Accreditation of human research protection program: An Indian perspective

With the increasing number of clinical trials being placed in India, it is the collective responsibility of the Investigator sites, Government, Ethics Committees, and Sponsors to ensure that the trial subjects are protected from risks these studies can have, that subjects are duly compensated, and credible data generated. Most importantly, each institution/hospital should have a strong Human Research Protection Program to safeguard the trial subjects. In order to look at research with a comprehensive objective approach, there is a need for a formal auditing and review system by a recognized body. As of now, only the sponsors are monitoring/auditing their respective trials; however, there is an increasing need to perform a more detailed review and assessment of processes of the institution and the Ethics Committee. This challenge can be addressed by going for accreditation by a reputed association that encompasses—the institutions, the ethics committees, and researcher/research staff. Starting their journey for the accreditation process in late 2010, Kasturba Medical College and Hospital [KMC], Manipal, and Manipal Hospital Bangalore [MHB] received full Association for the Accreditation of Human Research Protection Programs (AAHRPP) accreditation in Dec 2011—a first in India. This article delves into the steps involved in applying for AAHRPP accreditation from an Indian Perspective, the challenges, advantages, and testimonials from the two hospitals on the application experience and how the accreditation has improved the Human Research Protection Program at these hospitals.

**Key words:** Accreditation, Association for the Accreditation of Human Research Protection Programs, ethical clinical trials, human research protection, subject protection
offers nearly 700,000 specialty hospital beds. According to a Confederation of Indian Industry study, clinical trials in India in 2002 generated $70 million in revenues. It predicts that it would grow to $200 million by 2007 and anywhere between $500 million and $1 billion by 2010. India is continuing to gain importance as a clinical trial destination. The global clinical research outsourcing market is projected to touch US$ 23 billion by 2011, with consultancy firm, KPMG, estimating that India will corner 15% of this in two years.

The pace for drug trials in the country is so fast that the Clinical Data Interchange Standards Consortium (CDISC), USA, a non-profit organization committed to the development of clinical research organizations’ standards the world over, is looking at setting up its chapter in India.

This being the current scenario in India, where large number of trials are coming in with different sponsors and contract research organizations (CROs) playing a major role, it is the collective responsibility of the institutes/hospitals, government, nongovernmental organizations, statutory bodies, and ethics committees that the trial subjects are protected from risks these studies may pose, subjects are duly compensated, and credible data generated. Albeit subjectively, there are still a lot questions about the research process and the “Guinea Pig” cliché as illiteracy and economical backwardness leads to vulnerability. Therefore, each institution/hospital should have a strong Human Research Protection Program to safeguard the trial subjects.

**NEED FOR SUBJECT PROTECTION AND ETHICAL RESEARCH**

Robust regulations and guidelines [Schedule Y, Indian GCP and Indian council of medical research (ICMR) guidelines], rigorous training of investigators/research personnel, improvement of healthcare and research infrastructure are required for good clinical research. India needs to look at research with a different perspective—a comprehensive objective approach in order to protect the Human research participant rights, safety, and to see that the data generated are credible by strictly adhering to protocol, robust consent process, and robust review process by Ethics committee. It needs a formal auditing and review system by a recognized body. As of now, only the sponsors are monitoring/auditing their respective trials; however, there is an increasing need to perform a more detailed review and assessment of processes of the institution and the Ethics Committee. This challenge can be addressed by going for accreditation by a reputed association that encompasses—the institutions, the ethics committees, and researcher/research staff.

**ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAM**

Kasturba Medical College and Hospital, Manipal [KMC], and Manipal Hospital Bangalore [MHB], both of the Manipal group [MHEPL] have been engaged in clinical trials for the last 10 years, the majority of these being global trials that were approved by Drugs Controller General of India and Institutional Ethics Committee, were USFDA regulated. Recognizing the benefits and need to have a reputable accreditation, the Hospitals started their application process for Association for the Accreditation of Human Research Protection Programs (AAHRPP) in late 2010 and subsequently received full AAHRPP accreditation in December 2011—a first in India. The two Hospitals were supported in this initiative by the pharmaceutical company Pfizer resulting in a collaborative effort between a Sponsor and Hospitals working toward a single, simple goal—Ethical Research and Patient Safety and wellbeing.

**ASSOCIATION FOR THE ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS ACCREDITATION**

AAHRPP is the sole non-governmental organization in USA, which was established to promote accreditation as a way to improve the quality of research and protect research participants. Organizations that attain accreditation do so voluntarily and agree to adhere to research standards at par with the best institutions where research is conducted [Figure 1].

AAHRPP has defined Domains of responsibility: Organization, Institutional Review Board (IRB) or Ethics Committee (EC), and Researchers and Research Staff. Within each Domain are Standards, and for each Standard there are Elements that provide more specificity for the Standard. For each Element, there are essential requirements that all Organizations must follow. These

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**Figure 1: The accreditation process**
essential requirements meet many U.S. and international government requirements for protect human research participants.

WHY GO FOR ACCREDITATION?

Accreditation benefits research organizations, participants, and the research enterprise as a whole. The result is a more cohesive human research protection programs (HRPP), with the systems in place not only to protect research participants but also to advance research more efficiently and effectively.

Especially in a country like India where the media at times is hostile to research, accreditation helps in building public trust, confidence. Prospective participants and the public in general are looking to the research enterprise to take responsibility for ensuring that research is conducted safely and ethically.

ADVANTAGES OF HAVING AN ACCREDITATION

- The highest possible standards and protections.
- An assurance of quality. Accreditation is evidence of a quality research program
- Improves efficiency, effectiveness. Accreditation requires organizations to take an unprecedented view of their research protection programs—to make sure not just that policies and procedures are in place but also that they are documented and translated into practice. As a result, accredited organizations tend to have more streamlined and effective policies and procedures. These organizations also typically keep better records and are more likely to avoid costly shut downs and problematic inspections.
- A competitive edge. Sponsors and other funding agencies recognize that accredited organizations have more efficient operations, provide more comprehensive protection for subject, and produce high-quality data. Increasingly, accreditation is expected to be a condition of research support.
- Government recognition.

KMC AND MHB TESTIMONIALS—SHARING EXPERIENCE OF THE APPLICATION PROCESS

The accreditation process has helped KMC and MHB to take a comprehensive look at their HRPPs - to identify and address weaknesses and to build upon strengths.

STEPS FOR ASSOCIATION FOR THE ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS ACCREDITATION

Step 1 application— self evaluation

The most challenging part of accreditation was the self evaluation or the Step 1. It created a deep sense of commitment for protection of human subjects and that became the mission. There was support from the organization, ethics committee, and research staff. As the team studied every domain, standard, and element, they developed the key understanding that if research had to be conducted in the spirit of Declaration of Helsinki, i.e., protection of the Human subject above science, then the policies and procedures have to be objective. This realization gave clarity for the HRPP mission, vision, and an objectivity to create and meet the target and goal for human research protection program.

- Greater understanding of the regulations: Self evaluation for Step I was an opportunity to understand and incorporate the Schedule Y, Indian GCP, and ICMR guidelines effectively into the institutional policies and procedures.
- Process Re-engineering: During the self-assessment process, policies and procedures were reviewed and revised as necessary using the AAHRPP evaluation instrument. It was quickly realized that the institutes needed to put in place many policies and procedures for Domain I [organization] and Domain II [IRB/EC]. It enabled the teams to review the key important areas which had not been previously addressed and to develop procedures to cover these areas encompassing the Institutional policies of all the research Stakeholders—Organizational representatives, Ethics committee, Researchers, and research staff.

Key improvement areas identified

- Focused Education and training programs were developed
- Authority of organization and internalizing the organization for shared responsibility
- Ethics Committee composition and functioning. Example: Tools were established for assessing risk benefit ratio in trials.
- Conflict of Interest. It was initially challenging to understand and implement this standard as there was no clear objective cut-off point for the financial conflict in the Indian regulations with respect to the principal investigators [stocks included] or the organizational conflict. Example: It was decided to take a cue from the form 1572 and an organization financial limit was decided on and approved by the EC.
- Procedure of robust consent process: Factors considered were language barrier, economical backwardness, and illiteracy with a focus on protecting “vulnerable
subjects.” Example: The social work and help desk department of the hospital were engaged into the institute HRPP and a patient research advocate was introduced to evaluate and clear the consent process.

- **Clear procedures** were laid down on how to deal with unanticipated risks and events.
- **Participant outreach** outlined for the organization
- **Internal audits and evaluation** of all research stakeholders was done and organization audit plan developed.

### STEP 2 application—understanding the standards and believing in our processes

Step 2 was a very crucial evaluation process as the sites were contacted by the AAHRPP staff with review comments on Step 1 application. Based on the feedback received, an updated responses with required changes in SOPs and processed was submitted to AAHRPP as part of the Step 2 application.

A dedicated AAHRPP guide, Dr. Robert Hood, was assigned by AAHRPP to help the hospitals in reviewing and updating the processes for Step 2 preparation. The interactions with AAHRP personnel made the hospital teams realize the importance of making policies and procedures accountable and evaluable to give credibility to the HRPP program.

### Key learnings

- Understanding the relevance of the elements: The teams understood the relevance of all the elements and started believing their processes. Example: Novel process of having a patient research advocate to make the consent process robust.
- **Team building**: A collaborative network was formed between organization, ethics committee, researches, and research staff. Example: Consent process, conflict of interest, contract and budgets, training and education required inputs, and feedback from different organization stakeholders.

### Key areas where processes were re-defined and made more objective

- Organization **conflict of interest**
- Relevance to **contracts and budgets**
- **Ethics committee** inspection of the research activity
- New meaning to **vulnerability** [Economical, illiteracy]
- Understanding of **ethics committee quorum**
- **Ethics committee** review process and functioning. Example: Introducing new process of auditing EC and evaluating their functioning which was endorsed by the HRPP board. This lead to improvement in the many areas like approval timelines, Ethics Committee evaluations, documentation, monitoring, and training program.

### Site visit—living the process

The site visit is the acid test that determines whether the Hospital HRPP is robust enough to meet the stringent conditions and standards of accreditation.

- As this was the first time hospitals in India were going for the AAHRPP accreditation, the objective was to ensure that everyone was aware of the processes and there was uniformity in understanding across the organization. This involved many weeks of prior training, preparation, and awareness sessions for all individuals involved. Example: Based on the groups selected for the interview, team leaders were selected who was responsible for the group to understand the applicable process. Daily training sessions were conducted in order to internalize the process. Individuals were given questionnaires and assessed on their understanding.
- Two site visitors visited the Hospitals and reviewed records and interviewed researchers, senior management, and ethics committee members.
- The site visitors focused on assessing whether processes were consistently understood and followed by all individuals. Example: EC minutes, agendas, and documentation were reviewed to determine compliance and whether it accurately represented the processes outlined in the SOPs. Post site visit, a draft report was forwarded and a response was to be submitted within 30 days.

### Final accreditation determination

The application, site visit result, and report responses were reviewed by the AAHRPP council and final application status determined in the December Council Meeting. The Hospitals were granted Full AAHRPP accreditation, making them the first in India and 6th in Asia.

Even after receiving accreditation, the hospitals are aware that this is a continuous process improvement and is an ongoing commitment to ethical standards and quality.

### HOW THE ACCREDITATION PROCESS HELPED THE HOSPITALS

- **Revised processes**: As a prerequisite for this application, the hospitals created nearly 26 standard operating procedures and documents, which focused on the process for protecting Human subjects. Example - internal audit of clinical trials, evaluation of EC members, post trial obligation of the sponsors, robust documented consent process, and objectively evaluating conflict of interest.
- **Training**: All team members [investigators, study coordinators, EC members, institutional representatives,
stakeholders] were trained and sensitized on the need of SOPs on Human Research Protection Program as well as ICMR guidelines, Schedule Y, ICH GCP, and Indian GCP guidelines. Making Education and monitoring an ongoing process was a truly learning and improving process.

- **Collaboration and partnership across stakeholders**: It has brought the hospital team together and has also helped in developing a strong partnership with Sponsors like Pfizer.

- **Hospital HRPP**: The Accreditation process has enabled the hospital to create a robust HRPP program, where the institution, Ethics committee, and the research stakeholders work as a unit to protect the research participant. Evaluating the performance of EC, Institution, and research stakeholders with feedback ensures that the quality standards are maintained in the research process. It makes the system accountable and committed.

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