**Title:-Knowledge, Attitude and Practice of researchers about research ethics and laws on clinical trials in a tertiary medical college in India-a survey**

***Introduction***

The twenty-first century medical practice is an era of Evidence based medicine. As new drugs are developed, the need for evidence about their safety and efficacy becomes vital to all stakeholders of health care- the patient, the doctor, the ethicist, the regulator and the drug marketing company.

India has a rich history of medical research, including that in modern medicine. India had her own medical research fund named India Research Fund Association (IRFA) since 1911, which was later reconstituted to form the Indian Council of Medical Research in 1949.

Today, clinical trial industry is a booming market in India. It’s a 64 billion dollar global research industry. As per estimates countries other than USA, Canada and Western Europe account for nearly 25.9% of Phase I -IV sites with the number of studies in some emerging markets growing nearly two to three times faster than the global average.[[1]](#endnote-1) FICCI (*Federation of Indian Chamber of Commerce and Industries* ) stated position in their sectorial paper [[2]](#endnote-2) has been “*The vision is to catapult India into one of the top - five Pharma innovation hubs by 2020 with one out of every 5 to 10 drugs discovered worldwide, coming from India by 2020*.” In 2011, 15% of the global trials were also registered in India. There were more than 3000 trials being conducted which recruited more than 300,000 subjects. [[3]](#endnote-3) The turnover of the clinical research industry has grown by leaps and bounds from 50 crores INR in 2003 to more than 1.5 billion US $ in 2010.[[4]](#endnote-4) As on 3rd may 2014, there are 246 recruiting phase III and 94 phase III/IV trials in India as per search done on the website of Clinical Trials registry of India. [[5]](#endnote-5)

For the past two decades especially after 2005 when clinical trials regulations were relaxed there have been innumerable numbers of allegations about them. These allegations include poorly or unethically designed trials like Letrozole trial to induce fertility, inadequate consent or lack of consent- this is by far the most common allegation in most of the debated trials starting from the RCC trial to the recent HPV trial controversy, conflict in the role of researcher and clinician, how AE’s and SAE’s are handled till publication isssues or Questionable Research Practices (QRPs).

In response to the demands various guidelines and regulations have been put into place. Still the once epitomized faith in clinician researcher is yet to come back. The questions therefore today are Are our researchers aware of research ethics & regulations? Do they realize the need of ethics & regulations that have come? are they complying to that in word & spirit? In a word is the knowledge attitude and practice of research ethics among our researchers adequate or is there a KAP Gap?

***Objective:***

With this background in mind an offline survey was designed with the objective to know the level of knowledge, attitude and actual practice of post graduate students and faculty about Ethics & Law in clinical research

***Methodology:***

The survey was done with a self-administered questionnaire in English in a post graduate teaching department in a tertiary Medical College in Urban India. Consent was taken from all the participants in the study stating the objective and methodology of the study and that the results would be published anonymously. It was also informed that some identifying data regarding designation, years of research experience would be made available in the publication

***Results***

41 potential subjects were asked for consent. Two of them refused. One did not give any reason for refusal while the other on condition of anonymity informed that such questionnaire may throw up uncomfortable answers. Therefore 39 were included in the study. There were 31 post graduate students and 8 faculty members.

Out of 39, 28 had either done at least one clinical study (including PG thesis) or at present doing one. 15 of them had either published a paper in a peer reviewed journal or have presented a paper/poster in an academic body conference. 9 of them had undergone a research methodology course including GCP certification. Three of them are also PI or Co-PI in a sponsored trial or regulated clinical trial as we call it at present.

All faculties and those students who participated in research methodology course were aware of major regulations in biomedical research (Nuremberg Code, Declaration of Helsinki etc). Three however could not specify the ICMR guidelines on biomedical research. When asked specific questions regarding the codes and guidelines all those who have done a research methodology course (9) could recall the salient points of the codes. Out of other 30 only 16 could identify the salient points of all the codes.

Everybody stated that all the regulations are necessary for proper conduct of a trial. 20 of the 39 however commented that it was impractical to take informed consent in such a detailed manner. None of them had attended a research methodology course. The comments included that patients don’t understand the informed consent even if read in details and relies on the doctor most of the time. While one cannot deny the influence of the clinician concerned it also reflects the paternalistic attitude of the researcher clinician.

Only 10 out of 39 were aware of the audio-visual recording for regulated clinical trials as notified by the DGC(I). Out of these 10, 9 have had attended research methodology courses. However the attitude towards the issue of AV recording was positive throughout the sample. The researchers felt it would help in reducing the number of false allegations against inadequate consents or forged consents.

Regarding the knowledge of compensation clauses only 7 said that any harm while in clinical trials requires compensation as per laws. All of them felt that in case of death the subjects should receive compensation. For trial related injuries half of them (19) felt that adequate treatment should be enough while the rest (20) felt that they also should receive compensation. On the answer to the question who decides on the compensation, only five pointed out that IEC in consultation with an independent committee and DGCI decides on the compensation. 10 said it was IEC alone and 3 DGC(I). However there were 15 participants who thought the PI can decide on the compensation while 3 thought the sponsors can unilaterally decide whom to give and how much to give on the issue.

Out of the 39 participants all noted that they personally know more than one person, outside the list of study participant who has been involved in unethical conduct of clinical trial which include inadequate explanation of informed consent document, forging of number of study participants, data adjusting and offering guest authorship. Out of 39 hover 23 did not know any person who has received guest authorship.

***Discussion:***

The study was designed to assess the knowledge, attitude and practice of researchers towards research ethics regulations. While the names of various codes and regulations were well known the contents were not, especially to those who have not undergone any research ethics course. This may be due to the fact that the undergraduate medical education stresses more on information accumulation in a large amount rather than its assimilation. While the researchers in our sample were keen to follow regulations they were also worried that they may not be easy to follow. The attitude towards regulations was more of a compulsion. This unnecessary fear of regulatory tangles may lead to distancing of the clinicians from research. However we also see that those who had been into clinical research are comfortable with the regulations. This shows that the fear of regulations if dispelled can create new environment for medical research.

Compensation is a hotly debated topic in clinical research scenario. In India there were no clear guidelines on compensation for clinical trials till 2001. That year the CDSCO published its GCP guidelines which mentioned compensation in case of trial related injury or death. [[6]](#endnote-6) Paragraph 2.4.7 of the GCP Guidelines mentions the same. However despite best intentions there were very limited numbers of compensations.[[7]](#endnote-7) The Government of India amended the Drugs and Cosmetics Rules, 1945 vide G.S.R. 53(E) dated 30-01-2013 by inserting rule 122DAB and specifying procedures to analyse the reports of Serious Adverse Events occurring during clinical trials and procedures for payment of compensation in case of injury or death as per prescribed timelines.[[8]](#endnote-8) These regulations have been often criticized by the industry sometimes with valid reasons (compensation for injuries which is no way related to the trial) sometimes being a protectionist trend (compensation too high etc). However from our study it appears that those hues and cry has created lot of confusion about the regulations in mind of the researchers who do not want to get themselves in a legal tangle while conducting a clinical trial.

There have been a lot of noises from the clinical trial sponsors, CROs regarding the AV recording of informed consent. Kulkarni in his article[[9]](#endnote-9) lists a list of foreseeable constraints in implementation of AV recording. These include infrastructure, Indian culture, willingness to discuss disease status on camera, cost implications etc. In our sample there were two researchers who have been involved with AV recording for their trials. They felt that infrastructure (camera/ data storage/ place of storage/ confidentiality) are not of much issues. A digital camera in India costs less than a onetime investment of INR 5000/-, data storage can be done in a CD costing about INR 15/ maximum and that the place of storage used by them was the trial room with separate locker accessed only by the PI. None of the patients were unwilling to give consent on video. However all those patients were oncology related and therefore it may not be applicable to sensitive areas of research like HIV, or with vulnerable populations like the MSM, or any high risk groups.

Questionable research practices are of serious concern in India. In the data presented by T. A. Avinanadan at the “workshop on academic Ethics” in Chennai in 2011, for the decade 2000-2010 there were 69 retracted papers form India, 45 due to scientific misconduct, one of which was falsification. The rate was higher (18 per 100,000) than the world average of 4 per 100,000.[[10]](#endnote-10) Our survey too does show a very high cause for concern. This is not only because the quality or reliability of the work is at stake but also because as Steen showed that 180 retracted papers which enrolled 28,000 patients in between 2000 & 2010 were cited in another 851 secondary papers recruiting 400,000 participants putting them at risk. [[11]](#endnote-11)

A conducive attitude towards the regulations and incorporation of participants concerns were more reflected in those who have undergone research methodology courses and especially those who are actively involved in research. Premier Institutions have made attendance of post graduate students compulsory for research methodology courses like that in AIIMS, CMC Vellore, TMH, Mumbai. Some universities like TN Dr MGR medical University, Chennai do conduct Research methodology classes for their post graduate students who do not have the facilities in their institution. However, such scope is yet to be available for all students or faculties in all medical colleges all over India.

***Conclusion:***

There is deficiency of knowledge, along with a wide gap of knowledge and attitude of researchers regarding research ethics and regulations. It is an urgent need to sensitize all stakeholders including students who will be researchers of tomorrow about research ethics so that not only the quality is maintained but also the faith restored in researchers and research form India.

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2. Ibid. [↑](#endnote-ref-2)
3. Vikas Bajpai, “Rise of Clinical Trials Industry in India: An Analysis,” *ISRN Public Health* 2013 (2013): 1–17, doi:10.1155/2013/167059. [↑](#endnote-ref-3)
4. S. P. Vasireddy, “Destination India: Contract Research in Pharmaceuticals & Healthcare,” (Talk presented at the 1st Roundtable Conference by ACRO (Association of Contract Research Organisations), New Delhi, India, March 26, 2009), http://newsletters.cii.in/newsletters/quality\_news/iq\_February\_March09/pdf/quality\_news09.pdf. [↑](#endnote-ref-4)
5. “Search Result,Clinical Trials Registry - India (CTRI),” accessed May 3, 2014, http://ctri.nic.in/Clinicaltrials/advsearch.php. [↑](#endnote-ref-5)
6. Central Drugs Standard Control Organisation, Directorate General of Health Services, India, “Good Clinical Practices for Clinical Research in India. Good Clinical Practices: Guidelines for Clinical Trials on Pharmaceutical Products in India” (New Delhi: CDSCO, 2001). [↑](#endnote-ref-6)
7. Shoibal Mukherjee, “Compensation Conundrum,” *Perspectives in Clinical Research* 3, no. 1 (2012): 4, doi:10.4103/2229-3485.92300. [↑](#endnote-ref-7)
8. The Gazette of India Extraordinary. Part II- Section3-Subsection (i). Regd. No.D.L-33004/99.No. 47. Published by Authority [Internet]. New Delhi: Ministry of Health and Family Welfare (Dept of Health);2013 Jan 30, *Drugs and Cosmetics Rules, 1945, Rule 122 DAB,G.S.R. 53(E)*, 2013, http://www.pharmamedtechbi.com/~/media/Supporting%20Documents/Pharmasia%20News/2013/February/Clinical%20Trials%20Compensation%20Guidelines.pdf. [↑](#endnote-ref-8)
9. Niranjan Kulkarni, Jeroze Dalal, and Tejashree Kulkarni, “Audio-Video Recording of Informed Consent Process: Boon or Bane,” *Perspectives in Clinical Research* 5, no. 1 (January 1, 2014): 6–10, doi:10.4103/2229-3485.124547. [↑](#endnote-ref-9)
10. T A Abinandanan, “Scientific Misconduct in India: An Analysis of Retracted Papers in PubMed” (presented at the Workshop on Academic Ethics 2011, Ramanujan Auditorium, The Institute of Mathematical Sciences, Chennai, July 15, 2011), http://www.imsc.res.in/~ethicsmeet/abstracts/abinandanan.html. [↑](#endnote-ref-10)
11. R. G. Steen, “Retractions in the Scientific Literature: Do Authors Deliberately Commit Research Fraud?,” *Journal of Medical Ethics* 37, no. 2 (February 1, 2011): 113–17, doi:10.1136/jme.2010.038125. [↑](#endnote-ref-11)