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Office of Science and Technology Policy

Proposed Model Federal Policy for
Protection of Human Subjects; Response
to the First Biennial Report of the
President's Commission for the Study of
Ethical Problems In Medicine and
Biomedical and Behavioral Research;
Notice

**OFFICE OF SCIENCE AND
TECHNOLOGY POLICY**

**Proposed Model Federal Policy for
Protection of Human Subjects;
Response to the First Biennial Report
of the President's Commission for the
Study of Ethical Problems in Medicine
and Biomedical and Behavioral
Research**

AGENCY: Office of Science and
Technology Policy, Executive Office of
the President.

ACTION: Notice of proposed model policy
for department/agency implementation.

SUMMARY: This Notice sets forth the
Office of Science and Technology Policy
response to the recommendations in the
First Biennial Report of the President's
Commission for the Study of Ethical
Problems in Medicine and Biomedical
and Behavioral Research. This response,
made on behalf of all affected federal
departments and agencies, is based on
the work of the *Ad Hoc* Committee for
the Protection of Human Research
Subjects and further deliberations of the
Interagency Human Subjects
Coordinating Committee. The *First
Biennial Report* was published in the
Federal Register on March 29, 1982 (47
FR 13272-13305). Responses of the *Ad
Hoc* Committee were reviewed by the
Science Advisor to the President and,
with some modifications, accepted by
affected department and agency heads
in May 1985. This Notice includes in
response to the first and most important
recommendation, a Model Federal
Policy for the Protection of Human
Research Subjects (Model Policy)
involved in research conducted,
supported or regulated by federal
departments and agencies. The Notice
also contains a list of departments and
agencies that intend to adopt the Model
Policy and describes what, if any,
departures from the Model Policy
departments and agencies propose to
make at the time of their policy
implementation in order to meet
particular statutory requirements or
program needs.

Public comment and that of the
federal departments and agencies is
requested on the Proposed Model Policy,
proposed department and agency
departures, and other aspects of this
Notice. Based upon these comments, a
Final Model Policy will be published in
the **Federal Register**. Each department
and agency will expeditiously and in a
coordinated fashion promulgate the
Final Model Policy through its normal
procedures for implementing such
policies, e.g., through publication of
regulations in the **Federal Register**.

DATES: Comments must be received on
or before August 4, 1986. The
Interagency Human Subjects
Coordinating Committee will consider
these comments and refer them to the
Office of Science and Technology Policy
for use in development of a Final Model
Policy and to departments and agencies
for use in their policy implementation.

**ADDRESSES FOR COMMENT AND FURTHER
INFORMATION:** Comments and requests
for further information should be
addressed to: Joan P. Porter, Staff
Director, Interagency Committee for the
Protection of Human Subjects, Building
31, Room 4B09, Bethesda, Maryland
20892 (301-496-7041). Please specify
which recommendations or sections of
the Model Policy to which the comments
pertain.

John P. McTague,
*Acting Director, Office of Science and
Technology Policy.*

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Background

The President's Commission for the
Study of Ethical Problems in Medicine
and Biomedical and Behavioral
Research was established on November
9, 1978, by Pub. L. 95-622. One of the
charges to the President's Commission
was to report biennially to the President,
the Congress, and appropriate federal
departments and agencies on the
protection of human subjects of
biomedical and behavioral research. In
carrying out that charge, the President's
Commission was directed to conduct a
review of the adequacy and uniformity
(1) of the rules, policies, guidelines, and
regulations of all federal departments
and agencies regarding the protection of
human subjects of biomedical or
behavioral research which such
departments and agencies conduct or
support, and (2) of the implementation of
such rules, policies, guidelines, and
regulations by such agencies, such
review to include appropriate
recommendations for legislation and
administrative action.

In December 1981 the President's
Commission issued its *First Biennial
Report on the Adequacy and Uniformity
of Federal Rules and Policies, and their
Implementation, for the Protection of
Human Subjects in Biomedical and*

*Behavioral Research, Protecting Human
Subjects.* In transmitting the Report to
the President, Morris B. Abram,
Chairman of the Commission noted:

The Commission does not propose any
major changes in the substance of the rules
on human research, although a number of
adjustments are recommended to recognize
the flexibility needed by research
institutions, particularly in responding to
allegations of wrongdoing or other problems.
We also propose a simple improvement in the
reports filed by researchers, to provide
information on the number of subjects and on
any that are adversely affected by
participation in a research project.

The Commission does recommend one
major organizational change, namely that a
uniform core of regulations be adopted, based
upon the present rules of the Department of
Health and Human Services, and that HHS
become the lead agency in this field. This
consolidation would eliminate needless
duplication in the rules of the 23 other
Federal entities that support or regulate
research, thereby simplifying both local
compliance with the rules and Federal
oversight of the system. Copies of this report
are being sent to all affected Federal
agencies, with a request for action, pursuant
to the Commission's enabling legislation.

In accord with Pub. L. 95-622, each
federal department or agency which
receives recommendations from the
President's Commission with respect to
its rules, policies, guidelines or
regulations, must publish the
recommendations in the **Federal
Register** and provide an opportunity for
interested persons to submit written
data, views and arguments with respect
to adoption of the recommendations. On
March 29, 1982, (47FR 13272-13305) the
Secretary, HHS, published the report on
behalf of all the departments and
agencies affected by the
recommendations.

In May 1982 the Chairman of the
Federal Coordinating Council for
Science, Engineering and Technology
(FCCSET), appointed an *Ad Hoc*
Committee for the Protection of Human
Research Subjects under the auspices of
the FCCSET. The Committee, chaired by
Dr. Edward N. Brandt, Jr., Assistant
Secretary for Health, HHS, was
composed of the representatives and *Ex
Officio* members of affected
departments and agencies. In
consultation with the Office of Science
and Technology Policy (OSTP) and the
Office of Management and Budget, the
Ad Hoc Committee, after considering all
public comments, developed responses
to the recommendations of the
President's commission. After further
review and refinement, OSTP responded
on behalf of all affected department and
agency heads to the recommendations
of the President's Commission.

The first and most far-reaching recommendation of the President's Commission resulted in the development of a Proposed Model Federal Policy for the Protection of Human Research Subjects based on the January 1981 HHS regulations for the protection of human subjects (45 CFR Part 46):

The President should, through appropriate action require that all federal departments and agencies adopt as a common core the regulations governing research with human subjects issued by the Department of Health and Human Services (codified at 45 CFR Part 46), as periodically amended or revised, while permitting additions needed by any department or agency that are not inconsistent with these core provisions.

The *Ad Hoc* Committee agreed that uniformity is desirable among departments and agencies to eliminate unnecessary regulation and to promote increased understanding and ease of compliance by institutions that conduct federally supported or regulated research involving human subjects. Therefore, the *Ad Hoc* Committee developed a Model Policy, which applies to research involving human subjects that is conducted, supported or regulated by federal departments and agencies. In accordance with the Commission's recommendation, the Model Policy is based on Subpart A of the regulations of the Department of Health and Human Services (HHS) for the protection of human research subjects (45 CFR Part 46). The Proposed Model Policy developed by the *Ad Hoc* Committee was later modified by OSTP to enhance uniformity of implementation among the affected federal departments and agencies and to provide consistency with other related policies. The revised Policy was concurred in by all affected federal departments and agencies heads in March 1985.

The President's Commission also recommended that the President authorize and direct the Secretary, HHS, to designate an office with governmentwide jurisdiction to coordinate, monitor and evaluate the implementation of all federal regulations governing research with human subjects. For the reasons set forth in its response, the *Ad Hoc* Committee recommended that the Office for Protection from Research Risks (OPRR), National Institutes of Health, serve in a federal coordinating role for the protection of human subjects. The Director, OPRR, chairs the Interagency Human Subjects Coordinating Committee described below.

The Proposed Model Policy and the other responses to the President's Commission accepted by OSTP and the affected department and agency heads,

are set forth below. After a public comment period and publication of a Final Model Policy, each department and agency will promulgate the Model Policy expeditiously through whatever procedures are normally utilized for the implementation of policies or regulations, e.g. through publication as regulations in the **Federal Register**. Instances in which the policies of certain departments and agencies propose to depart from the Model Policy during their rulemaking or other implementation processes to accommodate statutory or program requirements are also described herein.

The interagency Human Subjects Coordinating Committee chartered in October 1983 under the auspices of FCCSET, is composed of representatives of all federal departments and agencies that conduct, support or regulate research involving human subjects. The Committee is advisory to department and agency heads, and among other responsibilities, evaluates the implementation of the Model Policy and recommends changes as necessary. OSTP responses to the recommendations of the President's Commission based on the report of the *Ad Hoc* Committee; the Proposed Model Policy; and the concurrences and intended departures of each affected federal department or agency head are presented below.

Response to Recommendations of the President's Commission

Response of the Office of Science and Technology policy (OSTP) to the recommendations of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in *Protecting Human Subjects; the First Biennial Report on the Adequacy and Uniformity of Federal Rules and Policies, and their Implementation for the Protection of Human Subjects in Biomedical and Behavioral Research* (December 1981).

This response is based on the work of the *Ad Hoc* Committee for the Protection of Human Research Subjects of the Federal Coordinating Council for Science, Engineering, and Technology which was modified to incorporate OSTP policy considerations in and accepted by affected Federal department and agency heads in June 1984.

Recommendation 1

The President should, through appropriate action, require that all federal departments or agencies adopt as a common core the regulations governing research with human subjects issued by the Department of Health and

Human Services (codified at 45 CFR Part 46), as periodically amended or revised, while permitting additions needed by any department or agency that are not inconsistent with these core provisions.

(A timetable of 180 days should be established by the President to provide an incentive for the interagency group to resolve any remaining questions about the HHS core regulations and identify an initial set of special rules beyond the core that are needed by various departments and agencies. If action is not prompt, the Commission suggests that Congress enact legislation directing the Executive branch to establish by a specified date a uniform set of regulations under a lead agency.)

The *Ad Hoc* Committee agreed in principle with this recommendation and developed a Model Federal Policy (Model Policy) statement based upon adaptations of HHS regulations for the protection of human subjects involved in research (45 CFR Part 46). The Office of Science and Technology Policy has made several modifications to increase uniformity of procedures among the federal departments and agencies and to increase compatibility with other current federal policies.

The Model Policy represented the *Ad Hoc* Committee's attempt to meet the concerns of the Commission that unnecessary and confusing regulations impose burdens on institutions that conduct or support research involving human subjects. The Committee attempted to make the Model Policy consistent with the HHS regulations while allowing for flexibility and adaptability in its application to the programs of diverse federal departments and agencies.

The *Ad Hoc* Committee believed that, insofar as possible, federal departments and agencies should employ consistent policies and procedures in dealing with nonfederal research institutions. Accordingly, the Model Policy was drafted in a mode that strives for uniformity in assurance and certification procedures; in all matters pertaining to the establishment, membership, functions and responsibilities of Institutional Review Boards (IRBs); and in procedural requirements including informed consent. Nevertheless, the Model Policy will allow agencies to continue to utilize time-tested directives and procedures in the conduct of their intramural research so long as these procedures are consistent with the Model Policy and adequately protect the rights and welfare of human research subjects.

Similarly, the Policy is designed to apply to research conducted, supported or regulated by United States departments or agencies in foreign situations. However, department or agency heads may accept other recognized standards in lieu of this Policy so long as these standards offer at least equivalent protections for research subjects.

The *Ad Hoc* Committee concurred with the findings of the President's Commission that there is already close correlation between the major provisions of the HHS regulations and current policies and procedures of other federal departments and agencies for protecting human subjects. The Model Policy is intended to further reduce the diversity so that nonfederal research institutions will not have to face inconsistent or contradictory requirements in their dealings with federal departments and agencies. The *Ad Hoc* Committee fully expected that adoption of the Policy will reduce the administrative burdens on institutions that conduct research involving human subjects.

The Model Policy document has been drafted in the form of a policy statement rather than in the form of a regulation so that it may be referenced by departments and agencies that will implement the Policy within a reasonable time and in a manner customary to each department or agency. In the future, department or agency heads may amend their policies so long as they note in advance in the **Federal Register** or other appropriate publications the way in which their amendments relate to provisions of the Model Policy.

Assuming a department or agency adopts the Model Policy it will retain the flexibility to waive individual requirements if waiver decisions are published in advance in the Federal Register or other appropriate publication. The *Ad Hoc* Committee believed that instances of waiver will be infrequent, and the requirement that each waiver be published will prevent inappropriate use of the waiver authority.

Highlights of key elements of the Model Policy for federal wide use are as follows:

Consistency with HHS Regulations

As noted previously, the *Ad Hoc* Committee Model Policy is patterned after HHS regulations. The word "Secretary" has been changed to "department or agency head" throughout the draft. Most of the provisions of the following subject areas

are the same in the Model Policy and HHS regulations:

(1) The characteristics of IRBs; (2) the role of IRBs in providing prior review of research protocols, including their duties and authorities in relation to investigators, to their institutions, and to the sponsors of research; (3) the standards and procedures that should govern IRB decision making and investigators' behavior; (4) the provisions of assuring compliance with the policy; (5) the procedures for expedited review; (6) the provisions for obtaining and documenting informed consent; and (7) the provisions for early termination of research support and evaluation of applications. The following highlights the major areas in which there is a difference in the Model Policy and Current HHS regulations.

Applicability

Sec. 101(a) specifies that

. . . [The policy] includes research conducted, supported, or otherwise subject to regulation by the federal government outside the United States.

(1) Research that is conducted or supported by a federal department or agency whether or not it is regulated as defined in Sec. 102(e) must comply with all sections of this policy.

(2) Research that is neither conducted nor supported by a federal department or agency but is subject to regulation as defined in Sec. 102(e) must be reviewed and approved, in compliance with Secs. 101, 102 and 107 through 117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.

It should be noted that federal support of an activity does not necessarily render the policy applicable to that activity. Federal "support" must be used in "research" involving "human subjects" as defined in the policy. For example, a private physician who conducts research unrelated to the Medicaid program would not come under this policy solely because the services he/she provides some of his/her patients are reimbursed by Medicaid. Nor would a research project sponsored by a State agency be covered solely because nonresearch services administered by the same agency are federally reimbursed. Alternatively, if a private physician or a State agency does employ federal support for research involving human subjects or if the physician or State agency voluntarily adopt this policy through the assurance mechanism, this policy would be applicable.

The Model Policy contains a definition of regulated research and indicates which sections of the policy are applicable to regulated research.

Sec. 102(e) defines regulated research.

'Research subject to regulation.' and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).

The provision in the HHS regulations which allows the Secretary to waive certain provisions is adapted to the Model Policy in the following manner:

Sec. 101(i) provides that

Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Protection from Research Risks, Department of Health and Human Services (HHS), and shall also publish them in the **Federal Register** or in such other manner as provided in department or agency procedures.

Consequently, waiver determinations must normally be published in the **Federal Register**, thus subjecting them to public scrutiny.

Changes in Exemptions

Sec. 101(b) sets forth exemptions for certain research activities from coverage of the Model Policy. The Model Policy combines exemptions 45 CFR 46.101(b)(2), (3) and (4) of the HHS regulations dealing with the use of educational tests, survey and interview procedures and observation of public behavior. The HHS exemptions are reflected in Model Policy exemptions sec. 101(b)(2) and (3):

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

(1) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

(ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing or employability.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures,

interview procedures or observation of public behavior that is exempt under paragraph (2), if:

(i) the human subjects are elected or appointed public officials or candidates for public office; or

(ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Thus, provision is made in the Model Policy for exempting certain social science research when federal statutes require without exception that the confidentiality of the personally identifiable information will be maintained.

Sec. 101(b)(6) is a new exemption

Taste and food quality evaluation studies, if wholesome foods without chemical additive are consumed or if a limited amount of a food is consumed that contains a food additive or agricultural chemical at or below a level approved by the Food and Drug Administration, the Environmental Protection Agency, or the Animal Plant Health Inspection Service of the U.S. Department of Agriculture.

This exemption, requested by the U.S. Department of Agriculture (USDA) but appropriate for several other agencies as well, is intended to exempt certain taste and food quality evaluation studies from IRB review. The current USDA policy exempts taste and food quality evaluation studies which involve consumer acceptance testing and quality evaluation studies if a limited amount of food will be consumed containing a food additive or agricultural chemical at a level approved by the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA) or the Animal Plant Health Inspection Service (APHIS) of the USDA; or if the food chemical is normally found in food at concentrations at least equal to those being tested. The exemption is not intended to apply to task tests and quality evaluation studies if the food additive is being tested and the test chemical is *not* (1) on FDA's Generally Recognized as Safe (GRAS) list; (2) a permitted food additive as tested; or (3) normally found in food at concentrations being tested. In addition, the exemption is not intended to apply if a pesticide or other chemical residue is present and the acceptable level has not been established by FDA, EPA or APHIS.

Foreign Research

Sec. 101(g) states clearly what is only implicit in the HHS regulations, namely that the Model Policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections for

human subjects. Furthermore, it allows department and agency heads discretion in accepting equivalent procedures for research carried out in foreign countries.

Sec. 101(h) provides that

When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the 1975 World Medical Assembly Declaration (Helsinki II) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the **Federal Register** or such other publications as provided by department or agency procedures. (Italics supplied)

Assuring Compliance with the Model Policy

Sec. 103(a) requires that

Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy.

Current HHS regulations permit institutions which hold an approved assurance to delay submission of certification of IRB review and approval until 60 days after submission of an application or proposal for financial support. The Model Policy does not include a grace period.

Sec. 103(g) requires that

Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived under Secs. 101(b) or (i). Along with the submission of an application or proposal for approval or support, an institution with an approved assurance covering the research shall certify that the application or proposal has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution,

IRB Membership

Sec. 107(a) includes a provision that

... The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. . . .

Sec. 107(a) of the Model Policy also replaces the current HHS requirement that if an IRB regularly reviews research that involves a vulnerable category of subjects, the IRB must include one or more individuals who are primarily concerned with the welfare of those subjects. Consideration of inclusion of such an individual(s) is left to the, institution (or other authority) establishing the IRB in the Model Policy.

The Model Policy requires instead in 1079(a) that

... If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

45 CFR 46.107(b) of the 1981 HHS regulations indicates that no IRB may consist entirely of men or entirely of women, or entirely of members of one profession.

Section 107(b) of the Model Policy reads

Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

This language was developed in consultation with the Department of Justice.

In seeking diverse membership on the IRB, the institution must consider both men and women who can contribute to the work of the IRB. Given the ready availability of well qualified persons of both genders, OSTP expects that only rarely, if ever, will an IRB consist solely of men or solely of women. In any event, no selection shall be made to the board on the basis of gender.

Recommendation 2

The President should authorize and direct the Secretary of Health and Human Services to designate an office with government-wide jurisdiction to coordinate, monitor and evaluate the implementation of all regulations governing research with human subjects

of Federal departments that conduct, support or regulate such research.

The *Ad Hoc* Committee endorsed the concept of the designation of an office to coordinate the implementation of the Model Policy developed under Recommendation 1. However, the *Ad Hoc* Committee did not believe that it is either necessary or useful to assign the coordinating office "government-wide jurisdiction to monitor and evaluate the implementation of all regulations governing research with human subjects." For example, the Food and Drug Administration (FDA) has jurisdiction over nearly 30 different categories of test articles—each covered by appropriate regulations governing clinical research. It would be entirely impractical to expect a central HHS office to monitor and evaluate each of these specialized regulations, but it is feasible and desirable that rules governing IRB review and informed consent be consistent throughout all of these regulations and consistent with procedures required by other departments and agencies. As the President's Commission notes, most departments and agencies already follow the HHS rules pertaining to IRBs and informed consent. To date, uniformity has been developing on a voluntary basis with assistance from OPRR.

Reporting Requirements for Institutions

In consideration of Recommendations 7 and 8 in the *Biennial Report*, language has been included in Sec. 103(b)(5) to indicate that assurances negotiated with supporting federal agencies or departments must specify

Written procedures for ensuring prompt reporting the IRB, appropriate institutional officials, and the department or agency head (i) any unanticipated problems or scientific misconduct involving risks to human subjects or others; (ii) any allegation or finding of serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval.

This sets forth the requirement that all concerned parties be informed of problems and misconduct based on noncompliance with the Policy for the protection of human subjects. It allows research institutions flexibility in developing procedures compatible with their organizational structures, while requiring them to meet a reasonable standard of accountability. (See discussion of Recommendations 7 and 8, following.)

Role of the Office for Protection from Research Risks (OPRR)

In anticipation of designation of OPRR as a key coordinating office (described below in the *Ad Hoc* Committee's response to Recommendation 2), the following responsibility for OPRR has been made explicit in the Model Policy.

Sec. 103(f) requires that

In lieu of negotiating a separate assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, approved by and on file with the Office for Protection from Research Risks, HHS.

This provision will considerably reduce the administrative burden on institutions conducting research and on federal departments and agencies conducting or supporting research.

The *Ad Hoc* Committee, therefore, recommended that the President's Science Advisor request the Secretary, HHS, to direct the OPRR to exercise federalwide coordination of policies and procedures for the protection of human research subjects. The Model Policy has been drafted to reflect an OPRR role.

The coordinating responsibilities of OPRR include at least the following:

(1) OPRR shall continue to negotiate and approve Assurances of Compliance with the HHS regulations based on the Model Policy for HHS conducted and supported research. In lieu of negotiating a separate assurance, individual departments and agencies shall accept a current HHS assurance approved by and on file in OPRR if it is appropriate to the research in question.

(2) OPRR shall facilitate an exchange of information among all federal departments and agencies that conduct, support or regulate research involving human subjects.

(3) OPRR shall, when appropriate, amend and republish the list of categories of research that may be reviewed under the expedited procedures outlined under Sec. 110 of the Model Policy.

(4) OPRR shall continue to develop educational materials and programs for the benefit of (a) research investigators; (b) research administrators; (c) IRB members; and (d) federal officials with responsibility for research involving human subjects.

(5) Department and agency heads shall forward to OPRR for review and comment all proposed department or agency policies and regulations for the protection of human research subjects. OPRR shall within 90 days of receipt call to the attention of any department or agency issuing a proposed rule or policy any provisions inconsistent with the Model Policy.

(8) The Director, OPRR, shall chair an Interagency Human Subjects Coordinating Committee to facilitate coordination of federal policies and regulations for the protection of human subjects. (This Committee was established in October 1983 by the Director, OSTP, under the auspices of the Federal Coordinating Council for Science, Engineering and Technology and is advisory to department and agency heads.)

The *Ad Hoc* Committee believed that if these coordinating steps are taken (including advising, guiding, educating and reviewing as described), the purposes of the recommendations of the President's Commission will be accomplished. The Interagency Committee is well-positioned to evaluate the implementation of the Model Policy when necessary and appropriate.

The *Ad Hoc* Committee further believed that over many years the OPRR has established sound credentials in the protection of human subjects. It noted that OPRR has operated effectively with all necessary backing from the Office of the Secretary, HHS. Because OPRR is located in a research milieu, it has ready access to experts in biomedical and behavioral research with experience in dealing with the delicate balance of promoting high quality research while maintaining proper safeguards for human subjects.

By designating OPRR as the coordinating office, the *Ad Hoc* Committee believed that the Secretary, HHS, would give emphasis to the importance of the coordinating function to be exercised. Establishment of a permanent federalwide advisory group assures the continuation of this emphasis. By designating an existing office in HHS rather than creating a new office, the Secretary is able to accomplish the goals of the President's Commission with only minimal increases in monetary and personnel expenditures.

Recommendation 3

Each Federal department or agency should have a comprehensive set of rules and procedures governing research with human subjects that applies consistently to all submits within the department or agency.

No action required on Recommendation 3 will be needed if the procedures outlined in response to Recommendations 1 and 2 are adopted.

Recommendation 4

All Federal departments and agencies that conduct or support research with

human subjects should require principal investigators to submit, as part of their annual reports to the IRB and the funding agency, information regarding the number of subjects who participated in each research project as well as the nature and frequency of adverse effects.

The *Ad Hoc* Committee questioned the feasibility of developing a major data collection of numbers of human subjects who participate in Federally conducted or supported research. It acknowledged the importance of sound data relating to research injuries and adverse reactions and recognized such data would be helpful in making sound policy decisions concerning compensation for research injuries. Nevertheless the *Ad Hoc* Committee recognized serious definitional problems associated with the collection of such data.

The President's Commission has acknowledged the difficulty in defining research-related injury. The Veterans Administration (VA) has made efforts to collect data of the type recommended by the President's Commission. The VA program, attempted as a pilot effort, has been fraught with technical difficulties.

The VA has described certain difficulties recently encountered in collecting data on human research subjects. The VA had issued circulars to its medical centers which were conducting research involving human subjects. The circulars requested that the centers collect data regarding the incidence of adverse results "or effects" of participation in biomedical and behavioral research. The collected data were forwarded to the central VA office. Figures received in November 1981 provided the VA with unreliable and incomplete reports of human subjects injured or otherwise adversely affected as the result of participation in research projects. Because of definitional problems, misunderstandings on the part of field research personnel, confounding of therapeutic and research data and instances of both underreporting and overreporting the data were considered misleading or meaningless. The data were not amenable to synthesis.

Given the existing definitional problems and the expected poor quality of resulting data, the *Ad Hoc* Committee believed that the expenditure of scarce resources for data collection was not warranted at this time. In fact, implementation of this recommendation could produce results that are misleading and could generate inappropriate policies and procedures. Therefore, the *Ad Hoc* Committee recommended that the matter of data collection be addressed by an

Interagency Human Subjects Coordinating Committee.

Recommendation 5

The Department of Health and Human Services and all other relevant Federal departments and agencies should proceed promptly to take action on the National Commission's recommendations concerning research involving children and research involving those institutions as mentally disabled, and other Federal agencies should also act on the final regulations of HHS governing such research....

In early February 1983 HHS Secretary Schweiker approved Subpart D of Title 45 CFR Part 46, "Additional Protections for Children Involved as Subjects in Research." These were published as a Final Rule in the **Federal Register** on March 8, 1983, and became effective June 6, 1983. HHS is now considering action on the proposed regulations addressing research involving those institutionalized as mentally disabled.

Recommendation 6

Congress should attach the following condition to any direct appropriations for "private" research entities: "No funds appropriated under this Act may be used, directly or indirectly, to support research involving human subjects unless such research is reviewed and conducted in compliance with either (1) appropriate regulations of (the disbursing agency) or (2) the regulations of the Department of Health and Human Services (45 CFR Part 46)."

The *Ad Hoc* Committee was unaware of any "private" research entity which receives direct appropriations other than the Gorgas Memorial Institute of Tropical and Preventive Medicine, Inc. OPRR has negotiated an HHS Multiple Project Assurance of Compliance with Gorgas Memorial Institute which has indicated its intention to comply with HHS regulations. Consequently this recommendation has been met by administrative action, and no legislation is required. If other such entities are identified, the federal disbursing agency should arrange for a proper Assurance of Compliance with HHS or Model Policy requirements.

Recommendations 7 and 8

7. 45 CFR 46.103, which specifies the minimum requirements for an institutional assurance, should be amended by inserting two new clauses under (b)(5) and (6): to—

- *designate a specific office at each institution that will be responsible for:*
 - (i) *receiving reports of alleged misconduct in research involving human subjects;*
 - (ii) *investigating promptly and*

fairly; and (iii) reporting formal findings of misconduct both to the institution's IRB which approved the research and to the Secretary. The institutional office so designated need not be created specifically for this purpose but may be the relevant IRB itself or another existing office already having responsibility for quality assurance with the institution. Such office shall report on all ongoing investigations of alleged research misconduct involving human subjects as well as formal findings to the IRB, and shall consult with the IRB on all matters relating to the conduct of research with human subjects. (paraphrased)

- *require written procedures for insuring prompt reporting to designated institutional officials, and by them to the Secretary, of the results of any investigation or inquiries carried out under the preceding subsection or under Sec. 46.108(c) that reveal research misconduct or serious or continuing noncompliance with Federal or institutional requirements for the protection of human subjects. (paraphrased)*

8. 45 CFR 46.108(c) should be revised to read as follows: (In order to fulfill the requirements of these regulations, each IRB shall) (c) be responsible for reporting to the appropriate institutional officials any serious or continuing noncompliance by investigators with the requirements and determinations of the IRB, or with the provisions of the regulations, or with good research practices, that is revealed during the IRB's continuing or annual review of research or through reports made directly to a member of the IRB or its staff (and that each IRB); (d) establish procedures for receiving and acting upon findings of misconduct in research involving human subjects, made in the office designated pursuant to Sec. 46.103(b)(5). (paraphrased)

After careful review of the recommendations of the President's Commission, the testimony to the Commissioners leading to these recommendations, and public and interagency comment, the *Ad Hoc* Committee proposed the following: *Sec. 103(b)(5)* of the proposed Model Policy requires that in assurances submitted to heads of departments or agencies conducting or supporting research involving human subjects institutions must include

Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head (i) any unanticipated problems or scientific misconduct involving risk to human subjects or others, (ii) any allegation or finding of

serious or continuing noncompliance with this policy or the requirements or determinations of the IRB, and (iii) any suspension or termination of IRB approval.

The *Ad Hoc* Committee concluded that addition of this language would permit deletion of the current 45 CFR 46.108(c) which states that an IRB ". . . be responsible for reporting to the appropriate institutional officials and the Secretary any serious or continuing noncompliance by investigators with the requirements and determination of the IRB."

By modification of current language in the HHS regulations, the *Ad Hoc* committee believed that (a) any implication is eliminated that the IRB is required to be an investigatory and reporting body in the institution. Institutions may develop their own procedures to assure that allegations are promptly investigated and reported to appropriate institutional officials as well as to supporting federal department or agency officials, and (b) the establishment of reporting lines is assigned to the institutions; and groups which need to be informed are identified. Institutions are, therefore, afforded flexibility in meeting requirements of the Policy. The assurance is the appropriate document for identifying the specific offices to be notified and the timing and nature of reporting which may be tailored to each institution's organizational structure. The *Ad Hoc* Committee members noted that the language proposed in Recommendations 7 and 8 was perhaps too detailed for verbatim incorporation into the Model Policy.

Recommendation 9

Federal departments and agencies should establish government-wide procedures for making determinations on suspension and debarment of grantees and contractors alleged to have engaged in misconduct in Federally supported research with human subjects. Final determinations and sanctions imposed should be entered onto a consolidated list of individuals and made known to all Federal agencies involved with human research, to state licensing boards, and to appropriate professional societies.

The *Ad Hoc* Comment generally concurred with the recommendation for the establishment of government-wide procedures for making determinations on suspension and debarment of grantees and contractors alleged to have engaged in misconduct in federally-supported research with human subjects. However, the *Ad Hoc* Committee believed that this recommendation should be carried out

as a part of an Executive Branch consideration of government-wide suspension and debarment procedures encompassing misconduct under all types of federal support.

The Executive Branch has undertaken several initiatives in this regard. With respect to contracts (i.e., procurement) the Office of Federal Procurement Policy on the OMB issued, on June 24, 1982, a Policy Letter setting forth government-wide policies and procedures for suspension and debarment of government contractors and for the establishment of a consolidated government-wide listing of these suspensions and debarments (47 FR 28854). The Policy Letter became effective on August 30, 1982, and the General Services Administration become responsible for maintaining the consolidated listing of suspensions and debarments of contractors on that date. The Policy Letter has now been incorporated in the Federal Acquisition Regulation (48 CFR Chapter 1) as Subpart 9.4, and on February 26, 1985 HHS published implementing procedures in 48 CFR 309.4.

With respect to grants and other forms of financial assistance (i.e., nonprocurement), on February 18, 1986, President Reagan signed Executive Order 12549 mandating the establishment, under the guidance of OMB, of a government-wide system for debarment and suspension from federal assistance programs. OMB published proposed Guidelines simultaneously with the Executive Order, which provided 60 days opportunity for comment. OMB is currently reviewing the comments and expects to publish the final Guidelines within six months. The Executive Order calls for implementing agency regulations within 12 months of the final OMB Guidelines. This will result in separate government-wide procedures for the suspension and debarment of contractors and of recipients of financial assistance. Although federally-supported research with human subjects is not specifically mentioned in the government-wide procedures, one or more of the specifically stated causes for suspension and debarment could arise in the course of such research. The Interagency Human Subjects Coordination Committee will monitor any suspension or debarment actions arising from research involving human subjects.

Model Federal Policy for Protection of Human Research Subjects

Sec. 101 To What Does This Policy Apply?
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Sec. 122 Use of Federal funds.
Sec. 123 Early termination of research support; Evaluation of applications and proposals.
Sec. 124 Conditions.

Sec. 101 To What Does This Policy Apply?

(a) Except as provided in paragraph (b) below, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the Federal government outside the United States.

(1) Research that is conducted or supported by a federal department or agency whether or not it is regulated as defined in Sec. 102(e) must comply with all sections of this policy.

(2) Research that is neither conducted nor supported by a federal department or agency but is subject to regulation as defined in Sec. 102(e) must be reviewed and approved, in compliance with Secs. 101, 102, and 107 through 117 of this policy, by an institutional review board

(IRB) that operates in accordance with the pertinent requirements of this policy.

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing or employability.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior that is not exempt under paragraph (2), if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) public benefit or service program; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for

benefits or services under those programs.

(6) Taste and food quality evaluation studies, if wholesome foods without chemical additives are consumed or if a limited amount of a food is consumed that contains a food additive or agricultural chemical at or below a level approved by the Food and Drug Administration, the Environmental Protection Agency, or the Animal Plant Health Inspection Service of the U.S. Department of Agriculture.

(c) Department or agency heads retain final judgment as to whether a particular activity is covered by this policy.

(d) Department or agency heads may require that specific research activities or classes of research activities conducted, supported, or otherwise subject to regulation by the department or agency but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

(e) Compliance with this policy requires compliance with pertinent federal laws or regulations which provide additional protections for human subjects.

(f) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(g) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research.

(h) When research covered by this policy takes place in foreign countries: procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the 1975 World Medical Assembly Declaration (Helsinki II) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the **Federal Register** or will be otherwise published as provided in department or agency procedures.

(i) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Protection from Research Risks, Department of Health and Human Services (HHS), and shall also publish them in the **Federal Register** or in such other manner as provided in department or agency procedures:

Sec. 102 Definitions.

(a) "Department or agency head" means the head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

(b) "Institution" means any public or private entity or agency (including federal, state, and other agencies).

(c) "Legally authorized representative" means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

(d) "Research" means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute "research" for purposes of this policy, whether or not they are conducted under a program which is considered research for other purposes. For example, some "demonstration" and "service" programs may include research activities.

(e) "Research subject to regulation," and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).

(f) "Human subject" means a living individual about whom an investigator (whether professional or student)

conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. "Intervention" includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

"Interaction" includes communication or interpersonal contact between investigator and subject. "Private information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

(g) "IRB approval" means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

(h) "Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(i) "Certification" means the official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

Sec. 103 Assuring compliance with this Policy—research conducted or support by any Federal Department or Agency.

(a) Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy.

(b) Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance approved as provided in this

section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to federally supported or conducted research shall at a minimum include:

(1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself. This requirement does not preempt provisions of this policy applicable to department- or agency-supported or regulated research and need not be applicable to any research exempted or waived under Secs. 101 (b) or (i).

(2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

(3) A list of the IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head.

(4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(5) Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head (i) any unanticipated problems or scientific misconduct involving risks to human subjects or others; (ii) any allegation or finding of serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval.

(c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.

(d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval.

(f) In lieu of negotiating a separate assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, approved by and on file with the Office for Protection from Research Risks, HHS.

(g) Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived under Secs. 101 (b) or (i). Along with the submission of an application or proposal for approval or support, an institution with an approved assurance covering the research shall certify that the application or proposal has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a

request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

Sec. 104 Section reserved.

Sec. 105 Section reserved.

Sec. 106 Section reserved.

Sec. 107 IRB Membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB's initial or continuing review of any project in

which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

Sec. 108 IRB functions and operations.

In order to fulfill the requirements of this policy each IRB shall:

(a) Follow written procedures in the same detail as described in Sec. 103(b)(4) and, to the extent required by, Sec. 103(b)(5).

(b) Except when an expedited review procedure is used (see Sec. 110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

Sec. 109 IRB review of research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with Sec. 116. The IRB may require that information, in addition to that specifically mentioned in Sec. 116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with Sec. 117.

(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

Sec. 110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Secretary, HHS, has established, and published in the **Federal Register**, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the **Federal Register**.

(b) With the approval of department or agency heads, an IRB may use the expedited review procedure to review either or both of the following: (1) Some or all of the research appearing on the list and found by the reviewers to involve no more than minimal risk, (2) minor changes in previously approved research during the period for which approval is authorized. Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in Sec. 108(b).

(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

(d) The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

Sec. 111 Criteria for IRB approval of research.

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks

and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by Sec. 116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by Sec. 117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Sec. 112 Review by institution.

Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

Sec. 113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

Sec. 114 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

Sec. 115 IRB records.

(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members in the same detail as described in Sec. 103(b)(3).

(6) Written procedures for the IRB in the same detail as described in Secs. 103(b)(4) and 103(b)(5).

(7) Statements of significant new findings provided to subjects, as required by Sec. 116(b)(5).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner.

Sec. 116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) below, in seeking informed consent the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained

(7) An explanation of whom to contact for answers to pertinent questions about

the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

(i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and

(2) The research could not practicably be carried out without the waiver or alteration.

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirements to obtain

informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

Sec. 117 Documentation of informed consent.

(a) Except as provided in paragraph (c) below, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the persons signing the form.

(b) Except as provided in paragraph (c) below, the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by Sec. 116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A "short form" written consent document stating that the elements of informed consent required by Sec. 116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the

representative, in addition to a copy of the "short form."

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

Sec. 118 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under Sec. 101 (b) or (i), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted to the department or agency.

Sec. 119 Research undertaken without the intention of involving human subjects.

In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted to the department or agency, and final

approval given to the proposed change by the department or agency.

Sec. 120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

(a) The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency through such officers and employees of the department or agency and such experts and consultants as the department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

(b) On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

Sec. 121 Section reserved.

Sec. 122 Use of Federal funds.

Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

Sec. 123 Early termination of research support; Evaluation of applications and proposals.

(a) The department or agency head may require that department or agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the department or agency head finds an institution has materially failed to comply with the terms of this policy.

(b) In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person who would direct or has directed the scientific and technical aspects of an activity has in the judgment of the department or agency head materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to federal regulation).

Sec. 124 Conditions.

With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.

Concurrences of Departments and Agencies Including Proposed Departures From the Model Policy

No Departures

Agency for International Development (AID)

Consumer Product Safety Commission (CPSC)

Department of Agriculture (USDA)

Department of Commerce (DOC)

Department of Defense (DOD)

Department of Energy (DOE)

Department of Housing and Urban Development (HUD)

Department of Justice (DOJ)

Department of Transportation (DOT)

Environmental Protection Agency (EPA)

National Aeronautics and Space Administration (NASA)

National Science Foundation (NSF)

Comment

Central Intelligence Agency (CIA)

The Central Intelligence Agency (CIA) is required by Executive Order 12333 to conform to the guidelines issued by the Department of Health and Human Services (HHS). Currently, the CIA follows the HHS regulations codified in 45 CFR Part 46. If, with respect to the CIA, HHS incorporates the Model Policy, the CIA will follow the model policy. The CIA fully concurs with the principles established in the Model Policy.

Proposed Departures

Department of Education (ED)

A departure for ED only that pertains only to research involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior, conducted under a program subject to the General Education Provisions Act: *Revise* the exception to the Model Policy stated in Section 101(b)(3)(ii) to read as follows: "The research is conducted under a program subject to the protections of the General Education Provisions Act (GEPA), including GEPA Sections 400A

(20 U.S.C. 1221-3), 438 (20 U.S.C. 1232g), and 439 (20 U.S.C. 1232h)."

Department of Health and Human Services (HHS)

1. Section 101(b)(6) of the HHS regulations (which becomes Section 101(b)(5) of the Model Policy) now has a qualifier found at 45 CFR 46.101(i): "(i) If, following review of proposed research activities that are exempt from these regulations under paragraph (b)(6), [of the HHS regulations] the Secretary determines that a research or demonstration project presents a danger to the physical, mental, or emotional well-being of a participant or subject of the research or demonstration project then federal funds may not be expended for such a project without the written informed consent of each participant or subject."

HHS intends to retain this qualifier to exemption 6 in future regulations.

2. Section 103(g)—The Model Policy requires that institutions holding an approved assurance which covers a proposed research projects submit certification of IRB review and approval *along with* an application for funding. Current HHS regulations permit institutions to submit such certification along with the application *or* within 60 days of application for funding [45 CFR 46.163(f)]. At the time HHS publishes proposed rules and technical amendments designed to implement the Model Policy, HHS will request comment on whether or not the "60-day grace period" should be reduced or eliminated.

Food and Drug Administration (FDA)

1. Section 101(h)—The section of the Model Policy addresses research that takes place in foreign countries. FDA must diverge from the Model Policy with regard to those clinical investigations that take place in a foreign country and are conducted under a research permit granted by FDA. Such investigations must be carried out in accordance with the Federal Food, Drug, and Cosmetic Act (FD&C Act), which establishes certain requirements for the conduct of such investigations [see, e.g., 21 U.S.C. 355(i), 357(d)(3), and 360j(g)]. For these investigations, FDA does not have the authority to accept the procedures followed in a foreign country in lieu of the procedures required by the FD&C Act.

2. Section 116(d)—This section of the Model Policy permits altering or waiving of the informed consent requirements. FDA must depart from this provision of the Model Policy (See 21 CFR 50.20). The FD&C Act requires that informed

consent be obtained from all subjects of clinical investigations except in very limited circumstances [see e.g., 21 U.S.C. 355(i), 357(d)(3), and 360j(g)(3)(D)], which establish requirements for the conduct of clinical investigations for drugs, antibiotic drugs, and medical devices, respectively. FDA does not have authority under the FD&C Act to waive this requirement.

Veterans Administration (VA)

VA will continue intramural research and development practices of not permitting exempted research [Section 101(2)(b)] or expedited review (Section 110), not permitting waiver of informed consent [Section 116(c)] or "short form" written consent [Section 117(b)(2)], and not requiring written institutional assurances from VA medical centers

[Section 103(a)]. Further, regarding cooperative research efforts under Section 114, VA requires that each VA medical center which participates in a cooperative or multi-hospital project must obtain the approval of its own Human Studies Subcommittee for such research.

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