U.S. DEPARTMENT OF TRANSPORTATION

NATIONAL HIGHWAY TRAFFIC SAFETY ADMINISTRATION

ORDER 700-1	
DATE OF ISSUANCE November 4, 1981	OPI: NRD-10

SUBJECT: Protection of the Rights and Welfare of Human Subjects in NHTSA-Sponsored Experiments

PARAGRAPH:

1. PURPOSE. This Order establishes policy and procedures to ensure the protection of human subjects involved in NHTSA-sponsored experiments in the United States and abroad.

2. EFFECT ON OTHER DIRECTIVES. NHTSA Order 700-l dated April 24, 1979 (Subject: Protection of the Rights and Welfare of Human Subjects Involved in NHTSA-Sponsored Experiments), is superseded.

3. BACKGROUND. As a result of growing concern over the rights of human subjects, the Department of Health, Education and Welfare (DHEW) issued regulations in 1976 to protect the rights and welfare of human volunteer subjects participating in research funded by DHEW. In order to protect the rights of subjects involved in NHTSA research and to fulfill Government obligations, this Order establishes NHTSA policy and procedures for the use of human subjects in NHTSA-sponsored experiments. These policies and procedures are closely patterned on the DHEW guidelines.

4. REFERENCES. ,

a. NHTSA Order 700-3, dated June 30, 1980, "Human Use Review Panel."

b. NHTSA Order 700-4, dated April 24, 1979, "Ethical Use of Human Surrogates in NHTSA-Sponsored Experiments."

Vertical lines denote change,

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5. DEFINITIONS.

a. "Subject at risk" means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

b. "Informed consent" means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. The basic elements of information necessary to such consent include:

(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental,

(2) A description of any attendant discomforts and risks reasonably to be expected,

(3) A description of any benefits to the subject or to society reasonably to be expected,

(4) A disclosure of any appropriate alternative procedures that might be advantageous for the subject,

(5) An offer to answer any inquiries concerning the procedures,

(6) An instruction that the person is free to withdraw his consent and to discontinue participation in the project at any time without prejudice to the subject,

(7) With respect to biomedical or behavioral research which may result in physical injury, an explanation as to the medical treatment available,

(8) With respect to biomedical or behavioral research which may result in physical injury, an explanation of the institution's applicable provisions, if any, for compensation for such injury.

(9) A statement that new information developed during the course of the research which my affect the subject's willingness to continue participation will be provided to the subject, and

(10) A statement describing the extent to which confidentiality of records identifying the subject will be maintained.

c. "Risk/Benefit Analysis" is an evaluation in which the person responsible for the conduct of the program presents his/her assessment of whether or not a proposed program involves subjects at risk. In the event subjects at risk are involved, the risk/benefit analysis includes the evaluator's judgment on the extent of the predictable risk to the human subject and the extent of the benefits to be derived fran conducting the program. The evaluator should also weigh the ham to society which might result fran not conducting the proposed program. Judgment on risk versus benefit should be consistent with contemporary public ethics and standards.

6. POLICY. It is the policy of NHTSA that:

a. Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from NHTSA is primarily the responsibility of the institution which receives or is accountable to NHTSA for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, no activity involving human subjects to be supported by NHTSA grants or contracts shall be undertaken unless an Institutional Review Board (IRB) (See 45 CFR Sec. 46.106(b)) or Human Use Review Panel (HURP) (See Order 700-3) has reviewed and approved such activity, and the institution or HURP has submitted to NHTSA a certification of such review and approval, in accordance with the requirements of this order, and 45 CFR Secs. 46.103 through 46.114.

(1) This review shall determine whether these subjects will be placed at risk, and, if risk is involved, whether:

(a) The risks to the subject are so outweighed by the sum ofthebenefittothe subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks:

(b) The rights and welfare of any such subjects will be adeguately protected: and

(c) Legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of this part.

(2) Where the IRB finds risk is involved, it shall review the conduct of the activity at timely intervals.

b. No grant or contract involving human subjects at risk be made to an individual unless he is affiliated with or sponsored by an institution which can and does assume responsibility for the subjects involved.

c. All NHTSA-sponsored programs involving human subjects be conducted in general accordance with procedures for the submission of assurances, established by DHEW in 45 CFR §§46.103 through 46.122 (see Appendix E). For purposes of this order, the designation "NHTSA" shall be substituted for "DHEW" wherever that term appears in sections 46.103 through 46.122, and

d. The Request for Proposals (RFP) for projects involving human subjects at risk and the Risk/Benefit Analysis be reviewed and concurred with by the HURP to ensure that the NHTSA and DHEW guidelines are followed.

7. RESPONSIBILITIES.

a. The Contract Technical Manager is responsible for:

(1) Indicating on HS Form 436, on the statement of work, and in the "Remarks" section of HS Form 112, "Procurement Initiation and Coordination" that the particular project involves the use of human subjects.

(2) Requesting that the HURP determine whether the project involves human subjects at risk.

(3) Preparation of the Risk/Benefit Analysis (see Appendix B) if any human subjects at risk are expected to be involved in the test activities.

(4) The nature of the risk to human subjects and the procedures developed to deal with that risk must be described in the Contractor's proposal. The Human Experimentation Considerations (see Appendix A) and NHTSA policy statement will be used to assist in this effort. The information required fran the Contractor shall be defined in the statement of work. The Contractor's proposed method of compliance with these procedures shall become part of the contract.

(5) Obtaining Branch Head, Division Chief, Office Director, and Associate Administrator approval for any study involving human subjects at risk (see Appendix C).

(6) Evaluation of the Contractor's procedures to protect the rights and welfare of human subjects at risk.

(7) Determining that any assurances needed are submitted and satisfactory. The HURP may be requested to assist in this process.

(8) Assuring that before work on the project commences an IRB, meeting DHEW and NHTSA guidelines, has approved the project.

(9) Monitoring of the Contractor's performance in providing protection for human subjects at risk.

(10) Assuring that the contractor submits immediate, monthly, and end of contract reports of any real or claimed injuries or unexpected results affecting the assessment of risk.

(11) Obtaining annual assurances that the Contractor is complying with approved procedures for the protection of human subjects.

(12) Advising the HURP of any injuries or unexpected results affecting the assessment of risk and requesting Associate Administrator and Chief Counsel approval for any changes in protocol which may affect the risk to subjects.

(13) Halting the project and notifying the HURP when results indicate that further research is unnecessary, inappropriate, or would expose subjects to greater than anticipated levels of risk.

b. In-house researchers are responsible for :

(1) Indicating on the research request whether the particular project involves human subjects.

(2) Requesting that the HURP determine whether the project involves human subjects at risk.

(3) If human subjects at risk are involved, preparation of the Risk/Benefit Analysis (see Appendix B).

(4) Obtaining Branch Head, Division Chief, Office Director, and

Associate Administrator approval for any study involving human subjects at risk.

(5) Assuring that before work on the project begins, an IRB, meeting DHEW and NHTSA requirements, has approved the project.

(6) Ensuring that informed consent guidelines are adhered to.

(7) Advising the HURP of any injuries or unexpected results affecting the assessemnt of risk and requesting Associate Administrator and Chief Counsel approval for any changes in protocol which may affect the risk to subjects.

(8) Halting the project and notifying the HURP when results indicate that further research is unnecessary, inappropriate, or would expose subjects to greater than anticipated levels of risk.

c. The HURP is responsible for:

(1) Reviewing the project and advising the Associate Administrator, whether a project involves human subjects at risk.

(2) On request of the Associate Administrator or his designee, advising the Contract Technical Manager in the preparation of the Risk/Benefit Analysis.

(3) Reviewing all projects involving human subjects at risk and recommending to the Associate Administrator approval, disapproval, or approval with modifications.

(4) Monitoring ongoing projects at the request of the Associate Administrator.

(5) Reviewing incidences of injuries or unexpected results affecting the assessment of risk, and changes in protocol, in a timely fashion, and assuring that the Associate Administrator, and the Chief Counsel are informed.

'd. The Contracting Officer is responsible for:

(1) The inclusion of an appropriate clause in contracts involving human subjects at risk that insures the protection of the subjects' rights and welfare (see Appendix D).

(2) Assuring that in any contract involving human subjects at risk an approved Risk/Benefit Analysis is included.

Vertical line denotes change.

(3) Assuring that NHTSA human use guidelines are followed.

(4) Assuring that prospective contractors submit examples of their informed consent forms.

e. The Associate Administrator is responsible for:

(1) Approving or disapproving the HURP's recommendations regarding the involvement of human subjects at risk.

(2) Reviewing the Risk/Benefit Analysis.

(3) Requesting review by the HURP of all projects involving human subjects.

(4) Approving or disapproving all projects involving human subjects at risk, and approving modifications to procedures during the course of the projects.

f. The Chief Counsel is responsible for approving or disapproving all projects involving human subjects at risk, and approving modifications to procedures during the course of the projects.

8. PROCEDURES. Listed below are the step-by-step procedures to be followed for projects involving human subjects to assure that the subjects' rights and welfare are protected.

a. The Contract Technical Manager or in-house researcher indicates whether a project involves human subjects.

b. The HURP determines, with the approval of the Associate Administrator, whether the project involves human subjects at risk.

c. The Contract Technical Manager or in-house researcher reviews the Human Experimentation Guidelines to become aware of considerations involved with human subjects at risk (see Appendix A).

d. The Contract Technical Manager or in-house researcher prepares a Risk/Benefit Analysis for the project. The Contract Technical Manager also prepares the contract work statement which includes a requirement for each bidder to present his/her procedures for protection of human subjects at risk including a copy of the Contractor's informed consent form.

e. The HURP reviews all projects involving human subjects at risk and makes appropriate recommendations to the Associate Administrator.

f. The Associate Administrator approves or disapproves the project. If the Associate Administrator approves a project involving human subjects at risk, he shall forward the project to the Chief Counsel for his approval.

g. The Chief Counsel approves or disapproves the project.

h. The prospective contractors submit their proposals, which include the proposed procedures and assurances for protection of human subjects at risk. In-house researchers submit their procedures for the protection of human subjects at risk directly to the HURP.

i. The Proposal Evaluation Committee evaluates the Contractor's proposals for protection of human subjects at risk. The HURP reviews those sections of acceptable contractor proposals which concern the protection of human subjects, if requested by the Associate Administrator responsible for the project. The HURP may recommend to the Associate Administrator approval, disapproval, or approval with change. In the event that changes are required in human use procedures and assurances, the HURP shall give guidance in the types of changes necessary. The HURP shall also review in-house proposals for human use procedures.

j. The Contracting Officer includes a compliance agreement (see Appendix D) in the contract. The HURP advises the Contracting Officer during the negotiation process as required.

k. The Contract Technical Manager or in-house researcher monitors the project, conducts a continuing review of human use procedures and advises the Associate Administrator and the Chief Counsel of any significant changes in the procedures. The Associate Administrator and the Chief Counsel approve or disapprove the changes. The Contract Technical Manager also reviews program progress and notifies the HURP of any injuries or unexpected results affecting the assessment of risk.

1. The Contract Technical Manager obtains from the Contractor the annual assurances required by paragraph 7a.(9), and includes these assurances and other documentation of internal review and approval of the project in the project file.

Vertical line denotes change.

9. APPENDICES. The procedures established by this Order require the use of certain documents. These documents are appended as follows:

a. Appendix A -- Human Experimentation Considerations

b. Appendix B -- Risk/Benefit Analysis Form

c. Appendix C -- Coordination Form (HS Form 436)

d. Appendix D -- Protection of Human Subjects Compliance Clause (#41)

e. Appendix E -- DHEW Guidelines

Joan Claybrook
Administrator

Attachments

APPENDIXA

Human Experimentation: Factors To Be Considered

These considerations indicate the most important questions which must be addressed in conducting programs involving human subjects at risk. Given the nature of the particular project, it may be the case that certain portions of the considerations are relevant/applicable at one stage of the research, e.g., preparation of the work statement, while others may become relevant only when certain levels of knowledge are reached. The Contract Technical Manager is thus advised to refer to the considerations at several time points in the life of the contract.

Appendix A
NHTSA Order 700-l
August 11, 1980

Considerations for the Preparation of Risk/Benefit Analyses

1. What is the nature and degree of risk to the subject involved (physical, medical, legal, psychological, social)?

2. Has equipment to be used been man-rated? By whom?

3. If drugs are involved, have they been approved for human use and experimentation by DHEW or an element of DHEW?

4. Are the proposed procedures adequate for minimizing risk to the subject?

5. What safeguards or alternate procedures can be employed to reduce risk to the subjects?

6. Are there other methods available to provide the desired information or data?

7. Will the people conducting the experiments be qualified scientifically and technically.

8. What are the benefits? How important are they?

9. Is the risk outweighed by the expected benefits?

10. Will the results be published and/or made generally available to the public and the scientific camunity?

Considerations for the Preparation and/or Evaluation of Test Protocol

1. What are the criteria for the selection of human subjects?

2. Will the subjects be given adequate physical and psychological evaluations by qualified personnel prior to or during the selection process?

3. Will the subjects receive medical and/or psychological mnitoring during the experiments?

4. What post-test physical/psychological exams and/or monitoring will be performed?

5. Are there trained medical personnel and adequate medical equipment for emergency treatment.

6. Will the procedures for emergency treatment and/or evaluation be satisfactory? Will periodic practice drills be conducted?

7. Will the tests be conducted usirq a "stepped-severity" system to contro1 the exposures of each subject (for example, progressively increasing of loads, velocities, dosages, etc.)?

8. Are there adequate safeguards or procedures to reduce the elements of risk?

9. Are there alternate methods or procedures to get the desired results which would reduce or eliminate the elements of risk?

Considerations for the Protection of the Rights of the Subjects

1. Has the Contractor established an Institutional Review Board, meeting DHEW/NHTSA requirements? (See Appendix E.)

2. Will the subjectsbe selected without bias regarding race, creed, sex, ornational originunless such criteria are required by the nature of the study?

3. Will any payment or inducment to the subjects be involved, and if so, what will be the scope of the payment or inducement?

4. Will the payment be likely to induce the subjects into taking undue risk because of financial or other need?

5. Have provisions been made to secure an "informed consent" in writing?

6. What are the plans andprovisions to insure confidentiality and anonymityofsubjectsand information obtained from or about subjects in accordance with the provisions of the Privacy Act of 1974 (Public Law 93-579)?

7. Will the subjects be given advance information and be adequately briefed on:

   a. Objectives of the test?

   b. The risks involved (physical, psychological, social, legal)?

   c. The physical and mental discomforts which may be encountered?

   d. The nature and extent of medical. supervision and emergency medical treatment and procedures?

   e. Their right to decline or to withdraw from participation at any time without prejudice?

f. Their right to ask questions at all times without prejudice to themselves?

g. Provisions for medical treatment and compensation in case of injury?

8. What are the plans for periodic review of the project?

9. Does the contractor have adequate means of determining whether subjects understand the risk involved?

APPENDIX B

Risk Benefit Analysis Form
Projects Involving Human Subjects

Contract No.:

Contract Title:

A. Description of project requirements:

B. Description of risks:

C. Analysis of benefits:

CTM _____ DATE _____

U.S. DEPARTMENT OF TRANSPORTATION
NATIONAL HIGHWAY TRAFFIC SAFETY ADMINISTRATION

PROJECTS INVOLVING HUMAN SUBJECTS AT RISK

(Coordination Form)

CONTRACT TITLE	CONTRACT NO.

	RISK/BENEFIT ANALYSIS		DATE	INITIALS
	Approved	Not Approved		
CONTRACT TECHNICAL MANAGER				
BRANCH HEAD				
DIVISION CHIEF				
OFFICE DIRECTOR				

HUMAN SUBJECTS INVOLVED ☐ YES ☐ NO

HUMAN SUBJECTS AT RISK ☐ YES ☐ NO

Chairman, HURP* _____ Date _____

Associate Administrator _____ Date _____

RECOMMENDATION BY HURP* REGARDING ACCEPTABILITY OF PROVISIONS FOR THE PROTECTION OF HUMAN SUBJECTS AT RISK.

☐ APPROVED

☐ DISAPPROVED

☐ APPROVED WITH ATTACHED MODIFICATIONS

Chairman, HURP* _____ Date _____

RULING BY ASSOCIATE ADMINISTRATOR REGARDING ACCEPTABILITY OF THE PROJECT AND PROVISIONS FOR THE PROTECTION OF HUMAN SUBJECTS AT RISK.

☐ APPROVED

☐ DISAPPROVED

☐ APPROVED PROVIDED ATTACHED MODIFICATIONS ARE IMPLEMENTED TO THE SATISFACTION OF THE HURP*

Associate Administrator _____ Date _____

RULING BY THE CHIEF COUNSEL REGARDING ACCEPTABILITY OF THE PROJECT AND PROVISIONS FOR THE PROTECTION OF HUMAN SUBJECTS AT RISK.

☐ APPROVED

☐ DISAPPROVED

☐ APPROVED PROVIDED ATTACHED MODIFICATIONS ARE IMPLEMENTED TO THE SATISFACTION OF THE HURP*

Chief Counsel _____ Date _____

* Human Use Review Panel

U.S. DEPARTMENT OF TRANSPORTATION
NATIONAL HIGHWAY TRAFFIC SAFETY ADMINISTRATION

PROJECTS INVOLVING HUMAN SUBJECTS AT RISK

(Coordination Form)

CONTRACT TITLE	CONTRACT NO.

	RISK/BENEFIT ANALYSIS		DATE	INITIALS
	Approved	Not Approved		
CONTRACT TECHNICAL MANAGER				
BRANCH HEAD				
DIVISION CHIEF				
OFFICE DIRECTOR				

HUMAN SUBJECTS INVOLVED ☐ YES ☐ NO

HUMAN SUBJECTS AT RISK ☐ YES ☐ NO

Chairman, HURP* _____ Date _____

Associate Administrator _____ Date _____

RECOMMENDATION BY HURP* REGARDING ACCEPTABILITY OF PROVISIONS FOR THE PROTECTION OF HUMAN SUBJECTS AT RISK.

☐ APPROVED

☐ DISAPPROVED

☐ APPROVED WITH ATTACHED MODIFICATIONS

Chairman, HURP* _____ Date _____

RULING BY ASSOCIATE ADMINISTRATOR REGARDING ACCEPTABILITY OF THE PROJECT AND PROVISIONS FOR THE PROTECTION OF HUMAN SUBJECTS AT RISK.

☐ APPROVED

☐ DISAPPROVED

☐ APPROVED PROVIDED ATTACHED MODIFICATIONS ARE IMPLEMENTED TO THE SATISFACTION OF THE HURP*

Associate Administrator _____ Date _____

RULING BY THE CHIEF COUNSEL REGARDING ACCEPTABILITY OF THE PROJECT AND PROVISIONS FOR THE PROTECTION OF HUMAN SUBJECTS AT RISK.

☐ APPROVED

☐ DISAPPROVED

☐ APPROVED PROVIDED ATTACHED MODIFICATIONS ARE IMPLEMENTED TO THE SATISFACTION OF THE HURP*

Chief Counsel _____ Date _____

* Human Use Review Panel

APPENDIX D

Protection of Human Subjects Canpliance Clause (#41)

The contractor will comply with the NHTSA policies and procedures for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts fra NHTSA, including the procedures for submission of assurances described in 45 CFR Secs. 46.103 through 46.122. Where the contractor has on file with the Department of Health, Education and Welfare a general assurance approved in accordancewith 45 CFR Sec. 46.108, additional assurances need not be submitted to NHTSA. In fulfillment of its assurance:

An Institutional Review Board meeting the requirements of 45 CFR Sec. 46.106(h) will be utilized by the contractor.

The Institutional Review Board will be assigned responsibility to determine for each activityas planned and conducted that:

The rights and welfare of subjects are adequately protected. The risks to subjects are outweighed by potential benefits. The informed consent of subjects will be obtained in writing by methods that are adequate and appropriate.

Institutional Review Board reviews are to be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded fran reviews of projects or activities in which they have an active role or a conflict of interests.

Continuing constructive communication between the Institutional Review Board and the project directors must be maintained as a means of safeguarding the rights and welfare of subjects.

The institution which administers the Institutional Review Board will maintain records of Institutional Review Board reviews of applications and active projects, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects. Detailed records shall be maintained of the circumstances of any unexpected results or injuries, and shall be provided upon request to the Institutional Review Board and the Contract Technical Manager. Unexpected results and injuries and changes in protocol which may affect the risk to subjects shall be immediately called to the attention of the Institutional Review Board and the Contract Technical Manager before proceedingwiththe experiment.

Facilities and professional attention required for subjects who may suffer injury as a result of participation in an activity will be provided.

Periodic reviews will be conducted by the contractor to assure, through appropriate administrative overview, that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied.

§ 46.103 Definitions.

(a) "Institution" means any public or private institution or agency (including Federal, State, and local government agencies).

(b) "Subject at risk" [1] means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

(c) "Informed consent" means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. The basic elements of information necessary to such consent include:

(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

(2) A description of any attendant discomforts and risks reasonably to be expected;

(3) A description of any benefits reasonably to be expected;

(4) A disclosure of any appropriate alternative procedures that might be advantageous for the subject;

(5) An offer to answer any inquiries concerning the procedures;

(6) An instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject; and

(7) With respect to biomedical or behavioral research which may result in physical injury, an explanation as to whether compensation and medical treatment is available if physical injury occurs and, if so, what it consists of or where further information may be obtained. This subparagraph will apply to research conducted abroad in collaboration with foreign governments or international organizations absent the explicit nonconcurrence of those governments or organizations.

(d) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(e) "DHEW" means the Department of Health, Education, and Welfare.

(f) "Approved assurance" means a document that fulfills the requirements of this part and is approved by the Secretary.

(g) "Certification" means the official institutional notification to DHEW in accordance with the requirements of this part that a project or activity involving human subjects at risk has been reviewed and approved by the institution in accordance with the "approved assurance" on file at DHEW.

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

[40 FR 11854, Mar. 13, 1975. Redesignated at 40 FR 33528, Aug. 8, 1975. Amended at 43 FR 51559, Nov. 3, 1978]

§ 16.101 Submission of assurances.

(a) Recipients or prospective recipients of DHEW support under a grant or contract involving subjects at risk shall provide written assurance acceptable to DHEW that they will comply with DHEW policy as set forth in this part. Each assurance shall embody a statement of compliance with DHEW requirements for initial and continuing Institutional Review Board review of the supported activities; a set of implementing guidelines, including identification of the Board and a description of its review procedures; or, in the case of special assurances concerned with single activities or projects, a report of initial findings of the Board and of its proposed continuing review procedures.

(b) Such 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 part, and shall be filed in such form and manner as the Secretary may require.

§ 46.105 Types of assurances.

(a) *General assurances.* A general assurance describes the review and implementation procedures applicable to all DHEW-supported activities conducted by an institution regardless of the number, location, or types of its components or field activities. General assurances will be required from institutions having a significant number of concurrent DHEW-supported projects or activities involving human subjects.

(b) *Special assurances.* A special assurance will, as a rule, describe those review and implementation procedures applicable to a single activity or project. A special assurance will not be solicited or accepted from an institution which has on file with DHEW an approved general assurance.

§ 46.106 Minimum requirements for general assurances.

General assurances shall be submitted in such form and manner as the Secretary may require. The institution must include, as part of its general assurance, implementing guidelines that specifically provide for:

(a) A statement of principles which will govern the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may include appropriate existing codes or declarations, or statements formulated by the institution itself. It is to be understood that no such principles supersede DHEW policy or applicable law.

(b) An Institutional Review Board or Board structure which will conduct initial and continuing reviews in ac-

[1] See interpretation document at 41 FR 26572, June 28, 1976.

cordance with the policy outlined in § 46.102. Such Board structure or Board shall meet the following requirements:

(1) The Board must be composed of not less than five persons with varying backgrounds to assure complete and adequate review of activities commonly conducted by the institution. The Board must be sufficiently qualified through the maturity, experience, and expertise of its members "The Board must be sufficiently qualified through the maturity, experience, and expertise of its members, and the diversity of the members' racial and cultural backgrounds, to insure respect for its advice and counsel for safeguarding the rights and welfare of human subjects." In addition to possessing the professional competence necessary to review specific activities, the Board must be able to ascertain the acceptability of applications and proposals in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The Board must therefore include persons whose concerns are in these areas.

(2) The Board members shall be identified to DHEW by name; earned degrees, if any; position or occupation; representative capacity; and by other pertinent indications of experience such as board certification, licenses, etc., sufficient to describe each member's chief anticipated contributions to Board deliberations. Any employment or other relationship between each member and the institution shall be identified, i.e., full-time employee, part-time employee, member of governing panel or board, paid consultant, unpaid consultant. Changes in Board membership shall be reported to DHEW in such form and at such times as the Secretary may require.

(3) No Board shall consist entirely of members of only one sex.

(4) No member of a Board shall be involved in either the initial or continuing review of an activity in which he has a conflicting interest, except to provide information requested by the Board.

(5) No Board shall consist entirely of persons who are officers, employees, or agents, of, or are otherwise associated with the institution, apart from their membership on the Board.

(6) No Board shall consist entirely of members of a single professional group.

(7) The quorum of the Board shall be defined, but may in no event be less than a majority of the total membership duly convened to carry out the Board's responsibilities under the terms of the assurance.

(c) Procedures which the institution will follow in its initial and continuing review of applications, proposals, and activities.

(d) Procedures which the Board will follow (1) to provide advice and counsel to activity directors and investigators with regard to the Board's actions, (2) to insure prompt reporting to the Board of proposed changes in an activity and of unanticipated problems involving risk to subjects or others, and (3) to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labeled drugs, or to medical devices, are promptly reported to DHEW.

(e) Procedures which the institution will follow to maintain an active and effective Board and to implement its recommendations.

[40 FR 11854, Mar. 13, 1975. Redesignated at 40 FR 33528, Aug. 8, 1975. Amended at 43 FR 53655 Nov. 3, 1978]

§ 46.107 Minimum requirements for special assurances.

Special assurances shall be submitted in such form and manner as the Secretary may require. An acceptable special assurance shall:

(a) Identify the specific grant or contract involved by its full title; and by the name of the activity or project director, principal investigator, fellow, or other person immediately responsible for the conduct of the activity.

(b) Include a statement, executed by an appropriate institutional official, indicating that the institution has established an Institutional Review Board satisfying the requirements of § 46.106 (b).

(c) Describe the makeup of the Board and the training, experience, and background of its members, as required by § 46.106(b)(2).

(d) Describe in general terms the risks to subjects that the Board recognizes as inherent in the activity, and justify its decision that these risks are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant the Board's decision to permit the subject to accept these risks.

(e) Describe the informed consent procedures to be used and attach documentation as required by § 46.110.

(f) Describe procedures which the Board will follow to insure prompt reporting to the Board of proposed changes in the activity and of any unanticipated problems, involving risks to subjects or others and to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or to medical devices are promptly reported to DHEW.

(g) Indicate at what time intervals the Board will meet to provide for continuing review. Such review must occur no less than annually.

(h) Be signed by the individual members of the Board and be endorsed by an appropriate institutional official.

§ 46.108 Evaluation and disposition of assurances.

(a) All assurances submitted in accordance with §§ 46.106 and 46.107 shall be evaluated by the Secretary through such officers and employees of DHEW and such experts or consultants engaged for this purpose as he determines to be appropriate. The Secretary's evaluation shall take into consideration, among other pertinent factors, the adequacy of the proposed Institutional Review Board in the light of the anticipated scope of the applicant institution's activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in the light of the probable risks, and the size and complexity of the institution.

(b) On the basis of his evaluation of an assurance pursuant to paragraph (a) of this section, the Secretary shall (1) approve, (2) enter into negotiations to develop a more satisfactory assurance, or (3) disapprove. With respect to approved assurances, the Secretary may determine the period during which any particular assurance or class of assurances shall remain effective or otherwise condition or restrict his approval. With respect to negotiations, the Secretary may, pending completion of negotiations for a general assurance, require an institution otherwise eligible for such an assurance, to submit special assurances.

§ 46.109 Obligation to obtain informed consent; prohibition of exculpatory clauses.

Any institution proposing to place any subject at risk is obligated to obtain and document legally effective informed consent. No such informed consent, oral or written, obtained under an assurance provided pursuant to this part shall include any exculpatory language through which the subject is made to waive, or to appear to waive, any of his legal rights, including any release of the institution or its agents from liability for negligence.

§ 46.110 Documentation of informed consent.

The actual procedure utilized in obtaining legally effective informed consent and the basis for Institutional Review Board determinations that the procedures are adequate and appropriate shall be fully documented. The documentation of consent will employ one of the following three forms:

(a) Provision of a written consent document embodying all of the basic elements of informed consent. This may be read to the subject or to his legally authorized representative, but in any event he or his legally authorized representative must be given adequate opportunity to read it. This document is to be signed by the subject or his legally authorized representative. Sample copies of the consent form as approved by the Board are to be retained in its records.

(b) Provision of a "short form" written consent document indicating that the basic elements of informed consent have been presented orally to the subject or his legally authorized representative. Written summaries of what is to be said to the patient are to be approved by the Board. The short form is to be signed by the subject or

his legally authorized representative and by an auditor witness to the oral presentation and to the subject's signature. A copy of the approved summary, annotated to show any additions, is to be signed by the persons officially obtaining the consent and by the auditor witness. Sample copies of the consent form and of the summaries as approved by the Board are to be retained in its records.

(c) Modification of either of the primary procedures outlined in paragraphs (a) and (b) of this section. Granting of permission to use modified procedures imposes additional responsibility upon the Board and the institution to establish: (1) That the risk to any subject is minimal, (2) that the use of either of the primary procedures for obtaining informed consent would surely invalidate objectives of considerable immediate importance, and (3) that any reasonable alternative means for attaining these objectives would be less advantageous to the subjects. The Board's reasons for permitting the use of modified procedures must be individually and specifically documented in the minutes and in reports of Board actions to the files of the institution. All such modifications should be regularly reconsidered as a function of continuing review and as required for annual review, with documentation of reaffirmation, revision, or discontinuation, as appropriate.

§ 46.111 Submission and certification of applications and proposals, general assurances.

(a) *Timely review.* Any institution having an approved general assurance shall indicate in each application or proposal for support of activities covered by this part (or in a separate document submitted with such application or proposal) that it has on file with DHEW such an assurance. In addition, unless the Secretary otherwise provides, each such application or proposal must be given review and, when found to involve subjects at risk, approval, prior to submission to DHEW. In the event the Secretary provides for the performance of institutional review of an application or proposal after its submission to DHEW, processing of such application or proposal by DHEW will under no circumstances be completed until such institutional review and approval has been certified. Except where the institution determines that human subjects are not involved, the application or proposal should be appropriately certified in the spaces provided on forms, or one of the following certifications, as appropriate, should be typed on the lower or right hand margin of the page bearing the name of an official authorized to sign or execute applications or proposals for the institution.

Human Subjects: Reviewed, Not at Risk.

(Date)

Human Subjects: Reviewed, At Risk, Approved

(Date)

(b) *Applications and proposals not certified.* Applications and proposals not properly certified, or submitted as not involving human subjects and found by the operating agency to involve human subjects, will be returned to the institution concerned.

§ 46.112 Submission and certification of applications and proposals, special assurances.

(a) Except as provided in paragraph (b) of this section, institutions not having an approved general assurance shall submit in or with each application or proposal for support of activities covered by this part a separate special assurance and certification of its review and approval.

(b) If the Secretary so provides, the assurance which must be submitted in or with the application or proposal under paragraph (a) of this section need satisfy only the requirements of §§ 46.107 (a) and 46.107(b). Under such circumstances, processing of such application or proposal by DHEW will not be completed until a further assurance satisfying the remaining requirements of § 46.107 has been submitted to DHEW.

(c) An assurance and certification prepared in accordance with this part and approved by DHEW shall be considered to have met the requirement for certification for the initial grant or contract period concerned. If the terms of the grant or contract recommend additional support periods, each application or proposal for continuation or renewal of support must satisfy the requirements of this section or § 46.111 whichever is applicable at the time of its submission.

§ 46.113 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications or proposals are submitted with the knowledge that subjects are to be involved within the support period, but definite plans for this involvement would not normally be set forth in the application or proposal. These include such activities as (a) institutional type grants where selection of projects is the responsibility of the institution, (b) training grants where training projects remain to be selected, and (c) research, pilot, or developmental studies in which involvement depends upon such things as the completion of instruments, or of prior animal studies, or upon the purification of compounds. Such applications or proposals shall be reviewed and certified in the same manner as more definitive applications or proposals. The initial certification indicates institutional approval of the applications or proposals as submitted, and commits the institution to later review of the plans when completed. Such later review and certification to DHEW should be completed prior to the beginning of the budget period during which actual involvement of human subjects is to begin. Review and certification to DHEW must in any event be completed prior to involvement of human subjects.

§ 46.114 Applications and proposals submitted with the intent of not involving human subjects.

If an application or proposal does not anticipate involving or intend to involve human subjects, no certification should be included with the initial submission of the application or proposal. In those instances, however, when later it becomes appropriate to use all or part of awarded funds for one or more activities which will involve subjects, each such activity shall be reviewed and approved in accordance with the assurance of the institution prior to the involvement of subjects. In addition, no such activity shall be undertaken until the institution has submitted to DHEW. (a) A certification that the activity has been reviewed and approved in accordance with this part, and (b) a detailed description of the proposed activity (including any protocol or similar document). Also, where support is provided by project grants or contracts, subjects shall not be involved prior to certification and institutional receipt of DHEW approval and, in the case of contracts, prior to negotiation and approval of an amended contract description of work.

§ 46.115 Evaluation and disposition of applications and proposals.

(a) Notwithstanding any prior review, approval, and certification by the institution all applications or proposals involving human subjects at risk submitted to DHEW shall be evaluated by the Secretary for compliance with this part through such officers and employees of the Department and such experts or consultants engaged for this purpose as he determines to be appropriate. This evaluation may take into account, among other pertinent factors, the apparent risks to the subjects, the adequacy of protection against these risks, the potential benefits of the activity to the subjects and to others, and the importance of the knowledge to be gained.

(b) Disposition. On the basis of his evaluation of an application or proposal pursuant to paragraph (a) of this section and subject to such approval or recommendation by or consultation with appropriate councils, committees, or other bodies as may be required by law, the Secretary shall (1) approve, (2) defer for further evaluation, or (3) disapprove support of the proposed activity in whole or in part. With respect to any approved grant or contract, the Secretary may impose conditions, including restrictions on the use of certain procedures, or certain subject groups, or requiring use of specified safeguards or informed consent proce-

dures when in his judgment such conditions are necessary for the protection of human subjects.

§ 46.116 Cooperative activities.

Cooperative activities are those which involve institutions in addition to the grantee or prime contractor (such as a contractor under a grantee or a subcontractor under a prime contractor). If, in such instances, the grantee or prime contractor obtains access to all or some of the subjects involved through one or more cooperating institutions, the basic DHEW policy applies and the grantee or prime contractor remains responsible for safeguarding the rights and welfare of the subjects.

(a) *Institution with approved general assurance.* Initial and continuing review by the institution may be carried out by one or a combination of procedures:

(1) Cooperating institution with approved general assurance. When the cooperating institution has on file with DHEW an approved general assurance, the grantee or contractor may, in addition to its own review, request the cooperating institution to conduct an independent review and to report its recommendations on those aspects of the activity that concern individuals for whom the cooperating institution has responsibility under its own assurance to the grantee's or contractor's Institutional Review Board. The grantee or contractor may, at its discretion, concur with or further restrict the recommendations of the cooperating institution. It is the responsibility of the grantee or contractor to maintain communication with the Boards of the cooperating institution. However, the cooperating institution shall promptly notify the grantee or contracting institution whenever the cooperating institution finds the conduct of the project or activity within its purview unsatisfactory.

(2) Cooperating institution with no approved general assurance. When the cooperating institution does not have an approved general assurance on file with DHEW, the DHEW may require the submission of a general or special assurance which, if approved, will permit the grantee or contractor to follow the procedure outlined in the preceding subparagraph.

(3) Interinstitutional joint review. The grantee or contracting institution may wish to develop an agreement with cooperating institutions to provide for an Institutional Review Board with representatives from cooperating institutions. Representatives of cooperating institutions may be appointed as ad hoc members of the grantee or contracting institution's existing Institutional Review Board or, if cooperation is on a frequent or continuing basis as between a medical school and a group of affiliated hospitals, appointments for extended periods may be made. All such cooperative arrangements must be approved by DHEW as part of a general assurance, or as an amendment to a general assurance.

(b) *Institutions with special assurances.* While responsibility for initial and continuing review necessarily lies with the grantee or contracting institution, DHEW may also require approved assurances from those cooperating institutions having immediate responsibility for subjects.

If the cooperating institution has on file with DHEW an approved general assurance, the grantee or contractor shall request the cooperating institution to conduct its own independent review of those aspects of the project or activity which will involve human subjects for which it has responsibility. Such a request shall be in writing and should provide for direct notification of the grantee's or contractor's Institutional Review Board in the event that the cooperating institution's Board finds the conduct of the activity to be unsatisfactory. If the cooperating institution does not have an approved general assurance on file with DHEW, it must submit to DHEW a general or special assurance which is determined by DHEW to comply with the provisions of this part.

§ 46.117 Investigational new drug 30-day delay requirement.

Where an institution is required to prepare or to submit a certification under §§ 46.111, 46.112, 46.113, or § 46.114 and the application or proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 312.1(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement: *Provided, however,* That in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received.

§ 46.118 Institution's executive responsibility.

Specific executive functions to be conducted by the institution include policy development and promulgation and continuing indoctrination of personnel. Appropriate administrative assistance and support shall be provided for the Board's functions. Implementation of the Board's recommendations through appropriate administrative action and followup is a condition of DHEW approval of an assurance. Board approvals, favorable actions, and recommendations are subject to review and to disapproval or further restriction by the institution officials. Board disapprovals, restrictions, or conditions cannot be rescinded or removed except by action of a Board described in the assurance approved by DHEW.

§ 46.119 Institution's records; confidentiality.

(a) Copies of all documents presented or required for initial and continuing review by the Institutional Review Board, such as Board minutes, records of subject's consent, transmittals on actions, instructions, and conditions resulting from Board deliberations addressed to the activity director, are to be retained by the institution, subject to the terms and conditions of grant and contract awards.

(b) Except as otherwise provided by law information in the records or possession of an institution acquired in connection with an activity covered by this part, which information refers to or can be identified with a particular subject, may not be disclosed except:

(1) With the consent of the subject or his legally authorized representative; or

(2) As may be necessary for the Secretary to carry out his responsibilities under this part.

§ 46.120 Reports.

Each institution with an approved assurance shall provide the Secretary with such reports and other information as the Secretary may from time to time prescribe.

§ 46.121 Early termination of awards; evaluation of subsequent applications and proposals.

(a) If, in the judgment of the Secretary an institution has failed materially to comply with the terms of this policy with respect to a particular DHEW grant or contract, he may require that said grant or contract be terminated or suspended in the manner prescribed in applicable grant or procurement regulations.

(b) In evaluating applications or proposals for support of activities covered by this part, the Secretary may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) Whether the applicant or offeror has been subject to a termination or suspension under paragraph (a) of this section, (2) whether the applicant or offeror or the person who would direct the scientific and technical aspects of an activity has in the judgment of the Secretary failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects in his, her, or its care (whether or not DHEW funds were involved), and (3) whether, where past deficiencies have existed in discharging such responsibility, adequate steps have in the judgment of the Secretary been taken to eliminate these deficiencies.

§ 46.122 Conditions.

The Secretary may with respect to any grant or contract or any class of grants or contracts impose additional

conditions prior to or at the time of any award when in his judgment such conditions are necessary for the protection of human subjects.