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**THE PUBLIC HEALTH SERVICE GUIDELINES
GOVERNING RESEARCH INVOLVING HUMAN SUBJECTS:
An Analysis of the Policy-Making Process**

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THE PUBLIC HEALTH SERVICE
GUIDELINES GOVERNING RESEARCH INVOLVING HUMAN SUBJECTS:

An Analysis of the Policy-Making Process

Introduction

The Public Health Service (PHS), largely through its National Institutes of Health (NIH), is the federal government's chief agency for supporting and conducting medical research. For the 1970 fiscal year NIH appropriations totaled \$1.5 billion¹ and NIH support for medical research was approximately 53% of total federal support for such research.² Thus, the tempo, character and direction of the nation's medical research effort is preeminently influenced by NIH programs and policies. Involved in this major research effort is a significant amount of clinical research using human subjects. In 1970 there were more than 11,000 research grants awarded by NIH and "slightly over 30%" of these involved human subjects.³ The NIH, of course, is responsible primarily for the support of a national program of research in the health sciences. In implementing this responsibility, the NIH maintains its own intramural research program, issues contracts for particular research studies, and distributes research grants to non-profit research institutions and their investigators.

¹United States Department of Health, Education and Welfare, Public Health Service, National Institutes of Health. NIH Almanac 1971 (Washington, D.C.: GPO, 1971), p. 99.

²Ibid., p. 109.

³Interview with Donald T. Chalkley, Chief, Institutional Relations Section, Division of Research Grants, NIH, Bethesda, Maryland, June 22, 1971.

While other PHS components maintain similar, though smaller programs, policy related to the administration of the extramural research program is largely determined by NIH. This study is concerned with one of these policies, the PHS Guidelines regarding the protection of the individual as a research subject. Part I of the study examines the evolution of the first issuance of the PHS Guidelines and subsequent revisions through the promulgation of the Protection Of The Individual As A Research Subject⁴ on May 1, 1969. Part II of the study analyzes the process by which these Guidelines were developed and examines the values, motivations and other underlying factors which led to their formulation. This analysis is constructed in the context of various theoretical and conceptual frameworks of decision-making and attempts to explain why the policy evolved as it did. It is not the purpose of this study to evaluate the Guidelines in principle or to assess their effectiveness. While the author recognizes the worth of a study "testing" the validity of many of the key decisions as well as of evaluating the efficacy of the Guidelines, such an effort would probably require another study equal to or greater in scope than this one.⁵

The importance of the PHS Guidelines is found most of all in their relationship to society, its health and its values. The Guidelines represent the government's attempt to protect the interest and investment

⁴United States Department of Health, Education and Welfare, Public Health Service, Division of Research Grants. Protection Of The Individual As A Research Subject (Washington, D.C.: GPO, 1969), Publication No. 0-348-095.

⁵Dr. Bernard Barber and his Research Group on Human Experimentation at Barnard College, Columbia University, have made such a study. Their findings were presented in a series of four papers at the American Association for the Advancement of Science (A.A.A.S.) Annual Meeting in Chicago, Illinois, December 1970.

of the American people. Such interest and investment are evidenced by the nation's annual commitment of more than one billion dollars to the NIH, which is "a decision by the American people, expressed through the Congress, to invest a substantial share of the nation's resources in research leading to the improvement of health."⁶ But while the American people accept health as an important value, they also recognize the value of individual worth and dignity. The Guidelines reflect the fact that society assigns great importance to protecting the individual against possible injury while simultaneously desiring to maximize the freedom of scientific inquiry. "This policy seeks to avoid the danger of direct federal intervention, case by case, on the one hand, and the dangers inherent in decision by an individual scientist on the other."⁷ The knowledge explosion has brought to the policy-making process a confrontation of scientific knowledge, ethical values and political responsibility. The Guidelines represent an attempt on the part of an administrative agency to reconcile those factors as they relate to a specific area of the quest for new knowledge and to develop a climate in which clinical research can prosper.

Examination of the Guidelines also focuses attention on public policy-making by a federal agency. By identifying the important substantive issues as well as the key decision-makers and the critical values which supported their policy decisions, one can more easily account for the

⁶William H. Stewart, Former Surgeon General, United States Public Health Service, in Committee on Government Operations, National Commission on Health Science and Society. Hearings before the Subcommittee on Government Research, United States Senate, on S.J. Res. 145, 90th Congress, 2nd session, 1968, p. 210.

⁷Ibid., p. 211.

resultant policy. At a time when new scientific and technological developments have rekindled the debate regarding the merits and feasibility of various approaches to making public policy, an analysis of this policy-making process may help one to evaluate this debate. At the very least, it should provide valuable insight into one instance of public policy as it was actually developed.

PART I: THE EVOLUTION OF THE P.H.S. GUIDELINES

In the Foreword to the Protection of the Individual as a Research Subject, former Surgeon General William H. Stewart wrote that "I believe that we have taken important steps toward protecting the human being who is a subject of research, while encouraging the conduct of excellent research on man."⁸ The steps of which Surgeon General Stewart wrote evolved over a long period of time. While the first official statement of government policy concerning its extramural research program was issued only in 1966, the issues underlying the development of the policy extend some years further back in time. In order to understand more fully the basis upon which recent policy decisions were made, it will be useful first to examine the thinking and practices relevant to medical research prior to the initiation of formal government involvement.

Historical Antecedents

Experimentation on man for scientific purposes dates back to the beginning of recorded history. Justification for such experimentation lies in the belief that, before any new technique may be considered acceptable medical practice or procedure for use in man, it must first be tested on a human being. "While prior experimentation in animals is

⁸William H. Stewart, Protection of the Individual as a Research Subject, p. iv.

absolutely necessary when possible, the crucial study of new techniques and agents must be carried out in man. The current development of human biochemistry, human physiology, human pharmacology has made it plain that man is the 'animal of necessity.'⁹ Paralleling this need for experimentation on man is the constant need to evaluate the procedures involved.

Prior to 1950 there were no specific federal or state statutes designed to regulate research institutions or investigators in their use of human beings for experimental purposes.¹⁰ In fact, there existed some uncertainty among those involved in medical research about what the law did say about medical research. In general, most hypothesizing about what such legal doctrines might state with respect to human experimentation derived from a long line of British and American court decisions involving common-law actions of medical malpractice. As far back as 1767, in Slater v. Baker and Stapleton,¹¹ an English court concluded that "many men very skillful in their profession have frequently acted out of the common way for the sake of trying experiments . . . they have acted ignorantly and unskillfully, contrary to the known rule

⁹ Henry K. Beecher, Experimentation in Man (Illinois: Charles C. Thomas, 1959), p. 9.

¹⁰ William J. Curran, "Governmental Regulation of the Use of Human Subjects in Medical Research: The Approach of Two Federal Agencies," Daedalus, vol. 98, No. 2, of the Proceedings of the American Academy of Arts and Sciences, Spring 1969, p. 54.

¹¹ 2 Wils. [K.B.] 359, 95 Eng. Rep. 860 (1767).

and useage of surgeons." The Court then disciplined the chief surgeon for failure to obtain the consent of the patient permitting the use of a new procedure. In the leading American case, Carpenter v. Blake (1871),¹² the Court cited the Slater opinion and concluded that "when the case is one as to which a treatment has been followed for a long time, there should be no departure from it . . . The rule protects the community against reckless experiments." The general conclusion drawn from these examples as well as subsequent decisions was that the scope of a physician's practice did not include the right to experiment with human beings. However, in a 1935 case, Fortner v. Koch,¹³ the Court did recognize the importance of clinical investigation for medical progress. "We recognize the fact that if the general practice of medicine and surgery is to progress, there must be a certain amount of experimentation carried on." The Court stated further that such experimentation must be done with the patient's knowledge and consent and "must not vary too much from the accepted methods of practice." This case, similar to the ones before it, appears to indicate that the judiciary associated experimentation with irresponsible behavior and professional negligence. "Experimentation was seemingly equated with ignorant and unskillful departure from approved methods."¹⁴ Yet none of these cases actually prohibited experimental procedures which took place in a controlled environment and which were directed toward the

¹²60 Barb. 488 N.Y. (1871).

¹³272 Mich. 273; 261 N.W. 762 (1935).

¹⁴Elwyn L. Cady, Jr., "Medical Malpractice: What About Experimentation?," Annals of Western Medicine and Surgery, vol. 6, March 1952, p. 164.

discovery of new knowledge not necessarily of direct benefit to the patient or subject. Past court decisions simply "failed to recognize the important distinction between poor medical practice and legitimate research."¹⁵ Yet, by the very nature of medical practice, physicians have always been involved in experimentation. "Every treatment is, in a sense, an experiment. There is no certainty that there will be complete safety for every patient, nor is there certainty that every diagnostic procedure will be safe. Each patient presents a unique and different research problem."¹⁶ Even no treatment at all can be a form of experimentation. In these instances the traditional safeguard was the fidelity of the physician to his patient. However, medical research directed primarily at the acquisition of new knowledge, like all other activities in our society, is subject to the application of the law. While the law regarding the liability of the investigator involved in clinical research remained undeveloped, it appeared that some experimentation was permissible and that,

since the courts rely on what the profession develops as acceptable practice, the principles and methods established by reputable public and private organizations will be employed as guidelines in determining whether the research has been properly performed and whether the patients or subjects have been safeguarded.¹⁷

¹⁵Irving Ladimer, "Human Experimentation: Medico-legal Aspects," New England Journal of Medicine, vol. 257, July 4, 1957, p. 23.

¹⁶Chauncey Leake, "Top Scientists Probe Dilemmas of Research Ethics," Medical World News, May 5, 1967, p. 37.

¹⁷Report of the National Conference on the Legal Environment of Medical Science. Published jointly by the National Society for Medical Research and the University of Chicago, Chicago, Illinois, May 27-28, 1959, pp. 82-83.

Thus, it was apparently in the best interest of the medical community to develop acceptable standards of care in their research.

Initial PHS Involvement

The PHS first became involved with the development of such standards with the opening of the NIH Clinical Center in 1953. The Center brought together talented young scientists and outstanding research leaders from throughout the world in order to seek new knowledge for the benefit of mankind. Edward J. Rourke, formerly of the Office of General Counsel, Department of Health, Education and Welfare (DHEW), emphasizes this primary goal. "If the Clinical Center meant anything at all, it was doing nonstandard things for more than therapeutic purposes . . . It sought to acquire new information."¹⁸ Individuals admitted to the Clinical Center were categorized into two classes: (1) Normal Volunteers--healthy persons who had volunteered to serve as normal controls for clinical investigation. Most of the volunteers were members of religious sects who served in this capacity as an obligation of service to their particular faith; and (2) Patients--individuals who had a disease that required further investigation, diagnosis, or treatment.

With the establishment of the Clinical Center, the ethical and moral problems connected with research on human subjects came sharply

¹⁸Interview with Edward J. Rourke, former Assistant General Counsel, Public Health Grants and Services Division, Office of General Counsel, DHEW, Arlington, Virginia, June 18, 1971.

into focus. The issues first arose "with respect to what limits should be applied in the case of normal subjects or volunteers."¹⁹ At that time it was felt that the use of experimental procedures for patients was part of the doctor-patient relationship; "a positive decision was made that it would be intrusive for an administrative body to interfere with that relationship."²⁰ That relationship, of course, did not apply to the normal volunteer and this was an important area of concern among NIH officials. "A fairly extensive effort was made to devise a set of guidelines and procedures governing the use of normal controls in clinical investigations within NIH and the clinical research programs."²¹ There were two important issues which came to the attention of NIH officials. "First, there was the degree of hazard or risk which we felt it was appropriate to subject anyone to. The second major question was the kind of information . . . which we felt should be made available to these people."²² To answer those questions, the NIH, on November 17, 1953, issued a set of principles and procedures for the protection of the individual. The guidelines, referred to as "Group Consideration of Clinical Research Procedures Deviating From Accepted Medical Practice or

¹⁹Interview with Joseph S. Murtaugh, former Director of the Office of Program Planning, National Institutes of Health, Washington, D.C., March 26, 1971.

²⁰Interview with James A. Shannon, former Director of the National Institutes of Health, New York City, May 13, 1971.

²¹Interview with Joseph S. Murtaugh.

²²Interview with Irving Ladimer, former Assistant Director of Research Planning, National Institutes of Health, New York City, May 14, 1971.

Involving Unusual Hazard,"* placed primary responsibility for the formulation and conduct of clinical research and medical care on the principal investigators. However, "in order to assist the principal investigator in making determinations with respect to research projects and medical procedures which may involve deviation from accepted medical practice or potential hazard to the life or well-being of the patient or subject, methods for obtaining group consideration and advice are established."²³

Such group consideration was instituted in the following manner. Each Institute Director and the Director of the Clinical Center was to establish a committee to review and make recommendations to him concerning clinical projects proposed by his staff that involved unusual hazard to the patient. A Medical Board, composed of representatives of each research institute and of the Clinical Center staff, established a Clinical Research Committee for the purpose of reviewing and reporting to the Medical Board on clinical research procedures involving unusual hazard or deviating from accepted medical practice. Cases were referred to the Committee by an Institute, by the Director of the Clinical Center, or by the Director of the NIH. This Committee reviewed the medical, scientific and ethical propriety of any questionable procedure. This procedure differed depending upon whether the project involved patients or normal volunteers. Projects involving patients were considered by the

*These guidelines were revised in July 1966.

²³Stuart M. Sessoms, "Guiding Principles in Medical Research Involving Humans," Hospitals, Journal of the American Hospital Association, vol. 32, January 1, 1958, p. 62.

Clinical Research Committee only if referred to it for the reasons cited above. On the other hand, all research projects involving normal volunteers were referred to the Committee. Recommendations of the Committee were submitted, through the Medical Board, to the Director of the NIH, who had the final authority to decide such matters. With respect to the question of how much information was to be given to the research subject, the guidelines provided that "the patient or subject of clinical study shall be considered a member of the research team and shall be afforded an understanding suited to his comprehension of the investigation contemplated, including particularly any potential danger to him." Where there was the possibility of an unusual hazard, the written consent of the subject was required and a statement was entered on the patient's chart or on a separate memorandum, indicating his understanding of the procedure and its purpose, including the potential hazards to him, and his consent to participate. Through these 1953 Guidelines, the general problems that one might experience in clinical research were discussed and means for avoiding those problems were established.

The Extramural Research Program

In its early years, the extramural research program was not subject to the same guidelines adopted for the intramural program. To cope effectively with the processing of these research grants, applications were subjected to a review process initiated at the request of the National Advisory Health Council in 1946. A grant application was first reviewed by the Division of Research Grants (DRG) to assure

basic compliance with NIH requirements. The grants were then assigned to various Study Sections made up of scientists with acknowledged competence in the scientific disciplines involved in the proposed research project. These panels passed judgment on the relative scientific merit of the proposal. Following the Study Section review, the proposals were forwarded to the Advisory Councils of each of the respective Institutes. These groups, composed of highly qualified individuals representing diverse backgrounds, provided the NIH with a mechanism of peer judgment augmented by wider considerations of social needs essential to a balanced and effective research program. Their concern was with the relevance and importance of the proposed project to the mission of the Institute. Since there was never any requirement that a Study Section or Advisory Council employ any particular set of ethical principles or guidelines, these official bodies

relied primarily on the collective experience and judgments of their members. Almost without exception, they were members of a profession which had established a code or set of principles, or they had subscribed to a particular code such as those developed by the American Medical Association or the World Health Organization.²⁴

Once a research proposal received approval, its conduct became the responsibility of the investigator and his institution for a period of up to seven years. The investigator was free to pursue his objectives, limited only by his own knowledge and ethical considerations and by any guidelines provided by his institution. In the late 1950's the NIH

²⁴Interview with Donald T. Chalkley.

explored the possibility of adopting the Nuremberg Code,²⁵ or one similar to it. This Code had developed from the trials of Nazi doctors who were tried for criminal action because of the experiments they had performed upon captives held in concentration camps and hospitals. The Code permitted some experimentation using human subjects, but explicitly enumerated the guidelines which should be followed when conducting such experimentation. "The effort foundered largely because of the difficulty of devising a single code that would cover with equal adequacy and equal flexibility the entire range of biomedical experimentation."²⁶ The pervasive posture of the NIH during these years was to permit researchers "to be guided by their own professional judgment and controlled by their own ethical standards as well as those of their institution."²⁷

While the NIH did not issue formal regulations or guidelines governing medical research, this is not to suggest that officials were unconcerned with ethical problems or with protecting human subjects from potential research hazards. There was a continuous flow of advice from the NIH to individual investigators and institutions. In addition the National Advisory Councils had discussed some of these problems. "The questions constantly arose, Is the institution aware of what this

²⁵ United States v. Karl Brandt, et. al., United States Adjutant General's Department, TRIALS OF WAR CRIMINALS BEFORE NUREMBERG MILITARY TRIBUNALS UNDER CONTROL COUNCIL LAW NO. 10 (October 1946-April 1949), The Medical Case, vol. 2 (1947).

²⁶ Interview with Donald T. Chalkley.

²⁷ Curran, op. cit., supra, n. 10 at 549.

individual investigator is intending to do? Have they really read this application over carefully?"²⁸ Former Surgeon General Stewart writes that "the National Advisory Heart Council had had discussions on human experimentation before I became Surgeon General (in 1965) and there had been developed at least a certification on grant applications that human subjects were protected."²⁹ Such concern developed primarily because of the rapid growth of medical research in the United States. By the latter part of the 1950's public expenditures for medical research had increased considerably as the NIH, by expanding its extramural research program, increased the capability for more clinical investigation throughout the country. Accompanying this expansion in medical research was a rapid increase in research involving human subjects. The nature of experimental procedures was also changing. The development of new surgical techniques made possible more complex and invasive surgical actions, culminating in the processes of organ transplantation. Initial efforts in the field of kidney transplantation had a special impact. Dr. James A. Shannon, Director of the NIH from 1955-1968, recalls an incident that occurred at a University hospital where a surgeon transplanted, without success, an animal kidney into a human being. What distressed Shannon most was that the surgeon "did it on his own without prior consultation with anybody" connected with the medical school or the University "and that the procedure as performed on the

²⁸Interview with Donald T. Chalkley.

²⁹William H. Stewart, in a letter to this author, February 16, 1971.

basis of then current information had neither likelihood of therapeutic benefit to the patient nor likelihood of providing new scientific information."³⁰ Thus there developed at the NIH a

clear consciousness that there wasn't an adequate scientific base for that action, that it was entirely experimental in character and that there was the growing need to make certain that all the implications of that act . . . had been clearly examined and that there was a valid basis for proceeding with that kind of experimentation in terms of the scientific objectives to be achieved and the protection and condition of the experimental subject involved.³¹

Similar problems also arose in the intramural program.

It became apparent from reading the protocols from the various Institutes that too frequently the statement was made that this is a safe procedure because it has been utilized on a patient with a particular type of disease. So it seemed that certain nontherapeutic procedures were being utilized in patients with disease quite properly to obtain specific types of information relative to the nature of the disease or its effect on certain systems. But at the same time these were nonstandard procedures and did not receive the careful review that the same procedures would have received in a normal individual.³²

The Clinical Center guidelines written in 1953 were, of course, very flexible with respect to treatment involving a doctor and his patient, which was dealt with in terms of the long-standing doctor-patient relationship. However, after reviewing some of the Institute protocols, Shannon began to inquire, on an Institute-by-Institute basis, about the types of programs of an experimental nature that were being conducted on diseased patients. "We found that much nonstandard diagnostic and

³⁰Interview with James A. Shannon.

³¹Interview with Joseph S. Murtaugh.

³²Interview with James A. Shannon.

therapeutic devices were being used."³³ It soon became evident to NIH officials that

the absence of any written guidelines on the . . . employment of investigative drugs or procedures with respect to the sick patient was no longer a tolerable situation and that something in the way of a set of basic guidelines to govern this area of activity had to be developed. The pressure internally was growing by virtue of the same advances in medical and surgical capability that was being reflected as well in the Clinical Center as it was throughout the teaching hospitals of the nation.³⁴

Another issue integrally linked to the expansion of the extramural program was "what kind of responsibility did the granting agency, the NIH, bear in respect to the circumstances and conditions in which investigative activity was carried out?"³⁵

In addition to this internal perception of the problem by key NIH officials, the medical community was reminded of the issues pertaining to human experimentation by a 1959 book called Experimentation in Man. Author Henry K. Beecher wrote,

Ethical and moral implications and problems surround every facet of experimentation in man. The central conclusion is that it is unethical and immoral to carry out potentially dangerous experiments without the subject's knowledge and permission. It also requires . . . profound thought and consideration on the part of the physician, for the complexities of medicine are in some cases so great, it is not reasonable to expect that the patient can be adequately informed as to the full implications of what his consent means.³⁶

³³Idem.

³⁴Interview with Joseph S. Murtaugh.

³⁵Idem.

³⁶Beecher, n. 9, supra, at p. 43.

Recognition of this myriad of problems prompted the NIH in January 1960 to award a three-year grant to the Boston University Law-Medicine Research Institute to conduct a study of actual practices in clinical research in the United States with regard to the legal, moral and ethical issues involved. Of the study's³⁷ findings, of special significance were the results of a 1962 survey which was sent to 86 departments of medicine and which produced 52 responses. The replies did not indicate any trend toward establishing guidelines or procedures concerning clinical research. Only nine institutions replied that they had a procedural document; an additional five indicated either that they were in the process of developing such a document or that they favored one for their institution. However, upon close examination of those documents, only two of the nine were guidelines generally applicable to all clinical research. The departments were also asked if they used special consent forms for research; only 16 answered positively.

As a result of their recognition of the problems related to human experimentation, it is not surprising that NIH officials began at this time to search for a mechanism to assure that experiments for which public money was being used would receive public screening. According to former Surgeon General Luther L. Terry, "the granting authorities in the Public Health Service were concerned about the Government's responsibility in the absence of such a policy."³⁸ The

³⁷Irving Ladimer and Donald B. Kennedy, Clinical Investigation in Medicine: Legal, Ethical and Moral Aspects (Boston University Law-Medicine Research Institute, 1963).

³⁸Luther L. Terry, in a letter to this author, February 23, 1971.

obvious problem was to develop a reasonable basis for judging the experimental activities of clinical investigators.

The Policy-Making Environment

During this period of time another federal agency was involved with a similar problem. Congressional hearings concerning the use and control of drugs were begun by Senator Estes Kefauver's Subcommittee on Antitrust and Monopoly in December 1958. As a result of the hearings, Congress passed the Drug Amendments of 1962,³⁹ which were explicit in requiring the Secretary of the Department of Health Education and Welfare, through the Food and Drug Administration (FDA), to issue regulations governing the testing of new drugs. Included in the amendments was a provision that made mandatory the consent of a subject before he became part of a procedure involving an experimental drug. The Congressional debate surrounding the introduction and use of experimental drugs had its effect on NIH policy-makers. It made clear to them "the inadequacy of the (PHS) Guidelines with respect to the physician-patient relationship" and also brought into focus the "question of what constituted consent."⁴⁰

In the latter part of 1963, persons from the Office of the Surgeon General and officials from the NIH began more in-depth discussions of the subject of human research. As a result of some preliminary

³⁹P.L. 87-781, 21 U.S.C. 355.

⁴⁰Interview with Joseph S. Murtaugh.

discussions, Shannon asked the Division of Research Facilities and Resources (DRFR),* which at that time supported the establishment of general clinical research centers, to investigate clearance procedures of current investigation in terms of the conventions that existed at that time and in terms of what they would recommend as a suitable set of controls. Selected to head this study was Dr. Robert B. Livingston, then Associate Chief for Program Development, DRFR. In a memorandum to Shannon, Livingston outlined the steps that he would follow in proceeding with his investigation:

Stage one would aim to define the scope of the study, outline the essential issues, identify the ethically responsible relationships, and specify procedures for carrying out the main study if such is to be undertaken. Stage one would naturally involve a careful assessment of the wisdom of a Government agency undertaking an examination of those problems.

The second stage would undertake an examination of the range and tenor of present professional practices and the nature of the educational, informational, and intellectual guidance processes involved in providing patterns of practice in this delicate area. These considerations would be essential to any recommendations which might be transmitted to you and the Surgeon General.⁴¹

In replying to Livingston's memorandum, Shannon generally agreed with the scope and plan that Livingston had outlined and emphasized his concern about the end results of such a study.

*Due to a NIH reorganization, this division is now the Division of Research Resources (DRR).

⁴¹Robert B. Livingston, Memorandum to Director, NIH, "Moral and Ethical Aspects of Clinical Investigation," February 20, 1964.

I think it is important to emphasize that our end objective in this matter is to clarify our responsibility as a supporting agency and to identify the courses of action that our responsibility imposes upon us.⁴²

Livingston, with assistance from NIH's Office of Program Planning, completed the study and submitted his report on November 4, 1964.⁴³ Concerning the background of the problem, the report made the following points:

Historically progressive changes in the kinds of clinical research possible to undertake are changing the nature of risks and values relating to clinical research.

There is no generally accepted professional code relating to the conduct of clinical research.

The legal status of clinical research is ambiguous.

The NIH supports clinical research in a wide variety of research institutions and hospitals. There exist conspicuous differences in institutional attitudes toward acceptable professional conduct of clinical research.

As the number of investigators, subjects and institutions engaged in clinical research increases and as the nature of the risks ventured changes according to the extension of research into new areas, a mounting concern is expressed over the possible repercussions of untoward events which are increasingly likely to occur and which may occur in an unfavorable pattern of context. Highly consequential risks are being taken by individuals and institutions as well as the NIH as a direct result of the complexity and ambiguity associated with research on man.⁴⁴

The report also referred to the wide publicity then being given

⁴²James A. Shannon, Memorandum to Dr. Robert B. Livingston, "Review of the Ethical Aspects of Clinical Investigation," March 5, 1964 (Hereinafter referred to as "Memorandum to Livingston").

⁴³Robert B. Livingston, Memorandum to Director, NIH, "Progress Report on Survey of Moral and Ethical Aspects of Clinical Investigation," November 4, 1964 (Hereinafter referred to as "Livingston Report").

⁴⁴Ibid., pp. 2-3.

to earlier experiments at the Jewish Chronic Disease Hospital in Brooklyn, New York, which had resulted in charges of unethical conduct against Dr. Chester M. Southam and Dr. Emanuel E. Mandel. This research project had been funded by grants from the PHS and the American Cancer Society. It is important to examine some of the details of the incident because it probably "stimulated a greater attention to the problems"⁴⁵ associated with research in humans.

Dr. Southam was a physician acting as an employee of the Sloan-Kettering Institute in New York and was conducting cancer research. Dr. Mandel was the Director of Medicine and Director of Medical Education at the Jewish Chronic Disease Hospital. Both doctors were found guilty, censured, and placed on probation for their "conduct in the planning and execution of a research project at the Jewish Chronic Disease Hospital . . . prior to and on or about and after July 16, 1963."⁴⁶ The two doctors were found "guilty of fraud or deceit and unprofessional conduct for injecting cancer cells into patients."⁴⁷ The doctors informed the patients that they were going to do something to them of an experimental nature, but they "did not tell the patients that they were receiving cancer cell injections, and . . . [the patients] were not asked for written consent."⁴⁸ This episode focused attention upon the

⁴⁵Interview with Edward J. Rourke.

⁴⁶Regents Committee on Discipline, University of the State of New York, Report on the Matter of Southam and Mandel, Nos. 158, 159 (undated).

⁴⁷"Two Physicians Put on Year's Probation," New York Times, December 15, 1965, p. 58.

⁴⁸Elinor Langer, "Human Experimentation: Cancer Studies at Sloan-Kettering Stir Public Debate on Medical Ethics," Science, vol. 143, February 7, 1964, p. 552.

actual and potential risk that humans could carelessly be used to achieve the objectives of clinical investigators whose ultimate goals may have been very commendable, but who were exercising unacceptable judgment in achieving those goals. Since NIH officials had been concerned with such problems prior to this incident, its impact upon them is not surprising.

It made all of us aware of the inadequacy of our guidelines and procedures and it clearly brought to the fore the basic issue that in the setting in which the patient is involved in an experimental effort, the judgment of the investigator is not sufficient as a basis for reaching a conclusion concerning the ethical and moral set of questions in that relationship.⁴⁹

The case also brought into focus the legal issues in which the PHS could become involved and dramatized the PHS responsibilities as a public agency. One participant at the National Advisory Health Council (NAHC) meeting on September 28, 1965, clearly expressed this concern when he stated that "if the Southam-Mandel case were to come to court, I think we [the PHS] would look pretty bad by not having any system or any procedure whereby we could be even aware of whether there was a problem of this kind being created by the use of our funds."⁵⁰ A related case, Fink v. Jewish Chronic Disease Hospital, did eventually reach a state court in New York. The defendant hospital demanded that the PHS, as one of the sponsors of the research, hold the hospital innocent and take over the defense of the action. The PHS rejected this demand and denied legal

⁴⁹Interview with Joseph S. Murtaugh.

⁵⁰Stenographic Transcript, National Advisory Health Council meeting in Washington, D.C., September 28, 1965 (Hereinafter referred to as "Transcript, NAHC meeting").

responsibility. The case was settled out of court; the plaintiff reportedly received a large sum of money. While no precedent was established in the area of a grantor's legal responsibility, government officials were clearly aware of the possible implications. One legal advisor, Edward J. Rourke, suggested at the time that "the greater need for the PHS is to define to what extent it has responsibility" with respect to its status as a granting agency.⁵¹

In his report, Livingston also directed his attention to the problem of NIH control.

NIH is not in a position to shape the educational foundations of medical ethics . . . More than that, whatever the NIH might do by way of designing a code or stipulating standards for acceptable clinical research would be likely to inhibit, delay, or distort the carrying out of clinical research . . . it would be advantageous to the national health research program if any general guidelines or code of clinical research behavior were developed by a nonfederal body . . . In our view, it would add to existing insecurities if the NIH were to assume an exclusive or authoritarian position concerning the definition of ethical boundaries or conditions mandatory for clinical research.⁵²

One of the participants in the Livingston group recalls the reluctance on the part of the group to suggest any action by the NIH. "It was very difficult to get that small group that was convened to agree on the necessity for any action on the part of the NIH. There was strong resistance on attempting to set forth any guidelines or restraints or policies in this area."⁵³ It was this particular part of the report,

⁵¹Edward J. Rourke, Memorandum to the Surgeon General, "Clinical Research," October 26, 1965, p. 3.

⁵²Livingston Report, pp. 7-8.

⁵³Interview with Joseph S. Murtaugh.

regarding the responsibility of the NIH, that Shannon found "wholly unsatisfactory, because what it said basically was that what a scientist does within his own institution is of no concern to the PHS and therefore there is no reason for you as Director of the NIH to be concerned with what was going on."⁵⁴ For Shannon this was an unsatisfactory resolution of a significant problem; it was his conviction that "we did have as an institutional responsibility the decision to assure that an institution had a mechanism that would have to be used to review the experimental work for suitability."⁵⁵

In July 1964, as part of the process of developing its report, the Livingston group held an informal, ad hoc meeting with a small number of NIH advisors knowledgeable about problems relating to clinical research and experienced in a variety of research institutions and professional societies. This ad hoc committee made four recommendations; they were included in Livingston's report.⁵⁶ These recommendations may be summarized as follows:

1. That an appropriate professional group be encouraged to formulate a statement of principles relating to the moral and ethical aspects of clinical investigation.
2. That there was a need for more factual information regarding actual research practices.
3. That the NIH should consider providing advice, at the request of grantees, concerning the ethical problems and risk-reducing practices appropriate for the development of clinical research.

⁵⁴Interview with James A. Shannon.

⁵⁵Idem.

⁵⁶Livingston Report, pp. 9-11.

4. That research grant documentation relating to clinical investigation using human subjects should be identified for special consideration throughout the NIH-PHS review process.

In his letter of transmittal to the Surgeon General, Shannon agreed in principle with all four recommendations, and urged "that the highest priority be given [to] the rapid accomplishment of the objectives" of the first and fourth recommendations.⁵⁷ However, he gave evidence of his belief that the first recommendation "did not constitute a means for executive action,"⁵⁸ and suggested an alternative course of action.

We are in full agreement with the advisory group that there is a need for a widely acceptable statement of principles relating to the moral and ethical aspects of clinical investigation. The problem is to conceive of a manner by which the statement of principles will be assured of endorsement as a consensus position which can serve as a positive guide to the conduct of clinical research. The advisors recommend that this statement of principles be developed by an appropriate professional group. We are inclined to think a broader approach may be necessary.

To win general acceptance within not only the medical research community but also our society at large, the final statement of principles should probably emerge from a group which includes representatives of the whole ethical, moral and legal interests of society. The nature of this group and the manner of its convening remains the critical question in acting upon recommendation number one. This question needs further discussion.⁵⁹

During 1965 Shannon continued discussion of this particular point with members of his own staff, with the hope of deriving a method by which to

⁵⁷James A. Shannon, letter of transmittal to the Surgeon General, "Moral and Ethical Aspects of Clinical Investigation," January 7, 1965 (Hereinafter referred to as "letter of transmittal").

⁵⁸Interview with James A. Shannon.

⁵⁹Shannon, letter of transmittal.

establish such a statement of principles. In the meantime, the issues surrounding experimental research on man were receiving world-wide attention. The World Medical Association issued its "Declaration of Helsinki," which permitted experimentation, with the patient's consent, if the experiment could be justified on therapeutic grounds.⁶⁰ The Medical Research Council of Great Britain declared that experimentation was permissible as long as "the true consent of the subject is explicitly obtained," at least in those cases where there is "no direct benefit to the individual and that, in consequence, if he is to submit to it he must volunteer in the full sense of the word."⁶¹ A decision was subsequently made by Shannon and Surgeon General Terry to bring the matter before the National Advisory Health Council (NAHC) at its September 1965 meeting. The Council, which had members representing both the medical and scientific professions, was designed to take up issues within the health field which had very broad policy implications.

The feeling was that we ought to have this kind of public concurrence for the procedural actions that we were going to take. That is why it was submitted to the Council. The report of the ad hoc committee was never considered a sufficient basis of action without some kind of broader concurrence. The National Advisory Health Council provided that mechanism.⁶²

Prior to that September meeting, however, another important policy development occurred within the NIH. In March 1965, the National

⁶⁰World Medical Association, "Declaration of Helsinki," Helsinki, Finland, 1964.

⁶¹Medical Research Council of Great Britain, "Responsibility in Investigations on Human Subjects," British Medical Journal, vol. 2, July 18, 1964, pp. 178-79.

⁶²Interview with Joseph S. Murtaugh.

Advisory Heart Council adopted for the National Heart Institute a special procedure relating to cases involving hazardous clinical research proposals. The procedure stated that

it is the responsibility of the applicant or grantee institution to furnish the Institute with a statement of acceptance of its responsibility in the use of the procedure or procedures in question. The Institute has the responsibility for deciding whether to issue a statement of grant award and whether to release grant funds with or without first having obtained such a statement.⁶³

Recognizing the problems faced by the NIH with respect to its responsibilities in the area of moral and ethical aspects of clinical investigation, Dr. John Sherman, then NIH Associate Director for Extramural Programs, urged that "each Institute adopt in principle the sense of the document as an interim measure until such time as it is superseded by a definite PHS policy."⁶⁴ At the July 1, 1965, meeting of the NIH Executive Committee for Extramural Affairs a motion to adopt the basic principles of the Heart Institute procedure was passed.

In a letter dated September 13, 1965, Congressman Cornelius E. Gallagher (N.J.), who was Chairman, Special Inquiry of the House Committee on Government Operations, notified Surgeon General Terry that he was conducting an investigation regarding the problem of the invasion of privacy as it was related to certain investigative activities of the Federal Government. Gallagher wrote that

⁶³"National Heart Institute Extramural Procedure In Case Of Hazardous Research Proposals," March 15, 1965.

⁶⁴John Sherman, Meeting of the NIH Executive Committee for Extramural Affairs, July 1, 1965.

One of our primary concerns has been the use of personality tests, inventories and questionnaires in research projects financed by grants and contracts under the Federal Government. It is our belief that the sponsoring agencies should adopt effective policies and guidelines to make certain that the protection of individual privacy is a matter of paramount concern and that the testing is without compulsion.⁶⁵

Terry referred this letter to Dr. Philip R. Lee, then Assistant Secretary for Health and Scientific Affairs, Department of Health, Education and Welfare, since the issues involved related not only to the activities supported by the PHS, but also to those of the Children's Bureau of the Welfare Administration and of the Vocational Rehabilitation Administration. In his reply, Lee wrote that "I do not believe that there is any disagreement on the principles involved. In my view, the main question is how to implement the principles and protect the individual against an invasion of privacy. We believe that this can best be done by a voluntary cooperative effort."⁶⁶ It is readily apparent, then, that throughout all levels of Government concerned with health affairs--NIH, PHS, and the upper levels of the Department of Health, Education and Welfare (DHEW)--there was, by 1965, a manifest concern with respect to the potential problems of experimenting with human beings and to the proposition that any proposal regarding the restraint of such activity should involve a minimum of federal intervention.

⁶⁵ Representative Cornelius E. Gallagher (N.J.), letter to Luther L. Terry, September 13, 1965.

⁶⁶ Philip R. Lee, letter to Representative Cornelius E. Gallagher, November 22, 1965.

The Government's Response

The general question of the ethical, moral and legal aspects of clinical investigation was discussed with the NAHC at its meeting on September 28, 1965. Shannon reviewed the issues that had been discussed by his ad hoc advisory committee and his staff for the Council. His remarks emphasized the following points:⁶⁷ There was a general awareness on the part of people engaged in clinical research activity that the present guidelines under which they operated were inadequate. The problems stemmed from the change in the nature of clinical investigation. In the past, such investigation was more in the line of observation and stemmed from the normal physician-patient relationship in an attempt to find a more accepted treatment. However, observation was being replaced by manipulation in not only the diseased individual but also in normal individuals. Shannon stressed that

we have the feeling that since such investigation departs from the conventional patient-physician relationship, where the patient's good has been substituted for by the need to develop new knowledge, that the physician is no longer in the same relationship that he is in the conventional medical setting and indeed may not be in a position to develop a purely or a wholly objective assessment of the moral nature or the ethical nature of the act which he proposes to perform. We would think that if indeed this is the case, that investigative procedures that depart from those which are purely therapeutic in nature perhaps might be the subject of discussion before the fact with the investigator's peers, so that the environment within which he resides could reach a sound judgment as to the worthwhileness and to the validity of the things that he chose to do.⁶⁸

⁶⁷This information has been taken from the Stenographic Transcript of the National Advisory Health Council Meeting, September 28, 1965 (Hereinafter referred to as "Transcript, NAHC Meeting"). See n. 50, *supra*.

⁶⁸Ibid.

Shannon told the Council that, while there had been various attempts to develop codes and declarations, in his opinion they had been produced to fit the need of very specific circumstances and did not apply generally. Shannon concluded that he felt that the PHS had

a dual responsibility. One is a minor one of keeping the Government out of trouble . . . but really the major one is through these programs to try to encourage the development of terms and conditions that will encourage the flourishing of sound clinical investigation rather than discouraging it. I am searching for some way of creating a more profound sense of an institutional awareness of the importance of this aspect of the problem without tying them down and immobilizing them in their capabilities.⁶⁹

Shannon and his associates hoped that their efforts would help to develop an institutional framework of review that would become "an integral part of the working process of biomedical research" and that "all investigative activity involving a human subject, regardless of the support, would be reviewed . . . as a part of the normal workings of a good scientific establishment."⁷⁰ Shannon also proposed for consideration by the NAHC a draft resolution which expressed the view that, in research involving human subjects,

the judgment of the investigator must be subject to review by his peers to assure an independent determination of the risk-benefit of the scientific work involved and maximum protection of the rights and welfare of the individual or individuals involved.

⁶⁹Ibid.

⁷⁰Joseph S. Murtaugh, in a letter to this author, October 4, 1971.

An arrangement to provide for this review by peers of proposed clinical investigation should be clearly provided for in every institution where such work is conducted.⁷¹

The Council expressed its concern with these issues and agreed that a restrictive code was not possible or warranted. It expressed a desire to study carefully the proposed resolution and to discuss it within the institutional environments of its members with the intent of taking a definitive stand on the issue in the Council's next meeting in December 1965.

Dr. Dael Wolfle, now Professor of Public Affairs at the University of Washington and a past member of the NAHC, explains the attitude of the Council toward the issues before it.

If rules were to be written that would apply generally over the country they would be either vague enough to require a good deal of interpretation or so specific as to try to cover a great variety of conditions. Neither alternative seemed desirable, in view of the fact that Federally supported research involving human subjects ranges over such a wide variety of conditions with respect to the kind of information to be secured from the subject, the methods of treatment, and possible harm.

Accordingly, we agreed that we should put the burden of responsibility on the experimenter and his professional colleagues. We thought the Government should have more protection than the mere statement by the principal investigator that his methods were sound and appropriate.⁷²

On December 3, 1965, the NAHC adopted a resolution reflecting much of the earlier work done by Shannon with his advisors and staff. The

⁷¹Draft Proposal for Discussion, "Resolution of the National Advisory Health Council on the Exercise of Ethical and Moral Judgment in the Conduct of Clinical Investigation," September 28, 1965.

⁷²Dael Wolfle, in a letter to this author, April 7, 1971.

Council resolved that the

Public Health Service support of clinical research and investigation involving human beings should be provided only if the judgment of the investigator is subject to prior review by his institutional associates to assure an independent determination of the protection of the rights and welfare of the individual or individuals involved, of the appropriateness of the methods used to secure informed consent, and of the risk and potential medical benefits of the investigation.

The recommendations of the NAHC were accepted by Surgeon General Stewart; on February 8, 1966, he issued the first official Policy and Procedure Order (PPO No. 129) outlining the position to be taken by the PHS regarding clinical research using human subjects.

The PPO maintained that

No new, renewal, or continuation research or research training grant in support of clinical research and investigation involving human beings shall be awarded by the Public Health Service unless the grantee has indicated in the application the manner in which the grantee institution will provide prior review of the judgment of the principal investigator or program director by a committee of his institutional associates. This review should assure an independent determination: (1) of the rights and welfare of the individual or individuals involved, (2) of the appropriateness of the methods used to secure informed consent, and (3) of the risks and potential medical benefits of the investigation. A description of the committee of associates who will provide the review shall be included in the application.

The statement also indicated that the policy applied to "all PHS research and research training grant regulations and research and research training policy statements." In addition, assurances of compliance with the PHS policy were required with each separate grant application.

The general reaction of the research community toward the policy statement was favorable. "Opposition to the guidelines was

minimal. There was no doubt that American science was ready for this type of regulation."⁷³ Some opposition both of a procedural and of a substantive nature did develop.

There were behavioral scientists who felt that this would interfere with their research. They said how can we possibly find out about people if we don't ask them these very personal questions. There is a whole class of studies in social psychology that depend on deception of the subjects. This was one issue. Another issue was that the individual investigator felt that he was being tied up with more red tape.⁷⁴

This opposition had little impact upon the policy-makers and their decision that such guidelines were required.

Once it was realized that the policy was necessary it was issued because we felt that we were going to the Congress to obtain money for certain types of investigation and we had a responsibility to see that amenities relative to the protection of individuals were not placed in jeopardy.⁷⁵

Experience with administering the policy, however, led by July 1, 1966, to a major revision. A memorandum from Dr. Mordecai Gordon of the Division of Research Grants to the Assistant General Counsel, DHEW, describes the major administrative problem. "The most frequent apparent misunderstanding is reflected in the submission of an assurance for an institution as a whole instead of for each application."⁷⁶ As a result of

⁷³Interview with James A. Shannon.

⁷⁴Interview with Mordecai Gordon, former Special Assistant to the Director, Division of Research Grants, National Institutes of Health, Bethesda, Maryland, April 27, 1971.

⁷⁵Interview with James A. Shannon.

⁷⁶Mordecai Gordon, Memorandum to Assistant General Counsel, Department of Health, Education and Welfare, "Clinical Research and Investigation Involving Human Beings," April 18, 1966.

this feedback, PPO No. 129, Revised Policy, eliminated the requirement of individual assurances of compliance with each grant application and provided instead for an institution-wide assurance to cover all subsequent grant proposals. The assurances were to include (1) agreement with the principles of the policy; (2) a description of the method of review; (3) the competencies represented in the review committee; (4) the administrative mechanism for surveillance and advice; and (5) the manner in which the institution would assure itself that the advice of the committee would be followed. In addition to resolving significant administrative problems, the single institution-wide assurance had another purpose. In their attempt to develop an institutional framework of review which would encompass all investigative activity involving human subjects, NIH officials "hoped that the use of a single but institutionally oriented assurance would, in most, if not in all situations, stimulate consideration also of reviews by a similar process of projects not supported by PHS grants."⁷⁷ The revision also extended the necessity for peer group review of research using human subjects to all PHS grants and required the institutions to report any changes in policy, procedures, or in the composition of review committees.

In the month prior to the issuance of the revised PPO No. 129, Dr. Henry K. Beecher published an article in which he cited 22 examples of experiments using human subjects which involved serious ethical problems. Beecher wrote that

⁷⁷John F. Sherman, Deputy Director, NIH, in a letter to this author, November 5, 1971.

Evidence is at hand that many of the patients in the examples to follow never had the risk satisfactorily explained to them, and it seems obvious that further hundreds have not known that they were the subject of an experiment although grave consequences have been suffered as a direct result of experiments described here.⁷⁸

While the article created quite an uproar in the medical research community, there is little doubt that the momentum to prevent such ethical errors was already strong within the PHS. If any problem did exist it was to find, to repeat an earlier statement by Shannon, "some way of creating a more profound sense of an institutional awareness of the importance" of the ethical and moral aspects of experimenting with man. The PHS Guidelines were an attempt to attain that objective.

On December 12, 1966, the Surgeon General, in order to clarify past statements as they related to the behavioral and social sciences, issued another policy statement. As indicated earlier, some investigators had complained that fully informed consent was impossible in much research, particularly in those cases involving psychological factors. The December clarification made it clear that the Guidelines applied to experiments of a behavioral or sociological nature, but PHS officials "tried to introduce into the clarification a little common sense. We tried to leave some leeway for judgments by both the investigators and the review committees."⁷⁹

The clarifying statement also noted that there were some studies in the behavioral sciences that "did not require the fully informed

⁷⁸ Henry K. Beecher, "Ethics and Clinical Research," The New England Journal of Medicine, vol. 274, June 16, 1966, p. 1354.

⁷⁹ Interview with Mordecai Gordon.

consent of the subject or even his knowledgeable participation." The clarification made clear the responsibility of the grantee institution to assure that experiments were "in accordance with the laws of the community in which the investigations are conducted and for giving due consideration to pertinent ethical issues." It also stressed concern for the protection of the subject as "most critical when the subject is not of age or competence to make an adequate judgment in his own behalf."

On January 24, 1967, the Surgeon General issued a further revision⁸⁰ of the July 1, 1966 statement. The primary purpose of this revision was to enunciate clearly the responsibility of the PHS:

Nothing in this institution-wide assurance should inhibit the PHS staff, advisory groups, or consultants from (1) identifying concern for the welfare of human subjects, and communicating this concern to the grantee institution, or (2) recommending disapproval of the application if the gravity of the hazards and risks so indicate.

The final major policy revision to be discussed in this paper was issued on May 1, 1969. The primary reason for this revision was the perceived need both to strengthen previous policy statements and to assure a greater consistency in interpreting and implementing their provisions.

It was on the basis of our experience with administering the policy that, for one thing, PPO No. 129 originally saw the light of day in February 1966, and over a period of months after that was revised and supplemented and pieced and patched together so many times that it became almost incoherent. So there was a need to put all of the policy in one pot, so to speak.⁸¹

⁸⁰PPO No. 129, Revised Supplement No. 3, January 24, 1967.

⁸¹Interview with Mark H. Conner, Institutional Relations Office, Division of Research Grants, Bethesda, Maryland, February 16, 1971.

On July 24, 1968, Dr. Philip Lee appointed a Task Force of various PHS-NIH officials to review and revise the guidelines for the protection of the individual as a research subject. The initial meeting of the Task Force was held on October 28, 1968. Eighteen months later, in a letter to the heads of institutions receiving PHS grants, the chairman of the Task Force summarized the group's findings. "The review confirmed the utility of the policy, but recommended changes in the policy statement to provide better understanding of the requirements."⁸²

The changes were more procedural than substantive. The revised policy statement, Protection Of The Individual As A Research Subject, once again emphasized that protecting the rights and welfare of human subjects was a responsibility of the grantee institution. Specifically, the policy required that a review committee within each institution be concerned primarily with: (1) the rights and welfare of the individual, (2) the appropriateness and adequacy of methods used to obtain informed consent from the subject, and (3) the risks and potential benefits of the investigation. It was made clear that the Guidelines applied to all research involving human subjects, whether concerned with medical or behavioral studies. The most significant change from the criterion enumerated in prior policy statements was in criterion (3),

which recognized that direct benefits to subjects could be other than medical, and that the importance of the knowledge to be gained might justify a committee in permitting an informed subject to accept risks in the interests to humanity, even though there was no direct benefit to him.⁸³

⁸²Eugene A. Confrey, Former Director, Division of Research Grants, National Institutes of Health, letter to Heads of Institutions Receiving PHS Grants, May 1, 1969.

⁸³Donald T. Chalkley, letter to Mrs. Lindsey Miller Lerman, Center for Criminal Justice, Harvard Law School, January 25, 1971.

There were two other important changes. The policy provided a more detailed description of what constituted "consent." It stipulated that for minors or other legally incompetent persons, consent could be obtained from parents, guardians or next of kin. The policy stated that "such consent is valid, however, only if the individual is given a fair explanation of the procedures to be followed, their benefits and attendant hazards and discomforts, and the reasons for pursuing the research and its general objectives." It made clear that the subject "may withdraw his consent at any time." This represented, by far, the greatest amplification of the term "consent" on the part of PHS officials. The other important change was of a procedural nature. It required certification of the review of individual applications. The July 1, 1966 policy revision had required that each application had been or would be reviewed by the institutional review committee. "This requirement was dropped in March 1967, on the insistence of some institutions that this was a bothersome requirement."⁸⁴ It was the opinion of the Task Force, however, that in order to prevent any problems from arising concerning the PHS's recognition that the institution was aware that the experiment involved human subjects, such certification should once again be required. "Our intent, therefore, was to provide a device that would enable an awarding unit within the PHS to be certain that the institution had in fact recognized that human subjects were involved in a particular proposal."⁸⁵

⁸⁴Interview with Donald T. Chalkley.

⁸⁵Idem.

It might be helpful at this juncture to summarize the major provisions of the Guidelines:

1. Broad guidelines, rather than detailed controls, are provided.
2. There are three basic guidelines:
 - a. the protection of the rights and welfare of the individual,
 - b. the judgment of methods used to obtain informed consent,
 - c. the determination of the risks and potential benefits of the investigation.
3. Compliance with these guidelines is accomplished by submitting an institution-wide assurance for all projects funded by the PHS. The institution is not required to adopt a specific set of ethical principles as long as its methods and procedures conform to the relevant principles outlined in the PHS Guidelines.
4. A system of self-regulation is established in the institutions funded by the PHS. This does not imply, however, a passive attitude on the part of the PHS. The Service retains its responsibility for a final overview of all research proposals.
5. Supervision of the Guidelines is vested in a review panel of the peers of the investigator within his own institution. Members of the panel cannot have a vested interest in any project that they review.
6. The committee review is not to be an independent review of the Guidelines for protecting the research subject. Rather it is a review of the judgment of the investigator and his methods for complying with the Guidelines. In this manner, the PHS places the primary responsibility for designing and carrying out the research project on the investigator.
7. The PHS has refrained from rigorously defining such terms as "informed consent," "rights and welfare of human subjects," and "invasion of privacy." However, it has attempted to provide the review committees, particularly in the May 1, 1969 statement, with a frame of reference for reaching a consensus regarding the meaning of such terms.

Rapid advances in biomedical science and the increase in the use of human subjects in research experiments have resulted in enormous benefits to the health of this nation. Such progress, however, has also brought into focus various ethical and social problems related to the

use of human beings as research subjects. Instances such as the Southam-Mandel case and those cited by Beecher provided ample evidence that the problems are real. In response to these developments, the PHS has felt it necessary to review its responsibility in the area of clinical research and to determine the course of action that such responsibility required. There were a variety of interests involved: among them the research subject, the clinical investigator, and the general public. The crucial question was how to balance those interests, weighing both the objectives being sought and the values held by key groups in society. This portion of the study has attempted to trace the evolution of the PHS's answer to that question. Whether well or badly done, government officials did define their responsibility and proceeded on a course of action designed to fulfill that responsibility. To explain why those officials defined their responsibility as they did and why they took a particular course of action may provide valuable insights into the policy-making process used to approach a very complex and sensitive problem.

PART II: THE P.H.S. GUIDELINES:
AN ANALYSIS OF THE POLICY-MAKING PROCESS

Government exists precisely for the reason that there is a need to have special persons in society charged with the function of promoting and protecting the public interest.⁸⁶

Paul Appleby
Big Democracy, 1945

The PHS Guidelines are the result of an effort by one agency of the government to protect and promote the public interest and to maintain the delicate balance between the welfare of the research subject and the expansion of medical research. In this specific case there existed a point of tension between these two objectives with respect to medical experimentation on human subjects, since procedures to be used for the benefit of man must first be tested on human beings. There have been instances when investigators, who have justified their action by the need to promote research, have disregarded the welfare of the individual. Clearly, there has been a conflict between two values, both strongly held in American society. The task which confronted government policy-makers, themselves former scientists, was to resolve that conflict without excessively sacrificing either the welfare of the individual or the benefits to be gained from future research. The comments of a past member of the NAHC illustrate the dilemma:

Some of us felt regretful at the necessity of writing an additional rule or regulation . . . for what we were doing was to impose one more "bureaucratic" restriction. However, we thought the "restriction" necessary, both in order to protect subjects against occasional lapses from good practice and also to assure Congress and the public that good practice was always to be insisted upon.⁸⁷

⁸⁶Paul Appleby, Big Democracy (N.Y.: Alfred A. Knopf, 1945), p. 5.

⁸⁷Dael Wolfle, in a letter to this author.

The purpose of this part of the study is to analyze the policy-making process outlined in Part I. That analysis will be based on an eclectic framework of various concepts of policy-making, drawn primarily from the literature of the social sciences. Within this framework, an attempt will be made to explain why the PHS Guidelines took the form that they did.

On the most basic level the Guidelines which resulted can best be explained in the context of what Amitai Etzioni refers to as a "mixed-scanning strategy." In such a strategy, policy-makers differentiate fundamental decisions from what Etzioni terms "bit decisions." Fundamental decisions

are made through an exploration of the main alternatives seen by the actor in view of his conception of his goals, but . . . details and specifications are omitted so that overviews are feasible. Bit decisions are made "incrementally" but within the contexts set by fundamental decisions.⁸⁸

It is the fundamental decisions, then, that set the basic direction of policy and it is the incremental or bit decisions that are made either to implement those basic decisions or to revise them. Etzioni also suggests that "the cumulative value of the incremental decisions is greatly affected by the underlying fundamental decisions."⁸⁹ The decisions by the PHS in the mid-1960's to assume formal responsibility in an area theretofore void of government involvement and to adopt a particular course of action represent such fundamental policy decisions. Actions subsequent to those decisions were for the most part attempts

⁸⁸Amitai Etzioni, The Active Society (N.Y.: The Free Press, 1968), p. 283.

⁸⁹Ibid.

by policy-makers to implement through bit decisions their initial decisions more effectively.

The most important task confronting the policy-makers in developing the PHS Guidelines was, to use Yehezkel Dror's concept, the "processing of values."⁹⁰ According to Dror, "values can be mutually independent, mutually reinforcing, contradictory or anywhere in between. In their 'raw' form, they are not very useful for evaluating problems or formulating goals for public policymaking . . . values should be specified at least enough to point out the main avenues of action and some rough priorities for them, including the basic values that must not be impaired."⁹¹ Prior to the 1960's, there was no formal policy by the PHS regarding research involving human subjects in its extramural program and there was no formal attempt to specify and to order values according to some scale of priorities so that such a policy might be established. That the PHS did not have such a policy by this time is not very surprising. The rationale underlying the lack of an explicit policy included, as this author views it, two major considerations. First, the problem was so complex that caution was generally accepted as the best way to approach the question of federal involvement. One authority felt that

it is not my view that many rules can be laid down to govern experimentation in man. In most cases, these are likely to do harm than good . . . legal development can be helpful and directed toward progress or can be harmfully restrictive. Which it shall be will be determined by the breadth of understanding expended on this complex subject.⁹²

⁹⁰Yehezkel Dror, Public Policymaking Reexamined (Pennsylvania: Chandler Publishing Co., 1968), pp. 164-66 contain a detailed explanation of this phase of policy-making.

⁹¹Ibid., pp. 164 and 165.

⁹²Henry K. Beecher, "Experimentation in Man," Journal of the American Medical Association, vol. 169, January 1959, p. 471.

Hence, if there was to be a fundamental change in policy it would have tended to evolve over a period of time, rather than to appear suddenly. The evolutionary process was well along by the start of the 1960's. The second factor which helped to determine the PHS's aloof stance on the issue of research guidelines was the traditional concept of the purpose of a research grant and of the inherent nature of scientific research.

The traditional grant is essentially string free. This was true in the early days of the National Cancer Institute program which started in 1937. The extramural program . . . has repeatedly emphasized the need of the Federal Government to disengage itself from direct control of the grant in any way. It was the feeling that it would not be in keeping with the traditions of scientific freedom for the government to exert any degree of control over the conduct of the work.⁹³

This "was a very strong tradition within the PHS . . . the limited approach in the clinical research field was due largely to this tradition."⁹⁴ These two factors--the complexity and uncertainty surrounding the problem and the traditional concept of the research grant--help explain the early attitude of the PHS. However, views and values of policy-makers frequently change as new experiences with a problem or a policy shed light on what is possible and desirable, and such was the case with respect to this policy issue as the 1960's unfolded.

Dror has written that "an intuitive awareness of 'problems' can be consciously cultivated by introspection and by systematically surveying subjectively-felt problems by means of, for instance, brainstorming sessions and panel discussions."⁹⁵ Certainly the efforts of Shannon and his staff

⁹³Interview with Donald T. Chalkley.

⁹⁴Interview with Edward J. Rourke.

⁹⁵Dror, op. cit., p. 170.

and the Livingston group represent mechanisms for the introspection and surveying cited by Dror. It was because of the meetings and discussions held by these groups that government officials came to realize in a concrete way that the expansion of the NIH clinical research program and the growth of new and complex medical procedures made the absence of some type of government policy no longer tolerable.

The basic force behind the Guidelines was an internal perception of the problem, arising out of the growing awareness that we had cultivated an investigative capability, particularly in the surgical area, that now presented a whole new set of issues in terms of the extent to which individuals could be submitted to that kind of capability for experimental and research purposes.⁹⁶

As an outgrowth of this recognition, two important considerations became of central importance. First, it became apparent that the judgment of the investigator was "not sufficient as a basis for reaching a conclusion concerning the ethical and moral set of questions in that relationship."⁹⁷ Second, it became clear that it was necessary to clarify the responsibility of the NIH "as a supporting agency and to identify the courses of action that that responsibility" imposed.⁹⁸ Implicit but inherent in these two interrelated considerations was the fundamental decision to intervene, to whatever degree was found necessary and desirable, in the research programs of institutions whose projects were funded by the PHS. Shannon, with reference to the PHS Guidelines, declares that "as soon as we decided that other institutions were not behaving responsibly as we felt that we should behave then it was inevitable that this development would come."⁹⁹ The next

⁹⁶Interview with Joseph S. Murtaugh.

⁹⁷Idem.

⁹⁸Shannon, Memorandum to Livingston.

⁹⁹Interview with James A. Shannon.

important decision to be made was to determine the direction that such intervention would take. It was in this stage of the policy-making process that the "processing of values" assumed such an important role.

Since this was so it might be useful at this point to discuss the concept of the "processing of values." Values are the principles by which one establishes priorities of importance among needs, demands and goals. The growth of new and complex medical procedures presented a whole new set of issues with respect to securing protection for the research subject without immobilizing the clinical investigator. Policy-makers realized that, as techniques of medical research became more sophisticated, the problems they now experienced would become more complex. The nature and degree of this complexity was unclear to them, nevertheless they believed that their most important task was to determine how the best possible balance between the welfare of the research subject and the requirements of medical research could be assured.

The obvious difficulty for policy-makers in this case was determining "the best possible balance" for all situations at all times in the future. The difficulty was very real, since what may be highly valued in one circumstance might be of only minor concern in another circumstance. Another important variable was that, as man's capability for doing and evaluating medical research increases, his practical information about certain experimental procedures will also increase, resulting in possible changes in the risks/benefits ratio. Thus as more or different factual information is obtained, there will be a greater tendency for a shift in those values viewed as relevant to attacking an explicit problem. Frequently, goals are altered

in light of both a change in available means and of a change in the cost of achieving an objective. Of course, one can also view the decision-making process as beginning first with a shift in values which then affects the design of policies and the role played by certain facts. Even during one particular point in time "we must deal continually with conflicts of value, where one person's gain is another's loss."¹⁰⁰ The ordering of priorities will differ among individuals, with one willing to sacrifice some value at the expense of another while another person remains unwilling to make the same sacrifice. Hence, the crucial problem for decision-makers arises "from multiplicity and fluidity of values and from social disagreement about values."¹⁰¹ Thus, it is not realistic to expect a precise and permanent ordering of values when a variety of persons and institutions are involved in the decision-making process.

There appear to have been five basic values articulated by the policy-makers which played an important role in the decision-making process. Each of these values were included in what Dror designates as the "basic values that must not be impaired." First, there was the strongly-held belief that no man had the right to risk the health and welfare of another human being without his knowledge and consent. This was apparent from the very beginning of the NIH attempt to assess the environment of clinical research. Shannon, in his request to Livingston to inquire into the existing state of clinical

¹⁰⁰Victor A. Thompson, Decision Theory, Pure and Applied (1971 General Learning Corporation), p. 7.

¹⁰¹Charles E. Lindblom and David Braybrooke, A Strategy of Decision: Policy Evaluation As A Social Process (London: Collier MacMillan, Ltd., 1963), p. 113.

investigation, expressed the desire for a mechanism that would "serve as some protection for the individual who submitted to these research procedures."¹⁰² Second, there was the belief in the impropriety of excessive government involvement. Dr. Eugene A. Confrey suggests that "surveillance by the Federal Government of research procedures and their ethical implications relating to tens of thousands of grants and contracts is . . . infeasible, to say nothing of its propriety."¹⁰³ While although the management of such a task was viewed as impracticable, it was the excessive surveillance by the Federal Government that was presumed to be improper and this was a crucial factor in determining the substance of the policy. This value judgment provided the basis for the next one. The policy-makers valued the importance of cooperation between the PHS, the institution, and the individual investigator. This value judgment was widely supported throughout all levels of the bureaucracy. There were three parties involved in this cooperating effort. Since the investigator designed the research, he was in the best position to evaluate the propriety of his procedures. However, "the investigator is first and foremost a scientist in search of new knowledge, and it would not be in accord with our understanding of human motivation to expect him always to be as vigilant for his subject's welfare as for the productiveness of his own research."¹⁰⁴ Thus, recognition was given to "the institution . . . [as] the proper agent for overseeing research programs involving human subjects."¹⁰⁵

¹⁰²Interview with James A. Shannon.

¹⁰³Eugene A. Confrey, "PHS Grant-Supported Research With Human Subjects," U.S. Public Health Reports, vol. 83, February 1968, pp. 127-33.

¹⁰⁴Office of Science and Technology, Privacy and Behavioral Research (Washington, D.C.: GPO, February 1967), pp. 5-6.

¹⁰⁵Confrey, "PHS Grant-Supported Research," op. cit.

The third party and spokesman for the public was the sponsoring agency. The agency was responsible for assuring that the investigator and his institution were cognizant of the importance of the ethical aspects of the proposed research and that they had done what was necessary to protect the welfare of the research subject. The fourth value considered by the policy-makers was the conviction that the diversity inherent in scientific research was desirable. They believed that the preservation of such diverse research precluded either a too broad or a too restrictive policy. Dael Wolfle expressed this belief earlier when he wrote that

neither alternative seemed desirable, in view of the fact that Federally supported research involving human subjects ranges over such a wide variety of conditions with respect to the kind of information to be secured from the subject, the methods of treatment, and possible harm.

Hence, there was no attempt on the part of the government to apply common rules to diverse situations. The policy-makers also valued highly the grant-oriented program, which they believed was of a special nature. This fifth value was, in part, held over from earlier years when the need was emphasized for "the Federal Government to disengage itself from direct control of the grant in any way."¹⁰⁶ Policy-makers still found it improper for the Government to constrain the investigator in his search for knowledge.

The agency has not contracted for a tangible product, to be produced under rigorously specified terms and conditions. On the contrary, a grant is interpreted as a form of financial assistance to an institution on behalf of an investigator so that he may pursue a problem in which he is interested and which coincides with an area of biomedical research relating

¹⁰⁶Interview with Donald T. Chalkley.

to a national objective. Given this concept, the agency will endeavor to optimize the conditions conducive to the advancement of knowledge, including maximal freedom of inquiry.¹⁰⁷

These, then, were the five basic values processed by the policy-makers and subsequently incorporated into the resolution promulgated by the NAHC on December 3, 1965. This resolution represents a fundamental decision in Etzioni's terms. The Council gave policy-makers the "broader concurrence"¹⁰⁸ they thought necessary to effectuate their policy aims. The use of such a mechanism reflects what Dror has identified as the "organizational and social distance between the units" involved in policy-making. Such distance is necessary, according to Dror, in order that the units "operate at high quality"¹⁰⁹ so that a policy will have a better opportunity to succeed. The policy-makers agreed that

it was much more important for an external group to make pronouncements that are going to be restrictive on themselves as they appear as professionals within an institution than for us as federal bureaucrats . . . to enunciate a restrictive policy.¹¹⁰

The Guidelines which subsequently evolved were a result of an effort by policy-makers to bring form and direction to their basic values in order to achieve their overall goal. That goal was to develop a mechanism that would both protect and promote the interests of the American people, and that would neither sacrifice the welfare of the individual nor deny the nation the benefits which would accrue from future research. In order to

¹⁰⁷Confrey, "PHS Grant-Supported Research," op. cit.

¹⁰⁸Interview with Joseph S. Murtaugh.

¹⁰⁹Dror, op. cit., p. 211.

¹¹⁰Interview with James A. Shannon.

develop a policy that would assure optimum protection of human subjects as well as achieve the goals of research, a consensus developed among policy-makers that a detailed code of ethics that "did not apply generally"¹¹¹ was neither practical nor desirable. Restrictions that might be warranted in a particular situation might be unjustified in another. The policy-makers reasoned, therefore, that "such control would be likely to inhibit, delay and distort the carrying out of research."¹¹² In their attempts to design a workable policy, within the context of their five basic values, the policy-makers were able to decide upon the basic direction that the Guidelines were to take: primary responsibility for executing the policy would reside at the local level. Of course, through the PHS-NIH review process federal officials maintained their responsibility of final judgment of all research proposals. It seems fair to conclude that in the case of this particular policy the five basic values specified by policy-makers formed the framework in which all later fundamental and incremental policy decisions were made. The construction of such a framework was an essential step because of the important role played by values in determining policy objectives, the kinds of implementing mechanisms that could be established to achieve them, and the resulting degree of success. General agreement among policy-makers regarding basic values remained constant throughout this decision-making process, but, as Dror writes, "values can be specified and ordered to

¹¹¹Shannon, Transcript, NAHC Meeting.

¹¹²Donald T. Chalkley, "Intent and Experience in the implementation of PHS Regulations Concerning Projects Involving Human Subjects," speech before the American Psychological Association, San Francisco, California, August 31, 1968.

various degrees" and what is required on this continuum "depends very much on the particular policy that has to be made."¹¹³ Since value considerations are intertwined with cognitive considerations and since both considerations may vary with changing conditions, policy-makers often choose to effect new policies through incremental changes. Incremental policy-making "proceeds through a sequence of approximations. A policy is directed at a problem; it is tried, altered, and tried in its altered form, altered again, and so forth."¹¹⁴ Dael Wolfle indicated in a statement cited earlier that "research involving human subjects ranges over a wide variety of conditions with respect to the kind of information to be secured from the subject, the methods of treatment, and possible harm." It was unreasonable, therefore, to expect an accurate forecast of those myriad of conditions. The incremental approach to decision-making focuses on margins or increments of change so that only small changes from the status quo are evaluated. The approach is "deliberately exploratory. Rather than attempting to foresee all of the consequences of various alternate routes, one route is tried, and the unforeseen consequences are left to be discovered and treated by subsequent increments."¹¹⁵ Any attempt to go beyond this, suggests Charles E. Lindblom, is usually unrealistic and perhaps unwise; policy-makers possess neither the knowledge to predict future outcomes, nor are they able to reach agreement on the ordering of the various values involved. Thus, by making policy decisions incrementally,

¹¹³Dror, op. cit., pp. 164 and 165.

¹¹⁴Lindblom and Braybrooke, op. cit., p. 73

¹¹⁵Etzioni, op. cit., p. 271.

variations in values and the degree to which they are valued by policy-makers, as well as new factual information, can more easily be incorporated into the decision-making process. As will be shown later, the policy revisions made subsequent to the initial and fundamental policy decisions to intervene and to intervene in a particular fashion reflected only incremental differences in the ranking of priorities rather than any deviation from the commitment to the primary values held by the policy-makers throughout the process under study.

Since the initial policy statement of February 8, 1966, represents the basic form of the Guidelines, it will be useful to examine that statement in light of the original decision made by the policy-makers concerning the direction that the policy would take. For the purposes of this analysis, it is important to see if the initial statement, as well as subsequent statements, reflect Etzioni's contention that "the cumulative value of the incremental decisions is greatly affected by the underlying fundamental decisions." Perhaps the most important substantive point in the initial statement was the requirement that each grantee institution provide for "prior review of the judgment of the principal investigator or program director by a committee of his institutional associates." This requirement was certainly consistent with the second through fifth values held by the policy-makers. It represents an attempt to avoid an unnecessarily restrictive "exercise of federal responsibility"¹¹⁶ and to create an "institutional awareness"¹¹⁷

¹¹⁶Curran, op. cit., p. 439.

¹¹⁷Shannon, Transcript. NAHC Meeting.

regarding the responsibility of the institution to promote a favorable environment for clinical research. If the primary responsibility for overseeing experimental procedures was to rest with the individual institutions, their review committees and their investigators, it was necessary for the policy-makers to instill the values underlying the overall policy into those review committees and scientists. This attitude was clearly expressed by one of the policy-makers: "We must use every opportunity in a continuing campaign of education among the grantees that . . . the grantee institution must accept and discharge in a forthright manner its responsibility for both scientific and administrative overview of grant-supported activities by its faculty or staff."¹¹⁸ Recognizing the diversity involved in clinical research, NIH officials sought to encourage the local review committee to solve their own problems. "We realized that we . . . couldn't possibly ride herd on the multiple situations that would arise. Our responsibility was satisfied if we were convinced that the individual institution within which the research took place had an adequate review mechanism."¹¹⁹

The review committees were given the responsibility to determine: (1) the rights and welfare of the individual involved; (2) the appropriateness of the methods used to secure informed consent; and (3) the risks and potential medical benefits of the investigation. Dror asserts that "policy-making must . . . often leave the concrete definitions of the policy to be

¹¹⁸John Sherman, Memorandum to members of the Interbureau Advisory Committee for Extramural Programs, National Institutes of Health, "Statement of Assurance With Respect to Clinical Investigation," January 23, 1966.

¹¹⁹Interview with James A. Shannon.

determined when it is applied to discrete issues during its execution."¹²⁰ Recognizing the diversity of research and the variety of situations that might arise, the policy-makers chose not to define rigorously these three responsibilities, but instead left their definition to the review committees. A good example of this aspect of the process is the policy-makers' attitude toward the meaning of "informed consent." The requirement that the investigator obtain the consent of his subject prior to initiating the experimental procedure was consistent with the belief that the subject be assured adequate protection. That requirement was equally consistent, however, with the other four principal values. Because of the absence of legal precedent and of the variety of possible interpretations of the meaning of informed consent, government officials refrained from developing a rigorous definition for it. "We had great debates over informed consent. The lawyers repeatedly said that there was very little legal precedent in law and, therefore, no real legal interpretation of informed consent. We did not think it was possible to construct a law. . . on informed consent."¹²¹ For the policy-makers to attempt such a construction might have meant the obstruction of future research and would certainly have violated the philosophy of a grant-operated support program, both important values. At the same time, however, "informed consent" was viewed as an important mechanism for which to strive and was, therefore, to be considered in any decision concerning a research project.

¹²⁰Dror, op. cit., p. 191.

¹²¹William H. Stewart, in a letter to this author.

Government officials were then confronted with the decision of how to determine whether or not the grantee institution had such a review mechanism. Once again, consistent with the principles of minimal federal encroachment and maximum local involvement, the decision was to require each institution to submit an assurance of compliance for any research project funded by the PHS. The assurance mechanism was designed to secure policy objectives and was selected within the context of the original fundamental decisions. In a similar fashion, examination of subsequent policy revisions will show that the incremental changes made between February 1966 and May 1969, were consistent with the original set of value premises articulated by the policy-makers. The first major revision was issued on July 1, 1966. Important to note, in light of Etzioni's framework for the analysis of policy-making, is that this revision did not include any substantive changes from the original policy statement. The most significant change was of a procedural nature--the replacement of the grant-by-grant assurances of compliance with an institution-wide assurance to cover all grant proposals. The change was made in order to implement original policy decisions more effectively, not to modify them. Etzioni explains the place of such implementing mechanisms in the policy-making process; he writes that "the decision-making and implementation processes . . . are closely interwoven, with decisions affecting implementations . . . Decision-making is hence not to be viewed as a passive process. There is a continual give-and-take between decision-making and implementation."¹²² The give-and-take of which Etzioni writes is made possible by the response of the policy-makers

¹²²Etzioni, op. cit., p. 303.

to feedback received from those executing the policy. Karl Deutsch writes that "in feedback processes . . . the system itself is not isolated from its environment but, on the contrary, depends for its functioning upon a constant stream of information from the environment."¹²³ The importance of recognizing and reacting to such feedback was realized by the policy-makers. At the conclusion of his policy statement of July 1, 1966, Surgeon General Stewart wrote that he would "be pleased to receive suggestions and information from officials and investigators of grantee institutions to assist the Service in the conduct of its study." That such feedback was heeded by the policy-makers is evident in statements such as that of December 12, 1966, which reflected "the advice of the American Psychological Association and the American Sociological Association."¹²⁴ In that policy statement, Surgeon General Stewart made it clear that there were some experiments that "did not require the fully informed consent of the subject or even his knowledgeable participation." However, the statement remained consistent with the basic values held by the policy-makers and their original fundamental policy decisions since it placed the responsibility to assure that experiments were "in accordance" with local laws and reflected consideration of "pertinent ethical issues"¹²⁵ on the grantee institution.

¹²³Karl Deutsch, The Nerves of Government (N.Y.: The Free Press, 1966), pp. 186-87.

¹²⁴Ernest M. Allen, former Grants Policy Officer, Office of the Surgeon General, Memorandum to Bureau Chiefs, December 16, 1966.

¹²⁵PP0, 129, Revised Supplement No. 2, December 12, 1966.

The policy revision of January 24, 1967, restated the responsibility of the PHS. Dror writes that "some 'motivation' must be introduced for executing the policy, which includes... 'pushing' the executing."¹²⁶ By emphasizing that the PHS was prepared to disapprove of an application "if the gravity of the hazards and risks so indicate,"¹²⁷ the policy-makers expressed their intent to assure the implementation of their original policy decisions.

The final major policy revision was issued on May 1, 1969. Once again, the changes were primarily procedural rather than substantive. On the basis of feedback from the individual institutions and their investigators, policy-makers realized the need to "put all of the policy in one pot"¹²⁸ in order to remove any confusion that may have arisen. An attempt was also made to amplify the meaning of "informed consent." At the same time, however, the revised policy insisted that primary responsibility for determining whether or not a "fair explanation"¹²⁹ had been given to the subject remained with the institutional review committees. One policy-maker explained, "We have never insisted on particulars. We have described in general what our conception of informed consent means. We can only offer suggestions and remind people of their obligations to the people that they experiment on."¹³⁰ This revision, like the ones preceding it, was basically an incremental decision designed to implement the initial policy decisions. In all instances of policy-making

¹²⁶Dror, op. cit., p. 188.

¹²⁷PPO No. 129, Revised Supplement No. 3, January 24, 1967.

¹²⁸Interview with Mark H. Conner.

¹²⁹Protection Of The Individual As A Research Subject, p. 3.

¹³⁰Interview with Mark H. Conner.

subsequent to formulation of the original policy, none of the revisions violated any of the fundamental value premises articulated by the policy-makers. Such incremental revisions were made "within the contexts set by fundamental decisions" and demonstrated the effect on them of those underlying fundamental decisions.

The PHS Guidelines were not a result of hastily-made decisions. The initial policy statement was developed over a period of years, during which time policy-makers set forth their basic values as a framework within which to evolve subsequent decisions. In order to fulfill their responsibility as a public agency as well as their responsibility as the chief supporter of medical research in the United States, NIH policy-makers sought to develop guidelines that would provide adequate protection for the research subject as well as bring into fruition the benefits to be gained from clinical research. The various mechanisms for executing the policy were not immediately clear. Confronted with the task of deciding upon the basic direction that their efforts would take, the policy-makers chose an approach of decentralized regulation, one consistent with their processed values. Subsequent revisions, products of the evaluation of feedback from those primarily responsible for executing the policy, were instituted in order to achieve original policy decisions.

The decision-making process used to develop the Guidelines is a good illustration of Etzioni's "mixed-scanning strategy." After fixing their basic values, the policy-makers proceeded with an "exploration of the main alternatives"--a detailed code or flexible guidelines, local versus national control--omitting details so that an overview of the alternatives was possible. The nature of subsequent policy decisions and the processes employed to make them also gives credibility to Etzioni's contention that

"the cumulative value of the incremental decisions is greatly affected by the underlying fundamental decisions."

The "mixed-scanning strategy," which employs elements of both comprehensive planning and incremental decision-making, must be considered when evaluating public policy-making. While it proposes that decision-makers formulate long-term goals and examine various alternative policies, it also recognizes the inherent limitations of policy-makers. "The likelihood that decisions can accomplish large social changes and, at the same time, be guided by a high level of intellectual comprehension of the problem is slim. Such decisions require prodigious feats of synoptic analysis, beyond human capacities."¹³¹ Each of the two elements in the "mixed-scanning strategy" --fundamental and incremental decision-making--help to neutralize the shortcoming of the other. The strategy permits a flexible response to the results of policy decisions, but does so within the context of broader policy considerations. Etzioni contends that

societal decision-making requires two sets of mechanisms: (a) a high-order, fundamental policy-making process which sets basic directions, and (b) an incremental process which prepares for fundamental decisions and revises them after they have been reached.¹³²

This case study suggests that, at the federal level, these two mechanisms may be an integral part of the policy-making process.

¹³¹Lindblom and Braybrooke, op. cit., p. 65.

¹³²Etzioni, op. cit., p. 290.

AFTERWORD

During the time that this paper was being prepared, the Department of Health, Education and Welfare announced the adoption of a new policy¹³³ governing research using human subjects. The policy is no longer restricted to the health field, but instead applies to all programs and activities supported by grants or contracts from the Department and in which the subjects may be at risk.

The new department-wide policy closely parallels the PHS Guidelines issued in May 1969. Perhaps the most important divergence in the new policy concerns the requirements for informed consent. The basic elements of informed consent are enumerated fully and clearly in the new policy. Furthermore, the policy requires that the procedure used to obtain informed consent and the basis for committee determinations that the procedures are adequate are to be fully documented. The documentation may follow one of three forms:

(1) The "provision of a written consent document embodying all of the basic elements of informed consent" which must "be signed by the subject or his authorized representative;" (2) the "provision of a 'short' form written consent document indicating that the basic elements of informed consent have been presented orally to the subject." This form is to "be signed by the subject or his authorized representative and an auditor-witness to the oral presentation and to the subject's or his authorized representative's signature;"

¹³³Chapter 1-40, "Protection of Human Subjects," Department of Health, Education and Welfare Grants Administration Manual, April 15, 1971.

(3) the "modification of either of the above two primary procedures" which "must be approved by the [institutional review] committee." While the latter alternative provides much the same freedom of action permitted under earlier versions of the policy, a greater burden is on the review committee to document its agreement to a particular consent procedure. The greater the departure from fully informed prior written consent, the greater the burden on the committee. This procedure is consistent with the PHS policy's emphasis on decentralized regulation, with primary responsibility resting with the research institution. At the same time, however, it represents a larger degree of involvement by the Federal Government. By placing this greater burden on the institutional review committee, the Government, in effect, exerts a new measure of influence that might well play an important part in committee decision-making. Greater care in obtaining informed consent will be of primary concern for all institutional review committees. Aside from this difference, however, the essential elements of the two policies remain quite similar. The PHS policy was clearly the model for the new HEW policy, which will affect a wide range of social research. The understanding of how the PHS policy evolved and the values underlying it is, therefore, an important element in evaluating the broader set of guidelines.

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