

monensin, salinomycin, narasin, semduramicin, and lasalocid) as adverse reactions may occur. If signs of toxicity occur, discontinue use. Withdraw 2 days before slaughter. As chlortetracycline calcium complex, Type A medicated articles containing the equivalent of 50 to 100 grams per pound of chlortetracycline hydrochloride provided by 000004 and 046573 in § 510.600(c) of this chapter.

Dated: February 6, 1997.

Stephen F. Sundlof,

Director, Center for Veterinary Medicine.

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21 CFR Part 812

[Docket No. 92N-0308]

Investigational Device Exemptions; Disqualification of Clinical Investigators

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its medical device regulations to include provisions for the disqualification of clinical investigators. These amended regulations parallel, with minor exceptions, the regulations for disqualification of clinical investigators of drugs, biologics, and animal drugs. The agency is finalizing this regulation to further implement its plan for consistent bioresearch monitoring procedures for all products regulated by FDA and to improve the remedies available to deal with clinical investigators who violate the law. This action is being taken under the Medical Device Amendments of 1976.

DATES: Effective May 13, 1997.

FOR FURTHER INFORMATION CONTACT: Rodney T. Allnut, Center for Devices and Radiological Health (HFZ-310), Food and Drug Administration, 2094 Gaither Rd., Rockville, MD 20850, 301-594-4718.

SUPPLEMENTARY INFORMATION:

I. Background

FDA has long intended to have clinical investigator disqualification procedures available for medical device investigations. Although the investigational device exemption (IDE) regulation part 812 (21 CFR part 812) allows FDA to initiate regulatory action against a study sponsor due to a noncompliant investigator, such as terminating the sponsor's IDE or imposing additional restrictions under

the IDE, the IDE regulation did not expressly provide for clinical investigator disqualification. The proposed IDE regulation, published in the Federal Register of August 20, 1976 (41 FR 35282 at 35311), contained disqualification provisions for clinical investigators in proposed § 812.119 that were not included in the final IDE regulations published on January 18, 1980 (45 FR 3732), which apply to device investigations generally. Disqualification provisions were included, however, in part 813 (21 CFR part 813) on investigational exemptions for intraocular lenses (IOL's) in § 813.119 (42 FR 58874, November 11, 1977). The preamble to the final IDE regulation, published in the Federal Register of January 18, 1980 (45 FR 3732 at 3749), noted that proposed § 812.119 was being removed and would be addressed in FDA's final agency-wide regulation on the obligations of clinical investigators, which had been proposed in the Federal Register of August 8, 1978 (43 FR 35186). This agency-wide regulation, however, was never finalized.

In the Federal Register of October 6, 1993 (58 FR 52142), FDA issued a proposed rule to remove part 813, the regulation on investigational exemptions for IOL's. FDA received two comments in response to the proposed rule. These comments were addressed in the preamble to the rule that removed part 813, which was published in the Federal Register of January 29, 1997 62 FR 4164.

In the Federal Register of October 6, 1993 (58 FR 52144), FDA also published a proposed rule governing disqualification of clinical investigators of medical devices, to be added to part 812. The proposed rule was virtually identical to the regulation for disqualification of clinical investigators of IOL's, which would be removed with the proposed removal of part 813. In the proposed rule, however, FDA expressly invited comments on whether the procedures for disqualification of clinical investigators of medical devices should be identical, or virtually identical to the regulation for the disqualification of clinical investigators of drugs and biologics in § 312.70 (21 CFR 312.70). FDA stated that if comments persuaded the agency to revise the proposed rule to follow § 312.70 precisely or closely, the agency might issue a final rule which parallels § 312.70.

FDA received three comments stating an explicit preference for rules governing disqualification of investigators of drugs as specified in § 312.70, over the rules that had been

proposed for disqualification of investigators of devices. Two other comments that did not specifically mention § 312.70 nevertheless suggested changes to the proposed rule that would make it more consistent with the drug investigator disqualification rule. The other three comments FDA received did not address this issue.

Two comments preferred § 312.70 to the proposed regulation because § 312.70 does not contain the perceived flaws found in the proposed regulation. These comments stated, e.g., that the threshold for disqualification in § 312.70 is set much higher and the terms are more clearly defined than in the proposed regulation. One of these comments requested that the Center for Devices and Radiological Health (CDRH) adopt § 312.70 in its entirety because of the perceived flaws in the proposed rule. That comment also noted that most medical device companies and investigators of devices are unfamiliar with § 312.70. Therefore, the comment recommended that FDA propose a rule similar to § 312.70 and give interested parties a chance to comment on the reproposal. The third comment stated that the regulation for disqualification of investigators of investigational new drugs is a better model because it is a relatively simple and clear regulation, it does not impose unfair and potentially harmful presumptions, and it would give FDA the immediate consistency it desires among product lines.

FDA has been persuaded by the comments that the regulation governing disqualification of investigators of medical devices should parallel the regulation for disqualification of investigators of drugs and biologics in § 312.70 (as well as the regulation for disqualification of investigators of animal drugs at § 511.1(c) (21 CFR 511.1(c))). This rule for disqualification of investigators of medical devices, therefore, adopts regulations that are basically the same as those governing disqualification of investigators of drugs, biologics, and animal drugs, with minor exceptions.

The agency has concluded, however, that a reproposal is unnecessary because the agency received sufficient and adequate comments to make a reasoned determination about the final rule and because the agency provided clear notice to interested persons that a final regulation paralleling § 312.70 would be adopted if the comments persuaded the agency that this approach represented the best option. (See the Federal Register of October 6, 1993, that stated "FDA is giving notice that, if comments persuade the agency to revise the proposed rule to follow § 312.70 * * *

the agency may issue a rule that parallels § 312.70.” (58 FR 52144.)

In response to the concern that medical device companies and investigators of medical devices are unfamiliar with § 312.70, the agency notes that this rule is consistent with FDA's regulatory program for investigators of drugs, which has existed for more than 30 years, and that interested persons were provided explicit notice in the proposal that the same disqualification procedures might be adopted for investigators of devices. Interested parties who may be unfamiliar with FDA's bio research monitoring activities for clinical investigations may find useful the description of the agency's investigator disqualification process that is provided in an FDA publication entitled "Food and Drug Administration INFORMATION SHEETS for Institutional Review Boards and Clinical Investigators" (October 1995 revision), which is currently available from the Office of the Associate Commissioner for Health Affairs.

This document explains why FDA was persuaded by the comments to adopt the approach being codified and also describes the ways in which the rule has been modified from the proposal in order to incorporate the changes suggested by the comments. In addition, this document identifies comments that are now moot because the agency adopted disqualification procedures that parallel § 312.70. Finally, this document also explains FDA's basis for not including other suggestions.

II. Summary of the Final Rule

The final rule consists of the following provisions:

A. Grounds for Disqualification

Section 812.119(a) establishes that disqualification proceedings will only begin if FDA has information indicating that the investigator has: (1) Repeatedly or deliberately failed to comply with the requirements of this part, part 50 (21 CFR part 50), or part 56 (21 CFR part 56); or (2) repeatedly or deliberately submitted false information either to the sponsor of the investigation or in any required report.

B. Informal Conference or Written Explanation and Opportunity for a Hearing on Proposed Disqualification

In accordance with § 812.119(a), when FDA determines that one of the grounds for disqualification may exist, CDRH will furnish the investigator written notice of the matter under complaint and offer the investigator an opportunity

to explain the matter in writing, or, at the option of the investigator, in an informal conference. If an explanation is offered and accepted by CDRH, the disqualification process will be terminated. If an explanation is offered but not accepted by CDRH, the investigator will be given an opportunity for a regulatory hearing under part 16 (21 CFR part 16) on the question of whether the investigator is entitled to continue to receive investigational devices.

C. Notification of Disqualification

In accordance with § 812.119(b), after evaluating all available information, including any explanation presented by the investigator, if the Commissioner of Food and Drugs (the Commissioner) determines that the investigator has repeatedly or deliberately failed to comply with the requirements of this part, part 50, or part 56, or has repeatedly or deliberately submitted false information either to the sponsor of the investigation or in any required report, the Commissioner will notify the investigator, the sponsor of any investigation in which the investigator has been named as a participant, and the reviewing Institutional Review Board (IRB), that the investigator is not entitled to receive investigational devices. The notification will provide a statement of the basis for such determination.

D. Actions Upon Disqualification

Under § 812.119(c), FDA shall examine each IDE and each cleared or approved application submitted under subpart E of part 807 (21 CFR part 807) or part 814 (21 CFR part 814), containing data reported by an investigator who has been determined to be ineligible to receive investigational devices to determine whether the investigator has submitted unreliable data that are essential to the continuation of the investigation or essential to the clearance/approval of any marketing application.

Under § 812.119(d), if the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation, the Commissioner will notify the sponsor, who shall have an opportunity for a regulatory hearing under part 16. If a danger to the public health exists, however, the Commissioner shall order withdrawal of approval of the IDE before any hearing. In such case, the sponsor shall have an opportunity for a regulatory hearing

under part 16 on the question of whether the IDE should be reinstated. (See § 812.30(c)(2).)

In accordance with § 812.119(e), if the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the continued clearance or approval of the marketing application for which the data were submitted cannot be justified, the Commissioner will proceed to withdraw approval or rescind clearance of the medical device in accordance with the applicable provisions of the act and the agency's regulations.

E. Reinstatement of a Disqualified Investigator

Under § 812.119(f), a disqualified investigator may be reinstated when the Commissioner determines that the investigator has presented adequate assurances, through written submissions, that the investigator will employ investigational devices solely in compliance with the provisions of parts 812, 50, and 56.

F. Scope

The final rule clarifies that the provisions for disqualification of investigators of devices apply to all cleared or approved and pending device applications containing or relying upon any clinical investigations performed by the disqualified investigator. Such applications include IDE's, premarket notifications (510(k)'s), and premarket approval applications (PMA's). Subsequent to publication of the proposed rule, FDA discovered that 510(k)'s were inadvertently omitted from proposed § 812.119(a). Because the provisions for disqualification of a clinical investigators are intended to apply to all device applications containing or relying upon any clinical investigations performed by the disqualified investigator, this final rule clarifies that such provisions apply to 510(k)'s, IDE's, and PMA's.

The final rule also clarifies that no clinical investigator of medical devices is exempt from the disqualification regulations. The exemptions and abbreviated requirements described in part 812 for certain investigations are intended to relate to those procedures and requirements under part 812 associated with submitting an IDE application or obtaining an IDE prior to conducting an investigation. Section 812.2 is not intended to eliminate the responsibility of clinical investigators of devices to abide by procedures and standards associated with good scientific practice. Whether or not an investigation requires an IDE, every

clinical investigator whose work may be considered in connection with a marketing application is expected to comply with the agency's regulations and scientific standards relating to informed consent, IRB oversight, inspections, adherence to investigational protocols, and pertinent reports and recordkeeping. The final rule amends § 812.2 to clarify that the provisions governing disqualification of investigators apply to all clinical investigations of devices, including those that do not require FDA approval of an IDE, e.g., clinical investigations involving nonsignificant risk devices, and those categories of exempted devices identified in the IDE regulation.

III. Identification and Explanation for the Differences Between the Regulation for Disqualification of Investigators of Devices and the Regulation for Investigators of Drugs and Biologics

Section 812.119(a) establishes that FDA may begin the disqualification process "if FDA has information indicating that an investigator has repeatedly or deliberately submitted false information either to the sponsor of the investigation or in any required report." This language is somewhat different from the parallel provision for investigators of drugs and biologics (§ 312.70(a)), which states that a disqualification process may begin when there is information that the investigator "has submitted to the sponsor false information in any required report." (The parallel regulation for investigators of animal drugs (§ 511.1(c)), requires FDA to have information indicating that the investigator "has submitted false information either to the sponsor of the investigation or in any required report.") FDA believes that the language in the final rule for disqualification of investigators of devices more clearly states the intent of both the drug and animal drug provisions.

As discussed in section IV. of this document, several comments raised concern that investigators would be unfairly penalized for submitting false information inadvertently or when it was beyond their individual control. The agency does not intend isolated or inadvertent failures to be the basis for disqualification and the addition of the phrase "repeatedly or deliberately" clarifies that the agency's threshold for taking action against a clinical investigator requires the submission of false information to be either deliberate or frequent enough to call into question the individual's eligibility to continue the investigation.

Section 812.119(b) establishes that, in addition to notifying the investigator and the sponsor of any investigation in which a disqualified investigator has been named as a participant (§ 312.70(b)), FDA will also notify the reviewing IRB of a final disqualification determination. FDA has made this addition in response to several comments received on the proposed rule and after concluding that this notification will better enable the reviewing IRB to meet an obligation for continuing review to ensure the protection of the rights and well-being of the subject.

Section 812.119(d) establishes that in addition to notifying the sponsor of any investigation (§ 312.70(d)), FDA will also notify the reviewing IRB that the Commissioner has determined that a danger to public health exists and has ordered withdrawal of approval of the IDE. FDA has considered the comments received on the proposed rule that prompted the adoption of notification of IRB's as provided under § 812.119(a), and has concluded that this notification will better enable IRB's to monitor an investigation that is ordered terminated to ensure continued protection of the rights and well-being of the subject.

FDA believes that these changes improve the medical device regulations for disqualification of clinical investigators without creating significant discrepancies between those procedures and the regulations that are now in place for clinical investigators of drugs, biologics, and animal drugs. FDA intends to consider making similar changes to § 312.70 in order to make the investigator disqualification regulations as consistent as possible.

IV. Comments

FDA published a proposed rule to revise its medical device regulations to include provisions for the disqualification of clinical investigators (58 FR 52144). Because of an inadvertent error, the date for submission of comments was incorrectly published as November 5, 1993, even though the preamble to the proposed rule provided an opportunity for interested persons to submit comments on the proposed rule until December 6, 1993. A correction notice was published in the Federal Register of October 14, 1993 (58 FR 53245). Subsequently, in the Federal Register of December 6, 1993 (58 FR 64209), FDA extended the comment period for the proposed rule from December 6, 1993, until January 5, 1994, in response to a request for an extension from a trade association.

The agency received a total of eight comments from trade associations, manufacturers, law offices, a medical device consultant, a medical center, and FDA's Center for Drug Evaluation and Research (CDER). A summary of the comments and the agency's response to them is provided below:

A. Secondary Studies; Proposed § 812.119(a)(2)

1. A comment suggested that the proposed provisions authorizing disqualification of secondary studies, i.e., clinical studies by the same investigator other than the one in which misconduct is shown, should be limited. The comment recommended that limits should be placed on retrospective disqualification of secondary studies because FDA has authority to monitor the integrity and performance of secondary studies. For instance, FDA has the opportunity to inspect clinical study sites, to review sponsor's monitoring of studies, and to analyze the results of studies. Because the agency already has the authority to monitor the integrity and performance of secondary studies, the comment requested FDA to establish the following provisions relating to disqualification of secondary studies: (1) Secondary studies should be disqualified only when there is specific, demonstrable basis for a charge of misconduct; (2) the burden of proof relative to disqualification of a secondary study should be with FDA; (3) sponsors of secondary studies should be notified of disqualification of investigators; and (4) the basis for disqualification of a secondary study should be limited to issues which represent ongoing threats to the safety of current or future users of the product.

Another comment suggested that proposed § 812.119(a)(2) should not apply to other ongoing IDE's in which the investigator is involved, unless particular information establishes that a potential problem exists with respect to that specific clinical investigation.

The agency agrees with these comments and is persuaded that the approach set forth in § 312.70 and now being adopted in part 812 is preferable to the proposal because it addresses these concerns. The final rule does not automatically disqualify all IDE's or secondary studies. Instead, § 812.119 establishes that FDA will examine each IDE to determine whether the disqualified investigator has submitted unreliable data that are essential to the continuation of any investigation in which the investigator has been named a participant. (See § 812.119(c).) If the Commissioner determines, after the

unreliable data submitted by the investigator are eliminated from consideration, that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation, the Commissioner will notify the sponsor, who shall have an opportunity for a regulatory hearing under part 16. (See § 812.119(d).)

Thus, in accordance with § 812.119(c) and (d), FDA may terminate "secondary" clinical investigations in which the disqualified investigator has been involved only after FDA: (1) Has determined that the disqualified investigator has submitted unreliable data that are essential to the continuation of any investigation in which the investigator has been named a participant; (2) eliminates the unreliable data from consideration and determines that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation; and (3) provides the sponsor with an opportunity for a regulatory hearing.

In accordance with § 812.119(d), the initial burden of proof relative to disqualification of secondary studies/IDE's rests with the agency. If FDA's initial determination is that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation, the sponsor will be provided with an opportunity to challenge FDA's findings during a regulatory hearing.

The comment's suggestion that sponsors of secondary studies be notified of the disqualification of investigators has already been incorporated into § 812.119(b), which requires, among other things, notification of the sponsor of any clinical investigation in which the disqualified investigator has been named as a participant.

B. Proposed § 812.119(a)

2. One comment requested that § 812.119(a), which was drafted to apply to the disqualification of an investigator "who has failed to comply with any" of the regulations applicable to clinical investigators, be changed to apply only to investigators who have engaged in serious violations.

The agency agrees with the basic concern raised by this comment and believes that the decision to adopt a final regulation that parallels § 312.70 has addressed this concern. Section 812.119(a) replaces "has failed to comply with any of the regulations set forth in this part" with "has repeatedly or deliberately failed to comply with the requirements of this part, part 50, or part 56 * * *." An investigator's failure

to repeatedly or deliberately comply with the requirements of this part, part 50, or part 56 constitutes a serious violation.

C. Proposed § 812.119(a)(1)

3. One comment noted that the use of the term "necessarily" in proposed § 812.119(a)(1) implies that a disqualification decision may or may not constitute a finding or recommendation that the investigator is not qualified to practice or teach medicine or should be subject to other sanctions by third parties. The comment suggested that these areas are outside the disqualification proceeding purview. As a result, the word "necessarily" should be omitted from § 812.119(a)(1) to ensure that a disqualification decision would not affect these areas of the investigator's life.

Proposed § 812.119(a)(1) has not been adopted in the final regulation. However, under § 812.119(b), the disqualification notification issued by the agency constitutes only a finding that the investigator is not entitled to receive investigational devices and a statement of the basis for a determination by the agency that the investigator is disqualified from participation in clinical investigations. The agency's disqualification does not constitute any other finding.

D. Proposed § 812.119(b)(1)

4. Proposed § 812.119(b)(1) provided that an investigator could be disqualified if he or she "caused false information to be submitted" to FDA or a sponsor. According to one comment, this language allows an investigator to be held responsible even if the investigator were unaware that the information was false. The comment said that this provision fails to recognize that all clinical studies have some degree of unavoidable error. Another comment stated that an investigator should not be disqualified because he or she submitted false information generated by a third person, unless the investigator knew of the falsehood. A third comment requested that proposed § 812.119(b)(1) be rewritten as follows: An investigator should be disqualified if "the investigator deliberately caused false information to be submitted to FDA or to the sponsor of a study with the understanding that information may be submitted to FDA."

It is not FDA's intention to disqualify an investigator for a single submission of false data for which the investigator was not responsible. The agency would not seek to disqualify investigators under such circumstances and FDA

believes that the adoption of § 812.119(a) ensures against such situations.

In accordance with § 812.119(a), an investigator may be disqualified "If FDA has information indicating that an investigator has * * * deliberately or repeatedly submitted false information either to the sponsor of the investigation or in any required report, * * *." Requiring submission of false information to be "deliberately" submitted ensures that investigators will not be held responsible for a single submission of false information if the investigator were unaware that the information was false.

Although the "repeated submission of false information" basis for disqualification does not ensure that an investigator will not be disqualified for the submission of false information if the investigator were unaware that the information was false, FDA believes that such a basis for disqualification is necessary. A clinical investigator who repeatedly causes false information to be submitted to FDA, whether through carelessness or mismanagement, jeopardizes the integrity of the study and safety of the patients. The agency believes that investigators who repeatedly submit false information should be disqualified from participation in such investigations.

E. Proposed § 812.119(b)(3)

5. Five comments suggested modifying the language in proposed § 812.119(b)(3) in order to clarify the grounds for disqualification and to afford clinical investigators and FDA a less severe remedy than disqualification for less serious violations. One comment recommended that FDA incorporate the standard used in § 312.70, which states that investigators may be disqualified for repeated or deliberate failures to comply with regulations.

The final rule addresses the concerns raised by these comments by adopting § 812.119(a), which parallels, with minor modifications, § 312.70(a). Section § 812.119(a) states that clinical investigators may be disqualified only under the following situations: (1) Repeated or deliberate failure to comply with the requirements of parts 812, 50, or 56; or (2) repeated or deliberate submission of false information either to the sponsor of the investigation or in any required report.

The agency believes that the concern regarding affording clinical investigators a remedy other than disqualification for less serious violations has also been addressed in § 812.119(a). Section 812.119(a) provides the investigator with an opportunity to explain the

matter in writing, or in an informal conference with the center. FDA believes that this opportunity is the appropriate time for a clinical investigator to dispute or explain any of the allegations cited in the written notice proposing disqualification. Based on the explanation given, CDRH may determine that the investigator's disqualification is not necessary and terminate the proceeding. The clinical investigator also may decide to enter into a consent agreement with the agency that terminates the disqualification proceeding.

F. Proposed § 812.119(c) and (d)

6. A comment requested that, in addition to the investigator receiving written notice, the sponsor of the clinical investigation, as well as IRB, should be informed about any written notice by FDA to the clinical investigator of an allegation involving noncompliance with regulations that may be grounds to justify disqualification of the investigator. Another comment requested that FDA be required to notify the sponsor, IRB, and other sponsors who are employing or have previously employed the investigator to conduct clinical studies requiring prior FDA review, that a potential problem exists at the same time FDA notifies the investigator about the opportunity for a written explanation, an informal conference, or a hearing. The comment contended that giving such notification will allow the sponsors to take actions to minimize the potential effect of disqualification.

One comment suggested adding the following provision to § 812.119(c):

The written notice to the investigator will be copied to the sponsor of the investigation, as well as the IRB reviewing the investigation. Sponsors of other clinical studies requiring prior FDA review which are being or have been conducted by the investigator will also be notified. FDA will issue this notice to the IRB and sponsors within 15 working days after the notice is issued to the clinical investigator.

Furthermore, it was requested that the disqualification process termination notice to the clinical investigator, provided for in § 812.119(c)(2), be required to be copied to the sponsor of the investigation, the IRB reviewing the investigation, and sponsors of other clinical studies requiring prior FDA review which are being or have been conducted by the investigator.

The agency does not believe that additional notification of preliminary findings should be required routinely as part of the investigation of an investigator who may be disqualified because further investigation may determine the investigator to be in

compliance with the relevant regulations, and also because sponsors and IRB's have access to Form FD-483 and warning letters relating to their clinical investigators. The agency does recognize, however, that there are times when it is reasonable or necessary for FDA to notify the sponsor of a study and the reviewing IRB prior to a final disqualification determination in order to ensure the integrity of a study or the rights and well-being of a subject. While there are circumstances that may warrant early notification to sponsors or IRB's, this final regulation, like its counterparts for investigators of drugs, biologics, and animal drugs, does not explicitly address this issue. However, separate from this rulemaking, the agency is establishing a working group, representing all FDA centers, to establish a uniform policy on the issue of prior disclosure to sponsors and IRB's.

The agency has adopted § 812.119(b), which parallels the language used in § 312.70(b) of the investigational new drug (IND) regulations for disqualification of investigators, and provides that "any sponsor of an investigation in which the investigator has been named as a participant and the reviewing IRB" shall be notified of the agency's final decision on the disqualification of the investigator and the basis for the disqualification. The agency has also adopted § 812.119(d), which parallels the language used in § 312.70(d) of the IND regulations, and provides that sponsors and IRB's shall be notified and sponsors given an opportunity for a hearing, when FDA intends to withdraw approval for an IDE, or if a danger to public health warrants immediate termination of an investigation, that the Commissioner shall order the immediate withdrawal of approval of the IDE and the sponsor shall be offered an opportunity for a hearing on whether the IDE should be reinstated.

G. Proposed § 812.119(c)(1) and (d)

7. A comment suggested that the written notice in § 812.119(c)(1) and (d) should describe the noncompliance with sufficient detail and particularity so that the investigator is informed fully of the alleged violation. An investigator cannot provide an informed response unless sufficient detail is provided.

The agency agrees with the concern expressed by this comment and has adopted § 812.119(a), which establishes the agency's responsibility to provide adequate details. Section 812.119(a) provides that " * * * the Center for Devices and Radiological Health will furnish the investigator written notice of

the matter under complaint * * *." FDA intends that such notices include a full description of the alleged violation(s) that are the basis for disqualification.

H. Proposed § 812.119(c)(2)

8. Proposed § 812.119(c)(2) provides for the termination of the proceeding if the investigator offers an explanation for the noncompliance that is accepted by FDA. One comment suggested that § 812.119(c)(2) be rewritten to allow for the termination of the proceeding if the investigator demonstrates that no regulatory violations actually occurred. Another comment recommended that the term "alleged" be placed before the word noncompliance in § 812.119(c)(2) to indicate that a noncompliance determination has not been made at this preliminary stage.

The agency believes that these modifications are unnecessary with the adoption of the final rule. In accordance with § 812.119(a), when FDA furnishes the investigator with a written notice of the matter under complaint, FDA will also offer the investigator an opportunity to explain the matter in writing, or at the option of the investigator, at an informal conference. If an explanation is offered by the investigator and accepted by CDRH, the disqualification process will be terminated. The scope of an investigator's explanation is not limited and may include a showing that no regulatory violations actually occurred.

The agency also believes that modifying § 812.119(a) by inserting the term "alleged" in the regulatory text is unnecessary because § 812.119(a), unlike proposed § 812.119(c)(2), does not indicate that a final noncompliance determination will be made at this preliminary stage.

I. Proposed § 812.119(c)(2) and (c)(3)

9. A comment requested that the terms "FDA" and "agency" in § 812.119(c)(2) and (c)(3) be replaced with "Center for Devices and Radiological Health," in order to clarify that informal conferences would not be held at the Commissioner's level.

The concern raised by this comment has been addressed with the adoption of § 812.119(a), which references CDRH, FDA. Also, FDA is taking this opportunity to notify interested persons that CDRH's Division of Compliance Operations has been eliminated through reorganization. The informal conferences will be held by the Division of Bioresearch Monitoring, Office of Compliance, CDRH.

J. Proposed § 812.119(d)

10. A comment stated that the text of proposed § 812.119(d) failed to mention that an opportunity for a hearing exists for an investigator who has received a proposed notice of disqualification.

This concern also has been addressed with the adoption of § 812.119(a). Section 812.119(a) specifically states, "If an explanation is offered but not accepted by the Center for Devices and Radiological Health, the investigator will be given an opportunity for a regulatory hearing under part 16 * * *."

K. Proposed § 812.119(f)(1)

11. Under § 812.119(a) and paragraph (f)(1) as proposed, a hearing on the disqualification of an investigator shall be conducted in accordance with the requirements for a regulatory hearing as set forth in part 16. One comment maintained that conducting a regulatory hearing under part 16 does not adequately protect the investigator's due process rights. The comment requested FDA to follow the procedures set forth in part 12 (21 CFR part 12) for a formal evidentiary public hearing when determining whether an investigator should be disqualified.

The agency disagrees with the comment that a part 16 regulatory hearing does not provide adequate due process. A part 16 regulatory hearing is initiated by a notice of opportunity for hearing from FDA. This notice specifies, among other things, the facts and the action that are the subject of the hearing and states the time in which a hearing may be requested. In accordance with part 16, if a hearing is requested, the Commissioner will designate a presiding officer, and the hearing will take place at a time and location agreed upon by the party requesting the hearing, FDA, and the presiding officer. A part 16 regulatory hearing, therefore, adequately protects an investigator's due process rights by providing the investigator with notice and an opportunity to be heard. Moreover, FDA has had extensive experience in the use of part 16 hearings for disqualification proceedings of clinical investigators of new drugs under part 312. FDA's experience has established that part 16 hearings are appropriate in these circumstances and protect the investigator's due process rights. Finally, a part 16 regulatory hearing is more streamlined than a part 12 evidentiary public hearing and will provide a quicker resolution of issues for both FDA and the investigator.

L. Proposed § 812.119(f)(3)

12. Section 812.119(f)(2) provides that a final order disqualifying a clinical investigator will be copied to the sponsor of each clinical investigation subject to requirements for prior submission to FDA that was or is being conducted by the investigator. A comment suggested adding a similar provision to § 812.119(f)(3) so that sponsors will be notified of any final order terminating the disqualification proceeding. Additionally, the comment suggested that FDA provide a copy of such orders to IRB's as well.

The agency has adopted § 812.119(b), which provides for notification of the interested parties after the Commissioner has made a final determination that an investigator is disqualified. After a final disqualification decision has been made, the investigator, the sponsors of any investigations in which the investigator was named as a participant, and the reviewing IRB shall be notified that the investigator is disqualified.

The agency's response to comments concerning notification of interested parties prior to a final disqualification decision has been provided previously. (See the response to comment 6 in section IV.F. of this document.)

M. Proposed § 812.119(g)

13. One comment said that proposed § 812.119(g), actions upon disqualification, may be interpreted to mean that the Commissioner is authorized to make decisions that directly affect the rights and responsibilities of sponsors even though sponsors may not be aware of the disqualification process or be given the opportunity to participate in the disqualification decisions. Another comment maintained that this section may violate sponsors' due process rights. The comment recommended that sponsors be given the opportunity to present their views before the agency takes any of the actions described in proposed § 812.119(g).

The agency has addressed these concerns with the adoption of § 812.119(d), which provides sponsors with the opportunity to participate in proceedings regarding termination of clinical investigations. Under this section, if the Commissioner determines, after the unreliable data submitted by the disqualified investigator are eliminated from consideration, that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation, the Commissioner will notify the sponsor, who shall have an

opportunity for a regulatory hearing under part 16. If a danger to the public health exists, however, the Commissioner shall terminate the clinical investigation immediately and notify the sponsor of that determination. In such case, the sponsor shall have an opportunity for a regulatory hearing under part 16 on the question of whether the clinical investigation should be reinstated.

The agency's adoption of § 812.119(e), which parallels § 312.70(e), also addresses the concerns about sponsors' rights raised by these comments. This new section provides that if the Commissioner determines, after the unreliable data submitted by the disqualified investigator are eliminated from consideration, that the continued clearance or approval of the device for which the data were submitted cannot be justified, the Commissioner will proceed to rescind clearance or withdraw approval of the marketing application in accordance with the applicable provisions of the act and regulations. These provisions provide adequate due process protections to the sponsor whose clinical investigations are subject to termination and/or whose marketing applications are subject to rescission of clearance or withdrawal of approval following disqualification of clinical investigators.

N. Proposed § 812.119(g)(2)

14. A comment suggested that proposed § 812.119(g)(2) was overly broad because it would allow FDA to terminate an entire study based on the disqualification of a single investigator.

The agency believes that the concern raised by this comment has been addressed with the adoption of § 812.119(d), which, like § 312.70(d), provides a sponsor with notification that the Commissioner has determined that the data are inadequate to support a conclusion that it is reasonably safe to continue the investigation, and an opportunity for a hearing under part 16, as indicated previously. (See the response to comment 13 in section IV.M. of this document.)

15. A comment suggested that there was an inconsistency between proposed § 812.119(g)(2) and proposed § 812.119(b). The comment stated that, under § 812.119(b), the Commissioner must base a disqualification order upon findings that address only limited factual issues. In contrast, § 812.119(g)(2) directed FDA to consider information that goes beyond the scope of the administrative record created during the disqualification proceedings. For example, nothing in proposed § 812.119(b) related to "the risks of the

subjects from suspension of the study," and yet FDA, under § 812.119(g)(2), would consider that factor. The comment recommended that this inconsistency be rectified.

The agency believes that the inconsistency indicated by this comment has been addressed with the adoption of § 812.119(b), which parallels § 312.70(b) and by the elimination of proposed § 812.119(g) in the final rule. Under § 812.119(b), a disqualification decision will be based upon the Commissioner's determination that the investigator has repeatedly or deliberately failed to comply with the requirements of this part, part 50 or part 56, or has deliberately or repeatedly submitted false information either to the sponsor or in any required report, after evaluating all available information, including any explanation presented by the investigator.

O. Proposed § 812.119(g)(2)(i)

16. One comment stated that the meaning of the phrase "another investigator accepts responsibility for the clinical investigation" was unclear in this proposed section.

Proposed § 812.119(g)(2)(i) was not adopted in the final rule, thus eliminating any need for clarification indicated by this comment. However, FDA believes that if continuation of an investigation is warranted after an investigator is disqualified, the sponsor of the investigation is responsible for selecting a qualified investigator who shall be responsible for the continuation of the investigation at that site. (See, also, the response to comment 18 in section IV.P. of this document.)

17. A comment expressed concern that proposed § 812.119(g)(2)(i) could be interpreted as broad FDA authority to suspend or terminate an entire clinical investigation, rather than the portion of the investigation conducted by the disqualified investigator. In order for the regulation to be explicit on this issue, this comment suggested that the phrase "under control of the disqualified investigator" should be added after "clinical investigation." Additionally, another comment requested that "clinical investigation" should be defined as that part of an investigation directly under the control of the disqualified investigator. Furthermore, the comment asked FDA to add the following sentence to this section for clarity: "Disqualification of an investigator or termination of a clinical investigation under control of a disqualified investigator shall not affect any investigation not under control of the disqualified investigator."

The agency has previously addressed other comments concerning the termination of an entire investigation or other investigations conducted by the disqualified investigator. (See the responses to comments 1 and 14 in sections IV.A. and N. of this document.)

P. Proposed § 812.119(g)(2)(iii)

18. One comment stated that it is inappropriate for a disqualified investigator to continue monitoring subjects. Instead, this comment recommended that another investigator be appointed to monitor the subject, or the subject should be withdrawn from the study.

The agency agrees that it is inappropriate for a disqualified investigator to continue monitoring clinical trial subjects who are either continuing to receive the test device or are in the followup phase of the trial. An investigator who is disqualified from eligibility to receive investigational devices is disqualified from participation in conducting investigations, including monitoring the subjects of investigations. Therefore, § 812.119(b) provides that once the Commissioner makes a final disqualification determination, the Commissioner will notify the sponsor of any investigation in which the investigator has been named as a participant and the reviewing IRB that the investigator is disqualified. Furthermore, the agency believes that if subjects are currently enrolled or receiving followup visits at the disqualified investigator's site, the sponsor is responsible for selecting, as soon as possible, a qualified investigator who shall be responsible at the site for completing the investigation, including subject followup.

Q. Proposed § 812.119(g)(2)(v)

19. One comment stated that proposed § 812.119(g)(2)(v) was too restrictive. Various comments suggested that § 812.119(g)(2)(v) be expanded to allow continued use if discontinuing use would cause a life-threatening problem, an immediate health problem, or involve significant risks to the person's health.

The agency has not adopted the provision that was the basis for this comment. However, under § 812.119(c) and (d), the Commissioner will determine whether the remaining data are adequate to support a conclusion that it is reasonably safe to continue an investigation, or whether approval should be withdrawn. If there is credible evidence that discontinuing an investigation would cause a life-threatening problem, an immediate

health problem, or involve significant risks to the health of a subject, this type of evidence will be considered in support of such determination.

R. Proposed § 812.119(g)(3)

20. Under proposed § 812.119(g)(3), once an investigator is disqualified, FDA would examine approved and pending applications relying on the work of this disqualified investigator. FDA would determine whether the investigation "is acceptable," notwithstanding the disqualification. According to several comments, proposed § 812.119(g)(3) was vague and unfair for various reasons. One comment suggested that FDA incorporate the language used in the IND regulations for disqualification of investigators, which provides that an application will be examined to determine whether the investigator has submitted unreliable data that are "essential to the continuation of the investigation or essential to the approval of any marketing application." (See § 312.70(c).)

The agency agrees with the comments and has adopted § 812.119(c), which parallels the language used in § 312.70(c) of the IND regulations, for disqualification of investigators.

21. Another comment said that the wording,

Any investigation done by an investigator before or after disqualification may be presumed to be unacceptable, and the person relying on the investigation may be required to establish that the clinical investigation was not affected by the circumstances which led to disqualification of the investigator, * * * has many flaws. First, the terminology "any investigation done by an investigator before or after disqualification may be unacceptable" is too broad. The comment recommended that the regulation state that an investigator's data will not be accepted to support a marketing application only if the evidence shows that the data are unreliable. The sponsor should then be given the opportunity to validate the data if possible, after exclusion of the adversely affected data. The comment also said that a "presumption" of invalidity for any investigation done by an investigator before or after disqualification is inappropriate because, under the proposed rule, that presumption would apply to any clinical investigation performed by the investigator.

The agency believes that the concerns expressed by this comment have been minimized with the adoption of a final rule that parallels § 312.70. Under § 812.119(c), each regulatory submission containing data reported by a

disqualified investigator will be examined to determine whether the investigator has submitted unreliable data that are essential to the continuation of the investigation or essential to the approval of any marketing application. It is not unreasonable, however, for FDA to presume that other work done by a disqualified investigator should be reviewed. Because this final rule states that a sponsor is entitled to a hearing before any particular investigation or approval is terminated, the opportunity to validate data will be available to sponsors.

22. Another comment stated that the use of the phrase "the person relying on the investigation may be required to establish that the investigation was not affected," improperly shifts the burden of proof to the sponsor; just because an investigator has failed to comply with the regulations in one study does not imply that all other studies are tainted. This comment recommended that, once FDA determines that an investigator has acted improperly, FDA should conduct an investigation to determine whether other clinical investigations conducted by the disqualified investigator are unreliable.

This recommendation is incorporated into the final rule, which parallels § 312.70. Under § 812.119(c), each IDE and each approved marketing application submitted under part 807 or 814 in which the disqualified investigator has been a participant will be examined by FDA. In essence, final § 812.119(c) places on FDA the initial burden of determining whether any unreliable data have been submitted by the disqualified investigator that are essential to the continuation of any other investigation or to the approval or clearance of any marketing application. (See the agency's responses to comments 1, 13, and 14 in sections IV.A., M., and N. of this document.)

23. A comment urged that an approval should not be withdrawn unless there is evidence that the device is unsafe or ineffective. If the device is found to be safe and effective, the device should remain available, regardless of irregularities in the investigation which led to the disqualification of an investigator.

The agency does not intend to withdraw approval or rescind clearance of devices under § 812.119(e) unless the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the continued approval or clearance of the marketing application for which the data were submitted cannot be justified. By its

very nature, unreliable data bring into question the safety and effectiveness of the device. If the marketing application contains data, other than the disqualified data, that support substantial equivalence or safety and effectiveness, FDA would have no reason to remove the device from the market. The course of action taken by FDA with respect to that device will be commensurate with the results of the agency's review, and may include withdrawal of approval of a PMA or rescission of a 510(k) if that is deemed necessary. Furthermore, as stated in response to comment 13 in section IV. M. of this document, § 812.119(e) parallels § 312.70(e) and provides sponsors with the opportunity to participate in proceedings regarding withdrawal of approval or recession of clearance of a marketing application.

24. A comment suggested that the regulation should include a reasonable time limit in which a sponsor must validate the data used in a study in which an investigator was disqualified.

The agency agrees with this comment. In accordance with § 812.119(d) and (e), when FDA has reviewed the remaining data after the disqualified investigator's data are eliminated and the Commissioner has determined that the remaining data are inadequate to support continued approval or clearance of an investigation or marketing application, the Commissioner will notify the sponsor, who shall have an opportunity for a regulatory hearing under part 16. The sponsor may request a hearing to present to FDA any new or additional factual information which challenges the determination, including any information that validates the disqualified investigator's data or that indicates the remaining data are adequate to support approval or clearance. The time limit for providing such information is governed by the procedures for conducting a regulatory hearing under part 16.

25. Another comment pointed out that § 812.119(d) and (e) requires a sponsor, in certain circumstances, to submit validating information to show that an IDE or PMA containing or relying upon a clinical investigation performed by a disqualified investigator is not adversely affected. This comment suggested that FDA should offer the sponsor periodic opportunities, i.e., quarterly, monthly, etc., to present validating information for any potentially adversely affected clinical investigation through segregated analysis, adding additional sites, or verification of existing data. According to this comment, offering such periodic opportunities to validate existing data would allow the sponsor to salvage

portions of valid data without having to gather clinical data through new investigations.

The agency agrees that such an opportunity may be appropriate. As part of FDA's examination under final § 812.119(c) to determine whether the disqualified investigator has submitted unreliable data that are essential to the continuation of an investigation or essential to the approval of any marketing application, FDA may request that sponsors submit to the agency, on a periodic basis, validating information for a potentially adversely affected clinical investigation or marketing application. Sponsors will receive written notification of such a request.

S. Proposed § 812.119(g)(4)

26. Under proposed § 812.119(g)(4), the determination that a clinical investigation may not be considered in support of an application would not relieve the applicant of any obligation under the statute to submit the results of the clinical investigation to FDA. A comment urged that an applicant should not be required to submit the results of the clinical investigation to FDA because, once a determination has been made that the clinical investigation will not be considered in support of an application, the usefulness of the clinical investigation is questionable.

The agency disagrees with this comment. Although the final rule no longer includes this explicit provision, it is imperative for FDA to review all available information collected on the investigational device, particularly information that may affect the rights, safety, or welfare of the subjects enrolled. Therefore, regardless of whether the clinical data will be used to support a marketing application, the reporting requirements described in other parts of the IDE regulation, e.g., §§ 812.40 and 812.150, must be maintained to provide adequate protection for subjects.

T. Proposed § 812.119(h)(1)

27. Proposed § 812.119(h)(1) would have required the notice of disqualification to state that the results of any investigations conducted by the investigator may not be considered by FDA in support of any IDE or PMA. According to one comment, proposed § 812.119(h)(1) would not permit validating information to be presented by a sponsor to save the IDE or PMA. Because of this, the comment requested that the contents of the disqualification notice not automatically reflect a determination that the study results are not to be considered in support of an IDE or PMA. Instead, the comment

requested that the contents of the disqualification notice state that the results will be evaluated by FDA to determine the effect of disqualification, if any, on the IDE or PMA.

Proposed § 812.119(h)(1), which is addressed in this comment, has not been adopted. However, under § 812.119(b), a disqualification notice is provided that states that the investigator is disqualified and the basis for such determination. Final § 812.119(c), (d), and (e) establish that FDA will review any IDE's, 510(k)'s or PMA's that contain data submitted by the disqualified investigator. If the agency finds that a withdrawal of approval is warranted, the sponsor of the application will be notified and offered an opportunity for a hearing under part 16. The sponsor may request a part 16 hearing to provide relevant information, such as validating information, which may influence a final decision.

28. Under proposed § 812.119(h)(1), upon issuance of a final order disqualifying an investigator or upon entry of a consent decree, FDA would have discretion to notify all or any interested persons. A comment recommended that it be a mandatory requirement that sponsors receive notice of an investigator disqualification both when FDA issues a final order and when FDA has reason to believe that an investigator may be subject to disqualification. Another respondent asked FDA to include in the regulation a provision requiring the notification of the sponsor by FDA when a consent agreement is executed, with a copy of the consent agreement included in the sponsor's notification. Three other respondents suggested that FDA, upon disqualification of a clinical investigator, inform the approving IRB that the investigator has been disqualified.

Proposed § 812.119(h)(1), which is addressed by these comments, has not been adopted in the final rule. However, FDA agrees with these comments in general and has adopted final § 812.119(b), which parallels § 312.70(b). This final rule provides that FDA will give notification of disqualification to the investigator who is disqualified, the sponsor of any investigation in which the investigator has been named a participant, and the reviewing IRB.

The agency's response to comments concerning notification of interested parties prior to a final disqualification decision has been provided previously. (See response to comment 6 in section IV.F. of this document.) Records relating to disqualification proceedings, such as inspectional findings, disqualification

determinations, administrative records of determinations and hearings, consent agreements, and reinstatement determinations are disclosable to the public upon request, subject to the provisions of part 20 (21 CFR part 20).

U. Proposed § 812.119(h)(3)

29. According to a comment, proposed § 812.119(h)(3) would not give sponsors notice that an investigator is facing disqualification proceedings. This comment requested that the regulation be revised to require FDA to notify the sponsor if one of its investigators may be facing disqualification.

A similar comment suggested the following wording:

Whenever FDA has reason to believe that an investigator may be subject to disqualification, the agency will so notify the sponsor of the clinical investigation in question, as well as the sponsor of each clinical investigation subject to requirement of prior submission to FDA that was or is being conducted by the investigator, and the IRB's under which the investigation(s) were conducted. This notification shall occur simultaneously with the agency's notice to the investigator describing the noncompliance and request for an explanation of the noncompliance under paragraph (c) of this section.

Proposed § 812.112(h)(3) addressed in these two comments has not been adopted in the final rule. However, the agency's response to similar comments concerning notification of interested parties prior to a final disqualification decision has been provided previously. (See response to comment 6 in section IV.F. of this document.)

V. Proposed § 812.119(j)

30. This proposed section would have required sponsors to notify FDA any time an investigator is removed from further participation in a clinical investigation. One comment stated that there is no need to require a sponsor to notify FDA when an investigator is removed from a study for nonregulatory reasons. Another comment maintained that requiring sponsors to report a termination, for whatever reasons, could inhibit sponsors from terminating investigators because of the reporting requirements.

Proposed § 812.119(j) addressed in these two comments has not been adopted in the final rule. However, § 812.40 of the existing IDE regulation currently requires sponsors to inform the agency of significant new information about an investigation, including any changes in or terminations of clinical investigators.

W. Publication of a List

31. A comment requested that disqualified investigators be added to a single list maintained by CDER or the Office of Health Affairs in FDA so that IRB's and sponsors are not required to search two (or more) separate lists.

Although the proposed rule did not specifically state that CDRH would maintain a list of clinical investigators who have been disqualified under this authority, FDA intends to compile such a list. This list will be combined with CDER's and the Center for Biologics Evaluation and Research's (CBER's) list of disqualified investigators. The newly combined disqualified clinical investigator list will be maintained by FDA's Office of Regulatory Affairs. This list is disclosable to the public under part 20. A request for the list should be sent in writing to the Freedom of Information Staff (HFZ-35), Food and Drug Administration, 5600 Fishers Lane, rm. 12A-16, Rockville, MD 20857.

V. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VI. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601-612). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the final rule specifies the procedures to be followed for investigator disqualification, the rule does not impose any burden on regulated industry. Procedures themselves are protections and do not

impose significant costs beyond what the underlying statute imposes. Thus, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

Lists of Subjects in 21 CFR Part 812

Health records, Medical devices, Medical research, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 812 is amended as follows:

PART 812—INVESTIGATIONAL DEVICE EXEMPTIONS

1. The authority citation for 21 CFR part 812 continues to read as follows:

Authority: Secs. 301, 501, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 701, 702, 704, 721, 801 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331, 351, 352, 353, 355, 356, 357, 360, 360c–360f, 360h–360j, 371, 372, 374, 379e, 381); secs. 215, 301, 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 262, 263b–263n).

2. Section 812.2 is amended by revising the introductory text of paragraph (c) to read as follows:

§ 812.2 Applicability.

* * * * *

(c) *Exempted investigations.* This part, with the exception of § 812.119, does not apply to investigations of the following categories of devices: * * *

* * * * *

3. New § 812.119 is added to subpart E to read as follows:

§ 812.119 Disqualification of a clinical investigator.

(a) If FDA has information indicating that an investigator has repeatedly or deliberately failed to comply with the requirements of this part, part 50, or part 56 of this chapter, or has repeatedly or deliberately submitted false information either to the sponsor of the investigation or in any required report, the Center for Devices and Radiological Health will furnish the investigator written notice of the matter under complaint and offer the investigator an opportunity to explain the matter in writing, or, at the option of the investigator, in an informal conference. If an explanation is offered and accepted by the Center for Devices and Radiological Health, the disqualification process will be terminated. If an explanation is offered but not accepted by the Center for Devices and

Radiological Health, the investigator will be given an opportunity for a regulatory hearing under part 16 of this chapter on the question of whether the investigator is entitled to receive investigational devices.

(b) After evaluating all available information, including any explanation presented by the investigator, if the Commissioner determines that the investigator has repeatedly or deliberately failed to comply with the requirements of this part, part 50, or part 56 of this chapter, or has deliberately or repeatedly submitted false information either to the sponsor of the investigation or in any required report, the Commissioner will notify the investigator, the sponsor of any investigation in which the investigator has been named as a participant, and the reviewing IRB that the investigator is not entitled to receive investigational devices. The notification will provide a statement of basis for such determination.

(c) Each investigational device exemption (IDE) and each cleared or approved application submitted under this part, subpart E of part 807 of this chapter, or part 814 of this chapter containing data reported by an investigator who has been determined to be ineligible to receive investigational devices will be examined to determine whether the investigator has submitted unreliable data that are essential to the continuation of the investigation or essential to the approval or clearance of any marketing application.

(d) If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation, the Commissioner will notify the sponsor who shall have an opportunity for a regulatory hearing under part 16 of this chapter. If a danger to the public health exists, however, the Commissioner shall terminate the IDE immediately and notify the sponsor and the reviewing IRB of the determination. In such case, the sponsor shall have an opportunity for a regulatory hearing before FDA under part 16 of this chapter on the question of whether the IDE should be reinstated.

(e) If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the continued clearance or approval of the marketing application for which the data were submitted cannot be justified, the Commissioner will proceed to withdraw approval or rescind clearance of the

medical device in accordance with the applicable provisions of the act.

(f) An investigator who has been determined to be ineligible to receive investigational devices may be reinstated as eligible when the Commissioner determines that the investigator has presented adequate assurances that the investigator will employ investigational devices solely in compliance with the provisions of this part and of parts 50 and 56 of this chapter.

Dated: March 3, 1997.

William B. Schultz,

Deputy Commissioner for Policy.

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DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[TD 8560; TD 8597; TD 8660]

RIN 1545-AQ69; 1545-AT58; 1545-AT51

Consolidated Returns; Consolidated and Controlled Groups; Correction

AGENCY: Internal Revenue Service, Treasury.

ACTION: Correcting amendments.

SUMMARY: This document contains technical corrections to final regulations [TD 8560; TD 8597; TD 8660] which were published in the Federal Register on Monday, August 15, 1994 (59 FR 41666); Tuesday, July 18, 1995 (60 FR 36671); and Thursday, March 14, 1996 (61 FR 10447); respectively. The final regulations amend the consolidated return investment adjustment provisions, intercompany transaction provisions and the provisions limiting losses and deductions from transactions between members of a nonconsolidated controlled group.

DATES: The correcting amendments affecting § 1.267(f)-1, 1.1502-13(f)(2)(ii), (g)(5), (l)(1), 1.1502-20, 1.1502-32(b), and 1.1502-80(b) are effective July 18, 1995. The correcting amendments affecting §§ 1.1502-11, 1.1502-19, 1.1502-32(f), 1.1502-43, 1.1502-76 and 1.1502-80(d)(1) are effective January 1, 1995. The correcting amendments affecting § 1.1502-13(f)(6) are effective March 14, 1996. For dates of applicability see §§ 1.267(f)-1(l), § 1.1502-11(b)(5), 1.1502-13(l)(1), 1.1502-13(f)(6)(v), 1.1502-19(h), 1.1502-32(h), 1.1502-76(b)(5), 1.1502-80(d), and other relevant provisions.

FOR FURTHER INFORMATION CONTACT: William Barry of the Office of Assistant