Corrective Actions and Investigator Sanctions to Remedy Non-Compliance

SACHRP

Subcommittee on Harmonization

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The Issue

- Problems occur in research that represent major deviations from approved protocols
- What are appropriate types of corrective actions and/or investigator sanctions?
- What are appropriate goals of corrective actions and/or sanctions?

Problems that Arise in Research

- Intentional non-compliance, such as forged signatures, falsification or fabrication of data, creation of fictitious subjects, failure to obtain consent or assent.
- Unintentional or accidental non-compliance, such as missed tests, dosing errors, missed visits, failure to pay subjects to whom compensation has been promised.

Problems that Arise in Research

- Unanticipated problems, such as unanticipated serious adverse events related to drugs, devices or procedures.
- Unanticipated problems such as lost laptops, lost data, etc..

Problems that Arise in Research

- Lots of overlap in the classification of unanticipated problem vs. serious or continuing non-compliance.
- Infinite variety of fact patterns.

Corrective Actions for Problems in Research

- Suspension or termination of research, by IRB or other parties, such as institutions and sponsors
- Re-consenting subjects
- Notifying subjects of non-compliance
- Training for investigators and staff
- Monitoring of ongoing activities

Corrective Actions for Problems in Research

- Restriction of funds or other resources
- Correction to publication, or retraction of publication
- Prohibition on use of data collected as part of protocol noncompliance
- Barring investigators from future submissions to IRB/suspensions of investigators

Corrective Actions for Problems in Research

- Required disclosures that data were collected unethically/outside protocol
- How far do prohibitions and requirements extend? To PI only or to all who participated in the noncompliance?
- What about other sites/investigators in a multi-site study?

Current OHRP Guidance

- When OHRP receives reports of serious and continuing noncompliance or unanticipated risks, OHRP routinely expects institutions to specify corrective action plans
- Current OHRP guidance documents are largely silent about the nature and extent of recommended sanctions and corrective actions
- OHRP guidance is similarly silent on any requirement of due process for investigators

Central IRBs/Independent IRBs

- Continued encouragement to increase use of these IRBs
- Yet these IRBs are independent of research institutions
- How can these IRBs require corrective actions or impose sanctions without clear basis in institutional authority?

Specific Questions

- What is the range of sanctions or corrective actions that IRBs and institutions should consider when faced with an investigator or research team that has seriously violated approved protocols or research regulations?
- Are there standards for when each such sanction or corrective action should be imposed?

Specific Questions

- How should sanctions or corrective actions be calibrated to the seriousness of protocol violations, or injuries or possible injuries to human subjects in an approved protocol?

Specific Questions

- Is it appropriate, if at all, for IRBs and/or institutions to require investigators to forego research use of data obtained outside of approved protocols or otherwise in violation of research regulations?
- Under what circumstances should such a sanction be imposed, if at all?

Specific Questions

- When an investigator has multiple active protocols, and there has been serious noncompliance in one or more, but not all, of those active protocols, how should sanctions be handled?
- Should serious noncompliance in one protocol lead to sanctions – such as suspension of privileges to conduct human subjects research – in all of that investigator's protocols?

Specific Questions

- How to determine sanctions on an investigator and corrective actions on a protocol when noncompliance was the result of actions of some, but not all, of the research team?
- For example, should failure of one investigator to gain informed consent prevent other members of the team who were compliant with the protocol from using data inappropriately obtained?

Specific Questions

- Other than the procedures set forth in 45 C.F.R. 46.109(d), are there basic requirements of due process for investigators before IRBs or institutions impose any sanction, including suspension or termination of research, or should this be defined by each IRB and its institution, consistent with other institutional policies?

Specific Questions

- When a central IRB has assumed responsibility for overseeing research at multiple institutions, how does that central IRB gain authority to impose sanctions other than suspension or termination of research?
- Should or must this authority be delegated to a central IRB in a “cede review” IRB authorization agreement?

Specific Questions

- When a central IRB (or any IRB) has assumed responsibility for overseeing research that is **not based at an institution** – such as research that occurs in private physician, psychologist, or psychotherapy practices – how does that IRB gain authority to impose these intermediate sanctions?
- Must this authority be included in an agreement entered into between an independent, non-institution-based investigator and an IRB?

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