# Ethics in biomedical research

### *Introduction*

'You cannot pluck a flower without disturbing a star.' This statement awakens in us a sense of the fundamental reality of the extent of inter-relatedness within our universe. The use of freon gas refrigerators in the northern hemisphere contributed to depletion of the ozone layer over the Antarctic. When mundane activities can influence remotely related phenomena, ethics becomes all the more pertinent to all deliberate human actions. It is not possible to subject every human action to ethical evaluation but moral and ethical codes have - over the years - been refined to enable mankind to lead an 'ethically just' existence. Notwithstanding continued refinement in ethical and moral codes, there are, and always will be, grey areas which create dilemmas in the practice of ethics.

Unlike most activities of everyday life, the pursuit of research is deliberate and elective. The end product of research - new knowledge or product - can, in turn, be harnessed for further change or manipulation bringing up an expanding chain of possibilities. It is therefore necessary for us to examine all the dimensions of research in terms of their implications. We must evaluate them on the basis of careful ethical considerations. The exercise becomes even more pertinent in case of biomedical or biotechnological research, relating as they do to living beings in more than one way.

Sharply focused research studies with wide ethical implications are of special concern for the latter may, at times, range beyond the expertise of primary concerns of the researcher. This is the basis for the plea that all research programmes, especially those in the fields of biomedicine and biotechnology, be subject to multidisciplinary and holistic ethical evaluation. Such analysis must cover each of the three principal components of the study - purpose, material and methods and the end result. It must start with the conception of the project and continue to the application of the research findings.

### *Questions to be answered even before research is contemplated*

The purpose of any research is to extend knowledge. Is the right to extend knowledge absolute? At first sight, this right does appear to be absolute. Reflection will show that since such studies and their findings might have far-reaching influences on society, the right must be subject to stipulations.

In his lecture on 'Knowledge, survival and the duties of science' delivered in Washington on November 20, 1973. Professor Julius Stone pointed out that the liberty to extend knowledge is not absolute but must be limited when it conflicts with other values.[2] He further urged that scientists have a moral duty to consider, along with others of competent knowledge, whether a line of inquiry should be desisted from as soon as it becomes clear that it is likely to bring about a mankind-endangering situation, which no one has any foreseeable capacity to handle.[2] The phrases 'along with others'; 'mankind-endangering situation' and 'which no one has any foreseeable capacity to handle' emphasise the role and responsibility of (a) the State; (b) the medical professional bodies (Medical Council of India, Indian Council of Medical Research (ICMR), medical associations...); (c) the health institutions where researches are carried out; (d) the other professional bodies (legal, social sciences etc.) in addition to the medical scientists themselves to ensure that the pursuit of research is ethically just. Thus whilst the medical scientist (researcher) must ensure that ethics is not flouted, it is equally important for the other competent bodies to ensure that they do not take a bystander approach.

### *Questions as soon as research is contemplated*

What is the intent behind the contemplated research? Does ethics enter into this area ? It certainly does. Research with mala fide intentions can never be ethically justified. There can be variations in geographic or societal perceptions of values. In some societies research on long acting contraceptives may be perceived as contributing to the welfare of the general population. Even here, ethical constraints will apply. It must be proven that such products do, indeed, empower women and are accepted by them for this purpose. This is particularly important because contraceptive intervention is carried out on healthy individuals to ward off a physiological event - pregnancy. There is no contraceptive, as yet, which is totally free from adverse effects. Therefore, unless women choose the contraceptive, its enforced use would violate ethical norms. Taking this example further, it would be necessary to hold discussions with women's groups to elicit the direction in which research is to be pursued and whether the products that are likely to result from the research do

meet the empowerment/convenience/reassurance values as they perceive them.

***Choosing live subjects and other resources whilst designing experiments for research***

All clinical research is expected to be preceded by experiments on non-human subjects to ensure (a) safety of human beings and (b) to justify proceeding to experiments on human beings. These subjects (animals, plants, etc. ) and other resources (time, money, facilities like computer-aided designing etc.) are organised based on their availability and utility in the experiments. The design of the experiment is expected to dictate which resource would be preferred. Nonetheless,, the ethics of such research should demand certain responsibilities on all concerned (researchers, the institute in which research is conducted, ethics committees or review boards and the law makers) to ensure that the programme does not drift into flippant use of resources.

There are many who feel that all experiments on animals must cease. Tom Regan[3], for instance, states that all such experiments, at whatever stage and however promising, ought to be stopped at once. Peter Singer[4] and Stephan Clark' advocate progressive or gradual cessation. On the other hand there are those who feel that animals do not matter morally and would allow any animal experiment for the benefit of mankind. R.G. Frey[6] justifies some but not all experiments on animals, while conceding the fact that they are of moral concern. Careful balancing of pros and cons over the use of animals and a sincere effort at minimising harm to them should form the golden rule.

We suggest the following guidelines for using resources ethically.

a) Use of non-living resources instead of living resources (e.g. computer-aided designing - of drugs) to preserve animal and plant resources.

b) Use of micro-organisms in place of higher animals wherever possible.

c) If higher animals are mandatory, care to ensure that the species is not threatened.

d) When experiments on animals are unavoidable, ensure optimal utility of the animal to be sacrificed. If Rhesus Monkeys are used, explore the possibility of the same animal serving two or more experiments within the institute.

e) Laws relating to protection of animals must be applied to experiments in medical research. It is the ethical responsibility of the law makers ( the State) to enunciate when exceptions to laws relating to protections of animals can be made in case of medical research. It is the ethical responsibility of the Medical Councils and Medical Associations to ensure that experiments are carried out responsibly.

A callous attitude to any resource - living or non-living - is unethical. Wastage of living resources is callousness. Wherever possible, used resources must be replenished.

***Clinical Research***

Clinical research starts after experiments on animals/ non-living materials provide substantial evidence that it is safe to conduct further researches on human beings. When such research is an extension or variation of existing procedure, proof from animal/non-living experiments may be waived.

***Drug research***

In addition to prior animal experiments, such research requires tests on humans in four stages.

Phase 1 conducted on normal human volunteers for validating safety in humans.

Phase 2 conducted on patients with the disease to be treated for validating efficacy under strict monitoring.

Phase 3. Multicentric trials on patients for validating safety and efficacy under a variety of conditions but under the strict vigil of heathcare providers and institutions.

Phase 4. Post marketing surveillance for monitoring adverse drug reactions under actual user-conditions. In case this proves unsafe, the drug is recalled from the market and re-evaluated for safety:

In India, to the best of our knowledge, there is no post marketing surveillance. A handful of Adverse Drug Reaction Monitoring Units appear to function erratically. Under these conditions, it is difficult to escape the conclusion that no drug has passed Phase 4 in India thus far.

***Informed consent***

The informed consent of participant volunteers in any research on human beings endorses the spirit of respect for autonomy of the volunteers and is an integral part of medical research. The convention of referring to volunteers as 'subjects' was intended to stress the fact that volunteers are being subjected to research procedures. Respect for the autonomy of volunteers implies concern and respect for the individuality of person and the provision of space for expression of this individuality at every stage of the research programme without any duress or impediment whatsoever and with the expectation of advice and provision of adequate facilities to ensure the integrity of the person.

Let us consider the example of volunteers participating in research on implanted contraceptives. There must be provision for [illegible] withdraw from the research at

any stage of the programme without duress or impediment. The volunteers have a right to.expect the facilities for removal of the implant whenever they so desire within the period of experimentation Further they have a right to be informed of the problems of non-removal of implants and the hazards of carrying the implants within their bodies for extended periods before they enrol.

Informed consent comprises of two elements, (a) information and (b) consent. Each of these has subdivisions; information comprising of the extent of information and its veracity and consent including volition and competence. (It is not possible to discuss details here. The interested reader is referred to Beauchamp and Childress' *Principles of Biomedical Ethics,* 3rd edition, Oxford University Press.) Each of these aspects poses considerable difficulties when implementing the requirement of informed consent.

The advances in science and technology are so rapid that a fully informed consent may be difficult in many cases. This leads to a perfunctory attitude unless there is acute sensitively and concern for the individual volunteer

We list some essentials when enlisting informed consent:

***Information***

1. Purpose of the trial
2. Benefits to the patient (volunteer) and to society
3. Possible risks of treatment (intervention)
4. Treatment offered in case complications develop during the trial
5. Right to refuse or withdraw from the trial at any time without prejudicing further treatment by doing so.
6. Implications of randomisation

The following additional information must be provided to volunteers:

a) The expertise and capabilities of the Research Unit with special reference to support in the event of a complication. Budgeted provisions for interventions/rehabilitation/compensation in the event of untoward manifestations.

b) Mechanisms and procedures for redressal of the volunteers complaints.

c) Names of persons who will contact the volunteers during the research. If the volunteer has serious objection to any of them, this may provide a ground for opting out right at the start.

d) Names and addresses of the members of the Ethics Committee to be approached for redressal.

The social value or implications of being associated with such a research programme. For instance, research on contraceptives for women may require discussion on the merits/demerits of provider-controlled contraceptive devices in the given social context.

***Voluntariness and the competence to consent***

Adequate provision must be made for the consent to be both voluntary and competent. One way of ensuring this is for several members of the research team, particularly the social worker, to interact with volunteers and test whether the volunteer has appreciated the nuances before offering consent. It has been suggested that when conducting research trials on tribes and races where communication barriers are evident, the informed consent of a chieftain could be adequate. [8] The ethics of this stand are debatable.

***Ethics Committee (Institutional Review Board)***

The Declaration of Helsinki suggested the setting up of Ethics Committees for reviewing research protocols with a view to ensuring the highest ethical standards before, during, and on completion of any research programme. It is important to ensure that ethics committees do not take on a perfunctory status merely because agencies providing grants require their sanction.

Ethics committees are increasingly incorporating collective expertise from varied disciplines in order to provide a holistic basis for evaluation, guidance and, when necessary, correction. In addition to physicians, lawyers, social workers and the theologist, nurses, ethicists and other professionals are being enlisted with increasing frequency. Most Ethics Committees hone their proficiency through intense internal debates and exchanges of information on the subject.

***How can we ensure meaningful Ethics Committees?***

Steps for doing so can be based on the goals set by the ethics committee. The principle of least restrictions for optimum practice of ethics is generally adopted. If, from the biomedical, legal, social and humanist perspective, the understanding and practice of ethics whilst conducting both research and clinical practice is seriously wanting, the powers to enforce corrective measures ought to be vested in the Ethics Committees. If, on the other hand, the research team is assessed as highly ethical, the Ethics Committee may play an advisory role. In any case the functioning of the Ethics Committee must be transparent and, itself, be subjected to review from time to time

The mission statement of ethics committees could include: to ensure adherence to ethical principles from the time the research programme is conceived to its completion, publication of results and implementation

a) to deepen understanding and appreciation of a holistic perspective of biomedical ethics;

b) to ensure that the research programme and its conduct is ethically just to participants (subjects) in particular and the people in general;

c) the ethics committee should have the powers to hold/suspend any research project as soon as it is evident that ethical principles are being violated. At the same time, it should be the responsibility of the Committee to report on its assessment of each research project from legal, biomedical, philosophical and humanistic stand point. The minutes of the meetings of the committee should be recorded in detail for the purpose of review;

d) the State and the institute must provide funds and facilities for adequate functioning of the committee. The ethics committee should preferably be autonomous and persons involved with the administration of the institute should not be included in it;

e) there should be periodic multicentric review to update information on the working of these committees. The findings of such review should be made publicly available;

f) the State and the institute must ensure institution of adequate redressal forum for any complaints against those conducting research.

The present state of indifference on the part of the State as the medical profession in India does not inspire confidence that things will improve. Voluntary bodies must try to force debates on the ethics of medical research and prod State and professional agencies into action.

### *Blatant malpractices*

Discussions on ethics are confined, in other countries, to grey areas in medical practice. This is how it ought to be because it is in these areas that clarity is required. The blatant malpractices - black areas - in India unfortunately force us to discuss what is taken for granted elsewhere.

It is not uncommon to find:

a) vested interests operating whilst allocating research grants;

b) superiors making juniors do the work and yet taking the credit for research;

c) fraudulent research / fabrication of results

We are told that the publish-or-perish compulsion has triggered such practices. It need not be so. The practice initiated by the Harvard University and now widely adopted will eliminate this cause. Each applicant for any position is asked to provide reprints of not more than five of his most valued publications.

### *Conclusion*

The mad race of commerce for producing powerful tools through biotechnological research seems to continue unabated the world over. Ingenuity of the scientific mind will continue to accelerate the pace. The impact of such tools cannot be confined to geographical zones. Inadequately informed over-criticism and inadequately informed over-enthusiasm in respect of such technologies are likely to be confusing and misdirectional. A holistic understanding of the social and environmental impact of technologies by professionals of every pursuit is vital to sagacious handling of the power of information generated through research. The exercise of ethical controls within all professional bodies and imaginative regulatory (legislative) mechanisms - national and international - are necessary.

In the present scenario, this is like asking for the moon. But is there an alternative ?

'Our knowledge of science has already outstripped our capacity to control it. We have many men of science, too few men of God... Man is stumbling blindly through a spiritual darkness while toying with the precarious secrets of Life and Death. The world has achieved brilliance without wisdom, power without conscience.' Omar N. Bradley

### *References*


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