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Statement Outlining the Philosophy and Ethical Principles Governing the Conduct of Research on Human Beings at the Harvard Medical School. (Prepared by Henry K. Beecher, M.D.)

Experimentation in man for scientific purposes is as old as recorded history. With progress in science and advances in ethical and moral concepts, the techniques and purposes of human experimentation become more complex than ever before.

Most breaches of ethical conduct arise in ignorance or thoughtlessness. They are not usually of willful or unscrupulous origin. Basic considerations in human experimentation at Harvard are the same as they are everywhere: protection of the subject, protection of the investigator and protection of research and the institutions involved, and the sound development of medicine. These all require a levelheaded approach to experimentation in man. It is everywhere recognized that man is the final essential test site -- the animal of necessity, so to speak, when it comes to the evaluation of new drugs and new procedures.

The clear-cut demonstrations in recent years that for some types of truly basic science, that is, science concerned with the discovery of new concepts and their establishment, the sick man is an essential starting point and that the study of disease in man is essential to the development of basic science (Beecher: Disease and the Advancement of Basic Science, 1960).

The social necessity for experimentation in man operates of course only when the desired ends cannot be obtained in other ways, as through experimentation in animals. It is recognized that it is often not possible to transfer observations made in animals directly to sick man, just as it is often not possible to transfer directly observations made in normal individuals to the sick.

The investigator must always keep in mind that consent on the part of the subject must be obtained in any except the most trivial case. At the same time it is folly to overlook the fact that valid, informed consent may be difficult to the point of impossible to obtain in some cases. (The risk involved in a new procedure often cannot be known -- for example, cardiac catheterization, now known to kill occasionally but of such value that it has been awarded three Nobel Prizes -- when the risk cannot be known, and this often includes the investigator as well as the subject, a fair question is whether in these circumstances valid consent is possible.) Earnest efforts must be made by the investigator to obtain formal consent, but to obtain the consent of the patient or subject to proposed investigation is not in itself enough. There is a special relationship of trust between subject or patient and the investigator and this must be honored far beyond the injunctions imposed by any code.

The inescapable responsibility for determining what investigations may be done on a particular patient must rest with the investigator or physician concerned, bearing in mind that present-day specialization in medicine and complexity of procedures proposed or undertaken are frequently beyond the grasp of the subjects involved.

All of the so-called codes as guides to human experimentation emphasize the necessity that the experimenter be well trained and adequate as a scientist to undertake the study proposed. Medical research, when it involves treatment of any physical procedures beyond the simplest, requires that the investigator or his close associate be a qualified physician. No other profession gives such prerogatives and no other profession, probably, presents such a generally high level of

WNRC: 21 Nov 94

RG: 112

Accession # 67A-4813

Box # 35

File Name: Human
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unselfishness and compassion in directly caring for the sick or in planning procedures for the future. Of the essential qualities of the investigator, unselfishness is the most important for subject and project alike. Imagination, objectivity and the power to generalize soundly are all essential. In the forefront of the qualities which lead to protection of subject and patient in investigation is a deep sense of responsibility on the part of the investigator, coupled with unselfishness and a keen and well-trained intelligence. Along with these requirements there is the corollary that whenever procedures are undertaken which involve even moderate risk, the matter should be discussed in complete detail with a group of the investigator's peers. These things will lead to the observance of all known precautions for the protection first of the subject and, secondly, of the honest, qualified investigator. These things are important, because the responsibility falling on those undertaking experimentation in man is so great that all possible safeguards must be set up.

The importance of any project undertaken must surely be commensurate with any risk involved. Insurance of this is a major responsibility of all who undertake experimentation in man. But having stated that important principle there is still a vast area where only judgment can and must operate.

Responsibility of the investigator extends also to propriety in publication. It must be made clear in any publication of work done, that the investigations described are unobjectionable. This must be made unmistakably clear to all readers. The suppression of certain details and complications to avoid criticism cannot be tolerated.

It must be recognized that medical research is significantly different from medical practice, as Ladimer has pointed out. It is different in hypothesis, in design of study, in general environment, including staff involved and in conduct.

It is essential to recognize that the only things that courts have had to say about experimentation in man is that the investigator "experiments to his peril". When accidents have occurred during the course of human experimentation these have always been judged in the past on the basis of whether or not what was done conformed to the accepted standards of the investigator's community. It is evident that any research which was fresh and new would not be in accord with community standards in many of its aspects.

The universal and long-standing recognition that research is essential to the advancement of medical science and the newer recognition that some aspects of basic science cannot advance without it, have led to a correct, although extra-legal, expansion of human experimentation. Curiously, such work when well conceived and soundly conducted is everywhere recognized as being properly within the ethical and moral concepts of our time, yet it remains outside legally. (Curiously, too, another branch of the Government, the Federal Drug Administration, requires the testing of new products in man.)

Comments on Codes Governing Experimentation in Human Beings

Earnest attempts to do so have not enabled any groups to arrive at specific codes which could be applicable in all cases.

The first attempt to set down a code in this country occurred in 1848, when the American Medical Association patterned a statement on Sir Thomas Percival's "Medical Ethics" of 1803.

The ethical problems of human experimentation do not lend themselves in most

cases to a series of rigid rules. It is helpful, of course, to inspect the views, concepts, "rules", codes that have been devised by one group or another. These will help the investigator troubled by a given problem to learn what past thinking on problems in this area has been. He can thus have a rough framework against which he can measure his problems in terms of conclusions of others in similar situations.

After some years of careful study of the available codes of the past which have been established to guide the medical investigator and after earnest attempts to write down a comprehensive code, the writer has had to conclude that it is not possible to lay down very many "rules" in terms of a code which can govern experimentation in man. In most cases these are more likely to do harm than good. Rules will not curb the unscrupulous.

There seems to be no sensible middle ground, as far as guides go; either they will be so general, platitudinous, as to be essentially useless, or if an attempt is made to cover all possible contingencies, a vast literature will have to be developed on the subject. At the same time this is done, any reasonably sophisticated investigator will realize that all contingencies cannot possibly be encompassed in a set of rules and that unscrupulous lawyers could use such a code as a starting point for endless law suits. It takes very little imagination to see how the precise statement of a code covering one contingency might easily be misapplied to another set of affairs, with disastrous legal implications.

It is the writer's point of view that the best approach concerns the character, wisdom, experience, honesty, imaginativeness and sense of responsibility of the investigator who in all cases of doubt or where serious consequences might remotely occur, will call in his peers and get the benefit of their counsel. Rigid rules will jeopardize the research establishments of this country where experimentation in man is essential.