proposed to use human subjects in the research, the research must first be reviewed and approved by the Institutional Review Board, as provided in these regulations, a certification submitted to the Department, and final approval given to the proposed change by the Department.

§ 46.116 Evaluation and disposition of applications and proposals.

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

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

§ 46.117 Cooperative research projects.

(a) Cooperative research projects are those projects, normally supported through grants, contracts, or similar arrangements, which involve institutions in addition to the grantee or prime contractor (such as a contractor with the grantee or a subcontractor with the prime contractor). In such instances, the grantee or prime contractor remains responsible to the Department for safeguarding the rights and welfare of subjects. However, except as provided in paragraph (b), when cooperating institutions in fact conduct some or all of the research involving some or all of these subjects, each cooperating institution must comply with these regulations as though it received support for its participation in the project directly from the Department.

(b) With prior approval by the Secretary, institutions involved in cooperative research projects may comply with these regulations through joint review or other arrangements aimed at avoidance of duplication of effort.

§ 46.118 Investigational new drug 30-day delay requirement.

Where an institution is required to prepare or to submit a certification under these regulations and the application or proposal involves an investigational new drug within the meaning of the Food, Drug, and Cosmetic Act, the drug must 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 the Department upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received.

§ 46.119 Confidentiality of records.

Except as otherwise provided by Federal, State, or local law, information in the records or possession of an institution acquired in connection with an activity covered by these regulations (including all subparts of these regulations), which information refers to or can be identified with a particular subject, may not be disclosed except:

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

(b) As may be necessary for the Secretary to carry out his responsibilities.

§ 46.120 Use of Federal funds.

Federal funds administered by the Department may not be expended for research involving human subjects unless the requirements of these regulations (including all subparts of these regulations) have been satisfied.

§ 46.121 Early termination of research support; 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 these regulations (including any subpart of these regulations), with respect to any particular research project, the Secretary may require that Department support for the project be terminated or suspended in the manner prescribed in applicable program requirements.

(b) In making decisions about funding applications or proposals covered by these regulations (including any subpart of these regulations), the Secretary may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) Whether the applicant has been subject to a termination or suspension under paragraph (a) of this section; (2) whether the applicant 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 Department funds were involved); and (3) whether, where past deficiencies have existed in discharging this responsibility, adequate steps have in the judgment of the Secretary been taken to eliminate these deficiencies.

§ 46.122 Research not conducted or supported by the Department.

Except for the categories of research exempted under § 46.101(c), prior and continuing review and approval by an Institutional Review Board is required for the conduct of all research involving human subjects not funded by the Department, if the research is conducted at or supported by any institution receiving funds from the Department for the conduct of research involving human subjects.

§ 46.123 Conditions.

The Secretary may with respect to any research project or any class of research projects impose additional conditions prior to or at the time of funding when in the Secretary's judgment conditions are necessary for the protection of human subjects.

[FR Doc. 79-24788 Filed 8-13-79; 8:45 am]

BILLING CODE 4110-08-M

Food and Drug Administration

[21 CFR Parts 16, 56, 71, 171, 180, 310, 312, 314, 320, 330, 361, 430, 431, 601, 630, 1003, and 1010]

[Docket No. 77N-0350]

Standards for Institutional Review Boards for Clinical Investigations; Withdrawal of Proposal

AGENCY: Food and Drug Administration.

ACTION: Withdrawal of Proposal.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing a proposal to establish standards for institutional review boards (IRB's) which review clinical investigations regulated by FDA. The National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (National Commission) published its IRB report after FDA published its IRB proposal. FDA is withdrawing its IRB proposal and issuing a new proposal that reflects a

consideration of the National Commission's IRB report.

EFFECTIVE DATE: August 14, 1979.

FOR FURTHER INFORMATION CONTACT: John C. Petricciani, Bureau of Biologics (HFB–4), Food and Drug Administration, Department of Health, Education, and Welfare, 8800 Rockville Pike, Bethesda, MD 20205, 301–496–9320.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of August 8, 1978 (43 FR 35186), FDA issued a proposal to establish standards for IRBs that review clinical investigations regulated by the agency. The proposal would have clarified IRB standards and extended the IRB requirement to articles other than new human drug products regulated by FDA.

Because the National Commission published its IRB report in the **Federal Register** on November 30, 1978 (43 FR 56174), FDA has decided to withdraw its IRB proposal of August 8, 1978, and issue a new proposal to take into account the National Commission's recommendations and the Department of Health, Education and Welfare's draft IRB proposal based on the National Commission's report.

Therefore, the proposal published in the **Federal Register** of August 8, 1978, on this matter is hereby withdrawn. Elsewhere in this issue of the **Federal Register,** the agency is reproposing an IRB regulation as well as a proposed revision of regulations governing informed consent.

This withdrawal is issued under the Federal Food, Drug, and Cosmetic Act (secs. 201, 502, 602, 701(a), 52 Stat. 1041–1042 as amended, 1050–1051 as amended by 76 Stat. 791, 1054 as amended, 1055 (21 U.S.C. 321, 352, 362, 371(a))), and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1).

Dated: August 6, 1979.

Sherwin Gardner,

Acting Commissioner of Food and Drugs.

[FR Doc. 79-24785 Filed 8-13-79; 8:45 am]

BILLING CODE 4110-03-M

[21 CFR Parts 16, 56, 71, 171, 180, 310, 312, 314, 320, 330, 361, 430, 431, 601, 630, 1003, and 1010]

[Docket No. 77N-0350]

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

AGENCY: Food and Drug Administration

ACTION: Withdrawal of Proposal; Reproposed Rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is reproposing regulations governing the activities of institutional review boards (IRB's) that review clinical investigations involving human subjects and new human drug products. This proposal would clarify and extend those regulations to include IRB's that review clinical investigations involving human subjects and articles other than new human drug products regulated by FDA. FDA has decided to repropose its IRB regulations to take into account the Report and Recommendations in Institutional Review Boards (DHEW Pub. No. (OS)78008) issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission) and to make the proposed regulation more compatible with the new revised regulations planned by the Department of Health, Education, and Welfare (HEW). The proposed regulations are intended to provide a common framework of operation for IRB's that review both HEW-funded research and research conducted under FDA regulatory requirements.

DATES: Comments by November 12, 1979. Public hearings on September 18, October 2, and October 16, 1979. The proposed effective date of the final rule is 60 days after the date of its publication in the **Federal Register.**

ADDRESS: Written comments, to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857. Public hearings in Bethesda, MD; San Francisco, CA; and Houston, TX.

FOR FUTHER INFORMATION CONTACT: John C. Petricciani, Bureau of Biologics (HFB–4), Food and Drug Administration, Department of Health, Education, and Welfare, 8800 Rockville Pike, Bethesda, MD 20205, 301–496–9320.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of August 8, 1978, FDA published proposed standards for institutional review boards for clinical investigations (43 FR 35186). Interested persons were given until December 6, 1978, to submit written comments on the proposal. By notice in the **Federal Register** of December 15, 1978 (43 FR 58574), the comment period was extended to June 6, 1979. During the comment period, the National Commission submitted its report and recommendations on IRB's and informed consent, and that document was published in the **Federal Register** of November 30, 1978 (43 FR 56174). In its report, the National Commission recommended revisions of the current HEW IRB regulations (45 CFR Part 46). Because the agency stated in the August 8, 1978 proposal that FDA's regulations should be compatible with, if not identical to, those of the Department, FDA is withdrawing its IRB proposal of August 8, 1978 and in this document is publishing a revised proposal developed in conjunction with HEW in response to the recommendations made by the National Commission. The agency is also publishing elsewhere in this issue of the **Federal Register** its proposed regulation concerning informed consent. HEW and FDA both agree in principle with the recommendation of the National Commission that IRB's should operate under one set of Federal regulations. Within the constraints of their independent statutory obligations and missions, HEW and FDA have developed IRB proposals that specify, for IRB's, virtually the same structural and functional requirements, so that IRB's will have essentially uniform requirements in areas such as scope of responsibility, quorum requirements, and record retention.

The agency emphasizes that, although this proposal will be essentially compatible and consistent with the regulations to be proposed by HEW, the two sets of regulations cannot be identical. The statutory authorities under which FDA regulates clinical research are different from the authorities relied upon by HEW to regulate research that it either funds or conducts. In addition, because HEW's regulations will encompass behavioral research (which FDA does not regulate), the scope of coverage and types of review required will be somewhat different.

This proposal is concerned with those IRB's that review clinical investigations regulated by FDA under sections 505(i), 507(d), and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as those clinical investigations that support applications for research or marketing permits for products regulated by FDA. This revised proposal represents the agency's attempt to achieve a common, flexible framework within which IRB's can operate, whether they are reviewing HEW-supported research or FDA-regulated research.

Because FDA is a regulatory agency, the compliance aspects of this proposal must be explicitly stated. In the initial proposal, the agency proposed sections that provide for inspection and disqualification of IRB's, and these sections have been retained without change. HEW, which employs the institutional assurance mechanism for dealing with institutions, and which may

cut off funding of projects for noncompliance, will not propose similar provisions. FDA will continue to consult with HEW during the development of final regulations so that, as much as possible, consistency of IRB structure and function can be maintained.

Opportunity for Public Hearing

The Food and Drug Administration stated in the August 8, 1978 proposal setting forth the standards for IRB's that three open hearings would be held to give the public an opportunity to make oral comments on both the IRB and the informed consent proposals. These hearings will be held under the administrative practices and procedures regulations, § 15.1(a) (21 CFR 15.1(a)), in (1) Bethesda, Maryland, September 18, 1979; (2) San Francisco, California, October 2, 1979; and (3) Houston, Texas, October 16, 1979.

The purpose of the hearings is (1) to provide an open forum to present views concerning the merit of the proposed regulations and their general applicability and practicability and (2) to foster greater consideration of the proposal among the scientific community, the regulated industry, and the public. Although the hearings will encompass all aspects of the proposed regulations, several specific areas of consideration on which the agency seeks advice are:

1. Administrative expense for IRB's;

2. IRB member compensation;

3. Paragraph (a) of § 56.26 *Relationship between members and investigator or investigation;*

4. § 56.81 *Quorum requirements;*

5. § 56.83 *Expedited review procedures for minor changes in the protocol of an approved clinical investigation;* and

6. Subpart K—Disqualification of an Institutional Review Board.

In preparing a final regulation, the agency will consider the administrative record of these hearings along with all other written comments received during the comment period specified in this proposal.

The hearings will take place at 9 a.m. as follows:

Bethesda Hearing (September 18, 1979)

Conference Room 4, Building 31, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20205

San Francisco Hearing (October 2, 1979)

Federal Building, Room 2007, 450 Golden Gate Avenue, San Francisco, CA 94102.

Houston Hearing (October 16, 1979)

University of Texas at Houston, Main Building Auditorium, 1100 East Holcombe Boulevard, Houston, TX 77030.

The presiding officer will be Dr. Mark Novitch, Associate Commissioner for Health Affairs.

A written notice of participation under the requirements of § 15.21 (21 CFR 15.21) must be filed with the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, not later than September 4 for the Bethesda hearing, September 18 for the San Francisco hearing, and October 2 for the Houston hearing. The notice of participation should contain Hearing Clerk Docket No. 77N–0350, the name, address, and telephone number of the person desiring to make a statement, along with any business affiliation, a summary of the scope of the presentation with references to the appropriate subpart of the proposed regulations, and the approximate amount of time requested for the presentation. A schedule for the hearing will be filed with the Hearing Clerk and mailed to each person who files a notice of participation within the specified filing time. Individuals and organizations with common interests are urged to consolidate or coordinate their presentations and to request time for a joint presentation.

If the response to this notice of hearing is such that insufficient time is available to accommodate the full amount of time requested in the notices of participation received, the agency will allocate the available time among the persons making the oral presentation to be used as they wish. Formal written statements on the issues may be presented to the presiding officer on the day of the hearing for inclusion in the administrative record.

If the response to this notice of hearing is such that all persons cannot be accommodated even though the agency has allocated the available time as indicated above, the hearings will be extended for an additional day, as appropriate, for each hearing site.

The hearings will be open to the public. Any interested person may be heard on matters relevant to the issues under consideration.

Comments Received on the August 8, 1978 Proposal

In formulating the final regulation, the agency will consider comments received in response to the August 8, 1978 proposal along with the comments responding to this reproposal. Thus, the agency urges that comments be directed especially to the provisions of the proposed regulation that are changed by this reproposal. To the extent that this proposal is not changed from the earlier proposal, the agency incorporates the preamble discussion that was published on August 8, 1978. The changes that have been made and the reasons for those changes are discussed below.

Definitions

The definitions remain largely unchanged. Some of the definitions will differ from those proposed by the Department and reflect the fact that FDA's major concern is biomedical and not behavioral research. The definitions proposed also are consistent with the definitions proposed as part of the other regulations that make up FDA's bioresearch monitoring program. The definition of "institutional review board" has been slightly modified to emphasize that the major function of an IRB is to review and approve clinical investigations, and is not to oversee the actual conduct of such investigations. However, IRB's do have a duty to engage in periodic review of ongoing studies, as specified in §§ 56.5(a) and 56.87(a) (21 CFR 56.5(a) and 56.87(a)).

Also, a definition of "minimal risk," which conforms to that proposed by HEW, has been added as new § 56.3(h) (21 CFR 56.3(h)).

Circumstances in Which an Institutional Review Board Is Required

Proposed § 56.5 *Circumstances in which an institutional review board is required* has been renumbered from its designation as § 56.2 in the August 8, 1978 proposal, and the provision covering waiver of the requirement has been set out separately as § 56.6. A paragraph has been added to § 56.5 to clarify that compliance with the proposed FDA IRB regulations does not relieve IRB's from compliance with other applicable Federal, State, or local laws or regulations.

Cooperative Clinical Investigations

New § 56.9 (21 CFR 56.9) has been added to explicitly reduce duplicative review of multi-institutional studies.

Diversity of Membership of an IRB

Proposed § 56.21 (21 CFR 56.21) has been modified to be consistent with the requirements to be proposed by HEW. The requirement that an IRB possess the competence to comprehend the scientific nature of the investigation has been deleted. Although it is necessary that a board have sufficient expertise to weigh the risks inherent in a clinical investigation, actual evaluation of the

scientific merits of a proposal is not intended as a major function of an IRB.

Relationship Between Members and Institution

Proposed § 56.25 (21 CFR 56.25) has been slightly modified to be consistent with HEW requirements. Paragraph (a) now states explicitly that members of the immediate family of persons affiliated with the institution may not serve as the only unaffiliated member of a board.

Relationship Between Members and Investigator or Investigation

Paragraph (a) of § 56.26 (21 CFR 56.26) has been modified to allow sponsors to participate in the selection of members of a board when that board will review a sponsor's study. The agency foresees situations in which an institution might act as the sponsor of a study conducted within that institution and might be required to have those studies reviewed by an IRB, the members of which were selected by the institution. To prohibit these institutional sponsors from participating in the selection of their own IRB, except by requesting a waiver, would be unnecessarily burdensome. The agency invites comments on this section.

Written Procedures for Review of Clinical Investigations by an IRB

The requirement that an IRB monitor a clinical investigation has been deleted from proposed § 56.80 (21 CFR 56.80) because the monitoring function is inconsistent with the generally accepted scope of IRB responsibilities and the recommendations of the national Commission.

Quorum Requirements

This section (§ 56.82 in the August 8, 1978 proposal) has been renumbered § 56.81 (21 CFR 56.81) and has been rewritten for consistency with HEW requirements. Because research regulated by FDA always involves some degree of medical risk, however, the minimum FDA IRB quorum requirement includes at least one licensed physician to help assure the protection of the human subjects in clinical investigations.

Procedures for Initial Review of a Clinical Investigation

This section (§ 56.85 in the August 8, 1978 proposal) has been renumbered § 56.82 (21 CFR 56.82). Paragraph (e) has been modified to require that if an IRB disapproves a proposal, it must give the clinical investigator an opportunity to respond in person or in writing.

Expedited Review Procedures for Minor Changes in the Protocol of an Approved Clinical Investigation

The agency is proposing new § 56.83 (21 CFR 56.83) in response to recommendation (5) of the National Commission, which said that expedited review procedures may be adopted by IRB's for carefully defined categories of research and for minor changes in an already approved study. The agency invites comments on what constitutes a minor change in a study. No provision has been made for applying the expedited review procedure to other than minor changes in an already approved protocol because FDA has been unable to identify any studies subject to these proposed regulations that would be limited to any of the low-risk procedures identified by the National Commission. However, the agency welcomes comment on whether there are specific examples of regulated research that are limited to and that fall into any of the following classes of low-risk procedures specifically mentioned by the National Commission so that the agency can include them in the final order. The categories cited by the National Commission as appropriate for expedited review are:

Research in which the only involvement of human subjects will be in one or more of the following activities:

(1) Collection (in a nondisfiguring manner) of hair, nail clippings, and deciduous teeth.

(2) Collection of excreta and external secretions including sweat, saliva, placenta expelled at delivery, umbilical cord blood after the cord is clamped at delivery, and amniotic fluid at the time of artificial rupture of the membranes prior to or during labor.

(3) Recording of data from adults through the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy. Such procedures include weighing, electrocardiogram, electroencephalogram, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography.

(4) Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in a 6-week period and no more often than two times per week, from subjects 18 years of age or older who are not anemic, pregnant, or in a significantly weakened condition.

(5) Collection of both supra- and subgingival plaque, provided the procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

(6) Voice recordings made for research purposes such as investigations of speech defects.

(7) Moderate exercise by healthy volunteers.

(8) Program evaluation activities that entail no deviation for subjects from the normal requirements of their involvement in the program being evaluated or benefits related to their participation in such program.

Criteria for Approval of a Clinical Investigation

New § 56.86 (21 CFR 56.86) describes for IRB's the basic elements required for an acceptable protocol for a clinical investigation. These elements coincide, where applicable within the limits of statutory authority, with the National Commission's recommendations and the HEW IRB proposal.

Procedures for Continuing Review and Suspension or Termination of the Approval of a Clinical Investigation

Proposed § 56.87 (21 CFR 56.87) has been changed to conform to language used by HEW and to provide IRB's with authority to suspend or terminate approval of a study rather than to suspend or terminate the study itself. Accordingly, § 56.87(b) makes it clear that if an IRB suspends or terminates the approval of a clinical investigation, the IRB must report the action immediately to FDA. The agency contemplates that when an IRB takes such serious action, the sponsor, FDA, or, in the case of funded studies, HEW, would promptly evaluate the situation and take necessary steps to suspend or terminate the clinical investigation if that were warranted on the basis of the IRB's report. Paragraph (c) responds to recommendation 3D of the National Commission as discussed in their comments on that recommendation, and conforms to proposed HEW requirements. It authorizes the IRB or its representative to observe the consent process or the clinical investigation. Paragraph (d) requires the IRB to report to institutional officials and to FDA any serious or continuing problems with clinical investigators. Paragraph (e) requires the IRB to review, at the time of periodic review of each clinical investigation, the adequacy of informed consent for subjects already entered into the study as well as for those who will be entered after the date of the periodic review. Adequacy of the

informed consent must be considered in terms of the new requirements of informed consent (see proposed Part 50, published elsewhere in this issue of the Federal Register).

Criteria for Disapproval, Suspension, or Termination of Approval of a Clinical Investigation

Proposed § 56.90 (21 CFR 56.90) has been slightly modified. The substance of proposed paragraph (b)(5) (i) through (iii) has been moved to § 56.86 (a) through (d). Paragraph (b)(5)(iv) has been deleted due to redundancy with § 56.87(a).

Suspension or Termination of Approval of a Clinical Investigation

The language of proposed § 56.92 (21 CFR 56.92) has been revised to conform to changes made in §§ 56.87 and 56.90, which specify that an IRB may suspend or terminate the approval of a clinical investigation, rather than the study itself.

Records of an IRB

Proposed § 56.185 (21 CFR 56.185) has been revised to be consistent with the recordkeeping requirements being proposed by HEW.

Retention of Records

Proposed § 56.195 (21 CFR 56.195) has been revised and simplified to conform to both the recommendations of the National Commission and proposed HEW requirements. IRB records are now required to be kept for a standard period of 5 years after completion of a study.

Disqualification of IRB's

Subpart K has been retained as originally proposed. The agency invites additional comments on this provision.

Conforming Amendments

The conforming amendments are reproposed without change.

The Food and Drug Administration has determined that this document does not contain an agency action covered by § 25.1(b) (21 CFR 25.1(b)), and consideration by the agency of the need for preparing an environmental impact statement is not required.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 601, 701(a), 706, and 801, 52 Stat. 1049–1054 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511–517 as amended, 72 Stat. 1785–1788 as amended, 74 Stat. 399–407 as amended, 76 Stat. 794–795 as amended, 90 Stat. 540–560, 562–574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c–360f, 360h–360j, 361, 371(a), 376, and 381)) and the Public Health Service Act (secs. 215, 351, 354–360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173–1186 as amended (42 U.S.C. 216, 262, 263b–263n)) and under authority delegated to the Commissioner of Food and Drugs, (21 CFR 5.1), the proposal published in the Federal Register of August 8, 1978 is withdrawn and it is reproposed that Chapter I of Title 21 of the Code of Federal Regulations be amended as follows:

SUBCHAPTER A—GENERAL

PART 16—REGULATORY HEARING BEFORE THE FOOD AND DRUG ADMINISTRATION

1. In § 16.1. by adding new paragraph (b)(27) to read as follows:

§ 16.1 Scope.

* * * * *

(b) * * *

(27) Section 56.204(b), relating to disqualifying an institutional review board.

2. By adding new Part 56 to read as follows:

PART 56—INSTITUTIONAL REVIEW BOARDS

Subpart A—General Provisions

Sec.
56.1 Scope.
56.3 Definitions.
56.5 Circumstances in which an institutional review board is required.
56.6 Waiver of requirement.
56.8 Review by institution.
56.15 Inspection of an institutional review board.

Subpart B—Organization and Personnel

56.21 Diversity of membership of an institutional review board.
56.9 Cooperative clinical investigations.
56.25 Relationship between members and institution.
56.26 Relationship between members and investigator or investigation.
56.34 Consultants.

Subparts C and D [Reserved]

Subpart E—Board Operations

56.80 Written procedures for review of clinical investigations by an institutional review board.
56.81 Quorum requirements.
56.82. Procedures for initial review of a clinical investigation.
56.83 Expedited review procedures for minor changes in the protocol of an approved clinical investigation.
56.86 Criteria for approval of a clinical investigation.
56.87 Procedures for continuing review and suspension or termination of the approval of a clinical investigation.
56.90 Criteria for disapproval, suspension, or termination of the approval of a clinical investigation.
56.92 Suspension or termination of the approval of a clinical investigation.

Subparts F through I [Reserved]

Subpart J—Records and Reports

56.185 Records of an institutional review board.
56.195 Retention of records.

Subpart K—Disqualification of an Institutional Review Board

56.200 Purpose.
56.202 Grounds for disqualification.
56.204 Notice of and opportunity for a hearing on proposed disqualification.
56.206 Final order on disqualification.
56.210 Actions on disqualification.
56.213 Public disclosure of information regarding disqualification.
56.215 Actions alternative or additional to disqualification.
56.219 Reinstatement of a disqualified institutional review board.

Authority: Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 601, 701(a), 706, and 801, Pub. L. 717, 52 Stat. 1049–1054 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511–517 as amended, 72 Stat. 1785–1788 as amended, 74 Stat. 399–407 as amended, 76 Stat. 794–795 as amended, 90 Stat. 540–560, 562–574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c–360f, 360h–360j, 361, 371(a), 376, and 381), secs. 215, 351, 354–360F, Pub. L. 410, 58 Stat. 690, 702 as amended, 82 Stat. 1173–1186 as amended (42 U.S.C. 216, 262, 263b–263n).

Subpart A—General Provisions

§ 56.1 Scope.

This part contains the general standards for the composition, operation, and responsibility of an institutional review board that reviews clinical investigations regulated by the Food and Drug Administration under sections 505(i), 507(d), and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, cosmetics, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Additional specific standards for the composition, operation, and responsibility of an institutional review board that reviews clinical investigations involving particular test articles and products may be found in other parts, e.g., Parts 312 and 812, of this chapter. Compliance with these parts is intended to protect the rights and safety of human subjects involved in such investigations and to help assure the quality and integrity of the data filed pursuant to sections 406, 408, 409, 502,

503, 505, 506, 507, 510, 513–516, 518–520, 601, 706, and 801 of the act and sections 351 and 354–360F of the Public Health Service Act.

§ 56.3 Definitions.

As used in this part:

(a) "Act" means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201–902, 52 Stat. 1040 et seq., as amended (21 U.S.C. 321–392)).

(b) "Application for research or marketing permit" includes:

(1) A color additive petition, described in Part 71 of this chapter.

(2) Data and information regarding a substance submitted as part of the procedures for establishing that a substance is generally recognized as safe for a use which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in §§ 170.35 and 570.35 of this chapter.

(3) A food additive petition, described in Part 171 of this chapter.

(4) Data and information regarding a food additive submitted as part of the procedures regarding food additives permitted to be used on an interim basis pending additional study, described in § 180.1 of this chapter.

(5) Data and information regarding a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.

(6) A "Notice of Claimed Investigational Exemption for a New Drug," described in Part 312 of this chapter.

(7) A new drug application, described in Part 314 of this chapter.

(8) Data and information regarding the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in Part 320 of this chapter.

(9) Data and information regarding an over-the-counter drug for human use submitted as part of the procedures for classifying such drugs as generally recognized as safe and effective and not misbranded, described in Part 330 of this chapter.

(10) Data and information regarding a prescription drug for human use submitted as part of the procedures for classifying such drugs as generally recorgnized as safe and effective and not misbranded, to be described in this chapter.

(11) Data and information regarding an antibiotic drug submitted as part of the procedures for issuing, amending, or repealing regulations for such drugs, described in Part 430 of this chapter.

(12) An application for a biological product license, described in Part 601 of this chapter.

(13) Data and information regarding a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, described in Part 601 of this chapter.

(14) An "Application for an Investigational Device Exemption", described in Part 812 of this chapter.

(15) Data and information regarding a medical device for human use submitted as part of the procedures for classifying such devices, described in section 513 of the act.

(16) Data and information regarding a medical device for human use submitted as part of the procedures for establishing, amending, or repealling a standard for such device, described in section 514 of the act.

(17) An application for premarket approval of a medical device for human use, described in section 515 of the act.

(18) A product development protocol for a medical device for human use, described in section 515 of the act.

(19) Data and information regarding an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for such products, described in section 358 of the Public Health Service Act.

(20) Data and information regarding an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in § 1010.4 of this chapter.

(21) Data and information regarding an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in § 1010.5 of this chapter.

(22) Data and information regarding an electronic product submitted as part of the procedures for obtaining an exemption from notification of a radiation safety defect or failure of compliance with a radiation safety performance standard, described in Subpart D of Part 1003 of this chapter.

(c) "Clincial investigation" means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research on marketing permit. The term does not include experiments that are subject to the provisions of Part 58 of this chapter, regarding nonclinical laboratory studies.

(d) "Institution" means a person (other than an individual) who engages in the conduct of research on subjects or in the delivery of medical services to individuals as a primary activity or as an adjunct to providing residential or custodial care to humans. The term includes, for example, a hospital, retirement home, prison, academic establishment, and pharmaceutical or device manufacturer. The word "facility" as used in section 520(g) of the act is deemed to be synonomous with the term "institution" for purposes of this part.

(e) "Institutional review board" means any board, committee, or other group formally designated by an institution for the purposes of reviewing clinical investigations or other types of biomedical research involving humans as subjects, approving the initiation and conducting periodic review of such investigations or research. The term has the same meaning as the phrase "institutional review committee" as used in section 520(g) of the act.

(f) "Institutionalized subject" means:

(1) A subject who is voluntarily confined for a period of more than 24 continuous hours on the premises of, and in the care of, an institution (e.g., hospital inpatient or a retirement home resident), whether or not that institution is a sponsor of the clinical investigation; and

(2) A subject who is involuntarily confined for any period of time in a penal institution (e.g., jail, workhouse, house of detention, or prison), or another institution (e.g., a hospital) by virtue of a sentence, order, decree, or judgment under a crminal or civil statute, or awaiting arraignment, commitment, trial, or sentencing under such a statute, or by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incareration in a penal facility.

(g) "Investigator" means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject).

(h) "Minimal risk" means that risk of harm that is no greater in probability and no greater in magnitude than that

risk of harm that is normally encountered in the medicial examination of healthy individuals.

(i) "Person" includes any individual, partnership, corporation, assocation, scientific or academic establishment, Government agency of organizational unit of a Government agency, and any other legal entity.

(j) "Sponsor" means a person who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(k) "Sponor-investigator" means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not inlcude a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

(l) "Subject" means a human who is or becomes a participant in a clinical investigation either as a recipient of the test article or as a control. A subject may be either a person in normal health or a patient to whom the test article might offer a therapeutic benefit or provide diagnostic information or a better understanding of a disease or metabolic process.

(m) "Test article" means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, cosmetic, electronic product, or any other article subject to regulation under the act or under sections 351 or 354–360F of the Public Health Service Act.

§ 56.5 Circumstances in which an institutional review board is required.

(a) Except as provided in § 56.6, the Food and Drug Administration will not accept any application for a research permit for a clinical investigation (as required in Parts 312, 812, and 813 of this chapter) unless that investigation has been reviewed and approved by, and remains subject to continuing review by, an institutional review board meeting the requirements of this part.

(b) Except as provided in § 56.6, the Food and Drug Administration will not consider in support of an application for a research or marketing permit any data or information that has been derived from a clinical investigation unless that investigation had been approved by, and was subject to initial and continuing review by, an institutional review board meeting the requirements of this part. The determination that a clinical investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable regulations to submit the results of the investigation to the Food and Drug Administration.

(c) Compliance with these regulations will in no way render inapplicable pertinent State or local laws or regulations, or other Federal laws or regulations, bearing upon activities covered by these regulations.

§ 56.6 Waiver of requirement.

(a) The Food and Drug Administration will waive the requirement for institutional review board review where an investigation commenced prior to and was completed within 1 year following (insert effective date of this section) and was not otherwise subject to requirements for insitutional reivew under Food and Drug Administration regulations prior to that date.

(b) Except as provided in this section, the Food and Drug Administration will waive the requirement on request of an applicant, if the Commissioner determines that the requirement is not necessary either for protecting the subjects involved or for assuring the validity or reliability of the scientific data, e.g., in a phase 3 investigational drug study (see § 312.1(a)(2), form FD–1571, item 10, of this chapter) on outpatient subjects. Any applicant for a research or marketing permit may include a request for waiver, with supporting information, in the application. In the case of an application for a research permit granted on an emergency basis, such request for waiver may be made over the telephone and be granted orally by the Food and Drug Administration at the same time the emergency application is approved on an oral basis; the approval may be conditioned upon subsequent review by an institutional review board. Written confirmation of any oral request for and grant of a waiver shall be included in the official application submitted subsequent to the emergency authorization of such application. Except in an emergency, the requirement will not be waived in any of the following situations:

(i) When the clinical investigation involves institutionalized human subjects.

(ii) When the clinical investigation is conducted on the premises of an institution that has an institutional review board meeting the requirements of this part:

(iii) When the Food and Drug Administration determines that the risks to the subjects justify such review.

§ 56.8 Review by institution.

Approval by an institutional review board of a clinical investigation may be subject to further appropriate review and approval or disapproval by officials of the institution. Disapproval of such an investigation by an institutional review board, however, may not be overruled by such officials.

§ 56.9 Cooperative clinical investigations.

Institutions involved in multi-institutional clinical investigations may comply with these regulations through joint interinstitutional review or through any other mechanism that complies with the requirements for institutional review but avoids duplication of effort.

§ 56.15 Inspection of an institutional review board.

(a) An institutional review board shall permit authorized employees of the Food and Drug Administration, at reasonable times and in a reasonable manner, for purposes of verification of case reports and other information prepared as part of the data and information to be submitted by the sponsor to the Food and Drug Administration and for purposes of assessment of compliance with the requirements set forth in this and other parts, e.g., Parts 312 and 812 of this chapter—

(1) To inspect records required to be made or kept by the institutional review board as part of, or relevant to, its activities relating to clinical investigations;

(2) To copy such records which do not identify the names of human subjects or from which the identifying information has been deleted; and

(3) To copy such records that identify the human subjects, without deletion of the identifying information, but only upon notice that the Food and Drug Administration has reason to believe that the consent of human subjects was not obtained, that the reports submitted by the investigator to the sponsor (or to the institutional review board) do not represent actual cases or actual results

obtained, or that such reports or other required records are otherwise false or misleading.

(b) The Food and Drug Administration may refuse to consider a clinical investigation in support of an application for a research or marketing permit if the institutional review board that reviewed the investigation refuses to allow an inspection under this section. The determination that a clinical investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable statute or regulation to submit the results of the investigation to the Food and Drug Administration.

Subpart B—Organization and Personnel

§ 56.21 Diversity of membership of an institutional review board.

(a) Each institutional review board shall be composed of not fewer than five individuals with varying backgrounds to promote complete and adequate review of any clinical investigation. The board shall be sufficiently qualified through the maturity, experience, and expertise of its members and the sufficient diversity of the members' racial and cultural backgrounds to promote 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 shall be able to ascertain the acceptability of clinical investigations in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The board shall therefore include persons familiar with these areas. If a board regularly reviews research that involves a vulnerable category of subjects (e.g., prisoners, children), the board should have one or more individuals who are primarily concerned with the welfare of those subjects.

(b) A board shall not consist entirely of members of one profession, nor entirely of men, nor entirely of women.

(c) Each board shall include at least one licensed physician, one scientist, and at least one individual whose primary concerns are in a nonscientific area (e.g., a lawyer, ethicist, or member of the clergy).

(d) The records of a board shall identify each member by name, earned degrees (if any), position or occupation, specialty field (if any), representative capacity, and by other pertinent indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to board deliberations.

§ 56.25 Relationship between members and institution.

(a) Each board shall include at least one member whose only affiliation with the institution is his or her board membership. A member of the immediate family of a person who is affiliated with the institution may not be appointed to serve as the board's unaffiliated member.

(b) The records of a board shall identify the employment or other relationship between each member and the institution, including the membership on the board (e.g., full-time employee, part-time employee, a member of governing panel or board, paid consultant, or unpaid consultant).

§ 56.26 Relationship between members and investigator or investigation.

(a) A member of a board shall not participate in the board's initial or continuing review of any clinical investigation in which the member has a conflicting interest, or of any investigation involving an investigator who participated in the member's selection for the board, except to provide information requested by the board. The board is responsible for determining whether a member has a conflicting interest. An investigator shall not participate in the selection of members for a board that will review his or her investigation. The Food and Drug Administration may waive the requirements of this section upon a request contained in the relevant application for a research or marketing permit; the request shall contain information describing the reasons why it is necessary for the investigator or sponsor to participate in the selection of board members.

(b) The records of a board shall identify the employment or other relationship between each member and the investigator or sponsor of any clinical investigation reviewed by the board (e.g., full-time employee, part-time employee, member of the governing board or panel, paid consultant, or unpaid consultant). If any such relationship exists, the records shall describe the extent to which the member participated in the initial or continuing review of the investigation.

§ 56.34 Consultants.

An institutional review board may, at its discretion, invite persons with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available on the board. Such persons may not vote with the board.

Subparts C and D [Reserved]

Subpart E—Board Operations

§ 56.80 Written procedures for review of clinical investigations by an institutional review board.

An institutional review board shall follow written procedures for conducting its initial and continuing review of clinical investigations and for reporting its findings and actions to the investigator, the institution and where appropriate, the sponsor. Such procedures may be promulgated by the institution or by the board.

§ 56.81 Quorum requirements.

Except when an expedited review procedure under § 56.83 is followed, an institutional review board shall conduct all significant business (e.g., approval or disapproval of a clinical investigation, or approval of a consent form) by a majority of its members present at a meeting. The majority shall include at least one licensed physician, one scientist, and one person who is neither a medical practitioner nor a scientist.

§ 56.82 Procedures for initial review of a clinical investigation.

(a) An institutional review board shall not approve a proposed clinical investigation until it has received in writing and reviewes the investigational plan or protocol, reports of pertinent prior animal and human studies conducted with the test article, and the materials to be used in obtaining consent of subjects.

(b) Upon receipt of a proposed investigation, the board shall inform in writing the investigator or sponsor, as appropriate, of the date of such receipt and that the investigation may not begin until the board notifies the investigator or sponsor, as appropriate, that it has approved the investigation and until the sponsor has complied with any other preinvestigation requirements of the Food and Drug Administration.

(c) If the board has any question regarding the proposed investigation or desires any further information, it may request the investigator or sponsor to provide the necessary information or materials as written amendments to the submission. The board may advise the investigator or sponsor, as appropriate,

on modifications, conditions, or other amendments to the investigational plan or protocol and/or the material to be used to obtain consent of subjects, which might improve the acceptability of the proposed investigation to the board. Any modifications, conditions, or other amendments to the investigational plan or protocol shall be made in writing as amendments to the submission.

(d) The board should review and approve or disapprove a proposed investigation as soon as possible after receipt of the submission and any amendments in response to requests or afvice from the board.

(e) The board shall notify in writing the investigator or the sponsor, as appropriate, and the institution, of its decision to approve or disapprove the proposed investigation. If the board decides to disapprove an investigation, it shall include in its written notification a statement of the reasons for its decision, and give the investigator an opportunity to respond in person or in writing.

§ 56.83 Expedited review procedures for minor changes in the protocol of an approved clinical investigation.

Review of any minor change in the protocol of an approved clinical investigation may be carried out by the board chairperson or by one or more experienced reviewers (who are members of the board) designated by the chairperson. The reviewer may approve the change if it meets the requirements set forth in § 56.86, may request the investigator to modify the change, or may refer the proposed change to the board for full review. If the reviewer has any significant doubt about whether the change in the protocol should be approved, the reviewer should refer the proposed change to the board for full review.

§ 56.86 Criteria for approval of a clinical investigation.

An institutional review board may approve a clinical investigation only where it determines that all of the following requirements are satisfied:

(a) The research methods are appropriate to the objectives of the clinical investigation.

(b) Selection of subjects is equitable, taking into account the purposes of the clinical investigation.

(c) Risks to subjects are minimized by using the safest procedures consistent with sound research design.

(d) Risks to subjects are reasonable in relation to anticipated benefits to subjects and importance of the knowledge to be gained. In making this determination, the board should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits the subjects would be exposed to or receive even if not participating in the research). The board should not consider possible long-range effects of applying knowledge gained in the research as among those research risks that fall within the purview of its responsibility.

(e) Informed consent will be sought from each prospective subject or his or her legally authorized representative, as required by Part 50 of this chapter.

(f) Informed consent will be appropriately documented, as required by § 50.27 of this chapter.

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

(h) There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(i) Applicable regulations for the protection of children, prisoners, and those institutionalized as mentally disabled are satisfied.

§ 56.87 Procedures for continuing review and suspension or termination of the approval of a clinical investigation.

(a) An institutional review board shall continue to review, periodically, a clinical investigation that it has approved until the investigation is concluded or is discontinued. Such continuing review shall be undertaken at intervals appropriate to the degree of risk, but not less often than once per year, to assure that the investigation is being conducted in compliance with the requirements and understandings of the board and with the requirements of the act and implementing regulations (e.g., Parts 312 and 812 of this chapter).

(b) A board may suspend and, if appropriate, terminate the approval of a clinical investigation that either is not being conducted in compliance with the requirements of § 56.86, or in which there is unexpected serious harm to the subjects. Any such suspension or termination of approval shall be reported immediately in writing to the investigator, appropriate institutional officials, and the Food and Drug Administration, and the report of such action shall include a statement of the reasons for the suspension or termination.

(c) Where appropriate, a board may observe, or may appoint a person not otherwise associated with the research or the investigator to observe, the consent process or the clinical investigation.

(d) A board shall report to the appropriate institutional officials and the Food and Drug Administration any serious or continuing noncompliance by an investigator with a requirement or determination of the board.

(e) At the time of the periodic review of studies in progress on the effective date of the informed consent order, the institutional review board shall determine whether or not: (1) revised informed consent should be obtained from human subjects already entered into the study; and (2) revised informed consent should be obtained from human subjects who will enter the study after the continuing review. In making those determinations, the institutional review board should consider the nature of the study, the degree of risk to human subjects in the study, and the adequacy of the informed consent initially approved. The decision of the institutional review board regarding the need for revised informed consent for studies in progress on the effective date of the informed consent order shall be recorded in the minutes of the meetings at which the studies undergo continuing review. Where such periodic review results in a finding that the consent obtained initially was inadequate (e.g., it contained exculpatory language, failed to reveal the experimental nature of the investigation, or did not reveal risks to the subjects), a second informed consent shall be obtained from all subjects continuing in the investigation.

§ 56.90 Criteria for disapproval, suspension, or termination of the approval of a clinical investigation.

(a) An institutional review board may disapprove, suspend, or terminate the approval of a clinical investigation for any of the reasons within the scope of the review authority conferred upon the board by the institution that created it. It shall state its reasons in writing. A board may reconsider its action, with or without submission of additional information, and the decision of a board of any one institution regarding a proposed clinical investigation shall not preclude a different decision by the board of another institution that might consider the same investigation.

(b) A board shall disapprove, and may suspend or terminate the approval of, a clinical investigation if it finds that:

(1) The information submitted to the board contains an untrue statement of fact material to the board or omits material information required by the board to review and evaluate the clinical investigation.

(2) The report of prior investigations with the test article is adequate to

support a conclusion that it is reasonably safe to initiate or continue the clinical investigation.

(3) The investigator does not possess the scientific training and experience appropriate to qualify the investigator as a suitable expert to investigate the safety and, where relevant, effectiveness of the test article.

(4) The available clinical laboratory facilities and medical support are inadequate to assure that the clinical investigation will be conducted properly and in conformity with the protocol.

(5) The clinical investigation exposes or will expose subjects to undue risks.

(6) The clinical investigation does not conform to, or is not being conducted in accordance with, the submission to the board and the requirements of the Act and implementing regulations (e.g., parts 312 and 812 of this chapter).

§ 56.92 Suspension or termination of the approval of a clinical investigation.

If an institutional review board decides to suspend or terminate the approval of a clinical investigation, it shall make recommendations to the institution, the Food and Drug Administration, and where appropriate, the Department of Health, Education, and Welfare regarding any subject who has previously been allowed to participate in the investigation and who either would (if the investigation were not suspended or terminated) continue to receive the test article or have it used involving him or her, or who would not continue to receive it or have it used involving him or her but who remains under the supervision of the investigator. In determining what recommendations to make, the board shall take into account, among other factors, the risks to the subject from the withdrawal of the test article or from its continued administration by another physician, the need for further medical supervision, the availability of qualified medical personnel, and the rights of the subject, including the right to participate in the decision as to future care.

Subparts F Through I [Reserved]

Subpart J—Records and Reports

§ 56.185 Records of an institutional review board.

An institutional review board shall prepare an maintain adequate documentation of its activities, including the following:

(a) A statement of the principles that will govern the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This statement may include appropriate existing codes, declarations, or statements of basic ethical principles, or principles formulated by the institution itself. However, the statement of principles does not supersede Food and Drug Administration policy or applicable law.

(b) Copies of all protocols of clinical investigations reviewed, scientific evaluations, if any, that accompany the protocol, approved sample consent forms, progress reports submitted by investigators, and reports of injuries to subjects.

(c) Information on board members required under Subpart B of this part.

(d) Attendance at and minutes of board meetings, including a written summary of the discussion of any substantive issues and their resolution. Minutes shall be in sufficient detail to show the basis of actions taken by the board.

(e) Board recommendations and actions, with a record of the number of members voting in favor of and the number voting against the decision.

(f) Records of continuing review activities.

§ 56.195 Retention of records.

An institutional review board shall retain the records required by this part regarding a particular clinical investigation for at least 5 years after completion of the clinical investigation. The board shall make the records accessible for inspection by authorized employees of the Food and Drug Administration, as required by § 56.15.

Subpart K—Disqualification of an Institutional Review Board

§ 56.200 Purpose.

The purpose of disqualification of an institutional review board that fails to comply with the standards set forth in this part (or other regulations regarding such boards in this chapter) may be one or both of the following:

(a) To preclude it from reviewing clinical investigations subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the Act until such time as it becomes likely that it will abide by such regulations or that such violations will not recur. Such preclusion will assure that all such clinical investigations are under the review of a board that complies with appropriate Federal standards. The determination to disqualify an institutional review board does not necessarily constitute a finding or recommendation that the board or any of its members should be subject to other sanctions by the institution that created it or by sponsors of clinical investigations under its review.

(b) To preclude the consideration of any clinical investigations in support of applications for a research or marketing permit from the Food and Drug Administration, which investigations have been conducted under the review of the board, until such time as the investigations are subject to review by an institutional review board that complies with the applicable standards, or it can be adequately demonstrated that such violations did not occur during, or affect the validity or acceptability of, a particular investigation or investigations. The determination that a clinical investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable statute or regulation to submit the results of the investigation to the Food and Drug Administration.

§ 56.202 Grounds for disqualification.

The Commissioner may disqualify an institutional review board upon finding all of the following:

(a) The institutional review board failed to comply with any of the regulations set forth in this part or other regulations regarding such boards in this chapter;

(b) The noncompliance adversely affected the validity of the clinical investigation or the rights or the safety of the subjects; and

(c) Other lesser regulatory actions (e.g., warnings or rejection of data from individual investigations) have not been or will proably not be adequate to assure that the board will comply with such regulations in the future.

§ 56.204 Notice of and opportunity for a hearing on proposed disqualification.

(a) Whenever the Commissioner has information indicating that grounds exist under § 56.202 which in the Commissioner's opinion may justify disqualification of an institutional review board, the Commissioner may issue to the board a written notice proposing that the board be disqualified.

(b) A hearing on the disqualification of an institutional review board will be conducted in accordance with the requirements for a regulatory hearing set forth in Part 16 of this chapter.

§ 56.206 Final order on disqualification.

(a) If the Commissioner, after the regulatory hearing or after the time for

requesting a hearing expires without a request being made, upon an evaluation of the administrative record of the disqualification proceeding, makes the findings required in § 56.202, the Commissioner shall issue a final order disqualifying the institutional review board. Such order shall include a statement of the basis for that determination and shall prescribe any actions (set forth in § 56.210(b)) to be taken with regard to ongoing clinical investigations being conducted under the review of the board. Upon issuing a final order, the Commissioner shall notify (with a copy of the order) the board of the action, as well as the institution that established the board, the sponsor of each clinical investigation subject to requirements for prior submission to the Food and Drug Administation which was under the review of the board, and the investigators of such investigations who were under the review of the board.

(b) If the Commissioner, after a regulatory hearing or after the time for requesting a hearing expires without a request being made, upon an evaluation of the administrative record of the disqualification proceeding, determines not to make the findings required in § 56.202, the Commissioner shall issue a final order terminating the disqualification proceeding. Such order shall include a statement of the basis for that determination. Upon issuing a final order, the Commissioner shall notify the board and provide a copy of the order.

§ 56.210 Actions on disqualification.

(a) No clinical investigation subject to a requirement for prior submission to the Food and Drug Administration and to a requirement for institutional review board review under § 56.5 will be authorized by the Commissioner if such investigation is to be conducted under the review of a disqualified board.

(b) The Commissioner, after considering the nature of each ongoing clinical investigation subject to a requirement for prior submission to the Food and Drug Administration which is being conducted under the review of the board, the number of subjects involved, the risks to them from suspension of the investigation, and the need for involvement of an acceptable institutional review board, may direct, in the final order disqualifying a board under § 56.206(a), that, among other things, one or more of the following actions be taken with regard to each such investigation:

(1) The investigation may be terminated or suspended in its entirety until the board is reinstated under § 56.219 or another board accepts responsibility for review of the investigation.

(2) No new subject shall be allowed to participate, or be requested to participate, in the investigation until the board is reinstated under § 56.219 or another board accepts responsibility for review of the investigation.

(3) Any subject who has previously been allowed to participate in the investigation and who remains under the supervision of an investigator, but who is no longer receiving the test article or having it used involving him or her (i.e., one having followup monitoring by the investigation or one acting as a control) should continue to be monitored by the investigator but shall not again receive the test article, or have it used involving him or her, until the board is reinstated under § 56.219 or another board accepts responsibility for review of the investigation.

(4) Any subject who has been allowed to participate in the investigation and who, but for suspension of the investigation, would continue to receive the test article or have it used involving him or her, shall not receive it or have it used until either.

(i) Another board accepts responsibility for review of the investigation, or

(ii) The clinical investigator determines in writing that it is contrary to the health of the subject to defer further use of the test article until another board can assume responsibility for review of the investigation. In such a case, the Commissioner may impose any further conditions that the Commissioner deems appropriate to protect the rights and safety of the subject.

(c) Once an institutional review board has been disqualified, each application for a research or marketing permit, whether approved or not, containing or relying upon any clinical investigation conducted under the review of the board may be examined to determine whether the investigation was or would be essential to a regulatory decision regarding the application. If it is determined that the investigation was or would be essential, the Commissioner shall also determine whether the investigation is acceptable, notwithstanding the disqualification of the board. Any investigation reviewed by a board before or after its disqualification may be presumed to be unacceptable, and the person relying on the investigation may be required to establish that the investigation was not affected by the circumstances which led to disqualification of the board, e.g., by submitting validating information. If the investigation is determined to be unacceptable, such investigation shall be eliminated from consideration in support of the application, and such elimination may serve as new information justifying the termination or withdrawal of approval of the application.

(d) No clinical investigation begun under the review of an institutional review board after the date of its disqualification may be considered in support of any application for a research or marketing permit, unless the board has been reinstated under § 56.219. The determination that a clinical investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable statute or regulation to submit the results of the investigation to the Food and Drug Administration.

§ 56.213 Public disclosure of information regarding disqualification.

(a) Upon issuance of a final order disqualifying an institutional review board, the Commissioner may notify all or any interested persons. Such notice may be given in the discretion of the Commissioner whenever the Commissioner believes that such disclosure would further the public interest or would promote compliance with the regulations set forth in this part. Such notice, if given, will include a copy of the final order issued under § 56.206(a) and will state that the disqualification constitutes a determination by the Commissioner that the board is not eligible to review clinical investigations subject to requirements for prior submission to the Food and Drug Administration and that the results of any clinical investigations conducted under the review of the board may not be considered by the Food and Drug Administration in support of any application for a research or marketing permit. The notice will further state that it is given because of the professional relations between the board and the person notified and that the Food and Drug Administration is not advising or recommending that any action be taken by the person notified.

(b) A determination that an institutional review board has been disqualified and the administrative record regarding such determination are disclosable to the public under Part 20 of this chapter.

(c) Whenever the Commissioner has reason to believe that an institutional review board may be subject to

disqualification, the Commissioner shall so notify other agencies in the Department of Health, Education, and Welfare that support research involving human subjects at the time of or after proposing disqualification of the board under § 56.204(a).

§ 56.215 Actions alternative or additional to disqualification.

Disqualification of an institutional review board under this subpart is independent of, and neither in lieu of nor a precondition to, other proceedings or actions authorized by the act. The Commissioner may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of, or after, disqualification. The Commissioner may also refer pertinent matters to another Federal, State, or local government agency for such action as that agency determines to be appropriate.

§ 56.219 Reinstatement of a disqualified institutional review board.

(a) An institutional review board that has been disqualified may be reinstated as eligible to review clinical investigations subject to requirements for prior submission to the Food and Drug Administration, or as acceptable to be the reviewer of clinical investigations to be submitted to the Food and Drug Administration, if the Commissioner determines, upon an evaluation of a written submission from the board, that the board has adequately assured that it will operate in compliance with the standards set forth in this part and other applicable regulations in this chapter, e.g., Parts 312 or 812.

(b) A disqualified board that wishes to be so reinstated shall present in writing to the Commissioner reasons why it believes it should be reinstated and a detailed description of the corrective actions it has taken or intends to take to assure that the acts or omissions that led to disqualification will not recur. The Commissioner may condition reinstatement upon the board's being found in compliance with the applicable regulations upon an inspection.

(c) If a board is reinstated, the Commissioner shall so notify the board and all persons who were notified under § 56.213 of the disqualification of the board. A determination that a board has been reinstated is disclosable to the public under Part 20 of this chapter.

PART 71—COLOR ADDITIVE PETITIONS

3. By amending Part 71:

a. In § 71.1 by adding new paragraph (i) to read as follows:

§ 71.1 Petitions.

* * * * *

(i) If clinical investigations involving human subjects are involved, petitions filed with the Commissioner under section 706(b) of the act shall include a statement regarding each such clinical investigation contained in the petition that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

b. In § 71.6 by adding a new sentence at the end of paragraph (b) to read as follows:

§ 71.6 Extension of time for studying petitions; substantive amendments; withdrawal of petitions without prejudice.

* * * * *

(b) * * * If clinical investigations involving human subjects are involved, additional information or data submitted in support of filed petitions shall include a statement regarding each such clinical investigation from which the information or data are derived, that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

SUBCHAPTER B—FOOD FOR HUMAN CONSUMPTION

PART 171—FOOD ADDITIVE PETITIONS

4. By amending Part 171:

a. In § 171.1 by adding new paragraph (m) to read as follows:

§ 171.1 Petitions.

* * * * *

(m) If clinical investigations involving human subjects are involved, petitions filed with the Commissioner under section 409(b) of the act shall include a statement regarding each such clinical investigation relied upon in the petition that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

b. In § 171.6 by adding a new sentence at the end of the paragraph to read as follows:

§ 171.6 Amendment of petition.

* * * If clinical investigations involving human subjects are involved, additional information and data submitted in support of filed petitions shall include a statement regarding each such clinical investigation from which the information or data are derived that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6) of this chapter.

PART 180—FOOD ADDITIVES PERMITTED IN FOOD ON AN INTERIM BASIS OR IN CONTACT WITH FOOD PENDING ADDITIONAL STUDY

Part 180 is amended in § 180.1 by adding a new paragraph (c)(6) to read as follows:

§ 180.1 General.

* * * * *

(c) * * *

(6) If clinical investigations involving human subjects are involved, such investigations filed with the Commissioner shall include, with respect to each investigation, either a statement that the investigation has been or will be conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter; or a statement that the investigation is not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

SUBCHAPTER D—DRUGS FOR HUMAN USE

PART 310—NEW DRUGS

§ 310.3 [Amended]

5. By amending Part 310 in § 310.3 *Definitions and interpretations,* by deleting and reserving paragraph (j).

PART 312—NEW DRUGS FOR INVESTIGATIONAL USE

6. By amending Part 312 in § 312.1 by redesignating paragraphs (d)(11) and (d)(12) as (d)(12) and (d)(13) and adding a new paragraph (d)(11) to read as follows:

§ 312.1 Conditions for exemption of new drugs for investigational use.

* * * * *

(d) * * *

(11) The clinical investigations are not being conducted in compliance with the requirements regarding institutional

review set forth in this part or Part 56 of this chapter, or

* * * * *

PART 314—NEW DRUG APPLICATIONS

7. Part 314 is amended:

a. In § 314.1 by adding a new item 17 to Form FD–356H in paragraph (c)(2) and by redesignating paragraphs (f)(7) and (f)(8) as (f)(8) and (f)(9) and adding a new paragraph (f)(7) to read as follows:

§ 314.1 Applications.

* * * * *

(c) * * *

(2) * * *

Form FD–356H—Rev. 1974:

* * * * *

17. *Conduct of clinical investigations.* A statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

(f) * * *

(7) A statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements the institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

b. In § 314.8 by adding a new paragraph (n) to read as follows:

§ 314.8 Supplemental applications.

* * * * *

(n) A supplemental application that contains clinical investigations involving human subjects shall include a statement by the applicant regarding each such investigation that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

c. In § 314.9 by adding new paragraph (e) to read as follows:

§ 314.9 Insufficient information in application.

* * * * *

(e) The information contained in an application shall be considered insufficient to determine whether a drug is safe and effective for use unless the application includes a statement regarding each clincial investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

d. In § 314.12 by adding new paragraph (e) to read as follows:

§ 314.12 Untrue statements in application.

* * * * *

(e) Any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

e. In § 314.110 by adding new paragraph (a)(11) to read as follows:

§ 314.110 Reasons for refusing to file applications.

(a) * * *

(11) The applicant fails to include in the application a statement regarding each clinical investigation involving human subjects contained in the application that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.26 of this chapter.

* * * * *

f. In § 314.111 by adding paragraph (a)(11) to read as follows:

§ 314.111 Refusal to approve the application.

(a) * * *

(11) Any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

* * * * *

g. In § 314.115 by adding new paragraph (c)(7) to read as follows:

§ 314.115 Withdrawal of approval of an application.

* * * * *

(c) * * *

(7) That any clinical investigation involving human subjects contained in the application subject to the requirements for institutional review set forth in Part 56 of this chapter was not conducted in compliance with such requirements.

* * * * *

PART 320—BIOAVAILABILITY AND BIOEQUIVALENCE REQUIREMENTS

8. Part 320 is amended:

a. In § 320.31 by adding a new paragraph (f) to read as follows:

§ 320.31 Applicability of requirements regarding a "Notice of Claimed Investigational Exemption for a New Drug."

* * * * *

(f) An in vivo bioavailability study in humans shall be conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter, regardless of whether the study is conducted under a "Notice of Claimed Investigational Exemption for a New Drug."

b. In § 320.57 by adding a new paragraph (e) to read as follows:

§ 320.57 Requirements of the conduct of in vivo bioequivalence testing in humans.

* * * * *

(e) If a bioequivalence requirement provides for in vivo testing in humans, any person conducting such testing shall comply with the requirements of § 320.31.

PART 330—OVER-THE-COUNTER (OTC) HUMAN DRUGS WHICH ARE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED

9. Part 330 is amended in § 330.10 by adding new paragraph (e) to read as follows:

§ 330.10 Procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded, and for establishing monographs.

* * * * *

(e) *Institutional review.* Information and data submitted under this section after (insert effective date of this paragraph) shall include a statement regarding each clinical investigation involving human subjects, from which the information and data are derived, that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

PART 361—PRESCRIPTION DRUGS FOR HUMAN USE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED: DRUGS USED IN RESEARCH

10. Part 361 is amended in § 361.1 by revising paragraph (d)(9) to read as follows:

§ 361.1 Radioactive drugs for certain research uses.

* * * * *

(d) * * *

(9) *Approval by an institutional review board.* The investigator shall obtain the review and approval of an institutional review board that conforms to the requirements for Part 56 of this chapter.

* * * * *

PART 430—ANTIBIOTIC DRUGS; GENERAL

11. Part 430 is amended in § 430.20 by adding new paragraph (g) to read as follows:

§ 430.20 Procedures for the issuance, amendment, or repeal of regulations.

* * * * *

(g) No regulation providing for the certification of an antibiotic drug for human use shall be issued or amended unless each clinical investigation in involving human subjects on which the issuance or amendment or the regulation is based was conducted in compliance with the requirements for institutional review set for the in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

PART 431—CERTIFICATION OF ANTIBIOTIC DRUGS

12. Part 431 is amended in § 431.17 by adding a new paragraph (l) to read as follows:

§ 431.17 New antibiotic and antibiotic-containing products.

* * * * *

(l) A statement regarding each clinical investigation involving human subjects contained in the request that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

SUBCHAPTER F—BIOLOGICS

PART 601—LICENSING

13. Part 601 is amended:

a. In § 601.2 by revising paragraph (a) to read as follows:

§ 601.2 Applications for establishment and product licenses; procedures for filing.

(a) *General.* To obtain a license for any establishment or product, the manufacturer shall make application to the Director, Bureau of Biologics, on forms prescribed for such purposes, and in the case of an application for a product license, shall submit data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed standards of safety, purity, and potency; with respect to each nonclinical laboratory study, either a statement that the study was conducted in compliance with the requirements set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a statement that describes in detail all differences between the practices used in the study and those required in the regulations; a statement regarding each clinical investigation involving human subjects contained in the application, that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter; a full description of manufacturing methods; data establishing stability of the product through the dating period; sample(s) representative of the product to be sold, bartered, or exchanged or offered, sent, carried or brought for sale, barter, or exchange; summaries of results of tests performed on the lot(s) represented by the submitted sample(s); and specimens of the labels, enclosures and containers proposed to be used for the product. An application for license shall not be considered as filed until all pertinent information and data have been received from the manufacturer by the Bureau of Biologics. In lieu of the procedures described in this paragraph, applications for radioactive biological products shall be handled as set forth in paragraph (b) of this section.

* * * * *

b. In § 601.25 by revising paragraph (h)(1) and adding a new paragraph (l) to read as follows:

§ 601.25 Review procedures to determine that licensed biological products are safe, effective, and not misbranded under prescribed, recommended, or suggested conditions of use.

* * * * *

(h) *Additional studies.* (1) Within 30 days following publication of the final order, each licensee for a biological product designated as requiring further study to justify continued marketing on an interim basis, pursuant to paragraph (f)(3) of this section, shall satisfy the Commissioner of Food and Drugs in writing that studies adequate and appropriate to resolve the questions raised about the product have been undertaken, or the Federal Government may undertake these studies. Any study involving a clinical investigation that involves human subjects shall be conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter, unless it is not subject to such requirements in accordance with § 56.6 of this chapter. The Commissioner may extend this 30-day period if necessary, either to review and act on proposed protocols or upon indication from the licensee that the studies will commence at a specified reasonable time. If no such commitment is made, or adequate and appropriate studies are not undertaken, the product licenses shall be revoked.

(j) [Reserved]

(k) [Reserved]

(l) *Institutional review.* Information and data submitted under this section after (insert effective date of this paragraph) shall include statements regarding each clinical investigation involving human subjects that it either was conducted in compliance with the requirements for institutional review set forth in Part 56 of this chapter or was not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

b. By revising § 601.30 to read as follows:

§ 601.30 Licenses required; products for controlled investigation only.

Any biological or trivalent organic arsenical manufactured in any foreign country and intended for sale, barter or exchange shall be refused entry by collectors of customs unless manufactured in an establishment holding an unsuspended and unrevoked establishment license and license for the product. Unlicensed products that are not imported for sale, barter or exchange and that are intended solely for purposes of controlled investigation are admissible only if the investigation is conducted in accordance with section 505 of the Federal Food, Drug, and Cosmetic Act and the requirements set forth in Parts 56, 58, and 312 of this chapter.

PART 630—ADDITIONAL STANDARDS FOR VIRAL VACCINES

14. Part 630 is amended:

By revising the first sentence of § 630.11 to read as follows:

§ 630.11 Clinical trials to qualify for license.

To qualify for license, the antigenicity of the vaccine shall have been determined by clinical trials of adequate statistical design conducted in compliance with Part 56 of this chapter, unless exempted under § 56.6. * * *

b. By revising the first sentence of § 630.31 to read as follows:

§ 630.31 Clinical trials to qualify for license.

To qualify for license, the antigenicity of the vaccine shall be determined by clinical trials of adequate statistical design conducted in compliance with Part 56 of this chapter, unless exempted under § 56.6 of this chapter, by subcutaneous administration of the product. * * *

c. By revising § 630.51 to read as follows:

§ 630.51 Clinical trials to qualify for license.

To qualify for license, the antigenicity of Mumps Virus Vaccine, Live, shall be determined by clinical trials conducted in compliance with Part 56 of this chapter, unless exempted under § 56.6 of this chapter, that follow the procedures prescribed in § 630.31, except that the immunogenic effect shall be demonstrated by establishing that a protective antibody response has occurred in at least 90 percent of each of the five groups of mumps-susceptible individuals, each having received the parenteral administration of a virus vaccine dose which is not greater than that which was demonstrated to be safe in field studies (§ 630.50(b)) when used under comparable conditions.

d. By revising § 630.61 to read as follows:

§ 630.61 Clinical trials to qualify for license.

To qualify for license, the antigenicity of Rubella Virus Vaccine, Live, shall be determinated by clinical trials conducted in compliance with Part 56 of this chapter, unless exempted under § 56.6 of this chapter, that follow the procedures prescribed in § 630.31, except that the immunogenic effect shall be demonstrated by establishing that a protective antibody response has occurred in at least 90 percent of each of the five groups of rubella susceptible individuals, each having received the parenteral administration of a virus vaccine dose which is not greater than that which was demonstrated to be safe in field studies when used under comparable conditions.

e. By revising the first sentence of § 630.81 to read as follows:

§ 630.81 Clinical trials to qualify for license.

In addition to demonstrating that the measles component meets the requirements of § 630.31, the measles and smallpox antigenicity of the final product shall be determined by clinical trials of adequate statistical design conducted in compliance with Part 56 of this chapter, unless exempted under § 56.6 of this chapter, and with three consecutive lots of final vaccine manufactured by the same methods and administered as recommended by the manufacturer. * * *

PART 1003—NOTIFICATION OF DEFECTS OR FAILURE TO COMPLY

15. In § 1003.31 by revising paragraph (b) to read as follows:

§ 1003.31 Granting the exemption.

* * * * *

(b) Such views and evidence shall be confined to matters relevant to whether the defect in the product or its failure to comply with an applicable Federal standard is such as to create a significant risk of injury, including genetic injury, to any person and shall be presented in writing unless the Secretary determines that an oral presentation is desirable. Where such evidence includes clinical investigations involving human subjects, the data submitted shall include, with respect to each clinical investigation, either a statement that each investigation was conducted in compliance with the requirements set forth in Part 56 of this chapter, or a statement that the investigation is not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

SUBCHAPTER I—RADIOLOGICAL HEALTH

PART 1010—PERFORMANCE STANDARDS FOR ELECTRONIC PRODUCTS: GENERAL

16. Part 1010 is amended:

a. By amending § 1010.4 by adding paragraph (b)(1)(xi) to read as follows:

§ 1010.4 Variances.

* * * * *

(b) * * *

(1) * * *

(xi) If the electronic product is used in a clinical investigation involving human subjects and subject to the requirements for institutional review set forth in Part 56 of this chapter, the investigation shall be conducted in compliance with such requirements.

* * * * *

b. In § 1010.5 by revising paragraph (c)(12) to read as follows:

§ 1010.5 Exemptions for products intended for United States Government use.

* * * * *

(c) * * *

(12) Such other information required by regulation or by the Director, Bureau of Radiological Health, to evaluate and act on the application. Where such information includes nonclinical laboratory studies, the information shall include, with respect to each nonclinical study, either a statement that each study was conducted in compliance with the requirements set forth in Part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a statement that describes in detail all differences between the practices used in the study and those required in the regulations. Where such information includes clinical investigations involving human subjects, the information shall include, with respect to each clinical investigation, either a statement that each investigation was conducted in compliance with the requirements set forth in Part 56 of this chapter, or a statement that the investigation is not subject to such requirements in accordance with § 56.6 of this chapter.

* * * * *

Interested persons may, on or before November 12, 1979, submit to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, written comments regarding this proposal. Four copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday.

In accordance with Executive Order 12044, the economic effects of this proposal have been carefully analyzed, and it has been determined that the proposed rulemaking does not involve major economic consequences as defined by that order. A copy of the regulatory analysis assessment supporting this determination is on file with the Hearing Clerk, Food and Drug Administration.

Dated: August 6, 1979.

Sherwin Gardner,

Acting Commissioner of Food and Drugs.

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