physicians' assistants, naturopaths, chiropractors, audiologists, and therapists);

(2) Educational personnel (for example, school teachers, counselors, early intervention team members, developmental center workers, and daycare center workers);

(3) Public and private social welfare agency personnel; and

(4) Other non-medical sources (for example, spouses, parents and other caregivers, siblings, other relatives, friends, neighbors, and clergy).

(e) *Completeness.* The evidence in your case record, including the medical evidence from acceptable medical sources (containing the clinical and laboratory findings) and other medical sources not listed in paragraph (a) of this section, information you give us about your medical condition(s) and how it affects you, and other evidence from other sources, must be complete and detailed enough to allow us to make a determination or decision about whether you are disabled or blind. It must allow us to determine—

(1) The nature and severity of your impairment(s) for any period in question;

(2) Whether the duration requirement described in § 416.909 is met; and

(3) Your residual functional capacity to do work-related physical and mental activities, when the evaluation steps described in § 416.920(e) or (f)(1) apply, or, if you are a child, your functioning.

* * * * *

13. Section 416.926 is amended by revising the second and fourth sentences of paragraph (c) to read as follows:

§ 416.926 Medical equivalence for adults and children.

* * * * *

(c) Who is a designated medical or psychological consultant. * * * A medical consultant must be an acceptable medical source identified in § 416.913(a)(1) or (a)(3) through (a)(5). * * * (See § 416.1016 for limitations on what medical consultants who are not physicians can evaluate and the qualifications we consider necessary for a psychologist to be a consultant.)

* * * * *

Subpart J—[Amended]

14. The authority citation for subpart J of part 416 continues to read as follows:

Authority: Secs. 702(a)(5), 1614, 1631, and 1633 of the Social Security Act (42 U.S.C. 902(a)(5), 1382c, 1383, and 1383b).

§ 416.1015 [Amended]

15. Section 416.1015 is amended by removing the last sentence of paragraph (d).

16. Section 416.1016 is revised to read as follows:

§ 416.1016 Medical or psychological consultants.

(a) What is a medical consultant? A medical consultant is a person who is a member of a team that makes disability determinations in a State agency, as explained in § 416.1015, or who is a member of a team that makes disability determinations for us when we make disability determinations ourselves.

(b) What qualifications must a medical consultant have? A medical consultant must be an acceptable medical source identified in § 416.913(a)(1) or (a)(3) through (a)(5); that is, a licensed physician (medical or osteopathic), a licensed optometrist, a licensed podiatrist, or a qualified speech-language pathologist. The medical consultant must meet any appropriate qualifications for his or her specialty as explained in § 416.913(a).

(c) Are there any limitations on what medical consultants who are not physicians can evaluate? Medical consultants who are not physicians are limited to evaluating the impairments for which they are qualified, as described in § 416.913(a). Medical consultants who are not physicians also are limited as to when they may serve as a member of a team that makes a disability determination. For example, a speech-language pathologist who is a medical consultant in a State agency may be a member of a team that makes a disability determination in a claim only if a speech or language impairment is the only impairment in the claim or if there is a combination of a speech or language impairment with another impairment but the speech or language impairment alone would justify a finding of disability. In all other cases, a physician will be a member of the team that makes a disability determination, except in cases in which this function may be performed by a psychological consultant as discussed in paragraph (f) of this section and § 416.1015(d).

(d) What is a psychological consultant? A psychological consultant is a psychologist who has the same responsibilities as a medical consultant explained in paragraph (a) of this section, but who can evaluate only mental impairments.

(e) What qualifications must a psychological consultant have? A psychological consultant used in cases where there is evidence of a mental impairment must be a qualified psychologist. For disability program purposes, a psychologist will not be considered qualified unless he or she:

(1) Is licensed or certified as a psychologist at the independent practice level of psychology by the State in which he or she practices; and

(2)(i) Possesses a doctorate degree in psychology from a program in clinical psychology of an educational institution accredited by an organization recognized by the Council on Post-Secondary Accreditation; or

(ii) Is listed in a national register of health service providers in psychology which the Commissioner of Social Security deems appropriate; and

(3) Possesses 2 years of supervised clinical experience as a psychologist in health service, at least 1 year of which is post masters degree.

(f) Are there any limitations on what a psychological consultant can evaluate? Psychological consultants are limited to the evaluation of mental impairments, as explained in § 416.1015(d). Psychological consultants also are limited as to when they can serve as a member of a team that makes a disability determination. They may do so only when a mental impairment is the only impairment in the claim or when there is a combination of a mental impairment with another impairment but the mental impairment alone would justify a finding of disability.

[FR Doc. 00–13607 Filed 5–31–00; 8:45 am]

BILLING CODE 4191–02–U

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 5

Delegations of Authority and Organization; Food and Drug Administration

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the general redelegations of authority from the Commissioner of Food and Drugs to other officers of FDA. On June 20, 1999, the Commissioner of Food and Drugs restructured FDA ''to create a more streamlined and efficient Office of the Commissioner that will provide leadership without compromising programmatic effectiveness.'' In this restructuring, organizational

components were abolished and established and functions and personnel were transferred. Therefore, FDA is updating the delegations of authority regulations to reflect these changes and to delegate authority to positions in newly established components. FDA is also updating some position titles that may have been affected by previous reorganizations.

DATES: This rule is effective June 1, 2000.

FOR FURTHER INFORMATION CONTACT: Donna G. Page, Division of Management Programs (HFA–330), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4816.

SUPPLEMENTARY INFORMATION: FDA is amending the delegations of authority regulations in various sections of 21 CFR part 5, subpart B, *Redelegations of Authority from the Commissioner of Food and Drugs*, to reflect the most significant changes that resulted from the June 20, 1999, restructuring. (See 64 FR 36361–36368, July 6, 1999, and 64 FR 38675, July 19, 1999.) The changes are as follows:

1. Updating the order of succession and who may perform all of the functions of the Commissioner of Food and Drugs.

2. Clarifying certain delegations of authority to appropriately reflect the Deputy Commissioners' authorities—there will be one principal Deputy Commissioner; however, two other Deputy Commissioner titles (International and Constituent Relations and Management and Systems) will be retained for incumbents only.

3. Amending certain delegations of authority and associated position titles to reflect the establishment of the Office of the Senior Associate Commissioner and the transfer of the Ombudsman, Executive Secretariat, Advisory Committee Oversight, Public Affairs, and Orphan Products Development functions to that component.

4. Removing position titles and delegations of authority associated with the abolished Office of Operations.

5. Removing references to the abolished Offices of Policy and External Affairs and updating position titles and associated delegations of authority, where appropriate, to reflect their conversions to the Office of Policy, Planning, and Legislation and the Office of International and Constituent Relations, respectively.

6. Updating position titles and associated delegations of authority to reflect the transfer of the health assessment, patent term extension, and scheduling controlled substances functions to the Center for Drug Evaluation and Research.

7. Updating position titles and associated delegations of authority to reflect the transfer of 21 CFR part 16 hearings functions; and to reflect the delegation of authority to make due diligence determinations, which pertain to patent term extensions, to the Office of the Ombudsman.

Unless stated otherwise, these authorities may not be further redelegated. Authority delegated to a position by title may be exercised by a person officially designated to serve in such position in an acting capacity or on a temporary basis, unless prohibited by a restriction in the document designating him/her as ''acting'' or unless not legally permissible.

List of Subjects in 21 CFR Part 5

Authority delegations (Government agencies), Imports, Organization and functions (Government agencies).

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 5 is amended as follows:

PART 5—DELEGATIONS OF AUTHORITY AND ORGANIZATION

1. The authority citation for part 5 continues to read as follows:

Authority: 5 U.S.C. 504, 552, App. 2; 7 U.S.C. 138a, 2271; 15 U.S.C. 638, 1261–1282, 3701–3711a; 15 U.S.C. 1451–1461; 21 U.S.C. 41–50, 61–63, 141–149, 321–394, 467f, 679(b), 801–886, 1031–1309; 35 U.S.C. 156; 42 U.S.C. 241, 242, 242a, 242l, 242n 243, 262, 263, 264, 265, 300u–300u–5, 300aa–1; 1395y, 3246b, 4332, 4831(a), 10007–10008; E.O. 11921, 41 FR 24294, 3 CFR, 1977 Comp., p. 124–131; E.O. 12591, 52 FR 13414, 3 CFR, 1988 Comp., p. 220–223.

2. Section 5.20 is amended by revising paragraphs (b), (c), (e), (f), and (g); by redesignating paragraph (i) as paragraph (j); and by adding a new paragraph (i) to read as follows:

§ 5.20 General redelegations of authority from the Commissioner to other officers of the Food and Drug Administration.

* * * * *

(b) The following officials are authorized to perform all of the functions of the Commissioner of Food and Drugs and this authority may not be further redelegated:

(1) Deputy Commissioner;

(2) Associate Commissioner for Regulatory Affairs;

(3) Senior Associate Commissioner;

(4) Deputy Commissioner for Management and Systems;

(5) Senior Associate Commissioner for Policy, Planning, and Legislation; and

(6) Deputy Commissioner for International and Constituent Relations.

(c)(1) During the absence or disability of the Commissioner, or in the event of a vacancy in that position, the first official who is available in the following positions, or who has been designated by the Commissioner to act in such position, shall act as Commissioner:

(i) Deputy Commissioner;

(ii) Associate Commissioner for Regulatory Affairs; or

(iii) Senior Associate Commissioner.

(2) This authority may not be further redelegated. However, for a planned period of absence, the Commissioner of Food and Drugs (or someone ''acting'' on his/her behalf) may specify a different order of succession.

* * * * *

(e)(1) The Senior Associate Commissioner is authorized to make determinations that advisory committee meetings are concerned with matters listed in 5 U.S.C. 552(b) and therefore may be closed to the public in accordance with § 5.10(a)(18). This authority may not be further redelegated.

(2) The Senior Associate Commissioner is authorized to perform other associated advisory committee functions (e.g., establishing technical and scientific review groups (advisory committees)); appointing and paying members; approving waivers to appoint members to established advisory committees; renewing and rechartering of established advisory committees; amending charters of established advisory committees; and terminating established advisory committees. This authority may not be further redelegated.

(3) The Senior Associate Commissioner is authorized to approve conflict of interest waivers for special Government employees serving on advisory committees in accordance with 18 U.S.C. 208(b)(3), as amended. This authority may not be further redelegated.

(4) The Senior Associate Commissioner is authorized to select temporary members to advisory committees if such voting members are serving on an advisory committee managed by another center. This authority may not be further redelegated.

(f)(1) The Senior Associate Commissioner for Policy, Planning, and Legislation and the Associate Commissioner for Policy are authorized to perform any of the functions of the Commissioner of Food and Drugs with respect to the issuance of **Federal Register** notices and proposed and final

regulations of the Food and Drug Administration. This authority may not be further redelegated.

(2) The Senior Associate Commissioner for Policy, Planning, and Legislation and the Associate Commissioner for Policy are authorized to issue responses to the following matters under part 10 of this chapter as follows, and this authority may not be further redelegated:

(i) Requests for waiver, suspension, or modification of procedural requirements under § 10.19 of this chapter;

(ii) Citizen petitions under § 10.30 of this chapter;

(iii) Petitions for reconsideration under § 10.33 of this chapter;

(iv) Petitions for stay under § 10.35 of this chapter; or

(v) Requests for advisory opinions under § 10.85 of this chapter.

(3) With respect to any matter delegated to the Senior Associate Commissioner for Policy, Planning, and Legislation and the Associate Commissioner for Policy under paragraph (f) of this section, the Senior Associate Commissioner for Policy, Planning, and Legislation and the Associate Commissioner for Policy are authorized to perform the function of the Commissioner of Food and Drugs under §§ 10.40, 10.45, 10.50, 10.55, 10.60, 10.65, 10.80, 10.90, and 10.95 of this chapter and of the Deputy Commissioner under § 10.206(g) and (h) of this chapter. This authority may not be further redelegated.

(4) The Senior Associate Commissioner for Policy, Planning, and Legislation and the Associate Commissioner for Policy are authorized under the Regulatory Flexibility Act (5 U.S.C. 605(b)) to certify that a proposed or final rule, if issued, will not have a significant economic impact on a substantial number of small entities. This authority may be further redelegated.

(g) The following officials are authorized to perform all of the functions of the officials under them in their respective offices, and this authority may not be further redelegated:

(1) Senior Associate Commissioner;

(2) Deputy Commissioner for International and Constituent Relations;

(3) Deputy Commissioner for Management and Systems; or

(4) Senior Associate Commissioner for Policy, Planning, and Legislation.

* * * * *

(i) The Deputy Commissioner is authorized to perform the due diligence determinations and informal hearings functions under 35 U.S.C. 156(d)(2)(B)(ii), as amended, relative to patent term extensions. This authority may not be further redelegated.

* * * * *

3. Section 5.22 is amended by revising paragraphs (a)(1), (a)(2), (a)(3), (a)(6), (a)(7), (a)(10)(ii), (a)(11)(ii), (a)(12)(ii), (b)(1), (b)(2), and (b)(3); by redesignating paragraph (c) as paragraph (d) and revising newly redesignated paragraph (d); and by adding new paragraph (c) to read as follows:

§ 5.22 Certification of true copies and use of Department seal.

(a) * * *

(1) The Deputy Commissioner, the Deputy Commissioner for International and Constituent Relations, and the Deputy Commissioner for Management and Systems.

(2) The Senior Associate Commissioners, the Associate and Deputy Associate Commissioners, and the Chief Counsel and Deputies.

(3) The Director, Office of the Executive Secretariat, Office of the Senior Associate Commissioner, Office of the Commissioner.

* * * * *

(6)(i) The Director, Office of Human Resources and Management Services, Office of Management and Systems, Office of the Commissioner.

(ii) The Director, Division of Management Programs, Office of Human Resources and Management Services, Office of Management and Systems, Office of the Commissioner.

(iii) The Chief, Dockets Management Branch, Division of Management Programs, Office of Human Resources and Management Services, Office of Management and Systems, Office of the Commissioner.

(7)(i) The Associate Commissioner for Public Affairs, Office of Public Affairs, Office of the Senior Associate Commissioner, Office of the Commissioner.

(ii) The Director, Freedom of Information Staff, Office of Public Affairs, Office of the Senior Associate Commissioner, Office of the Commissioner.

* * * * *

(10) * * *

(ii) The Director and Deputy Director, Office of Management and Communications, Center for Veterinary Medicine (CVM).

* * * * *

(11) * * *

(ii) The Director and Deputy Director, Office of Management and Communications, CVM.

* * * * *

(12) * * *

(ii) The Director, Office of Management, Facilities, and Research Support, NCTR.

* * * * *

(b) * * *

(1) The Deputy Commissioner, the Deputy Commissioner for International and Constituent Relations, and the Deputy Commissioner for Management and Systems.

(2) The Senior Associate Commissioners, the Associate and Deputy Associate Commissioners, and the Chief Counsel and Deputies.

(3) The Director, Office of Human Resources and Management Services, Office of Management and Systems, Office of the Commissioner.

(c) The authorities under § 5.22 (a) and (b), where appropriate, may be further redelegated by the Deputy Commissioners; Senior Associate Commissioners; Associate Commissioner for Regulatory Affairs and Deputy; Chief Counsel and Deputies; Center Directors and Deputies; and Executive Officers (i.e., Executive Assistant, Office of the Commissioner; Director, Office of Management, CBER; Director, Office of Management, CDER; Director, Office of Management and Systems, CFSAN; Director, Office of Systems and Management, CDRH; Director, Office of Management and Communications, CVM; Director, Office of Management, Facilities, and Research Support, NCTR; and the Director, Office of Resource Management, ORA).

(d) The Chief, Regulations Editorial Section; Regulations Policy and Management Staff; Office of Policy, Planning, and Legislation; Office of the Commissioner, and his/her alternates are authorized to certify true copies of **Federal Register** documents. The Chief, Regulations Editorial Section; Regulations Policy and Management Staff; Office of Policy, Planning, and Legislation; and the Office of the Commissioner may designate alternates as required.

4. Section 5.23 is amended by revising paragraphs (a)(1), (a)(2), (a)(4), and (d).

§ 5.23 Disclosure of official records.

(a) * * *

(1) The Deputy Commissioner, the Deputy Commissioner for International and Constituent Relations, the Deputy Commissioner for Management and Systems, Senior Associate Commissioners, Associate and Deputy Associate Commissioners.

(2)(i) The Executive Assistant to the Commissioner, Office of the Commissioner.

(ii) The Director, Office of the Executive Secretariat, Office of the

Senior Associate Commissioner, Office of the Commissioner.

* * * * *

(4)(i) The Director, Office of Human Resources and Management Services, Office of Management and Systems, Office of the Commissioner.

(ii) The Director, Division of Management Programs, Office of Human Resources and Management Services, Office of Management and Systems, Office of the Commissioner.

(iii) The Chief, Dockets Management Branch, Division of Management Programs; Office of Human Resources and Management Services, Office of Management Services, Office of the Commissioner.

* * * * *

(d) The Director, Office of Resource Management, Office of Regulatory Affairs is authorized to sign affidavits regarding the presence or absence of records in the files of that office.

* * * * *

5. Section 5.25 is amended by revising paragraphs (a)(7) and (c) to read as follows:

§ 5.25 Research, investigation, and testing programs and health information and health promotion programs.

(a) * * *

(7) The Director, Office of Orphan Products Development, Office of the Senior Associate Commissioner, Office of the Commissioner.

* * * * *

(c) The Deputy Commissioner for Management and Systems, Office of Management and Systems, Office of the Commissioner; the Director and Deputy Director, Office of Facilities, Acquisitions, and Central Services, Office of Management and Systems, Office of the Commissioner; the Director, Division of Contracts and Procurement Management, Office of Facilities, Acquisitions, and Central Services, Office of Management and Systems, Office of the Commissioner; and the Chief Grants Management Officer and the Grants Management Officer, Division of Contracts and Procurement Management, Office of Facilities, Acquisitions, and Central Services, Office of Management Systems, Office of the Commissioner are authorized to sign and issue all notices of grant awards and amendments thereto and sign and issue notices of suspension and termination thereof for grants approved under the authority delegated in paragraphs (a) and (b) of this section.

* * * * *

6. Section 5.27 is revised to read as follows:

§ 5.27 Patent term extensions for human drug products, medical devices, and food and color additives; and due diligence determinations.

(a) The Director, Center for Drug Evaluation and Research (CDER) and the Associate Director for Policy, CDER, are authorized to perform the functions delegated to the Commissioner of Food and Drugs under 35 U.S.C. 156, as amended, except for making due diligence determinations and holding of informal hearings under 35 U.S.C. 156(d)(2)(B).

(b) The Chief Mediator and Ombudsman, Office of the Ombudsman, Office of the Senior Associate Commissioner, Office of the Commissioner, is authorized to perform the functions delegated to the Commissioner to make due diligence determinations under 35 U.S.C. 156(d)(2)(B), as amended, except for holding of informal hearings under 35 U.S.C. 156(d)(2)(B)(ii).

7. Section 5.30 is amended by revising paragraph (c)(1) to read as follows:

§ 5.30 Hearings.

* * * * *

(c) * * *

(1) The Chief Mediator and Ombudsman, Office of the Ombudsman, Office of the Senior Associate Commissioner, Office of the Commissioner.

* * * * *

8. Section 5.32 is revised to read as follows:

§ 5.32 Authority relating to determination of product classification and assignment of primary jurisdiction.

The Chief Mediator and Ombudsman, Office of the Ombudsman, Office of the Senior Associate Commissioner, Office of the Commissioner, as product jurisdiction officer is authorized to make a determination under section 563 of the Federal Food, Drug, and Cosmetic Act (the act) respecting the classification of a product as a drug, biological product, device, or a combination product subject to section 503(g) of the act, and to assign primary responsibility respecting the organizational component of the Food and Drug Administration that will regulate the product.

9. Section 5.34 is amended by revising paragraph (a) to read as follows:

§ 5.34 Authority to select temporary voting members for advisory committees and authority to sign conflict of interest waivers.

(a) Each center director is authorized to select members of, and consultants to, scientific and technical FDA advisory committees under that center's management to serve temporarily as voting members on another advisory committee under that center's management when expertise is required that is not available among current voting standing members of a committee or to comprise a quorum when, because of unforeseen circumstances, a quorum will be lacking. When additional voting members are added to a committee to provide needed expertise not available among current voting standing members of a committee, a quorum will be based on the total of regular and added members. Authority to select temporary voting members to advisory committees if such voting members are serving on an advisory committee managed by another center has not been redelegated. This authority will continue to be exercised by the Commissioner or the Senior Associate Commissioner, Office of the Commissioner.

* * * * *

10. Section 5.58 is amended by revising introductory text of paragraphs (a) and (b) to read as follows:

§ 5.58 Orphan products.

(a) The Director, Office of Orphan Products Development, Office of the Senior Associate Commissioner, Office of the Commissioner, is authorized to issue notices, and amendments thereto, inviting sponsorship for orphan products (human and animal drugs, biological products, and medical devices) and submission of:

* * * * *

(b) The Director, Office of Orphan Products Development, Office of the Senior Associate Commissioner, Office of the Commissioner, is authorized:

* * * * *

11. Section 5.81 is revised to read as follows:

§ 5.81 Responses to Drug Enforcement Administration temporary scheduling notices.

The Director, Center for Drug Evaluation and Research (CDER) and the Director, Executive Operations Staff, Office of the Center Director, CDER are authorized to provide responses to the Drug Enforcement Administration's temporary scheduling notices under the Controlled Substances Act, as amended (Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, 21 U.S.C. 811(h)(4), as amended hereafter). The delegation excludes the authority to submit reports to Congress. Further redelegation may only be authorized with the Commissioner of Food and Drugs' approval.

Dated: May 17, 2000.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 00–13586 Filed 5–31–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 312

[Docket No. 97N–0030]

Investigational New Drug Applications; Amendment to Clinical Hold Regulations for Products Intended for Life-Threatening Diseases and Conditions

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the regulations governing investigational new drug applications (IND's) to permit FDA to place a clinical hold on one or more studies under an IND involving a drug that is intended to treat a life-threatening disease or condition affecting both genders. The amendments permit the agency to place a clinical hold on such studies if *men or women* with reproductive potential who have the disease or condition are otherwise eligible but are categorically excluded from participation solely because of a perceived risk or potential risk of reproductive or developmental toxicity from use of the investigational drug. This rule was developed in response to the past practice of excluding women with reproductive potential from early clinical trials because of a perceived risk or potential risk of reproductive or developmental toxicity. The final rule does not impose requirements to enroll or recruit a specific number of men or women with reproductive potential.

DATES: The regulation is effective July 31, 2000.

FOR FURTHER INFORMATION CONTACT: Andrea C. Masciale, Center for Drug Evaluation and Research (HFD–7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–2041.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of September 24, 1997 (62 FR 49946), FDA proposed to amend its regulations in § 312.42 (21 CFR 312.42) governing clinical holds. A clinical hold is an order that FDA may issue to a sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation for the development of a new drug or biological product (§ 312.42(a)). Under the proposed amendments, FDA could impose a clinical hold on any proposed or ongoing clinical trial for a life-threatening disease or condition that affects both genders if men or women with reproductive potential who have the disease or condition being studied were excluded from eligibility in any phase of the clinical investigation solely because of a risk or potential risk of reproductive toxicity or developmental toxicity from use of the investigational drug. As explained in the preamble to the proposed rule (62 FR 49946 at 49947), the amendments address the exclusion from clinical trials of members of either gender who have a life-threatening disease or condition. Because such exclusions have in the past been applied primarily to women, however, it is expected that the impact of the amendments will be to ensure that women who have a life-threatening disease or condition are not categorically excluded from investigational trials of drug products for that disease or condition solely because of a perceived risk or potential risk of reproductive or developmental toxicity from the use of the investigational drug. FDA provided 90 days for public comment on the proposed rule.

II. Description of the Final Rule

FDA regulations identify the grounds for placing a clinical hold on proposed or ongoing phase 1 studies (§ 312.42(b)(1)) and on proposed or ongoing phase 2 or phase 3 studies (§ 312.42(b)(2)). FDA is amending these clinical hold regulations to provide an additional ground for placing a phase 1, phase 2, or phase 3 study on clinical hold. Under these amendments, FDA may impose a clinical hold on any proposed or ongoing clinical trial for a life-threatening disease or condition that affects both genders if men or women with reproductive potential who have the disease being studied are excluded from eligibility in any phase of the investigation because of a risk or potential risk of reproductive or developmental toxicity from use of the investigational drug.

The proposed rule refers to studies under an IND involving a drug that is intended to treat a life-threatening illness or disease affecting both genders. As stated in the proposal (62 FR 49946 at 49951), the definition of life-threatening illness or disease is intended to be consistent with the agency's IND regulations (§ 312.81(a)(1)). Under the IND regulations, the term life-threatening is applied to ''conditions'' or ''diseases.'' To remain consistent with current terminology, the agency is amending the final rule to refer to ''life-threatening diseases or conditions.''

The clinical hold under these amendments would not apply to clinical studies conducted under special circumstances, such as studies pertinent to only one gender (e.g., to evaluate the excretion of a drug in semen or its effects on menstrual function).

As described in the proposed rule, a clinical hold would not be applied to a clinical study conducted in men, as long as a study that does not exclude subjects with reproductive potential has been planned or is being conducted in women. The agency expects that in an active IND, studies that do not exclude women or men with reproductive potential will be underway or will commence in a timely manner. To clarify this expectation, the final rule has been modified to state that a clinical hold would not be ordered for a study conducted only in men or only in women, as long as a study that does not exclude members of the other gender with reproductive potential is being conducted concurrently or will take place within a reasonable time agreed upon by the agency (§ 312.42(b)(1)(v)(B)). FDA expects that a discussion between the sponsor and the agency concerning a reasonable time for carrying out the study would take place at a pre-IND meeting or with the submission of the IND.

As stated in the proposed rule, this amendment to the IND regulations would not apply to clinical studies conducted exclusively in healthy volunteers (62 FR 49946 at 49951). The final rule has been modified in § 312.42(b)(1)(v) by adding paragraph (C) to clarify that the rule applies to clinical investigations that are conducted only in subjects who have the disease or condition that the drug is intended to treat.

III. Comments on the Proposed Rule

FDA received 26 letters, including letters from manufacturers, individuals, advocacy groups, and trade associations, commenting on the proposed rule. The majority of comments supported FDA's proposal to prohibit the exclusion of women from investigational studies through the clinical hold mechanism. Many comments suggested changes that would have narrowed or broadened the proposal.