
GENERAL REVIEW AND ENFORCEMENT POLICIES

**CLINICAL INVESTIGATOR SANCTIONS AND THE VIDEOTEX METHOD OF
OBTAINING INFORMATION ON INELIGIBLE INVESTIGATORS**

Issues involved in the promulgation of this guide are two-fold. First, CVM wishes to avoid the possibility that clinical studies conducted by ineligible investigators may be inadvertently used in support of application approvals. Second, CVM wishes to ensure that information on clinical investigators, disqualified or otherwise restricted, be readily available at the time action is taken and the ineligible list is updated. The withdrawal of eligibility is described.

Purpose

This guide identifies the procedures for:

- 1) Identification of ineligible investigators prior to drug approvals
 - 2) Notification of investigator ineligibility to relevant offices in the Center and Agency
 - 3) Withdrawal of eligibility, examination of INADs for unreliable data, and elimination of unreliable data.
1. The Center for Drug Evaluation and Research on its Vax Videotex system maintains a disqualified/restricted and assurances list of clinical investigators including input from all Centers. The identification codes and definitions are as follows:

- D = Investigators ineligible to receive investigational products-DISQUALIFIED
- R = Investigators agreeing to some RESTRICTION of the use of investigational products
- A = Investigators whose assurances for the performance of future studies with investigational products were accepted after regulatory hearing or through consent agreement. These are investigators whose work is found to be in

violation of regulations but on whom no sanctions were imposed because of the assurance given for future compliance. They are not disqualified.

The Videotex bulletin board additionally contains data on permanent debarment from FDA, temporary debarment/administrative sanctions, federal procurement debarment, AIP firms.

This source should be consulted by the primary reviewer to establish that no ineligible clinical investigator is conducting or has conducted trials under an INADA. The access and search information was distributed by E-MAIL to the Office of New Animal Drug Evaluation staff in July, 1994.

2. The Center Bioresearch Monitoring Staff is responsible for notifying concerned groups agency-wide by updating the Videotex list.
3. The Food and Drug Administration (FDA) may initiate a proceeding to withdraw eligibility of a clinical investigator from receiving investigational use articles if the agency has information that the investigator has repeatedly or deliberately violated FDA's regulations or has submitted false information to the sponsor in a required report. The proceeding is as follows:

Offer for Informal Conference or Written Explanation:

Whenever FDA has information indicating that an investigator has repeatedly or deliberately failed to comply with FDA regulatory requirements or has submitted false information to the sponsor in any FDA required report, the appropriate Center will send the investigator a written notice describing the noncompliance or false information and offer the investigator an opportunity to respond to the notice at an informal conference or in writing. The agency will specify a time period within which the investigator must respond. While the conference is informal, a transcript may be made, and the investigator may have legal representation.

If the investigator offers and the Center accepts a timely and satisfactory explanation for the noncompliance, the process is terminated, and the investigator is notified in writing. If the investigator offers an explanation that the Center rejects, or if the investigator fails to respond within the specified time period, FDA will offer the investigator an opportunity for an informal regulatory hearing, under Part 16 of FDA's regulations (21 CFR Part 16), to determine whether the investigator should remain eligible to receive investigational new animal drugs.

Opportunity for Hearing on Proposed Withdrawal of Eligibility:

FDA initiates a Part 16 hearing when it sends the investigator a written Notice of Opportunity for Hearing. The Notice specifies the allegations that are the subject of the hearing and other relevant information. An investigator must respond to the Notice within a specified time. If the investigator does not respond within that time period, FDA considers the offer for a hearing to have been refused, and no hearing will be held. The Commissioner will then consider all relevant information available to FDA to determine whether the investigator should be disqualified.

If a hearing is requested, the Commissioner will designate a presiding officer from FDA, and the hearing will take place at a mutually agreeable time at FDA headquarters. If agreement cannot be reached, the presiding officer will designate a hearing date.

Part 16 Hearing and Final Order on Disqualifications:

Before the hearing, FDA gives the investigator notice of the matters to be considered at the hearing:

A comprehensive statement of the basis for the proposal to disqualify the investigator and a general summary of the information that the Center will present. The Center and the investigator exchange written notice of any published articles or written information to be presented or relied on at the hearing. If it seems unreasonable to expect the other party to have, or able to obtain, a copy of a particular document, a copy of the document is provided.

The hearing is informal, and the rules of evidence do not apply. Any participant may comment upon or rebut all data, information, and views presented.

The presiding officer conducts the hearing. The hearing begins with Center employees giving a complete statement of the action that is the subject of the hearing and describing the information and reasons supporting disqualification. They may present any oral or written information relevant to the hearing. The investigator, who may be represented by legal counsel, then may present any oral or written information relevant to the hearing. All parties may confront and question any person who makes a statement at the hearing, other than the presiding officer and counsel for the parties.

After the hearing, the presiding officer prepares a written report which includes a recommended decision and the reasons for the recommendation. The administrative record of the hearing includes all written material presented at the hearing and the hearing transcript. The parties are given the opportunity to review and comment on the presiding officers's report. The report and the comments of the parties are transmitted to the Commissioner who considers them along with the administrative

record to determine whether the investigator should be disqualified. The Commissioner issues a written decision giving the basis for the action decided upon.

Actions Following Disqualification:

If the Commissioner determines that the investigator has repeatedly or deliberately failed to comply with the requirements, or has repeatedly or deliberately submitted false information to the sponsor in any required report, the Commissioner will:

- a. Notify the investigator and the sponsor(s) of any investigation(s) in which the investigator has participated that the investigator is not entitled to receive investigational animal drugs. The notification will include a statement explaining the basis for this determination.
- b. Notify the sponsors of studies conducted under each Investigational New Animal Drug (INAD) application or each approved application containing data reported by the investigator that with our validating information, establishing that the study results were unaffected by the investigator's misconduct, the agency will not accept the investigator's work in support of claims of safety and efficacy.
- c. Determine, after the investigator's unreliable data are eliminated from consideration, whether the data remaining support a conclusion that studies under the INAD may continue. If the Commissioner determines that the remaining data are inadequate, the sponsor will be notified and will have an opportunity for a regulatory hearing under 21 CFR Part 16. If a public health danger exists the Commissioner will terminate the INAD immediately and notify the sponsor of the determination. The sponsor will then have an opportunity for a Part 16 regulatory hearing to determine whether the INAD should be reinstated.
- d. Determine, after the investigator's unreliable data are eliminated from consideration, whether the continued approval of the product for which the data were submitted can be justified. If it cannot, the Commissioner will move to withdraw approval in accordance with applicable provisions of the Federal Food, Drug, and Cosmetic Act.

Public Disclosure of Information Regarding Disqualification:

Notification of impending or contemplated action is limited to those persons who have a legitimate

interest in knowing that the clinical investigator may be disqualified, e.g., the sponsor of studies conducted or to be conducted by the investigator, federal, state, or local agencies, and institutions in which the investigator practices or teaches. Similar notification may be provided at the time of a consent agreement.

FDA may notify a sponsor about a disqualification proceeding pending against a clinical investigator when the circumstances clearly establish a need to do so. Notification generally will be made when FDA sends a Notice of Opportunity for a Hearing under Part 16 to the investigator. However, when safety considerations warrant earlier notifications, the agency will act accordingly. FDA will notify other government agencies of a proposed disqualification whenever the agency deems such notification to be appropriate.

If the agency notifies other parties of its preliminary findings prior to final disqualifications, FDA will provide a description of these findings, state that the agency has yet to reach a final decision, and will not recommend that any action be taken by the third party. If the disqualification proceeding does not result in a disqualification or a consent agreement, the agency will so advise those third parties who had been contacted. A copy of each notification will be sent to the investigator.

If the agency gives notice of the disqualification to a third party, FDA will provide a copy of the final disqualification order, explain its legal meaning, and state that FDA is not advising or recommending that the person notified take any action upon the matter. A copy of each notification will be sent to the investigator.

Reinstatement of a Disqualified Investigator:

An investigator who has been disqualified may be reinstated if the Commissioner determines that the investigator has presented adequate assurances that he/she will employ investigational drugs in compliance with FDA regulations. A notice of availability of the agency's reinstatement guidelines, entitled "Procedures for Reinstating Eligibility of Disqualified Clinical Investigators to Receive Investigational Articles," was published in the Federal Register on November 19, 1982 (47 FR 52228). These guidelines are available through FOI.

Consent Agreements:

In addition to an opportunity for an informal conference or to responding in writing to the Center's

allegations, the Center may offer investigators the opportunity to enter into a consent agreement whereby the investigator agrees to meet certain conditions mutually acceptable both to FDA and the investigator. This agreement obviates the need to proceed further with the disqualification process. Consent agreements generally take one of two forms:

- (1) the individual agrees to refrain from further studies within FDA's jurisdiction, or
- (2) the individual agrees to specific restrictions in the use of investigational products, such as oversight by an individual acceptable to both the investigator and the agency.

The consent agreement option is available to the clinical investigator at all stages of the disqualification process.

Criminal Prosecution:

A final order after a Part 16 proceeding, or entry into a consent agreement, constitutes final agency administrative action. Final agency administrative action does not preclude institution of criminal proceeding against an investigator. Those investigators referred for criminal prosecution are generally clinical investigators who have knowingly or willingly submitted false information to a sponsor in a report required by FDA regulations.