CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE

Site Interviews

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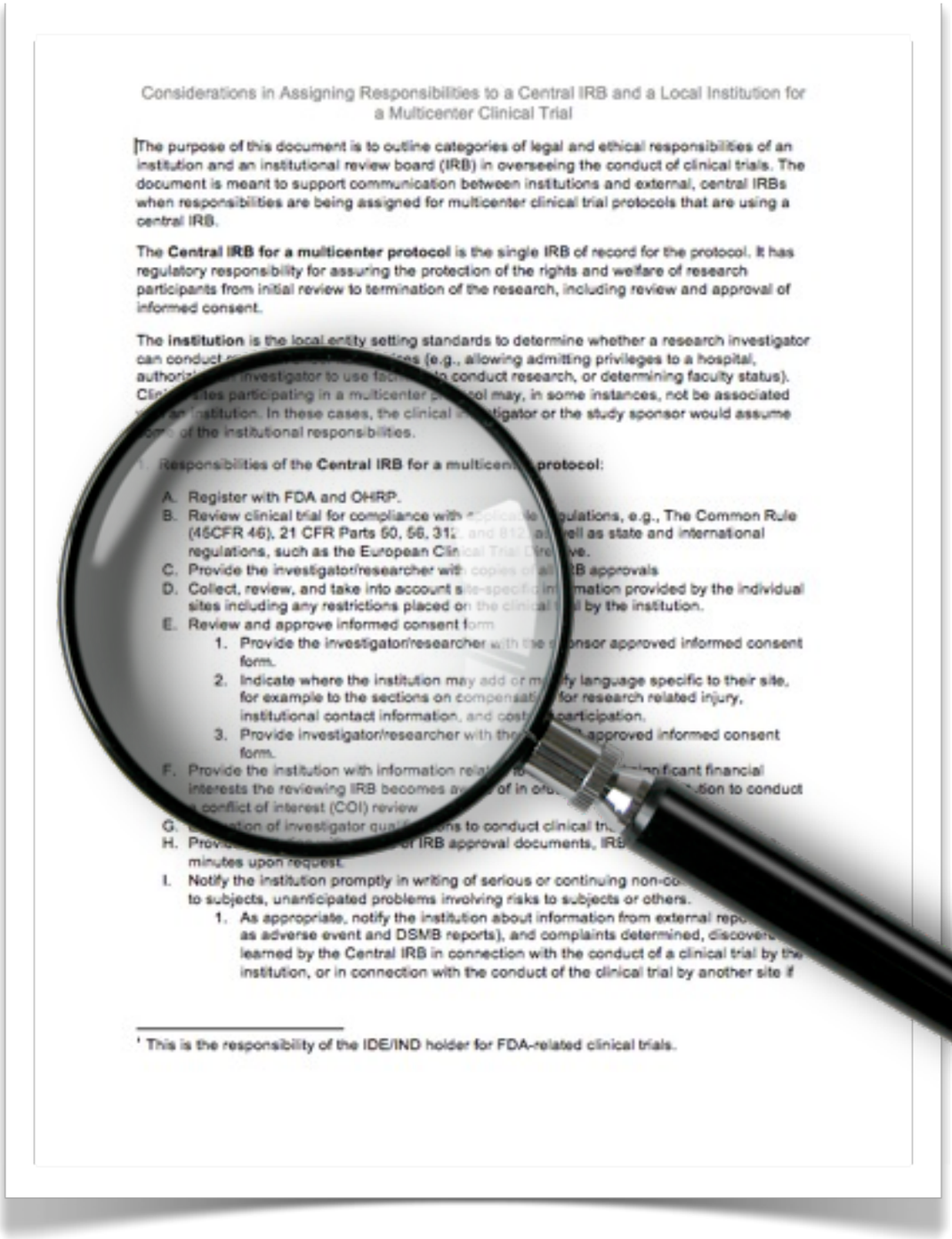
on behalf of CTTI Team

Considerations Document



Considerations in Assigning Responsibilities to a Central IRB and a Local Institution for a Multicenter Clinical Trial

The purpose of this document is to outline categories of legal and ethical responsibilities of an institution and an institutional review board (IRB) in overseeing the conduct of clinical trials. The document is meant to support communication between institutions and external, central IRBs when responsibilities are being assigned for multicenter clinical trial protocols that are using a central IRB.

The **Central IRB for a multicenter protocol** is the single IRB of record for the protocol. It has regulatory responsibility for assuring the protection of the rights and welfare of research participants from initial review to termination of the research, including review and approval of informed consent.

The **institution** is the local entity setting standards to determine whether a research investigator can conduct [illegible] (e.g., allowing admitting privileges to a hospital, authoriz[illegible] investigator to use fac[illegible] to conduct research, or determining faculty status). Clin[illegible]sites participating in a multicenter p[illegible]col may, in some instances, not be associated with an institution. In these cases, the clinical [illegible]tigator or the study sponsor would assume some of the institutional responsibilities.

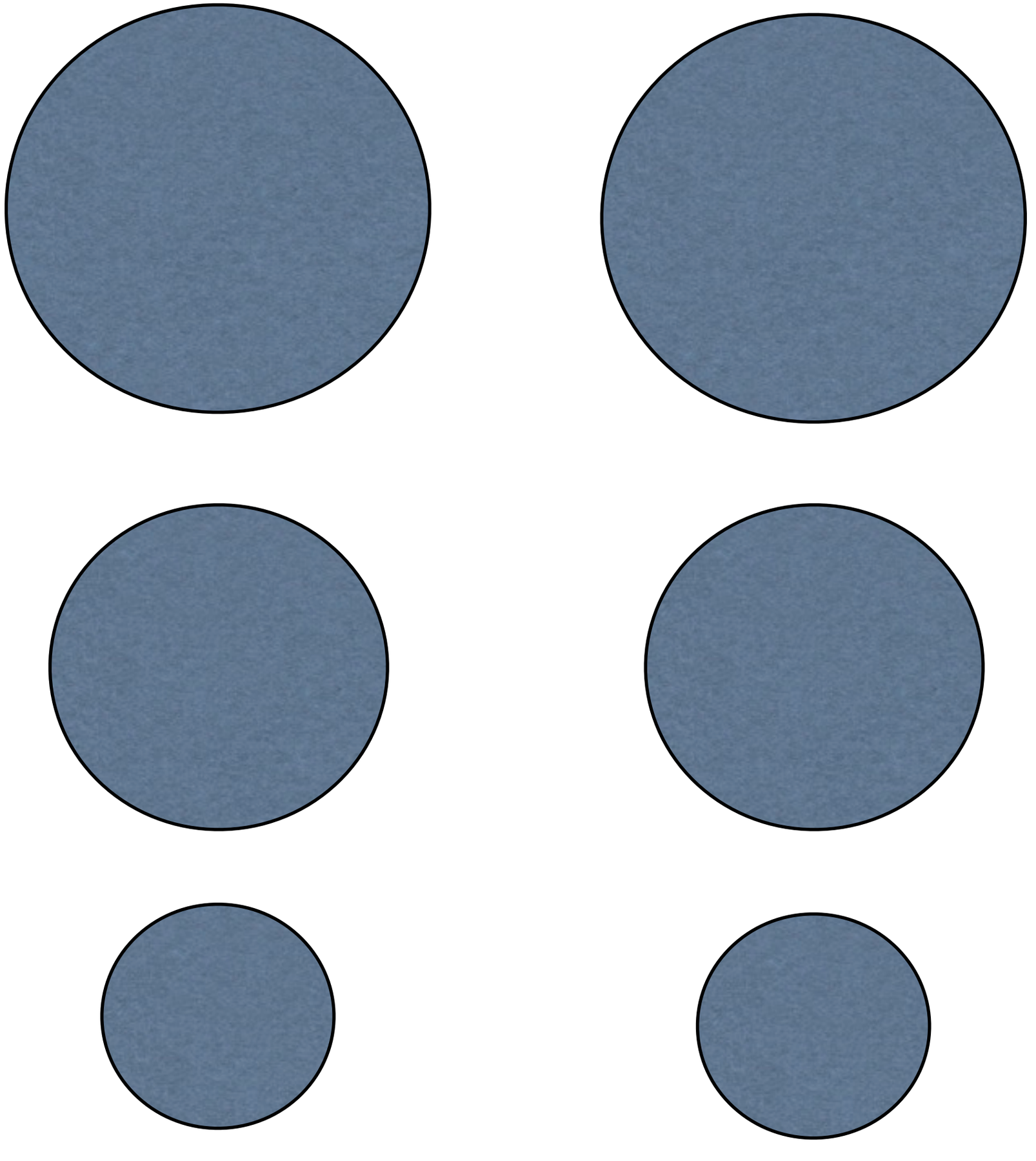
1. Responsibilities of the **Central IRB for a multicen[illegible] protocol**:
   A. Register with FDA and OHRP.
   B. Review clinical trial for compliance with [illegible]gulations, e.g., The Common Rule (45CFR 46), 21 CFR Parts 50, 56, 31[illegible] and 812 as well as state and international regulations, such as the European Clinical Trial Directive.
   C. Provide the investigator/researcher with copies of all IRB approvals
   D. Collect, review, and take into account site-specific information provided by the individual sites including any restrictions placed on the clinical trial by the institution.
   E. Review and approve informed consent form
      1. Provide the investigator/researcher with the sponsor approved informed consent form.
      2. Indicate where the institution may add or modify language specific to their site, for example to the sections on compensation for research related injury, institutional contact information, and costs of participation.
      3. Provide investigator/researcher with the [illegible] approved informed consent form.
   F. Provide the institution with information relating to [illegible]nificant financial interests the reviewing IRB becomes aware of in order [illegible]tion to conduct a conflict of interest (COI) review
   G. [illegible]tion of investigator qualifications to conduct clinical tr[illegible]
   H. Provide [illegible] IRB approval documents, IRB minutes upon request.
   I. Notify the institution promptly in writing of serious or continuing non-co[illegible] to subjects, unanticipated problems involving risks to subjects or others.
      1. As appropriate, notify the institution about information from external repo[illegible] as adverse event and DSMB reports), and complaints determined, discovered learned by the Central IRB in connection with the conduct of a clinical trial by the institution, or in connection with the conduct of the clinical trial by another site if

[1] This is the responsibility of the IDE/IND holder for FDA-related clinical trials.

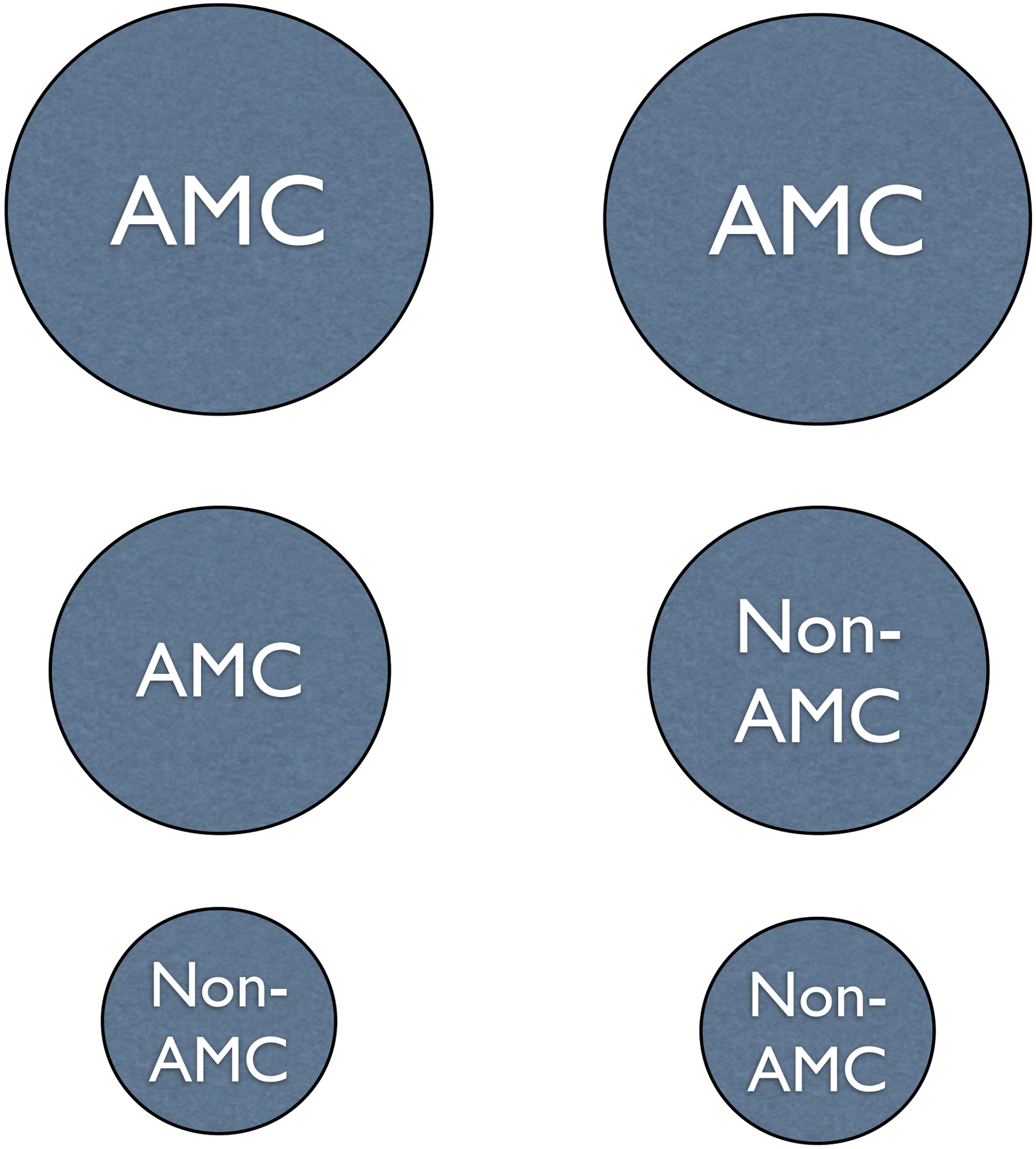
Delineates ethical/ regulatory responsibilities of IRB and local institution

Methods

The Sites



AMC = Academic Medical Center



participants

3

5

4

3

6

3

IRB Chair

IRB administrator/coordinator

Director of Human Research Protections

General Counsel

Corporate Responsibility

Research Integrity/Compliance officers

Institutional Official for Research (VP)

Interviews

General query first

Follow-up of specific barriers/issues

Review of Considerations Document

Findings

Meta-Themes

Enthusiastic support for project and Considerations Document

Comfort and *Trust*

Categories of Barriers

Legal & regulatory

Local context

Administrative & logistic

Financial

Conflicts of interest

Legal & Regulatory Barriers

Who will be held responsible in event of noncompliance?

Adherence to state regulations

Bear the risk without control

And one [concern] is the most common that I think I've heard from other institutions, as well, is our legal responsibility to the patients through our consent forms and through our contracts. And if we have not a lot of say in those contracts or in that information, we feel like we're taking the legal responsibility but without the ability to actually negotiate that on our own behalf.

IRB Chair

The oversight and main control, the ability to be the IRB of record and to make sure that they know exactly when to stop the studies, when something is happening within the studies . . . It's a control issue.

Senior Vice President of Research

Legal/Regulatory Solutions

Clarify responsibilities: Considerations Document

Clarification of OHRP policy to take action against IRB-of-record for noncompliance

Accreditation of central IRB

Plan for timely communication

By utilizing the central IRB, our IRB may be saying, "Hmm. Okay. Well, how long's it take for them to notify us of all of this? . . . Is this going to come in writing? How long is it going to take for us to get it? Is it going to be..." You know, just little small things.

Senior Vice President of Research

Local Context Barriers

Investigators / staff

Patient population

Appropriateness and consistency of compensation

There was an NIH sponsored study where they were going to try and prophylactically treat signs of fever. And this was with regard to the fly from the South which produces that fever. But the frequency of the side effect of the prophylactic medication was higher than the rate of that flu virus here in [state]. So [we] declined to participate in study.

IRB Chair

Local Context Solutions

Systematic plan for incorporating local concerns into central IRB review (need models)

Consent form with customizable section for state/local concerns

Local institution has authority to participate or not

Administrative/Logistic Barriers

Need to review/maintain records for auditing

Different paperwork & software for each external IRB

How to coordinate what should be done centrally vs locally?

Administrative/Logistic Solutions

Delineating site vs IRB responsibility: Considerations Document

Standardized forms and software

Need models here!

Financial Barriers

Lose overhead from industry-sponsored trials

Preserving IRB jobs

Financial Solutions

Institutional administration fee to replace IRB review fee

Conflicts of Interest Barriers

Concern about relationship between industry sponsor and independent IRB

Unease with sending sensitive COI info outside of institution

Institution may not want to communicate certain knowledge about investigators to an outside body

COI Solutions

Need reassurance about integrity of independent IRB

Need models for sharing COI information

Awesome

Understand how issues live within institution

Great examples

Move from barriers to needs, needs to solutions

Utility of *Considerations Document*