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Single-site review of Multi-site research: Institutional and Investigator perspectives

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Contemparary Issues in Human Subjects Protections
Institute of Medicine

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Ethical Considerations in Clinical Research

Barbara E. Bierer, MD

• **No Conflict of Interest :** The speaker has no significant financial relationships with industry to disclose relevant to the content of this lecture.

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Challenge Depends on Perspective

- Sponsor
- **PI**
- **Institution**
- Local IRB
- Research participant

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Mandate for coordinated, single IRB review

- Potentially improve the substantive IRB review
- End redundant, sometimes conflicting reviews and expectations
- End hours and hours of repetitive negotiations with individual IRBs
- Increase efficiency of study start-up
- Ease administrative burden

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Challenges to adoption of single-site review for multi-site research

- Many different stakeholders
  - Each may have own preferences, experience, biases
- Many different models of reliance
  - Independent IRBs
  - NCI Central IRB, NINDS Neuronext IRB
  - Many models of institutional reliance agreements
- Administrative confusion
- Administrative burden
- Institution knows their players best
- Fear of liability
- Trust

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Before Harvard Catalyst:

Separate institutions, legally and financially

Faculty not Harvard employees

Harvard School of Public Health

Harvard School of Dental Medicine

Harvard Medical School

Beth Israel Deaconess Medical Center

Brigham and Women's Hospital

Cambridge Health Alliance

Radcliff Institute for Advanced Study

Kennedy School

Harvard University Health Services

Children's Hospital

Dana Farber Cancer Institute

Harvard School of Engineering and Applied Sciences

Forsyth Institute

Harvard Law School

Harvard Graduate School of Education

Harvard Pilgrim HealthCare

Hebrew SeniorLife

Harvard Graduate School of Design

Immune Disease Institute

Joslin

Harvard Divinity School

Judge Baker Children's Center

Harvard Business School

Massachusetts Eye and Ear Infirmary

Harvard University

Massachusetts General Hospital

Broad Institute of MIT and Harvard

MIT

Boston College Connell School of Nursing

Veteran Affairs Boston Healthcare System

Spaulding Rehabilitation Hospital

Schepens Eye Research Institute

Mount Auburn Hospital

McLean Hospital

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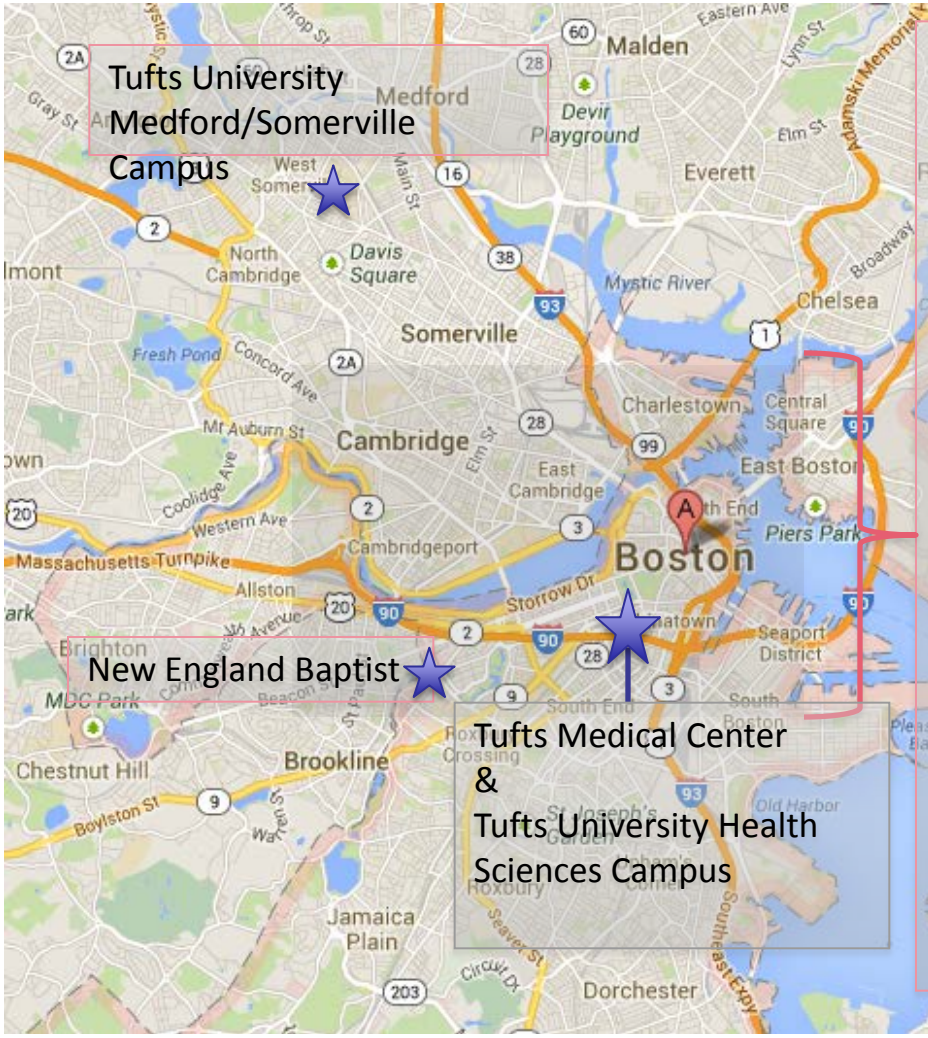
Harvard Catalyst Reliance Agreement is now the New England Reliance Agreement



Harvard Catalyst Institutions:

Beth Israel Deaconess Medical Center
Boston Children's Hospital
Brigham and Women's Hospital
Broad Institute
Cambridge Health Alliance
Dana-Farber Cancer Institute
Forsyth Institute
Harvard Medical School *
Harvard Pilgrim Health Care
Harvard School of Public Health
Harvard University (FAS) *
Hebrew SeniorLife
Joslin Diabetes Center
Judge Baker Children's Center
Massachusetts Eye & Ear
Massachusetts General Hospital
McLean Hospital
Mount Auburn Hospital
Schepens Eye Research Institute
Spaulding Rehabilitation Hospital

* The Harvard School of Dental Medicine (which comes under the auspices of the HMS IRB) and the University's non-medical professional schools (all of which receive regulatory coverage from the FAS IRB) are also participating in the agreement.

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Overview

The Harvard Catalyst Reliance Agreement

- A Master Common Agreement creating the framework for a "reviewing IRB" and a "relying IRB" to accept review on a case-by-case basis
- Request for reliance is made before submitting a full IRB application
- Eliminates duplicative IRB review
- Promotes collaborative research
- Reduces administrative burden and costs for IRBs and study teams
- Flexible and scalable

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IRB Reciprocity: Contractual Terms as a Contract layout

- Federal Wide Assurance
- Investigator Conflicts of Interest
- HIPAA
- Notice of Deadlines
- Policies
- Sponsored research agreements
- IRB Approval does not automatically activate a study
- Procedures for managing serious or continuing non-compliance
- Subject Injury and Unanticipated problems
- Research compliance
- Audits
- Record keeping
- Confidentiality

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Characteristics of the Harvard Catalyst Reliance Agreement

1. Electronic "CEDE REVIEW FORM" to allow investigators to request reliance
2. Agreement as to which IRB take the lead by determining primary employment of the principal (lead) investigator
3. HIPAA Flexibility
4. Common Subject Injury Language in informed consents
5. Reviewing IRB retains authority
6. Definition of IRB approval vs activation to ensure integration with contracting offices for agreements
7. Procedures for managing serious or continuing non-compliance
8. Common Policies and Procedures (e.g. COI, Education, Audit SOP, Security and Breach SOP)

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Serious or continuing non-compliance

- Agreed to notifications based on the timeline of discovery (ie. Discovery, Investigation, Suspension, Disapproval or Termination, Findings, etc.)
- Who would investigate what, and expectation of cooperation
- Findings and reporting
- Access to records and corrective actions
- Audits
- Record keeping
- Confidentiality

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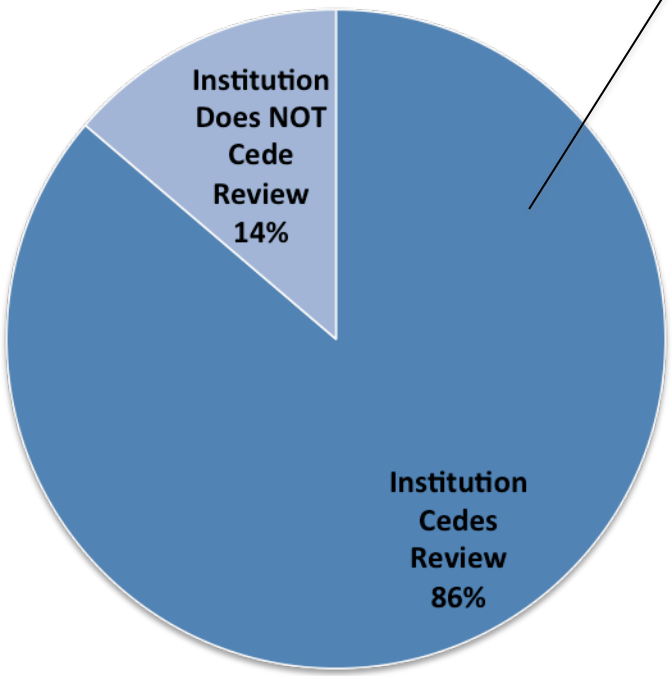
Reliance:

Institutions CEDE REVIEW ~90% of the time



From launch thru 2013, **86%** of **>1100** reviewed applications represent a **reduction in duplicative review**, with the reviewing IRB accepting review for at least 1 additional site

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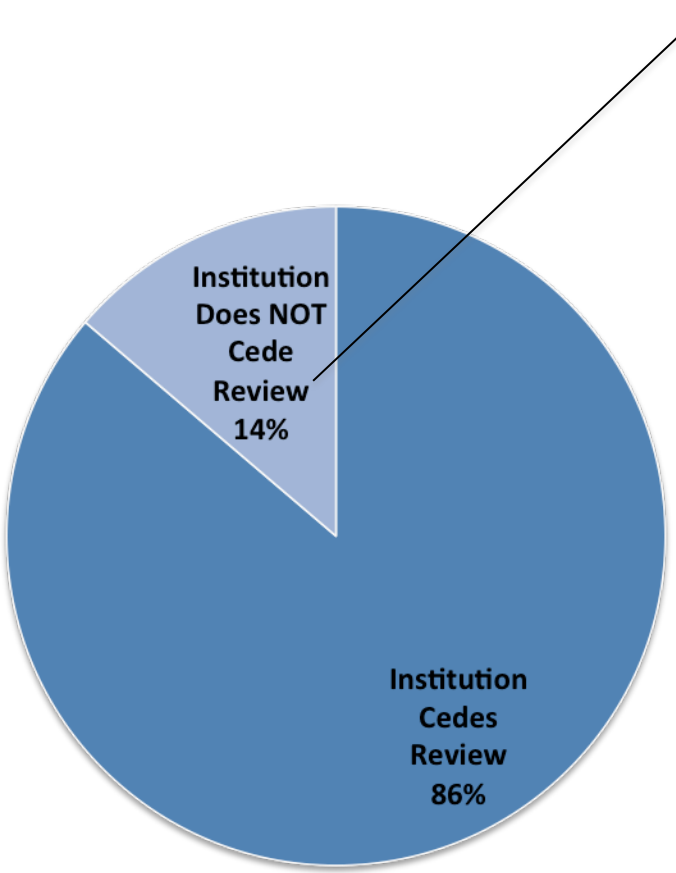
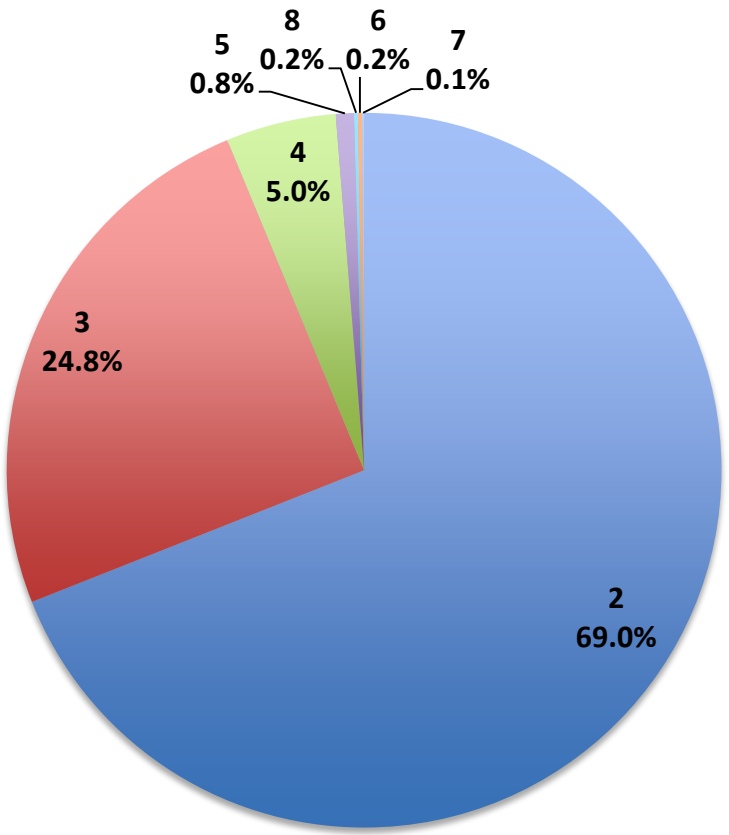


Why do institutions elect NOT to cede review?

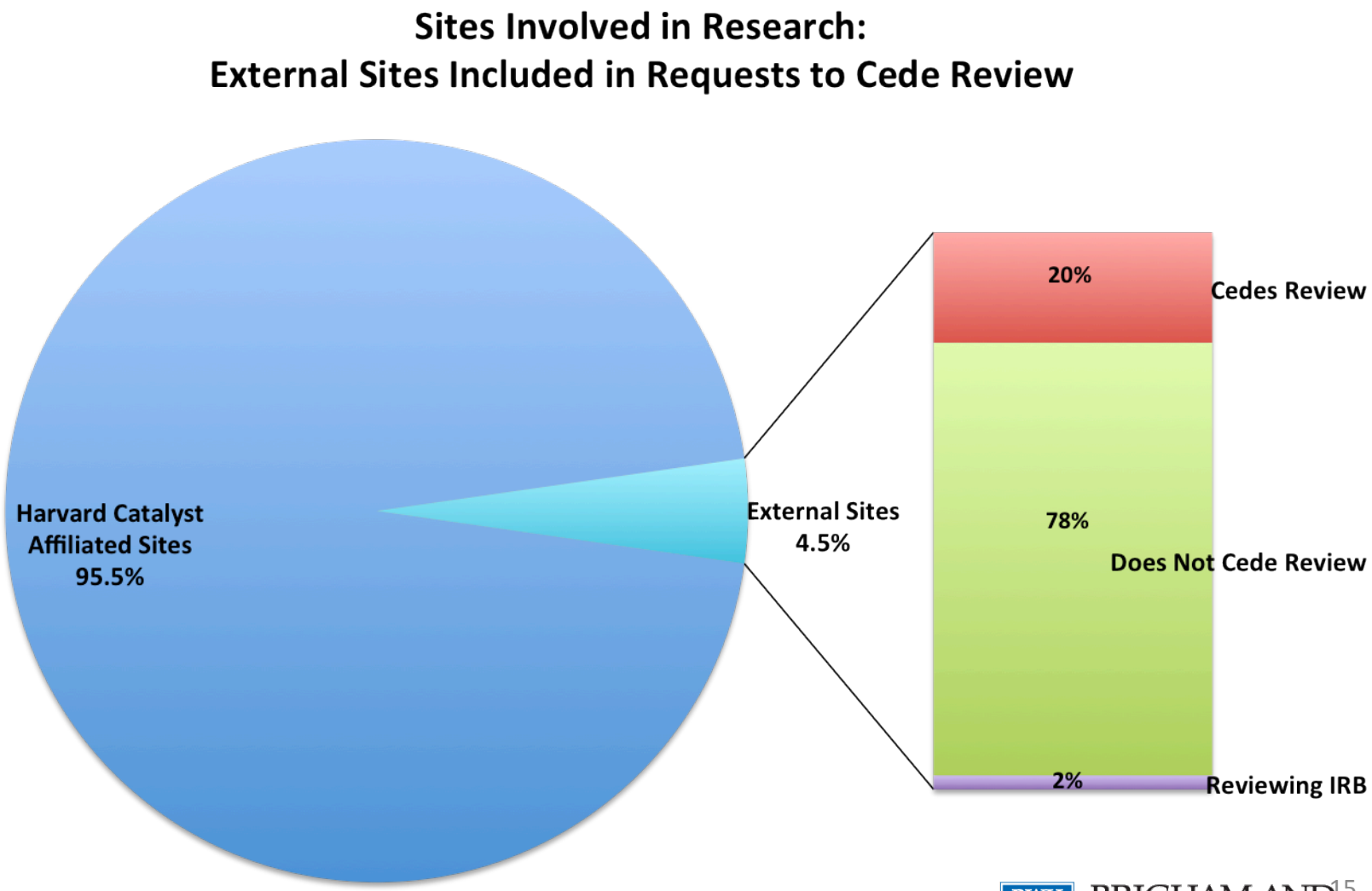
- Not Applicable / Not Human Subjects Research
- Not Engaged in Research
- Feedback from IO, Chair, IRB, etc.
- Local Review Planned/Required
- Cede arrangement already in place
- Relying IRB chooses not to cede review
- Request or Project Withdrawn
- Error in request

IRB Cede Review Request Form: Sites Involved in Research



- Most applications include 2 sites
- 25% of requests included 3 sites
- Max sites on an application = 8
- Greatest reduction in review: 7 institutions ceded review

IRB Cede Review Request Form: Non-Harvard Catalyst Sites



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Required elements to adoption

- Written IRB Authorization Agreement
- Clarity of role of reviewing IRB and relying institution
- Clarity and channels of communication
- Agreement on template IC language

For institution:

- State Law responsibilities
- Investigator and team competencies and education
- COI review and management
- System integration with other institutional functions: grants, contracts, IBC, Nursing, Pharmacy, Privacy
- Non-compliance and reporting

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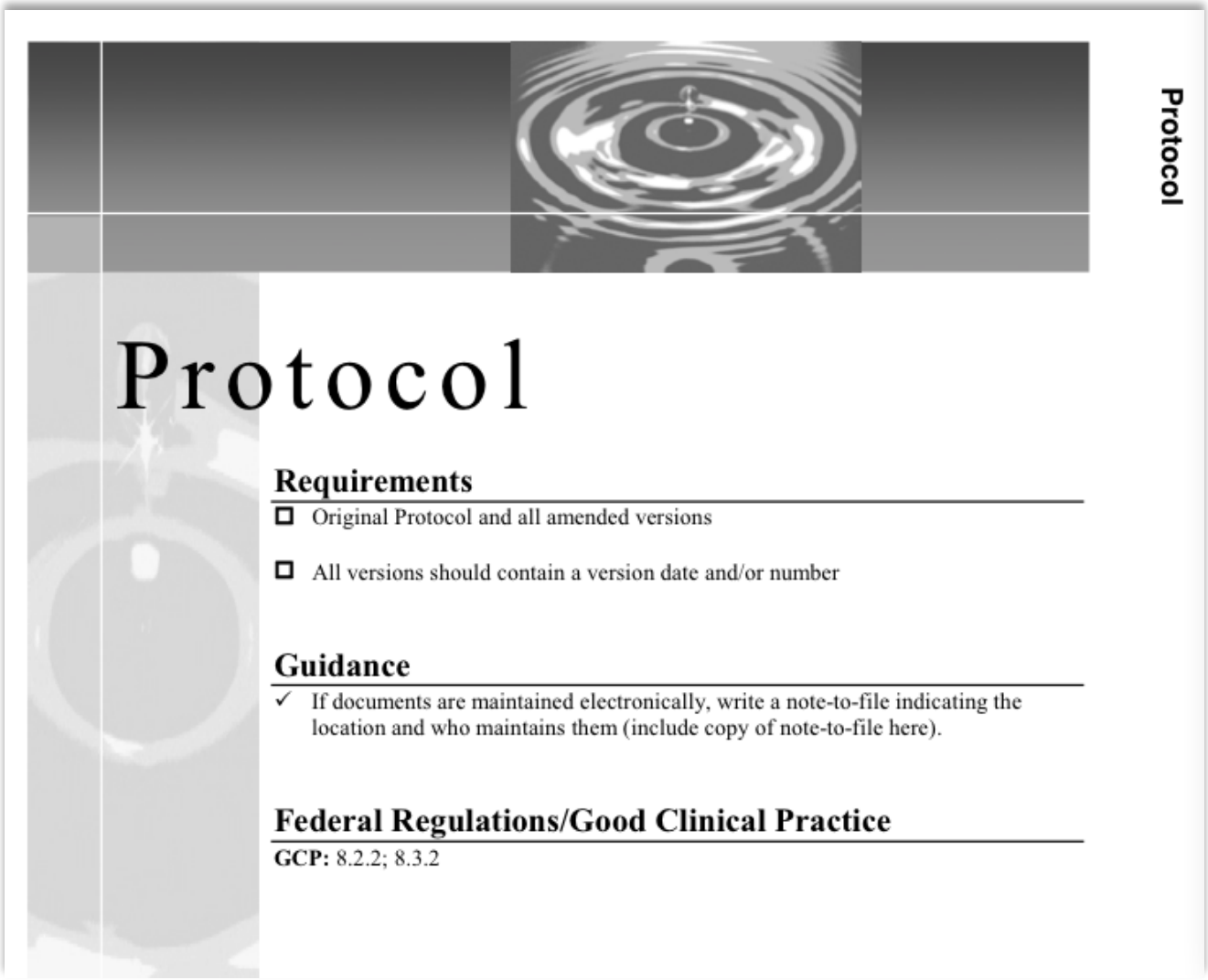
Resources: PI Binder



Protocol

Protocol

Requirements

- ☐ Original Protocol and all amended versions
- ☐ All versions should contain a version date and/or number

Guidance

- ✓ If documents are maintained electronically, write a note-to-file indicating the location and who maintains them (include copy of note-to-file here).

Federal Regulations/Good Clinical Practice

GCP: 8.2.2; 8.3.2

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Path Forward

- Agreement on necessity of increasing single-site IRB review of multi-site research
- Advantage of multiplicity of central IRBs
- Compromise on a Central Central IRB model
- Clarity of roles and responsibilities

On the wish list:

- Compensation for subject-related injury

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Thank you

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