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EXPERIENCES IN REVIEW OF CLINICAL TRIALS

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ABSTRACT

The purpose of an IHEC (Institutional Human Ethics Committee) review is to ensure that appropriate steps are taken to protect the rights and welfare of participants as subjects of research. If the risks to participants are found to be too great, the IHEC will not approve the research, or it will specify changes that must be made before the research can be done. The EC (Ethics committee) review process of a trial protocol includes three different considerations: science, ethics and data quality. Any clinical trial with poor science, poor ethics or poor data quality puts participants at unnecessary risk of harm. This study aims to list out the scientific and ethical issues identified during review of clinical trials at IHEC. On IHEC approval, all the clinical trials approved over the past five years in IHEC, were analyzed using a proforma by the investigators (1-3) who are IHEC members & the anonymized raw data was given to the investigator number 4 who is not an IHEC member. 33 clinical trials were included for the study. Scientific and ethical considerations that were raised by IHEC was noted. The results of the study revealed that the issues were mainly related to the methodology and selection of participants as well as on the risks involved, insurance aspects and post-trial access. Most of the clinical trials were approved after the required modifications and some required major revision. Few unacceptable projects were rejected. The data indicate that the ethical committee reviews both scientific as well as ethical aspects.

Key words: experiences, review, Clinical trials.

INTRODUCTION

Research in humans represents our aspiration to know and to advance our society. Research has improved our lives and will continue to so, and we must acknowledge that good research can benefit society. Research seeks to understand the unrevealed, which means that it may come with risks. There have been examples of trial participants needlessly harmed by research. But on the other hand, there have been tens of thousands of ethically sound and successful research studies. Human research ethics is about the balance between recognizing potential benefits and the need to protect participants from research-related risks – in other words, the risk-benefit balance.

The purpose of an IHEC (Institutional Human Ethics Committee) review is to ensure that appropriate steps are taken to protect the rights and welfare of participants as subjects of research. If the risks to participants are found to be too great, the IHEC will not approve the research, or it will specify changes that must be made before the research can be done. The EC review process of a trial protocol includes three different Considerations: science, ethics and data quality. Any clinical trial with poor science, poor ethics or poor data quality puts participants at unnecessary risk of harm.

There is a persistent demand, in addition to a great need, to develop new medical treatments that are as effective and safe as, or more effective or safer for specific types of patients than, treatments already on the market. Research also enables discovery of new therapeutic uses for currently available medications, as well as enabling development of innovative treatments for currently untreated conditions. New medicinal products are commonly discovered by means of laboratory research and animal studies before they can be tested in humans – through clinical trials – and eventually used in medical care [1].

A clinical trial that will not advance knowledge about a certain medical test article should not be conducted, since the risk-benefit balance for participants will be unacceptably high As part of their review, IRBs (Institutional Review Board) consider participant

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inclusion and exclusion requirements to be sure that appropriate people have been identified as eligible for the trial. They often look at how and where recruitment for clinical trials will occur. IHEC is committed to protecting the participants of clinical trials, as well as helping to ensure that reliable information is provided to those interested in participating. Although efforts are made to minimize risks to clinical trial participants, some risk may be unavoidable because of the uncertainty inherent in clinical research involving new medical products. It's important, therefore, that people make their decision to participate in a clinical trial only after they have a full understanding of the entire process and the risks that may be involved. IRBs review the adequacy of the informed consent document to ensure that it includes all the elements required by law, and that it is at an appropriate reading level and understandable to study participants Clinical trials should be carefully designed to answer certain research questions. A trial plan called a protocol maps out what study procedures will be done, by whom, and why. Products are often tested to see how they compare to standard treatments or to no treatment [2].

A study on published articles of 767 trials and found the following indicators of lower methodological quality to be independent predictors for failure to disclose Ethics approval or Informed consent process: absence of concealment of allocation, lack of justification for unblinded trials, not using a treatment for the patients in the control group, absent information on statistical methods, not including sample size estimation, not establishing the rules to stop the trial, and omitting the presentation of a baseline comparison of groups [3].

A study on hidden risks associated with clinical trials reported the requirement for the involvement of research ethics committees in the risk evaluation process [4]. There are several studies that have found deficiencies in reporting the design and conduct of trials, to the best of our knowledge this study is first of its kind to list out the scientific and ethical issues pertaining to review of clinical trials.

OBJECTIVES

- To identify common ethical & scientific considerations in IHEC review of clinical trials.
- To create awareness among investigators and IHEC members on this deliberations.
- To facilitate the IHEC members for sound scientific & ethical review of clinical trials.

METHODOLOGY

All the clinical trials approved over the past five years in IHEC, were included for the study. Ethical and scientific considerations that are raised by IHEC were filled up using proforma after obtaining ethics committee clearance.

Inclusion Criteria

Clinical trials approved by IHEC, in the last five years.

Exclusion Criteria

Proposals other than clinical trials that are approved by IHEC in the past five years.
Data was statistically analyzed.

RESULTS

There were 33 clinical trials reviewed over the past five years. Among these projects 58.8%, were phase 3 clinical trials and there were no Phase 1 clinical trials (Figure 1).

Majority (80.6%) of the clinical trials were Randomized double blinded studies (Figure 2).
48.48% of projects required modifications before approval and 3.03% were rejected (Figure 3).

91.8% of the queries were related to the participant protection, 81.6% were related to methodology and 36.7% were regarding regulatory bodies (Figure 4)

Among the queries related to regulatory bodies, majorities were regarding DCGI (Drug controller general of India) approval letter (10.2%) and CTRI (Clinical trial registry India) number (10.2%) and rest of them were regarding CTA (Clinical trial agreement), International transfer of biological sample & others (Table 1).

Among the queries related to methodology, 32.65% were regarding participant selection and rest were regarding study design, sample size, regarding dose, washout period, previous study data, uniformity in standard of care, test dose & outcome measures(Table 2).

Among the queries related to participant protection, 32.65% were regarding Insurance and rest were regarding risk, benefit, vulnerable population, criteria for withdrawal, informed consent, financial burden on participants, post trial access, unblinding.

Table 1. Queries related to regulatory bodies

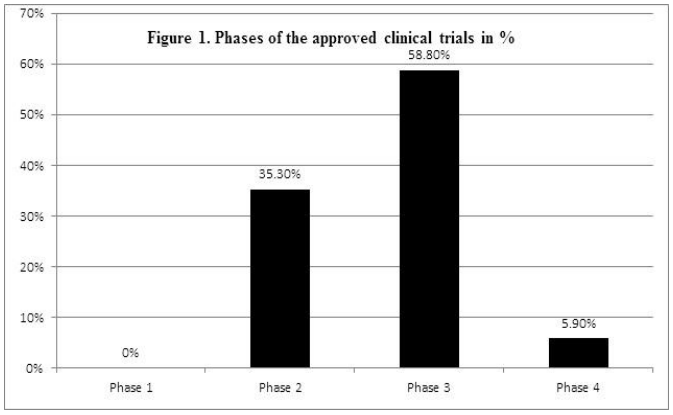
Queries related to regulatory bodies	%
DCGI approval	10.2%
CTRI Number	10.20%
CTA	6.12%
International transfer of biological samples	8.16%
Others	2.04%

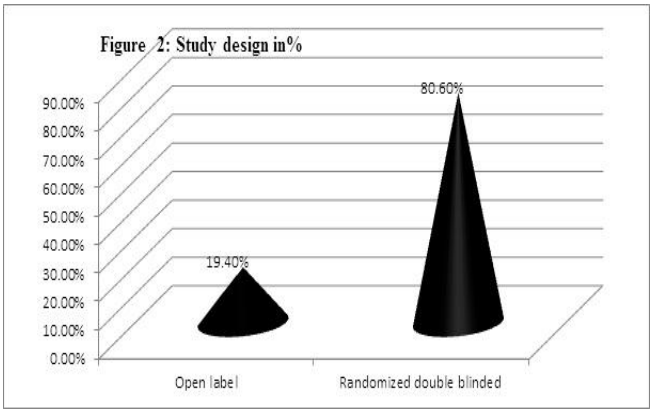
Table 2. Queries related to methodology

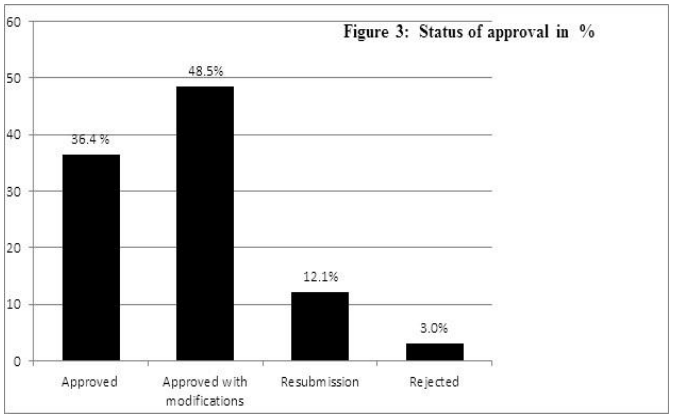
Queries related to methodology	%
Study design	16.32%
Sample size	10.20%
Participant selection	32.65%
Dose related	4.08%
Wash out period	2.04%
Previous study data	6.12%
Uniformity in standard of care	2.04%
Test dose	4.08%
Outcome measures	4.08%

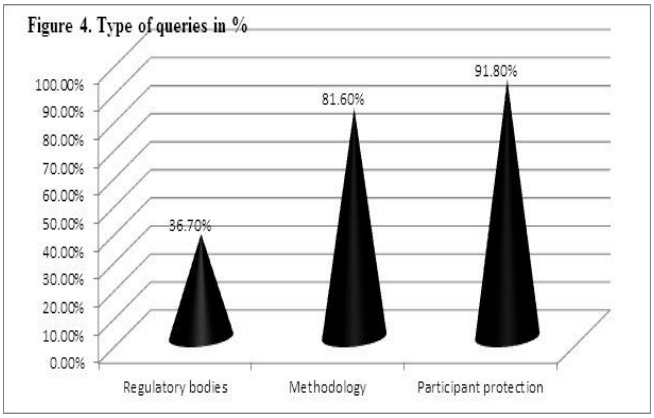
Table 3: Queries related to participant protection

Queries related to participant protection	
Risk	28.57%
Benefit	2.04%
Vulnerable Population	2.04%
Criteria for withdrawal	6.12%
Informed consent	12.24%
Financial burden on participants	4.08%
Post trial access	2.04%
Insurance	32.65%
Unblinding	2.04%









DISCUSSION AND CONCLUSION

The results of the study revealed that the issues were mainly related to the methodology and selection of participants as well as on the risks involved, insurance aspects and post-trial access. Most of the clinical trials were approved after the required modifications and some required major revision. Few unacceptable projects were rejected. The data indicate that the ethical committee reviews both scientific as well as ethical aspects.

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