From: OC GCP Questions
To: [redacted]
Subject: RE: IRB Review Models
Date: Friday, January 16, 2015 3:37:00 PM

Dear [redacted] -

Thank you for your question I had the opportunity to discuss your question with some of my FDA colleagues and will outline some thoughts here in response

As you know, both sets of regulations (21 CFR 56 114 for FDA and 45 CFR 46 114 for HHS) permit institutions involved in multi-institutional studies to use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort I am only able to address the FDA regulations, but if you have questions about 45 CFR 46, you can always contact OHRP (see contact information at http://www hhs gov/ohrp/contact/index html) You indicate that your concerns might be more applicable to federally conducted or supported research so I suggest you contact OHRP with any specific concerns

The FDA regulations at 21 CFR 56 114 allows for cooperative research and provides flexibility in how IRBs meet the requirements for cooperative review FDA has a guidance document for Industry titled; "*Using a Centralized IRB Review Process in Multicenter Clinical Trials*" (see http://www fda gov/downloads/RegulatoryInformation/Guidances/ucm127013 pdf) This guidance is intended to assist sponsors, institutions, IRBs, and clinical investigators involved in multicenter clinical research in meeting the requirements of 21 CFR part 56 by facilitating the use of a centralized IRB review process (use of a single central IRB), especially in situations where centralized review could improve efficiency of IRB review The guidance (1) describes the roles of the participants in a centralized IRB review process, (2) offers guidance on how a centralized IRB review process might consider the concerns and attitudes of the various communities participating in a multicenter clinical trial, (3) makes recommendations about documenting agreements between a central IRB and the IRBs at institutions involved in the centralized IRB review process concerning the respective responsibilities of the central IRB and each institution's IRB, (4) recommends that IRBs have procedures for implementing a centralized review process, and (5) makes recommendations for a central IRB's documentation of its reviews of studies at clinical trial sites not affiliated with an IRB

You mentioned some concerns with some flexible model IRBs including not being able to tell from the minutes which alternate substituted for which member, and not being able to discern whether the alternate was an appropriate substitution You also mentioned some concerns about alternates attending meetings and their role when a member is present, or if a member leaves the room Your concerns should first be addressed with the appropriate institutional officials at [Redacted] Your institution may wish to inquire with the IRB in question about providing more information or clarification [Redacted] may have a mechanism in place to determine when studies can rely on an external IRB You may wish to look into what this mechanism is and whether there is a process for you to bring forth your concerns

As you know, FDA generally assesses IRB compliance through on-site inspections, so FDA is not able to determine whether any of the IRB models you briefly describe in your question are acceptable FDA developed its Bioresearch Monitoring (BIMO) Program to ensure the protection of the rights, welfare, and safety of human subjects and the quality and integrity of data submitted to the Agency Among other things, the FDA BIMO Program involves site visits to IRBs, clinical investigators, sponsors, monitors, contract research organizations, nonclinical (animal) laboratories, and bioequivalence analytical laboratories FDA has Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors titled; "*FDA Institutional Review Board Inspections*" (see http://www fda gov/downloads/RegulatoryInformation/Guidances/UCM126555 pdfU S DepartmentofHealthandHumanServicesFoodandDrugAdministrationJanuary2006InformationSheetGuidanceForIRBs) This guidance document addresses site visits to IRBs that review clinical investigations that are regulated by FDA under 21 USC 355(i) and 21 USC 360(j) and clinical investigations that support applications for research or marketing permits for products regulated by FDA FDA also has the Compliance Program Guidance Manual (CPGM) for BIMO inspections of IRBs (see http://www fda gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/ucm133768 pdf) CPGM 7348 809 was developed to provide uniform guidance and specific instructions for inspections of IRBs

I suggest you discuss your concerns internally with the appropriate institutional officials at [Redacted]

Just for reference, FDA has information on our web site for reporting complaints related to FDA-regulated clinical trials and you can find this information at the following web location: http://www fda gov/scienceresearch/specialtopics/runningclinicaltrials/complaintsrelatingtoclinicaltrials/default htm

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

This communication does not constitute a written advisory opinion under 21 CFR 10 85, but rather is an informal communication under 21 CFR 10 85(k) which represents the best judgment of the employee providing it This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed

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From [redacted]
Sent: Wednesday, January 14, 2015 9:35 AM
To: OC GCP Questions
Subject: RE: IRB Review Models

Also, the IRB SOPs rarely describe the IRB model It is not always clear who decides what alternates will be deployed and whether they are qualified to do so

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From [redacted]
Sent: Wednesday, January 14, 2015 9:21 AM
To: 'OC GCP Questions'
Subject: RE: IRB Review Models

Yes Thank you I am not speaking official for [Redacted] in any capacity other than my work I am seeking information The [Redacted] has about [Redacted] Medical Centers that use the IRBs operated by our Academic Affiliates – Medical and Dental Schools Most of them have adopted what they call "flexible IRB models" The models vary

One model is simply to have one or more IRB panels of Primary Members Alternates are "Pooled" and any MD can alternate for any MD Any allied health scientist can alternate for any allied health scientist Any nonscientist professional for another (Often the IRB staff vote, and any unaffiliated for another They are not identified on the IRB Registration by name It is very difficult for us to exercise oversight We often cannot tell from the minutes who alternated for whom and whether or not their experience is comparable

Another model has essentially the same structure, and alternates attend with the primary members, offering the benefit of their reviews if they have done them They participate in the IRB discussion, functioning essentially as consultants or ad hoc reviewers However, if the Primary member leaves the room, the alternate then votes in the Member s stead, essentially being both an ad hoc reviewer and a voting member in the same meeting Per FDA guidance, Ad Hoc consultants and consultants may present and respond to questions but not participate in deliberations or vote with the IRB

Some of them have "unchecked the box" on the FWA indicating that the OHRP oversight does not extend to their nonfederal research, but I think there is confusion about the federally conducted or supported research

Also there are new "Central" type IRBs, such as PCori CAPriCORN and StrokeNet, that want to implement these models I don t speak for [Redacted] but I can see [Redacted] being reluctant to become involved in these IRBs to the detriment of [Redacted] patients

Are these types of arrangements acceptable to FDA? We cannot tell our academic affiliates how to operate their IRBs We can only ask for a solution that we at [Redacted] feel is compliant with federal regulations and guidance

From: OC GCP Questions [mailto:gcp.questions@fda.hhs.gov]
Sent: Wednesday, January 14, 2015 9 02 AM
To: [redacted]
Subject: IRB Review Models

Dear [redacted] –

I am trying to get you to the right office at FDA. Can you explain to us what you mean by flexible IRB models and perhaps expand on your question?

Thank you, Doreen

Doreen M Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Tuesday, January 13, 2015 9:18 AM
To: OC GCP Questions
Subject: IRB Review Models

Who at FDA can I talk with about the flexible IRB models in use by academic affiliates? I work in the [Redacted] I am seeing these IRB models get increasingly complex rather than streamlined I think some of their practices, which may be ok if the research is not Federally conducted or supported, are noncompliant for federally conducted research Thanks

[redacted]