SMG 7714

FDA STAFF MANUAL GUIDES, VOLUME IV – AGENCY PROGRAM DIRECTIVES

COMPLIANCE ACTIVITIES

DISQUALIFICATION OF AN INSTITUTIONAL REVIEW BOARD (IRB), PARENT INSTITUTION, OR COMPONENT OF PARENT INSTITUTION

Effective Date: August 27, 2014

1. PURPOSE

This Staff Manual Guide (SMG) provides to FDA staff the procedures to follow for a proceeding to disqualify:

- an Institutional Review Board ("IRB"), or

- the parent institution responsible for the operation of an IRB or a component of the parent institution determined to be responsible for formal designation of the IRB (together, referred to as "institution").

Adherence to the procedures described in this document will help ensure that disqualification actions brought under Title 21 Code of Federal Regulations, section 56.121, "Disqualification of an IRB or an institution," are processed consistently and efficiently.

2. POLICY

A. General Policy

Under FDA's inspectional authority FDA conducts inspections to determine if IRBs are operating in compliance with current FDA regulations and statutory requirements. FDA regulations pertinent to IRBs include 21 CFR Part 50 (Protection of Human Subjects), Part 56 (Institutional Review Boards), Part 312 (Investigational New Drug Application), and Part 812 (Investigational Device Exemptions).

If FDA determines there is significant noncompliance with the relevant regulations concerning FDA-regulated research, FDA may send a letter to the IRB or institution describing the noncompliance (see 21 CFR 56.120(a)). This initial "Institutional Review Board – Restrictions Imposed" letter (IRB Restrictions Letter)[1] will include some or all of the restrictions provided in 21 CFR 56.110(d), and 56.120(b).

- All involved parties[2] should be kept informed throughout the process following issuance of the IRB Restrictions Letter.

  Because an IRB's noncompliance may affect studies under the jurisdiction of more than one of FDA's Centers or Offices, internal communication among the relevant Centers and Offices is essential. Also, the relevant Center should ensure that the Office of Regulatory Affairs (ORA)/Office of Enforcement and Import Operations (OEIO), as well as the ORA district office that conducted the IRB inspection and the Office of Good Clinical Practice (OGCP) are informed about the ongoing status of the matter. In the event that the Center recommends disqualification, OGCP should inform the Office for Human Research Protections (OHRP), U.S. Department of Health and Human Services (DHHS), about FDA's intent to initiate an IRB disqualification action

[1] See the definition of "Institutional Review Board – Restrictions Imposed (IRB Restrictions Letter)" in section 3 of this document.
[2] Those parties include relevant contacts in FDA Centers and Offices who deal with human subject protection compliance issues.

(e.g., by directing OHRP to FDA's webpage where the relevant information is posted).

- The Center should contact the OGCP Project Manager[3] for assistance with the proper routing of documents.

- When ongoing clinical research may be disrupted because of an IRB's or institution's noncompliance and there is concern about potential harm to study subjects, consideration should be given to the transfer of IRB review responsibilities.[4] The IRB is responsible for notifying the affected sponsors and clinical investigators about any sanctions or restrictions placed on the IRB, including a disqualification.[5]

- All timeframe references are to calendar days, unless stated otherwise.

B. Responsible Party

The parent institution is presumed to be responsible for the operation of an IRB, and FDA will ordinarily direct any administrative action under 21 CFR Part 56, Subpart E, against the institution. However, depending on the evidence of responsibility for deficiencies in a particular case, FDA may restrict its administrative actions to the IRB or a component of the parent institution determined to be responsible for the formal designation of the IRB (see 21 CFR 56.120(c)).

Examples of situations where FDA would proceed with an administrative action against entities other than the parent institution include the following:

- if an IRB, including a Central IRB, reviews clinical investigations for more than one institution, and the IRB is found not to be in compliance with the regulations, it would be appropriate to take action directly against the IRB;[6] and

- if a single institution has multiple IRBs and one of the IRBs is found to be noncompliant, disqualifying all of the IRBs at the institution may not be appropriate. Therefore, FDA may take action against the individual IRB, and not against the institution, when the institution has taken all appropriate steps within its power to correct the IRB's deficiencies, but the IRB remains out of compliance.[7]

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[3] For updated contact information about the OGCP Project Manager for disqualification matters, call 301-796-8340.
[4] See http://www.fda.gov/RegulatoryInformation/Guidances/ucm307757.htm.
[5] Note: for drug and biologic studies, clinical investigators are responsible for securing IRB approval under 21 CFR 312.66; for device studies, the sponsor is responsible under 21 CFR 812.35(a)(1) and (3).
[6] See 46 Federal Register 8958, January 27, 1981; response to comment 119.
[7] *Id.*

3. DEFINITIONS

A. Commissioner. Commissioner includes the Commissioner of Food and Drugs and certain FDA officials under general redelegations of authority (see SMG 1410.21).[8]

B. Disqualification of an IRB or an Institution. A process through which the Commissioner issues an order disqualifying an IRB or an Institution. The disqualification order is issued to the IRB, the parent institution responsible for the operation of an IRB, or a component of that parent institution determined to be responsible for formal designation of the IRB, whichever is applicable.

C. Institutional Review Board (IRB). Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of the Federal Food, Drug, and Cosmetic Act. (See 21 CFR 56.102(g)).

D. Institutional Review Board (IRB) Restrictions Imposed (IRB Restrictions Letter).[9] An IRB Restrictions Letter is a letter issued under 21 CFR 56.120(a) describing the IRB's noncompliance and imposing restrictions on the IRB in accordance with 21 CFR 56.110(d) and 56.120(b). It informs the IRB that the IRB is responsible for notifying all affected sponsors and clinical investigators of the restrictions described in the letter. The letter also should include a request for the IRB to provide a complete list of all sponsors and investigators notified and the date of notification. Additionally, the letter will request a list of all studies currently being conducted that are affected by the restrictions including the titles of the studies (with IDE or IND numbers, if applicable and known), the names of the test articles, the names of the clinical investigators, dates of initial reviews and approvals, and dates of continuing reviews. (See Attachment A).

E. Motion for Summary Decision. In the proceeding, a written brief filed with the Presiding Officer explaining the issues in the proceeding and requesting a determination. The determination will be incorporated into the Presiding Officer's Report.

F. Notice of Opportunity for Hearing. The Notice of Opportunity for Hearing (NOOH) provides a person with the opportunity for a hearing on a regulatory action before a Presiding Officer designated by the Commissioner. When the Commissioner determines that an IRB, or the IRB's parent institution's

[8] See http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/staffmanualguides/ucm273783.pdf
[9] For information about administrative guidance and choosing the appropriate correspondence, see the Compliance Program Guidance Manual, Program 7348.809, Part V, sections A. and B., at http://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/ucm133768.pdf

noncompliance may justify disqualification, proceedings are instituted in accordance with the requirements for a regulatory hearing set forth in Title 21 Code of Federal Regulations, Part 16 (see 21 CFR 56.121(a)).

G. **Presiding Officer.** An official to whom the Commissioner delegates authority to conduct a regulatory hearing,[10] or consistent with 5 CFR 930.209(b) or (c), an administrative law judge to whom such authority is delegated (21 CFR 16.42).

H. **Repeated Violation.** More than one violation, including the same violation, in the review of one or more studies.[11]

I. **Separation of Functions.** Under separation of functions, agency personnel who are involved in advocating a proposed regulatory action (disqualification) do not participate in the agency's decision on the action. Upon receipt of a request for a Part 16 hearing, the agency observes separation of functions, even though under 21 CFR 16.44(a), regulatory hearings are not subject to the separation of functions rules in 21 CFR 10.55. The principal purpose of observing separation of functions is to ensure: fairness; both sides have equal access to the decision-maker; and, neither party can be accused of exerting improper influence. Separation of functions also ensures the independence of the decision-maker and that the decision is based only on the record and not on information that might have come to the attention of the decision-maker in some other way. The agency's adherence to separation of functions in disqualification Part 16 hearing proceedings has been adopted as a matter of policy.

4. BACKGROUND

Under FDA's inspectional authority, FDA conducts inspections to determine if IRBs are operating in compliance with current FDA regulations and statutory requirements. FDA regulations pertinent to IRBs include 21 CFR Part 50 (Protection of Human Subjects), Part 56 (Institutional Review Boards), Part 312 (Investigational New Drug Application), and Part 812 (Investigational Device Exemptions).

Upon completion of an inspection, the FDA investigator issues a FDA Form 483 – Inspectional Observations, summarizing the observations. The applicable Center, in

[10] See SMG 1410.29, 1.B., (http://www.fda.gov/AboutFDA/ReportsManualsForms/StaffManualGuides/ucm049562.htm) for a list of officials who have been delegated as authorized to serve as presiding officers for Part 16 hearings.

[11] In the context of clinical investigator disqualifications, FDA has addressed what is meant by repeated violations. See Report of the Presiding Officer, In the Matter of James A. Halikas (2000), findings adopted by the Commissioner (2001); Report of the Presiding Officer, In the Matter of Chaovanee Aroonsakul, M.D. (1990), findings adopted by the Commissioner (1991); Report of the Presiding Officer, In the Matter of Ronald R. Fuller, D.V.M (1987), findings adopted by the Commissioner (1988); Report of the Presiding Officer, In the Matter of Stephen Steen, M.D., at 25 ("I do not interpret the term, 'repeated,' to require proof of violations in two different studies") (1982), findings adopted by the Commissioner (1984); Report of the Presiding Officer, In the Matter of John H. Hopkinson III, M.D. (1982), findings adopted by the Commissioner (1983); Report of the Presiding Officer, In the Matter of Michael C. Gelfand, M.D. (1980), findings adopted by the Commissioner (1981).

consultation with ORA/OEIO and the ORA district office that conducted the IRB inspection, determines what action(s) should be taken (e.g., Warning Letter, regulatory meeting).[12] The regulations specifically authorize FDA to send a letter describing the noncompliance and requiring the IRB to respond to FDA within a specified time describing corrective actions that will be taken to achieve compliance. (21 CFR 56.120(a)). In addition, until the IRB takes appropriate corrective action, FDA may impose restrictions on the operation of the IRB under 21 CFR 56.110(d) and 56.120(b). In other words, the Center/District could issue a letter imposing restrictions without first issuing a Warning Letter, or could issue a Warning Letter, and then because of the seriousness of the violations and until the IRB takes corrective action, impose restrictions on the operation of the IRB.

Whenever the IRB or the institution has failed to take adequate steps to correct the noncompliance stated in the letter issued under 21 CFR 56.120(a) (a Warning Letter or IRB Restrictions Letter), and the Commissioner determines that this noncompliance may justify the disqualification of the IRB or the parent institution, the Commissioner will institute proceedings under Part 16 to disqualify the IRB or parent institution.

If an IRB or institution is disqualified, oversight of all ongoing clinical investigations will need to be transferred to another IRB. For FDA's recommendations about what to consider when review and oversight responsibility for an ongoing clinical investigation is transferred from one IRB to another IRB, see "Guidance for IRBs, Clinical Investigators, and Sponsors: Considerations When Transferring Clinical Investigation Oversight to Another IRB".[13] This guidance document explains how to carry out such a transfer.

5. RESPONSIBILITIES AND PROCEDURES

- If FDA determines there is significant noncompliance with the relevant regulations concerning FDA-regulated research that cannot be addressed with a Warning Letter, FDA may send a letter to the IRB or institution describing the noncompliance (see 21 CFR 56.120(a)). This IRB Restrictions Letter[14] will include some or all of the restrictions provided in 21 CFR 56.110(d), 56.120(b), and 56.103(a).

- FDA will require that the IRB or institution respond to the IRB Restrictions Letter within a time period specified by FDA describing the corrective actions proposed or that have been implemented by the IRB or institution to achieve regulatory compliance. (See 21 CFR 56.120(a)). (See Attachment A).

[12] See FDA Compliance Program 7348.809 – Part V – Regulatory/Administrative Strategy, Section A., 4., a. – "Administrative Actions for noncompliance," at http://www.fda.gov/ICECI/EnforcementActions/BioresearchMonitoring/ucm282649.htm
[13] See http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM307779.pdf
[14] See the definition of "IRB Restrictions Letter" in section 3 of this document.

- Although not required by the regulations, FDA may request a regulatory meeting with the IRB or institution to discuss corrective actions proposed or implemented by the IRB or institution.

- Based on information provided by the IRB or institution, FDA may lift the restrictions imposed in the IRB Restrictions Letter.

- FDA may schedule a reinspection to confirm the adequacy of the implementation of the proposed corrective actions. (See 21 CFR 56.120(b)).

- When an IRB or institution takes adequate steps to correct the deficiencies in the IRB Restrictions Letter, FDA does not intend to pursue disqualification under 21 CFR 56.121.

- In the event the Center, with concurrence from the FDA Office of the Chief Counsel (OCC), determines that an IRB's actions warrant the initiation of disqualification proceedings, the Center will prepare materials for ORA to send to the Commissioner requesting that the Commissioner initiate proceedings to disqualify the IRB in accordance with the requirements for a regulatory hearing under 21 CFR Part 16.

- The Center should prepare a cover memo or routing and transmittal form recommending disqualification to the Director of the Division of Enforcement (DE/OEIO/ORA) indicating the date by which the recommendation should be reviewed and action should be completed, as recommended in this SMG.

- Whenever the IRB or the institution has failed to take adequate steps to correct the deficiencies listed in the IRB Restrictions Letter sent by FDA and the Commissioner determines that this noncompliance may justify the disqualification of the IRB or of the parent institution, the Commissioner will initiate a disqualification proceeding in accordance with the requirements for a regulatory hearing set forth in part 16.[15]

    - FDA will consider an IRB or institution as having failed to correct the deficiencies in the IRB Restrictions Letter if the IRB or institution fails to respond to the letter, submits an incomplete or inadequate response, or is found (e.g., during reinspection) to have violated any restrictions imposed by FDA or failed to comply with the regulations set forth in 21 CFR Part 56.

- A regulatory hearing is initiated by the Commissioner through issuance of a Notice of Opportunity for Hearing (NOOH)[16] to the IRB or institution (21 CFR 16.22(a)).

[15] See 46 Federal Register 8958, January 27, 1981; response to comment 122.
[16] See section 3 of this document for a definition of a NOOH.

The Center is responsible for drafting the NOOH, obtaining OCC concurrence, and sending to ORA (the Commissioner's delegate) the electronic version of the document. The Director of DE/OEIO/ORA is responsible for reviewing and issuing the NOOH with the signature of the Associate Commissioner for Regulatory Affairs (ACRA).

A. The IRB's Response to the NOOH

The NOOH directs the IRB or institution to respond to the Director/DE/OEIO/ORA, who will send a copy of any response to OCC, the OGCP Director and Project Manager, and the Center's Bioresearch Monitoring (BIMO) unit.

Within 10 business days of receiving the NOOH, the IRB or institution may:

- fail to respond;
- decline the opportunity for a hearing and request in writing that the agency make a determination based on the available information;
- ask for additional time to respond; or
- request a hearing.

1. **Fails to respond** – When an IRB or institution fails to respond within the time specified in the NOOH, the offer is deemed to have been refused and no hearing will be held (see 21 CFR 16.22(b)). If the IRB or institution fails to respond by the deadline specified, the Director/DE/OEIO/ORA informs the Center and OGCP's Director and Project Manager.[17]

   Within 60 days of ORA's notification to the Center, based on available information, the Center's BIMO unit prepares, in consultation with the Center's OCC counsel, a Center Decision Memorandum (see Attachment C), and Order of Disqualification (see Attachment D). The proposed Order of Disqualification explains the basis for the determination and prescribes any actions to be taken with regard to ongoing clinical research conducted under the review of the IRB (21 CFR 56.121(c)).

   The Center should consult with the OGCP Project Manager to determine the proper routing of documents after the Center, and Center OCC counsel, have cleared the Center Decision Memorandum and Order of Disqualification. Typically, the Center would route these documents to the Commissioner's

[17] Delivery of the NOOH is confirmed when a signed mail receipt is received or a similar confirmation of delivery is documented. If, however, reasonable attempts to deliver the NOOH have been unsuccessful, the Center should promptly consult with OCC Center counsel regarding how to proceed.

counsel and the Commissioner for review and decision, with a copy to the OGCP Director. (See section 5.C.1. of this document).

2. **Declines a hearing** – If the IRB or institution declines a hearing and requests that FDA make a determination based on the available information, the Director/DE/OEIO/ ORA informs the Center and OGCP's Director and Project Manager of the declination.

   Within 60 days of ORA's notification to the Center, based on the available information, the Center's BIMO unit prepares, in consultation with Center OCC counsel, a Center Decision Memorandum (see Attachment C) and Order of Disqualification (see Attachment D).

   The Center should consult with the OGCP Project Manager to determine the proper routing of documents following Center and Center OCC counsel clearance, of the Center Decision Memorandum and Order of Disqualification. Typically, the Center would route these documents to the Commissioner's counsel and the Commissioner for review and decision, with a copy to the OGCP Director. (See section 5.C.1. of this document).

3. **Requests additional time to respond** – If the IRB or institution requests additional time to respond, the Director/DE/OEIO/ORA will consult with the Center and Center OCC counsel for a determination of whether granting the request for additional time to respond to the NOOH is warranted, and will respond to the IRB or institution within five business days of receipt of the IRB's or institution's request. ORA will send a copy or otherwise notify the Center and OGCP's Director and Project Manager of the decision whether to allow additional time to respond to the NOOH.

4. **Requests a hearing** – A written request for a hearing must present specific facts showing there is a genuine and substantial issue of fact that warrants a hearing (21 CFR 16.26(a)). A hearing will not be granted on issues of policy or law. If the IRB or institution requests a hearing:

   a. Generally, within one business day, the Director/DE/OEIO/ORA forwards to the Center and OGCP's Director and Project Manager a copy of the request.

   b. Generally, within three business days, the Project Manager forwards to OCC the hearing request and requests that OCC designate counsel to work with the Commissioner during the hearing process.

   c. Within seven days of receipt of the request for a hearing, OCC will provide the Project Manager the name of counsel to represent the Commissioner.

d. Within 60 days of receipt of the request for a hearing, the Center, with the assistance of Center OCC counsel, may evaluate the hearing request to determine whether the IRB or institution has raised any genuine and substantial issue of fact.

   If they conclude that no genuine and substantial issue of fact has been raised, the Center, within the 60 day time frame, may prepare and forward to the OGCP Project Manager, a Motion to Deny the Request for a Hearing and for Disqualification, with an accompanying memorandum. Please note that this Motion and memorandum should be cleared through the Center Director and Center OCC Counsel within this 60 day time frame.

   Generally, within three business days, the OGCP Project Manager will forward to the Commissioner and Commissioner's OCC counsel the Center's Motion to Deny the Request for a Hearing and for Disqualification.

   The Commissioner, with the assistance of counsel, will review the Center's Motion within 60 days of receipt from the OGCP Project Manager and determine whether a hearing is warranted. If the Commissioner agrees that no hearing is warranted, the Commissioner, with the assistance of counsel, will issue within 120 days of receipt a Commissioner's Decision.

   If the Commissioner also agrees that the IRB or institution should be disqualified, the Commissioner will issue an Order of Disqualification (see Attachment D), disqualifying the IRB or institution. The Commissioner's Decision will explain why the hearing was denied and will prescribe any actions to be taken with regard to ongoing clinical research conducted under the review of the IRB. (See section 5.C.2.). The Commissioner will send to the Project Manager the Commissioner's Decision and Order of Disqualification. Within seven days of receipt, the Project Manager will forward the Order of Disqualification and Commissioner's Decision to the IRB or institution, and Center.

   If the Commissioner determines that the material submitted by the IRB or institution raises a genuine and substantial issue of fact, the Commissioner will issue a decision letter granting the Part 16 hearing and send it to the Project Manager. The OGCP Project Manager is responsible for ensuring a Presiding Officer is designated.[18] Within

[18] An Administrative Law Judge (ALJ) is authorized to serve as Presiding Officer. (See 21 CFR 16.42(a); and, Staff Manual Guide 1410.29, paragraph 1.,B.,13., at http://www.fda.gov/AboutFDA/ReportsManualsForms/StaffManualGuides/ucm049562.htm .)

three business days of receipt, the Project Manager will forward the decision letter to the IRB or institution and Center.

e. If the Center does not file a Motion to Deny the Request for a Hearing and for Disqualification, the IRB's or institution's request for hearing is deemed granted.

B. A Part 16 Hearing

Fundamentals:

- Federal rules of evidence do not apply to the Part 16 hearing (21 CFR 16.60(c)); no specific format for the hearing is required of the parties.

- Any party to the hearing has the right at all times to be advised and accompanied by counsel (21 CFR 16.62).

- Off the record (or ex parte) communication by the Center or the IRB or institution with the Commissioner or Presiding Officer should be avoided in accordance with 21 CFR 16.44(b).

- Part 16 hearings are generally open to the public. However, the Commissioner may close all or part of the hearing on the Commissioner's own initiative or on the request of the party asking for the hearing to prevent a clearly unwarranted disclosure of personal privacy; to prevent disclosure of a trade secret or confidential commercial or financial information that is not available for public disclosure under 21 CFR 20.61; or to protect investigatory records complied for law enforcement purposes that are not available for public disclosure under 21 CFR 20.64 (see 21 CFR 16.60(a)).

- The Commissioner or Presiding Officer may, either voluntarily or at the request of a participant, waive, suspend, or modify any provisions in 21 CFR Part 16 applicable to the conduct of a public hearing by announcement at the hearing or by notice in advance of the hearing if no participant will be prejudiced, the ends of justice will thereby be served, and the action is in accordance with the law (21 CFR 10.19).

After a request for a hearing is granted, the OGCP Project Manager arranges for the designation of a Presiding Officer[19] to conduct the regulatory hearing.[20] The Project Manager schedules as soon as possible a telephone conference[21] with the Presiding Officer, Center, and the IRB or institution, and their respective

[19] *Id.*
[20] The Project Manager may identify for the Presiding Officer consultants who have expertise in the relevant disciplines (e.g., a medical officer or scientist to provide scientific or technical advice).
[21] The process described above in section 5.A.4.d. or 5.A.4.e., as applicable, should be completed before the Project Manager schedules the telephone conference.

counsels, to establish a date for the hearing and a schedule for the submission of documents and materials relevant to the hearing, and to refine or narrow the issues to be resolved, if necessary.

1. **Submission of Motions for Summary Decision** – After the request for a hearing is granted, the Center and/or the IRB or institution may submit Motions for Summary Decision within the timeframe specified at the telephone conference, generally within 90 days.[22] Motions for Summary Decision are appropriate when there is no "genuine and substantial issue of fact" regarding the issues in the proceeding (21 CFR 16.26(b)).

   Motions for Summary Decision with attached memoranda:

   - are informal in nature;
   - may incorporate statements and documents by attaching them without the support of an affidavit; and
   - have no set format, although the Presiding Officer may set a page limit to the Motions. This will be communicated during the telephone conference previously described.

   NOTE: Center Motion. The Center will forward its Motion for Summary Decision to Center counsel to review, and revise, if necessary. Center counsel will then forward the document to the Presiding Officer, Project Manager, IRB or institution and IRB's or institution's counsel, if any.

   IRB's or Institution's Motion. The IRB or institution will be directed during the conference call with the Presiding Officer to forward a copy of its Motion for Summary Decision to the Presiding Officer, Project Manager, and Center's counsel.

2. **Summary Decision After the Hearing has Commenced** – Within 90 days of receipt, the Presiding Officer, with the assistance of counsel (if requested), will review the Motions for Summary Decision and any other matters officially noticed[23] and may issue a Summary Decision[24] (see 21 CFR 16.26 (b)) explaining whether there exists any genuine and substantial issue of fact to be decided at a hearing. Specifically, the Summary Decision explains whether the evidence presented shows that the IRB (1) has refused or repeatedly

[22] The Presiding Officer will establish the time frames. Ninety days will include filing of motions by both parties and any opposition to such motions.
[23] Official notice is a means of entering evidence into the administrative record and allows the Presiding Officer to take notice of commonly acknowledged facts, and any other matter peculiarly within the general knowledge of FDA as an expert agency. If official notice is taken of a material fact not appearing in the evidence of record, the parties will be afforded the opportunity to show the contrary.
[24] The Summary Decision will be incorporated in a Presiding Officer's Report.

failed to comply with any of the regulations set forth in 21 CFR Part 56, and (2) the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

a. If the Presiding Officer determines that there is no genuine and substantial issue of fact to be decided at a hearing regarding whether the IRB has refused or repeatedly failed to comply with any of the regulations set forth in 21 CFR Part 56 and that the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation, the Presiding Officer may issue a Summary Decision granting the Center's Motion in whole or in part, and recommending that the IRB or institution be disqualified. A hearing will not be scheduled.

   The Project Manager, within seven days of issuance of the Presiding Officer's Report, will forward the Report to the parties.[25] The parties have 30 days after receipt to review the Report and request review by the Commissioner (see 21 CFR 16.26(c)). Within the same 30 days after receipt, the parties may submit to the Project Manager[26] comments on the Presiding Officer's Report.

   The Project Manager will forward promptly to the Commissioner (or delegate) the request from a party for the Commissioner's review and/or a party's comments. The Commissioner, on the Commissioner's own initiative or at the request of either party, may review the Presiding Officer's Report and all related materials (21 CFR 16.26(c)). At the end of the 30 day comment period, the Project Manager will forward to the Commissioner the Presiding Officer's Report, any request for review, and any comments received. Within 90 days of receipt of the Presiding Officer's Report and any comments received, the Commissioner will issue a decision on whether to disqualify the IRB or institution. (See section 5.C.3.).

   If the Presiding Officer determines that the materials submitted by the IRB or institution do raise an issue of fact as to whether the IRB or institution violated the regulations and that the IRB's or institution's noncompliance adversely affects the rights or welfare of the human subjects in an investigation, the Presiding Officer will issue a Summary Decision, denying the Center's Motion. A hearing will be scheduled.

b. If the Presiding Officer determines that the materials submitted by the IRB or institution and Center do not raise any issue of fact as to the IRB's or institution's actions, but the undisputed facts do not support the charges

[25] Note that the template cover letter (Attachment F) directs the parties to submit to the Project Manager any request for the Commissioner's review or any comments on the Presiding Officer's Report.
[26] *Id.*

made by the Center, the Presiding Officer will issue a Summary Decision recommending that the IRB or institution not be disqualified.

The Project Manager, within seven days of issuance of the Presiding Officer's Report, will forward the Report to the parties with a cover letter (see Attachment F).[27] The parties have 30 days after receipt to review the Report and request review by the Commissioner (see 21 CFR 16.26(c)). Within the same 30 days after receipt, the parties may submit to the Project Manager[28] comments on the Presiding Officer's Report.

The Project Manager will forward promptly to the Commissioner (or delegate) the request from a party for the Commissioner's review and/or a party's comments. The Commissioner, on the Commissioner's own initiative or at the request of either party, may review the Presiding Officer's Report and all related materials (21 CFR 16.26(c)). At the end of the 30 day period provided to the parties for comment, the Project Manager will forward to the Commissioner the Presiding Officer's Report, any request for review, and any comments received. Within 90 days of receipt of the Presiding Officer's Report and any comments received, the Commissioner will issue a decision on whether to disqualify the IRB or institution. (See section 5.C.3. below).

3. **Hearing Process** – The following steps apply to the hearing process.

   a. **Scheduling the hearing,** when indicated – If the Commissioner determines that a hearing is justified, the Presiding Officer will send a letter to all parties. Within 10 days of the Presiding Officer issuing the letter, the Project Manager and the Presiding Officer will notify the Center, the IRB or institution and their respective attorneys to arrange a date (preferably within 30 days), time, and location for the hearing. If the parties cannot agree, the Presiding Officer will designate a reasonable time and location (21 CFR 16.22(c)).

   b. **Prior to hearing** – At least one business day before the hearing, if feasible, the Center and the IRB or institution will provide each other with written notice of any published or written information to be presented or relied on at the hearing. A copy will also be provided in advance if the other party could not reasonably be expected to have or be able to obtain a copy. If written notice or a copy is not provided, the Presiding Officer may, if time permits, allow the party who did not receive the notice or copy additional time after the close of the hearing to make a submission concerning the article or information (21 CFR 16.24(g)).

[27] *Id.*
[28] *Id.*

c. **Hearing Transcript** – The Presiding Officer may order the hearing to be transcribed. The party requesting the hearing may have the hearing transcribed, at the party's expense, in which case a copy of the transcript is to be furnished to FDA. Any transcript of the hearing will be included with the presiding officer's report of the hearing (21 CFR 16.60(d)). In the event that the party requesting a hearing chooses not to have the hearing transcribed and the Agency wishes to have a transcript made, it is the responsibility of the Center to arrange for a transcript to be made of the hearing. The Center should provide the Project Manager with the name of the firm (and individual, if available) who will be preparing the transcript. Costs associated with transcription services will then be borne by the Center.

d. **Witnesses** – The Center should identify and contact any witnesses to be used by the Center during the hearing (usually FDA employees). At a hearing, witnesses typically provide oral testimony and submit documentary evidence to the Presiding Officer.

e. **Conduct of the Hearing** – FDA employees will first give a full and complete statement of the action which is the subject of the hearing, together with the information and reasons supporting it, and may present any oral or written information relevant to the hearing. The party requesting the hearing may then present any oral or written information relevant to the hearing. All parties may confront and conduct reasonable cross-examination of any person (except for the presiding officer and counsel for the parties) who makes any statement on the matter at the hearing. (See 21 CFR 16.60(b)).

f. **Presiding Officer Report** – Within 90 days after the conclusion of the hearing, the Presiding Officer will prepare a Report of the hearing. All written material presented at the hearing will be attached to the Report (21 CFR 16.60(e)). The Report will include a finding on the credibility of the witnesses (other than expert witnesses) whenever that is a material issue in the proceeding, and must include a recommended decision, with a statement of reasons, unless the Commissioner directs otherwise (21 CFR 16.60(f)). (See section 5.C.4.).

   Within seven days, the Project Manager will send the Report to the parties with a cover letter (see Attachment G). Whenever time permits, the parties to the hearing will be given the opportunity to review and comment on the Report (21 CFR 16.60(e)).

C. Commissioner's Decision

The Commissioner will issue an order explaining the basis for the disqualification determination and prescribing any actions to be taken with regard to ongoing clinical research conducted under the review of the IRB (21 CFR 56.121(c)), under one of the following four pathways:

1. Commissioner's Decision When the IRB or Institution Does Not Request a Hearing

If the IRB or institution fails to respond to the NOOH or declines the opportunity for a hearing, the Commissioner will review the Center Decision Memorandum and issue a decision within 90 days. The Commissioner may accept, in whole or in part, the findings of the Center regarding the alleged violations committed by the IRB and the conclusion that the IRB's alleged noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation. If the Commissioner adopts the Center's recommendation for disqualification of the IRB or institution, the Commissioner will sign the Center Decision Memorandum and the Order of Disqualification prepared by the Center (see section 5.A.1. above) and forward these documents to the OGCP Project Manager. The Order of Disqualification must state the reasons for the Commissioner's administrative action and the basis in the record (21 CFR 16.95(b)(2) and 21 CFR 56.121(c)).

Within seven days, the Project Manager will:

(1) Issue the signed Order of Disqualification to the IRB or institution and their counsel by certified mail (return receipt) or other documented method of transmission;

(2) Notify the Center when receipt of the Order of Disqualification by the IRB or institution and their counsel is confirmed; and

(3) Provide a copy of the Order of Disqualification to the Center and Center's counsel.

Within 14 days of confirmed delivery, the Center will:

(1) Provide copies of the Order of Disqualification to other appropriate FDA offices;

(2) Forward the Order of Disqualification to the Center's Freedom of Information (FOI) program for redaction (ensuring that the letter is compliant with Section 508 of the Rehabilitation Act);[29]

(3) Forward information about the IRB's or institution's disqualification to ORA so that the IRB's or institution's name can be included in the list of disqualified IRBs or institutions on FDA's webpage; and

(4) Notify OHRP and other parties with a direct interest, such as sponsors and clinical investigators, about the disqualification. The Center may provide notification by sending a notice of the disqualification.[30] In addition, FDA may elect to publish in the Federal Register a notice about the disqualification action. (See 21 CFR 56.121(c)).

If the Commissioner does not adopt the Center's recommendation to disqualify, the Commissioner, with the assistance of counsel, will prepare, and forward to the Project Manager, a letter to notify the IRB or institution.[31] Within seven days, the Project Manager will send the letter to the IRB or institution by certified mail (return receipt) or other documented method of transmission. A copy of the letter (and memorandum, if any) is sent to the Center.

Within 14 days of confirmed delivery, the Center will:

(1) Provide copies of the letter to other appropriate FDA offices; and

(2) Forward the letter to the Center's FOI program for redaction (ensuring that the letter is compliant with Section 508 of the Rehabilitation Act), and request posting by ORA on FDA's webpage, as appropriate.

2. Notice When the IRB's or Institution's Request for a Hearing is Denied

If the Commissioner grants the Center's Request to Deny the Hearing and to Disqualify (see section 5.A.4.e. above), the Commissioner, with the assistance of counsel, will issue a Notice of Denial of Hearing and Order of Disqualification and forward the Notice and Order to the OGCP Project Manager.

Within seven days, the Project Manager will:

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[29] In 1998, Congress amended the Rehabilitation Act of 1973 to require that Federal agencies make their electronic and information technology accessible to people with disabilities. "Section 508" refers to the portion of the law containing this requirement, which applies to Web applications, Web pages, and all attached files. (29 U.S.C.794d, as amended). See http://www.section508.gov/# .

[30] Note when sharing a document in this manner, certain information may need to be redacted.

[31] We recommend that the Commissioner issue a memo to the file, outlining the basis for the determination.

(1) Issue the signed Notice of Denial of Hearing and Order of Disqualification to the IRB or institution and their counsel by certified mail (return receipt) or other documented method of transmission;

(2) Notify the Center when receipt of the Notice of Denial of Hearing and Order of Disqualification by the IRB or institution and their counsel is confirmed; and

(3) Provide a copy of the Notice of Denial of Hearing and Order of Disqualification to the Center and Center's counsel.

Within 14 days of confirmed delivery, the Center will:

(1) Provide copies of the Notice of Denial of Hearing and Order of Disqualification to other appropriate FDA offices;

(2) Forward the Notice of Denial of Hearing and Order of Disqualification to the Center's FOI program for redaction (ensuring that the letter is compliant with Section 508 of the Rehabilitation Act),[32] and request posting by ORA on FDA's webpage, as appropriate. In addition, FDA may elect to publish in the Federal Register a notice about the disqualification action. (See 21 CFR 56.121(c));

(3) Forward information about the IRB's or institution's disqualification to ORA so that the IRB's or institution's name can be included in the list of disqualified IRBs or institutions on FDA's webpage; and

(4) Notify OHRP and other parties with a direct interest, such as sponsors and clinical investigators, about the disqualification. The Center may provide notification by sending a notice of the disqualification.[33]

3. Commissioner's Decision After the Presiding Officer's Summary Decision (Included in the Presiding Officer's Report)

The Commissioner may review any Summary Decision issued. Either party may request this review or the Commissioner may review the Summary Decision on the Commissioner's own initiative (21 CFR 16.26(c)). The Presiding Officer's Summary Decision is forwarded to the Commissioner, who will issue, within 90 days, a written Commissioner's Decision[34] either disqualifying the IRB or institution, or determining that the standard for disqualification has not been met. The Commissioner's Decision must state

[32] See http://www.section508.gov/#
[33] Note when sharing a document in this manner, certain information may need to be redacted.
[34] The Commissioner's Decision need not repeat all of the underlying arguments and basis contained in the Presiding Officer's Report; it may be as simple as a one page letter stating that the Presiding Officer's Decision has been adopted by the Commissioner.

the reasons for the Commissioner's administrative action and the basis in the record (21 CFR 16.95(b)(2)).

a. Commissioner Determines that the IRB or Institution Should Be Disqualified

If the Commissioner determines that the IRB or institution should be disqualified because the IRB refused or repeatedly failed to comply with the relevant regulations and the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation, within the above 90 days, the Commissioner, with the assistance of counsel, will issue a Commissioner's Decision. The Commissioner, with the assistance of counsel, will also prepare an Order of Disqualification to inform the IRB or institution that it is disqualified and forward a copy to the Project Manager. The notification will include a statement of the basis for such determination (21 CFR 56.121(c)).

Although the Commissioner may find that the IRB or institution did not violate all the regulations cited by the Center in the NOOH, the IRB or institution may still be disqualified if the IRB has refused or repeatedly failed to comply with some of the relevant regulations and the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

Within seven days, the Project Manager will:

(1) Issue the signed Order of Disqualification and a copy of the Commissioner's Decision to the IRB or institution and their counsel by certified mail (return receipt) or other documented method of transmission;

(2) Notify the Center when receipt of the Order of Disqualification by the IRB or institution and their counsel is confirmed; and

(3) Provide a copy of the Order of Disqualification and Commissioner's Decision to the Center and Center's counsel.

Within 14 days of confirmed delivery, the Center will:

(1) Provide copies of the Order of Disqualification to other appropriate FDA offices;

(2) Forward the Order of Disqualification and Commissioner's Decision to the Center's FOI program for redaction (ensuring that the letter is compliant with Section 508 of the Rehabilitation Act),[35] and request posting by ORA on FDA's webpage, as appropriate. In addition, FDA

[35] See http://www.section508.gov/#

may elect to publish in the Federal Register a notice about the disqualification action. (See 21 CFR 56.121(c));

(3) Forward information about the IRB's or institution's disqualification to ORA so that the IRB's or institution's name can be included in the list of disqualified IRBs or institutions on FDA's webpage; and

(4) Notify OHRP and other parties with a direct interest, such as sponsors and clinical investigators, about the disqualification. The Center may provide notification by sending a notice of the disqualification.[36]

b. Commissioner Determines that the IRB or Institution Should Not Be Disqualified

If the Commissioner does not adopt the Center's recommendation to disqualify, the Commissioner, with the assistance of counsel, will prepare, and forward to the Project Manager, a Commissioner's Decision explaining the decision. Within seven days of receipt of the Commissioner's Decision, the Project Manager will send a copy of the Commissioner's Decision to the IRB or institution by certified mail (return receipt) or other documented method of transmission. A copy of the Commissioner's Decision is sent to the Center.

Within 14 days of confirmed delivery, the Center will:

(1) Provide copies of the Commissioner's Decision to other appropriate FDA offices; and

(2) Forward the Commissioner's Decision to the Center's FOI program for redaction and posting on FDA's webpage (ensuring that the letter is compliant with Section 508 of the Rehabilitation Act).

4. Commissioner's Decision After the Presiding Officer's Report on the Regulatory Hearing

The Presiding Officer's Report on the Part 16 hearing, including any attachments and comments, will be forwarded to the Commissioner. With the assistance of counsel, the Commissioner will issue a written Commissioner's decision within 90 days of receipt. The Commissioner's decision shall state the reasons for the Commissioner's administrative action and the basis in the record (21 CFR 16.95(b)(2)). The Commissioner's decision may be in the form of a report or a letter.

a. Commissioner Determines the IRB or Institution Should Be Disqualified

[36] Note when sharing a document in this manner, certain information may need to be redacted.

If, after reviewing the administrative record, including the Presiding Officer's Report, the Commissioner determines that the IRB has refused or repeatedly failed to comply with the regulations in 21 CFR Part 56 and the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation, the Commissioner with the assistance of counsel will prepare a Commissioner's Decision and an Order of Disqualification (see Attachment D) and send those documents to the Project Manager.

Within seven days, the Project Manager will:

(1) Issue the signed Order of Disqualification and a copy of the Commissioner's Decision to the IRB or institution and their counsel by certified mail (return receipt) or other documented method of transmission;

(2) Notify the Center when receipt of the Order of Disqualification by the IRB or institution and their counsel is confirmed; and

(3) Provide a copy of the Order of Disqualification and Commissioner's Decision to the Center.

Within 14 days of confirmed delivery, the Center will:

(1) Provide copies of the Order of Disqualification to other appropriate FDA offices;

(2) Forward the Order of Disqualification and Commissioner's Decision to the Center's FOI program for redaction (ensuring that the letter is compliant with Section 508 of the Rehabilitation Act),[37] and request posting by ORA on FDA's webpage, as appropriate. In addition, FDA may elect to publish in the Federal Register a notice about the disqualification action. (See 21 CFR 56.121(c));

(3) Forward information about the IRB's or institution's disqualification to ORA so that the IRB's or institution's name can be included in the list of disqualified IRBs or institutions on FDA's webpage; and

(4) Notify OHRP and other parties with a direct interest, such as sponsors and clinical investigators, about the disqualification. The Center may provide notification by sending a notice of the disqualification.[38]

b. Commissioner Determines the IRB or Institution Should Not Be Disqualified

[37] See http://www.section508.gov/#
[38] Note when sharing a document in this manner, certain information may need to be redacted.

If, after reviewing the administrative record, including the Presiding Officer's Report, the Commissioner determines not to disqualify, within 90 days, the Commissioner with the assistance of counsel will prepare a Commissioner's Decision. Within seven days of receiving the Commissioner's Decision, the Project Manager will send the Commissioner's Decision to the IRB or institution and their counsel by certified mail (return receipt) or other documented method of transmission. A copy of the document is sent to the Center.

Within 14 days of confirmed delivery, the Center will:

(1) Provide copies of the Commissioner's Decision and/or letter to other appropriate FDA offices; and

(2) Forward the Commissioner's Decision and/or letter to the Center's FOI program for redaction (ensuring that the letter is compliant with Section 508 of the Rehabilitation Act),[39] and request posting by ORA, as appropriate, on FDA's webpage.

D. Administrative Record, Posting of Documents, and Disqualified IRBs and Data Review

Copies of all documents should be sent to the OGCP Project Manager for purposes of recordkeeping. The Center is responsible for forwarding the documents to the Center's FOI contact and ORA, so that as appropriate, all applicable documents may be posted on the agency webpage (after redaction), e.g., the IRB Restrictions Letter,[40] NOOH, Order of Disqualification, Notice of Denial of Hearing and Order of Disqualification, the Presiding Officer's Report, and Commissioner's Decision.

A listing of all final actions related to disqualification matters should be posted on FDA's webpage.[41] If an IRB is disqualified, FDA should notify OHRP for purposes of updating the OHRP database for IRB registrations and Federalwide Assurances.

FDA will review the studies conducted at a disqualified institution or reviewed by a disqualified IRB to decide on a case-by-case basis whether to reject the data[42]

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[39] See http://www.section508.gov/#

[40] See the Institutional Review Boards – Restrictions Imposed Letters webpage at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ComplianceEnforcement/ucm369514.htm.

[41] A determination that an IRB or institution is disqualified is disclosable to the public (see 21 CFR 56.122). See also, the Freedom of Information Act (5 U.S.C. § 552) and the Privacy Act of 1974 (5 U.S.C. § 552a); and the Privacy Act System of Records 09-10-0010 for the "Bioresearch Monitoring Information System, HHS/FDA."

[42] See 46 Federal Register 8958 at 8975, January 27, 1981; response to comment 132.

generated by clinical studies reviewed by the IRB and submitted to FDA or to take further action.

6. EFFECTIVE DATE.

This FDA Staff Manual Guide is effective as of August 27, 2014.

7. HISTORY -- SMG 7714, Disqualification of an Institutional Review Board (IRB), Parent Institution, or Component of Parent Institution

STATUS (I, R, C)	DATE APPROVED	LOCATION OF CHANGE HISTORY	CONTACT	APPROVING OFFICIAL
Initial	08/27/2014	N/a	Doreen Kezer, Senior Health Policy Analyst, OGCP, OSPM/OMPT	Joanne R. Less, Ph.D., Director, OGCP, Office of Special Medical Programs, Office of Medical Products and Tobacco (OSMP/OMPT)

ATTACHMENT A

[Institutional Review Board -- Restrictions Imposed]

[DATE]

By Certified Mail [or other documented method of transmission] - **Return Receipt Requested** [or] **Hand Delivered**

[**NOTE:** See 21 CFR 56.120(c) for addressee information]

[IRB/PARENT INSTITUTION and/or IRB/PARENT INSTITUTION'S COUNSEL]
[ADDRESS]

Dear [IRB/PARENT INSTITUTION and/or IRB/PARENT INSTITUTION'S COUNSEL]:

This letter imposing restrictions (IRB Restrictions Letter) informs you of objectionable conditions observed during the U.S. Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB) that was conducted between [INSPECTION START DATE] and [INSPECTION END DATE][OPTIONAL: ", by [MR./MS./DR. XXXXX], representing FDA"]. The purpose of this inspection was to determine whether the IRB procedures for the protection of human subjects complied with the regulations set forth in Title 21 of the Code of Federal Regulations (CFR), Parts 50 and 56. These regulations apply to clinical investigations of products regulated by FDA and help ensure that human subjects are protected from undue hazard or risk during the course of clinical investigations.

At the conclusion of the inspection, [ENTER FDA INVESTIGATOR NAME OR "the FDA investigator"] presented and discussed with [ENTER "you" OR APPROPRIATE INDIVIDUAL(S)] FDA Form 483, Inspectional Observations. We acknowledge receipt of the IRB's [DATE] written response to the FDA Form 483 and a follow-up response dated [DATE]. We have reviewed the FDA inspection report, the Form FDA 483, and your responses. The IRB's written responses are unacceptable, as explained below.

[INSERT THIS SECTION ONLY IF APPLICABLE] Until [IRB or PARENT INSTITUTION] takes appropriate corrective action, FDA is [INSERT ONE OR MORE OF THE FOLLOWING:]

(1) Withholding approval of new studies subject to the requirements of 21 CFR Part 56 that are conducted at [INSTITUTION] or reviewed by [IRB]. (21 CFR 56.120(b)(1)).

(2) Directing that no new subjects be added to ongoing studies subject to 21 CFR Part 56. (21 CFR 56.120(b)(2)).

(3) Terminating the following ongoing studies subject to 21 CFR Part 56. (21 CFR 56.120(b)(3)). [LIST STUDIES, AS APPROPRIATE]

(4) Notifying relevant State and Federal regulatory agencies and other parties with a direct interest in FDA's action of the deficiencies in the operation of the IRB because the apparent noncompliance creates a significant threat to the rights and welfare of human subjects. (21 CFR 56.120(b)(4)).

(5) Restricting OR suspending OR terminating the IRB's use of the expedited review procedure to protect the rights or welfare of subjects. (21 CFR 56.110(d)).

This IRB Restrictions Letter provides you with written notice describing the noncompliance with (violations of) applicable regulations governing the operation and responsibilities of IRBs

under 21 CFR Part 56. The [IRB or PARENT INSTITUTION] is required to respond in writing to FDA's [APPLICABLE CENTER] ("the Center") with a description of the corrective actions that will be taken by the IRB, the institution, or both to achieve compliance with FDA regulations [21 CFR 56.120(a)]. A listing of the violations follows. The applicable provisions of the CFR are cited for each violation.

[INSERT LIST OF VIOLATIONS & APPLICABLE CITATIONS]

This letter is not intended to be an all-inclusive list of the deficiencies. It is your responsibility to ensure adherence to each requirement of the law and relevant regulations.

Based on our evaluation of information obtained by the FDA, the IRB does not meet the requirements of 21 CFR Part 56. We have no assurance that the IRB procedures are adequately protecting the rights and welfare of the human subjects involved in research. For this reason, and effective immediately:

- FDA will withhold approval of all new studies subject to 21 CFR Part 56 and reviewed by the IRB; and

- No new subjects are to be enrolled in any ongoing studies subject to 21 CFR Part 56 and approved by the IRB.

These restrictions will remain in effect until such time as FDA has evidence of adequate corrective actions and notifies you in writing that the IRB's corrective actions are satisfactory. You are responsible for notifying the affected sponsors and clinical investigators about these restrictions. See [INSERT RELEVANT PROVISIONS: device studies (notifying sponsors) – 21 CFR 812.35(a)(1) and (3) / drug/biologic studies (notifying CIs) – 21 CFR 312.66]. These restrictions do not relieve the IRB of its responsibility for receiving and reacting to reports of unanticipated problems involving risks to human subjects or others and routine progress reports from ongoing studies.

Within 30 business days of receipt of this letter, you should respond in writing with a description of the corrective actions that will be taken or that have been implemented to achieve compliance with the regulations.

Your response should address each item of noncompliance listed above. If you do not believe your IRB is in violation of FDA requirements, include your reasoning and any supporting information for our consideration. If you assert that full and adequate correction has been achieved, you should include any documentation necessary that affirms your corrective actions. For each action to be accomplished, include the projected completion dates.

Include with your response a copy of the IRB's written communication to each of the affected sponsors and clinical investigators, notifying them of the current FDA-imposed restrictions. In addition, please provide a list of all studies being reviewed by your IRB that are subject to 21 CFR Part 56, and list all studies that are affected by the above restrictions.

Your failure to adequately respond to this letter may result in further administrative actions, as authorized by 21 CFR 56.121.

Your written reply should be sent to [CENTER CONTACT].

[CONSIDER INCLUDING, IF A REGULATORY MEETING IS DESIRED:]After receipt of your written response, FDA may request your participation in a regulatory meeting. If such a meeting is scheduled, we ask that you provide us with a full and complete explanation of the violations listed above. You should bring with you all pertinent documents. A representative of your choosing may accompany you.

The Center will carefully consider your written response. If your explanation is accepted by the Center, the restrictions imposed above in this letter will be lifted. FDA will verify that your corrective actions are implemented during future inspections.

Sincerely yours,

[DESIGNATED CENTER SIGNATORY & TITLE]

bcc:

[*To blind copy electronically, send to the relevant party at firstname.lastname@fda.hhs.gov; for hardcopy distribution at the White Oak (WO) campus, include the building and room numbers*]
OCC; WO31/WO32
DFOI; HFI-30
OGCP; WO32-5129
ORA, Division of Enforcement (DE), Office of Enforcement and Import Operations (OEIO), Office of Operations (OO); WO32
[*Relevant District Office – District Personnel, including the District Director; Director, Investigations Branch; and the District Investigators*]
CDER, OSI; WO51
CBER, BIMO Group; HFM-664, CBERBIMONotification@fda.hhs.gov
CVM, BIMO Group; HFV-234
CDRH, BIMO Group; WO66, BIMO@cdrh.fda.gov
CFSAN, BIMO Group; HFS-205
CFSAN, OCD; HFS-265
CTP, Office of Compliance and Enforcement, CTPCompliance@fda.hhs.gov
[*Originating Center – Center files and distribution]*

ATTACHMENT B

[Notice of Opportunity for Hearing]

[DATE]

By Certified Mail [or other documented method of transmission] - **Return Receipt Requested** [or] **Hand Delivered**

[IRB/INSTITUTION and/or IRB/INSTITUTION'S COUNSEL]

[ADDRESS]

NOTICE OF OPPORTUNITY FOR HEARING

Dear [IRB/INSTITUTION and/or IRB/INSTITUTION'S COUNSEL]:

The [CENTER], Food and Drug Administration (FDA) has information indicating that [IRB/INSTITUTION] has refused or repeatedly failed to comply with any of the regulations set forth in Title 21 Code of Federal Regulations (CFR), Part 56, and the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation. The violations and the effect of the noncompliance on human subjects provide the basis for disqualification of [IRB/INSTITUTION].

Pursuant to 21 CFR § 56.120, the Center informed you, by letter dated [DATE OF LETTER], of the specific matters complained of (noncompliance) and offered you an opportunity to respond to them in writing. [STATE HOW THE IRB/INSTITUTION RESPONDED, WHETHER BY NOT RESPONDING OR RESPONDING IN WRITING]. [The Center has concluded that your written explanation is unacceptable because it fails to adequately address the violations set forth below.] [By failing to respond to the letter of [DATE OF LETTER], you waived your opportunity to provide a written response.]

Accordingly, [IRB/INSTITUTION] is being offered an opportunity for a regulatory hearing pursuant to 21 CFR Part 16 and § 56.121(a), on the question of whether to disqualify [IRB/INSTITUTION]. [IRB/INSTITUTION] has the right to be advised and represented by counsel at all times. Any regulatory hearing on this matter will be governed by the regulations in 21 CFR Part 16 and FDA's guidelines on electronic media coverage of administrative proceedings, 21 CFR Part 10, Subpart C. Enclosed you will find copies of these regulations.

A listing of the specific violations follows. These are the matters that will be considered at the regulatory hearing. Applicable provisions of the CFR are cited for each violation.

[SET OUT VIOLATIONS IN NUMBERED PARAGRAPHS. CITE CFR PROVISION FOR EACH VIOLATION. STATE THE RESTRICTIONS, IF ANY, THAT FDA HAS IMPOSED ON THE IRB.]

A request for a hearing should be made, in writing, within ten (10) business days of receipt of this letter and should be directed to [NAME AND TITLE OF ORA CONTACT], Office of Regulatory Affairs, Telephone [CONTACT PHONE NUMBER], Fax [CONTACT FAX NUMBER]. If no response to this letter is received by that time, [IRB/INSTITUTION] will be deemed to have waived any right to a regulatory hearing, and a decision in this matter will be made based on the facts available to FDA. No hearing will be held.

A request for a hearing may not rest upon mere allegations or denials but must present specific facts showing that there is a genuine and substantial issue of fact that warrants a hearing. Pursuant to 21 CFR § 16.26, a request for a hearing may be denied, in whole or in part, if the Commissioner or the Commissioner's delegate determines that no genuine and substantial issue of fact had been raised by the material submitted. A hearing will not be granted on issues of policy or law. Written notice of a determination of summary judgment will be provided, explaining the reasons for denial of the hearing.

Please inform [NAME OF ORA CONTACT] within ten (10) business days your request for a hearing or if you wish to have this matter resolved by information available to FDA.

Sincerely,

[NAME]
Associate Commissioner for
Regulatory Affairs

bcc:

[*To blind copy electronically, send to the relevant party at firstname.lastname@fda.hhs.gov; for hardcopy distribution at the White Oak (WO) campus, include the building and room numbers*]
OCC; WO31/WO32
DFOI; HFI-30
OGCP; WO32-5129
ORA, Division of Enforcement (DE), Office of Enforcement and Import Operations (OEIO), Office of Operations (OO); WO32
[*Relevant District Office – District Personnel, including the District Director; Director, Investigations Branch; and the District Investigators*]
CDER, OSI; WO51
CBER, BIMO Group; HFM-664, CBERBIMONotification@fda.hhs.gov
CVM, BIMO Group; HFV-234
CDRH, BIMO Group; WO66, BIMO@cdrh.fda.gov
CFSAN, BIMO Group; HFS-205
CFSAN, OCD; HFS-265
CTP, Office of Compliance and Enforcement, CTPCompliance@fda.hhs.gov
[*Originating Center – Center files and distribution*]

ATTACHMENT C

[Center Decision Memorandum]

Date:

To: Commissioner of Food and Drugs [OR DELEGATE]

From: Director (Office, Mailing Code)

Through: Director (Center, Mailing Code)

[NAME]/Center Counsel, Office of the General Counsel, GCF-1

[NAME]/Commissioner's Counsel, Office of the General Counsel, GCF-1

Subject: Proposed Disqualification of [IRB/INSTITUTION], [CITY, STATE] – ACTION

ACTION REQUESTED

I request your decision, under 21 CFR Parts 16 and 56, regarding our recommendation (below) to disqualify [IRB/INSTITUTION]. If you agree with the recommendation, I request your signature on the last page of this recommendation, and on the attached "Order of Disqualification" (Attachment 1), to be issued to [IRB/INSTITUTION].

BACKGROUND

[PROVIDE SUMMARY OF MATTER]

CONCLUSION

DECISION

Pursuant to 21 CFR Parts 16 and 56, the Food and Drug Administration hereby disqualifies [IRB/INSTITUTION].

Approved_____ Disapproved _____

_____ _____

Signature Date
Name
Title

ATTACHMENTS

Attachment 1 – Order of Disqualification of [IRB/INSTITUTION]

[SUPPORTING DOCUMENTATION, AS APPROPRIATE, e.g., IRB Restrictions Letter, evidence of receipt of IRB Restrictions Letter, response to IRB Restrictions Letter, transcript of informal hearing (if any), NOOH, evidence of response to NOOH, hearing transcript, relevant correspondence.]

[Order of Disqualification]

[DATE]

By Certified Mail [or other documented method of transmission] - **Return Receipt Requested**

[IRB/INSTITUTION]
[ADDRESS]

[NAME OF COUNSEL]
[ADDRESS]

Order of Disqualification

Dear [IRB/INSTITUTION] [and/or COUNSEL]:

I have reviewed the administrative record of the regulatory disqualification proceeding involving [IRB/INSTITUTION]. After reviewing all information available to FDA, I have determined that [IRB] has refused or repeatedly failed to comply with the regulations set forth in 21 CFR Part 56 and that [IRB]'s noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation. In accordance with 21 CFR Part 16 and § 56.121, [IRB/INSTITUTION] is disqualified. [IF SIGNED BY THE COMMISSIONER'S DELEGATE, ADD: Under authority delegated to me by the Commissioner of Food and Drugs, I am issuing this Commissioner's Decision disqualifying [IRB/INSTITUTION]].

The basis for this disqualification determination is [ENTER BASIS]. [NOTE: a Commissioner's Decision may be referenced and enclosed with this order.]

FDA will not approve an application for a research permit for a clinical investigation that is under the review of a disqualified IRB or that is to be conducted at a disqualified institution, and FDA may refuse to consider in support of a marketing permit the data from a clinical investigation that was reviewed by a disqualified IRB or conducted at a disqualified institution, unless the IRB or the parent institution is reinstated as provided in 21 CFR § 56.123.

An IRB or an institution may be reinstated if [I or THE COMMISSIONER determine/determines, depending on who signs the Order], upon an evaluation of a written submission from the IRB or institution that explains the corrective action that the institution or IRB plans to take, that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in 21 CFR Part 56.

Sincerely,

Commissioner of Food and Drugs [OR DELEGATE]

Enclosure

bcc:

[*To blind copy electronically, send to the relevant party at firstname.lastname@fda.hhs.gov; for hardcopy distribution at the White Oak (WO) campus, include the building and room numbers*]
OCC; WO31/WO32
DFOI; HFI-30
OGCP; WO32-5129
ORA, Division of Enforcement (DE), Office of Enforcement and Import Operations (OEIO), Office of Operations (OO); WO32
[*Relevant District Office – District Personnel, including the District Director; Director, Investigations Branch; and the District Investigators*]
CDER, OSI; WO51
CBER, BIMO Group; HFM-664, CBERBIMONotification@fda.hhs.gov
CVM, BIMO Group; HFV-234
CDRH, BIMO Group; WO66, BIMO@cdrh.fda.gov
CFSAN, BIMO Group; HFS-205
CFSAN, OCD; HFS-265
CTP, Office of Compliance and Enforcement, CTPCompliance@fda.hhs.gov
[*Originating Center – Center files and distribution*]

ATTACHMENT E

[Notice of Denial of Hearing and Order of Disqualification]

[DATE]

By Certified Mail [or other documented method of transmission] - **Return Receipt Requested**

[IRB/INSTITUTION]
[ADDRESS]

[NAME OF COUNSEL]
[ADDRESS]

Notice of Denial of Hearing and Order of Disqualification

Dear [IRB/INSTITUTION] [and/or COUNSEL]:

I have reviewed the administrative record of the regulatory disqualification proceeding involving [IRB/INSTITUTION]. On the basis of all information available to FDA, I have determined that no genuine and substantial issue of fact has been raised by the material submitted by [IRB], and [IRB] has refused or repeatedly failed to comply with the regulations set forth in 21 CFR Part 56 and that [IRB]'s noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation. I am therefore granting [CENTER]'s Request for Hearing Denial and, in accordance with 21 CFR Part 16 and § 56.121, [IRB/INSTITUTION] is disqualified. [IF SIGNED BY THE COMMISSIONER'S DELEGATE, ADD: Under authority delegated to me by the Commissioner of Food and Drugs, I am issuing this Commissioner's Decision disqualifying [IRB/INSTITUTION]].

The basis for this disqualification determination is [ENTER BASIS]. [NOTE: a Commissioner's Decision may be referenced and enclosed with this notice.]

FDA will not approve an application for a research permit for a clinical investigation that is to be under the review of a disqualified IRB or that is to be conducted at a disqualified institution, and FDA may refuse to consider in support of a marketing permit the data from a clinical investigation that was reviewed by a disqualified IRB as conducted at a disqualified institution, unless the IRB or the parent institution is reinstated as provided in 21 CFR § 56.123.

An IRB or an institution may be reinstated if [I or THE COMMISSIONER determine/determines, depending on who signs the Notice and Order], upon an evaluation of a written submission from the IRB or institution that explains the corrective action that the institution or IRB plans to take, that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in 21 CFR Part 56.

Sincerely,

Commissioner of Food and Drugs [OR DELEGATE]

Enclosure

bcc:

[*To blind copy electronically, send to the relevant party at firstname.lastname@fda.hhs.gov; for hardcopy distribution at the White Oak (WO) campus, include the building and room numbers*]
OCC; WO31/WO32
DFOI; HFI-30
OGCP; WO32-5129
ORA, Division of Enforcement (DE), Office of Enforcement and Import Operations (OEIO), Office of Operations (OO); WO32
[*Relevant District Office – District Personnel, including the District Director; Director, Investigations Branch; and the District Investigators*]
CDER, OSI; WO51
CBER, BIMO Group; HFM-664, CBERBIMONotification@fda.hhs.gov
CVM, BIMO Group; HFV-234
CDRH, BIMO Group; WO66, BIMO@cdrh.fda.gov
CFSAN, BIMO Group; HFS-205
CFSAN, OCD; HFS-265
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[*Originating Center – Center files and distribution*]

[Notice to a Party under 21 CFR 16.26(c) of Issuance of Presiding Officer Report]

[DATE]

By Certified Mail [or other documented method of transmission] - **Return Receipt Requested** [or] **Hand Delivered**

[IRB/INSTITUTION] [IRB/INSTITUTION'S COUNSEL]
[ADDRESS]

[or]

[CENTER COUNSEL]
[ADDRESS]

Regarding: In the Matter of [IRB/INSTITUTION]

Dear [IRB/INSTITUTION] [and/or COUNSEL] [or] [CENTER COUNSEL]:

Enclosed you will find the "Report of the Presiding Officer," issued on [DATE], concerning the above referenced matter. The Presiding Officer issued this Report under Title 21, Code of Federal Regulations, Section 16.26(b). The Report is provided to you as a party to the matter or as counsel to a party.

In accordance with 21 CFR §16.26(c), you may request that the Commissioner or his or her delegate review the enclosed Report. Within thirty days of the date you receive the Report, submit any request for review and any comments you may have on the Report to the Project Manager, [NAME, ADDRESS, FAX NUMBER OF PROJECT MANAGER].

The Commissioner (or delegate) will consider as part of the administrative record any comments you submit (see 21 CFR §16.80(a)). The Commissioner (or delegate) will issue a written decision on the basis of the administrative record pursuant to 21 CFR §16.95(a).

Sincerely,

[PROJECT MANAGER SIGNATURE]

[NAME/TITLE]

Enclosure

bcc:

[*To blind copy electronically, send to the relevant party at firstname.lastname@fda.hhs.gov; for hardcopy distribution at the White Oak (WO) campus, include the building and room numbers*]
OCC; WO31/WO32
DFOI; HFI-30
OGCP; WO32-5129
ORA, Division of Enforcement (DE), Office of Enforcement and Import Operations (OEIO), Office of Operations (OO); WO32
[*Relevant District Office – District Personnel, including the District Director; Director, Investigations Branch; and the District Investigators*]
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[*Originating Center – Center files and distribution*]

[Notice to a Party under 21 CFR 16.60(e) of Issuance of Presiding Officer Report]

[DATE]

By Certified Mail [or other documented method of transmission] - **Return Receipt Requested** [or] **Hand Delivered**

[IRB/INSTITUTION] [IRB/INSTITUTION'S COUNSEL]
[ADDRESS]

[or]

[CENTER COUNSEL]
[ADDRESS]

Regarding: In the Matter of [IRB/INSTITUTION]

Dear [IRB/INSTITUTION] [and/or COUNSEL] [or] [CENTER COUNSEL]:

Enclosed you will find the Presiding Officer's written report dated [DATE], of the hearing referenced above held on [DATE OF HEARING]. The Presiding Officer prepared this report under Title 21, Code of Federal Regulations, Section 16.60(e). The report is provided to you as a party to the Part 16 regulatory hearing, or as counsel to a party.

In accordance with 21 CFR §16.60(e), you may review and comment on the Presiding Officer's report of the hearing. Within thirty days of the date you receive the report, submit any comments you may have on the report to the Project Manager, [NAME, ADDRESS, FAX NUMBER OF PROJECT MANAGER].

The Commissioner (or delegate) will consider as part of the administrative record any comments you submit (see 21 CFR §16.80(a)). The Commissioner (or delegate) will issue a written decision on the basis of the administrative record pursuant to 21 CFR §16.95(a).

Sincerely,

[PROJECT MANAGER SIGNATURE]

[NAME/TITLE]

Enclosure

bcc:

[*To blind copy electronically, send to the relevant party at firstname.lastname@fda.hhs.gov; for hardcopy distribution at the White Oak (WO) campus, include the building and room numbers*]
OCC; WO31/WO32
DFOI; HFI-30
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