DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
WASHINGTON, D.C. 20201

REFER TO:

February 8, 1966

TO : The Heads of Institutions Conducting Research with Public Health Service Grants

FROM : Surgeon General, Public Health Service

SUBJECT: Clinical research and investigation involving human beings

Expanding Public Health Service support of clinical research and investigation involving human beings emphasizes the need for more formal attention to the critical issues raised by such research.

In December 1965 the National Advisory Health Council, after study of these critical issues, made certain recommendations to me which I have now formulated as the following Public Health Service grant policy:

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

Effective immediately, this policy will be included in all future statements of Public Health Service research and research training grant policy. The wisdom and sound professional judgment of you and your staff will determine what constitutes the rights and welfare of human subjects in research, what constitutes informed consent, and what constitutes the risks and potential medical benefits of a particular investigation.

I wish to define more explicitly, however, what is meant by a committee of his institutional associates to assure an independent determination because the policy requires that the application include a description of the associates who will provide the review. The committee would need to be made up of staff of, or consultants to, your institution who are at the same time acquainted with the investigator under review, free to assess his judgment without placing in jeopardy their own goals, and sufficiently mature and competent to make the necessary assessment. It is important that some of the members be drawn from different disciplines or interests that do not overlap those of the investigator under review.

The policy does not ask for the names of the members of the committee. It does ask for a description of its composition; e.g., the number of members and the professional or public interests they reflect.

I have directed all my staff who administer the initial review of applications for grants for clinical research and investigation involving human beings -- regardless of whether these applications are for new, supplemental, renewal, or continuation support -- to ascertain that each application includes the information required by this policy and to obtain this information, when necessary, in a document signed by both the principal investigator or program director and the official for the institution.

I know that you are as deeply concerned with this issue as are any of us in the Public Health Service. I urgently request that you give my staff your cooperation in making this policy an effective instrument for the good of the public and science.

William H. Stewart

William H. Stewart, M.D.

U. S. Public Health Service
Division of Research Grants
Bethesda, Maryland 20014

PPO # 129
POLICY
February 8, 1966

SUBJECT : Clinical Investigations Using Human Subjects

APPLICABILITY : All PHS Research and Research Training Grants in Support of Such Clinical Investigations (including General Research Support Grants)

EFFECTIVE DATE: Immediately

BACKGROUND:

The National Advisory Health Council on December 3, 1965, recommended to the Surgeon General as follows:

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

The Surgeon General accepted the recommendation of the Council and instructed the Grants Policy Officer to develop implementing procedures for research and research training grants.

STATEMENT OF POLICY:

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

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PROCEDURE:

The above policy becomes effective immediately and will be incorporated in all PHS research and research training grant regulations and research and research training policy statements as soon as possible. In the meantime, the attached memorandum from the Surgeon General explains the policy to grantee institutions.

The PHS staff who administer the initial review of applications for clinical research and investigation involving human beings (including the administrative review for continuation applications) shall ascertain that each application includes the information required by this policy and shall obtain this information, if necessary, in a document signed by both the principal investigator or program director and the official authorized to sign for the institution.

Attachment

ORIGINATING OFFICE: The Surgeon General, Public Health Service

APPROVED BY: Grants Policy Officer, OSG

Ernest M. Allen

Date: 2/8/66

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Human Subjects: Clinical Investigations

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
9000 ROCKVILLE PIKE
BETHESDA, MD. 20014

July 1, 1966

TO : Heads of Institutions Receiving Public Health Service Grants

FROM : Surgeon General, Public Health Service

SUBJECT: Revised procedure on clinical research and investigation involving human subjects

On February 8, 1966, I issued a policy statement relating to investigations involving human beings, including clinical research, pointing out the need for group review to protect the rights and welfare of the human subjects involved. The original policy involved only the support of research and research training. The application of this policy has been extended to all grants and awards of the Public Health Service in the support of research, training, or demonstration projects, including the projects supported through general research support and those of fellows and trainees. The policy is not applicable to grants in support of construction, alterations, renovations, or research resources -- it is obviously applicable to the Public Health Service projects using these facilities and resources.

Experience gained in administering this policy has led to revision and simplification of procedure. The major procedural revision is one for making agreements between each grantee institution and the Public Health Service which will obviate the necessity for providing detailed assurance with each application. Attached to this memorandum is a statement of revised policy and procedure (Policy and Procedure Order 129) which has been issued at my instruction.

The Public Health Service will continue its study of the issues of investigations involving human subjects. As experience shows the need for revised or augmented policy or procedures, these will be developed. I shall be pleased to receive suggestions and information from officials and investigators of grantee institutions to assist the Service in the conduct of its study.

I trust that these revisions, reflective of the advice I have received from many of you, will facilitate your discharge of this important obligation.

William H. Stewart

William H. Stewart, M.D

Attachment

U. S. Public Health Service
Division of Research Grants
Bethesda, Maryland 20014

PPO #129, Revised
POLICY
July 1, 1966

SUBJECT : Investigations Involving Human Subjects, including Clinical Research: Requirements for Review to Insure the Rights and Welfare of Individuals

APPLICABILITY : All Public Health Service Grants and Awards

EFFECTIVE DATE: Immediately

SUPERSEDES : PPO #129, February 8, 1966
PPO #129 Supplement, April 7, 1966

I. BACKGROUND:

Culminating several years of study by various Public Health Service staff and advisory groups, the National Advisory Health Council passed the following resolution on December 3, 1965:

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

II. POLICY:

The Surgeon General accepted the resolution of the National Advisory Health Council and promulgated the following policy statement on February 8, 1966:

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

III. REVISED POLICY:

By decision of the Surgeon General, the application of this policy has been extended to all grants and awards of the Public Health Service in the support of research, training, or demonstration projects, including the projects supported through general research support and those of fellows and trainees. The policy is not applicable to grants in support of construction, alterations, renovations, or research resources -- it is obviously applicable to the PHS projects using these facilities and resources.

This policy will be included in all pertinent grant program policy and instruction statements, and will be among the conditions of award agreed upon by grantee institutions and the Public Health Service. The policy applies to all investigations involving human subjects, including clinical research.

A. Assignment of Responsibility

Safeguarding the rights and welfare of human subjects involved in research support by PHS grants is the responsibility of the institution to which the grant is awarded. The institution must assure the Public Health Service that in the case of investigations and activities supported directly by the PHS, it will provide group review and decision, maintain surveillance, and provide advice for investigators on safeguarding the rights and welfare of human subjects. The institution also has the responsibility to provide whatever professional attention or facilities may be required for the safety and well-being of human subjects. The institution shall be responsible for developing the administrative mechanism for review, surveillance, and advice; however, the PHS requires that, prior to inception of each course of investigation, objective decisions be made on the three points cited in the Surgeon General's policy statement (above) by an appropriate committee of associates of the investigator having no vested interest in the specific project involved. The grantee institution may utilize staff, consultants, or both to carry out the review. Any group responsible for review should possess not only specific scientific competence to comprehend the scientific content of the investigations reviewed, but also other competencies pertinent to the judgments that need to be made.

The grantee is required to make and keep written records of the group reviews and decisions on the use of human subjects and to obtain and keep documentary evidence of informed consent relating to investigations carried out with the assistance of PHS financial support.

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B. Timing of Review

While this policy requires that review be conducted prior to the use of human beings as subjects, there are advantages to both the PHS and the grantee in having the review conducted prior to application for PHS support. The PHS encourages the institution to do so, if the review can be accomplished without causing unreasonable delay in the application process and if the application is of the type that normally contains a reviewable scientific protocol.

IV. PROCEDURAL REVISIONS -- ASSURANCES OF APPLICANTS AND GRANTEES:

Upon issuance of this policy statement, the PHS will require necessary assurances from the grantee institutions which sponsor investigations involving human subjects, including clinical research. These assurances will cover both the general principles of safeguarding human rights and welfare in the conduct of research and the specific points of the Surgeon General's policy. The assurance should provide explicit information on the policy and procedure it employs for review and decision on the propriety of plans of research involving human subjects. The descriptions will include the competencies represented in the committees of associates utilized for review, the sources of consultants (if used), the administrative mechanisms by which surveillance is provided for projects involving human subjects -- particularly to deal with changes in protocol or emergent problems of investigations, the means of guidance and advice provided for investigators, and the manner in which the institution will assure itself that the advice of the committee of associates will be followed. Copies of documents of institutional policies on these issues should be attached to the memorandum of assurance. An example of an acceptable assurance is attached.

Assurances can be provided which apply only to individual major components of universities or other large institutions in those instances where assurances covering the total institution are impracticable or inadvisable.

Each assurance and its attachments shall be transmitted to the Public Health Service, in care of the Chief, Division of Research Grants. When the Public Health Service has reviewed and accepted the assurance, the Chief, Division of Research Grants, shall so notify both the responsible official of the grantee institution involved and all Public Health Service extramural research program offices.

Each grantee institution shall report currently any changes in its policies, its procedures, or the competencies represented on its committee of associates.

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For each application that includes or is likely to include investigations involving human subjects, including clinical research, the applicant institution should make reference to the certification as follows:

> "The investigations encompassed by this application have been or will be approved by the committee of associates of the investigator(s) in accordance with this institution's assurance on clinical research dated _____."

Until an institution-wide assurance has been accepted by the PHS, the institution can fulfill requirements of this policy for individual studies by submitting an assurance with each application for PHS financial support, stating that prior to inception of investigations, the requirements of section III. A. of this Policy and Procedure Order will be followed. The statement must also describe the composition of the group which will conduct the review.

This interim procedure will be acceptable until November 1, 1966. After that date no new, supplemental, renewal, or continuation application for a Public Health Service grant or award to support investigations involving human subjects will be accepted for review unless the PHS has approved an institution-wide assurance.

Nothing in the institution-wide assurance or in the interim policy procedure used in some cases until November 1, 1966, should inhibit PHS staff, advisory groups, or consultants (1) from identifying concern for the welfare of human subjects, and communicating this concern to the grantee institution, or (2) from recommending disapproval of the application if the gravity of the hazards and risks so indicate.

In the case of awards to U.S. citizens receiving fellowships for training abroad, special conditions or circumstances relating to the place at which the training is being provided may upon occasion justify modification of these requirements. Requests from the sponsor for approval of such modifications must be reviewed by the Office of International Research, NIH, and approved by the PHS bureau chief concerned.

Attachment

ORIGINATING OFFICE: Office of the Surgeon General, PHS

APPROVED BY: Grants Policy Officer, OSG

Edwin A. Allen

Date: July 1, 1966

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Individuals, Rights and Welfare of