investigation is such that mentally competent adults would not be competent subjects.' On the other hand, the Declaration of Helsinki states, and the AMA guidelines do not, that '(a)t any time during the course of clinical research the subject or his guardian should be free to withdraw permission for research to be continued.' No explanation is provided for the differences nor is any mechanism available to guide physician-investigators in adopting or rejecting part or all of either document, based on its disagreement with the other or for any additional reasons." [18]

In retrospect, the promulgation of so many varying codes of ethics can be viewed as a tacit recognition within the professions that self-regulation by investigators could not be relied on to control research practices. When it was also realized that the codes themselves had serious shortcomings, new and quite different proposals for ordering the research process began to emerge. Procedures were gradually developed to apply the general principles contained in codes of research ethics in the formal evaluation of individual research projects by institutional review committees.

The National Institutes of Health (NIH) first developed such procedures in order to regulate clinical research performed at its Clinical Center in Bethesda, Maryland. Since 1953, human research has not been conducted there without prior approval of a review committee responsible for the protection of subjects.[19] In 1966, Surgeon General William H. Stewart extended the requirement of prior review by "a committee of (the investigator's) institutional associates" to all "extramural" research supported by United States Public Health Service (PHS) grants and awards.[20] This review was to 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.[21]

Prior committee review was also instituted, in 1967, for all "intramural" research programs of the Public Health Service.[22] The Tuskegee Syphilis Study, conducted by PHS investigators, was an intramural activity.

In 1971, the Department of Health, Education, and Welfare formulated its policy for the protection of human subjects [23] which superseded the Public Health Service extramural program guidelines. Institutional committee review was retained as the central feature of the new DHEW policy. The DHEW regulations apply to all research supported by Departmental grants or contracts, regardless of whether the research is medical in nature. However, the new regulations do not apply to intramural PHS activities, which are still governed by separate and sometimes divergent PHS guidelines. Also in 1971, the Food and Drug Administration promulgated additional regulations,[24] patterned on the DHEW framework, to govern the testing of "investigational new drugs." And recently, in response to the Tuskegee Syphilis Study revelations, Senator Jacob Javits introduced a bill which would enact most of the current DHEW requirements into law.[25] Senator Hubert Humphrey also responding to the Tuskegee Study, introduced another bill, quite different in conception.[26] It would create within the executive branch an independent board to establish guidelines for human experimentation, to review research practices and to enjoin the conduct of certain investigations.

Due to the Federal Government's prominent role in funding biomedical research, the PHS-DHEW regulations have had a noticeable impact on the conduct of human research in this country. Over 700 American research institutions have established review committees in order to satisfy DHEW or PHS

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[18] Katz and Capron, *Social Factors Affecting the Modern Treatment of Catastrophic Diseases* (Unpublished Manuscript, 1973) (hereinafter, *Katz and Capron*).

[19] Sessoms, "Guiding Principles in Medical Research Involving Humans, National Institutes of Health," 32 *Hospitals, Journal of American Hospital Association* 44 (1958).

[20] Memorandum of Surgeon General William H. Stewart to the Heads of Institutions Conducting Research with Public Health Grants. (February 8, 1966).

[21] *Ibid.*

[22] DHEW—Public Health Service, *Protection of the Individual as a Research Subject*—Intramural Programs (May 1, 1969) (hereinafter *Intermural Guidelines*).

[23] DHEW Grants Administration Manual Chapter 1-40 (1971) (hereinafter *Grants Administration Manual*). The Department publishes *The Institutional Guide to DHEW Policy on Protection of Human Subjects* (1971) (hereinafter *Institutional Guide*) to help institutions sponsoring research to implement DHEW policy.

[24] 36 Fed. Reg. 5037-38 (1971).

[25] S. 3935, 92d Cong., 2d Sess. (1972).

[26] S. 3951, 92d Cong., 2d Sess. (1972).

requirements.[27] Although these committees are required to review only Federally-funded research, they often have extended their review to all research on human subjects conducted at their institutions.[28]

B. Description of DHEW Policy [29]

At present DHEW policies vest primary responsibility for the protection of research subjects in institutional review committees. These committees are charged with the initial review of all project proposals and are also expected to subject research activities to "continuing review." Once a committee has approved a research protocol, its decision is reviewed again by the DHEW study section which considers the protocol for funding. When either group disapproves a protocol, that decision cannot be appealed to the Department, and the protocol cannot be Federally funded. In contrast to the DHEW requirements, PHS intramural policy does not require continuing review. Instead, the burden is on the investigator to bring "significant proposed changes in protocol and emergent problems of investigation to the attention of the review group involved." [30] Nor does PHS intramural policy specify distinct stages of protocol review.

DHEW requires institutional committees to review all aspects of "any activity" which might expose a subject to the possibility of harm if the activity "goes beyond the application of those established and accepted methods necessary to meet his needs." [31] Recognizing that this jurisdictional standard leaves much to the discretion of committees and investigators the Department concedes that "(a)cceptance is a matter of professional response, and determination as to when a method passes from the experimental stage and becomes 'established and accepted' is a matter of judgment." [32]

Before the committee can approve an activity under review, it must "determine that the rights and welfare of the subjects involved are adequately protected, that the risks to an individual are outweighed by the potential benefits to him or by the importance of the knowledge to be granted, and that informed consent is to be obtained by methods that are adequate and appropriate." [33] Like the jurisdictional standard, these review standards are phrased in general terms, although the "basic element" of "informed consent" are set forth in greater detail.[34] DHEW policy also requires each institution to provide written assurance that it will abide by DHEW policy. The assurance must include "a statement of compliance with DHEW requirements for initial and continuing committee review of the supported activities; a set of implementing guidelines, including identification of the committee, and a description of its review procedures." [35] As part of the "implementing guidelines," each institution is asked to adopt a "statement of principles that will assist the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects." [36] These statements are typically derived from existing codes of ethics not much more explicit than the DHEW review standards themselves.[37]

Unlike DHEW policy, the intramural guidelines of the PHS make specific, albeit limited, reference to "(s)tudies involving children, the mentally ill or the mentally defective." [38] Such studies "shall be carried out only when there is no significant risk of physical or mental harm to the subject or when direct

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[27] For a description of the spread of institutional review committees following the promulgation of the PHS guidelines, see *Barber et al., supra*, footnote 3, at 145–148.

[28] Barber *et al.* estimate that 85% of the institutional review committees they surveyed review "all clinical research" conducted at their institutions, regardless of funding. *Barber et al., supra*, footnote 3, at 149.

[29] This description is based on the *Intramural Guidelines, supra*, footnote 22, and the *Institutional Guide, supra*, footnote 23. Hereinafter, the policy of the Manual and the Guide will be referred to as "DHEW" policy, while the policy of the Intramural Guidelines will be referred to as "PHS intramural" policy.

[30] *Intramural Guidelines, supra*, footnote 22, at 5.

[31] *Grants Administration Manual, supra*, footnote 23, § 1-40-10.

[32] *Institutional Guide, supra*, footnote 23, at 3.

[33] *Grants Administration Manual, supra*, footnote 23, § 1-40-20(A). The PHS *Intramural Guidelines, supra*, footnote 22, contain essentially equivalent standards for review, at 4–5.

[34] See *infra*., pp. 31–32.

[35] *Grants Administration Manual, supra*, footnote 23, § 1-40-40 (A).

[36] *Grants Administration Manual, supra*, footnote 23, § 1-40-40 (C) (2) (a).

[37] *Ibid.* See also *Institutional Guide, supra*, footnote 23, at 5, footnote 2, and at 23.

[38] *Intramural Guidelines, supra*, footnote 22, at 10.

benefit to the subject is anticipated."[39] The intramural guidelines also explicitly provide that "(s)tudies of individuals with limited civil freedom shall also be subject to group consideration and approval."[40] Although the references to minors, incompetents, and prisoners do not impose additional substantive restrictions on research, they may alert review committees and investigators to the special problems presented by research with such subjects.[41]

Since institutional review committees are entrusted with such difficult decision-making responsibilities, their composition is a matter of Departmental concern. The committee must be composed of sufficient members with varying backgrounds to assure complete and adequate review of projects and activities commonly conducted by the institution. The committee's membership, maturity, experience, and expertise should be such as to justify respect for its advice and counsel. No member of an institutional committee shall be involved in either the initial or continuing review of an activity in which he has a professional responsibility, except to provide information requested by the committee. In addition to possessing the professional competence to review specific activities, the committee should be able to determine acceptability of the proposal in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The committee may therefore need to include persons whose primary concerns lie in these areas rather than in the conduct of research, development, and service programs of the types supported by the DHEW.[42]

Beyond this, the Department does not specify any particular size or membership requirements, believing instead that disparity in institutional situations demands flexibility. For the same reason the Department does not provide any directions for the conduct of initial or continuing review. Instead, as already noted, institutions are required to submit for Departmental approval a description of the procedures their committees will follow to implement review.

When DHEW funding is sought, a research proposal approved by an institutional committee is reviewed again within the Department.[43] A study section, composed of scientists not connected with the proposal or its sponsoring institution, examines the proposal and transmits its recommendation to the particular National Advisory Council authorized to grant the requested research funds. This Departmental review is not restricted to a reconsideration of the "ethical soundness" of the proposed research. Instead, it encompasses all other factors which enter into any research funding decision, such as the scientific rigor of the proposal, the scientific significance of the proposed project, and the relationship of budgetary estimates to the proposed study. As a result, the review of ethical issues at this stage cannot be as thorough as it is intended to be at the institutional level.

The adoption of this institutional review committee approach promised to be a significant advance toward the goal of ethical human research. For the first time, codes of research ethics were to be applied in concrete situations by means of a definite procedure providing for independent scrutiny of individual research proposals. Moreover, a decentralized, pluralistic approach, emphasizing decision-making at the institutional level, seemed to offer other advantages. The exploration of problems from different points of view could ultimately lead to a fuller appreciation of the issues requiring resolution. Concern for the rights and welfare of subjects could be more easily communicated to individual investigators. The review of research protocols could be handled in depth and yet with dispatch.

Despite these hopes, the present DHEW regulatory framework can only be considered a qualified success. The continued existence of two varying sets of guidelines to govern intramural and extramural human research activities respectively serves no purpose and generates confusion. As to the content of the guidelines, although from a historical perspective institutional committee review was a major improvement over prior practices, many deficiencies, to which we now turn, have precluded successful supervision of human experimentation for the protection of human subjects.

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[39] *Ibid.*
[40] *Ibid.*
[41] PHS intramural policy does impose stricter consent requirements for experiments with such subjects. These consent requirements are discussed *infra*, at pp. 25 *ff.*
[42] *Grants Administration Manual, supra*, footnote 23, § 1-40-40 (C)(2)(6).
[43] *Grants Administration Manual, supra*, footnote 23, §§ 1-40-20 (B) and 1-40-50 (B). See also NIH Manual § 4107 "Grants Involving Human Subjects," § 4107 (G) (1972).

IV. CRITIQUE OF DHEW POLICY

A. Vagueness of Standards

At bottom, the difficulties which face review committees derive from the generality of the standards which are to guide their determinations in specific cases under either the intramural or extramural policies. To illustrate, if a review committee had evaluated the Tuskegee Syphilis Study under current guidelines, questions calling for searching examination would have surfaced.

(1) If the requirement of informed consent[46] is to be taken seriously, should impoverished and uneducated Blacks from rural Alabama have been selected as subjects in the first place? Or should a concerted effort have been made to find subjects from among the most educated within the population at large, or at least to select from the given subgroup those subjects most capable of giving "informed consent"? Put more generally, what general principles should guide the selection of subjects? The philosopher Hans Jonas has given one answer to this question: "(O)ne should look for (subjects) among the most highly motivated; the most highly educated, and the least 'captive' members of the community."[45]

(2) If "(t)he welfare of the individual is paramount (and) the subject must have available to him the facilities and professional attention necessary for the protection of his health and safety,"[46] what special efforts should have been made by investigators to provide medical treatment beyond the economic reach of the subjects before enlisting them in the Tuskegee Study? Or should the institutional review committee have turned down the Tuskegee Syphilis Study because no adequate treatment facilities were available in Macon County?

(3) How should "continuing review" operate? For example, at what point in time, after penicillin treatment for syphilis became available, should the subjects of the Tuskegee Syphilis Study have been apprised of this new development? Since it generally takes time before medical consensus is reached on the value of a new medication, and is reported in the medical literature, when should the subjects have been told that drug was available which at least some competent physicians considered effective treatment?

(4) How should the risks inherent in this study have been weighed against the predicted advancement of medical knowledge? The rule that "the risks to an individual . . . (must be) outweighed by the potential benefits to him or by the importance of the knowledge to be gained,"[47] is perhaps the most difficult guideline for review committees to implement. The seeming simplicity of this command belies its complexity. How are such tangibles as "risks," "benefits," and "importance of knowledge" to be measured and weighed? Can serious harm to research subjects ever be outweighed solely by additions to the sum of human knowledge?[48] If so, what kind of knowledge, in what circumstances, would outweigh what risks to subjects? The difficulties inherent in evaluating the scientific merits of a particular study are demonstrated by the ongoing differences of opinion among scientists of the PHS as to whether continuation of the Tuskegee Syphilis Study can still be defended on the ground of scientific merit. It is necessary for review committees to scrutinize carefully the research design of every proposed study if the requirement that risks be balanced against benefits is to be taken seriously, for the acquisition of knowledge depends so much on the soundness of the research protocol.[49] Does the informed willingness of the subject to accept certain risks have any bearing on the committee's balancing of risks against benefits? Finally, since the design of the Tuskegee Study could not completely exclude the possibility

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[46] The requirement of informed consent is analyzed in greater detail *infra*, at pp. 31 ff.

[45] Jonas, "Philosophical Reflections on Experimenting with Human Subjects," 98 *Daedalus* 219, 235 (1969).

[46] *Intramural Guidelines*, *supra*, footnote 22, at 1.

[47] *Grants Administration Manual*, *supra*, footnote 23, § 1-40-20 (A); see also *Intramural Guidelines*, *supra*, footnote 22, at 2, 4-5.

[48] Although PHS policy does proscribe seriously risky experimentation which cannot benefit the subject, *Intramural Guidelines*, *supra*, footnote 22 at 2, DHEW policy for extramural research does not categorically prohibit such research. The *Institutional Guide*, *supra*, footnote 23 states at 6: "If the potential benefits are insubstantial, or are outweighed by risks, the committee may be justified in permitting the subjects to accept these risks in the interests of humanity."

[49] *Intramural Guidelines*, *supra*, footnote 22, at 1.

that non-subjects might contract syphilis from untreated subjects, how should a review committee have balanced risks to nonsubjects against benefits to society?[50]

(5) Review committees are also required to "determine that the rights and welfare of the subjects involved are adequately protected."[51] What rights did the Tuskegee Study subjects possess? The tremendous confusion which exists in the area of patient subjects' rights is in part the result of the traditional but largely unexamined prerogative of professionals to intervene in their patients' best interests." The doctrine of "informed consent" has had little impact on this longstanding professional practice. Since much medical research is carried out in the context of "patient care" the right to make decisions for patients has more often than not unwittingly been carried over into the research domain. The confusion about patient-subjects' rights is bolstered by the scientist's felt obligation to advance knowledge for the good of society, although society has inadequately defined the extent of this obligation.

To illustrate the confusion about subject's rights: Can the subject claim the right to be indemnified for any harm he suffers as a result of the research, regardless of the investigator's fault and in spite of consent? If so, who is responsible for informing him that an injury has occurred which is not the result of the natural progression of his illness? Do Tuskegee Study subjects have a cause of action because they did not receive suitable medical treatment? If so, who may be liable—the individual investigators, the PHS, the Milbank Memorial Fund, the Tuskegee Institute? The intramural guidelines of the PHS and *The Institutional Guide to DHEW Policy on Protection of Human Subjects* also identify confidentiality as a right which must be protected.[52] Does confidentiality extend only to the subject involved in the study or does it also include the group of which he is a part? If the latter, what are the limits of group confidentiality? The Tuskegee Syphilis Study, in common with many other studies, singled out one particular group and revealed much that was intimate and private about all its members. Where can review committees seek guidance in devising procedures which safeguard subjects' rights in general, and their rights to confidentiality, privacy and respect, in particular?[53]

(6) The jurisdiction of institutional review committees encompasses "any activity which goes beyond the application of those established and accepted methods necessary to meet (the subject's) needs."[54] How are "established and accepted" methods to be ascertained? Among "established" treatments should distinctions be made between those of "proven" and those of "dubious" value? What are the criteria for a "necessary" intervention? Since there is so much professional disagreement as to when a procedure becomes "therapeutic," the question must be posed: "accepted" by whom? Was the withholding of arsenic and heavy metal treatments at the beginning of the Tuskegee Study a "therapeutic" intervention since the effectiveness of such treatments was in doubt, particularly for late syphilis? When did penicillin treatment become an "established and accepted method"? What degree of certainty is required of investigators and review committees? Certainly no clear line can be drawn between experimental and routine treatment since, as has so frequently been asserted, "the therapy of disease is, and always will be, an experimental aspect of medicine."[55]

The vagueness and generality of the governing standards have disadvantaged all participants in the research decision-making process. For conscientious review committees, they have meant hard work and, insofar as the committees

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[50] The *Intramural Guidelines, supra,* footnote 22, at 1, state: The health and safety of persons other than the subject, if endangered by the research procedures, must be protected. DHEW policy neglects this problem.

[51] *Grants Administration Manual, supra,* footnote 22, § 1-40-20 (A), see also *Intramural Guidelines, supra,* footnote 22, at 1, 4-5.

[52] *Intramural Guidelines, supra,* footnote 22, at 9; *Institutional Guide, supra,* footnote 23, at 6.

[53] The *Institutional Guide, ibid.,* does make an effort to suggest procedures for safeguarding confidentiality.

[54] *Grants Administration Manual, supra,* footnote 23, § 1-40-10 (B); see also *Intramural Guidelines, supra,* footnote 22; at 2-3,7-8.

[55] Ivy, "The History and Ethics of the Use of Human Subjects in Medical Experiments" 108 *Science* (July, 1948). Barber *et al.* have recently documented the prevalence of professional uncertainty over the definition of "research." See *Barber et al., supra,* footnote 3 at 150.

are overwhelmed by the enormity of their task, superficial examination of protocols. For subjects, the inevitable result has been to deprive them in some measure of the protection which review committees were supposed to provide. For investigators, the pervasive uncertainty about what kind of human studies are now permissible has impeded their research. And for society, fears about the protection of its citizens in the research enterprise have not been stilled. Especially because review committees work in isolation from one another and no mechanisms have been provided for disseminating the knowledge gained from their individual experiences, each committee is condemned to repeat the process of finding their own answers to all the questions we have raised. This is an overwhelming, unnecessary and unproductive task for which they are not prepared and which we doubt they are willing to assume.

What is needed, is an overall official body authorized to formulate more detailed policies with respect to research on human beings. The need for such a policy making body has in point of fact already been perceived, and other bodies, official and non-official, have partially and on an *ad hoc* basis attempted to fill the gap. For example, the FDA has promulgated comprehensive rules for the conduct of drug research,[56] although on many crucial issues of subject protection it has simply copied DHEW policy.[57] Similarly, in the wake of organ transplantation, an *Ad Hoc* Committee of the Harvard Medical School redefined the criteria of "death" in order to facilitate the removal of needed organs.[58] Moreover, the Division of Research Grants of NIH,[59] which at present supervises the implementation of DHEW policy, has occasionally transmitted memoranda to review committees "concerning the interpretation and implementation of (its) policy."[60] Recent memoranda focused on potential hazards of screening programs for sickle cell trait, the definition of "human subject," and guidelines for fetal studies. These policy making activities need to be consolidated, under the auspices of a broadly representative body, about which we shall have more to say below. Such a body would not only provide guidance to review committees but would also enable them to obtain advice whenever difficult problems arise.

B. Invisibility

The creation of institutional review committees could have led to increased visibility of decisions regarding the protection of subjects. But since neither publication nor free access to their findings was specifically planned for, increased visibility has not been realized. A low level of visibility hampers efforts to evaluate and learn from attempts to resolve the complex problems of human research. Especially so long as guidelines for human research remain so indefinite, high-visibility decision-making is an essential feature of a well-functioning regulatory framework. Moreover, since committee disapprovals can block research, with no recourse to higher level review, invisibility may impede the acquisition of valuable knowledge.

The 1969 committee review of the Tuskegee Syphilis Study illustrates the problems which a low level of visibility creates. Our knowledge of that proceeding comes from an unofficial summary which constitutes the only available report on that committee's deliberations. From this summary it is impossible to determine the factors which the committee considered or the grounds on which the committee based its decision to approve a continuation of the study. This state of affairs is not atypical. Because institutional committee decisions are not published, committee decision-making operates at a primitive level, uninformed by pertinent prior decisions of other committees or by scholarly outside criticism. A mechanism for self-improvement over time is lacking. Professor Guido Calabresi has observed:

". . . The best way of broadening the inputs to the committee—lies in another device: publication of the cases decided by the committees. Such cases could well be anonymous (at least at first). They could be collected and published in much the same way that decisions of courts are collected. The

[56] See 21 C.F.R. §§ 130.3, 130.37.
[57] *Ibid.*; see also 36 Fed. Reg. 5037 (1971).
[58] *Ad Hoc* Committee of the Harvard Medical School, "A Definition of Irreversible Coma," 205 J.A.M.A. 337 (1968).
[59] *Grants Administration Manual, supra*, footnote 23, § 1-40-50 (A).
[60] Memorandum of January 24, 1972, from Stephen P. Hatchett, Director, Division of Research Grants, NIH, DHEW, to Officers Responsible for Institutional Implementation of DHEW Policy on Protection of Human Subjects.

reports on any case could include, first a factual part describing, among other things, the experience of the experimenter, the intecedent tests in non-human subjects, the major risks perceived, the scientific gains perceived possible, the availability of subsequent controls to limit the risks, the origin and life expectancy of the subjects, and the nature of the consent and the manner in which it was obtained; and, second, a jurisprudential section containing the decision of the committee (whether favorable or unfavorable), together with the principal arguments made for and against the decision reached.

"Such published cases would soon become the subject of intense study both inside and outside the medical profession. Analyses in learned journals by lawyers, doctors, and historians of science would inevitably follow. These would undoubtedly re-argue the more important or pathbreaking cases. If law cases are any guide, the analyses would sometimes conclude that the cases were wrongly decided, but frequently that they were rightly decided, and perhaps more frequently that they were rightly decided but for the wrong reasons. To the extent that Law Reviews consider themselves courts of last appeal beyond the highest courts in the land, so would the learned journals in which this *giurisprudenza* would be dissected. From all this, a sense of what society at large deems proper in medical experiments might well arise. This sense would, in turn, guide the committees and make their decisions more sophisticated. The result would not only be better thought out decisions, but also a more complex system of controls, which, in effect, took into account much broader sources of information as to societal values. . . ." [61]

In the Recommendation section of our report we incorporate Calabresi's suggestions in a comprehensive framework for the regulation of human experimentation.

C. Subject Consent

1. *The Definition of "Informed Consent".*—Institutional review committees are expected to ascertain "that informed consent is . . . obtained by methods that are adequate and appropriate." [62] The DHEW Grants Administration Manual, in contrast to its treatment of other important matters, defines "informed consent" in some detail: Informed consent is the agreement obtained from a subject, or from his authorized representative, to the subject's participation in an activity.

The basic elements of informed consent are: 1. A fair explanation of the procedures to be followed, including an identification of those which are experimental; 2. A description of the attendant discomforts and risks; 3. A description of the benefits to be expected; 4. A disclosure of appropriate alternative procedures that would be advantageous for the subject; 5. An offer to answer any inquiries concerning the procedures; and 6. An instruction that the subject is free to withdraw his consent and to discontinue participation in the project or activity at any time.[63]

The PHS Intramural Guidelines also explicate informed consent in some detail: The individual must be free to choose whether or not to be a subject in research. His participation shall be accepted only after he has received a fair explanation of the procedures to be followed, benefits, and attendant hazards and discomforts, and, suited to his comprehension, the reasons for pursuing the study and its general objectives. He must be informed of his right to withdraw from the study at any time.[64]

For no apparent reason, two "basic elements" of informed consent identified in DHEW policy are ignored by the PHS intramural policy. Nothing is said in the intramural policy statement about disclosure of alternative procedures ("basic element" number four) or response to inquiries ("basic element" number five).

Despite the commendably greater detail with which DHEW policy on obtaining informed consent is set forth, major gaps do remain. For instance, the DHEW directives permit consent to be obtained from the subject's "authorized representative" in lieu of the subject himself. But the circumstances in which third party consent may properly be substituted for the consent of subjects

[61] Calabresi, "Reflections on Medical Experimentation in Humans," 98 *Daedalus* 387, 400–401 (1969).
[62] *Grants Administration Manual*, *supra*, footnote 23, § 1–40–20 (A).
[63] *Grants Administration Manual*, *supra*, footnote 23, § 1–40–10 (C).
[64] *Intramural Guidelines*, *supra*, footnote 22, at 1.

are undefined. Committees are not advised as to who can validly consent in place of the subject or whether consent can be obtained from another person besides the subject only for certain investigations, such as those specifically designed to benefit the subjects themselves. Thus, committees are left to their own devices in fashioning rules about the participation in research of such subjects as the very young or the very old, the mentally incompetent or the emotionally disturbed, the imprisoned or those otherwise under duress, or, as in the Tuskegee Study, those who are ill-prepared as a consequence or cultural deprivation or inadequate education.

In contrast to the DHEW extramural guidelines, the PHS intramural research rules do address the problems of substitute consent for special subjects in more detail: Studies involving children, the mentally ill or the mentally defective should be carried out only when there is no significant risk of physical or mental harm to the subject or when direct benefit to the subject is anticipated. . . . In general, written informed consent of the parent or guardian shall be required for all medical or dental studies with such subjects, except in studies of an observational nature or in those conducted during the administration of accepted health care procedures that do not require specific informed consent in ordinary practice. Any exception shall be carefully considered and fully documented. Written informed consent of parent or guardian may be desirable in certain other studies with these groups and shall be required of conditions warrant. . . . Studies of individuals with limited civil freedom shall also be subject to group consideration and approval. Informed consent of the responsible institutional authority shall be required in all cases. Written informed consent of the individual shall also be required except for studies of an observational nature conducted during the administration of accepted health care procedures that do not require specific informed consent in ordinary practice.[65]

The major difficulties with these provisions result from the exceptions to the general requirement of substitute consent. "Studies of an observational nature" and "accepted health care procedures that do not require specific informed consent in ordinary practice" are phrases too vague to be meaningful. For example, was the Tuskegee Syphilis Study "of an observational nature"? In what "other" kinds of studies may investigators dispense with the consent of parent or guardian unless unspecified "conditions warrant" it? Moreover, the PHS instructions ignore the issue of the capacity of third parties to represent the interests of special subjects adequately, and the subtle inducements which may persuade prisoners to consent.

Prisoners in particular are a group whose participation in research has long been controversial.[66] Because prisoners are a captive group, the danger is great that their consent to participate in research will be obtained by duress. Jessica Mitford has recently documented some of the abuses to which prisoner participants in experimentation have been subjected, and she comments:

"The (Institutional) Guide expresses a 'particular concern' for 'subjects in groups with limited civil freedom. These include prisoners. . . .' Having uttered this praiseworthy sentiment, HEW has apparently let the matter drop. Dr. D. T. Chalkley, chief of the Institutional Relations Branch, Division of Research Grants, and signer of the Guide, tells me that HEW does not even maintain a list of persons in which HEW-financed research programs are in progress and has 'no central source of information' on the scope of medical experiments on prisoners by drug companies. . . .

"What efforts have been made by HEW to enforce its guidelines in HEW-financed medical research behind prison walls? 'We do give some grants that involve prisoners. But there's no convenient way of recovering the information as to whether our guidelines are being followed,' said Dr. Chalkley. 'That responsibility lies with the principal investigator. . . .' Has HEW ever brought any action to enforce its regulations in any prisons anywhere? 'None, to date'."[67]

Most new drug testing is initially conducted on prisoners, and is subject to FDA regulations, but the FDA also has no list of persons in which such research is carried out.[68]

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[65] *Intramural Guidelines*, *supra*, footnote 22, at 10–11.

[66] See, e.g., Lasagna, "Special Subjects in Human Experimentation," 98 *Daedalus* 449 (1969); *Katz*, *supra*, note 12, pp. 1018–1052; Mitford, "Experiments Behind Bars," *The Atlantic Monthly* 64 (January, 1973).

[67] Mitford, "Experiments Behind Bars," *supra*, footnote 67, at 67–68.

[68] See Mitford, "Experiments Behind Bars," *supra*, footnote 67, at 68.

We regard the failure of the DHEW policies to include comprehensive guidelines for safeguarding prisoners, children, mental incompetents, and other special subjects in research, as a major shortcoming which must be rectified. Detailed policy must be formulated specifying the kinds of research which may be carried out with special subjects of different types, the inducements which are permissible, the circumstances in which third-party consent is necessary, the identity of those who can validly consent for the subject, additional precautions which must be taken for such subjects, and other matters.

2. *Exceptions to the Consent Requirement.*—In its *Institutional Guide to DHEW Policy on the Protection of Human Subjects*, the Department sets forth the following additional exceptions to the requirement of informed consent:

"The review committee will determine if the consent required, whether to be secured before the fact, in writing or orally, or after the fact following debriefing, or whether implicit in voluntary participation in an adequately advertised activity, is appropriate in the light of the risks to the subject, and the circumstances of the project.

"Where an activity involves therapy, diagnosis, or management and a professional/patient relationship exists, it is necessary 'to recognize that each patient's mental and emotional condition is important . . . and that in discussing the element of risk, a certain amount of discretion must be employed consistent with full disclosure of fact necessary to any informed consent'." [69]

The first exception which permits obtaining consent "after the fact," is so general in scope and so extensive in the discretion it accords review committees that it almost staggers the imagination. What are "the circumstances of the project" which could ever permit such an invasion of subjects' rights to self-determination and privacy? Is this exemption limited to investigations with normal subjects employing placebos or to deception studies so frequently employed by psychologists? In one sentence the requirement of prior [70] informed consent is seriously undermined.

Furthermore, another exeception provides for a departure from informed consent in situations in which "a professional/patient relationships exists." Since most medical research is carried out in such settings, it can apply to almost all medical interventions. It is particularly in clinical settings that overreaching in obtaining consent, however unwitting, is a constant danger.[71] Thus the unqualified provision that "a certain amount of discretion must be employed consistent with full disclosure of fact" is particularly unsatisfactory.[72]

PHS intramural policy also contains loopholes in its consent provisions. First, the guidelines state that an explanation so detailed as to bias his response or otherwise to invalidate findings is not necessary in those procedures that involve no risk of physical harm to the subject.[73]

This qualification is apparently designed to minimize interference with behavioral and other studies common to the social sciences. These guidelines elsewhere state that "a major class of procedures in the social and behavioral sciences does no more than observe or elicit information about the subject's status by means of tests, inventories, questionnaires or surveys of personality or background. In such instances, the ethical considerations of voluntary

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[69] *Institutional Guide, supra*, footnote 23, at 8.

[70] It is implicit that consent is normally to be obtained prior to the subject's participation in research, although DHEW policy nowhere so states.

[71] See *infra*, pp. 40ff.

[72] Compare the more satisfactory provisions on informed consent adopted by the FDA, 21 CFR § 130.37, which require that consent be obtained "in all but exceptional cases." This is defined as follows:

(d) Exceptional cases," as used in paragraph (b) of this section, which exceptions are to be strictly applied, are cases where it is not feasible to obtain the patient's consent or the consent of his representative, or where, as a matter of professional judgment exercised in the best interest of a particular patient under the investigator's care, it would be contrary to that patient's welfare to obtain his consent.

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(f) "Not feasible" is limited to cases where the investigator is not capable of obtaining consent because of inability to communicate with the patient or his representative; for example, where the patient is in a coma or is otherwise incapable of giving informed consent, his representative cannot be reached, and it is imperative to administer the drug without delay.

(g) "Contrary to the best interests of such human beings" applies when the communication of information to obtain consent would seriously affect the patient's disease status and the physician has exercised a professional judgment that under the particular circumstances of this patient's case, the patient's best interests would suffer if consent were sought.

[73] *Intramural Guidelines, supra*, footnote 22, at 1-2.

participation, confidentiality, and propriety in use of the findings are the most generally relevant ones. The procedures may in many instances not require the fully informed consent of the subject or even his knowledgeable participation." [74]

The lack of concern in the quoted passages for psychological—as opposed to physical—harm to subjects is striking. Despite acknowledged ethical problems, the guidelines suggest that in "many instances" the "knowledgeable participation" of the subject may be unnecessary. Here again, the regulations fail to provide meaningful guidance to review committees.

3. *The Quality of "Informed Consent".*—Another difficulty which seriously undermines the implementation of informed consent has not been dealt with at all in the DHEW policies. It has long been recognized that consent is far too often obtained in form alone, and not in substance. As the Department itself admits in its Institutional Guide (c ing Doctor Henry K. Beecher of Harvard Medical School): "The informed ent of the subject, while often a legal necessity is a goal toward whic must strive, but hardly ever achieve except in the simplest cases." [75]

For as Doctor Beecher has written elsewhere, "Lay subjects, sick or well, are not likely to understand the full implications of complicated procedures, even after careful explanation." [76]

Even with the best of intentions, investigators may fail to "get through" to their subjects for a variety of reasons. The subjects themselves may have great difficulty in understanding or little interest in knowing the nuances of what the investigator tries to explain to them. As Senator Hubert Humphrey recently lamented in response to the Tuskegee Syphilis Study:

"Who are the people who have been the subjects of medical experiment? The clear and shocking implications of the most recently revealed experiments indicate that the powerless, the poor, the least educated, and members of minority groups are the likeliest human guinea pigs.

"It is those who cannot understand what is being done to them that constitute by far the largest numbers among human experimentation subjects." [77]

Moreover, the circumstances in which consent is sought may foster or hinder an informed and voluntary decision. The subject may be under stress or distracted by other pressing concerns. For example, he may be a patient, desperately hoping for successful treatment of his condition, whose judgment is distorted by the natural tendency to grasp at any straw in reach. The likelihood of this result is magnified by the profound dependence which many patients develop on their attending physicians, who are often responsible for obtaining consent. Indeed, however wrongly, the patient may well fear that his refusal to consent to experimental treatment will anger his physician and deprive him of adequate medical care.

Lastly, the investigator himself may fail to describe his own research objectively, or unwittingly create subtle pressures on a subject to consent. To suggest this is not to deny the integrity of the researcher, but only to acknowledge the reality of investigators' bias toward their work. Their scientific curiosity and excitement make it difficult for them to take a detached view of the research they wish to conduct with their subjects.

D. Continuing Review

Although extramural research projects supported by DHEW grants or contracts must be reviewed on a continuing basis, intramural research activities of the Public Health Service need not be reviewed again after initial committee approval. This omission for intramural programs of what the Depart-

[74] *Intramural Guidelines, supra*, footnote 22, at 9.
[75] *Institutional Guide, supra*, footnote 23, at 7.
[76] Beecher, *Research and the Individual* (Little, Brown and Co. (1970).
[77] 118 Cong. Rec. S 14041 (Sept. 5, 1972). Senator Humphrey's assertion is corroborated by the recent study of research practices conducted by Barber *et al.* In the two institutions they analyzed, they found that studies in which the risks were relatively high in proportion to therapeutic benefits to the subjects were "almost twice as likely as more favorable studies to be done using subjects more than three-fourths of whom (were) ward and/or clinical patients," as opposed to private and/or semi-private patients. Moreover, this proportion is not significantly altered when studies in which the risk exceeds all possible benefits, to the subjects or to medic , generally are examined: "the 'least favorable' studies (where) still almost twice as likely as the more favorable to be done using three-forths or more ward or clinical patients." *Barber et al., supra*, footnote 8 at 55, 56.

ment itself calls "an essential part of the review process"[78] explains the long neglect of the Tuskegee Study. Begun long before committee review became a reality, the Study was not reviewed by any committee until 1969, three years after Surgeon General Stewart had inaugurated the policy of committee review. Moreover, the 1969 review was undertaken at the behest of the principal investigators themselves, and not as the result of the Public Health Service review policy. The Tuskegee Study was not reviewed again until this Panel was appointed. We have been unable to ascertain why intramural research programs are exempt from the continuing review requirement.

Although DHEW extramural policy does require "continuing review," a better definition of the nature and extent of this obligation is needed. The present indefinite regulations invite a perfunctory performance of the continuing review function. Essentially the Department expects that the committees "will . . . adopt a variety of continuing review mechanisms. They may involve systematic review of projects at fixed intervals set by the committee commensurate with the project's risk. Thus, a project involving an untried procedure may initially require reconsideration as each subject completes his involvement. A highly routine project may need no more than annual review. Routine diagnostic service procedures, such as biopsy and autopsy, which contribute to research and demonstration activities generally require no more than annual review. Spot checks may be used to supplement scheduled reviews. Actual review may involve interviews with the responsible staff, or review of written reports and supporting documents and forms. . . ."[79]

Institutional review committees, already overburdened by the task of examining all new research projects, are thus also responsible for re-examining from time to time all ongoing research. If something has to give first, it tends to be this assignment. Pressed for time, the review committees assume that the initial review has satisfactorily resolved all existing problems and that a cursory review is sufficient.

E. Structure and Composition of Institutional Committees

Institutional review committees are charged with carrying out a number of distinct functions. They are required to formulate policies and regulations to guide the conduct of research at their institutions,[80] often under the rubric of protocol review; to communicate these policies to investigators; to administer the policies they have promulgated through the prior appraisal of research proposals, the supervision of the attempt to obtain consent and the continuing review of approved research activities; to review the consequences of their decisions; and to keep informed of DHEW policy changes and suggestions in order to reformulate institutional policies and rules when necessary.

In recognition of the variety of tasks which have been delegated to committees, DHEW policy stresses the composition of committee membership. . . . In addition to possessing the professional competence to review specific activities, the committee should be able to determine acceptability of the proposal in terms of institutional commitments and regulations, *applicable law, standards of professional conduct and practice, and community attitudes.* The committee *may* therefore need to include persons whose primary concerns lie in these areas rather than in the conduct of research, development, and service programs of the types supported by DHEW (emphasis supplied).[81]

In carrying out their functions, the institutional review committees are thus also asked: "to determine acceptability of the proposal in terms of . . . applicable law, standards of professional conduct and practice, and community attitude." By assigning these tasks to a broadened committee membership, DHEW recognizes that decision-making in the human experimentation process cannot be left solely to professionals, but requires the participation of informed and concerned non-scientists, who may be laymen, lawyers, clergymen, and appropriate others. However, the functions of these non-professional participants are not spelled out. And the assumption that they can make their most

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[78] *Institutional Guide, supra,* footnote 23, at 8.
[79] *Institutional Guide, supra,* footnote 23, at 8-9.
[80] Although the parent institutions are charged by DHEW with the responsibility of formulating policies to guide institutional review committees, *Grants Administration Manual, supra,* footnote 23, § 1-40-40, to our knowledge this task is generally delegated to those committees. As we have previously described, the burden of formulating policy weighs heavily on local institutions because the DHEW policy is vague and incomplete.
[81] *Grants Administration Manual, supra,* footnote 23, § 1-40-40 (C) (2) (b).

effective contribution at the administrative stage, when individual protocols are reviewed, rather than at other stages of the process remains unexamined. The DHEW policies attempt to consolidate all phases of research regulation—formulation of detailed policies, administration of research, and review of decisions and consequences—in one committee structure. Asking each review committee to determine far-reaching policies by itself overburdens the review committee structure. The policy issues which must be resolved with the assistance of lay members are so complex that to require *each* committee to work them out by itself is at best inefficient and at worst self-defeating.

It would be more functional and efficient to leave the administration of research, like the administration of therapeutic interactions between physicians and patients, primarily in the hands of the professionals. If review committees were guided by comprehensive policies formulated by a broadly representative body, the review of individual protocols could focus on technical matters, such as degree of risk, likely benefits, research design, competence of investigators, safety precautions, and the like. This allocation of authority would help to reduce the widespread concern among physician-investigators about "meddlesome outsiders."

F. Enforcement

The DHEW guidelines on enforcement are written in permissive and general language:

"The Division of Research Grants (DRG), NIH, will follow up reports by reviewers, evaluators, consultants, and staff of the DHEW indicating concern for the welfare of subjects involved in approved and funded grants or contracts, and of subjects potentially involved in activities approved but not funded, and in disapproved proposals. On the basis of these reports and of other sources of information, the DRG, NIH, may, in collaboration with the operating agency concerned, correspond with or visit institutions to discuss correction of any apparent deficiencies in its implementation of the procedures described in its institutional assurance.

"If, in the judgment of the Secretary, an institution has failed in a material manner to comply with the terms of this policy with respect to a particular DHEW grant or contract, he may require that it be terminated in the manner provided for in applicable grant or procurement regulations. The situation shall be promptly notified of such finding and of the reason therefor.

"If, in the judgment of the Secretary, an institution fails to discharge its responsibilities for the protection of the rights and welfare of the individuals in its care, whether or not DHEW funds are involved, he may question whether the institution and the individuals concerned should remain eligible to receive future DHEW funds for activities involving human subjects. The institution and individuals concerned shall be promptly notified of this finding and of the reasons therefor." [82]

These enforcement guidelines delegate sole responsibility for the detection of failures to comply to the Division of Research Grants. But staff members of the DRG are probably the last persons to hear of any infractions once they have occurred, and then only when, as in the Tuskegee Study, they are of major proportions. Indeed, no procedures have been established to require institutional review committees to report to DHEW any evidence on noncompliance. Moreover, DHEW has made no efforts to define categories of noncompliance [83] which should lead to the imposition of sanctions or to specify different kinds of sanctions which would be imposed in particular cases. Finally, institutional review committees and DHEW are not authorized to take disciplinary action, except for the Secretary's prerogative to terminate grants or make the investigator or his institution ineligible to receive future funds.

G. Compensation of Subjects

Existing DHEW policy provides no mechanism for the compensation of subjects harmed as a consequence of their participation in research, in spite of the growing recognition that no matter how careful investigators may be,

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[82] *Grants Administration Manual, supra*, footnote 23, § 1-40-50 (E).

[83] Because the requirement of "continuing review" has not been elaborated, committees themselves only haphazardly come across evidence of noncompliance.

harm still will befall some subjects.[84] Unavoidable injury to a few is the "cost" of engaging in research which ultimately benefits the many. But unless the injured individuals can prove carelessness, failure to obtain informed consent, or actual malice, their participation bars recovery for the harm done to them. Those subjects whose injury does result from negligence are faced with the usual difficulties and uncertainties inherent in a law suit. For his part, any investigator who is sued as a result of his research may find that his ordinary malpractice insurance does not cover medical research.[85] If it does not—and the question is as yet unsettled—the personal liability of the investigator can be substantial. In addition, the economic vulnerability of subject and investigator adds to society's uneasiness about human experimentation, and may deter some persons from engaging in research activities.

H. Applicability of DHEW Policies

The DHEW guidelines quite appropriately were formulated for research grants and contracts to be funded by the Department. While much research in this country is supported by DHEW funds, a great deal of research is also funded or conducted by other Federal agencies, such as the Department of Defense.[86] Additionally, many research activities receive no Federal support. Is there any justification for permitting less stringent protective controls for human experimenation supported by other governmental agencies, private foundations, or other private sources than for research conducted or supported by DHEW?[87] Since a major restructuring in existing policies is necessary, we believe that serious consideration should be given to developing, through Congressional action, rules and procedures which apply to the entire human research enterprise without reference to the source of funding. A tentative step in this direction has already been taken by DHEW. Its enforcement section provides for the discontinuation of funds to any institution which has failed "to discharge its responsibilities for the protection of the rights and welfare of the individuals in its care, *whether or not DHEW funds are involved.*"[88] If it is concluded, however, that such broad coverage is beyond the power of Congress, then Congress should at least act to bring all federally funded research within a comprehensive regulatory framework.

When this is done, the existing anomaly in the applicability of DHEW policies should be corrected. We refer to the different policies described earlier which govern intramural and extramural research. We can find no justification for differential protection of subjects on this basis. Moreover, the conduct of human research by DHEW employees and under the Department's aegis lends additional support to our call for an independent Government body to oversee all research. For to expect DHEW to scrutinize and judge its own activities as critically and strictly as it supervises outside research projects is arguably unrealistic and unnecessarily strains internal Departmental relationships.

V. RECOMMENDATIONS

A. Preface

Before turning to our specific recommendations we would like to anticipate three possible criticisms of our proposals. First, the argument may be advanced that any regulation of human research is an unwarranted infringement of the "freedom of inquiry." But freedom of inquiry is only one facet of freedom in

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[84] See Ladimer, "Protection and Compensation for Injury in Human Studies," *In Experimentation With Human Subjects* (Paul A. Freund, ed.) 247, (George Braziller, 1970) (hereinafter *Ladimer*).

[85] See *Ladimer, supra*, footnote 84 at 251.

[86] For documentation of the human research conducted by the armed services, see the Legislative Reference Service's report "Medical Experimentation on Human Beings, March 1967," placed in the Congressional Record by Senator Jacob Javits, 118 Cong. Rec. S. 13789, 13793–95 (August 17, 1972). The report states: "There is very little information available on the number and types of military persons who serve as subjects in research. Intuitively appraised, however, the number of topics and of human subjects must be large," 118 Cong. Rec. S. 13793.

[87] Barber *et al.*, found that in 15% of the institutions they surveyed some clinical research was not reviewed by an institutional committee. Moreover, 35% of these institutions were medical schools, "the type of institutional setting most productive of biomedical investigations using human subjects." They concluded that "a perhaps significant volume of human research is still not subject to review by peer review committees." *Barber et al., supra*, footnote 3, at 149.

[88] *Grants Administration Manual, supra*, footnote 23, § 1-40-50 (15).

general. When scientists use other human beings as subjects of experimentation and in so doing jeopardize their rights and welfare, the scientists' freedom of inquiry clashes headon with the right of every individual in our society to personal autonomy. Therefore, society must retain the right to define and limit the human costs it is willing to bear in order to benefit from advances of knowledge.

Second, whenever it is suggested that representatives of society at large participate in decision-making of significance to both science and society, concerns about the intrusion of "outsiders" in the domain of professionals are voiced. This position was forcefully expressed by Dr. Owen W. Wangensteen in a letter to Senator Walter F. Mondale prior to congressional hearings in 1968 on a proposed Commission to study the social and ethical problems raised by biomedical advances.

"Senator, I would urge you with all the strength I can muster to leave this subject to the conscionable people in the profession who are struggling valiantly to advance medicine. We are living through an era in which the innovator is often under suspicion, being second-guessed by self-appointed arbiters more versed in the art of criticism than in the subject under scrutiny. We need to take great care lest the wells of creativity and the spring of the mind of those who break with tradition are not manacled by well-intentioned but meddlesome intruders.

"I would urge you to leave these matters in the hand of their proponents, the persons who are actually doing the work. They know more about all this than any of us possibly could. They have wrestled with the problem day and night, almost invariably over many years. Theirs are not overnight judgments or convictions. In the academic community in which I have worked and spent my entire professional life of almost 50 years, you will find as warm, sympathetic human beings as are to be found on this earth. . . .

"It is important that we look back as well as forward. To have no concern for history is tantamount to having a physician with total amnesia. If we leave this matter alone, it will simmer down. Discussion should not be restrained, but legislative action, never." [89]

We appreciate Dr. Wangensteen's fears, which have been echoed by others. But not all intrusions by "outsiders" into medical decision-making are viewed by the profession as unwarranted interferences with the practice of medicine. Authorized representatives of society have the right to circumscribe some activities of professionals and this has been accepted; for example, the discretion of physicians to commit patients against their will or to prescribe addictive drugs is limited. Thus, the pertinent questions are: under what circumstances, to what extent, and by what means should the activities of the medical professional be controlled?

We have already mentioned that the human research decision-making process can be divided into three functionally distinct stages: the *formulation* of research policies, the *administration* of research, and the *review* of research decisions and their consequences. The participation of "outsiders"—which is to say, of persons deemed capable of representing the interests of society in the proper conduct of research—is highly desirable in the formulation and review stages. Such decisions as the allocation of resources for research, the extent of hazardous experimentation, the degree of respect to be shown for the autonomy of research subjects, and the extent of the participation of children, prisoners, members of minority groups, and other captive or disadvantaged persons in research, are of momentous consequence to society as well as to science. These decisions implicate general social policies and must not be left to the sole discretion of scientists.

Nonetheless, we agree that the often expressed fear of interference by laymen with the immediate clinical research decisions which physician-investigators must make has merit. However, we believe that the two positions can be reconciled. Once satisfactory rules and procedures for the protection of human subjects have been formulated and research practices are adequately reviewed by "insiders" and "outsiders," society should feel safe in leaving the actual administration of research and therapy to physician-investigators within the

[89] *Hearings on S.J. Res. 145 before the Subcommittee on Government Research of the Senate Committee on Government Operations*, 90th Cong., 2d Sess. 98-99 (1968).

restraints imposed by peer review (through the already established institutional review committees).

Current DHEW policies fail to identify the different stages in the regulation of research. Instead, institutional review committees are charged with formulating policies, administering policies, and evaluating the consequences of their decisions. Taken together these tasks are too burdensome for such committees. Moreover, because these committees must formulate policy and evaluate decisions, the demand for outsiders to sit on them has intensified, justifying the fear of interference in professional day-to-day decision-making by persons not qualified to do so. Our recommendations seek to reverse this development by confining the role of the institutional committees largely to the implementation of policies already adequately formulated by others.

A third criticism may be leveled against our recommendation that a National Human Investigation Board be established to oversee human experimentation. Some may fear that this Board will promulgate such detailed rules and impose so many legal duties that progress in research and innovation in treatment will be seriously impaired. The danger of cumbersome bureaucracy cannot be lightly dismissed and every effort must be made to avert it.[80] At the same time we doubt that society, if properly informed, would tolerate any serious impediments to the acquisition of knowledge, for the pervasive and compelling desire to benefit from advances in medicine should counteract any tendency to stifle research.

A national Board to regulate human research is needed for many reasons. One central group should be responsible for formulating policy, instead of the many different Federal agencies and the hundreds of individual review committees which, as we have argued, cannot be expected to assume this complex task. Moreover, "outsiders" who could represent and protect individual and societal values and interests could then be included in policy formulation and review, where they are most needed, without thereby hindering physician-investigators in their professional decision-making. The national Board would provide a forum in which the competing interests of science and society could be debated openly before authoritative decisions are made.

B. National Human Investigation Board

A permanent Governmental agency, to be called the National Human Investigation Board (NHIB), should be established to oversee *at a minimum* all Federally-supported research involving human subjects. The jurisdiction of this Board should extend to all extramural and intramural research sponsored by DHEW (including human research currently governed by FDA regulations) as well as to research supported by Government agencies other than DHEW, such as the Department of Defense. Ideally, the authority of this Board should also extend to all human research activities, even if not Federally supported. However, despite its apparent merits, such a sweeping proposal may raise insurmountable jurisdictional problems. We leave it to others to determine whether Congressional authority to regulate research may encompass investigations not conducted or financed by the Federal Government.[81]

The primary function of the NHIB would be to formulate policies and procedures to govern research with human beings. For this reason the Board must include, in addition to eminent medical and other professional researchers, lay members who can represent the interests of society in the ethical conduct of research with human subjects. Such lay members should be selected for their ability to make disinterested judgments about research issues of societal concern. Because medical and other research professionals have been trained to pursue other goals, they should not be expected to shoulder the added burden of speaking for the concerns of society.

Senator Hubert Humphrey has called for the establishment of a National

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[80] Another commonly expressed fear is that detailed regulations may adversely affect the well-being of patient-subjects because the physician-investigator's authority to intervene quickly, whenever his professional judgment dictates it, is unduly restricted. But discretionary authority must of course be delegated to physician-investigators in the exercise of purely professional judgments regarding their patient's health.

[81] Senator Jacob Javits has also recently introduced a bill, in response to the Tuskegee Study, for the protection of research subjects. S. 3935, 92d Cong., 2d Sess. However, this proposed amendment to the Public Health Service Act is in essence simply a statutory enactment of current DHEW regulations. As we have argued, more than this is needed for the protection of research subjects.

Human Experimentation Standards Board which in some respects resembles the Board we propose. His bill [92] provides as follows:

Sec. (2) (a) There is hereby established, as an independent agency in the executive branch, a National Human Experimentation Standards Board (hereinafter referred to as the "Board").

(b) The Board shall be composed of 5 members to be appointed by the President by and with the advice and consent of the Senate from among individuals who by virtue of their service, experience, or education are especially qualified to serve on the Board. . . .

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(3d) Members should be chosen from persons who are representative of the fields associated and concerned with clinical investions.

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Sec. 5. (a) It shall be the function of the Board to——

(1) establish guidelines for the involvement of human beings in medical experiments which are funded in whole or in part with Federal funds;

(2) review all planned medical experiments that involve human beings which are funded in whole or in part with Federal funds to determine if the guidelines established under paragraph (1) are being complied with;

(3) obtain an injunction to prevent such experimentation in a case where such experiments are found not to comply with established guidelines; and

(4) prepare and submit an annual report to the President, for transmittal to the Congress recommending legislation, if required, and detailing the performance of the Board during the preceding year.

Senator Humphrey's bill assigns to his Board policy making, administrative and review powers. We believe that some of these functions should not be delegated entirely to the NHIB and that those functions which the NHIB should be given must be spelled out in greater detail. Senator Humphrey's bill also does not provide for the continuation of the institutional review committee system. We believe that institutional review committees should be maintained, although in modified form. We now turn to a discussion of the functions of the NHIB and institutional committees in the formulation, administration and review of policies for human research.

1. *Formulation of Policy.*—The National Human Investigation Board must establish guidelines for the conduct of research with human beings with respect to such matters as:

a. Selection of Subjects—The Board must formulate criteria for the selection of subjects. It will have to reexamine the contemporary research practice of choosing subjects from the less educated, disadvantaged, or captive groups within society. In doing so, the Board will have to confront many questions. For example, should every effort be made, consistent with research objectives, to obtain a subject sample which represents a cross-section of the population at large? Or should subjects first be selected from among the best educated before turning to the less educated, since the former are more capable of giving "informed consent"? How should the recruitment of subjects be effectuated to implement whatever rules for their selection are adopted? Under what circumstances should non-comprehending subjects such as children or severely mentally disturbed individuals, or captive subjects such as prisoners or other institutionalized persons, be barred from participating in research?

b. Ambit of Informed Consent—The Board must not only formulate the overall criteria of informed consent but must also specify the circumstances in which the consent requirement can be modified, and to what extent, in order to accomplish important research objectives. In doing so, the Board will have to find answers to such policy questions as: Under what circumstances can what benefits to individuals or society justify modifications in the informed consent requirement? Should certain groups or potential subjects be excluded from participating in research or high-risk investigations be proscribed unless informed consent can be obtained? When is third party consent permissible, and what safeguards should be introduced whenever the consent of a third

[92] S. 3951, 92d Cong., 2d Sess.

party is invoked? The Board may have to promulgate separate guidelines for the conduct of investigations which are predicated on the absence of informed consent, such as placebo, double blind, deception and secret observation studies. The latter two procedures are employed by sociologists and psychologists on such an extensive and repetitive scale, and constitute such a significant exception to the general requirement of informed consent, that serious consideration should be given to restricting their use.

This may be an appropriate place to introduce a note of caution. The policies we have in mind cannot be formulated overnight or without serious study of the problems inherent in this field. An example from the literature on informed consent illustrates this point. It has traditionally been assumed that the consent requirements should be more stringent in research with "healthy" volunteers than with patients. This assumption ought to be reexamined. Perhaps, as Alexander Capron has written:

". . . higher requirements for informed consent should be imposed in therapy than in investigation, particularly when an element of honest experimentation is joined with the therapy. The 'normal volunteer' solicited for an experiment is in a good position to consider the physical, psychological and monetary risks and benefits to him in consenting to participate. How much harder that is for the patient to whom an experimental technique is offered during a course of treatment. The man proposing the experiment is one to whom the patient may be deeply indebted (emotionally as well as financially) for past care and on whom he is probably dependent for his future well-being; the procedure may be offered, despite its unknown qualities, because more conventional modalities have proved ineffective." [93]

Finally, more attention must be given to the nature and quality of the interactions between investigator and subject if the ensuing consent is to be truly informed and voluntary. In this connection, consideration should also be given to make an adviser available to a subject whenever he thinks that his decision to participate or not might benefit from disinterested advice.[94] The authority and obligations of such advisers must be carefully defined and, as we have said repeatedly, with regard to policy formulation, cannot be left to each individual research committee to work out.

c. Definition of "Research"—To clarify the jurisdiction of the Board and of the institutional review committees, distinctions must be made between "research" activities and "accepted and established procedure." We have pointed out already that the borderline between research and therapy is difficult to draw. Physician-investigators have often wittingly or unwittingly added to the obfuscation by calling some investigations "therapy" in order to escape the obligations which the research designation entails. Such practices diminish the protection afforded subjects, and also undermine the scientific validity of the results of such investigations, because they were not established in carefully controlled clinical trails.

d. Application of Risk-Benefit Criteria—We have already suggested that the risk-benefit equation is one of the most difficult guidelines to implement. To evaluate risk taking, distinctions must be made between research designed to benefit its participants and those which may benefit society at large. With respect to societal benefits, answers will have to be found to such crucial questions as: Do even minimal risks from participation require an intensive scrutiny of the benefits to be derived from the study or should "minimal" risks, however defined, be exempted from this burdensome requirement? How often can risky experiments be repeated for the sake of verification, if results have already been reported in the literature? Must certain groups, such as children and mentally defective subjects, be excluded from all risky studies that are not designed to benefit them? When the risks and benefits of therapeutic measures are unknown, as in all first clinical trials of a new drug, should the tests be randomized with a limited number of patients in order to ascertain a scientifically valid estimate of effectiveness? In research with so-called normal volunteers or other subjects who are able to give a satisfactory consent, can greater risks be taken than a weighing of risks against benefits would in general permit? Should dying patients who are

[93] Capron, "The Law of Genetic Therapy," in *The New Genetics and the Future of Man*, M. Hamilton, ed. (Eerdmans Pub. Co., 1972).
[94] We elaborate upon this recommendation *infra*, pp. 44 ff.

willing to participate in risky experiments be exempted from the rule that no experiments are to be conducted which might hasten death?

e. Promulgation of a Compensation Scheme—An insurance plan should be devised and implemented for the compensation of subjects harmed as a consequence of their participation in research activities. Though many schemes for compensating subjects deserve consideration, we mention one which we believe has substantial merit: "no fault" clinical research insurance paid for by each institution sponsoring research. Subjects would be compensated for any injurious consequences of their participation in research whether or not caused by the fault of the investigator. This plan would provide full protection for subjects and relieve investigators of the threat of liability. As to cost, one of the principal promoters of research insurance, Irving Ladimer, has asserted that:

". . . it is unlikely that the costs will be great, probably a small fraction of customary malpractice premiums. First, there are few compensable occurrences within responsible research institutions, where most of the studies are conducted. Second, the assumption of medical care, most likely at the sponsor's premises, will reduce such costs. Third, the adoption of such a system should tend to improve prior protection, controls, and research design; this is especially true for studies approved by research review committees. Fourth, the spirit and philosophy of this form, which should be fully explained in advance in discussions with participants, should serve to diminish rather than induce any questionable claims." [95]

The cost of the insurance would probably vary directly with institutional safety records and thus might provide an additional impetus to careful consideration of research proposals. Guido Calabresi has called attention to this possibility:

". . . Requiring compensation of injured subjects causes the full cost of research in humans to be placed on the research center. Accordingly, approval by the center of a particular experiment will require conscious consideration not only of the possible payoff (either in market or scientific terms), but also of the risks, converted to money, that the project entails. This may not deter many experiments, but it may cause those involved in the most risky or least useful ones to consider carefully whether the experiment is worth it, whether it is best done by those who propose to do it, and whether there is an alternative, and safer, way of obtaining approximately the same results. It may well be that all these considerations are already firmly in the minds of the experimenters. If so, nothing is changed by requiring compensation. But if researchers—like auto makers, coal mine owners and the rest of mankind—tend to consider costs and benefits a bit more carefully when money is involved, a useful added control device will have been imposed." [96]

If "no fault" research insurance, or any other mechanism, is adopted as a device for compensating subjects, regulations will have to be established for adjudicating disputes over such matters as causation—whether the worsened condition of the subject was caused by the research in which he participated or whether it was merely the inevitable outcome of the subject's particular illness—or the amount of compensation. Similarly, the NHIB will have to work out procedures for implementing whatever compensation scheme is adopted.

f. Promulgation of Sanctions—Senator Humphrey's bill authorized his Board "to obtain an injunction to prevent . . . experimentation in a case where . . . experiments are found not to comply with established guidelines." Though the promulgation of sanctions raises many sensitive issues, more is needed than has been provided in Senator Humphrey's bill. Other sanctions tailored to specific violations of the policies governing research are required. For example, an investigator's failure to submit a protocol for review, his departure from an approved research protocol or a review committee's failure to follow its established procedures might in some circumstances justify suspension of further Federal funding of the investigator or the sponsoring institution.

It is beyond the scope of this report to detail the offenses which should lead to the invocation of sanctions, the particular penalties which should be imposed, or the procedures which must be followed to satisfy due process requirements. We also leave open the question of who—the National Human Investiga-

[95] *Ladimer, supra,* footnote 84, at 259.
[96] Calabresi, "Reflections on Medical Experimentation in Humans," 98 *Daedalus* 387, 398 (1969).

tion Board or Congress—should promulgate the regulations which will govern the imposition of sanctions.

g. Delegation of Authority to Administer and Review the Research Process—The National Human Investigation Board must also promulgate rules and procedures for the administration and review of the human research process. We now turn to these issues under their appropriate headings.

2. *Administration of Research.*—a. Institutional Human Investigation Committees—Once adequate research policies have been formulated by a broadly representative body, "outsiders" should intervene as little as possible in the administration of those policies. For when research policies are put into effect, limitations imposed by colleagues are better tolerated by investigators than restrictions imposed by outsiders. The administration of research should therefore be performed principally by researchers' professional peers sitting on institutional review committees. Thus we seek to reverse the trend [97] toward outsider membership on institutional review committees and outsider interference with day-to-day professional decision-making. In our proposed restructuring of institutional review committees, we have sought to restrict the participation of outsiders to those areas where they have the most to contribute.

Senator Humphrey's bill does not specify the status of the institutional review committees which are not required by DHEW. The advantages of institutional committees are numerous, and we propose that they be retained, though with redefined functions. Among other things, administration at the institutional level simplifies the task of prior review of research protocols; permits closer scrutiny of research activities; encourages investigator involvement in and respect for the problems of ethical research; enables different institutions to deal with complex new problems from different vantage points, and facilitates responsiveness to difficulties in the research process as they arise. Instead of eliminating institutional committees, they should be restructured to enable them to perform their functions better than they now do.

We recommend the creation of a structured institutional body, to be called the Institutional Human Investigation Committee (IHIC), in place of the existing unspecialized institutional review committee. Each institution which is subject to the jurisdiction of the NHIB would be required to provide written assurance to the NHIB that it had appointed an IHIC. This would be similar to current practice which requires institutions to negotiate assurances with the NIH's Division of Research Grants.[98] As outlined below, each IHIC would be responsible for the conduct of research in its institution, and would be required to file with the NHIB its plans for carrying out the responsibility. Thus the NHIB would pass on the suitability of the IHIC membership, local policies, and administrative procedures, and NHIB approval would be required before Federally funded research [99] could be conducted at the institution.[100]

IHIC members should be appointed by their institutions to serve for a period of years, so as to accumulate expertise in the problems of human experimentation. The membership should represent a cross-section of the disciplines involved in research at the institution. It ought also to include a few "outsiders," who can make a valuable contribution to the supervision of the consent process, as described below.

The main functions of each IHIC would be: to establish local policies, consistent with the uniform national guidelines promulgated by the NHIB, which are responsive to the individualized needs of the institution, to bring to the attention of the NHIB any procedural modifications deemed necessary for effective functioning; to inform local participants in the research enterprise of their

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[97] Current DHEW regulations suggest, and FDA regulations require, that outsiders be members of institutional review committees. See *Grants Administration Manual, supra,* footnote 23, § 1-40-40 (C) (2) (b); 21 CFR § 130.3; 36 Fed. Reg. 5037, 5038 (March 17, 1971).

[98] See *Grants Administration Manual, supra,* footnote 23, § 1-40-40 (A):

"The assurance shall embody a statement of compliance with DHEW requirements for initial and continuing committee review of the supported activities; a set of implementing guidelines, including identification of the committee; and a description of its review procedures . . ."

[99] Or all research—see *supra,* p. 39.

[100] It should be noted that, as in present DHEW policy, different requirements might be established for institutions "having a significant number of concurrent" research projects and for institutions sponsoring only one, or a limited number, of such projects. See *Grants Administration Manual, supra,* footnote 23, § 1-40-40 (B), (C), and (D). The description of the IHIC presented in our report hereinafter is for an institution with a number of research activities.

rights and obligations; and to establish two subcommittees to carry out its administrative functions—a Protocol Review Group and a Subject Advisory Group. Although the membership of the subcommittees should be drawn largely from the IHIC, these subcommittees could also include others associated with the institution. Our recommendations regarding the two subcommittees are modeled on a similar proposal recently advanced by Jay Katz and Alexander Capron in a somewhat different context, and in what follows we quote from the draft document they have prepared.

b. Protocol Review Groups—The heart of IHIC's will be their Protocol Review Groups (PRG) which will be responsible for approving, disapproving or offering suggestions for modification in protocols for experimental and therapeutic interventions which come within the policies on risk and consent formulated earlier in the process. The PRG's task is to apply the rules and policies already set down, but this should not be a matter of "clockwork" or mere routine. Realistically, it is unlikely that even if policy formulation proceeded with much more rigor (as we urge) it will result in directives that settle all issues faced by the PRG's. This does not suggest, however, that Protocol Review Groups set policies themselves, though these rules may give them some discretion in light of local institutional conditions and so as to permit experimentation with a variety of alternative policies which are still consistent with the general directives. This sort of flexibility is vital if the PRG's are to operate effectively and secure the services of thoughtful, devoted members.

Membership in the Protocol Review Group should consist primarily of professionals with competence in biomedicine. This reflects the committee's function, which is to scrutinize protocols in light of the policy guidelines and directives, to evaluate whether the procedure should be undertaken, and to give advice to the physicians and scientists involved. In most instances these group members will be members of the university or research center's staff and faculty, but when the presence of more than one institution in a locality permits it, the crossfertilization of having some people from one center serve on another's PRG would probably be advisable. Such an arrangement would provide "outsiders" in the sense of people free of the personal ties and biases of the institution's own employees, while maintaining the biomedical expertise that should characterize "insiders." [101]

c. Subject Advisory Groups—Katz and Capron also propose "the establishment of Subject Advisory Groups (SAG) to aid patient-subjects in decision-making." [102] We do not lightly suggest the creation of another subgroup within the IHIC, since we have no desire to overburden the process with excessive bureaucracy. But, as we have emphasized, present procedures for obtaining consent are concerned with form to the neglect of substance. If informed and voluntary subject consent is to become a reality in human experimentation, efforts must focus on improving the quality of the communications between investigator and subject. We therefore endorse the Katz and Capron proposal that an adviser be made available to counsel any prospective subject who thinks his decision to participate or not might benefit from disinterested advice. "Not all patient-subjects may wish to seek out representatives of the Subject Advisory Group, for some may be satisfied with the information obtained from physician-investigators. But patient-subjects should be well apprised of the availability of these representatives prior to their participation in projects which have to be submitted to the PRG because of the risk involved or because of the problems anticipated with obtaining valid consent. Patient-subjects may also wish to avail themselves of the SAG's services when they begin to wonder whether continuation of the intervention is worth the pain and suffering they have to endure. At such times the Subject Advisory Group assumes the important function of administering the procedures formulated for the termination of experimental treatments." [103]

The SAG should also aid investigators in developing fair methods of obtaining consent, and in avoiding inadvertent bias or coercion when seeking consent. It ought to go without saying that . . . (c)reating an opportunity for someone in addition to physician-investigators to talk with patient-subjects does not suggest a lack of trust in the investigators' integrity, rather it recognizes the reality that investigators cannot help but plead, however unconsciously, their

[101] *Katz and Capron, supra,* footnote 18.
[102] *Ibid.*
[103] *Ibid.*

interests in the research and therefore must find it difficult fully to safeguard the interests of their subjects.[104]

Because the work of the SAG would be restricted to issues relating to consent, laymen could make a significant contribution in this subcommittee. They, more than professionals, would appreciate the difficulties prospective subjects might have when faced with an invitation to participate in research. And potential subjects might be less overawed in interactions with their peers, than in interactions with physicians.

d. Appeals—From time to time disagreements will arise between investigators and the Protocol Review Groups. No opportunity for appeal from an adverse institutional review committee ruling exists at present, and committees can cut investigators off from Federal funding without possibility of reconsideration. This may not only hinder the acquisition of knowledge; it may also undermine the legitimacy of peer review. Barber *et al.* have written:

"We have heard researchers object to peer review as they know or understand it because they believe that research proposals having real potential for medical scientific advances, or even 'pioneering breakthroughs,' frequently either are not or will not be approved by those who sit on institutional review committees. The reasons for these rejections they are especially concerned about do not involve the ethical defectiveness of the proposals. Rather they include local institutional politics and conflicts as well as resistance to innovations just because they depart from accustomed ways of scientific thinking and proceeding . . . (T)o forestall rejections of this kind, the biomedical community may have to go beyond the establishment of local appeal procedures by institutions. Perhaps what is necessary is the establishment of a hierarchy of 'courts of appeal' throughout the nation, culminating, as a final resort, in a 'supreme court' composed of eminent peers including both 'insiders' and 'outsiders' with respect to any field. Such a system might be the best safeguard available against the object of these concerns—unjustified hindrance of medical progress by the peer review process." [105]

Procedures should be established for appeals to the National Human Investigation Board.[106] After a hearing of the controversy, the NHIB should be empowered to sustain or overrule the judgment of the Protocol Review Group.

Since the NHIB has a role to play in the administration of research, it must employ expert staff to evaluate research protocols and to prepare detailed findings. This staff would take over the reviewing function currently handled by DHEW study groups. However, it is beyond the scope of this report to set forth all the specific functions which the NHIB should assume. In particular, we have refrained from deciding how many of the protocols approved by the PRG's should be reviewed again by the NHIB. Though a certain number will have to be examined in order to provide the NHIB with sufficient information to carry out its most important function—policy formulation—it may not be necessary to review all protocols a second time. This would be a time consuming task.

3. *Review of Decisions and Consequences.*—The NHIB must create mechanisms for the overall review of the human experimentation process in order to assess the continuing efficacy of its own policies and of the institutional peer group review. Thus, the Board has to keep itself informed about ongoing research practices, and a number of already existing resources would facilitate this task: scientific journals which publish research studies, legal cases in which conflicting claims about research have been brought before courts, newspaper accounts (such as the initial reports of the Tuskegee Syphilis Study), reports from Institutional Human Investigation Committees, etc.[107]

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[104] *Ibid.*

[105] *Barber et al., supra,* footnote 3, at 156–157. (footnote omitted).

[106] IHIC's might also find it appropriate to establish an internal appeals procedure. This would be more convenient than, and would sometimes obviate the need for, appeals to the national level.

[107] The NHIB might consider inviting others—for example, editors of scientific journals—to submit for review studies which raise ethical questions. Editorial boards should welcome such an opportunity, particularly in the light of the recent debate about the publication of articles based on "unethical" research. Some commentators have favored non-publication, while others have felt that "(s)uch an editorial policy would maintain the low visibility of unethical experimentation and preclude not only review but also careful and constant appraisal of the conflicting values inherent in experimentation." (Katz, "Human Experimentation," 275 New Eng. J. of Med. 700 (1966)). Journal censorship creates difficult problems. If editorial boards could be assured that violations of "ethical" practice would be dealt with by an authorized body, they might prefer to call them to the attention of the NHIB and judge acceptability of articles on the basis of scientific merits.

The NHIB must also establish rules and procedures for the direct review by IHIC's and by NHIB staff members of ongoing previously approved research projects. The current requirement of systematic review of all projects at fixed intervals is burdensome and inefficient and encourages perfunctory review. Instead of requiring continuing review of all research projects on a routine basis, it would reduce the burden on IHIC's and maximize the effectiveness of continuing review if investigators were asked to report immediately any contemplated or necessary deviations from approved research protocols, all inconveniences and injuries suffered by any subjects which has not been anticipated in the original protocol, or any medical advances which might benefit subjects and which has not been anticipated in the original protocol. Moreover, periodic "spot checks" of selected interventions which are now discretionary should be made a requirement. It is apparent that some approved research projects are carried out improperly. For example, in a recent study involving subjects subsequent to their participation in a medical research project which had been approved by an institutional review committee, an interviewer found that—"(m)ost of these subjects learned of the existence of the study during the interviews done for my research. Second, many more subjects (the exact number awaits further analysis), while aware of the research, had significant gaps in their understanding of the project and consented on a more or less uninformed basis. These included women who had no knowledge of whether there were alternatives to participation, women who did not know of the double-blind nature of the study (it was not part of the research design to withhold this information), and women who were not aware of the fetal monitoring procedures and extra blood samples required by the research. Others were not aware beforehand that their consent to have the baby observed would be sought by a separate researcher." [108]

Spot checks would determine the extent of noncompliance with existing procedures. Should the checks reveal widespread noncompliance, then remedial steps could be taken, such as better education of physician-investigators about their responsibilities, more careful evaluation of protocols, or routine monitoring of all research activities for a period of time.

The NHIB should also invite the IHIC's to submit their most difficult decisions for an evaluation. Significant cases, including the original PRG rulings and the subsequent NHIB opinions, should be published to give direction to the deliberation of local committees, to provide material for scholarly analysis, and to foster and sustain public awareness of the issues raised by human experimentation. Indeed, all important decisions rendered at the local or national level should be published and preserved in easily accessible form. These cases would serve as precedents for future opinions. Thus publication would be a first step toward the case-by-case development of sound policies for human experimentation. We regard such a development, analogous to the growth of the common law, as the best hope for ultimately providing workable standards for the regulation of the human experimentation process.

Finally, we emphasize again that the review of research decisions and their consequences requires the participation of persons representing a wide variety of societal interest and should not be limited to members of the biomedical professions. It is at the policy-formulation and review stages of the human experimentation process that "outsiders" have an important role to play by championing individual and societal rights and interests. Professionals have been trained to pursue other goals and should not be expected, even if they could, to shoulder the added burden of speaking for the concerns of society.

C. Education.

Our last recommendation pertains to the education of investigators, particularly when they are still students, for the responsible practice of human research in a democratic society. Recently, Senator Jacob Javits introduced a bill [109] in the Senate which addresses itself to this problem. The bill "would authorize special project grants for medical schools to develop and operate programs which provide increased emphasis on the ethical, social, moral, and legal implications of advances in biomedical research and technology.

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[108] Gray, "Some Vagaries of Consent," a preliminary report (1971) on data collected for the author's doctoral thesis, reproduced in *Katz, supra*, footnote 12, at 660.
[109] S. 974, 93d Cong., 1st Sess.

"The bill . . . provides the opportunity for our Nation's medical schools to develop the appropriate program curriculums regarding ethical, moral, and social issues to meet the need—the protection of human subjects at risk in medical research and improved understanding of the consequences and implications for the individual and society of the advances in biomedical science—and through their own initiative and leadership construct and appropriate continuing professional institutional activity to safeguard human subjects in research." [110]

Senator Javits referred to the findings of Professor Bernard Barber *et al.*, and to document further the need for such an educational effort, we quote briefly another passage from their study:

"It is clear from our date that medical schools are presently giving very little serious attention to these matters in their curriculum. Of the 307 physicians interviewed, only 13% reported that they had had a seminar, a lecture or part of a course devoted to the issues involved in the use of human subjects in biomedical research, and only one researcher said that he had had a complete course dealing with these issues. Thirteen per cent of the respondents said that the issues of research ethics came up when as students they did practice procedures on one another, and 24% said that they became aware of the issues of balancing risk of suffering against potential benefits when doing experimental work with animals. Thirty-four per cent remembered discussions with instructors or other students of the ethical issues involved in specific research project which they had read about or learned of in class. But 57% of the physicians interviewed reported none of these experiences, even those peripheral to work with humans, such as those involving animal experimentation." [111]

It has sometimes been asserted that the human subject in experimentation is best safeguarded "by the presence of an intelligent, informed, conscientious, compassionate, responsible investigator." [112] Whatever merit underlies such a contention, sufficient attention has not been paid by educators in all professional schools to exploring the responsibilities of the professional toward his patients, clients, or research subjects. Without training, even a "conscientious" investigator is poorly prepared to deal knowledgeably or systematically with these problems.

Though in recent years there has been an upsurge in efforts to expose students to the issues raised by professional responsibility, considerably more thought and support must be given to this work. Professional schools must recruit faculty members who are interested in pursuing the complex problems created by human research in particular and contemporary professional practices in general. The task is not limited to educating students but must ultimately include a re-examination of the entire scope of professional decision-making.

VI. CONCLUSION

Human experimentation reflects the recurrent societal dilemma of reconciling respect for human rights and individual dignity with the felt needs of society to overrule individual autonomy for the common good. Throughout this report we have expressed our concern for the lack of attention which has been given to the protection of the rights and welfare of human subjects in research. Society can no longer afford to leave the balancing of individual rights against scientific progress to the scientific community alone. The revelations of the Tuskegee Syphilis Study once again dramatically confirmed this conclusion.

We offer our far-reaching proposals in the hope that the decision-making process for human research will become more open and more effectively regulated. We have amply documented the need for implementing this most basic recommendation. Precise rules and efficient procedures, however, are not by themselves proof against a repetition of Tuskegee. For, however well designed the system of regulation, the danger of token adherence to ethical standards and evasion in the guise of flexibility will persist. Ultimately, the spirit in which an aware society undertakes to use human beings for research ends will determine the protection which those human beings will receive. Therefore, we

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[110] 110 Cong. Rec. S 3114 (Feb. 22, 1973).
[111] *Barber et al.*, supra, footnote 3, at 101.
[112] Beecher, "Ethics and Clinical Research," 274 New Eng. J. Med. 1354, 1360 (1966).

have urged throughout a greater participation by society in the decisions which affect so many human lives.

Respectfully submitted,

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[Item I.B.4]

DRAFT SPECIAL POLICY STATEMENT ON THE PROTECTION OF HUMAN SUBJECTS INVOLVED IN RESEARCH, DEVELOPMENT, AND DEMONSTRATION (EXCERPTS)*

Summary

The mission of the Department of Health, Education, and Welfare includes the improvement of the health of the nation's people through research, development, and demonstration activities which at times involve human subjects. Thus, policies and procedures are required for the protection of subjects on whose participation these activities depend.

Informed consent is the keystone of the protection of human subjects involved in research, development, and demonstration activities. Certain categories of persons have limited capacity to consent to their involvement in such activities. Therefore, as a supplement to DHEW policies, special protections are proposed for *children*, *prisoners*, and the *mentally infirm* who are to be involved in research, development, and demonstration activities.

Agency "Ethical Review Boards" are to be established to provide rigorous review of the ethical issues in research, development, and demonstration activities involving human subjects, in order to make judgments regarding societal acceptability in relation to scientific value. "Protection Committees" are to be established by the applicant to provide "supplementary judgment" concerning the reasonableness and validity of the consent given by, or on behalf of, subjects. The intent of this policy is that institutions which apply for DHEW funds or submit research in fulfillment of DHEW regulations, must be in compliance with these special protections, whether or not particular research, development, or demonstration activities are Federally financed.

1. CHILDREN

If the health of children is to be improved, research activities involving their participation is often essential. Limitation of their capacity to give informed consent, however, requires that certain protections be provided to assure that scientific importance is weighed against other social values in determining acceptable risk to children. Therefore, research, development, and demonstration activities which involve risk to children who participate must: a. include a mechanism for obtaining the consent of children who are 7 years of age or older; b. include the applicant's proposal for use of a Protection Committee which is appropriate to the nature of the activity; c. be reviewed and approved, in conformity with present DHEW policy, by an Organizational Review Committee; and d. be reviewed by the appropriate agency Primary Review Committee, the Ethical Review Board, and the appropriate secondary review group.

2. SPECIAL CATEGORIES

a. *The Abortus.*—No research, development, or demonstration activity involving the non-viable abortus shall be conducted which: 1. will prolong heart beat

* Received by Constitutional Rights Subcommittee on October 19, 1973.

and respiration artificially solely for the purpose of research; 2. will terminate heart beat and respiration; 3. has not been reviewed by the agency Ethical Review Board; and 4. has not been consented to by the pregnant woman and by a Protection Committee.

(An abortus having the capacity to sustain heart beat and respiration is in fact a premature infant, and all regulations governing research on children apply.)

b. *The Fetus in Utero.*—No research involving pregnant women shall be conducted unless: 1. Primary Review Groups assure that the activity is not likely to harm the fetus; 2. the agency Ethical Review Board has reviewed the activity; 3. a Protection Committee is operating in a manner approved by the agency; and 4. the consent of both prospective legal parents has been obtained, when reasonably possible.

c. *Products of In Vitro Fertilization.*—No research involving implantation of human ova which have been fertilized *in vitro* shall be approved until the safety of the technique has been demonstrated as far as possible in sub-human primates, and the responsibilities of the donor and recipient "parents" and of research institutions and personnel have been established. Therefore, no such research may be conducted without review of the Ethical Review Board and of a Protection Committee.

3. PRISONERS

Research, development, and demonstration activities involving human subjects often require the participation of normal volunteers. Prisoners may be especially suitable subjects for such studies, although there are problems concerning the voluntariness of the consent of normal volunteers who are confined in institutions. Certain protections are required to compensate for the diminished autonomy of prisoners in giving voluntary consent. Research, development, and demonstration activities involving prisoners must: a. include the applicant's proposal for use of a Protection Committee which is appropriate to the nature of the activity; b. be reviewed and approved by an Organizational Review Committee which may already exist in compliance with present DHEW policy or which must be appointed in a manner approved by the appropriate DHEW agency; c. be reviewed by the agency Primary Review Committee; and d. be conducted in an institution which is accredited by the Secretary of Health, Education, and Welfare.

4. THE MENTALLY INFIRM

Insofar as the institutionalized mentally infirm might lack either the competency or the autonomy (or both) to give informed consent, their participation in research requires additional protection:

a. Research, development and demonstration activities involving the mentally infirm will be limited to investigations concerning (1) diagnosis, etiology or treatment of the disability from which they suffer, or (2) aspects of institutional life, *per se.*

b. All research, development and demonstration activities involving such persons must: 1. include the applicant's assurance that the study can be accomplished *only* with the participation of the mentally infirm; 2. include the applicant's proposal for use of a Protection Committee which is appropriate to the activity; and 3. be reviewed and approved by an Organizational Review Committee, in conformity with present DHEW policy.

[Item I.B.5]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

Report on the Biomedical Research Aspects of Brain and Aggressive Violent Behavior, October 23, 1973 (Excerpts)

INTRODUCTION

The development and use of biomedical methods for the treatment of behavioral disorders during the past decade has generated discussion in the scientific community about issues of efficacy and safety and about appropriate cri-

teria for their use on humans. Psychosurgery (i.e.: the neurological treatment of behavioral disorders) more recently has generated public concern about matters such as informed consent of human subjects in either experimental or clinical care situations, the criteria for differentiating experimental from clinical procedures and the use of neurosurgical methods of treatment on institutionalized persons. The issues have become particularly sensitive with the use of psychosurgical methods for the treatment of uncontrollable violence and rage behavior.

In order to provide a background for development of a public policy position on these matters, the Department of Health, Education, and Welfare (DHEW) asked the National Institute of Neurological Diseases and Stroke (NINDS) to prepare a Report on the biomedical research aspects of brain and aggressive violent behavior and the National Institute of Mental Health (NIMH) to prepare a Report on clinical psychosurgery.

The NINDS invited forty-eight distinguished leaders in basic science and clinical research to review and evaluate the scientific literature and available unpublished data on brain and aggressive behavior, particularly uncontrollable violence and rage. (Attachment). Their deliberations were divided into four workshops: (1) neuroanatomical and neurophysiological studies; (2) biochemical, endocrine, pharmacological and genetic studies; (3) behavioral studies; and (4) clinical studies. Although social factors undoubtedly play a role in the etiology and expression of violent behavior, the workshops were limited to discussions of the biological, psychological and medical research aspects of aggressive violent behavior. Workshop participants were asked to document and evaluate only established facts and to avoid speculation.

The NINDS Report on The Biomedical Research Aspects of Brain and Aggressive Violent Behavior is divided into two parts: I. Summary and Evaluation of The Biomedical Research Aspects of Brain and Aggressive Violent Behavior; II. Recommendations on Public Policy and DHEW Procedures.

The focal point for the development of the NINDS Report was The National Advisory Neurological Diseases and Stroke Council, an officer of the Institute and a member of the Council serving as project directors. (Attachment II). Part I of the Report was prepared by a panel of workshop discussion leaders, discussants, editorial consultants and the project directors; Part II was prepared by the NINDS. The National Advisory Council has reviewed the Report and endorsed it with enthusiasm.

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National Advisory Neurological Diseases and Stroke Council.

SEPTEMBER 24, 1973.

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PART II. RECOMMENDATIONS ON PUBLIC POLICY AND DHEW PROCEDURES

A. SUMMARY OF RECOMMENDATIONS

It is recommended that:

1. Research on the biomedical bases of aggressive violent behavior continue to receive DHEW support.

2. The NINDS-NIMH give attention to the cooperative planning and sponsoring of a research program on the fundamental aspects of brain and aggressive behavior in experimental animals, particularly violent and rage behavior. This program should include the neurosciences and behavioral sciences, investigator-initiated fundamental research, and coordination by NIH staff.

3. The NINDS-NIMH give attention to the cooperative planning and sponsoring of a research program on the clinical aspects of brain and aggressive violent behavior. The program should include the clinical neurological and clinical behavioral sciences, be investigator initiated and university based, include special procedures for protection of human subjects and be continuously monitored by NIH staff.

4. An appropriate number of clinical research groups be supported for multidisciplinary clinical investigations of aggressive violent behavior.

5. A human subjects advocacy committee be established in each institution proposing to conduct clinical studies on aggressive violent behavior. The appropriateness of the participation of each human subject in such studies should be reviewed by this committee.

6. The Department's position on the biomedical therapy of violent and rage behavior be that the scientific and medical literature available at this time is inconclusive in regard to the efficacy of these procedures.

B. RECOMMENDATIONS AND DISCUSSION

1. Part I of this Report clearly indicates that no conclusions can be derived about the etiology, pathophysiology, diagnosis or therapy of aggressive violent behavior from available, scientifically reliable biomedical information; this is specifically true about both the neurological and behavioral science aspects of violence.

2. The neurosurgical treatment of behavioral disorders (sometimes referred to as "psychosurgery") recently has generated discussion and concern in both the scientific community and general public. Reasons for this include the poor delineation between the clinical care and the investigative aspects of these neurosurgical procedures; also, procedures for the treatment of epilepsy, pain and brain tumor have been confused with those for the diagnosis and treatment of behavioral disorders in patients who also have a convulsive disorder, are in intractable pain or suffer a brain tumor. The evidence available at this time does not demonstrate a difference in the incidence of violent behavior in patients with epilepsy from that in the general population. The rare patient with both epilepsy and violent behavior, however, is more liable to become a subject in a clinical investigation of violence; this occurs because procedures for the diagnosis and treatment of epilepsy provide the clinical investigator with an opportunity also to study the patient's aggressive behavior.

3. With the advancement of experimental medical, surgical and behavioral methods for diagnosis and therapeutic intervention, issues of informed consent, the protection of human subjects participating in investigations and the several factors contributing as etiologies of violence have become concerns for public, legal and scientific interchange.

Recommendation 1.

It is recommended that research on the biomedical bases of aggressive violent behavior continue to receive DHEW support.

1. Irrespective of the several possible etiologies, the final common pathway for the manifestation of behavior is the nervous system. The development of adequate preventive and theraputic measures is dependent upon meaningful investigations of the neurological mechanisms underlying aggressive behavior, including violence.

2. Fundamental studies of the neural and behavioral mechanisms of aggression and rage behaviors, particularly animal-based investigations, are progressing at a modest pace; however, increased opportunities have evolved for the understanding of these basic mechanisms. Clinical studies, particularly those including the use of human subjects, generally have been unstructured and often inconclusive. This has occurred because clinical studies usually have been conducted secondary to the needs of clinical care and have utilized case-by-case protocols; the development and evaluation of quantitative mensuration techniques essential to the interpretation of clinical results too often have had to be an integral part of the clinical situation. Despite these difficulties, technical advances have been made resulting in meaningful opportunities for the conduct of carefully structured clinical investigations.

Recommendation 2.

It is recommended that the NINDS–NIMH give attention to the cooperative planning and sponsoring of a research program on the fundamental aspects of brain and aggressive behavior in experimental animals, particularly violent and rage behavior. This program should include the neurosciences and behavioral sciences, investigator-initiated fundamental research, and coordination by NIH staff.

1. Fundamental studies on the genetic, neurochemical, enzymatic and morphophysiologic substrates of aggressive behavior, particularly violent behavior, offer the key to a better understanding of the biological mechanisms by which

psychosocial factors evoke different behavioral responses in individuals. Stimulation and encouragement of these studies are needed, particularly investigations such as those concerned with the development of the neural network, the role of synaptic organization and reorganization, the interrelationship of the limbic system, hypothalamus and cerebral cortex with brain stem, and the histochemical delineations of relevant neural pathways. These studies require not only financial support but also NINDS–NIH planning and program development activity.

2. Paralleling and complementing these neuroscience investigations, a focused program of behavioral science research on aggression and violence also is needed. This latter program should include: exploration of perinatal and endocrine influences on behavior; ethology and killing behavior in animals; and the characteristics of the several varieties of aggressive behavior.

Recommendation 3.

It is recommended that the NINDS–NIMH give attention to the cooperative planning and sponsoring of a research program on the clinical aspects of brain and aggressive violent behavior. The program should include the clinical neurological and clinical behavioral sciences, be investigator initiated and university based, include special procedures for protection of human subjects and be continuously monitored by NIH staff.

1. Clinical studies on the pathophysiology of aggressive violent behavior, its diagnosis, prevention and therapy, must finally rely upon studies of man. With the exception of violent rage behavior occasionally reported in "killer" animals, the models of aggressive behavior utilized in animal studies (defense, attack, ritual and predatory aggression) do not coincide with rage or uncontrollable violence observed in man. Man, therefore, must be studied if man's violence is to be understood.

2. Human studies evoke concern because of both the inadequacy of a firm conceptual basis for violence from animal studies and public uneasiness about the social consequences of investigation in this area. This situation is particularly sensitive because of the nature of the population prone to such investigations—prisoners, the mentally ill, wards of the state—and the short and long-term effects on the individual of experimental therapy.

3. A DHEW policy position at either of the extremes of reactions to these concerns would be an inadequate response to a situation of importance both to the health of society and the individual and to the responsibilities of the DHEW.

Recommendation 4.

It is recommended that an appropriate number of clinical research groups be supported for multidisciplinary clinical investigation of aggressive violent behavior.

1. The establishment of multidisciplinary research groups is needed to provide for coordinated investigations of improved methods of clinical diagnosis, prevention and the treatment under carefully defined and monitored conditions. Such groups would provide for the size, composition and quality of the research team essential for such studies. They would also provide for a pool of patients from which an adequate and appropriate selection can be made to satisfy both the requirements of precise research protocols and the protections of the rights of subjects participating in the research.

Recommendation 5.

It is recommended that a human subjects advocacy committee be established in each institution proposing to conduct clinical studies on aggressive violent behavior. The appropriateness of the participation of each human subject in such studies should be reviewed by this committee.

1. For DHEW to provide federal support for clinical research on aggressive violent behavior without recognition of the potential for abuse to the individual and to society would be irresponsible: for DHEW to impose regulations which would either prevent such research or drive it "underground," would be equally irresponsible. Within the tenets of both the Helsinki Declaration and the Nüremberg Code and within the concepts presently evolving within DHEW for the protection of human subjects in research, it is possible and desirable that clinical studies of violence be developed and supported with DHEW assistance.

2. As with ALL biomedical investigations involving human subjects, four criteria must be considered in the evaluation of clinical studies of aggressive violent behavior. These are:

1. *Scientific Excellence.*—Every study involving human subjects must have a high probability of providing meaningful information. A scientifically poor or minimally acceptable study involving human subjects should be considered unacceptable.

2. *Informed Consent.*—Informed consent requires that the human subject recognizes and understands with certainty the relative risks and benefits to his or her physical and social well being of the procedures in which the subject will participate; furthermore, that the human subject agrees to these procedures freely and without overt or subtle duress. If the human subject either cannot be informed (e.g., mentally ill) or is in a situation where the ability to provide consent without duress is subject to question (e.g., a prisoner), protection of the legal and social rights of the subject must be assured.

3. *Risk-Benefit Ratio to the Human Subject.*—Nearly every biomedical clinical procedure, investigative or accepted practice, involves some degree of risk to the human subject undergoing the procedure. The potential benefit to the subject must be weighed against the potential harm. In investigative situations, these judgments often are most difficult because the body of experience about the procedure may still be too meager to establish the precise parameters of the clinical situation. Investigative procedures should be carried out on human subjects only after full and meaningful evaluation in experimental animals. To provide maximal assurance that the risk-benefit ratio to the human subject has been adequately and appropriately considered, documentation of the relevant factors considered and conclusions reached must be provided independently by the investigator, by the institution in which the investigation is to be conducted and by a board of independent reviewers appointed by the granting agency (e.g., a National Advisory Council). All must agree that the risk-benefit ratio to the human subject warrants the use of the investigative procedure before it can be utilized.

4. *Risk to the Human Subject and Benefit to Society.*—Studies of "normal" human subjects or studies of human subjects who may not benefit directly from the investigation (e.g., responses to brain stimulation in patients being studied for convulsive disorders) necessitate sensitive and often scientifically less precise decisions. If society is to understand the unusual or abnormal, it must understand the usual and normal; but at what risk to the individual human subject being studied? The decision is a "societal" decision which depends upon law and the needs and mores of society. The technical expert (e.g., the physician, the biomedical scientist, the social scientist) is an expert witness, but ought not be asked to be the decision maker. It is a firm premise of our society that "every human being of adult years and sound mind has a right to determine what shall be done with his own body."[1] The procedure of informed consent is a major protection of that right of the individual. Situations do occur, however, in which the individual cannot be informed because of mental deficiency, illness or age. Other situations occur in which the concept of consent is questionable because of imprisonment, hospitalization, institutionalization or promise of unusual reward. To ensure that the interests of the individual are adequately protected in investigative situations in which issues of either the adequacy of being informed or the appropriateness of giving consent can be questioned, a Human Subject Advocacy Committee (HUSAC) should be involved. The HUSAC should comprise members of society (e.g., theologians, jurists, community representatives) drawn from the local geographic area who are selected for their dedication to the protection of the individual rights of the human subject. The HUSAC should function at the institutional level and should have no employees of the institution as voting members. On a case-by-case basis, the HUSAC should rule on the participation of every human subject in an investigative procedure that either cannot benefit the subject or in which a question is posed about the ability of the subject to provide informed consent. All human subjects participating in investigations of violent behavior should be reviewed by the HUSAC.

[1] Justice Benjamin N. Cardozo in *Santaendorff v. Society of New York Hospitals*, 211 N.Y. 125, 105 N.E. 92, 93 (1914).

Recommendation 6.

It is recommended that the department's position on the biomedical therapy of violent and rage behavior be that the scientific and medical literature available at this time is inconclusive in regard to the efficacy of these procedures.

1. Therapeutic interventions including surgical procedures (e.g., neurosurgical), physical methods (e.g., heat, cold, electricity, ultrasound), pharmacologic agents (chemical and biological) and psychotherapeutic regimens are ALL examples of biomedical clinical procedures being utilized at the present time for the treatment of uncontrollable rage. However, the scientific and medical literature is characterized by a lack of adequate investigations providing precise or meaningful results about either the efficacy or safety of these procedures. On the other hand, several approaches have reached the stage where carefully controlled human studies would be meaningful and need to be considered if further progress is to be made on the biomedical aspects of rage.

In conclusion, the biomedical aspects of uncontrollable violence or rage are proper and necessary concerns of biomedical investigation. A more adequate conceptual basis for such investigations needs to be developed through fundamental neurological and behavioral science research. Proper and adequate clinical studies in man need to be continued but under the most careful and monitored conditions. The participation of human subjects in biomedical research represents a privilege, a privilege which biomedical scientists and society jointly must protect by means of the continuing review and monitoring of the scientific, medical and societal facets of the proposed research.

[Item I.B.6]

Psychosurgery Report of the National Institute of Mental Health, January 21, 1974

INTRODUCTION

In preparing this report, NIMH staff have relied heavily on consultation with numerous outside experts in scientific, clinical, legal, and ethical matters. Two separate groups were convened, one group composed of scientists and clinicians, and a second comprised of legal, philosophical, and ethical experts, as well as representatives of various population groups alleged to be "at risk" as potential psychosurgery candidates. A membership list for each of these two panels appears as Attachment A.

NATURE OF THE PROBLEM

Psychosurgery is the destruction of brain tissue with the primary intent of altering behavior, thought, or mood. The current controversy about psychosurgery stems from a number of factors spanning scientific, philosophical, political, and moral issues. In order to understand the nature and source of the psychosurgery controversy, it is necessary to make explicit some of the different viewpoints that are often unstated when the psychosurgery issue is discussed.

1. A fundamental concern about psychosurgery derives from differing philosophical views of the relationship between mind (the self) and the brain. Much opposition to psychosurgery, and often the most vociferous opposition, is based on the conviction that any physical damage to the brain is tantamount to destruction of the "self." This viewpoint is most strongly illustrated by some of the rhetoric used by opponents of psychosurgery who equate it with "murder of the mind." Proponents of psychosurgery, while usually not articulating an alternative philosophy, do not equate the brain with the self and take a pragmatic approach to mental or behavioral disorders in which the primary criterion for selection of a treatment is the question of whether it works or not.

2. A closely related issue is the differing viewpoints about the causal factors in mental illness. Some psychosurgeons rationalize surgical treatment on the hypothesis that mental or behavioral disorders arise from biological dysfunction in the brain, and that appropriate treatment must be based on manipulating or changing the biological substrate of behavior. Others, however, hold the view that disturbed behavior is a result of adverse environmental influences and that the solution to mental illness or behavior disorders is to manipulate or change environmental variables. While both of these views are ex-

treme positions held only by a few, and are untenable in view of our current knowledge about the complex interrelations between environmental and biological causative factors, they illustrate another philosophical argument that, in frequently more subtle form than illustrated here, is one of the roots of the psychosurgery controversy.

3. Although virtually all psychosurgical procedures and technical innovations, including the first lobotomies, were suggested by experimental brain research with animal subjects, the scientific rationale for any psychosurgical procedure is still quite tenuous. Generalizations from animal research have often been based on incomplete understanding of the complexity of behavior, logical deductions of dubious validity, and an uncritical acceptance of similarities of brain-behavior relationships in animals and man. Although we know a great deal about how the brain influences a variety of specific and limited animal behaviors, our understanding of the complex emotional and cognitive behaviors of man is extremely limited. On the other hand, many proponents of psychosurgery would argue, quite rightly, that many medical therapies are based on a pragmatic criterion of effectiveness rather than an understanding of the physiological mechanisms underlying the disease or its treatment.

4. In contrast to most physical illnesses, many of the functional mental and behavioral disorders constitute a class of poorly defined and difficult to diagnose diseases or disorders. Thus, there is considerable concern about treating with surgical means any disorder which cannot be clearly defined and diagnosed. Such problems also come to the fore in any attempt to judge the outcome of psychosurgical treatment, with the criteria for cure or amelioration not being clear or universally agreed upon.

5. A key issue in the psychosurgery controversy is whether or not psychosurgery is an experimental procedure. Most psychosurgeons regard it as an accepted practice of proven efficacy while critics claim it is an experimental therapy in view of an alleged unpredictability of outcome, lack of evidence about efficacy, and lack of scientific rationale.

6. Alternative therapies to psychosurgery is another division issue. Although a great deal of research is being done on drug therapies and various forms of psychotherapy or behavior therapy, there are numerous instances in which none of these alternatives seem to offer any relief, and the patient is faced with a dehumanizing fate in an institution, often with pharmacological restraints that equal or exceed any personality destruction that is claimed to be caused by psychosurgery. In these instances, psychosurgery might be seen as a reasonable last-resort therapy. On the other hand, there is no agreement or guidelines among practioners about the duration, intensity, or degree to which other therapies should be tried before resorting to psychosurgery. Psychosurgery critics claim, often correctly, that confinement in an institution does not guarantee adequate attempts at therapeutic measures short of psychosurgery, and that psychosurgery is frequently performed before other alternatives are tried to an adequate extent.

7. Closely related to the problem of psychiatric diagnosis is the issue of the extent to which mental or behavioral disorders are socially defined. This issue most often surfaces in the context of the psychosurgical treatment of aggressive or violent behavior in which critics of psychosurgery express the fear that it will be used for nefarious purposes as a means of controlling political or social dissidents. Stated in more general terms, the critics charge that psychosurgery has been or can be used to change behavior for the convenience or comfort of persons other than the patient himself. Thus, there is claimed to be a bias toward the use of psychosurgery in blacks, women, and other minority or disadvantaged population groups. There is no reliable data available on this point.

IMMEDIATE NEEDS AND ACTIVITIES

Extensive discussion of these areas of concern with scientific, clinical, legal, and ethical experts, as well as representatives of the lay public and of some of the population groups claimed to be "at risk" for psychosurgery, has led NIMH staff to propose a number of specific activities that will be necessary in order to resolve some of the above-discussed issues, and to some interim recommendations that may be subject to modification as further information is obtained.

The following issues must be resolved before any informed and reasonable position can be taken on psychosurgery:

1. To what extent does the currently-available scientific and clinical literature provide a basis for an informed judgment about the efficacy of psychosurgery and the severity of untoward effects? Knowledgeable scientists and clinicians with whom we have consulted are of the opinion that the existing literature will not, by itself, provide a sound basis for such a judgment. Inadequacy of pre- and post-operative behavioral and psychological testing, lack of long-term followup of patients, and general inadequacies of clinical and behavioral reporting characterize much of the published literature. However, despite these deficiencies, NIMH staff and consultants feel that an updated literature survey and analysis could provide some useful data that, in combination with other sources of information, may permit us to come to a more objective evaluation about the efficacy and adverse effects of psychosurgical treatment. What is needed goes beyond a simple compilation of psychosurgical publications and must include a critical evaluation and analysis of the published data by the various relevant scientific and clinical exports. There should also be developed a system for the continuous monitoring and updating of the literature in psychosurgery.

One of the most useful outcomes of this literature survey and analysis would be the development of a uniform reporting protocol for literature in psychosurgery. By identifying deficiencies in the existing literature, recommendations could be made for the types of clinical and behavorial data that appear to be necessary to provide a scientifically valid contribution to the future psychosurgery literature.

2. Estimates of the number of psychosurgical procedures conducted in this country each year have varied from 100 to 1000. It would seem to be important to have a more realistic figure for the extent of psychosurgery practice, since we are presently dealing with a problem of unknown dimensions. A survey of the current extent of psychosurgical practice is an important and immediate need.

3. There exists an unkown but presumably large number of patients who have undergone psychosurgery in the past. No systematic attempt has been made to determine their current status. Although such a follow-up project would depend on the cooperation of the patient and the medical and psychiatric staff involved in his case, and would present problems of confidentiality in the physician-patient relationship, we feel that such an effort could provide badly needed information relevant to the efficacy issue.

4. Relying on activities 1-3, and using the resources of the NIMH staff, its outside consultants, and by contract with outside organizations, a concerted effort should be made to develop guidelines for the conduct of psychosurgery. Such guidelines should include criteria for the selection of patients, what alternate therapies should be attempted (and for how long) before performing psychosurgery, development of informed consent procedures to meet the special problems posed by treatment of the mentally ill, and (if the information obtained in 1-3 above permits) guidelines for the type of operation that seems to be most beneficial for the various categories of behavior, thought, or mood disorders.

INTERIM RECOMMENDATIONS

The activities outlined above will require considerable time, probably on the order of two or three years. Since psychosurgery practice will continue during this time period, the NIMH makes the following recommendations with the intent of providing the maximum possible protection for potential psychosurgery candidates without unduly inhibiting practice for those cases which, judged by our present standards and knowledge, appear to require psychosurgery for relief of extreme mental illness or behavioral disorders.

1. *Psychosurgery should be regarded as an experimental therapy at the present time.*—As such, it should not be considered to be a form of therapy which can be made generally available to the public because of the peculiar nature of the procedure and of the problems with which it deals. Special constraints that apply to any experimental therapeutic procedure are required and the procedure should be only undertaken in those circumstances where there is special competence and experience and in institutional environments where appropriate safeguards are documented to be available.

The designation of psychosurgery as an experimental therapy imposes a number of stringent but essential constraints on practice: comprehensive re-

search protocols must be developed whenever psychosurgery is undertaken in order to assure that the maximum scientific value and information is obtained; psychosurgery should be conducted only in hospitals with strong and intimate affiliation with, and commitment to, academic sciences; it is absolutely essential that informed consent procedures be given primary consideration; every effort must be made to insure that all reasonable alternative therapies, based on our present state of knowledge, are attempted to an adequate extent before resorting to psychosurgery.

2. *No psychosurgery should be performed on involuntarily confined persons or persons incapable of giving consent, either by reason of age or mental condition.*—The NIMH is in full and complete accord with the recent decision of the Circuit Court for the County of Wayne, State of Michigan, which concluded that involuntarily confined mental patients cannot give informed and adequate consent to psychosurgery. We would also apply this judgment to prisoners and to persons under the age of consent.

3. *A registry should be established to monitor psychosurgery practice and to provide a continually updated source of information about the extent of the practice, the type of patients selected, and the outcome of the treatment.*—We would also suggest that the registry have provisions for indicating intent to perform psychosurgical procedure, so that scientific and clinical experts in psychology, psychiatry, and neurology have an opportunity to assess the patient's status prior to operation, as well as to study the short- and long-term effects of psychosurgical treatment.

CONCLUSION

In the many discussions held between NIMH staff and consultants, the possibility of recommending a voluntary moratorium on psychosurgery practice was frequently brought up. However, we have concluded that this would not be an appropriate action, for at least three reasons: (1) it would constitute an unprecedented Federal prescription of the parameters of permissible and impermissible surgery for the medical profession; (2) the difficulty of arriving at a precise and consensually agreed-upon definition of psychosurgery, specifically in the cases of surgical treatment for epilepsy and intractable pain, would vitiate the effectiveness of any moratorium—psychosurgery could, in many cases, continue under the guise of treatment for epilepsy or other neurological disease; and (3) the interim recommendations listed above amount to at least a partial moratorium, calling for cessation of that psychosurgery practice which is most subject to criticism.

With regard to the various activities outlined above, which are designed to provide a sound basis for judging the value of and indications for psychosurgery, the NIMH is soliciting contract proposals from outside organizations possessing the special expertise necessary for approaching these problems. However, we have received no satisfactory responses to a recent "sources sought" notice in the Commerce Business Daily. This fact, combined with our discussions with consultants and potential contractors, has made it clear that some of the projects that we consider essential for reasoned judgments about psychosurgery practice will be quite difficult to accomplish. A number of serious problems present themselves, including whether or not the necessary degree of cooperation can be obtained from the professional disciplines involved in psychosurgery and difficulties in the area of the physician-patient relationship and confidentiality of clinical records. Thus it is difficult to provide at this time any timetable for completion of these tasks. We will continue our activities in trying to develop a contract that will satisfy the necessarily stringent scientific, clinical, and managerial criteria that must be applied to such an effort.

NIMH Psychosurgery Panel—Legal, Ethical, and Lay Group

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[Item I.B.7]

CONFERENCE REPORT ON HR 7724 (P.L. 93-348)

Mr. Staggers submitted the following conference report and statement on the bill (H.R. 7724) to amend the Public Health Service Act to establish a

national program of biomedical research fellowships, traineeships, and training to assure the continued excellence of biomedical research in the United States, and for other purposes:

CONFERENCE REPORT (H. REPT. NO. 93-1149)

"The committee of conference on the disagreeing votes of the two Houses on the amendments of the Sente to the bill (H.R. 7724) to amend the Public Health Service Act to establish a national program of biomedical research fellowships, traineeships, and training to assure the continued excellence of biomedical research in the United States, and for other purposes, having met, after full and free conference, have agreed to recommend and do recommend to their respective Houses as follows:

"That the House recede from its disagreement to the amendment of the Senate to the text of the bill and agree to the same with an amendment as follows:

"In lieu of the matter proposed to be inserted by the Senate amendment to the text of the bill insert the following:

"Section 1. This Act may be cited as the 'National Research Act'.

"TITLE I—BIOMEDICAL AND BEHAVIORAL RESEARCH TRAINING

"SHORT TITLE

"SEC. 101. This title may be cited as the 'National Research Service Award Act of 1974'.

"FINDINGS AND DECLARATION OF PURPOSE

"SEC. 102. (a) Congress finds and declares that—

"(1) the success and continued viability of the Federal biomedical and behavioral research effort depends on the availability of excellent scientists and a network of institutions of excellence capable of producing superior research personnel;

"(2) direct support of the training of scientists for careers in biomedical and behavioral research is an appropriate and necessary role for the Federal Government; and

"(3) graduate research assistance programs should be the key elements in the training programs of the Institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration.

"(b) It is the purposes of this title to increase the capability of the institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration to carry out their responsibility of maintaining a superior national program of research into the physical and mental diseases and impairments of man.

"BIOMEDICAL AND BEHAVIORAL RESEARCH TRAINING

"SEC. 103. The part II of the Public Health Service Act relating to the appointment of the Directors of the National Institutes of Health and the National Cancer Institute is redesignated as part I, section 401 of such part is redesignated as section 471, and such part is amended by adding at the end the following new sections:

"'NATIONAL RESEARCH SERVICE AWARDS

"'SEC. 472. (a) (1) The Secretary shall—

"'(A) provide National Research Service Awards for—

"'(i) biomedical and behavioral research at the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration in matters relating to the cause, diagnosis, prevention, and treatment of the disease (or diseases) or other health problems to which the activities of the Institutes and Administration are directed,

"'(ii) training at the Institutes and Administration of individuals to undertake such research,

"'(iii) biomedical and behavioral research at non-Federal public institutions and at nonprofit private institutions, and

"'(iv) pre- and postdoctoral training at such public and private institutions of individuals to undertake such research; and

"'(B) make grants to non-Federal public institutions and to nonprofit private institutions to enable such institutions to make to individuals selected by them National Research Service Awards for research (and training to undertake such research) in the matters described in subparagraph (A)(i).

A reference in this subsection to the National Institutes of Health or the Alcohol, Drug Abuse, and Mental Health Administration shall be considered to include the institutes, divisions, and bureaus included in the Institutes or under the Administration, as the case may be.

"'(2) National Research Service Awards may not be used to support residencies.

"'(3) Effective July 1, 1975, National Research Awards may be made for research or research training in only those subject areas for which, as determined under section 473, there is a need for personnel.

"'(b)(1) No National Research Service Award may be made by the Secretary to any individual unless—

"'(A) the individual has submitted to the Secretary an application therefor and the Secretary has approved the application;

"'(B) the individual provides, in such form and manner as the Secretary shall by regulation prescribe, assurances satisfactory to the Secretary that the individual will meet the service requirement of subsection (c)(1); and

"'(C) in the case of a National Research Service Award for a purpose described in subsection (a)(1)(A)(iii) or (a)(1)(A)(iv), the individual has been sponsored (in such manner as the Secretary may by regulation require) by the institution at which the research or training under the Award will be conducted.

An application for an Award shall be in such form, submitted in such manner, and contain such information, as the Secretary may by regulation prescribe.

"'(2) The award of National Research Service Awards by the Secretary under subsection (a) and the making of grants for such Awards shall be subject to review and approval by the appropriate advisory councils to the entities of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration (A) whose activities relate to the research or training under the Awards, or (B) at which such research or training will be conducted.

"'(3) No grant may be made under subsection (a)(1)(B) unless an application therefor has been submitted to and approved by the Secretary. Such application shall be in such form, submitted in such manner, and contain such information, as the Secretary may by regulation prescribe. Subject to the provisions of this section other than paragraph (1) of this subsection, National Research Service Awards made under a grant under subsection (a)(1)(B) shall be made in accordance with such regulations as the Secretary shall prescribe.

"'(4) The period of any National Research Service Award made to any individual under subsection (a) may not exceed three years in the aggregate unless the Secretary for good cause shown waives the application of the three-year limit to such individual.

"'(5) National Research Service Awards shall provide such stipends and allowances (including travel and subsistence expenses and dependency allowances) for the recipients of the Awards as the Secretary may deem necessary. A National Research Service Award made to an individual for research or research training at a non-Federal public or nonprofit private institution shall also provide for payments to be made to the institution for the cost of support services (including the cost of faculty salaries, supplies, equipment, general research support, and related items) provided such individual by such institution. The amount of any such payments to any institution shall be determined by the Secretary and shall bear a direct relationship to the reasonable costs of the institution for establishing and maintaining the quality of its biomedical and behavioral research and training programs.

"'(c)(1)(A) Each individual who receives a National Research Service Award shall, in accordance with paragraph (3), engage in—

"'(i) health research or teaching,

"'(ii) if authorized under subparagraph (B), serve as a member of the National Health Service Corps or serve in his specialty or

"'(iii) if authorized under subparagraph (C), serve in a health related activity approved under that subparagraph, for a period computed in accordance with paragraph (2).

"'(B) Any individual who received a National Research Service Award and who is a physician, dentist, nurse, or other individual trained to provide health care directly to individual patients may, upon application to the Secretary, be authorized by the Secretary to—

"'(i) serve as a member of the National Health Service Corps,

"'(ii) serve in his specialty in private practice in a geographic area designated by the Secretary as requiring that specialty, or

"'(iii) provides services in his specialty for a health maintenance organization to which payments may be made under section 1876 of title XVIII of the Social Security Act and which serves a medically underserved population (as defined in section 1302(7) of this act),

in lieu of engaging in health research or teaching if the Secretary determines that there are no suitable health research or teaching positions available to such individual.

"'(C) Where appropriate the Secretary may, upon application, authorize a recipient of a National Research Service Award, who is not trained to provide health care directly to individual patients, to engage in a health-related activity in lieu of engaging in health research or teaching if the Secretary determines that there are no suitable health research or teaching positions available to such individual.

"'(2) For each year for which an individual receives a National Research Service Award he shall—

"'(A) for twelve months engage in health research or teaching or, if so authorized, serve as a member of the National Health Service Corps, or

"'(B) if authorized under paragraph (1)(B) or (1)(C), for twenty months serve in his specialty or engage in a health-related activity.

"'(3) The requirement of paragraph (1), shall be complied with by any individual to whom it applies within such reasonable period of time, after the completion of such individual's Award, as the Secretary shall by regulation prescribe. The Secretary shall (A) by regulation prescribe (i) the type of research and teaching which an individual may engage in to comply with such requirement, and (ii) such other requirements respecting such research and teaching and alternative service authorized under paragraphs (1)(B) and (1)(C) as he deems necessary; and (B) to the extent feasible, provide that the members of the National Health Service Corps who are serving in the Corps to meet the requirement of paragraph (1) shall be assigned to patient care and to positions which utilize the clinical training and experience of the members.

"'(4)(A) If any individual to whom the requirement of paragraph (1) is applicable fails, within the period prescribed by paragraph (3), to comply with such requirement, the United States shall be entitled to recover from such individual an amount determined in accordance with the formula—

$$A = \phi \frac{t - 1/2s}{t}$$

in which 'A' is the amount the United States is entitled to recover; 'ϕ' is the sum of the total amount paid under one or more National Research Service Awards to such individual and the interest on such amount which would be payable if at the time it was paid it was a loan bearing interest at a rate fixed by the Secretary of the Treasury after taking into consideration private consumer rates of interest prevailing at the time each Award to such individual was made; 't' is the total number of months in such individual's service obligation; and 's' is the number of months of such obligation served by him in accordance with paragraphs (1) and (2) of this subsection.

"'(B) Any amount which the United States is entitled to recover under subparagraph (A) shall, within the three-year period beginning on the date the United States becomes entitled to recover such amount, be paid to the United States. Until any amount due the United States under subparagraph (A) on account of any National Research Service Award is paid, there shall

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accrue to the United States interest on such amount at the same rate as that fixed by the Secretary of the Treasury under subparagraph (A) to determine the amount due the United States.

"'(4)(A) Any obligation of any individual under paragraph (3) shall be canceled upon the death of such individual.

"'(B) The Secretary shall by regulation provide for the waiver or suspension of any such obligation applicable to any individual whenever compliance by such individual is impossible or would involve extreme hardship to such individual and if enforcement of such obligation with respect to any individual would be against equity and good conscience.

"'(d) There are authorized to be appropriated to make payments under National Research Service Awards and under grants for such Awards $207,947,000 for the fiscal year ending June 30, 1975. Of the sums appropriated under this subsection, not less than 25 per centum shall be made available for payments under National Research Service Awards provided by the Secretary under subsection (a)(1)(A).

"'STUDIES RESPECTING BIOMEDICAL AND BEHAVIORAL RESEARCH PERSONNEL

"'SEC. 473. (a) The Secretary shall, in accordance with subsection (b), arrange for the conduct of a continuing study to—

"'(1) establish (A) the Nation's overall need for biomedical and behavioral research personnel, (B) the subject areas in which such personnel are needed and the number of such personnel needed in each such area, and (C) the kinds and extent of training which should be provided such personnel;

"'(2) assess (A) current training programs available for the training of biomedical and behavioral research personnel which are conducted under this Act at or through institutes under the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration, and (B) other current training programs available for the training of such personnel;

"'(3) identify the kinds of research positions available to and held by individuals completing such programs;

"'(4) determine, to the extent feasible, whether the programs referred to in clause (B) of paragraph (2) would be adequate to meet the needs established under paragraph (1) if the programs referred to in clause (A) of paragraph (2) were terminated; and

"'(5) determine what modifications in the programs referred to in paragraph (2) are required to meet the needs established under paragraph (1).

"'(b)(1) The Secretary shall request the National Academy of Sciences to conduct the study required by subsection (a) under an arrangement under which the actual expenses incurred by such Academy in conducting such study will be paid by the Secretary. If the National Academy of Sciences is willing to do so, the Secretary shall enter into such an arrangement with such Academy for the conduct of such study.

"'(2) If the National Academy of Sciences is unwilling to conduct such study under such an arrangement, then the Secretary shall enter into a similar arrangement with other appropriate nonprofit private groups or associations under which such groups or associations will conduct such study and prepare and submit the reports thereon as provided in subsection (c).

"'(c) A report on the results of such study shall be submitted by the Secretary to the Committee on Interstate and Foreign Commerce on the House of Representatives and the Committee on Labor and Public Welfare of the Senate not later than March 31 of each year.'

CONFORMING AMENDMENTS

"SEC. 104. (a)(1) Section 301 of the Public Health Service Act is amended (A) by striking out paragraph (c); (B) by striking out in paragraph (d) 'or research training' each place it occurs, 'and research training programs', and 'and research training program'; and (C) by redesignating paragraphs (d), (e), (f), (g), (h), and (i) as paragraphs (c), (d), (e), (f), (g), and (h), respectively.

"(2)(A) Section 303(a)(1) of such Act is amended to read as follows:

"'(1) to provide clinical training and instruction and to establish and maintain clinical traineeships (with such stipends and allowances (includ-

ing travel and subsistence expenses and dependency allowances) for the trainees as the Secretary may deem necessary);'

"(B) Section 303(b) of such Act is amended by inserting before the first sentence the following: 'The Secretary may provide for training, instruction, and traineeships under subsection (a)(1) through grants to public and other nonprofit institutions.'

(3) Section 402(a) of such Act is amended (A) by striking out 'training and instruction' in paragraph (3) and inserting in lieu thereof 'clinical training and instruction', and (B) by striking out paragraph (4) and by redesignating paragraphs (5), (6), and (7) as paragraphs (4), (5), and (6), respectively.

"(4) Section 407(b)(7) of such Act is amended (A) by striking out 'and basic research and treatment', and (B) by striking out 'where appropriate'.

"(5) Section 408(b)(3) of such Act is amended by inserting 'clinical' before 'training' each place it occurs.

"(6) Section 412(7) of such Act is amended by striking out '(1) establish and maintain' and all that follows down through and including 'maintain traineeships' and inserting in lieu thereof ', provide clinical training and instruction and establish and maintain clinical traineeships'.

"(7) Section 413(a)(7) is amended by inserting 'clinical' before 'programs'.

"(8) Section 415(b) is amended by inserting before the period at the end of the last sentence thereof the following: '; and the term "training" does not include research training for which fellowship support may be provided under section 472'.

"(9) Section 422 of such Act is amended (A) by striking out paragraph (c) and by redesignating paragraphs (d), (e), and (f) as paragraphs (c), (d), and (e), respectively, and (B) by striking out 'training and instruction and establish and maintain traineeships' in paragraph (e) (as so redesignated) and inserting in lieu thereof 'clinical training and instruction and establish and maintain clinical traineeships'.

"(10) Section 434(c)(2) of such Act is amended by inserting '(other than research training for which National Research Service Awards may be made under section 472)' after 'training' the first time it occurs.

"(11) Sections 433(a), 444, and 453 of such Act are each amended by striking out the second sentence thereof.

"(12) The heading for part I of title IV of such Act (as so redesignated by section 103) is amended by striking out 'Administrative' and inserting in lieu thereof 'General'.

"(b) The amendments made by subsection (a) shall not apply with respect to commitments made before the date of the enactment of this Act by the Secretary of Health, Education, and Welfare for research training under the provisions of the Public Health Service Act amended or repealed by subsection (a).

"SEX DISCRIMINATION

"SEC. 105. Section 799A of the Public Health Service Act is amended by adding at the end thereof the following: 'In the case of a school of medicine which—

"'(1) on the date of the enactment of this sentence is in the process of changing its status as an institution which admits only female students to that of an institution which admits students without regard to their sex, and

"'(2) is carrying out such change in accordance with a plan approved by the Secretary,

the provisions of the preceding sentences of this section shall apply only with respect to a grant, contract, loan guarantee, or interest subsidy to, or for the benefit of such a school for a fiscal year beginning after June 30, 1970.'

"FINANCIAL DISTRESS GRANTS

"SEC. 106. Section 773(a) of the Public Health Service Act is amended (1) by striking out '$10,000,000' and inserting in lieu thereof '$15,000,000', and (2) by striking out '1972' each place it occurs in the last sentence thereof and inserting in lieu thereof '1974'.

"TITLE II—PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH

"Part A—National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

"ESTABLISHMENT OF COMMISSION

"SEC. 201. (a) There is established a Commission to be known as the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (hereinafter in this title referred to as the 'Commission').

"(b)(1) The Commission shall be composed of eleven members appointed by the Secretary of Health, Education, and Welfare (hereinafter in this title referred to as the 'Secretary'). The Secretary shall select members of the Commission from individuals distinguished in the fields of medicine, law, ethics, theology, the biological, physical, behavioral and social sciences, philosophy, humanities, health administration, government, and public affairs; but five (and not more than five) of the members of the Commission shall be individuals who are or who have been engaged in biomedical or behavioral research involving human subjects. In appointing members of the Commission, the Secretary shall give consideration to recommendations from the National Academy of Sciences and other appropriate entities. Members of the Commission shall be appointed for the life of the Commission. The Secretary shall appoint the members of the Commission within sixty days of the date of the enactment of this Act.

"(2)(A) Except as provided in subparagraph (B), members of the Commission shall each be entitled to receive the daily equivalent of the annual rate of the basic pay in effect for grade GS-18 of the General Schedule for each day (including traveltime) during which they are engaged in the actual performance of the duties of the Commission.

"(B) Members of the Commission who are full-time officers or employees of the United States shall receive no additional pay on account of their service on the Commission.

"(C) While away from their homes or regular places of business in the performance of duties of the Commission, members of the Commission shall be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as persons employed intermittently in the Government service are allowed expenses under section 5703(b) of title 5 of the United States Code.

"(c) The chairman of the Commission shall be selected by the members of the Commission from among their number.

"(d)(1) The Commission may appoint and fix the pay of such staff personnel as it deems desirable. Such personnel shall be appointed subject to the provisions of title 5, United States Code, governing appointments in the competitive service, and shall be paid in accordance with the provisions of chapter 51 and subchapter III of chapter 59 of such title relating to classification and General Schedule pay rates.

"(2) The Commission may procure temporary and intermittent services to the same extent as is authorized by section 3109(b) of title 5 of the United States Code, but at rates for individuals not to exceed the daily equivalent of the annual rate of basic pay in effect for grade GS-18 of the General Schedule.

"SEC. 202. (a) The Commission shall carry out the following:

"(1)(A) The Commission shall (i) conduct a comprehensive investigation and study to identify the basic ethical principles which should underlie the conduct of biomedical and behavioral research involving human subjects, (ii) develop guidelines which should be followed in such research to assure that it is conducted in accordance with such principles, and (iii) make recommendations to the Secretary (I) for such administrative action as may be appropriate to apply such guidelines to biomedical and behavioral research conducted or supported under programs administered by the Secretary, and (II) concerning any other matter pertaining to the protection of human subjects of biomedical and behavioral research.

"(B) In carrying out subparagraph (A), the Commission shall consider at least the following:

"(i) The boundaries between biomedical or behavioral research involving human subjects and the accepted and routine practice of medicine.

"(ii) The role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects.

"(iii) Appropriate guidelines for the selection of human subjects for participation in biomedical and behavioral research.

"(iv) The nature and definition of informed consent in various research settings.

"(v) Mechanisms for evaluating and monitoring the performance of Institutional Review Boards established in accordance with section 474 of the Public Health Service Act and appropriate enforcement mechanisms for carrying out their decisions.

"(C) The Commission shall consider the appropriateness of applying the principles and gudelines identified and developed under subparagraph (A) to the delivery of health services to patients under programs conducted or supported by the Secretary.

"(2) The Commission shall identify the requirements for informed consent to participation in biomedical and behavioral research by children, prisoners, and the institutionalized mentally infirm. The Commission shall investigate and study biomedical and behavioral research conducted or supported under programs administered by the Secretary and involving children, prisoners, and the institutionalized mentally infirm to determine the nature of the consent obtained from such persons or their legal representatives before such persons were involved in such research; the adequacy of the information given them respecting the nature and purpose of the research, procedures to be used, risks and discomforts, anticipated benefits from the research, and other matters necessary for informed consent; and the competence and the freedom of the persons to make a choice for or against involvement in such research. On the basis of such investigation and study the Commission shall make such recommendations to the Secretary as it determines appropriate to assure that biomedical and behavioral research conducted or supported under programs administered by him meets the requirements respecting informed consent identified by the Commission. For purposes of this paragraph, the term 'children' means individuals who have not attained the legal age of consent to participate in research as determined under the applicable law of the jurisdiction in which the research is to be conducted; the term 'prisoner' means individuals involuntarily confined in correctional institutions or facilities (as defined in section 601 of the Omnibus Crime Control and Safe Streets Act of 1968 (42 U.S.C. 3781); and the term 'institutionalized mentally infirm' includes individuals who are mentally ill, mentally retarded, emotionally disturbed, psychotic, or senile, or who have other impairments of a similar nature and who reside as patients in an institution.

"(3) The Commission shall conduct an investigation and study to determine the need for a mechanism to assure that human subjects in biomedical and behavioral research not subject to regulation by the Secretary are protected. If the Commission determines that such a mechanism is needed, it shall develop and recommend to the Congress such a mechanism. The Commission may contract for the design of such a mechanism to be included in such recommendations.

"(b) The Commission shall conduct an investigation and study of the nature and extent of research involving living fetuses, the purposes for which such research has been undertaken, and alternative means for achieving such purposes. The Commission shall, not later than the expiration of the 4-month period beginning on the first day of the first month that follows the date on which all the members of the Commission have taken office, recommend to the Secretary policies defining the circumstances (if any) under which such research may be conducted or supported.

"(c) The Commission shall conduct an investigation and study of the use of psychosurgery in the United States during the five-year period ending December 31, 1972. The Commission shall determine the appropriateness of its use, evaluate the need for it, and recommend to the Secretary policies defining the circumstances (if any) under which its use may be appropriate. For purposes of this paragraph, the term 'psychosurgery' means brain surgery on (1) normal brain tissue of an individual, who does not suffer from any physical disease, for the purpose of changing or controlling the behavior or emotions of such individual, or (2) diseased brain tissue of

an individual, if the sole object of the performance of such surgery is to control, change, or affect any behavioral or emotional disturbance of such individual. Such term does not include brain surgery designed to cure or ameliorate the effects of epilepsy and electric shock treatments.

"(d) The Commission shall make recommendations to the Congress respecting the functions and authority of the National Advisory Council for the Protection of Subjects of Biomedical and Behavioral Research to be established under section 217(f) of the Public Health Service Act.

"SPECIAL STUDY

"SEC. 203. The Commission shall undertake a comprehensive study of the ethical, social, and legal implications of advances in biomedical and behavioral research and technology. Such study shall include—

"(1) an analysis and evaluation of scientific and technological advances in past, present, and projected biomedical and behavioral research and services;

"(2) an analysis and evaluation of the implications of such advances, both for individuals and for society;

"(3) an analysis and evaluation of laws and moral and ethical principles governing the use of technology in medical practice;

"(4) an analysis and evaluation of public understanding of and attitudes toward such implications and laws and principles; and

"(5) an analysis and evaluation of implications for public policy of such findings as are made by the Commission with respect to advances in biomedical and behavioral research and technology and public attitudes toward such advances.

"ADMINISTRATIVE PROVISIONS

"SEC. 204. (a) The Commission may for the purpose of carrying out its duties under sections 202 and 203 hold such hearings, sit and act at such times and places, take such testimony, and receive such evidence as the Commission deems advisable.

"(b) The Commission may secure directly from any department or agency of the United States information necessary to enable it to carry out its duties. Upon the request of the chairman of the Commission, the head of such department or agency shall furnish such information to the Commission.

"(c) The Commission shall not disclose any information reported to or otherwise obtained by it in carrying out its duties which (1) identifies any individual who has been the subject of an activity studied and investigated by the Commission, or (2) which concerns any information which contains or relates to a trade secret or other matter referred to in section 1905 of title 18 of the United States Code.

"(d) Except as provided in subsection (b) of section 202, the Commission shall complete its duties under sections 202 and 203 not later than the expiration of the 24-month period beginning on the first day of the first month that follows the date on which all the members of the Commission have taken office. The Commission shall make periodic reports to the President, the Congress, and the Secretary respecting its activities under sections 202 and 203 and shall, not later than ninety days after the expiration of such 24-month period, make a final report to the President, the Congress, and the Secretary respecting such activities and including its recommendations for administrative action and legislation.

"(e) The Commission shall cease to exist thirty days following the submission of its final report pursuant to subsection (d).

"DUTIES OF THE SECRETARY

"SEC. 205. Within 60 days of the receipt of any recommendation made by the Commission under section 202, the Secretary shall publish it in the Federal Register and provide opportunity for interested persons to submit written data, views, and arguments with respect to such recommendation. The Secretary shall consider the Commission's recommendation and relevant matter submitted with respect to it and, within 180 days of the date of its publication in the