SURGEON GENERAL'S DIRECTIVES ON HUMAN EXPERIMENTATION

THE Surgeon General, Public Health Service, United States Department of Health, Education, and Welfare, has issued the following directives concerning research and investigation involving human subjects in institutions receiving Public Health Service grants:

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 investigaiton 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, M.D.

Attachment

PPO #129, Revised
POLICY
July 1, 1966

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

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 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.

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 protocal or emergent problems of investigations, the means of guidance and advice provided for in-

vestigators, 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.

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
Ernest M. Allen
Date: July 1, 1966

Index: Clinical Research
Human Subjects, Investigations Involving
Individual, Rights and Welfare of

EXAMPLE OF AN ACCEPTABLE ASSURANCE

Institutional Assurance on Investigations Involving Human Subjects, Including Clinical Research

The (name of institution) agrees with the principles of the Public Health Service policy (identified as Policy and Procedure Order 129 dated July 1, 1966) with regard to investigations involving human subjects, including clinical research. This institution agrees that review independent of the investigator is necessary to safeguard the rights and welfare of human subjects of research investigations and assures the Public Health Service that it will establish and maintain advisory groups competent to review plans of investigation involving human subjects, prior to initiation of investigations, to insure adequate safeguard. Group reviews and decisions will be carried out in reference to (1) the rights and welfare of the individuals involved, (2) the appropriateness of the methods used to obtain informed consent, and (3) the risks and potential medical benefits of the investigations.

The institution also agrees to exercise surveillance of PHS-supported projects using human subjects for changes in protocol which may alter the investigational situation with regard to the criteria cited above. The institution further assures the Public Health Service that it will provide advice and consultation to investigators on matters of employing human subjects in investigation, and also that it will provide whatever professional attention or facilities may be required to safeguard the rights and welfare of human subjects involved in investigation. Records of group review and decision on the use of human subjects and of informed consent will be developed and kept by the institution.

Attached as part of this statement are copies of policy and procedure of this institution with regard to use of human subjects in investigation, as well as a description of the groups utilized to review projects for enforcement of these policies and the manner in which the institution will assure itself that the advice of the committee of associates is followed.

Signature:
Title:
Date:

Attachments

. . .

December 12, 1966

TO: Heads of Institutions Receiving Public Health Service Grants

FROM: Surgeon General, Public Health Service

SUBJECT: Clarification of procedure on clinical research and investigation involving human subjects

The attached report of December 12, 1966, on the above subject, is to clarify issues raised by Public Health Service grantees and staff since the issuance by this office of PPO #129, Revised, dated July 1, 1966, subject: "Investigations Involving Human Subjects, Including Clinical Research: Requirements for Review to Insure the Rights and Welfare of Individuals."

This policy refers to all investigations that involve human subjects, including investigations in the behavioral and social sciences. It does not reflect a change in policy, but is a clarification only of the current policy for the use of grantees.

William H. Stewart, M.D.

Attachment

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

December 12, 1966

SUBJECT: Investigations Involving Human Subjects, Including Clinical Research: Requirements for Review of Insure the Rights and Welfare of Individuals: *Clarification*

APPLICABILITY: All PHS Grants and Awards

REFERENCE: PPO #129, Revised, July 1, 1966

This report is to clarify issues raised by PHS grantees and staff regarding the meaning of the requirements of PPO #129, Revised, July 1, 1966, subject: "Investigations Involving Human Subjects, Including Clinical Research: Requirements for Review to Insure the Rights and Welfare of Individuals."

This policy refers to all investigations that involve human subjects, including investigations in the behavioral and social sciences. The grantee institution is responsible for assuring that the investigations are in accord with the laws of the community in which the investigations are conducted and for giving due consideration to pertinent ethical issues. Appropriate groups of associates within the institution, and outside consultants if needed, are to be utilized to provide the necessary review. Institutions may designate separate groups in order to assure competence and independence of review for particular areas.

The principles of this policy apply most directly and comprehensively in those instances of social, behavioral, and medical science investigations where a procedure may induce in the subject an altered state or condition potentially harmful to his personal welfare. Surgical procedures, the administration of drugs, the requirement of strenuous physical exertion, and participation in psychologically or socially harmful activities are examples of experimental arrangements which require thorough scrutiny by institutional review groups. Such procedures require continuing overview and full documentation for the record.

Aside from the above types of procedures, there is a large range of social and behavioral research in which no personal risk to the subject is involved. In these circumstances, regardless of whether the investigation is classified as behavioral, social,

medical, or other, the issues of concern are the fully voluntary nature of the participation of the subject, the maintenance of confidentiality of information obtained from the subject, and the protection of the subject from misuse of the findings. For example, a major class of procedures in the social and behavioral sciences does no more than observe or elicit information about the subject's status, by means of administration of tests, inventories, questionnaires, or surveys of personality or background. In such instances, the ethical considerations of voluntary participation, confidentiality, and propriety in use of the findings are the most generally relevant ones. However, such procedures may in many instances not require the fully informed consent of the subject or even his knowledgeable participation. In such instances full and specific documentation is necessary for the record.

Many investigations in the social and behavioral sciences involve procedures designed to alter the status of the individual as, for example, studies of human learning, social perception, or group effectiveness. In such research the effects, if any, on the subject may be transitory or even more or less permanent, but they must be judged clearly not to be harmful or not to involve the risk of harm.

Whatever the nature of the investigation, the concern for the protection of the subject and for the assurance of voluntary participation becomes most critical when the subject is not of age or competence to make an adequate judgment in his own behalf.

These are only some examples of issues which may arise. The fundamental point is that every project must be considered on an individual basis to clarify which, if any, such issues are present and to insure that these are adequately resolved by the specific design of its procedures. For this reason, it is essential that the grantee institution be responsible for the clarification and resolution of all ethical and other pertinent issues. The appropriate mechanism for this purpose is the utilization of groups of associates, established at the institution to provide competent, independent review. Based on its knowledgeable scrutiny of the specifics of the investigation involved, such a review group can decide which issues are germane and ascertain the adequacy of provisions for protecting the rights and welfare of human subjects in research, the appropriateness of the methods used to secure informed consent, and the risks and potential benefits of the investigation.

ORIGINATING OFFICE: Office of the Director, Division of Research Grants

APPROVED BY: Grants Policy Officer, OSG
Ernest M. Allen
Date: 12/15/66

Index: Clinical Research
Human Subjects: Behavioral Investigations
Clinical Investigations
Medical Science Investigations
Social Science Investigations

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TO: Heads of Institutions Receiving Public Health Service Grants

FROM: Director, Office of Extramural Programs, OSG

SUBJECT: Institutional assurances relating to investigations involving human subjects

On July 1, 1966, Dr. William H. Stewart, Surgeon General, Public Health Service, issued PPO #129, Revised; Subject: Revised procedure on clinical research and investigation involving human subjects. Among the procedural revisions was the statement, on page 4, that each application including or likely to include investigations involving human subjects, including clinical research, must refer to the institution's assurance 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 ———.

Since the normal processing of each application routinely includes the verification of this acceptance, the application itself no longer needs to include this reference. Accordingly, printed on the reverse side of this memorandum is a revised page 4 to the July 1, 1966 document. The revised page 4 deletes the first two paragraphs of page 4, PPO #129, Revised, July 1, 1966, and eliminates the reference to the interim procedure which is no longer effective.

Ernest M. Allen, Sc.D.

(To be substituted for page 4, PPO #129, Revised, July 1, 1966)

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 this institution-wide assurance should inhibit PHS staff, advisory groups, or consultants from (1) identifying concern for the welfare of human subjects, and communicating this concern to the grantee institution, or (2) recommending disapproval of the application if the gravity of the hazards and risks so indicate.

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.

ORIGINATING OFFICE: Office of the Surgeon General, PHS

APPROVED BY: Director, Office of Extramural Programs, OSG
Ernest M. Allen
Date: 1/24/67

Index: Clinical Research
Human Subjects, Investigations Involving
Individuals, Rights and Welfare of