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# Guidance for IRBs, Clinical Investigators, and Sponsors

## Considerations When Transferring Clinical Investigation Oversight to Another IRB

**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Center for Biologics Evaluation and Research  
Center for Devices and Radiological Health  
Office of Good Clinical Practice  
May 2014**

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# Guidance for IRBs, Clinical Investigators, and Sponsors Considerations When Transferring Clinical Investigation Oversight to Another IRB

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# **Guidance for IRBs, Clinical Investigators and Sponsors<sup>1</sup> Considerations When Transferring Clinical Investigation Oversight to Another IRB**

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

## **I. INTRODUCTION**

This guidance discusses the regulatory responsibilities of institutional review boards (IRBs), clinical investigators, and sponsors when oversight of a previously approved, ongoing clinical investigation under FDA's jurisdiction is transferred from one IRB to another IRB. This guidance also addresses questions that have been previously raised concerning procedures and processes that are required and/or recommended by FDA when such oversight is transferred. FDA encourages individuals to contact the agency directly to discuss any unusual circumstances.

To enhance human subject protections and reduce regulatory burden, FDA and the Office for Human Research Protections (OHRP) have been actively working to harmonize the agencies' regulatory requirements and guidance for human subjects research. This guidance document was developed as a part of these efforts. For studies subject to 45 CFR part 46 (i.e., studies that are funded, conducted, or supported by the Department of Health and Human Services), OHRP issued a draft guidance entitled, "Considerations in Transferring a Previously Approved Research Project to a New IRB or Research Institution."<sup>2</sup>

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

## **II. BACKGROUND**

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<sup>1</sup> This guidance has been prepared by the Office of Good Clinical Practice, Office of Medical Products and Tobacco with input from the Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER) and Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration.

<sup>2</sup> OHRP's guidance is available at: <http://www.hhs.gov/ohrp/newsroom/rfc/transferdraftdoc.html>.

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An IRB is any board, committee, or other group formally designated by an institution to review, approve the initiation of, and 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.<sup>3</sup> To prevent lapses in human subject protection, it is generally preferred that the same IRB retain oversight responsibility throughout the conduct of the trial, if possible. FDA recognizes, however, that clinical investigations that were originally approved by one IRB are sometimes transferred to another IRB for subsequent review and oversight. These transfers may give rise to a number of legal, regulatory, administrative, and logistical considerations for the parties involved.

The research entities involved in a transfer of IRB review responsibilities for a clinical investigation include:

- The *original* IRB, which for the purpose of this guidance means the IRB originally designated to review a clinical investigation and that transfers oversight responsibility to another IRB;
- The *receiving* IRB, which for the purpose of this guidance means the IRB that accepts responsibility for oversight of the clinical investigation;
- The sponsor who initiates the clinical investigation; and
- The clinical investigator who conducts the investigation.

The transfer of review responsibility for a clinical investigation from one IRB to another should be accomplished in a way that assures continuous IRB oversight with no lapse in either IRB approval or the protection of human subjects, and with minimal disruption of research activities. This guidance discusses possible actions that sponsors, clinical investigators, and IRB staff for the original and receiving IRBs should consider before, during, and after any such transfer. Ideally, IRBs will have their own procedures and/or institutional policies in place to provide general guidance if oversight of a clinical investigation must be transferred to another IRB.

We recommend that the original IRB work closely with the clinical investigator, the sponsor, and the receiving IRB, as appropriate, throughout the transfer process to ensure an orderly transition and continued protection of human subjects. Effective communication among the IRBs, sponsors, clinical investigators, FDA, and others (e.g., institutional members, Data Safety Monitoring Board, Contract Research Organization (CRO)) is critical to ensuring a smooth transition to another IRB. FDA recommends that any impending changes in oversight be communicated as early as possible in the transfer process. In some situations, a transfer may disrupt study enrollment or other aspects of a clinical investigation, whether because of unforeseen difficulties in the transfer process or because of concerns arising from the study. FDA believes that providing this guidance will help to ensure that serious disruptions are rare.

FDA's requirements place the responsibility for securing IRB review and approval on the clinical investigator in clinical investigations of new drugs and biological products,<sup>4</sup> and on the

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<sup>3</sup> 21 CFR 56.102(g).

<sup>4</sup> 21 CFR 312.66.

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sponsor in clinical investigations of medical devices.<sup>5</sup> In practice, however, the party that actually initiates the transfer process varies depending on the circumstances necessitating the transfer and the parties involved. For example, an institution's IRB may decide to transfer oversight for its pediatric clinical investigations to an IRB with such expertise within the same institution. Whoever initiates the transfer of oversight, the clinical investigator and sponsor continue to be responsible for their respective regulatory obligations (e.g., making any modifications to the informed consent document required by the receiving IRB).<sup>6</sup>

Although FDA regulations at 21 CFR parts 50, 56, 312, and 812 do not specifically address the issue of transfer of oversight from one IRB to another, the requirements governing review, oversight, and conduct of clinical investigations apply nonetheless. While this guidance provides recommendations to facilitate such a transfer, it does not create or imply new requirements and/or responsibilities for IRBs, sponsors, or clinical investigators.

Transfers of IRB oversight of a clinical investigation may occur for a number of different reasons, including cessation of IRB operations, consolidation of multiple IRBs into a single IRB, temporary inability of an IRB to meet its obligations, or as a result of IRB non-compliance. Specific examples include:

- A medical school decides to transfer oversight responsibility for a category of its clinical investigations (e.g., drug research, device research) to another IRB.
- A hospital's IRB realizes it has an excessive workload, but the institution does not want to establish an additional IRB and transfers oversight of some clinical investigations to another IRB.
- A large multi-campus university decides to consolidate its human subject protection system by closing one or more of its existing IRBs and transfers oversight to an independent IRB.
- A small institution has an insufficient number of clinical investigations to justify maintaining its own IRB and decides to cease operations of its IRB and transfer oversight of its clinical investigations to another IRB.
- A sponsor decides to transfer IRB oversight from one IRB to another.
- Financial or other considerations cause an IRB to cease operations.
- An institution realizes its current IRBs are overburdened and establishes another IRB to share the workload.
- A fire, flood, or other disaster temporarily prevents an IRB from fulfilling its review/oversight responsibilities.
- An IRB is subject to administrative actions under 21 CFR 56.120 or has been disqualified under 21 CFR 56.121.<sup>7</sup>
- A sponsor decides to transfer a clinical investigation when an investigator moves to a new research site.

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<sup>5</sup> 21 CFR 812.40.

<sup>6</sup> See, e.g., 21 CFR 56.109, 21 CFR 312.66, and 21 CFR 812.40.

<sup>7</sup> 21 CFR 56.121(b) provides that an IRB may be disqualified if FDA determines that the IRB has refused or repeatedly failed to comply with the applicable regulatory requirements and the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

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The complexity and duration of the IRB transfer process itself is expected to vary, depending on the reasons for the transfer, the parties involved, and the number and risk of the studies being transferred. For example, transfer of IRB oversight due to purely administrative reasons such as consolidating IRB workload may be relatively quick and straight-forward, whereas a transfer of oversight due to the original IRB's non-compliance might be lengthier and involve more complicated legal, regulatory, administrative, and logistical considerations. In general, the type of IRBs involved (e.g., academic, hospital-based, independent) would not affect the steps to consider when transferring oversight.<sup>8</sup>

Section III of this guidance document provides recommendations concerning the transfer of IRB oversight from one IRB to another IRB that is not part of the same institution (including independent IRBs). Section IV of this document addresses several special situations: the transfer of oversight from one IRB to another IRB operating within the same institution, the temporary transfer of clinical investigation oversight to another IRB that occurs as a result of a natural disaster or for other reasons, and the transfer of a clinical investigation to a new research site requiring IRB review.

### **III. WHEN OVERSIGHT OF A PREVIOUSLY APPROVED CLINICAL INVESTIGATION TRANSFERS FROM THE ORIGINAL IRB TO ANOTHER IRB NOT PART OF THE SAME INSTITUTION**

When transferring IRB review and oversight of clinical investigations from one IRB to another IRB, FDA recommends that a plan for the transfer process be documented in a written agreement between the original and receiving IRBs, if appropriate.<sup>9,10</sup> The agreement should address how the IRBs should handle, and document as appropriate, the following eight steps. We describe each of these steps in more detail below. Please note, this list is not meant to be exhaustive. Additional actions may be necessary and/or appropriate.

- (1) Identifying those studies for which IRB oversight is being transferred;
- (2) Ensuring the availability and retention of pertinent records;
- (3) Establishing an effective date for transfer of oversight, including records, for the clinical investigation(s);
- (4) Conducting a review of the study(ies) by the receiving IRB, where appropriate, before it accepts responsibility for the study(ies);
- (5) Confirming or establishing the date for the next continuing review;
- (6) Determining whether the consent form needs to be revised;

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<sup>8</sup> FDA encourages the use of central IRBs, in appropriate circumstances, as a mechanism to reduce burden and delays in the conduct of multicenter clinical trials. The goal of the centralized process is to increase efficiency and decrease duplicative efforts that do not contribute to meaningful human subject protection. For additional information relating to the use of central IRBs, see FDA's Guidance, "Using a Centralized IRB Review Process in Multicenter Clinical Trials," available at <http://www.fda.gov/RegulatoryInformation/Guidances/ucm127004.htm>.

<sup>9</sup> FDA recognizes that for transfer of oversight to an IRB at the same institution, a written agreement may not be necessary as the process may be addressed by the institution's established procedures (assuming all appropriate steps described in Section III are covered).

<sup>10</sup> In general, some IRBs may have a policy not to transfer or accept a study until a final transfer contract or similar agreement is signed by both the original and receiving IRBs.

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- (7) Notifying the key parties; and
- (8) Updating IRB registration information.

### **(1) Identifying those studies for which IRB oversight is being transferred.**

One of the first steps in the transfer process is determining for which studies IRB oversight is being transferred. FDA recommends that the original and receiving IRBs have a clear understanding of this as it will help to bring certainty and continuity to the process and allow for effective planning, particularly when a large number of studies is being transferred. The number of studies, the risk posed by them, and the circumstances leading to the transfer, as discussed below, will influence subsequent steps in the transfer process (e.g., whether records are obtained from the original IRB or the clinical investigator/sponsor, how the transfer date is established, and whether the receiving IRB decides to conduct a review before accepting responsibility for the research).

### **(2) Ensuring the availability and retention of pertinent records.**

Before the receiving IRB accepts oversight of the transferred clinical investigation, it should obtain copies of pertinent records to allow it to meet its review and ongoing oversight responsibilities for the study once transferred.<sup>11</sup> Pertinent records include documents such as the research protocol and significant amendments; approved consent form; investigator's brochure; minutes of IRB meetings at which the research was reviewed; reports of unanticipated problems involving risk to human subjects and others; reports of IRB-conducted audits, if any; and correspondence with the investigator, sponsor, and/or FDA.

#### **(a) Availability of pertinent records.**

With concurrence of the sponsor, the original IRB should make pertinent records available to the receiving IRB.<sup>12</sup> This can be accomplished by providing the receiving IRB with paper or electronic copies of the pertinent records.<sup>13</sup> It is important to note that the sponsor's concurrence is necessary because the records may contain confidential commercial information. Alternatively, the receiving IRB may decide to obtain the records directly from the clinical investigator and/or sponsor. If records are obtained in this manner, the receiving IRB should also obtain meeting minutes from the original IRB as this information may be critical to the receiving IRB's assessment of the adequacy of the previous review (e.g., discussion of controverted issues, quorum, etc). The receiving IRB may choose to obtain records directly from the clinical investigator and/or sponsor,

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<sup>11</sup> Obtaining pertinent records about studies in advance of oversight transfer should help receiving IRBs meet their procedural and review obligations for the studies once transfer is complete. For example, under 21 CFR 56.108(a) and (b), IRBs must follow written procedures for certain review activities; these written procedures may be an important resource for determining the records that should be transferred.

<sup>12</sup> In some cases, sponsors may not agree to the transfer of records to a proposed IRB. In such cases, the sponsor and/or investigator should work expeditiously to arrange for oversight by another IRB.

<sup>13</sup> For more information on creating, maintaining, and archiving electronic records for regulatory purposes, see FDA's guidance, "Computerized Systems Used in Clinical Investigations," available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf>.

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for example, when a transfer occurs as a result of non-compliance actions of the original IRB.

Both the original IRB and the receiving IRB should maintain adequate records regarding the clinical investigations affected by the transfer.<sup>14</sup> Such records should include: any written agreement between the original and receiving IRBs; the title of the protocols being transferred; the expiration dates of IRB approval; the research sites affected; the names of the associated sponsors, clinical investigators, and CROs; the identities of the original IRB and the receiving IRB; and the date(s) on which the receiving IRB accepts responsibility for oversight of the clinical investigations. In addition, the original and receiving IRBs should keep adequate records of all communications to all affected sponsors, clinical investigators, and FDA, and comply with all other recordkeeping requirements.<sup>15</sup>

### **(b) Retention of IRB records.**

Under FDA regulations, IRB records related to the review of a clinical investigation must be retained for at least three (3) years after the completion of the research, and the records must be accessible for inspection and copying by FDA at reasonable times and in a reasonable manner.<sup>16</sup> Because FDA may require access to the records at any reasonable time, it is important for the agency to know whether the original IRB, the receiving IRB, the institution that housed the original IRB, a CRO or other responsible third party will maintain the records once clinical investigation oversight has been transferred. The party that assumes responsibility for the records is responsible for ensuring that they are retained in accordance with 21 CFR 56.115(b).

As a general matter, the original and receiving IRBs have the flexibility to work out any suitable arrangement for handling the transfer and maintenance of the records as long as the records remain accessible for inspection and copying by authorized representatives of FDA at reasonable times and in a reasonable manner. For example, the original IRB may decide to transfer to the receiving IRB the records related to the clinical investigations that are still active and retain the records for “closed” clinical investigations, or the receiving IRB may choose to receive all of the records.<sup>17</sup> When the original and receiving IRBs agree to share record retention responsibilities, FDA recommends that

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<sup>14</sup> Under some circumstances (e.g., if the original and transferring IRBs are located at the same institution), FDA recognizes that the records may be stored in a mutually accessible location. Duplication of the study records would not be necessary. If the files are mutually accessible, the IRBs should make appropriate arrangements for viewing and using the files.

<sup>15</sup> Under 21 CFR 56.115(a)(4), IRBs are required to keep copies of all correspondence between the IRB and the investigator(s).

<sup>16</sup> 21 CFR 56.115(b). IRBs may have their own record-keeping requirements that supplement FDA’s requirements.

<sup>17</sup> If storage space is a concern, the receiving IRB could, for example, scan the records as certified copies of the originals so that they can be stored electronically, as long as the records remain accessible for inspection and copying by FDA. For additional information, see FDA’s guidance, “Computerized Systems Used in Clinical Investigations,” available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf>.

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they reach a clear understanding of their respective roles to avoid confusion and to ensure appropriate responsibility for and access to the documents.

There may be circumstances when the original IRB reaches an agreement with the receiving IRB to retain some of the documentation for the transferred trials, yet may not be able to commit to retaining the documents for at least 3 years after the completion of the research. For instance, if an IRB ceases operations but retains responsibility for some records for trials that are still ongoing, either by physically maintaining these records or by reaching a storage arrangement with a responsible third party. In this instance, we recommend that the original IRB contact FDA to discuss possible retention arrangements.<sup>18</sup> In this situation, the original IRB should make arrangements to transfer the documents to the receiving IRB or to another, responsible party.

#### **(3) Establishing an effective date for transfer of oversight, including records, for the clinical investigation(s).**

FDA recommends establishing a transfer date for each clinical investigation, including records, for which oversight is being transferred. Although there is no regulatory requirement to establish a transfer date, such an action promotes continuity, helps prevent a lapse in IRB coverage, and minimizes confusion regarding which IRB is responsible for review and action if an unanticipated problem should arise or if the clinical investigation needs to be quickly suspended or terminated. When choosing a transfer date, the affected IRBs should allow enough time for all appropriate actions, communications, and agreements to occur.

Depending on the circumstances of the transfer, the transfer date may be established using one of a variety of methods, such as the following:

- In the written agreement, the exact date is specified in advance between the original IRB and the receiving IRB; or
- In the written agreement, the date is made contingent upon the review and acceptance of the clinical investigation by the receiving IRB. For example, if the receiving IRB decides to perform an initial review of the clinical investigation, the transfer may take effect on the date the receiving IRB makes its decision to approve, require modification in (to secure approval), or disapprove the clinical investigation. In this situation, the receiving IRB should notify the original IRB and other involved parties of the date of its approval and acceptance of oversight responsibilities.

Note that if both the original and receiving IRBs are located within the same institution, the transfer date may be determined according to the established procedures of that institution.

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<sup>18</sup> Factors to consider in selecting an appropriate record retention arrangement may include the reasons for the transfer, as well as the nature of the clinical investigations and the records. Generally speaking, and depending on the specific facts, FDA would expect an IRB that has accepted record keeping responsibilities to retain the documentation for at least 3 years after closure of the IRB, in accordance with 21 CFR 56.115(b), or transfer the records to the receiving IRB.

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When a large number of clinical investigations are being transferred, it may be preferable to phase-in the transfer over a period of weeks or months to facilitate a smooth transition.

If oversight is being transferred because of the closure of an IRB, the original IRB is expected to inform all clinical investigators and/or sponsors, as appropriate, of the pending closure date. If oversight by a new IRB cannot be obtained by the closure date, approval for the research would be considered suspended or terminated with no further subject enrollment.<sup>19, 20, 21</sup> The original IRB must follow its written procedures for ensuring prompt reporting to its institutional officials and FDA of the suspension or termination, as required under 21 CFR 56.108(b)(3).<sup>22</sup> In addition, sponsors of device studies must report to FDA and all reviewing IRBs and participating investigators any instances of IRB withdrawal of approval of an investigation or a part of an investigation within 5 working days after receipt of the withdrawal of approval.<sup>23</sup> Sponsors of drug/biologic studies must report to FDA the discontinuance of a clinical investigation.<sup>24</sup>

### **(4) Conducting a review by the receiving IRB, where appropriate, before it accepts responsibility for the study(ies).**

Because the regulations do not address transfer of IRB oversight, it is left to the receiving IRB to decide whether to conduct a review of the clinical investigation prior to the next continuing review date established by the original IRB.<sup>25</sup> In practice, however, IRBs often choose to perform some type of review before accepting responsibility for a study, as part of their own due diligence efforts.

A number of options are available to the receiving IRB, depending on the circumstances. The receiving IRB may decide to:

- **Undertake an *initial* review**, either by the convened IRB or under an expedited review procedure,<sup>26</sup> if appropriate. Review by the receiving IRB is strongly recommended where the quality of the review by the original IRB may be questionable, for example, where the transfer occurs because of noncompliance by the original IRB, as reflected in an FDA Warning Letter to that IRB. In addition, the receiving IRB should also consider conducting an initial review for higher risk studies, such as those involving an exception

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<sup>19</sup> See 21 CFR 56.103.

<sup>20</sup> See 21 CFR 312.60, 21 CFR 312.66, 21 CFR 812.40, 21 CFR 812.42 and 21 CFR 812.64.

<sup>21</sup> When IRB approval of a clinical investigation is suspended or terminated, IRBs should establish procedures to ensure that the rights and welfare of currently enrolled subjects are protected, subjects are not put at risk, and subjects receive appropriate care during any period in which the IRB and clinical investigator are attempting to resolve any remaining issues. For more information regarding suspensions or terminations of IRB approval, you may refer to FDA's guidance, "IRB Continuing Review after Clinical Investigation Approval," available at: <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf>.

<sup>22</sup> See "IRB Continuing Review after Clinical Investigation Approval," available at: <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf>.

<sup>23</sup> 21 CFR 812.150(b)(2).

<sup>24</sup> 21 CFR 312.31(a)(2).

<sup>25</sup> In other contexts, FDA recognizes that one IRB may rely on the review of another qualified IRB to avoid duplication of effort. See 21 CFR 56.114 (Cooperative research).

<sup>26</sup> For categories of research that are eligible for review through an expedited review procedure, see: <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm119074.htm>.

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from the informed consent requirements under 21 CFR 50.24, unapproved therapies with a high risk of morbidity and/or mortality, novel therapies including new cellular or gene therapies, and those flagged by the original IRB for more frequent review. The receiving IRB may also decide to conduct an initial review if, for example, the IRB believes that there may be local issues that would warrant its review. Initial review should also be considered where the receiving IRB has no familiarity with the original IRB, such that it may not be comfortable wholly relying on the original IRB's review and approval. The IRB should consider whether to conduct an initial review of device studies to make an independent determination of significant or non-significant device risk, particularly when the transfer occurs because of noncompliance by the original IRB.<sup>27</sup>

- **Undertake a *continuing review at the time of transfer***, either by the convened IRB or under an expedited review procedure, if appropriate. Continuing review may be appropriate when the receiving IRB already has responsibility for a site in a multi-site study (i.e., is familiar with the study because the receiving IRB has already reviewed and approved the study protocol).
- **Not undertake a review until the next continuing review date.** This option may be most appropriate for transfers due to logistical, administrative, or economic reasons. In practice, however, IRBs often choose to perform some sort of informal assessment to ensure that the records appear to be in order and to help prepare for the continuing review when it comes due. Because a request for IRB approval of a protocol or informed consent change may occur even before the continuing review date, it is important to note that receiving IRBs must perform either an initial or continuing review before approving substantive changes to the research or the informed consent document to ensure that they are sufficiently familiar with the study.<sup>28</sup>

FDA regulations at 21 CFR part 56 make no provision for a grace period extending the conduct of research beyond the expiration date of IRB approval. When the receiving IRB's review of the transferred research does not occur prior to the end of the approval period specified by the original IRB, IRB approval expires automatically and all research activities involving human subjects must stop. Enrollment of new subjects cannot occur after the expiration of IRB approval.<sup>29, 30</sup> Overall, FDA expects that lapses of IRB approval will be a rare occurrence.

FDA reminds receiving IRBs that they also have the authority to suspend or terminate approval of research in circumstances where the clinical investigation is not being conducted in accordance with the receiving IRB's requirements or has been associated with unexpected serious harm to subjects.<sup>31</sup> The receiving IRB must promptly report any suspension or termination of IRB approval, including the reasons for the action, to the clinical investigator,

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<sup>27</sup> 21 CFR 812.66.

<sup>28</sup> See 21 CFR 56.103(a), 21 CFR 56.108(a)(4), and 21 CFR 56.110(b)(2). There is an exception to this general requirement: changes necessary to eliminate apparent immediate hazards to human subjects may be initiated without IRB review and approval, as described in 21 CFR 56.108(a)(4).

<sup>29</sup> See, e.g., 21 CFR 56.103(a).

<sup>30</sup> For information regarding lapses in IRB approval and temporary continuing participation of already enrolled subjects, see FDA's guidance, "IRB Continuing Review after Clinical Investigation Approval," available at: <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf>.

<sup>31</sup> 21 CFR 56.113.

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appropriate institutional officials, and FDA.<sup>32, 33</sup> FDA recommends that sponsors also be informed of any suspension or termination and the reasons for such action.<sup>34</sup> Informing sponsors of an IRB suspension or termination of the study allows sponsors the opportunity to address the IRB's concerns so that disruptions of the study can be minimized and any human subject protection issues can be addressed.

Sponsors must also report such information to FDA. Sponsors of drug/biologic studies are required under 21 CFR 312.31(a)(2) to report to FDA any information regarding the discontinuation of a clinical investigation in an information amendment to the Investigational New Drug (IND) application. Sponsors of device studies are required under 21 CFR 812.150(b)(2) to notify FDA and all reviewing IRBs and participating investigators of any withdrawal of IRB approval of an investigation or a part of an investigation within 5 working days after receipt of the withdrawal.

### **(5) Confirming or establishing the date for the next continuing review.**

If the receiving IRB performs a review at the time of clinical investigation transfer (whether an initial or a continuing review), it may choose to maintain the anniversary date of approval established by the original IRB or decide to establish a new anniversary date. If the receiving IRB decides to establish a new anniversary date, the new date must be within one year of the receiving IRB's review.

If the receiving IRB does not conduct a review of the clinical investigation at the time of transfer, the date of clinical investigation approval by the original IRB is presumed to remain in effect for the full approval period established at the time of the most recent review by the original IRB. For example, if the original IRB initially approved the clinical investigation for one year effective July 1, 2011, and the clinical investigation is transferred to a new IRB effective October 1, 2011, the expiration date of IRB approval would continue to be July 1, 2012, unless or until the receiving IRB establishes a new expiration date. Note that review in accordance with a newly established expiration date would nonetheless need to be conducted prior to the original July 1, 2012 expiration date.

### **(6) Determining whether the consent form needs to be revised.**

The informed consent document is required to contain “[a]n explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject.”<sup>35</sup> Therefore, when a change in IRB oversight results in changes in the contact information regarding subject rights and/or whom to contact in the event of research-related injury, the new contact information must be provided

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<sup>32</sup> Ibid.

<sup>33</sup> For further information about reporting of suspensions or terminations of IRB approval, refer to FDA's guidance on “IRB Continuing Review after Clinical Investigation Approval,” available at: <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf>.

<sup>34</sup> We note that, the device regulations place this responsibility on investigators. However, IRBs may nonetheless also choose to inform sponsors of a termination or suspension and the reasons for doing so. 21 CFR 812.150(a)(2).

<sup>35</sup> 21 CFR 50.25(a)(7).

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to subjects. For subjects who are already enrolled (whether or not they are active), this may be accomplished in a number of ways, including sending a letter providing the relevant contact information.<sup>36</sup> For new subjects, the informed consent, assent, and/or parental permission form must be revised to reflect the new contact information.<sup>37</sup> The clinical investigator should promptly notify the IRB of any such administrative changes to the consent form.

Other changes to the consent form may also be necessary, for example, if the receiving IRB requires modifications to the consent form at the site(s) under its jurisdiction as a condition of approval (e.g., changes in template language, changes in risks, etc.).<sup>38</sup> Depending upon the types of changes needed, they may be conveyed to the clinical investigator and sponsor as required modifications to secure IRB approval for the clinical investigation at that site or sites and may require reporting to FDA.<sup>39</sup>

### **(7) Notifying the key parties.**

As discussed above, all key parties involved in the transfer of oversight (e.g., clinical investigator, sponsor, and original and receiving IRBs) should discuss their respective responsibilities before implementing the transfer. In addition, the sponsor should notify pertinent entities involved in the clinical investigation (e.g., institutional members, Data Safety Monitoring Board, CRO), as and when appropriate. After IRB transfer of oversight for the clinical investigation is complete, the sponsor must update the associated IND<sup>40</sup> or IDE<sup>41</sup> with the name and contact information of the receiving IRB and should include the effective date of transfer.

For studies for which the original IRB acts as a central IRB, those local institutions/IRBs that have written agreements with the original IRB (to transfer review responsibility to that original IRB) should be notified that responsibility for the study is now being transferred to a new central IRB (receiving IRB). We recommend that those local institutions/IRBs be given the option to enter into new written agreements with the receiving IRB or opt out of the central review arrangement if they do not believe central review by the receiving IRB is appropriate for their local institution (e.g., are concerned about the ability of the receiving IRB to adequately address local issues).<sup>42</sup>

Additionally, when an IRB declines to accept oversight of a clinical investigation, FDA recommends that the IRB notify the appropriate party(ies) who initiated the transfer process (refer to page 3 for further information; parties responsible for initiating the transfer may not be those responsible for securing IRB review) to enable the clinical investigator and/or sponsor to make alternate arrangements for IRB review.

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<sup>36</sup> FDA does not require subjects who are already enrolled (whether or not they are active) to be re-consented for such minor changes; however, IRBs may choose to do so.

<sup>37</sup> 21 CFR 50.25(a)(7).

<sup>38</sup> 21 CFR 56.109(a) and (b).

<sup>39</sup> See, e.g., 21 CFR 56.109(a), 21 CFR 312.31, and 21 CFR 812.35.

<sup>40</sup> 21 CFR 312.31(a).

<sup>41</sup> 21 CFR 812.35(a)(4).

<sup>42</sup> For more information on the responsibilities of central IRBs and local institutions/IRBs with respect to central IRB review, see “Using a Centralized IRB Review Process in Multicenter Clinical Trials,” available at: <http://www.fda.gov/RegulatoryInformation/Guidances/ucm127004.htm>.

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### **(8) Updating IRB registration information.**

The IRB registration rule at 21 CFR 56.106(e) requires that any IRB that decides to review FDA-regulated research involving new types of FDA-regulated products, or decides to discontinue reviewing FDA-regulated research, must revise its registration within 30 days of the change in product type review or permanent cessation of the IRB's review of research. A receiving IRB may therefore need to revise its registration if it previously did not review clinical investigations of FDA-regulated products or if it will assume the review for a new type of FDA-regulated product upon the acceptance of clinical investigations from an original IRB (e.g., the receiving IRB will now review clinical investigations of medical devices, whereas the IRB previously reviewed only clinical investigations of drugs). Similarly, the original IRB may need to update its registration information if it will no longer be reviewing a certain type of FDA-regulated product, will no longer be reviewing FDA-regulated research, or plans to disband. IRBs must revise their registration within 30 days of any such changes and may do so electronically through <http://ohrp.cit.nih.gov/efile>.<sup>43</sup>

## **IV. SPECIAL SITUATIONS**

### **A. Transfer of IRB Oversight from one IRB to Another IRB within the Same Institution and Temporary Transfer of IRB Review Responsibility**

Transfer of oversight may occur from one IRB to another IRB that operates within the same institution for logistical, administrative, and/or budgeting reasons (e.g., consolidating IRB workload). Transfer of oversight might also occur temporarily when a natural disaster or other disruptive event briefly suspends the functioning of the original IRB; in this case, the transfer is only temporary because responsibility for IRB review will eventually revert back to the original IRB.

When the transfer occurs within the same institution (e.g., for logistical, budgeting or administrative reasons), the transfer process is generally expected to be simpler and more expeditious than the transfers described above in Section III as not all eight steps may be applicable. For example, when oversight is transferred to another IRB at the same institution, the receiving IRB may decide not to conduct an initial or continuing review prior to the next continuing review date established by the original IRB, as such review may not be expected to substantively add to human subject protection. The guidance provided in Section III for institution-to-institution transfers may be useful for within-institution transfers.

When a temporary transfer of IRB oversight occurs (e.g., due to a natural disaster) whether within the same institution or to a different institution, the guidance provided in Section III should be useful, but again, not all eight steps may apply. The appropriate steps to effectuate oversight transfer will depend on the specific circumstances, including

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<sup>43</sup> IRBs that lack the ability to access the electronic registration system may send revisions, in writing, to the Office of Good Clinical Practice, Office of Special Medical Programs, Food and Drug Administration, 10903 New Hampshire Avenue, WO32-5103, Silver Spring, MD 20993-002.

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the reasons for the transfer and the risk posed by the study. In the case of a natural disaster, although the transfer may initially be thought to only be required for a short period of time, additional time may ultimately be needed before the original IRB is able to resume its oversight responsibilities. The original and receiving IRBs would need to ensure that study oversight does not lapse; adverse events are reported to the appropriate IRB, etc. during this interim period.

### **B. Transfer of a Clinical Investigation to a New Research Site Requiring IRB Review**

A sponsor may decide to transfer a clinical investigation to a different research site when, for instance, a clinical investigator relocates to that new site. Because the transfer involves changes to the research (i.e., conducting the research in a new location, consent form revisions, possible changes in key staff, etc.), the sponsor or investigator must submit these changes to the receiving IRB for review and approval, prior to implementing the changes.<sup>44</sup> In many cases, these changes represent a “minor change” to the research, which the IRB may review under an expedited review procedure.<sup>45</sup>

Such a move to a new research site may or may not entail changing the IRB. If the reviewing IRB changes as a result, then the considerations described in Section III apply, except initial or continuing IRB review must be conducted (an IRB may not approve a change in research without first conducting an initial or continuing review).<sup>46</sup>

FDA notes that, even if the IRB remains the same when a study is transferred to a new research site, IRB review/approval for the new research site is required because such a move is considered a change in previously approved research.<sup>47</sup> Additionally, the sponsor must notify FDA of any change in research site, clinical investigator, and/or IRB. For drug or biologics studies, this notification can generally be accomplished through an IND protocol or information amendment, whereas for device studies it can generally be accomplished in an IDE annual report.<sup>48</sup>

## **V. ADDITIONAL QUESTIONS ABOUT TRANSFERRING OVERSIGHT OF A CLINICAL INVESTIGATION**

Occasionally, during the course of its initial or continuing review of a transferred clinical investigation or at other times during oversight transfer, an original or receiving IRB may have

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<sup>44</sup> 21 CFR 56.108(a)(4). For drug/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).

<sup>45</sup> 21 CFR 56.110(b)(2).

<sup>46</sup> See 21 CFR 56.103(a), 21 CFR 56.108(a)(4), and 21 CFR 56.110(b)(2). There is an exception to this general requirement: changes necessary to eliminate apparent immediate hazards to human subjects may be initiated without IRB review and approval, as described in 21 CFR 56.108(a)(4).

<sup>47</sup> *Ibid.*

<sup>48</sup> See 21 CFR 312.30, 21 CFR 312.31, 21 CFR 812.35, and 21 CFR 812.150(b)(5). For a discussion of the types of changes in an IND study that require a new Form 1572, refer to Question 7 of FDA’s Guidance “Frequently Asked Questions -- Statement of Investigator (Form FDA 1572),” available at <http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm214282.pdf>

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questions that are not resolvable through communications with the sponsor or clinical investigator. In such situations, either IRB may contact FDA for additional guidance. Affected sponsors and clinical investigators may also contact FDA in these situations. Please use the following as an initial point of contact:

- Center for Biologics Evaluation and Research (CBER) - Bioresearch Monitoring Branch, Division of Inspections and Surveillance, Office of Compliance and Biologics Quality
  - Phone: (301) 827-6221
  - Email: [industry.biologics@fda.gov](mailto:industry.biologics@fda.gov)
- Center for Drug Evaluation and Research (CDER) - Office of Scientific Investigations, Office of Compliance
  - Phone: (301) 796-3150
  - Email: [cdersosi@fda.hhs.gov](mailto:cdersosi@fda.hhs.gov)
- Center for Devices and Radiological Health (CDRH) - Division of Bioresearch Monitoring, Office of Compliance
  - Phone: (301) 796-5490
  - Email: [bimo@cdrh.fda.gov](mailto:bimo@cdrh.fda.gov)

If you have specific questions about how to interpret this guidance, please contact FDA by phone at (301) 796-8340 or by e-mail at [gcp.questions@fda.hhs.gov](mailto:gcp.questions@fda.hhs.gov).