be addressed. To think right in the beginning the other extreme that may create a very elaborate legislative and regulatory frame work where no mistake will ever occur which would be a long way to look at world . Finally he assured his full support to the participants in this endeavour. While recalling his interactions with ASCI when he was looking after industrial finances he looked forward to ASCI's collaboration in furthering public healthcare in the country. In clinical trials there would be a tendency for high cost drugs that would drive high profit and hence need for appropriate financial process for a good size clinical trial. But cost effective clinical trials for Indian centric diseases and their remedies also have to be considered adequately to look to the need of earning foreign exchange by throwing open our country and to improve the research content of our own country. For academic medicine it is said that only 3-4%of research is existing and needs to be increased considerably. India has to be self reliant and has to do much more for its own medical industry. So this could also be achieved by allowing global players to come into India for conducting the necessary clinical trials. This was followed by the speech of Padma Vibhushan Dr.M.S. Valiathan. He gave an overall look at the landscape of clinical trials and highlighted few important areas and also suggested a few elements in the strategy

of action. Clinical trial is not a new thing, in fact the first was done more than 200 years ago by Dr James Lint who gave fresh citrus fruits to sailors who are traveling on steam boats for months, deprived of all the fresh foods they used to get which developed Scurvy, a bleeding disease. James had the idea that perhaps fresh fruit might be the remedy. So he gave first citrus fruit to some sailors while others were denied and found that it really worked. Now the product was simply the citrus food he was trying, subjects were captives available readily and the ethical guidelines that were provided by his own conscience. That was a simple and very effective start for clinical trials. Since the second world war today the picture is extremely complex. Highlight the area of the research and development looking at the products today which are being subjected to clinical trials he said the first is the very large obvious area of drugs about which several references have been made. That is a very large area but India has also its own complement of herbal drugs which has its own discipline, its own protocol, its own way of testing and is essential part of the health care system. The second large area is the of devices, not at all highlighted in this country except when there is a crisis somewhere and that consist of essentially disposables like disposable syringes, or a blood bag, simple things or gloves go on to the complex things like or implantable hip prosthesis and so on.. Now these and the medical instruments, in India today we are importing worth more than 5000 crores as per figure from British department of commerce . These again, were used after subjecting to clinical trial. Another large area is the bio-technology products, diagnostics where recombinant DNA technology, therapeutics like human insulin and a whole lot all genetically engineered products need to be tested and finally the crucial area of vaccines with all complex issues. Many people believe that the biotechnology products will dominate the market in this century, as far as India is concerned 90% of these are being imported today. In the area of instruments for example, in 2003 5000 US patents issued to Japan, India got only 5. That gives an idea where we stand in terms of innovation. In the area of drugs we have moved from intelligent copying to innovation mainly because of the TRIPS agreement but there again India has to go a long way . So in this whole area of R & D in relation to clinical trial it is to recognize subjects are being tested in clinical trial for technologies essentially developed abroad. So when clinical trials are done here it needs to be realized that the R and D done in the other countries

is really supported and not advancing the R and D in this country anyhow. Then he highlighted the area of ethics he said everybody knows the Nuremberg code, what the Nazi doctors could do to prisoners, everyone thought that was only relation to crazy doctors in Germany . It doesn't apply else where, but this illusion was sorted in 1966 when Beecher from Harvard published a report. Twenty two reports he collected from contemporarily literature in the United states where all kind of things were done in reputed hospitals which would not be acceptable by any ethical standards. That woke up the medical conscience and today there is a wide sort of recognition everywhere that this is a serious matter, be it an informed consent, beneficence which have universal applications. In India itself, ICMR is a pioneer in this area, Justice Venkatachaliah committee, have issued the ethical guidelines for conducting research in patients, experiments, clinical trials etc. But in these ethical guidelines the area of weakness is identification of the institutions where clinical trial are going to be done and this is a problem because the institutions to do clinical trials must have an investigative culture. A nursing home which is functioning very well, overnight it cannot conduct clinical trials. They do not have a culture to do it. While talking about the a research paper on publications he said 18000 papers published from India in Medline journals. had very interesting revelations . Out of these 18000 papers picked up in Medline journals, less than 100 came in high impact journals, with an impact of more than four and out of this 90, I think most of these came from institutions like Indian institute of Science, CCMB in Hyderabad, National Institute of Immunology and AIIMS but none from the medical colleges in India and now these are more than 160 or 200 but none from any other institution. The health ministry has the top priority diseases in India like lower respiratory tract infection, infection between one and five years age group is the biggest killer and there are no papers on that subject . India has nine million blind of which two millions are children , there were hardly any papers on that. Where as papers were all being published on heart disease or on neurologic disorders, which are not the priority according to the health ministry statistics. So our priorities have been skewed. Drug act has been in operation for many years ,but assumptions are there in the beginning drug that is being subjected to the clinical trials . Large number of devices are there and every time there is a crisis, there is a strength problem, some where processs break down, then after waking up there is fire fighting

operation followed by everybody forgetting it. Still there is no devices legislation in this country. Ambiguities are in relation to biotechnology products also. Very often Government makes the situation by issuing notifications, executive orders but there is no force of legislation. Today, for example, a device which is recalled in the United States, where ten thousand is a lot, if one of this is faulty the entire ten thousand is recalled by law of the FDA. Now suppose if FDA also permit what is not accepted in the United States, they can export. This is specifically permitted. Now nothing stops the rejected lot if the sale is in India as there is no mechanism stop it. Dr. Madhav Menon in one of the meetings in our ethics committee pointed out emphatically that notification, executive orders do not have the force of law, a court can struck it down. This is what is required in the regulatory domain. In the future in R&D when it is planned to do clinical trials in this country on all these drugs, devices, bio-technology products so as to reach the patient aclearcut vision has to be developed keeping in mind a scientific strength culture and tradition of the country. It is inconceivable to keep on 80 or 90% of the trials that are done will be the products developed abroad. There should have a clear vision that in five years or ten years 50% of those that are tried will be developed in this country. That's the way clinical trial will also act as stimulus to R&D in this country and that stimulus should come with which a clear vision about the clear-cut achievement after a trial in a certain period of time. Otherwise India is going to become the world capital for clinical trial. Also there is a great need to define which institution - the criteria for authorising institutions to do clinical trials for which some standards need to be set up. Similarly principal investigators training of GCP, role of ethics committees - institutional ethics committee & Central ethics committee need to be identified. The ICMR guidelines laid on how the institutional ethics committee should be set up, but the fact of the matter is that many of the institutional ethics committee member are not trained about what they are supposed to do? what type of question should be asked?. So there is no mechanism to give a course of training to the institutional ethics committee members and also to update them because the ethical regime is changing all over the world and documents are being issued practically every year by the WHO, UNESCO, national bodies. Therefore there is need to update our knowledge for which a mechanism to be developed before inducting a person as a member of ethics

committee. He or she should go through a certain period of training may be one week or three days. Similarly there should also be a mechanism for them to update their knowledge and perhaps there is even a reason to think that the institutional ethics committee should be accredited. Institutional ethics committee could be used as instruments for monitoring of the clinical trials. Therefore, it is absolutely necessary that very competent people with a conscience are the member of the committee. And there should be a mechanism to strengthen the ethical regime as far as the regulatory part is concern in relations to drugs , devices and bio technology products Various efforts are being made infact the devices legislation, the efforts started some more then 15 years ago, it is still to become a legislation . It is absolutely necessary to move fast when globalisation is considered which will affect each one of these domains. If through R&D a product is produced in India it is no longer for Indian market but for the global market and should be able to compete with a product in the Europe or in the United States . The globalisation affects similarly the ethical domain. Human rights are universal like the beneficence or informed consents no two standards are in place from one country to another. When it comes to regulation again it is necessary that fast action is required for effective lagislations to be in place. But the only caution to make in the globalisation is remembering the international standards & rules and to accept them with the pre-statutory moves towards the local changes in ethics. There is communitism in India where a women consent is not considered necessary, the husbands consent is enough or the community leader the village head's consent is important .For this kind of problems local adjustments have to be made and local fine tuning may be necessary Many years ago tilting disk valve was developed at his institute that was tried for global testing. The whole device is putting a tester of it which goes on for 400 million times. When our effort is going on as there was no WTO at that time but a new recommendations from the ISO (international standard organisation) that each drug should be seperately tested came to notice which required very heavy investment in testing equipment, special skills and if the product in the united states gets failed. On the basis of this a change was suggested by The Association for Medical instrumentation in the United States and the ISO faithfully copied it. If one would accept unthinkinly like that there is no way that

the test could be done with each single strap to be tested and would cripple our own development process .

Dr Ashwani Kumar, DCGI while appreciating the initiative taken by the Dr. Falguni Sen and the motivation provided by the health secretary Mr. Hota and the support provided by ICMR said about very panoramic view of the whole clinical trial situation in India brought about in the background paper by Dr. Falguni Sen. The roles and responsibilities as well as the inadequacy , the infirmities and the preventions every thing that's is very, so interesting that this will serve a great purpose of our further discussion and the regulatory issues are very important the issues of ethics, the issues of auditing the issue of the quality, issues pertaining to clinical trials the integrity of the data all those things are so important but at the same time this is a high end of science. So, as regulatory agencies dealing with the this high end of science there is need of that kind of capacity and systems in place. So, this all issues is very-very complex and since it is an evolving thing is a kind of learning process. Even for a small regulatory agencies DCGI need to expand further. He talked about the how DCGI system has evolved and still what are the infirmities in the systems and the way things should improve from the deliberation of the workshop with very specific suggestions and recommendations on some policy formulation and all that the government will have to quickly absorb into their processes Regarding what has been the background specifically in context of the clinical trials or the clinical research in the country and what are the challenges and constraints, how the evolution the regulations have evolved specially in the clinical trials, what is the current situation what are the some of the initiatives being taken and what are the challenges and constraints The whole issue or the central point for any regulatory framework for the government is to provide public assurance of safe guarding rights safety and well being of study subjects when it comes to clinical trials and then to ensure the credibility of data submitted to support new drug applications because ultimately the regulatory agencies have to approve new drug. It also adds the medical device or any health care product. The credibility of the data ultimately is responsible to ensure long term safety and has been well structured into the regulatory framework. The regulatory framework is also dynamic process dependent upon our understanding of the issues , to keep pace with advances in science and technology , what are the

contemporary global regular standards , the country specific scenario whether political geographical that need to be absorbed in the regulatory evolution of the regulatory systems . In clinical trials all reservation may be about the guinea pigs in syndromewhich has been addressed beautifully even in the paper prepared by Dr. Falguni Sen . These are the some of the perspectives at the highest policy level which has also prompted to bring in some more changes in our legislation . This is one of the part of vision statement for 2010 of government of India which says become a preferred global destination for clinical research custom synthesis and genomic research including bio-informatics . The pharmaceutical research and development committee headed by Dr. Mashelkar wrote in 1999 government to focus on all the researching areas concerning pharmaceutical research in India and how to leverage our strength and all that at the global level there again it has been very clearly mentioned that the citing the unique opportunities for India to become a leading center for clinical trial the committee has called for the basic changes and the legislation allowing import of animals contract research and legal status for institutional animals ethics committees further more establishment and operationalisation of a current GLP, GMP and GCP monitoring authority has been recommended, So this is in that shell the whole idea was . The pharmaceutical policies 2002 of government of India, which is framed by Ministry of Chemical & Fertilizers but it is done in co-ordination with Ministry of health and Family Welfare, has said that the health ministry would do certain things like, encourage research and development in pharma sector progressively , harmonize standards for clinical testing with international practices , streamline the procedures , steps for quick relations and clearance of new drug application etc.This gives a policy perspectives of our moving forward. About the regulations in Drugs and Cosmetic act 1940 it has kept pace with the changing times which influence law making started from 1988 when for the first time some rules were introduced which defined what is new drug and how basic norms to be adopted to be adopted in the clinical trials that was brought through shedule Y . Now clinical trials have been defined under the law that includes requirement of a mendatory permission for conducting clinical trials,. Definition of investigational new drug , the forms for the submission of IND application, the fee structure etc is laid down in this. National pharmaco vigilance programme has been initiated , which is still in infacny, but it is

likely to address some of the issues concerning clinical trials. For the clinical trial situation there are certain facilitating provisions also, the policy initiatives have been taken up by government of India which provides an indication for a responsible kind of partnership in the global arena and in clinical trials that the government should encourage. That is why the import of custom duty relaxation has been given on all clinical trial supplies in 2003. Under drugs and cosmetic rules, exemption has been given from registration requirements and for import of any clinical trial material. In the meantime also a separate website of regulatory office is provided to show that whatever information can be shared very speedily with all the stake holders. There were more bottlenecks which were expressed earlier by the stake holders regarding export of clinical trial related biological material that has been taken care of by schedule by amendment which was very intricate and has been made easier. In 2001 definition of new chemical entity, even fixed dose combination of the existing drug, the new indication for the existing drug everything that is considered as a new drug was included. Also in 2001 because of many media concern and some episode and the people asking that who permits the clinical trial what happens if somebody is doing unauthorized trials also led the regulatory system to provide a very clear provision in rule 122DA that made it mandatory that no clinical trials in the country can take place without the permission of the concerned competent authority but at the same time even for those trials which have been approved by the competent authority there is a provision to withdraw them or to cancel them if something goes wrong. There is a provision for appeal, in case the stake holders feel a wrong decision has been taken. Till January 2005 no clear definition of what is clinical trial which is essential from the regulatory perspectives, unless and until we have definition of a product it is very difficult to move ahead legally if something goes wrong. The clinical trial definition has been first stage introduced in the law in 2005. The major instrument in our system which prescribed the norms for clinical trials etc. is schedule Y, in the Drug and Cosmetic rules. Schedule Y first introduced in 1988 and it was after 17 years that a major revision undertaken with a view to improve the clinical trials situation or the climate in the country that has more or less taken care of global requirements the of data production, the responsibility of the investigators, the responsibility of the sponsors, the responsibility of the ethics committees, the composition of the ethics committees, the

informed consents the details of the informed consents form etc. Subsequently National Guidelines on Good Clinical Practices and Bio-liability and Bio-equivalence Guidelines were developed and are again in the process of revision on the basis of the feedback. The section 27D in the Drug and Cosmetic act which stipulated certain penalties and punishments for contravention provision of similar things in the clinical trial scenario can be covered under this section 27D which could be punishable with the imprisonment for term not less than one year and may extend to two years with fine. About the CRO's some panel discussion have been held. This being complex issue because of interlinking of sponsors and CRO's. The recommendations of the workshop could workout certain strategies for the same. Contract research organization or clinical research organization can be independent as well as they can perform a role of the sponsors and runs whatever is the responsibility of the sponsors which has been prescribed in Schedule Y automatically that is a responsibility of a CRO but there are details which need to be worked out intricately. The issue of regulatory capacities and the regulatory systems, whether able to audit or evaluate regulatory system, what is going on and what kind of a confidence a regulatory agency has, that can be provided to the public at large or the policy makers that the ethics are being followed, the science is being followed, the integrity of that eye is there is very important. A process has been started now which is still in infancy. The process includes integrating many of the consolidated things where number of stake holders have been involved in organizing various workshops. Around 500 personnel right from ethics committee to investigators to sponsors etc. have been sensitized to these issues and only a fortnight back or may be even last week a workshop was held where first time some of the experts are being identified who can become a kind of inspectors, for inspections of clinical trial sites and what kinds of norms they have to follow, what is their understanding about the clinical trials, conduct of the clinical trial and all those complex issues. People are trained to undertake audits of the trials. There is need to advise further on these challenges before the regulatory agencies specially in term of new drugs or new health care products as well as clinical trials, regulatory evaluation capacity - whether it is in terms of investigational new drugs, whether it is in terms of medical devices, whether it is in terms of bio-tech drugs and all that,

the capacity for evaluating data which is lacking in the regulatory system which cannot be possible also for a country like ours to have everything under one roof and there is need to share, outsource with the experts available in the country and that mechanism is being involved. Regulation of inspection capacity also needs to be evolved. Challenge facing in the vaccine, the, biogenetics, the medical devices diagnostic and the plant based medicine herbal products like that all there are so complex when it comes to clinical research sciences evaluation, audits etc. There is also an international debate on whether India can take a lead in GCP . Debates are going on whether the next edition GCPc guidelines be re-nomenclature as good clinical research practices, off level use of drugs, which is also many times media also reports off level use as a clinical trial ,debate on phase I trials in India etc .

Dr. Dhananjay Bakhle from OPPI which is the organization of Pharmaceuticals producers of India and has more than 50 big pharmaceutical companies as members including multinational as well as the Indian big pharma companies like Ranbaxy, Dr. Reddy's and all the research based pharmaceutical companies are member of OPPI gave a brief overview of the industry perspectives with respect to clinical trials. Looking at the clinical research scenario today worldwide India is actually at the crossroads . By and large it is proven that the randomized clinical trials are essential for the medical advances of the past 50 years. Number of times the differences between the case control trials between of the studies which are not controlled versus the controlled studies have been clearly documented. The randomized control trials are established now as a corner stone for advances and hope for the patient of incurable diseases. While looking at the scenario in US and Europe, the high cost and inefficient patient recruitment are the major factors that are now leading to global trials moving into emerging countries and various part of the world. Latin America , eastern Europe and Asia these are three favorite continent where the clinical trial are moving. India obviously offers a very attractive destination for global studies but for this there is need of building a capacity on a very-very large scale. Looking at the changing research environment worldwide in terms of the clinical trials as such the industries sponsors are becoming more and more prominent in the field of clinical trials. The number of studies in the complexities of these is significantly increasing as compared to 5 to 10

years back especially in some of the studies of cardiology, oncology are getting more and more complex whereas sometimes it could be logistical nightmare to conduct and there is a significance in shift research from the academic center to the private clinic and same phenomenon is being seen also in India. There are tremendous pressure internally for the pharmaceuticals industries which is regulated in most big countries, whether a cost containment effort going on because it is a risky research and it takes anywhere between 5 hundred million dollar to 1 billion dollar for bringing out one new chemical entity. Because the ratio is about ten thousands chemicals to one product that actually hits the market. There is tremendous expectations of a short development time for each molecule because there is a pressure within the R&D department of the pharma industry to shorten this period and as a result of all these factors sometimes there is a rush to recruit subject and there are aggressive timelines for completing the studies because the data has to be submitted to the authorities and therefore there is more intense search for expanding research science beyond US and Europe for many years this was in effect of domain the geographical domain for clinical trials. On this background looking at the potential of clinical research very clearly India provides a very rich pool of talents and there is significant clinical research training organization now coming up. Therefore, what NIIT did to the IT sector is beginning to happen for the clinical research industries as well as with number of private institutes setting teaching training centers and there is a highly qualified physician pool which is now turning into metamorphosis to very well trained investigators. There is relatively ease of patient enrolment facilitating completion of target number. The moment India is added to a global study the chances of completing the number are definitely there and the CRO's which are now increasing in numbers are changing the scenario by also adding number of non-metro cities and the clinical trials which should be done principally in the big metro cities are now diversifying to different parts of India without limiting the major cities. There is significant advantage because these are the places where the trials can be conducted very well. There is developed IT industry which can provide a back office support and the number of alliances that are happening in the IT industry have also been identified. With global pharmaceuticals the measures have to be taken to obtain this support. And now we have an emergence of a new era of new chemical entities

which are home grown on the Indian soil are ready for testing in phase I, phase II and it will be interesting to see how do they move through clinical development phase within India. In 2003 a report was written for one of the London based publication where specific graphs were put which shows the typical India advantage where you have cost as one of that advantages, speed of recruitment, a large patient pool, the language which is definitely an advantage over China and the regulatory reforms and this scale only shows the level of importance in terms of pharma centered industries. Overall in the last 5 to 10 years significant development of capacity within the investigators and clinical trial sites has been observed. While comparing the regulatory and easy review time in different countries he said India is seen very much on par with no. of countries like Germany, Italy. Even in some of the countries Russia for example it is done in ten weeks and in India it was between 12 to 16 weeks and there are no. of examples where clinical trial approval can happen much faster than that. So it is a very-very important parameter where India is ways ahead of China and Korea and this part of the world where there is a tremendous competition for clinical trials. On this background there is need to look at no. of reports that talk about the potential for CRO. This conference is very important to set and identify all the issues so that plan a strategy to cross all the hurdles in a concerted and orchestrated manner. Looking at some of the reports that have come recently for the last 4 and 5 years on the international scenario talking specifically about clinical development in emerging countries and really identify lots of issues e.g., national bio-ethics advisories commission report on ethical and policies issues for developing countries, OIG report from US which is entitled as the globalization of clinical trial if identified alongwith number of issues and in the European group on ethics in science and new technology in February 2003 and India would be no exceptions to this kind of reports. While summarizing the kind of issues and anxieties generated is the level of protection to human subject. The fear of infringement of informed consent apprehension about compromise of patient confidentiality as there are no privacy laws as yet strictly identified and an advertent enrolment of ineligible subjects some of the issues that are identified in these reports. Starting with the subject protection the scale is only about level of risk involved for clinical trials from not only the pharma industry point of view but also from the societal point of view. GCP compliance for clinical trials

overall India is in a nascent stage. The newness of GCP to various sites is very-very important because right now there are about not more than 400-500 sites which have been conducted as GCP compliant studies. Safety reporting is one issue that needs to be addressed from marketing point of view as most of the times when products have been prescribed by the physicians the level of reporting has been very low . To ensure the safety reporting it is very important that the investigators are properly trained by taking specific measures at the at the sponsors level as well at the regulatory level . Timely amendments of schedule y as per our requirements to be addressed appropriately. Data quality is also important because source data that exist in the case paper of the patient in the hospital also is not currently of high quality as result of which it becomes difficult to trace the data. Sometimes transcription of this data into case record forms is a big issues at some centers . Lastly he mentioned about the sites infrastructure hospitals need to be geared for the centralized suppliers of medicine and at the trial site departments have to ensure that all the facilities are available for good clinical services. From the industry point of view for the potential solution efforts are made individually to enhance the sanctity of informed consent from the strengthen ethics committee, for proper documentation, independent auditing through CRO's and concentration on quality to cope up with the the multinational perspectives. A whole hearted support of the academics, industry regulators and civil society in building national capacity can create a very robust mechanism for cooperation between all the stake holders and such linkages have to be formed in a formal and informal manner for taking this forward. Pfizer and other members of OPPI are individually putting efforts for clinical excellence and no. of workshops for GCP and other related activities have been undertaken in the last 5-10 year. A forum could be developed where people can put their funds and do thing in a consented manner to create center for clinical excellence will be something which should be very novel, different from other countries. If you look at the complementarily of the academia industry there are different incentives normally because academic research will produce papers and the industry research created products so the way then we try to collaborate with the academia or the academic sites its very important that there is an adequate blend from the Industry and academia and how they are complementary to each other. Academia has the clinical infrastructure and access to patient

whereas industry has the funds and the projects. It is possible that network could be formed of this type which will be public private type and will definitely move forward in a very systematic manner . To make clinical research a big success that there is need to worship GCP so that in the next few years it is possible that we can prevent such stories coming out in the press about guinea pigs. Also there is need of scientist amongst the media which will not only increase the public understanding of science but also establish a very clear connection between science policy , the broader public interest , provide information about genuine benefits for human health which may involve the selfless participation of the set individuals who may not themselves benefits from the research study and therefore building trust within the patients and changing public perceptions about clinical trials. There is need for forming patient association in the country who can represent the patient groups as well. While concluding his talk he said there are five M's first in medical clinical research , the Motivation which is already there, Mindset are created, Money flowing , Methods identified but what is really required is a Mission with the kind of government support new scenario for clinical research can be created .

EXECUTIVE SUMMARY

Recent events worldwide have challenged the adequacy and integrity of research on pharmaceutical products and have triggered calls by legislators, medical associations, the International Committee of Medical Journal Editors, the World Health Organization and others, for increased accountability and transparency in health products research and development. India, which is projected to have accelerated growth in this sector with the entry of a number of major global and domestic players and a more research focused pharmaceutical industry, is poised to face formidable challenges. This report is presented as a result of an interactive workshop on "Building and Managing Clinical Trial Capacity in India: Challenges in Ethics, Equity and Efficiency" held in Hyderabad on October 21/22 in collaboration with the Indian Council of Medical Research (ICMR), Administrative Staff College of India (ASCI) and Fordham University of New York. The purpose of this workshop was to create a multi-stakeholder forum for discussions on issues related to the conduct of clinical trials in India. Discussions were held on existing provisions, policy guidelines that need to be developed and the actions to be taken by different stakeholders in the clinical trials industry to make it grow in an efficient and ethical way. Sixty participants representing a wide cross-section of stakeholders including industry, government, patient advocacy, medical practice, ethics review boards, clinical research organizations, media and independent investigators attended the workshop. Invited speakers made formal presentations and/or comments followed by discussions. A summary of the main issues and recommendations are included here. Building the right kind of capacity to meet the anticipated demand for clinical trials in India is an important issue. Along with the optimism for growth in this industry is the fear that vulnerable populations may be exploited. Access to experimental drugs, exposure to latest therapies, improvement in equipment and infrastructure, and creation of new knowledge assets are among the many benefits of this growth. However, being used as guinea pigs with high-risk therapies, creating expectations difficult to meet and moving local

resources away from basic healthcare are among the costs and risks of this

growth. The regulatory regime will have to identify ways of creating a balance between these benefits and costs/risks. There may be a need at the present time for a strong centralized regulatory regime which can guide high quality development of ethical capacity with extra vigilance but an informed understanding of acceptable risk. Such a system while conforming to international standards needs to be uniquely Indian. It needs to include indigenous medicine, devices, drugs and therapies while incorporating the advent of biotechnology in general and genomics and proteomics in particular. India can lead the way in an industry at a time when no country can boast of adequate regulations to ensure safety. While Good Clinical Practices (GCPs) have been clearly spelt out and ethical guidelines have been articulated, the experience with implementation is relatively short. The regulatory system is already stretched in terms of its ability to monitor proper implementation.

The expected fast growth in the industry is going to further stretch the capabilities of the system and highlight complexities and unintended consequences. The workshop covered the following topics:

- Prioritization of Clinical Trials
- Creating a review mechanism for clinical trials
- Building ethical capacity
- Building expertise
- Regulating CROs
- Registries and the role of the media

Prioritization:

Setting clear-cut priorities can help in providing a balance between benefits and

risks/costs of the clinical trial enterprise. Such priorities can allocate public resources in a manner that meets national interests. For the private sector, priorities could mean speedier approvals with a possibility of closer monitoring. It could also mean private public partnership in high priority trials. It is recommended that India have a system of prioritization based on national interest and patient safety. Criteria for prioritization should be clearly spelt out, and legitimate authority to

identify such priorities be identified. Clinical trials have different types of risk associated with them. Ability to safely perform a trial is also a risk and should be factored into the prioritization process. Thus, a placebo trial with vulnerable population (including socio-economically vulnerable) will have a higher risk and may be given a different priority from an identical trial without subject recruitment from vulnerable populations. Higher risk trials need to have special monitoring and more intense review. Risk should include a "site's" ability to safely conduct the trial and the pool from which trial subjects are sought. A number of operational issues to implement such a system of priorities need to be discussed and procedures developed. It is recommended that a working group be formed to develop these. Such a working group should decide on the level of risk attributed to different situations and how to measure them (such as placebo trials using a pool of subjects from a vulnerable population, pediatric trials etc). It should also decide on how to measure risk associated with "site capabilities". This may be particularly relevant for approval of Phase 1 trials. Criteria for "disallowed" trials as well as guidelines for exceptions should be specified by this group and made transparent.

Ethical Review

Ethics committees at different levels, ethical guidelines and norms, independent institutional review boards are all different ways of ensuring compliance with established ethical guidelines and good practices. Critical however, is the preparedness of the members of the ethics committees to take on this onerous task and actually implement some of the guidelines. Ethics committees cannot conduct their task responsibly unless they get the type of data needed to evaluate ethical behavior. Evaluating conflict of interest is an important task of ethics committees for which they may need special training and easy access to financial and other information. Cultural specificities in conducting informed consent may place some special burden in India. Vulnerable populations may need special consideration in the implementation of informed consent. A subject's ability to independently determine risk and the availability of guaranteed medical care might obscure his/her desire to do a risk-benefit assessment before

providing informed consent. The lack of punitive measures and/or legal liability may reduce the importance of the findings of the ethics committees. Training of ethics committee members, accreditation of these committees and the development of more stringent guidelines with detailed operating procedures in response to the issues raised above are the primary recommendations of the workshop. Other recommendations include funding for the ethics committee members, distinction between scientific and ethical reviews, operating procedures for implementation of informed consent and harmonization of the guidelines and rules between different parts of the regulatory process. It is also suggested that different guidelines might need to be developed for ethics committees to deal with preventive (vaccine) trials.

Capacity building

There has been some systematic and some ad-hoc growth in capacity in different parts of the clinical trial process. Much of this growth is taking place without any guidelines and is often uncoordinated. The lack of quality control in some of these capacity building measures has caused public concern. More regulatory capacity to evaluate NDAs and more trained principal investigators are needed. There is also a need for more GLP laboratories, a pharmacovigilance program and the ability to monitor GCP sites. The availability of insurance for subjects of trials is another matter that needs to be urgently addressed. The workshop suggests the creation of a working group to specify the needs for the urgent development of regulatory capacity in monitoring, oversight, enforcement and approval of trials. An innovative structure with “consultants” is suggested rather than a replication of the USFDA structure. A definition of “conflict of interest” in the Indian context for these consultants is also recommended as a task for this working group. The workshop also recommends the creation of a department of Human Research Subject Protection within MoHFW. It is suggested that this be complemented by required legislative changes for the enforcement of such protection. The creation of a public sector CRO for the conduct of need-based trials and curriculum changes in medical colleges to teach GCP, ethics, and research methodology is also recommended. A certification for Principal Investigators is also suggested. The workshop recommends the creation of a committee to investigate the possibility of providing insurance to clinical trial and research subjects. This committee should involve insurance providers. Dispute resolution capacity in trials needs to be enhanced. There is also a need for more systematic collection of data relevant to clinical trials. It is felt that a database for clinical trial capacity would help in monitoring such capacity

especially for Phase 1. A database of prevalent diseases, therapies and largescale epidemiological studies will also be helpful.

Initiatives for expertise building

While growth in clinical trials is being fuelled by business opportunities there are

several other outcomes. Development of world-class expertise in this area is one such outcome. However, care has to be taken to see that knowledge transfer from abroad and local expertise building takes place in a coordinated fashion. This workshop focused on a few aspects of such expertise building. Quality control and joint-trials with reputed global players can give rise to building expertise in this area. Partnerships between public and private sector and with international organizations are a great way to increase expertise. It is recommended that guidelines be provided to ensure that learning does indeed occur through such partnerships. It is also recommended that human resource planning be done carefully to deal with clinical trials of the future (such as molecular diagnostics and molecular epidemiology as well as latest social science techniques) to ensure that required expertise is available.

Regulation of CROs

There has been an unprecedented growth in clinical research organizations

(CROs) in India. Almost all the major multinationals have set up operations in India either directly or as joint ventures with local partners. A large number of Indian companies have started their own CROs and a number of small operations have begun as well. At the present time there is no way of registering or approving the growth of such organizations. Quality control and potential for abuse remain a major concern for the nation. This workshop discussed the pros and cons of self-regulation through accreditation as well as legislation that might be required, in order to maintain high standards in these organizations. In the initial stages of high growth, extra care needs to be taken to see that all trials are registered. Pending the implementation of adequate monitoring by the sponsoring company and the regulatory agency, it is recommended that CROs be registered.

Clinical trials registries and database management

There has been a demand that all clinical trials be registered. Recently this has been further emphasized by the international editors of medical journals who have made some minimum requirements for data to be included in such registries without which they will not publish the results of trials. The World Health Organization (WHO) has suggested a structure of the registry with a minimum required data set to be followed by all countries.

The workshop recommends the creation of an Indian registry with the minimum data set and requirements suggested by WHO. A working group should be formed to implement this registry and should include stakeholders from industry, national laboratories and regulatory authority. Simultaneously, there have been great strides in database management of clinical trials especially in the arena of multi site, multi country trials. Indian IT companies are trying to establish a leadership position in these technological platforms. The government should be proactive in working with ITeS companies to see how this could be stimulated. Media has been criticized for sensationalizing a few cases without investigating systemic issues. Media on the other hand, have complained of lack of transparency on clinical trials conduct and results. What is the responsible role of the media in reporting issues related to clinical trials? It was felt that the media plays a very critical role in locating abuse of the system especially in identifying unethical trials and unreported serious adverse events (SAEs). Media should be seen as a partner in this enterprise and has to be provided training to better understand clinical trials as well as more transparency to do more in depth reporting. It was felt that this would increase public trust in the enterprise that was fast eroding. Public trust is a critical issue for survival and growth in this industry. A few transgressions can erode this trust considerably. It is recommended that human subjects be offered the same protections in all activities. It is recommended that GCP encompass clinical trials, clinical research, devices, drugs and procedures and all these get formally registered and approved. It is also recommended that a working group be formed to investigate different ways in which adequate post-trial care of subjects can be provided. This working group should also look into the feasibility of restricting Phase 1 trials to urban educated subjects. Finally, it is recommended that this

workshop be followed up with another workshop to evaluate the actions taken and the outcome of the different working groups.

STRUCTURE OF THE WORKSHOP

A *Public Policy forum* on clinical trials began at 11:00 AM Friday, October 21st, with presentations by senior policy makers. The *stakeholder forum* for invitees only began at 2 PM that day and continued till 6:00 PM on Saturday, October 22nd. Arrangement for stay was made at the Administrative Staff College of India. Travel to Hyderabad and stay was provided courtesy the Indian Council of Medical Research (ICMR). Financial and intellectual support from Fordham University in New York was also provided. Six panels formed the basis of the workshop. Invited speakers in each panel made formal presentations and/or comments. This was followed by around a one-hour discussion by invited stakeholders (see attached agenda in Appendix 1).

All presentations and discussions were taped under confidentiality. This report is based on the transcripts as well as the formal presentations and background material.

BACKGROUND SITUATION

Recent events worldwide have challenged the adequacy and integrity of research on pharmaceutical products and have triggered calls by legislators, medical associations, the International Committee of Medical Journal Editors, the World Health Organization and others, for increased accountability and transparency in health products research and development. India, projected to have accelerated growth in this sector with the entry of a number of major global and domestic players and the expected transformation in the pharmaceutical industry giving research a higher priority, is poised to face formidable challenges. There is an increase in demand for clinical trials arising out of changes in the global competitive environment in the pharmaceutical industry, new technological possibilities and changes in the regulatory environment in some countries. Demand for clinical trials in India has skyrocketed in the

recent years and is expected to grow exponentially in the next few years. A number of factors make India a very attractive location for clinical trials. There is optimism amongst a variety of stakeholders, about the potential for growth. There is a spurt of entrepreneurial and business activity in this area. Pharmaceutical companies have increased their number of trials, there has been a rapid growth of contract research organizations (CROs) and locations where clinical trials are being conducted have tripled. Secondary and tertiary organizations have also sprouted such as site managers, social workers and subject advocacy groups. There appear to be four major reasons for this rapid growth in clinical trials in India. These are 1) local demand, 2) global demand, 3) supply conditions, and 4) favorable regulatory and technology changes. Building the right kind of capacity to meet the anticipated demand for clinical trials in

India is an important issue. There are a number of stakeholders involved in this process. The Ministry of Health has a very important role to play in regulating this industry through its departments/directorates and councils. The hospitals where such trials are conducted must have systems in place including efficient and independent ethics committees that can best deliver the ethical and efficient conduct of the trial. The doctors who are engaged in the trials are critical to this process and need to be properly trained in being principal investigators.

The pharmaceutical companies need to have adequate databases to monitor and track the trials and must possess clinical research expertise in design and implementation. The independent clinical research companies need to develop systems to monitor the implementation of the trials. Good clinical practices need to be constantly reviewed for effectiveness in reaching the

stated goals. Finally, the volunteers of the clinical trials need to trust the entire system and believe that its primary objective is protecting human subjects and improving healthcare in specific disease categories. Advocacy groups and responsible media are important stakeholders in ensuring that decision-makers hear volunteers concerns and appropriate transparency is assured. Along with the optimism for growth in this industry is the fear that vulnerable populations may be exploited. The benefits and costs anticipated in the fast growth of this enterprise may be summarized in the table below:

TABLE
BENEFITS AND COSTS OF CLINICAL TRIAL ENTERPRISE

BENEFITS	COSTS/RISKS
1. Access to experimental drugs	1. Possibility of exploitation of vulnerable populations
2. Doctors exposure to latest therapies	2. Indians used as guinea pigs (unscrupulous activities going unchecked and unpunished)
3. Overall quality improvement in clinical practice and diagnostics	3. Focus of healthcare shifting to income from trials at the cost of patient care
4. Availability of latest therapies	4. High risk new therapies not allowed in other countries being tried here
5. Improvement in equipment and infrastructure	5. Creating expectations of cure and access to drugs we cannot meet
6. Business opportunity and employment generation	6. Focus of research shifting to diseases of the west
7. Competitive advantage to Indian Pharmaceutical industry	7. Limited governmental resources being hogged by clinical trial activity
8. Stimulate FDI in pharmaceuticals	8. Good doctors losing interest in routine patient care and shifting to research
9. Give India competitive advantage in biotechnology	9. A greater shift from rural into urban health care as research sites remain primarily located in urban areas
10. Give India competitive advantage in gene-based new drug discoveries	10. Lack of post-trial/post approval availability of tested drug; or availability of continued medical care for the subjects.

11. Access to healthcare in economically vulnerable populations	
12. Ability to create sustainable new knowledge assets	

The stakeholders who are independent members of the clinical trials value chain are actively debating the benefits and costs of the enterprise. Their objectives and goals are different and a dialogue between them will go a long way towards clarifying issues, debating priorities and creating the necessary trust. This is what the interactive workshop focused to achieve. The regulatory regime in India has to strike a balance between the benefits and costs/risks of this enterprise. In the initial stages of evolution an industry may not have the ability to self-regulate or implement decentralized decision making without some informed guidelines. Conversations such as those provided during the workshop help build a culture of common goals and priorities so that self-regulatory and decentralized systems can indeed evolve with growth in the industry. Till that happens however, there may be a need for a strong centralized regulatory regime which can guide high quality development of ethical capacity. There is a need to professionalize the culture of this industry. Since this industry deals with the lives of people it has some unique norms. It cannot be viewed in purely commercial terms. It has to develop a culture of caring for human safety. Unlike many other industries however, risk is essential to the nature of experimentation in this industry but errors can kill the reputation of this enterprise or even that of this country. This industry is very sensitive to issues of ethics and morality since it deals with the lives of people. Thus extra vigilance is paramount if this industry is to succeed. There has to be a system that quickly rectifies mistakes but understands the notion of acceptable risk. The regulatory system has a further responsibility of providing public assurance of safe guarding the rights and safety of the study subjects while ensuring the credibility of the data submitted for new drug applications. The system has to simultaneously assure that limited budgetary resources are being spent on issues of national priority. Scientific research and clinical trials in India may be skewed towards lifestyle diseases and less towards public health issues. India has a system of herbal and indigenous medicine that a large number of its

population depends upon and is part of our health care system. Any discussion on clinical trials should incorporate ways of improving the effectiveness of the indigenous system. Another area that needs to come under the clinical trial regulatory regime is that of medical devices. In some areas the distinction between devices, drugs and therapies is being obfuscated. Innovations in devices are happening very rapidly and clinical trials need to be done in a scientific manner to establish superiority over existing therapy. This is because these devices can be very expensive and are mostly imported. There is currently a weak system to prevent the sale of rejected lots of devices in this country since trials on devices is not mandatory. The advent of biotechnology in general and genomics and proteomics has created issues in assessing risk and safety that no regulatory system in the world has perfected. India is entering this industry at a time when no country can boast of adequate regulations to ensure

safety. There is thus no other country to emulate. India has to come up with its own procedures unique to its realities and the technologies of its times. It is also an opportunity for India to be able to be at the forefront of this regulatory venture. It is important that India develops a regulatory system that conforms to international standards. However, there are unique situations in India that may make the "copying" of another country's regulations inadequate or irrelevant. India needs to develop a system that corresponds to its own culture, risk taking profile, legal system, implementation capabilities and priorities. India also needs to be aware that the "blind" following of another country's system may inhibit innovation and development indigenously. There is already a lot of awareness in India regarding clinical trials. Good Clinical Practices (GCPs) have been clearly spelled out and ethical guidelines have been articulated. A system to register and approve clinical trials is in place. An "investigational new drug" and a "clinical trial" have been operationally defined. A national pharmacovigilance program, while in its infancy is likely to address some of the other concerns. However, the experience with implementation is relatively short. The regulatory system is already stretched in terms of its ability to monitor proper implementation. The expected fast growth in the industry is going to further stretch the capabilities of the system and highlight complexities and unintended consequences. This conference covered the issues discussed above in greater depth and developed some recommendations. While senior policy

makers developed the themes presented in this section and provided the backdrop and a sense of urgency to the workshop the stakeholder summit that followed was structured around the following six panels:

Panel 1: Issues of prioritization of clinical trials in India

Panel 2: Strengthening ethical review mechanisms

Panel 3: Critical issues in capacity building

Panel 4: Initiatives for expertise building

Panel 5: Regulation of CROs

Panel 6: Clinical trials registries and database management

The next section describes the issues covered in each of these panels.

The

recommendations from each panel are provided in the final section.

PANELS: SUMMARY OF ISSUES AND VIEWS

Panel 1: Issues of prioritization of clinical trials in India

The panel addressed broad questions dealing with the philosophy of prioritization as well as some of its operational complexity:

Philosophy of prioritization:

There are a number of issues that underscore the debate on prioritization. Market forces can allocate priorities and the need to establish a national priority system has to be debated. Stakeholders from industry were concerned that unless a legitimate basis for prioritization is established it could distort the type of clinical trials approved and could even provide a disincentive to conduct trials in India due to legislative delays. However, a number of instances of trials conducted in India that may not reflect the national needs were identified. To the extent that trials can consume limited regulatory and other capacity, a prioritization process would help. Such a prioritization may result in speedier approvals and alliances with national institutes where resources may be shared. It was however felt that criteria for prioritization should be clearly spelt out, a legitimate authority to identify such priorities be identified. Clinical trials have different types of risk associated with them. Ability to safely perform a trial is also a risk. This should be included in the decision on prioritization, which should basically be based on national interests and risk. High-risk trials may be given a high priority if that means closer monitoring will occur. Thus priority should be associated with different monitoring schemes. Disallowing trials is an extreme way of giving a low priority. There was discussion on whether all Phase 1 trials should be banned, whether the current practice of only allowing Phase 1 trials for indigenous molecules and national priority projects be continued or whether all Phase 1 trials be allowed. There were differing views on this, as a number of industry stakeholders would like to see that all Phase 1 trials are allowed. It is possible that if the issue of risk based prioritization is implemented (where risk is defined also as ability to

safely conduct the trial) then this issue may be automatically resolved. In this scenario, Phase 1 may be allowed for any trial if, along with other factors, the site where the trial is to be conducted is considered safe for such trials. A way to establish safety of sites for Phase 1 will then need to be developed.

Other questions addressed were:

- a) Should India have a system of priorities where it clearly prefers the conduct of clinical trials in some therapeutic/disease areas and discourages others?
- b) What would a high priority mean? Should a high priority mean a speedier approval process and a monitoring and review process based on trust? Or should a high priority trial mean greater scrutiny and control.
- c) Should priorities be assigned to different phases of a trial process or within each phase of a trial?
- d) What will prioritization achieve?

Operational issues dealing with prioritization:

- a) Should there be a prioritization at all? What criteria should be used for such prioritization? Some examples for debate and discussion: should a higher priority be given to drugs that deal with illnesses more prevalent in the Indian population? Should a low priority or denial be given to drugs not approved for trials by other countries? Should paediatric trials and trials on pregnant women come under special scrutiny? Should placebo trials be automatically given a different priority?
- b) Should internationally funded research, nationally funded research and commercially funded research have a different regulatory evaluation system due to differences in internal controls and procedures and public versus private interests?
- c) Do we need different approaches for prioritizing drugs and vaccines?

- d) Should all Phase 1 trials be disallowed or the present policy of not allowing Phase I trial for drugs developed outside be continued/re-examined?
- e) Are there drugs that we should not allow to be tested in India?
- f) Should the prioritization process factor in the study design and protocol? For example, should placebo trials being tested on vulnerable populations be assigned a low/high priority?

- g) What does a high or low priority mean? Quick approval? Access to best resources? Allocation of capacity? Availability or access to national institutes? Reporting of intermediate results? Adverse event reporting? Aggressive monitoring?

- h) Should the public be informed of the criteria for prioritization (if one is established)?

- i) Should the regulatory bodies charge higher fees to applicants in order to increase capacity and provide speedier responses?

Panel 2: Strengthening ethical review mechanisms

Ethics committees at different levels, ethical guidelines and norms, independent institutional review boards are all different ways of ensuring compliance with established ethical guidelines and good practices. While there are a number of such mechanisms in place this panel discussed some of the pros and cons of the existing procedures and structures. Harmonization of guidelines and rules between different parts of the regulatory process as well as with international standards is an important issue. Critical however, is the preparedness of the members of the ethics committees to take on this onerous task and actually implement some of the guidelines. Issues of training of ethics committees were discussed in this panel as well as the role, played by IRBs in the other countries. Critical in this panel was also the issue of informed consent in different trial phases. Do cultural specificities in conducting informed consent place some special burden in India? Do vulnerable populations need special considerations in the implementation of informed consent? The presentations and discussion covered the above issues and elaborated on:

- a) Ethics Committees: need for training, need to re-evaluate structure and composition, need to have proper SOPs for ethics committees, need to identify rules for conflict of interest in ethics committees
- b) Informed consent: evaluating a subject's ability to determine risk and impact of guaranteed medical care obscuring a subject's desire to do a risk-benefit assessment before providing informed consent
- c) SAE reporting: the need to have clear procedures and implementation
- d) GCP compliance
- e) Post-trial issues such as availability of therapy: how to evaluate these concerns
- f) Penalties for violations and enforcement issues

- g) Conflicts of interest: training on how to evaluate conflict of interest and rules to require the availability of data, especially financial data. The need to have someone in the ethics committee who understands financial data was mentioned.
- h) Public's right to know
- i) Problem of the same group doing both scientific as well as ethical review.
More guidelines are needed
- j) The need to look at vaccine and other preventative trials differently in ethics committees was discussed at length. Greater community involvement is needed in these cases and may require the creation of a community advisory board
- k) The lack of an appellate procedure to address grievances in many trials causes serious ethical dilemmas and need to be addressed
- l) There was much discussion on the need for accreditation of ethics committees. This was positively received but caution in implementation was urged.
- m) There was discussion on the pros and cons of independent ethics committees including those for profit. Experiences from the US were discussed.
- n) There was a sentiment that the complexities of running ethics committees should be available on a privately accessible website. In general the issue of transparency of ethics committee deliberations needs to be considered.

Panel 3: Critical issues in capacity building

There is anticipation of a rapid growth in demand for clinical trials to be performed in India. This is partly due to the changing strategies of the Indian pharmaceutical industries, the demand for testing Indian traditional medicines more rigorously, and the growth in outsourcing of clinical trials by global pharmaceutical companies. The characterization of India as a 'preferred location' for global clinical trials has further fuelled this demand. The result has been some systematic and some adhoc growth in capacity in different parts of the clinical trial process. Much of this growth is taking place without any guidelines and is sometimes very uncoordinated. The lack of quality control in some of these capacity building measures has caused public concern. This panel identified critical issues in capacity building for clinical trials. In order to do that the discussion was structured around the different parts of the clinical trial process. The main focus of this panel was to identify what we have to keep in mind as a nation as we invest in building capacity in different parts of the clinical trial process. For the sake of simplicity the clinical trial process was broken down into the following:

- 1) Study design and protocol development
- 2) PI recruitment
- 3) Site selection
- 4) Subject recruitment
- 5) Clinical trial management
- 6) Data management
- 7) Supplies management
- 8) Regulatory interface

This panel looked at each of the four phases (Phase I through IV) and just identified the critical issues in the eight steps listed above. The following issues, were raised during the course of discussions in this panel:

1. Availability of sufficient number of trained Principal Investigators
2. Need for certification of Principal Investigators
3. Introducing training in medical colleges on the conduct of clinical trials

4. The acute need to increase the regulatory capacity in the center
5. Availability of insurance coverage for subjects
6. Capability of addressing all trial related consequences for subjects
7. Manufacturing and importing of clinical trial supplies
8. Need for more *GLP* laboratories
9. The need to create a data base on available clinical trial capacity in India was suggested
10. The need for a national pharmacovigilance programme was highlighted
11. Need for capacity to monitor and oversee *GCP* compliance. There was discussion on whether small sample techniques used in the US to monitor compliance can be used

Panel 4: Initiatives for expertise building

While growth in clinical trials is being fuelled by business opportunities there are several other outcomes. Development of world-class expertise in this area is one such outcome. However, care has to be taken to see that knowledge transfer from abroad and local expertise building takes place in a coordinated fashion. This panel focused on a few aspects of such expertise building. Quality control in clinical trials management is one such area. Joint-trials with reputed global players can give rise to building expertise in this area. Panelists discussed examples of how this can be achieved and the policies that might help to foster this. Certification is another initiative that can lead to creating world-class expertise. Training of high quality principal investigators is critical. Specialized diagnostics capabilities are necessary in different phases of the clinical trial process. Many CROs are working with specific hospitals in order to build expertise to world-class standards. The success of this was discussed. The focus in this panel was to identify successful initiatives and facilitating policies that not only bring us to world-class standards but also prepare us for the future as the demands on expertise change with the increase of genetic based drugs. This panel focused on:

- a) Joint trials
- b) PI certification
- c) CRO partnerships
- d) Training
- e) Preparing for future expertise

Panel 5: Regulation of CROs

There has been an unprecedented growth in CROs in India. Almost all the major multinationals have set up operations in India either directly or as joint ventures with local partners. A large number of Indian companies have started their own CROs and a number of small operations have begun as well. At the present time there is no way of registering or approving the growth of such organizations. Quality control and potential for abuse remain a major concern for the nation. This panel discussed the pros and cons of self-regulation through accreditation as well as legislation that might be required, in order to maintain high standards in these organizations. Experience with these problems and ways to resolve them in other countries was discussed. The relevance to India was elaborated.

Panel 6: Clinical trials registries and database management

There has been a demand that all clinical trials be registered. This demand has come recently from the international editors of medical journals who have made some minimum requirements for data to be included in such registries without which they will not publish the results of trials. WHO has suggested the structure of a registry with a minimum required data set to be followed by all countries. There is a European registry in place as well. The first part of this panel discussed the elements of existing proposals and the policies India may like to follow in this regard. Specifically the issue of an Indian registry was discussed. Simultaneously, there have been great strides in database management of clinical trials especially in the arena of multi site, multi country trials. Indian IT companies are trying to establish a leadership position in these technological platforms. Some Indian firms have secured large contracts from multinationals to manage their clinical trials databases. Finally with the increased use of internet based trial management protocols such as eClinicaltrials, India may wish to consider leapfrogging into this system. The second part of this panel discussed these issues. Media has been criticized for sensationalizing a few cases without investigating systemic issues. Media have complained of lack of transparency on clinical trials conduct and results. What is the responsible role of the media in reporting issues related to clinical trials? What can be done to facilitate their playing a responsible role? This panel also addressed some of these issues.

PANELS: CONCLUSIONS AND RECOMMENDATIONS

Based on the presentations, discussions and other background material

at the workshop, the following recommendations are offered

Prioritization of clinical trials in India

1) India should have a system of prioritizing clinical trials based on national

interests. National interests for the purposes of clinical trials may be defined as:

- a) Drugs, whose approval will provide benefits to a substantial segment of the Indian population
- b) Drugs, for diseases relevant to Indian populations which may or may not have a high priority in other countries including orphan drugs,
- c) Clinical trials, which will give Indian manufacturers/researchers a competitive advantage in the global pharmaceutical market and knowledge,
- d) Trials that leverage private and public resources (partnership trials such as those private sector trials which allow "piggy-backing" of public interest hypotheses testing).

2) A high priority trial should benefit from speedier and/or earlier approvals, and sharing of resources and risks by government institutions. Details of intellectual property/knowledge sharing need to be worked out where resources and/or risks are being shared by the public sector. Different types of priority approvals may be looked into, such as:

- a) Priority review (end of Phase 2 for life threatening)

- b) Expedited review (for minimal risk trials)
 - c) Accelerated review (me-too drugs)
 - d) Fast track review (testing for "superiority" of product over another)
 - e) Fast track development (Phase 0, or proof of concept)
 - f) Post market survey (currently does not have any monitoring)
 - g) Spontaneous reporting of ADR (adverse drug reactions)/Effective Pharmacovigilance program
 - h) Letters written by the regulatory authorities after approval of trial to principal investigators if new information warrants it (such as SAEs discovered in international sites)
 - i) Supplemental NDA (label change, OTC)
 - j) Abbreviated New Drug Application (ANDA)
(Note: the above are similar in many respects to USFDA practices)
- 3) There should be a system of intense review for trials that are considered to be higher risk. A system of assigning risk to clinical trials needs to be devised. This should be a uniquely Indian system which factors in not only technoscientific risks but risks of conducting the trial given India's state of the capacity in that area and specific social and cultural milieu. Such a review may need extra information and may be slower in approval. It is however, necessary to differentiate approvals based on risks.
 - 4) A low risk high priority trial may have speedier approval process as well as a self-reporting monitoring and review process. A high-risk high priority trial may have speedier approval but a more formal and rigorous monitoring, reporting and review process.
 - 5) A number of operational issues need to be specified. It is recommended that a working group comprising of stakeholders be formed to develop these procedures. Such a working group should consider issues such as whether priorities should vary between different phases of a trial and on issues of concern such as placebo trials, pregnancy indications, pediatric trials, use of other vulnerable groups etc.
 - 6) This group should also look into issues of transparency of criteria for prioritization.

7) A list of criteria for trials that will not be allowed in India should be publicized. Such criteria may include, banned drugs in other countries, Phase I for drugs developed outside India unless justified. etc.

Ethical review mechanisms

- 1) Training of ethics committee members needs to be vigorously implemented. Such training should include international and local concerns and programs should clarify "equivalent" protections - i.e., what India considers equivalent to those internationally adopted.
- 2) Accreditation of ethics committees will help in improving the quality of such committee's operations and continuously reviewing their performance. An accreditation system should be set up in a stepwise manner.
- 3) While the tasks and decisions of the ethics committees have been developed there is a need to develop more detailed guidelines on the specifics of the operating procedures to implement these tasks and decisions. Such operating procedures must include types of information and infrastructural facilities and access that must be accorded to committee members and their deliberations. Guidelines for funding of such committees need to be developed to ensure effectiveness without conflict of interest.
- 4) The operating procedures should distinguish between scientific review of trials and ethical review and simultaneously have a system in place that allows a combined review as well wherever needed.. The expertise needed for scientific and ethical reviews are different and the operating procedures should account for that.
- 5) Preventive trials (vaccine) need special considerations. Community involvement should be mandated in such trials. The experience with community advisory boards should be investigated to see the appropriateness of mandating such structures for preventive trials or research in life-threatening settings where commonly accepted ethical principles (such as obtaining informed consent prior to enrolling research participants) may not exist.

- 6) While elements of informed consent forms are well laid out, the operating procedures for implementing these forms need to be standardized. Guidelines need to be issued and approval should be conditional to following these guidelines. Ethics committees may be given the added responsibility to monitor the informed consent process.

- 7) Harmonization of guidelines and rules between different parts of the regulatory process needs to be done. At the present time there is some confusion regarding the role of departments outside the jurisdiction of MoHFW in the trial approval process. The criteria and timing of referrals and intervention of such departments need to be formalized and publicized.

Capacity building

- 1) There is need for the urgent development of regulatory capacity regarding clinical trials. Capacity in monitoring, oversight, enforcement and approvals is needed in that order of priority. A working group needs to be urgently formed to specify these resource needs.
- 2) In order to achieve the above, innovative structures may have to be created. Specialists in disease categories as well as disciplines need to be identified who will act as paid regular consultants to the regulatory body for a period of five years. A sub-committee of the above working group should be formed to develop the details of this "virtual matrix structure". Replicating the USFDA structure may be too ambitious given the number of trials conducted in India. An India specific regulatory structure with appropriate capacity is urgently required. Indian definitions of when "conflict of interest" for consultants/experts exists, need to be developed.
- 1) Human subject protection capacity needs to be enhanced. The possibility of an OHRP (Office of Human Research Subject Protection, USA) type department within MOHFW should be investigated. Given the large vulnerable population in India and the dependence by them on the government for their protection, the need for such a structure is acute.
- 4) The creation of such a department should be complemented by required legislative changes to allow for enforcement of such protection.
- 5) For need-based trials the creation of a public sector CRO should be investigated. Priority trials with public and private participation can be coordinated through such an organization. Such a CRO will act as an example of good clinical practices and will help train professionals for such work. Such a public sector CRO should have multi-departmental relevance (in particular be relevant to the work of DBT, DST, CDSCO, ICMR).

- 6) Teaching and training of Principal Investigators should be introduced in medical colleges. *GCP*, together with research methodology and ethics, should be taught as part of the regular curriculum of medical programs.
- 7) Certification of Principal Investigators will add to the capacity for trained investigators. A system for such certification should be developed.
- 8) **A database for capacity available in India for Phase I, II and III trials may be created. This should be part of a GCP certification process for clinical trial sites.**
- 9) Phase I trial capacity is particularly limited and of high risk. There is need to monitor this carefully. Demand for Phase I through IIa in India is likely to be high. Caution should be used in the approval process for Phase I and special rules may need to be written into the Indian *GCP* to ensure that Phase I sites are capable of handling the risks involved.
- 10) A committee should be formed to investigate the possibilities /develop the modalities of insurance for clinical trial and research subjects.
- 11) Dispute resolution capacity in trials needs to be enhanced. A committee should investigate the ways in which disputes could be best resolved in the interests of the subjects as well as that of good science.
- 12) Standardization of laboratories and a list of labs approved to conduct clinical trials tests should be identified. More labs to be *GLP* certified.
- 13) Data needed to prioritize effectively has to be generated. Currently there is a lack of data on diseases prevalent, therapies recommended and results of large-scale epidemiological studies. A system to generate and disseminate such data needs to be established.

Expertise building

- 1) Global trials should be used to transfer knowledge locally. Ways in which to do this need to be investigated.
- 2) Training should be given to building expertise for the next generation of clinical trials that will be based heavily on genomics and proteomics routes to drug discovery and will need new skills.
- 3) Expertise needs to be built in the area of molecular diagnostics and molecular epidemiology as well as the social sciences geared towards the conduct of clinical trials.
- 4) Incentives need to be provided to develop capacity in research design, data management and analytics aspects of clinical trials. Trends in outsourcing these tasks as well as India's skills in these areas can provide competitive advantage to Indian firms.
- 5) Public health expertise needs to be urgently enhanced. This may require the setting up of more public health education capacity.

Regulation of CROs

- 1) In the initial stages of high growth in the number of CROs in India, care must be taken to ensure that all trials being conducted by CROs are indeed registered and approved.
- 2) Pending the implementation of adequate monitoring by the sponsoring company and the regulatory agency of clinical trials, CRO's may need to be registered.

Clinical trials registries and database management

- 1) A registry for all clinical trials should be created. While there is already a group within ICMR working on creating such a registry it is imperative that multiple stakeholders are part of the design process of such a registry for it to be meaningful. There is a need to create such a stakeholder group that goes beyond a simple advisory role.
- 2) Such a registry should have a public and a confidential element. Some key items may need to be blocked from public view (such as raw data pertaining to SAEs and proprietary information) but necessary for regulatory enforcement purposes and scientific research. 3) Such a registry should incorporate all the necessary items required by the WHO registry as well as by the International Editors of Medical Journals. This will ensure that research based on trials conducted in India will be publishable in top tier international journals.\
- 3) Such a registry should have "hot links" to results databases of marketed drugs that are being introduced by a number of industry associations and individual firms. At the present time it is too onerous to include a results database into the registry.
- 4) The ministry should begin dialogue with ITES companies to facilitate the growth of the clinical trial database management industry in India. A committee should be formed to identify initiatives with public-private participation.
- 5) Public trust is critical to the growth of this industry and the ministry needs to improve its education and information dissemination to the media in the area of clinical trials. While a publicly accessible registry will increase transparency, clinical trials are a complex process and much more needs to be done to inform the media.

7) The media plays a very critical role in locating abuse of the system especially in identifying unethical trials and unreported serious adverse events (SAEs). There should be a way in which the media can be seen as a partner in this enterprise to ensure responsible reporting on their part.

Miscellaneous

- 1) No distinction should be made between clinical trials and clinical research with respect to human subject protection. The same protection should be available to both. This implies that there should be a way to ensure that the same GCPs are being used for research as well. This will put India ahead of other countries that are now trying to correct the mistakes made in legislation due to separating research subjects from trial subjects with respect to protections provided.
- 2) Most of the discussion on clinical trials is usually restricted to drugs. There is a need to integrate the needs of trials on devices as well as procedures into the regulatory system and bring them within GCP purview.
- 3) Some symbolic gestures are needed to increase public trust in this enterprise. This will happen if the government shows in no uncertain terms that it is willing to punish abusers in the area of clinical trials. The proposed legislation of the ICMR guidelines to be expedited to protect all research participants.
- 4) Unregistered trials are a main perpetrator of abuse. The government needs to "crack down" on some of these as soon as possible. This will have a major prophylactic effect on other such trials, which will remain the main culprits in providing a poor image to India's ability to conduct trials ethically.
- 5) Availability of post-trial care is an issue unique to conducting trials in countries like India. There is a huge cost advantage to

conducting trials in India and some of this should be used to defray the costs of life-long care of clinical trial subjects. The possibility of using a levy to create a fund that will adequately take care of this issue should be investigated. Alternatively, regulations could require sponsors to guarantee life-long care for any trial related illness to all subjects. The costs of this will not be so exorbitant as to make the conduct of clinical trials in India no longer an attractive economic proposition for sponsors. A committee should be formed to specify the details of this issue.

- 6) A working group should be formed to look into the feasibility of restricting Phase I trials to urban educated subjects due to the difficulty in understanding risks and meaningfully providing informed consent.

- 7) A working group should look into the feasibility of approving trials only if the principal investigator can demonstrate that no more than one-third of his/her income in a given year comes from clinical trial participation (wherever applicable).

APPENDIX 1

Agenda of the workshop and speakers

Agenda
JOINT ICMR – ASCI – FORDHAM UNIVERSITY
WORKSHOP
ON
BUILDING AND MANAGING CLINICAL TRIAL CAPACITY IN
INDIA:
CHALLENGES IN ETHICS, EQUITY AND EFFICIENCY
21-22 OCTOBER 2005
AT
THE ADMINISTRATIVE STAFF COLLEGE OF INDIA (ASCI),
HYDERABAD

21 October 2005

Inaugural Session

11.00 A.M. - 11.05 A.M.	Welcome Dr. S.K. Rao, DG ASCI
11.05 A.M. - 11.20 A.M.	New initiatives/trends in healthcare in India Sh. P. Hota, Secretary Health
11.20 A.M. - 11.40 A.M.	Global trends of clinical trials Dr. M.S.Valiathan , MAHE, Manipal
11.40 A.M - 12.00 P.M.	Emerging regulatory scenario on clinical trials in India Sh. Ashwani Kumar, DCGI
12.00 P.M. - 12.20 P.M.	Clinical trials and Indian Industry perspective Dr. Dhananjay Bakhle,OPPI
12.20 P.M. - 12.40 P.M.	Public health perspectives in clinical trials Dr. Lalit Dandona, ASCI, Hyderabad
12.40 P.M. - 1.00 P.M.	Objectives and expected outcome from the conference Dr. Falguni Sen & Dr. Vasantha Muthuswamy

1.00 P.M - 2.00 P.M.

Lunch break

Panel I

<i>2.00 P.M - 3.30 P.M.</i>	<i>Issues of prioritization</i> <i>Chair Dr. Lalit Kant, ICMR, New Delhi</i>
<i>Speakers</i>	Dr.Lalit Kant,ICMR,NewDelhi Dr. N.R.Srinivas, Dr Reddy's Lab, Hyderabad Sh. Ashwani Kumar,New Delhi Dr Pushpa Bhargava, Bangalore Dr Krishna Ella,Hyderabad
3.30 P.M. - 4.00 P.M	Discussion for Panel I

4.00 P.M. -4.15 P.M.

Tea break

Panel II

<i>4.15 P.M. – 5.30 P.M.</i>	<i>Strengthening Ethical Review Mechanisms</i> <i>Chair: Dr Vasantha Muthuswamy</i>
<i>Speakers</i>	Evaluating current policies and mechanisms on ethical review Dr. Rajni Kaul, ICMR, New Delhi Ethical Review at various levels: from community review board (CRB) to national ethics committee (NEC) Dr. Sanjay Mehandale, NARI Being proactive and not intrusive: the sponsor as adviser Dr. Narges Mahaluxmiwala, Quintiles Spectral, Mumbai IRBs and institutional ethics committees: working together and separately in the US Dr. Felix Khin-Maung-Gyi, Chesapeake Res. Review, USA Accrediting ethics committees: is it the answer? Dr. Marjorie A. Speers, Washington, USA
5.30 P.M. -6.30 P.M.	Discussion for Panel II
6.30 P.M. - 7.30 P.M.	Cocktails
8.00 P.M.	Dinner for invitees

22 October 2005

Panel III

<i>9.00 A.M. - 10.15 A.M.</i>	<i>Critical issues in capacity building</i> <i>Chair: Dr. M.S. Valiathan</i>
<i>Speakers</i>	Certification of Principal Investigators- international experience Dr. Felix Khin-Maung-Gyi, Chesapeake Res. Review, USA Improving benefit/risk ratios: insurance and other issues Dr. Rajat Goyal, PATH, New Delhi Meeting international standards in capacity building Dr. Vis Niranjan, RDxMD, Chennai
<i>10.15 A.M-11.00A.M.</i>	Discussion for Panel III
11.00 P.M. - 11.30 P.M.	<i>Tea</i>

Panel IV

<i>11.30 A.M. – 12.30 P.M</i>	<i>Initiatives for expertise building</i>
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	<i>Chair: Dr Laxman Prasad</i>
<i>Speakers</i>	<p>Growing clinical trials activities in India: an impact on critical expertise building Dr. Satyajit Rath, NII</p> <p>Future expertise building potential if we do it right - a multinational perspective Dr. Dhananjay Bakhle, Sanofi-Aventis</p> <p>Participating in clinical trials as a way of building international expertise for doctors Dr. D.Prabhakaran, AIIMS, New Delhi</p> <p>Quality assurance audits from phase I to phase IV Dr. Banu Priya, Health Care Solutions, Bangalore</p>
12.30 P.M. - 1.00 P.M.	Discussion for Panel IV

1.00 P.M. - 2.00 P.M.

Lunch break

Panel V

<i>2.00 P.M. - 2.45 P.M.</i>	<i>Regulation of CROs</i> <i>Chair: Sh. Ashwani Kumar, DCGI</i>
<i>Speakers</i>	<p>From bio-equivalence studies to full fledged CRO: Challenges in making the transition Dr. Vasi Reddy, Vimta Laboratories, Hyderabad</p> <p>Challenges of a new entrant Ms. Jamila Joseph, Reliance Clinical Research, Mumbai</p> <p>Maintaining quality in CRO operations: self-regulation, accreditation and legislative issues Dr. Douglas Peddicord, ACRO, USA</p>
2.45 P.M. - 3.15 P.M.	Discussion for Panel V

3.15 P.M. - 3.30 P.M.

Tea break

Panel VI

<i>3.30 P.M. - 4.45 P.M.</i>	<i>Clinical Trial Registries & Data Management</i> <i>Chair: Dr Falguni Sen</i>
<i>Speakers</i>	<p>Building India's registry: where we stand Dr. Arvind Pandey, ICMR, New Delhi</p> <p>Is a human subjects national registry desirable and possible? Dr. Indira Ghosh, Pune University, Pune</p> <p>Building world class data management capacity at Manipal Dr. Ramanand Nadig, Manipal Acunova, Bangalore</p> <p>Key issues in outsourced clinical trial data management Mr. Bala Sankaranarayanan, Cognizant, Mumbai</p> <p>Responsible reporting of clinical trials: issues Ms. Mohuya Chaudhuri, NDTV</p>
4.45 P.M. - 5.30 P.M.	Discussion for Panel VI
5.30 P.M. - 6.30 P.M.	Summary of workshop and recommendations

APPENDIX 2

List of participants

1. Dr O.P.Agarwal
Emeritus Scientist
(CSIR) ,ICMR New Delhi
op_agarwal@yahoo.com

2. Dr Abha Agarwal
Assistant Director
Institute For Research In Medical Statistics
ICMR Head Quarters Campus Ansari Nagar
New Delhi - 110029 .

3. Dr Dhananjay Bakhle
Aventis house
54A Sir M.V.Road
Andheri East
Mumbai 93
Dhananjay.bakhle@sanofi-aventis.com
Mobile: 9821511880

4. Dr Pratul K Banerjee
Director
Defence Institute of Physiology And Allied Sciences
DRDO, Ministry of Defence
Delhi- 110054
Tel: 23946257
23914790
Fax 23914790
Pratul47@yahoo.com

5. Dr. Pushpa M. Bhargava
Padma Bhushan
Founder Director, CCMB
Nveshna, Furqan Cottage
12-13-100 Lane #1, Street #3, Tarnaka,
Hyderabad 500 017

6. Miss Mohuya Chaudhuri
News Editor
New Delhi television Limited
Archana
Greater Kailash - 1
New Delhi- 110 048
tel: 011 2621 8621, 011 5157 7777
fax: 011 2646 1740
mohuya@ndtv.com

7. Dr Sudhir Dagaongkar
Professor,
Somayya Medical College,
Mumbai

8. Dr Lalit Dandona
Director,
Health Study Center"
Administrative Staff College of India, (ASCI)
Bella Vista
Hyderabad - 500082
Tel: 040-23376958
E-mail dandona@asci.org.in

9. Dr. Bhawani Shanker Das
Consultant
Department of Biotechnology
Block 2, 7th floor
CGO Complex, Lodi Road
New Delhi-110003.
FAX –24362884

10. Dr Taraprasad Das
L.V.Prasad Eye Institute
Hyderabad

11. Dr Krishna Ella
Bharat Biotech
Hyderabad

12. Dr Indira Gosh
Professor
University of Pune
indira@bioinfo.ernet.net
Tel: 02025698751
+919890397771

13. Dr. Rajat Goyal
Director
Vaccine and Health Technologies India
Sangha Rachna Building
53 Lodhi Estate
New Delhi 110 003
India
Phone: 91.11.2465.6062
Fax: 91.11.2463.1240
Email: info@path.org

14. Dr Felix Gyi
CEO
Chesapeake Research Review, Inc.
7063 Columbia Gateway Drive
Suite 110 ,Columbia MD 21046
Ph: 410-884-2900 Fx: 410-997-5959
fgyi@irbinfo.com
www.chesapeakeirb.com

15. Sh. P. K. Hota
Secretary
MOHFW
Govt. of India
Nirman Bhawan
New Delhi

16. Dr Jamila Joseph
Reliance Clinical Research Services
Mumbai

17. Dr Lalit Kant
Sr DDG , ICMR
New Delhi

18. Dr. Rajni Kaul
DDG(BMS)
ICMR , New Delhi

19. Sh Ashwani Kumar
Drugs Controller General of India
Nirman Bhawan
New Delhi
Tel 01123061806
Fax 01123062648
dci@nb.nic.in

20. Dr Nandini K Kumar
DDG
Division of BMS
ICMR
New Delhi

21. Dr Nargis Mahalaxmiwala
M/s Quintiles Spectral (India)
Muthuswamy and Sen muthuswamyv@icmr.org.in & fsen@fordham.edu 51
3 Ashok Nagar Bungalows
Behind Sundervan, Satellite Road
Ahmedabad
Tel 022-56774201
022-56774343
9819301085
Narges.Mahaluxmivala@Quintiles.com

22. Dr. S.M.Mehendale
Deputy Director
National AIDS Research Institute
Plot No. 73, Block G, MIDC Complex
Bhosari,
Pune-411026
smehendale@nariindia.org
mehendalesm@icmr.org.in
Tel: 020-27121342

23. Mr Rajendra Mehrotra
Ministry of Health and Family Welfare
rajendra.mehrotra@rediffmail.com

24. Dr Ganapati Mudur
Telegraph, New Delhi
gsmudur@hotmail.com

25. Dr Somsheila Murthy
L.V.Prasad Eye Institute
Hyderabad

26. Dr. Vasantha Muthuswamy
Sr.DDG(BMS)
ICMR ,
New Delhi
Tel: 011 26589791
muthuswamyv@icmr.org.in

27. Dr Ramananda Nadig
Chief Technology Officer
Acunova Pvt. Ltd.
Manipal Tower

14, Airport Road,
Bangalore 560008
080-25217617
Fax 25217619

28. Dr M.U.R Naidu
Nizam's Institute of Medical Sciences
Hyderabad

29. Dr Ashwin Naik
Vaatsalya Healthcare Solutions Pvt. Ltd.
314, 5th main 1st Block Koramangala,
Bangalore 34

30. Dr Balasankara Narayanan
Cognizant Solution Ltd.
Mumbai

31. Mr Neelkantan
Vaatsalya Healthcare Solutions Pvt. Ltd.
314, 5th main 1st Block Koramangala,
Bangalore 34

32. Dr Vis Niranjan, MD
74, Kasturi Rangan Road
Chennai- 600018
Mobile: 9841096081
Vis.niranjan@rxmd.com

33. Dr. Arvind Pandey
Director
Institute For Research In Medical Statistics
ICMR Head Quarters Campus Ansari Nagar
New Delhi – 110029

34. Dr Rajul Parikh
L.V.Prasad Eye Institute
Hyderabad

35. Dr Douglas Peddicord, Ph.D.
ACRO Executive Director
Association of Clinical Research Organizations
227 Massachusetts Avenue NE
Suite 300,
Washington DC 20002
doug.peddicord@whaonline.org
www.acrohealth.org

36. Dr Chandrashekar Potkar
Pfizer Centre
Patel Estate, S V Road,
Muthuswamy and Sen muthuswamyv@icmr.org.in & fsen@fordham.edu 53
Jogeshwari (West),
Mumbai - 400 102.
India.
Tel : +91- 22 - 5693 2000
Fax : +91- 22 - 5693 2444
Mobile: +919833277484
potkac@pfizer.com

37. Dr D. Prabhakaran
Additional Prof
Deptt. of Cardiology
AIIMS,
New Delhi 110029
Tel: +919810118696

38. Dr. Laxman Prasad
Advisor
Department of Science & Technology, Technology Bhavan,
New Mehrauli Road,
New Delhi - 110016"
Phone 26510686(o)
22712420 (R)

39. Dr. Banu Priya
Vaatsalya Healthcare Solutions Pvt. Ltd.
314, 5th main 1st Block Koramangala,
Bangalore 34
priya@vaatsalya.com

40. Dr Radhika, MD
VIMTA Labs Ltd.
#142, IDA, Phase-2, Cherlapally
Hyderabad - 500 051

India
Tel: +91 40 2726 4444
Fax: +91 40 2726 3657
Email: mdo@vimta.com
URL: www.vimta.com

41. Dr Radha Rajgopalan
Apollo Hospitals
Chennai

42. Dr Siripurapu.K.Rao,
Director General
Administrative Staff College of India (ASCI)
Muthuswamy and Sen muthuswamyv@icmr.org.in & fesen@fordham.edu 54
Bella Vista
Hyderabad - 500082
Tel 040-2331-0852
Fax 040-2332-1401
Email: skrao@asci.org.in

43. Dr D Prasada Rao
Nizam's Institute of Medical Sciences
Hyderabad

44. Dr B Venkata Rao
Administrative Staff College
Hyderabad

45. Dr Satyajit Rath
National Institute of Immunology
New Mehrauli Road
satyajit@nii.res.in
Tel: 01126703649

46. Dr Vasi Reddy
Chairman & MD
VIMTA Labs Ltd.
#142, IDA, Phase-2, Cherlapally
Hyderabad - 500 051
India
Tel: +91 40 2726 4444
Fax: +91 40 2726 3657
Email: mdo@vimta.com
URL: www.vimta.com

47. Dr Chander Shekhar K Reddy
APIDC Venture Capital Pvt Ltd
Hyderabad

48. Dr Shyamla Sasikaran
Apollo Hospitals 21,
Greems Lane, Off Greems Road,
Chennai - 600006.
Phone No.: 8293333 Ext. 2511
Fax: 8291761
Website: www.apollohospitals.com
www.medvarsity.com

49. Dr K Satyanarayana
Sr DDG
Muthuswamy and Sen muthuswamyv@icmr.org.in & fsen@fordham.edu 55
Division of P & I
ICMR,
New Delhi

50. Dr Falguni Sen
Professor of Management
Graduate School of Bussiness
Fordham University
113 W 60th Street
"New York,NY 10023"
Tel +1212 636 6160
Fax +1 212 765 5573
Email: fsen@fordham.edu

51. Dr S.D.Seth
Chair in Clinical Pharmacology
ICMR,
New Delhi

52. Dr Veena Shatrugana
National Institute of Nutrition
Hyderabad

53. Dr Majorie A Speers
Executive Director
Association for the Accreditation of Human
Research Protection Program
915 15th Street, NW Suite400
Washington DC20005
Phone: (202) 783-1112

Fax: (202) 783-1113
mspeers@aahrpp.org
www.aahrpp.org

54. Dr Nuggehally R Srinivas
Vice President
Discovery Research
Dr Reddy's Lab
Hyderabad

55. Dr Urmilla Thatte
BYL Nair Hospital
Mumbai
clinpharm@vsnl.net

56. Dr M.S Valiathan
Honorary Advisor Manipal Academy of higher education
Muthuswamy and Sen muthuswamyv@icmr.org.in & fsen@fordham.edu 56
Madhav Nager
Manipal -576119

□□