Authority: 5 U.S.C. 301; 42 U.S.C. 300v–1(b).

Frederick M. Bernthal,

Acting Director.

DEPARTMENT OF TRANSPORTATION

49 CFR Part 11

RIN 2105–AB74

List of Subjects in 49 CFR Part 11

Human subjects, Research, Reporting and record-keeping requirements.

Title 49 of the Code of Federal Regulations is amended by adding part 11 as set forth at the need of this document.

PART 11—PROTECTION OF HUMAN SUBJECTS

Sec.

11.101 To what does this policy apply?
11.102 Definitions.
11.103 Assuring compliance with this policy—research conducted or supported by any Federal Department or Agency.
11.104 [Reserved]
11.105 [Reserved]
11.106 [Reserved]
11.107 IRB Membership.
11.108 IRB functions and operations.
11.109 IRB review of research.
11.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.
11.111 Criteria for IRB approval of research.
11.112 Review by institution.
11.113 Suspension or termination of IRB approval of research.
11.114 Cooperative research.
11.115 IRB records.
11.116 General requirements for informed consent.
11.117 Documentation of informed consent.
11.118 Applications and proposals lacking definite plans for involvement of human subjects.
11.119 Research undertaken without the intention of involving human subjects.
11.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.
11.121 [Reserved]
11.122 Use of Federal funds.
11.123 Early termination of research support: Evaluation of applications and proposals.
11.124 Conditions.

Authority: 5 U.S.C. 301; 42 U.S.C. 300v–1(b).

Dated: February 4, 1991.

Samuel K. Skinner,

Secretary of Transportation.

[FR Doc. 91–14258 Filed 6–17–91; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Agency Forms Submitted to the Office of Management and Budget for Clearance

The following request has been submitted to the Office of Management and Budget (OMB) for clearance in compliance with the Paperwork Reduction Act (44 U.S.C. chapter 35). Expedited review by OMB has been requested as described below.

(Call PHS Reports Clearance Officer on 202–245–2100 for copies of submission)

Federal Policy for the Protection of Human Subjects—New—This submission is for approval of the information requirements associated with the common rule for the protection of human subjects of research conducted, supported or regulated by the following Federal departments and agencies: Department of Agriculture, Department of Energy, National Aeronautics and Space Administration, Department of Commerce, Consumer Product Safety Commission, Agency for International Development, Department of Housing and Urban Development, Department of Justice, Department of Defense, Department of Education, Department of Veterans' Affairs, Environmental Protection Agency, Department of Transportation, Central Intelligence Agency, and Department of Health and Human Services.

Adoption of the common Federal policy by these departments and agencies will implement a recommendation of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. The Office of Science and Technology Policy established an Interagency Human Subjects Coordinating Committee under the Federal Coordinating Council for Science Engineering and Technology. This group prepared a proposed Model Federal Policy for the Protection of Human Subjects that was published as a proposed policy in 1986 and again as a proposed common rule on November 10, 1988. After revision of the proposed common rule in response to public comments, the final common rule is being published elsewhere in this issue of the **Federal Register.** The common rule is based on Department of Health and Human Services (DHHS) regulations (45 CFR part 46, subpart A), the basic HHS Policy for the Protection of Human Subjects.

Respondents: Individuals or households, State or local governments, businesses or other for-profit, Federal agencies or employees, non-profit institutions, small businesses or organizations.

The total number of respondents affected by these information requirements is estimated at 3,831. The total annual response burden for these requirements including all Federal departments and agencies subject to the common rule, is estimated at 187,408 hours divided as follows: 22,982 hours for recordkeeping requirements and 164,426 hours for reporting and disclosure requirements.

Additional Information:

DHHS has submitted this request for approval to OMB on behalf of all Departments and Agencies governed by this final rule. It is critical to receive OMB review and approval for the information requirements so that the common rule for the Protection of Human Subjects may be effective 60 days after publication. Federal Departments and Agencies have ongoing research programs to which the common rule will apply, and they are seeking the most expeditious time frame in which to begin protection of human subject policies and procedures. In addition, institutions supported or regulated by the involved Departments and Agencies have requested implementation of the final rule as soon as possible to lessen burden of compliance with numerous, sometimes inconsistent, procedures for the protection of human subjects required by the various Federal Departments and Agencies.

OMB has been requested to review and approve the information requirements in the common rule on an expedited basis no later than August 2, 1991. In keeping with the requirements for expedited review, we are publishing this announcement in the same issue as the proposed final rule. The information requirements are separately identified in the preamble to the rule, printed elsewhere in this issue. There are no separate forms or instructions for which approval is being sought.

OMB Desk Officer: Shannah Koss-McCallum.

Because of the time frame in which OMB has been asked to act on this request, any comments and recommendations for the proposed information collection should be provided directly to the OMB Desk Officer designated above by telephone at (202) 395–7316 or by express mail at the following address: Human Resources and Housing Branch, New Executive Office Building, room 3002, Washington, DC 20503.

Dated: May 31, 1991.

Sandra K. Mahkorn,

1Deputy Assistant Secretary for Public Health Policy.

[FR Doc. 91–14259 Filed 6–17–91; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 50 and 56

[Docket No. 87N-0032]

RIN 0905-AC52

Protection of Human Subjects; Informed Consent; Standards for Institutional Review Boards for Clinical Investigations

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulations on institutional review boards (IRB's) and on informed consent to conform them to the "Federal Policy for the Protection of Human Research Subjects" (Federal Policy) published elsewhere in this issue of the **Federal Register**. Existing FDA regulations governing the protection of human subjects share a common core with the Federal Policy and implement the fundamental principles embodied in that policy.

EFFECTIVE DATE: August 19, 1991.

FOR FURTHER INFORMATION CONTACT: Richard M. Klein, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-1382.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is charged by statute with ensuring the protection of the rights, safety, and welfare of human subjects who participate in clinical investigations involving articles subject to section 505(i), 507(d), or 520(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(i), 357(d), or 360j(g)), as well as clinical investigations that support applications for research or marketing permits for products regulated by FDA, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.

In the **Federal Register** of January 27, 1981, FDA adopted regulations governing informed consent of human subjects (21 CFR part 50; 46 FR 8942) and regulations establishing standards for the composition, operation, and responsibilities of IRB's that review clinical investigations involving human subjects (21 CFR part 56; 46 FR 8958). At the same time, the Department of Health and Human Services (HHS) adopted regulations on the protection of human research subjects (45 CFR part 46; 46 FR 8366). The FDA and HHS regulations share a common framework.

In December 1981, the President's Commission for the study of Ethical Problems in Medicine and Biomedical and Behavioral Research (the commission) issued its "First Biennial Report on the Adequacy and Uniformity of Federal Rules and Policies, and their Implementation, for the Protection of Human Subjects in Biomedical and Behavioral Research, Protecting Human Subjects." The commission recommended that all Federal departments and agencies adopt the HHS regulations (45 CFR part 46).

In May 1982, the President's Science Advisor, Office of Science and Technology Policy (OSTP), appointed an ad hoc Committee for the Protection of Human Research Subjects (the committee), under the auspices of the Federal Coordinating Council for Science, Engineering, and Technology (FCCSET), to respond to the recommendations of the commission. The committee, composed of representatives and ex officio members from departments and agencies that conduct, support, or regulate research involving human subjects, developed responses to the commission in consultation with OSTP and the Office of Management and Budget (OMB).

The committee agreed that uniformity of Federal regulations on human subject protection is desirable to eliminate unnecessary regulations and to promote increased understanding by institutions that conduct federally-supported or regulated research. The committee developed a model policy which OSTP later modified and, with the concurrence of all affected Federal departments and agencies, published as a proposal in the **Federal Register** of June 3, 1986 (51 FR 20204). More than 200 comments were submitted in response to the proposal. Published elsewhere in this issue of the **Federal Register** is the final rule on the Federal Policy.

FDA concurs in that final rule. In the **Federal Register** of November 10, 1988 (53 FR 45678), the agency proposed to amend its regulations in 21 CFR parts 50 and 56 to conform them to the Federal Policy to the extent permitted by the act. The agency is committed to being as consistent with the final Federal Policy as it can be, given the unique requirements of the act and the fact that FDA is a regulatory agency that rarely supports or conducts research under its regulations. However, as explained in the proposed rule, FDA must diverge from §§ _____.101(h) and _____.116(d) of the Federal Policy.

FDA received 22 comments on the proposed rule from sponsors of regulated research, institutional review board members and staff, academic institutions, medical societies, and lawyers. Several comments were prepared by organizations, each representing a consortia of institutions that had been polled concerning the proposed rule.

A. General Comments

1. The majority of comments supported the agency's efforts to conform to the Federal Policy.

2. The majority of comments received concerned the proposal to amend § 56.108(b) to require that IRB's follow written guidelines for ensuring the reporting of scientific misconduct and of unanticipated problems to the IRB, institutional officials, and FDA. Two comments noted that this provision would make the IRB the institutional body that investigates alleged fraud severely damaging the IRB/investigator relationship and possibly diminishing the effectiveness of the IRB in protecting human subjects. Several comments noted that the proposed additional reporting requirements would duplicate investigator and sponsor reporting requirements and would be difficult for the IRB to enforce. One comment said that this section may adversely affect the IRB/institution relationship and asked how FDA intended to ensure that reporting occurred. One comment interpreted the provision as applicable to animal studies and wondered whether IRB's would be responsible for contacting sponsors. One comment expressed concern that the workload of the IRB would increase and adversely affect the recruitment of new members. One comment sought to exclude Adverse Drug Reaction reports. One comment argued that the reporting requirement was unauthorized by law.

Two comments from sponsors requested that sponsor notification be added under proposed § 56.108(b), noting that an investigator engaged in misconduct is unlikely to report that misconduct to the IRB, and that the sponsor is the entity that frequently detects misconduct through its extensive monitoring practices. In addition, these comments requested clarification of the office in FDA to which scientific misconduct should be reported. Several comments requested that FDA define or clarify "scientific misconduct" and "unanticipated problems."

Since the proposed model policy was published, the Public Health Service published a final rule concerning fraud and misconduct in science (54 FR 32446,

August 8, 1989). Because that rule directs institutions to establish provisions for the investigation of alleged scientific fraud and misconduct, the mention of "scientific misconduct" has been deleted, as unnecessary, from the model policy. Because FDA only proposed to require that IRB's report scientific misconduct to be consistent with the model policy, it has deleted this requirement from its final rule. This action should allay many of the concerns expressed in the comments.

Moreover, FDA believes that the comments misconstrued the intent of § 56.108(b). This section requires simply that an IRB have procedures by which it checks to ensure in reviewing each study presented, that provision has been made in the study to notify the IRB, appropriate institutional officials, and FDA in the specified circumstances. Section 56.108(b) does not require that the IRB itself provide the notification to either the institution or to FDA, unless such reporting would not otherwise occur. Although FDA's regulations include reporting requirements for certain types of investigational articles (see, e.g., 21 CFR parts 312 (investigational drugs) and 812 (investigational devices)), there are no such provisions for other articles that may be the subject of an investigation (e.g. food additives). Because all regulated research to be conducted at an institution will come before the IRB, FDA finds that the IRB is the appropriate entity to charge with the responsibility for ensuring that reporting of the specified problems to the IRB, the institution, and the agency will occur.

3. One comment urged FDA to move toward the adoption of an assurance system as established for the other agencies within HHS to guarantee compliance with regulations for the protection of human subjects.

FDA continues to believe that it would be inappropriate for it to adopt this mechanism. As stated in the final rule in the **Federal Register** of January 27, 1981 (46 FR 8959, comment 2), the benefits of assurance from IRB's that are subject to FDA jurisdiction, but not otherwise to HHS jurisdiction, do not justify the increased administrative burdens that would result from an assurance system. FDA relies on its Bioresearch Monitoring Program, along with its educational efforts, to assure compliance with these regulations.

4. One comment expressed concern over FDA's proposed divergences from sections 101(h) and 116(d) of the Federal Policy. The comment contended that it is sometimes impossible to obtain informed consent, as defined by FDA's regulations, in foreign clinical trials.

As stated in the proposed rule (53 FR 45679), FDA does not have the authority to accept the procedures followed in a foreign country in lieu of informed consent as required by the act for studies that are conducted under a research permit that it grants. The comment did not provide any information that would compel a different conclusion.

B. Comments on Definitions

5. One comment suggested that the word "discomfort" used in proposed §§ 50.3(i) and 56.102(i) is difficult to define and is subjective.

FDA believes that the meaning of "discomfort" is sufficiently clear. FDA interprets this term to have its ordinary meaning; that is, to mean the extent to which a subject may be made uncomfortable by the article that is the subject of the research.

6. One comment asserted that proposed § 56.102(m), the definition of "IRB approval," suggests an intent to change the procedural requirements of IRB approval.

FDA proposed to add this definition to make the regulations conform to the Federal Policy and to clarify the meaning of the phrase "IRB approval" under this rule. The addition of this definition is not intended to effect a substantive change in part 56. In the preamble to its August 8, 1978 proposal of the IRB regulation (43 FR 35186 at 35197), FDA presented a thorough discussion of its authority to require IRB review.

7. One comment stated that the reference to "other institutional and Federal requirements" in proposed § 56.102(m) goes beyond FDA's ability to determine other institutional requirements and may be counterproductive where there is conflict between the institutional requirements and FDA or HHS requirements. The suggestion is made to delete "and other institutional * * * requirements."

This definition is intended to make clear that IRB approval is to be based on a determination that the proposed research is acceptable under any applicable institutional requirements, applicable law, and standards of professional conduct and practice. If there are conflicts between the institutional requirements and Federal law, those conflicts obviously must be resolved in favor of the Federal law. However, institutional requirements often address matters not addressed by Federal law. Therefore, FDA finds it appropriate to mention both institutional and Federal requirements in this definition.

8. One comment suggested substituting "clinical investigation" for the word "research" in § 56.102(m).

FDA rejects the suggestion. FDA has defined "clinical investigation" in § 56.102(c) to be synonymous with "research" (46 FR 8976). Because FDA desires to conform to the Federal Policy and in the absence of a compelling argument to diverge from it, FDA is using the word used in the Federal Policy.

9. Several comments suggested deleting "at an institution" from § 56.102(m), contending that this phrase may confuse the original intent of the meaning of IRB approval. Another comment noted that much research today is conducted outside the institutional setting.

FDA rejects the comments. In 1981, when FDA adopted the IRB regulations, FDA intentionally defined "institution" broadly to include "any public or private entity or agency" (§ 56.102(f); 46 FR 8963, comment 27). Thus, § 56.102(m) is consistent with the original intent of the IRB regulations.

10. One comment suggested revising § 56.102(m) to read "IRB approval means * * * that the research has been reviewed for undue risk to the subject and may be conducted * * *."

FDA rejects the suggestion. The suggested change does not adequately describe the role of the IRB. The IRB's review of studies and informed consent documents includes numerous considerations in addition to whether the study presents undue risks to the human subjects involved.

C. Comments on Exemptions From IRB Requirements

11. One comment requested that no exemptions from IRB requirements be granted for those populations already identified as vulnerable.

FDA did not propose that studies involving vulnerable populations be exempt from IRB review. The only exemptions from the IRB review requirements were established in the 1981 final rule (46 FR 8942; 21 CFR 56.104). The use of an investigational article is exempt from IRB review if the investigation started before July 27, 1981, before the requirement of IRB review was in effect, or if it involves an emergency use of the test article, in which case there is not time for IRB review before the article is used. The agency found that in these circumstances, the considerations that support granting an exemption outweigh those that would support denying it (46 FR 8965, comment 48). The comment did not provide any basis for reconsidering

or revising this judgment. The agency points out that the latter consideration (emergency use), which is the only basis on which a new study would be exempt, applies only to particular uses of an article and would not provide the basis for an exemption for the use of an article in a particular population. Therefore, FDA finds that this comment provides no basis for modifying its regulations.

12. One comment suggested that FDA completely exempt "minimal risk" studies from IRB review.

FDA rejects the comment. The determination of minimal risk can be made only by members of the IRB, not the investigator or the sponsor. The burden of an expedited review of a protocol to determine if it presents minimal risk is not so great as to justify the requested exemption.

D. Comments on IRB Membership

13. Three comments suggested that FDA define in § 56.107 the specific members to be included on an IRB. Several comments suggested that FDA define, in new § 56.107(c), "non-scientific" and "scientific." Two comments suggested that the IRB include "one member who has an understanding of the medical risks involved." Another comment suggested that § 56.107(c) be clarified to include a statement requiring that at least one member of the IRB have an understanding of the scientific method.

FDA rejects these comments. FDA has chosen not to prescribe professional membership requirements for IRB members. The regulations allow for flexibility in the makeup of the IRB (see 46 FR 8966, comment 55). They require, however, that there be at least one member whose concerns are in nonscience areas and one member who has the professional competency to review the proposed research, such as a physician. FDA interprets "competency" in this context to include the ability to understand the scientific method. The agency believes that the membership requirements that it has adopted are adequate to ensure that an IRB will be able to fully consider the issues presented by a study.

14. One comment suggested that the proposed change in § 56.107(a), allowing IRB's that regularly review studies that involve vulnerable categories of subjects to consider including as a member an individual knowledgeable about, and experienced in, working with vulnerable populations, will afford less human subject protection than the current regulation.

The current regulation states that an IRB that regularly reviews research involving vulnerable populations should include as members individuals who are primarily concerned with the welfare of vulnerable subjects. Revised § 56.107(a) lists categories of subjects who are considered vulnerable and requires that the institution, or other authority, consider including individuals knowledgeable and experienced in working with these types of subjects as voting members on the IRB. This revision is not intended to lessen in any way the protections for vulnerable populations under FDA's regulations. As explained in the proposal (53 FR 45679), FDA is making this change only to conform to the language of the Federal Policy.

FDA on its own initiative is adding parenthesis to the word "reviewers" in § 56.110(b)(1) to permit a continuance of existing IRB review procedures.

E. Comments on IRB Functions and Operations

15. Several comments sought clarification of new § 56.108(b)(1) with regard to the definition and interpretation of "any unanticipated problems involving risks to human subjects and others" and the level of risk to be reported.

FDA interprets this phrase to mean an unexpected adverse experience that is not listed in the labeling for the test article. Such experience includes an event that may be symptomatically and pathophysiologically related to an event listed in the labeling but that differs from the event because of greater specificity or severity. The word "others" has previously been defined as persons who are participating in clinical trials under the same or similar protocols or who may be affected by products or procedures developed in those trials (see 53 FR 45661, 45665; November 10, 1988).

F. Comments on Expedited Review Procedures

16. One comment read the parenthetical change in § 56.110(b), "of one year or less," as affecting a change from the current regulations.

FDA disagrees with the comment. Under current regulations, the IRB may approve a study that will continue beyond 1 year, such as a longitudinal followup study. The IRB is obligated, however, under § 56.109(e) (21 CFR 56.109(e)), to conduct continuing review of the research at intervals appropriate to the degree of risk that it presents but not less than once a year.

17. One comment stated that expedited review procedures should never be used in research that involves vulnerable populations.

FDA disagrees with the comment. Expedited review procedures may only be used to review research that involves minimal risk as defined in § 56.102(i) or to review minor changes in previously approved research (§ 56.110(b)). The determination that such conditions apply must be made by the chairperson of the IRB, or by one or more experienced members of the IRB designated by the chairperson. Thus, research involving vulnerable populations will not be subject to expedited review unless a member of the IRB has affirmatively determined that the subjects will not be exposed to any greater risk of harm than they encounter in daily life or during routine physical or psychological examinations or tests, or that a change in research that has been reviewed by the whole IRB is minor. Obviously, in making these determinations, the IRB member must consider the nature of the subject population. Moreover, if expedited review is undertaken, the reviewer may exercise all the authority of the IRB, including the authority under § 56.111(a)(3) to ensure that any special problems of vulnerable populations have been addressed. Thus, FDA believes that vulnerable populations will not be involved in research that has been subject to expedited review procedures without full consideration of whether such research should be subject to expedited review at all and, if so, of their interests. Therefore, FDA does not agree with the comment.

G. Comments on Criteria for IRB Approval of Research

18. One comment suggested deleting "* * * economically or educationally disadvantaged persons * * *" from new § 56.111(a)(3), stating that it would be impossible for the IRB or the clinical investigator to make that determination.

FDA disagrees with the comment. As stated in § 56.111(b), FDA expects the IRB to make sure that adequate protections are included in those clinical investigations in which vulnerable subjects will be participating. There is no requirement for the IRB to make a determination that individual subjects are disadvantaged. However, the IRB is required to determine whether it is likely that vulnerable individuals will be involved in the study, and, if so, whether adequate safeguards have been included to protect the study subjects or whether additional safeguards are necessary.

II. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) that this action is of a type that does not individually or

cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

III. Economic and Regulatory Assessments

FDA has examined the economic consequences of the final amendments to its regulations pertaining to IRB's and to informed consent in accordance with the criteria in section 1(b) of Executive Order 12291 and found that these amendments would not be a major rule under the Executive Order. The agency also has considered the effect that the final rule would have on small entities including small businesses in accordance with the Regulatory Flexibility Act (Pub. L. 96–354). The agency certifies that there will not be a significant economic impact on a substantial number of small entities. FDA explained the basis for these conclusions in the proposal (53 FR 45681). The agency did not receive any comments that suggest contrary conclusions. This final rule contains information collections subject to the Paperwork Reduction Act of 1980. These information collections have been approved under OMB control number 0910–0130.

List of Subjects in

21 CFR Part 50

Prisoners, Reporting and recordkeeping requirements, Research, Safety.

21 CFR Part 56

Reporting and Recordkeeping requirements, Research, Safety.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, 21 CFR parts 50 and 56 are amended as follows:

PART 50—PROTECTION OF HUMAN SUBJECTS

1. The authority citation for 21 CFR part 50 continues to read as follows:

Authority: Secs. 201, 406, 408, 409, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 701, 706, 801 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c–360f, 360h–360j, 371, 376, 381); secs. 215, 301, 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 262, 263b–263n).

2. Section 50.3 is amended by revising paragraph (l) to read as follows:

§ 50.3 Definitions.

* * * * *

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

* * * * *

PART 56—INSTITUTIONAL REVIEW BOARDS

3. The authority citation for 21 CFR part 56 continues to read as follows:

Authority: Secs. 201, 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 701, 706, 801 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360c–360f, 360h–360j, 371, 376, 381); secs. 215, 301, 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 262, 263b–263n).

4. Section 56.102 is amended by revising paragraph (i) and by adding new paragraph (m) to read as follows:

§ 56.102 Definitions.

* * * * *

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

* * * * *

(m) *IRB approval* means the determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

5. Section 56.104 is amended by adding new paragraph (d) to read as follows:

§ 56.104 Exemptions from IRB requirement.

* * * * *

(d) Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

6. Section 56.107 is amended by revising paragraphs (a), (b), and (c) to read as follows:

§ 56.107 IRB membership.

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

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

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

* * * * *

7. Section 56.108 is amended by revising paragraph (a), by removing paragraph (c), by redesignating paragraph (b) as paragraph (c), by adding a new paragraph (b), and by adding a parenthetical statement to the end of the section to read as follows:

§ 56.108 IRB functions and operations.

(a) Follow written procedures: (1) For conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (2) for determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review; (3) for ensuring prompt reporting to the IRB of changes in

research activity; and (4) for ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.

(b) Follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of: (1) Any unanticipated problems involving risks to human subjects or others; (2) any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or (3) any suspension or termination of IRB approval.

* * * * *

(Information collection requirements in this section were approved by the Office of Management and Budget (OMB) and assigned OMB control number 0910–0130)

8. Section 56.110 is amended by revising paragraph (b) to read as follows:

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

* * * * *

(b) An IRB may use the expedited review procedure to review either or both of the following: (1) Some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk, (2) minor changes in previously approved research during the period (of 1 year or less) for which approval is authorized. Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the IRB chairperson from among the members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the nonexpedited review procedure set forth in § 56.108(c).

* * * * *

9. Section 56.111 is amended by revising paragraphs (a)(3) and (b) to read as follows:

§ 56.111 Criteria for IRB approval of research.

(a) * * *

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

* * * * *

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

10. Section 56.115 is amended by revising paragraph (a)(6) and by adding a parenthetical statement to the end of the section to read as follows:

§ 56.115 IRB records.

(a) * * *

(6) Written procedures for the IRB as required by § 56.108 (a) and (b).

* * * * *

(Information collection requirements in this section were approved by the Office of Management and Budget (OMB) and assigned OMB control number 0910–0130)

Dated: March 29, 1991.

David A. Kessler,

Commissioner of Food and Drugs.

Louis W. Sullivan,

Secretary of Health and Human Services.

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DEPARTMENT OF EDUCATION

34 CFR Parts 350 and 356

Protection Of Human Subjects—Disability and Rehabilitation Research: General Provisions, Disability and Rehabilitation Research: Research Fellowships

AGENCY: Department of Education.

ACTION: Interim final regulations with an opportunity to comment.

SUMMARY: The Secretary amends program regulations for the National Institute on Disability and Rehabilitation Research to add certain protections for handicapped children and mentally disabled persons who are the subjects of research conducted or sponsored by those programs. Specifically, the program regulations would require that when an institutional review board (IRB) reviews research involving these research subjects, the IRB must include at least one person who is primarily concerned with the welfare of the research subjects. The regulations are necessary as the result of the Department of Education's (Department) withdrawal of a departure from the common regulations for the protection of human research subjects.

DATES: Comments must be received on or before August 2, 1991. These regulations take effect either August 19, 1991, or later if the Congress takes certain adjournments. If you want to know the effective date of these regulations, call or write the Department of Education contact person. A document announcing the effective date will be published in the **Federal Register.**

ADDRESSES: All comments concerning these interim final regulations should be addressed to Mr. Edward Glassman; Office of Planning, Budget and Evaluation; U.S. Department of Education, Federal Building #6, room 3127, 400 Maryland Avenue SW., Washington, DC 20202–4132.

FOR FURTHER INFORMATION CONTACT: Edward B. Glassman, Telephone: (202) 401–3132. Deaf and hearing impaired individuals may call the Federal Dual Party Relay Service at 1–800–877–8339 (In the Washington DC area, 202 708–9300) between 8 a.m. and 7 p.m. Eastern Time.

SUPPLEMENTARY INFORMATION: The Office of Science and Technology Policy, Executive Office of the President (OSTP), published a "Proposed Model Policy for the Protection of Human Subjects" in the **Federal Register** on June 3, 1986 (51 FR 20204). OSTP adopted a final policy for the protection of human research subjects on November 10, 1988 (53 FR 45660). The Final Policy adopted by OSTP was included in proposed common regulations published in the **Federal Register** on November 10, 1988 (53 CFR 45661) by sixteen departments and agencies in the Executive Branch of the Federal Government, including the Department of Education. The final common regulations are published in another section of this **Federal Register** part.

The notice of proposed rulemaking (NPRM) for the common regulations specifically asked for comments addressing what effect promulgation of the Model Policy would have on each of the agencies involved in the proposed rulemaking. The Secretary proposed a departure from the common regulations that would require representation on an Institutional Review Board (IRB) of at least one person primarily concerned with the welfare of the research subjects whenever the research involves handicapped children or mentally disabled persons. As discussed below,

the Secretary has decided to withdraw this across-the-board departure in favor of program-specific regulations under those programs of the Department that are likely to support covered research that involves these research subjects.

Composition of the IRB

Comment

The Department proposed a departure to § ____.107(a) of the common regulations that would have required that, for all programs of the Department, "when an IRB reviews research that deals with handicapped children or mentally disabled persons, the IRB shall include at least one person primarily concerned with the welfare of the research subjects." The remainder of the departure reiterated the common rule's provision, which required institutions to consider representation on the IRB of persons who are knowledgeable about and experienced in working with certain vulnerable subjects if the IRB regularly reviews research involving those vulnerable subjects. Twenty-one institutions focused on this proposed departure in their comments. The majority of these comments were opposed to the proposed departure.

Some commenters, while supporting the proposed general language in § ____.107, stated their belief that the departure was not necessary because the policy in § ____.107 already addresses representation of the special concerns of vulnerable subjects on the IRB. Thus, the rights of handicapped children and mentally disabled persons should be represented on any IRB that regularly reviews proposals involving those individuals and there is nothing to be gained by emphasizing these two categories of subjects. Such an emphasis was seen as a precedent with the potential for discrimination against other categories of vulnerable subjects. When special expertise is required, IRBs already have the option, and, they believed, the obligation to seek informed consultants. However, one commenter stated "If in future staffing of our IRB, someone with expertise in this area is available and willing to serve, we would be happy to encourage such participation."

One commenter suggested that only when an IRB regularly reviews research that deals with handicapped children or mentally disabled persons should the IRB include at least one person primarily concerned with the welfare of the research subjects. Otherwise, consultation should take place when appropriate. Another suggestion was that handicapped children be added to the list of examples of vulnerable subjects for which an IRB that regularly reviews research might want to consider inclusion of one or more members who are knowledgeable about and experienced in working with these subjects.

Some commenters objected to the lack of consistency among Federal agencies and cited the Department of Education's proposed departure as inconsistent with the purpose of the common rule. One commenter indicated that the departure would not pose any problem.

Response

The language of the proposed departure was rooted in the Secretary's concern that the welfare of research subjects who are handicapped children or mentally disabled persons be adequately protected because of the diminished capacity of such persons to protect their own interests and their corresponding greater potential for harm. It should be noted that, while the common rule does, in general, protect the interests of vulnerable populations, it does not specifically command representation of their interests in all cases. For example, the common rule only requires that when an IRB regularly reviews research involving vulnerable subjects, consideration should be given to including on the IRB a researcher experienced in working with such subjects. Thus, the Department believes it is appropriate to offer special protection for handicapped children and mentally disabled persons, and the protection proposed in the departure would have satisfied that need.

The comments also appear to misunderstand the intent of the Department's proposed departure. Some commenters believed that the departure would require that an IRB include a permanent member to represent the special populations covered by the departure. Others appeared to believe that the departure would apply to all research of the institution that involved the special populations covered by the departure. The proposed departure would have produced neither of these results. Instead, the proposed departure would have required the addition of one member on an *ad hoc* basis only when the research is sponsored or funded by the Department of Education and purposefully requires the inclusion of handicapped children or mentally disabled persons.

As explained above, the Secretary believes that there is a special need to protect handicapped children and mentally disabled persons. However, given the broad policy objective of providing consistent treatment through common regulations, the Secretary has decided that the IRB special representation requirements contained in the proposed departure are not necessary for most of the programs of the Department, because most programs of the Department do not support research likely to involve those persons. Thus, the Secretary has decided to withdraw the departure. However, the Secretary believes that the concerns addressed by the proposed departure have a particular urgency in those programs of the Department that support a significant amount of research involving handicapped children and mentally disabled persons. Therefore, the Secretary is amending the regulations for the programs of the National Institute on Disability and Rehabilitation Research (34 CFR parts 350 and 356) to ensure that the protections that would have been afforded under the departure are implemented in those specific programs.

Although the Secretary has decided to publish this regulation in final form, due to the strong public interest created by the proposed departure, and because a number of commenters appeared to misunderstand the effect of the proposed rule, the Secretary has also decided to offer the public an additional opportunity to comment on the final rule. The address to which commenters should send their comments and the date by which those comments must be received is stated at the beginning of this preamble.

Changes

In the notice of proposed rulemaking, the proposed departure was stated as follows: "When an IRB reviews research that deals with handicapped children or mentally disabled persons, the IRB must include at least one person primarily concerned with the welfare of the research subjects." The Secretary has decided to change this language in the program-specific regulations adopted in this document to make clear that the regulation specifically protects handicapped children and mentally disabled persons when those persons are purposefully included in a research protocol, rather than incidentally. Therefore, the language has been changed to state: "When an IRB reviews research that purposefully requires inclusion of handicapped children or mentally disabled persons in the research sample, the IRB must include at least one person primarily concerned with the welfare of the research subjects."

Executive Order 12291

These regulations have been reviewed in accordance with Executive Order 12291. They are not classified as major because they do not meet the criteria for major regulations established under the Order.

Regulatory Flexibility Act Certification

The Secretary certifies that these interim final regulations will not have a significant economic impact on a substantial number of small entities.

The small entities that are affected by these interim final regulations are small institutions receiving research grants or contracts under the programs of the National Institute on Disability and Rehabilitation Research. However, the regulations do not have a significant economic impact on these entities because the regulations do not impose excessive regulatory burdens. These regulations impose minimal requirements that are necessary to ensure the proper treatment of handicapped children and mentally disabled persons under the programs of the National Institute on Disability and Rehabilitation Research.

Invitation To Comment

Interested persons are invited to submit comments and recommendations regarding these interim final regulations. Comments are specifically invited on whether other research programs of the Department should have added protections for handicapped children and mentally disabled persons.

All comments submitted in response to these regulations will be available for public inspection, during and after the comment period, in room 3127, 400 Maryland Avenue, SW., Washington, DC between the hours of 9 a.m. and 4:30 p.m., Monday through Friday of each week except Federal holidays.

To assist the Department in complying with the specific requirements of Executive Order 12291 and the Paperwork Reduction Act of 1980 and their overall requirement of reducng regulatory burden, the Secretary invites comment on whether there may be further opportunities to reduce any regulatory burdens found in these interim final regulations.

Assessment of Educational Impact

The Secretary has determined that the regulations in this document do not require transmission of information that is being gathered by or is available from any other agency or authority of the United States.

List of Subjects

34 CFR Part 350

Education, Education of the handicapped, Educational research, Grant programs—education.

34 CFR Part 356

Education, Education research, Fellowships.

(Catalog of Federal Domestic Assistance Number does not apply.)

Dated: June 6, 1991.

Lamar Alexander,

Secretary of Education.

The Secretary amends title 34 of the Code of Federal Regulations by amending parts 350 and 356 as follows:

PART 350—DISABILITY AND REHABILITATION RESEARCH: GENERAL PROVISIONS

3. The authority citation for part 350 continues to read as follows:

Authority: 29 U.S.C. 760–762, unless otherwise noted.

4. Section 350.3 is amended by revising paragraph (d) and the authority citation at the end of the section to read as follows:

§ 350.3 What regulations apply to these programs?

* * * * *

(d)(1) The regulations in 34 CFR part 97, PROTECTION OF HUMAN SUBJECTS, except § 97.107(a).

(2) Each Institutional Review Board (IRB) established under part 97 must have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB must be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB must be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB must therefore include persons knowledgeable in these areas. When an IRB reviews research that purposefully requires inclusion of handicapped children or mentally disabled persons as research subjects, the IRB must include at least one person primarily concerned with the welfare of these research subjects. If an IRB regularly reviews another vulnerable category of subjects, such an non-handicapped children, prisoners, pregnant women, or handicapped adults, consideration must also be given to the inclusion of one or more individuals who are knowledgeable about the experience in working with these subjects.

(Authority: 20 U.S.C. 761a, 762, 42 U.S.C. 300v-1(b))

PART 356—DISABILITY AND REHABILITATION RESEARCH: RESEARCH FELLOWSHIPS

1. The authority citation for part 356 continues to read as follows:

Authority: 29 U.S.C. 761a(d), unless otherwise noted.

2. Section 356.3 is amended by revising paragraph (c) and the authority citation at the end of the section to read as follows:

§ 356.3 What regulations apply to this program?

* * * * *

(c)(1) The regulations in 34 CFR part 97, PROTECTION OF HUMAN SUBJECTS, except § 97.107(a).

(2) Each Institutional Review Board (IRB) established under part 97 must have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB must be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB must be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB must therefore include persons knowledgeable in these areas. When an IRB reviews research that purposefully requires inclusion of handicapped children or mentally disabled persons as research subjects, the IRB must include at least one person primarily concerned with the welfare of these research subjects. If an IRB regularly reviews another vulnerable category of subjects, such as non-handicapped children,

prisoners, pregnant women, or handicapped adults, consideration must also be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

(Authority: 29 U.S.C. 761a(d), 42 U.S.C. 300v–1(b))

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

45 CFR Part 46

Federal Policy for the Protection of Human Subjects: Additional Protections for Children Involved as Subjects in Research

AGENCY: Department of Health and Human Services.

ACTION: Technical amendment.

SUMMARY: This technical amendment is to correct a reference in 45 CFR part 46 subpart D (Additional Protection for Children Involved as Subjects in Research) to subpart A of that part of the **Federal Register**.

In the revision to subpart A, published elsewhere in this issue, the numbering of exemptions in 45 CFR part 46.101(b) changes.

The reference to those exemptions in subpart D 45 CFR part 46.401(b) is now amended accordingly.

EFFECTIVE DATE: This regulation shall become effective on August 19, 1991.

FOR FURTHER INFORMATION CONTACT: Dr. Joan P. Porter, staff Director, Interagency Human Subjects Coordinating Committee, building 31, room 5B59, Bethesda, Maryland 20892 Telephone (301) 496–7005.

List of Subjects in 45 CFR Part 46

Human subjects, Research, Reporting and record-keeping requirements, Infants and children.

PART 46—PROTECTION OF HUMAN SUBJECTS

1. The authority for part 46 is revised to read:

Authority: 5 U.S.C. 30; Sec. 474(a), 88 Stat. 352 [42 U.S.C. 289*l*–3(a)].

2. In subpart D—Additional Protections for Children Involved as Subjects in Research, § 46.401, paragraph (b) is revised to read as follows:

§ 46.40§ To what do these regulations apply?

* * * * *

(b) Exemptions at § 46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at § 46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at § 46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

* * * * *

Dated: March 29, 1991.

Louis W. Sullivan,

Secretary of Health and Human Services.

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