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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

**Investigational Biological Product Trials; Procedure to Monitor Clinical Hold Process;
Meeting of Review Committee and Request for Submissions**

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the 1999 meetings of the clinical hold review committee, which reviews the clinical holds that the Center for Biologics Evaluation and Research (CBER) has placed on certain investigational biological product trials. FDA is inviting any interested biological product company to use this confidential mechanism to submit to the committee for its review the name and number of any investigational biological product trial placed on clinical hold during the past 12 months that the company wants the committee to review.

DATES: The meetings will be held on February 9, 1999; May 11, 1999; August 10, 1999; and November 9, 1999. Biological product companies may submit review requests for the February meeting by January 5, 1999; for the May meeting by March 30, 1999; for the August meeting by June 29, 1999; and for the November meeting by September 28, 1999.

ADDRESSES: Submit clinical hold review requests to Amanda Bryce Norton, FDA Chief Mediator and Ombudsman, Office of the Commissioner (HF-7), Food and Drug Administration, 5600 Fishers Lane, rm. 14-105, Rockville, MD 20857, 301-827-3390.

FOR FURTHER INFORMATION CONTACT: Stephen M. Ripley, Center for Biologics Evaluation and Research (HFM-17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448, 301-827-6210.

SUPPLEMENTARY INFORMATION: FDA's regulations in part 312 (21 CFR part 312) provide procedures that govern the use of investigational new drugs and biologics in human subjects. If FDA determines that a proposed or ongoing study may pose significant risks for human subjects or is otherwise seriously deficient, as discussed in the investigational new drug regulations, it may order a clinical hold on the study. The clinical hold is one of FDA's primary mechanisms for protecting subjects who are involved in investigational new drug or biologic trials. Section 312.42 describes the grounds for ordering a clinical hold.

A clinical hold is an order that FDA issues to a sponsor to delay a proposed investigation or to suspend an ongoing investigation. The clinical hold may be ordered on one or more of the investigations covered by an investigational new drug application (IND). When a proposed study is placed on clinical hold, subjects may not be given the investigational drug or biologic as part of that study. When an ongoing study is placed on clinical hold, no new subjects may be recruited to the study and placed on the investigational drug or biologic, and patients already in the study should stop receiving therapy involving the investigational drug or biologic unless FDA specifically permits it.

When FDA concludes that there is a deficiency in a proposed or ongoing clinical trial that may be grounds for ordering a clinical hold, ordinarily FDA will attempt to resolve the matter through informal discussions with the sponsor. If that attempt is unsuccessful, a clinical hold may be ordered by or on behalf of the director of the division that is responsible for the review of the IND.

FDA regulations in § 312.48 provide dispute resolution mechanisms through which sponsors may request reconsideration of clinical hold orders. The regulations encourage the sponsor to attempt to resolve disputes directly with the review staff responsible for the review of the IND. If necessary, the sponsor may request a meeting with the review staff and management to discuss the clinical hold.

CBER began a process to evaluate the consistency and fairness of practices in ordering clinical holds by instituting an oversight committee to review clinical holds (see 61 FR 1033, January 11, 1996). CBER held its first clinical hold review committee meeting on May 17, 1995, and plans to conduct further quality assurance oversight of the IND process. The review procedure of the committee is designed to afford an opportunity for a sponsor who does not wish to seek formal reconsideration of a pending clinical hold to have that clinical hold considered “anonymously.” The committee consists of senior managers of CBER, a senior official from the Center for Drug Evaluation and Research, and the FDA Chief Mediator and Ombudsman.

Clinical holds to be reviewed will be chosen randomly. In addition, the committee will review some of the clinical holds proposed for review by biological product sponsors. In general, a biological product sponsor should consider requesting review when it disagrees with FDA’s scientific or procedural basis for the decision.

Requests for committee review of a clinical hold should be submitted to the FDA Chief Mediator and Ombudsman, who is responsible for selecting clinical holds for review. The committee and CBER staff, with the exception of the FDA Chief Mediator and Ombudsman, are never advised, either in the review process or thereafter, which of the clinical holds were randomly chosen and which were submitted by sponsors. The committee will evaluate the selected clinical holds for scientific content and consistency with FDA regulations and CBER policy.

The meetings of the oversight committee are closed to the public because committee discussions deal with confidential commercial information. Summaries of the committee deliberations, excluding confidential commercial information, may be requested in writing from the Freedom of Information Office (HFI-35), Food and Drug Administration, 5600 Fishers Lane, rm. 12A-16, Rockville, MD 20857, approximately 15 working days after the meeting, at a cost of 10 cents per page. If the status of a clinical hold changes following the committee’s review, the appropriate division will notify the sponsor.

For each meeting, FDA invites biological product companies to submit to the FDA Chief Mediator and Ombudsman the name and IND number of any investigational biological product trial that was placed on clinical hold during the past 12 months that they want the committee to review. Submissions should be made by January 5, 1999, for the February meeting;

by March 30, 1999, for the May meeting; by June 29, 1999, for the August meeting; and by September 28, 1999, for the November meeting to Amanda Bryce Norton, FDA Chief Mediator and Ombudsman (address above).

Dated: December 1, 1998
December 1, 1998



William K. Hubbard
Associate Commissioner for Policy Coordination

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL

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