**From:** OC GCP Questions
**To:** [redacted]
**Subject:** RE: Question re: IRB oversight
**Date:** Thursday, December 18, 2014 9:39:00 AM

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Dear [Redacted]-

Thank you for your question. I am not able to provide you information about OHRP's position but if you would like to get OHRP's perspective, you must separately contact OHRP. You can contact OHRP at:

Toll-Free Telephone within the United States: (866) 447-4777
Telephone: (240) 453-6900
Fax: (240) 453-6909
E-mail: OHRP@hhs.gov

It is very important that you consult the appropriate institutional officials and IRB at your institution to determine if there are any institutional policies and procedures that must be followed.

Based on the limited information provided, I'm not able to give you a definitive response as there is a lot of information that would need to be considered in the scenario you describe. However, I will try to provide you with some points to consider. For purposes of providing points to consider, I will assume that the study in question is an FDA-regulated study, and I will use the drug regulations at 21 CFR 312 as the basis for these considerations.

It is not clear from your question whether or not the study you refer to is an FDA-regulated clinical investigation, and if so, whether it involves a drug, biologic, device, or other FDA-regulated product. You may consider consulting the sponsor of the study and any appropriate institutional officials and IRB at your institution to make a determination as to whether or not the "clinical protocol" you refer to is a clinical investigation that is subject to FDA regulations, and if so, which FDA regulations.

You may also consider discussing with the sponsor of the study whether, based on the proposed study activities of your researcher in this study, the sponsor considers your researcher to be an investigator or a subinvestigator on the proposed study. FDA has guidance for Industry titled, "Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects" that can be found at http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm187772.pdf. Section IIIA3 (What is Adequate Supervision of the Conduct of an Ongoing Clinical Trial?) of this guidance says:

For each study site, there should be a distinct individual identified as an investigator who has supervisory responsibility for the site. Where there is a subinvestigator at a site, that individual should report directly to the investigator for the site (i.e., the investigator should have clear responsibility for evaluating the subinvestigator's performance and the authority to terminate the subinvestigator's involvement with the study) and the subinvestigator should not be delegated the primary supervisory responsibility for the site.

FDA's IND regulations at 21 CFR 312.3(a) define an investigator:

Investigator means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team.

While there is not a separate definition in these regulations for subinvestigator, the ICH GCP E6 Good Clinical Practice: Consolidated Guidance, (which is recognized as official FDA guidance – see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf) provides a definition for both investigator and subinvestigator as follows:

1.34 Investigator: A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator. See also Subinvestigator.

1.56 Subinvestigator: Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). See also Investigator.

The Statement of Investigator, Form FDA 1572 (1572), is an agreement signed by the investigator to provide certain information to the sponsor and assure that the investigator will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic. Whenever a sponsor selects a new investigator to participate in a clinical investigation that is being conducted under an IND, the sponsor must obtain a completed and signed 1572 before permitting the investigator to begin participation in the clinical investigation (21 CFR 312.53(c)).

Box #3 of the 1572 requires the name and address of any medical school, hospital, or other research facility where the clinical investigation(s) will be conducted. FDA has Information Sheet Guidance for Sponsors, Clinical Investigators and IRBs titled, "Frequently Asked Questions – Statement of Investigator (Form FDA 1572)" that can be found at http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm214282.pdf. Section IV of this guidance document includes information about what address(es) should be entered into box #3 on the 1572 - question 26 states:

26. What qualifies as a research facility for Section #3?

Section #3 is intended to identify facilities where study activities will be conducted and clinical data will be generated or collected. This includes facilities where subjects will be seen and study procedures performed. For example, this might include locations such as health care facilities where the test article will be administered, or where physical exams will be performed. Facilities where other important clinical investigation functions are performed may also be identified in Section #3. For example, a research laboratory where the test article is prepared, a special storage facility where the test article will be kept, or a location where tissue specimens are collected should be listed in this section.

Does the sponsor of the study consider University A to be a facility where other important clinical investigation functions are performed (e.g., data analysis)? Since the 1572 is a sponsor document, I suggest you discuss with the sponsor of the study and the appropriate institutional officials and IRB at your institution whether, based on the study activities to be performed by your researcher at University A, he/she should be considered an investigator or subinvestigator on this study. The answer to that question may also inform you about whether University A should be considered a site to be included in box #3 of the 1572. The sponsor you are working with should contact their assigned IND project manager at FDA to request additional assistance if needed.

In accordance with the regulations at 21 CFR 312.66, an investigator must ensure IRB oversight of the proposed clinical study. The FDA regulations at 21 CFR 56.114 (cooperative research) allow institutions involved in multi-institutional studies to use joint review, reliance on the review of another qualified IRB, or similar arrangements to avoid duplication of effort. It is not clear if there is a single IRB of record for this study, whether or not that single IRB will extend its oversight to cover study activities being conducted at University A, University B and University C, or whether or not the local IRB(s) currently permit oversight from an IRB located outside their institution. This type of information should also be considered when assessing the study scenario you are presented with.

I hope this information is useful. If you need further information and/or have additional questions, please feel free to contact us at the official GCP mailbox, gcp.questions@fda.hhs.gov. You may also find it useful to access the set of redacted GCP e-mails found at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm since we find that many questions and concerns are repeated over time.

Best Regards,

Janet

Janet Donnelly, RAC, CIP
Policy Analyst, Office of Good Clinical Practice
Office of Special Medical Programs, Food and Drug Administration



-----Original Message-----
From: [Redacted]
Sent: Tuesday, December 16, 2014 12:41 PM
To: OC GCP Questions
Subject: Question re: IRB oversight

Hello!

Can you please tell me what the FDA/OHRP's position is regarding IRB oversight in the following scenario:

A researcher from University A decides to collaborate as a sub-investigator with Universities B and C on a clinical protocol. The protocol will be conducted at Universities B and C only. No research will be conducted at University A (no patients or employees will be subjects, no samples will be received - nothing).

The University A researcher's role is merely analysis of anonymized data. The final paper will reflect that this Sub-Investigator worked at University A.

My question is – what is the role of University A's IRB in this scenario. My feeling is that it is limited in that –yes, it is human subjects research but none of the human subjects fall under University A's purview. I think University A's IRB should be notified that an employee is conducting research – but that's it. However, I now hear from others that University A needs to be considered a "site" on the study and actually completely review the research or formally defer it to another IRB. I looked in the regulations and it was not clear. Can you help me with this question please.

Thanks (again) and Happy Holidays!