CTSA Program: Moving Toward a Single IRB for Multi-Site Research

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NIH HCS RESEARCH COLLABORATORY STEERING COMMITTEE MEETING
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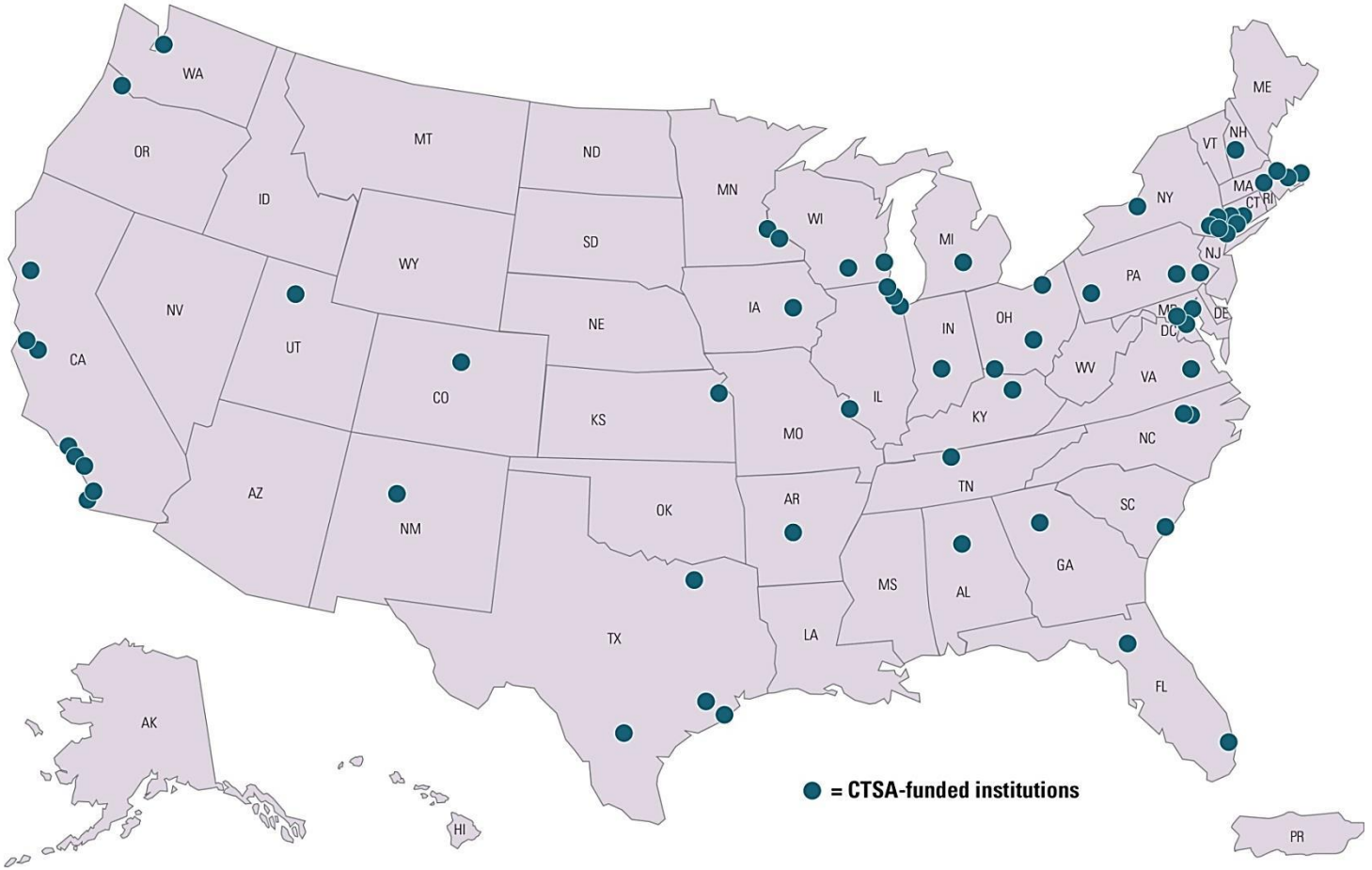
NCATS

National Center for Advancing Translational Sciences

Clinical and Translational Science Awards (CTSA) Program Hubs



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Background

- Patients are frustrated with the slow pace of translational clinical research
- Research teams spend too much time on bureaucratic tasks
- Start-up time for NIH-funded trials often exceeds 1 year
- Separate local IRB review at each site adds delays and cost (Ravina et al, 2010)
- Uncertain value-added
  - Inconsistencies in IRB assessment between sites (Hirshon et al, 2002)
  - Distributed accountability; no IRB takes charge? (Meninkoff 2010)
- FDA Guidance available on “Centralized IRB Process” – 2006
- OHRP allows for use of central IRB (April 30, 2010 letter)
- Draft NIH Policy on the Use of a Single Institutional Review Board (December 3, 2014)

Challenges: Some reasons for reluctance to defer IRB review

- Liability
- Administrative challenges
- Possible confusion of responsibilities
- Quality of review by other IRBs (trust)
- Ensuring local requirements are addressed
- Additional burden of changing internal processes to accommodate different methods of review

Proposed Solutions

- **Central IRB (cIRB)**: One IRB as IRB of record for all sites involved in multi-center protocols. cIRBs generally focus on particular topic or disease (e.g., NeuroNext, NCI CIRB).
- **Commercial IRB:** Often used for industry-sponsored multi-center trials; also called "independent IRBs."
- **IRB Share:** A joint review model and "Shared Review Process" in which a Lead IRB approves a study, but the Local Oversight IRB verifies agreement with the determination of the Lead IRB, and reviews local context issues.
- **Reliance model:** A single or consolidated IRB of record, chosen on a study-by-study basis, for the life of a study, involving a "reviewing IRB" and "relying institutions."

Example: Wisconsin IRB Consortium (WIC)

- **Includes 4 major research institutions across the state**
  - Aurora Health Care
  - Marshfield Clinic
  - Medical College of Wisconsin
  - University of Wisconsin-Madison

- Since January 2008, more than 170 studies qualified for single IRB review
- Expanding model across state lines to MARCH (6 institutions) & GPC (10 institutions focused on PCORI research), so far -
- *MARCH: 1 study involving 3 sites
- *GPC: 2 studies involving up to 10 sites each

Example: Harvard Catalyst – New England Reliance

- From January 2010 – November 20, 2014
- 32 Federalwide Assurance (FWA) signatories
  (22 Catalyst institutions; 10 non-Catalyst institutions)
- 1,413 applications requesting reliance
- 1230 applications (87%) represent a reduction of duplicative review
- 78% of the time the Reviewing IRB is that of the PI's primary employer

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Value of Reliance Agreement and Network: Boston Marathon Bombing

- Doctors at Mass Eye and Ear in Boston realized that they could learn more about the nature of blast-related ear injuries by studying bombing victims.
- **Harvard CTSA already had an IRB reliance network in place.** With 7 other hospitals, rapid IRB approval was obtained to study a large number of ear injuries from the same blast, and to observe patients as they healed.

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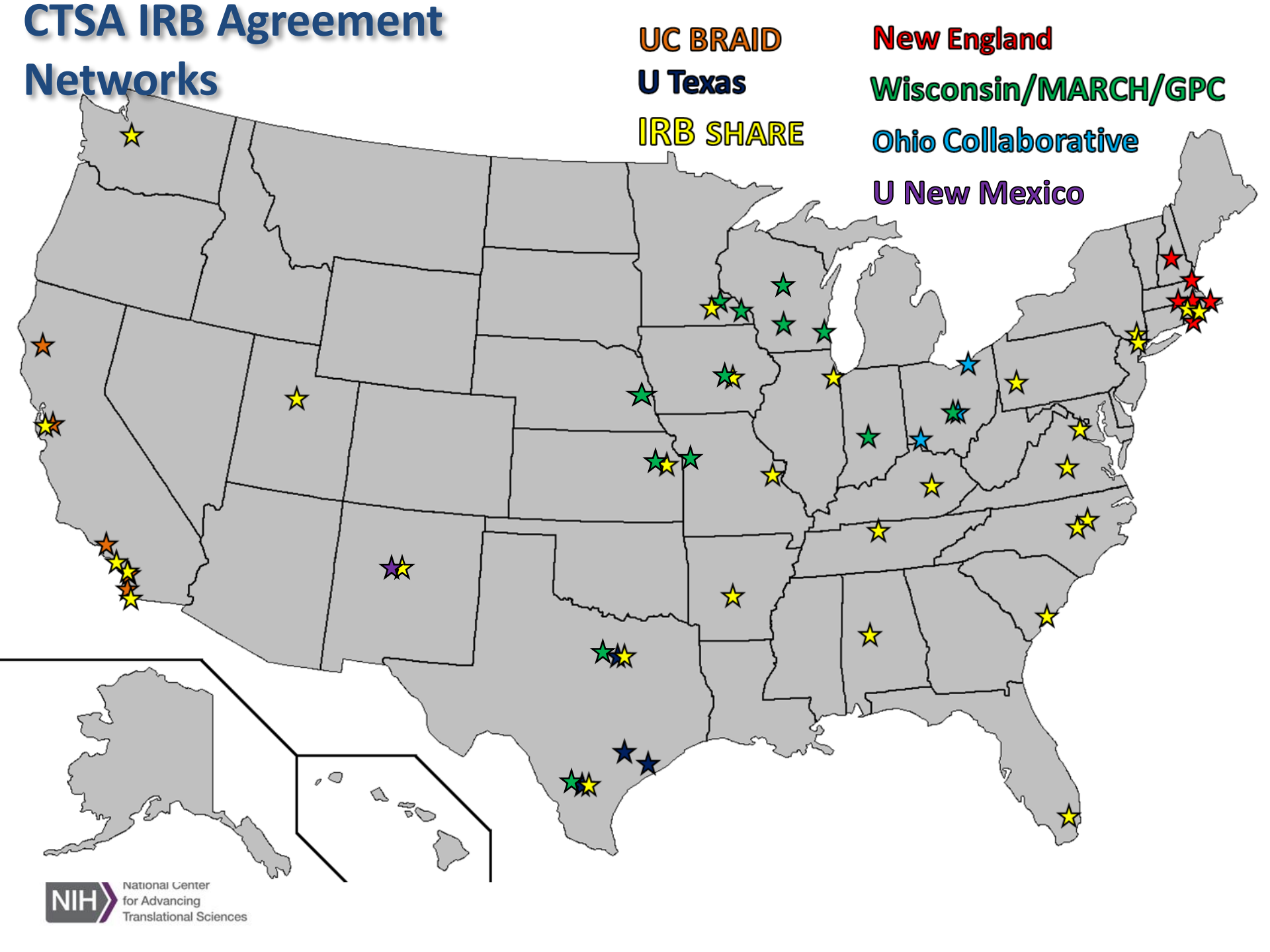
CTSA IRB Agreement Networks



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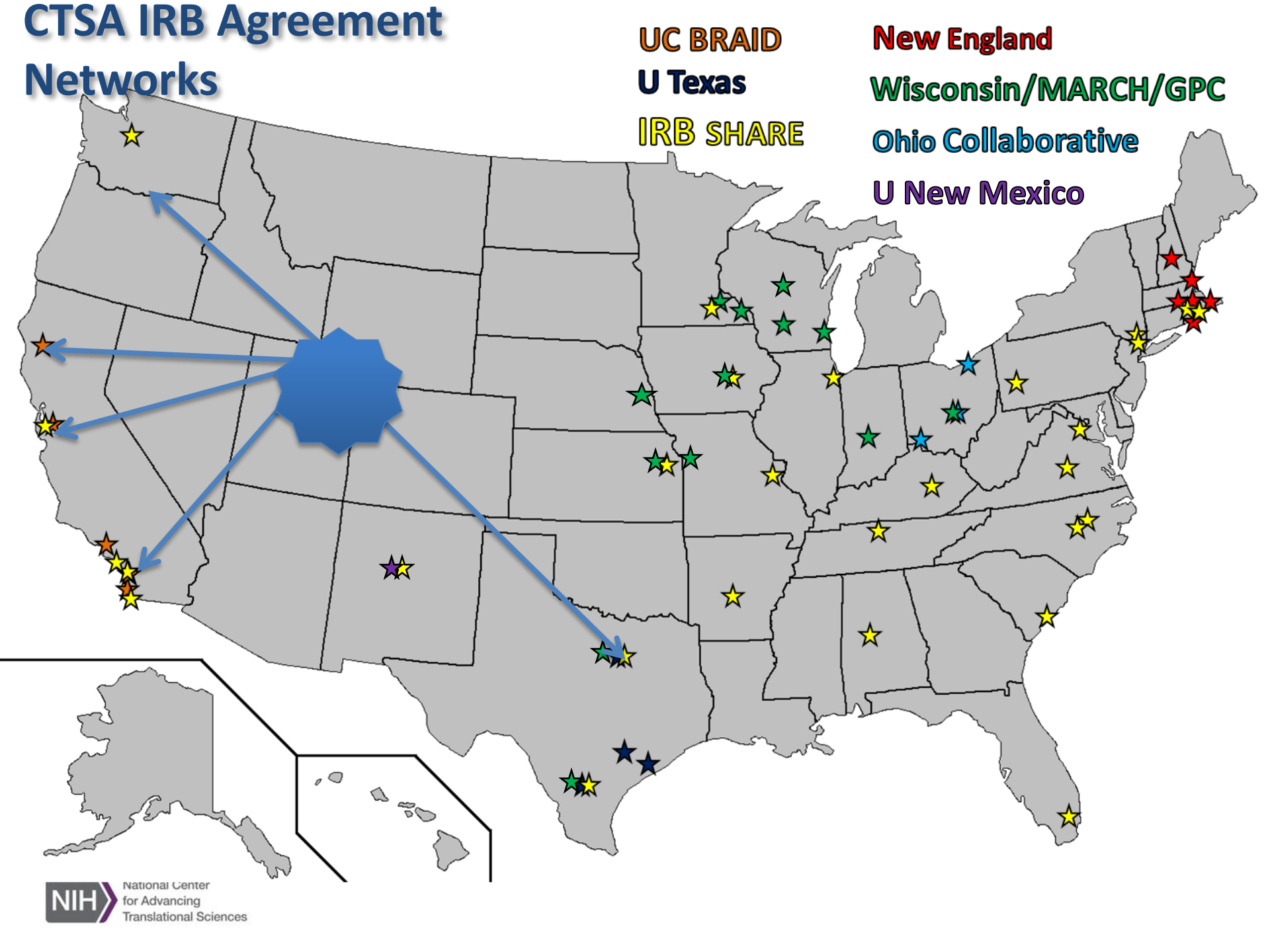
CTSA IRB Agreement Networks



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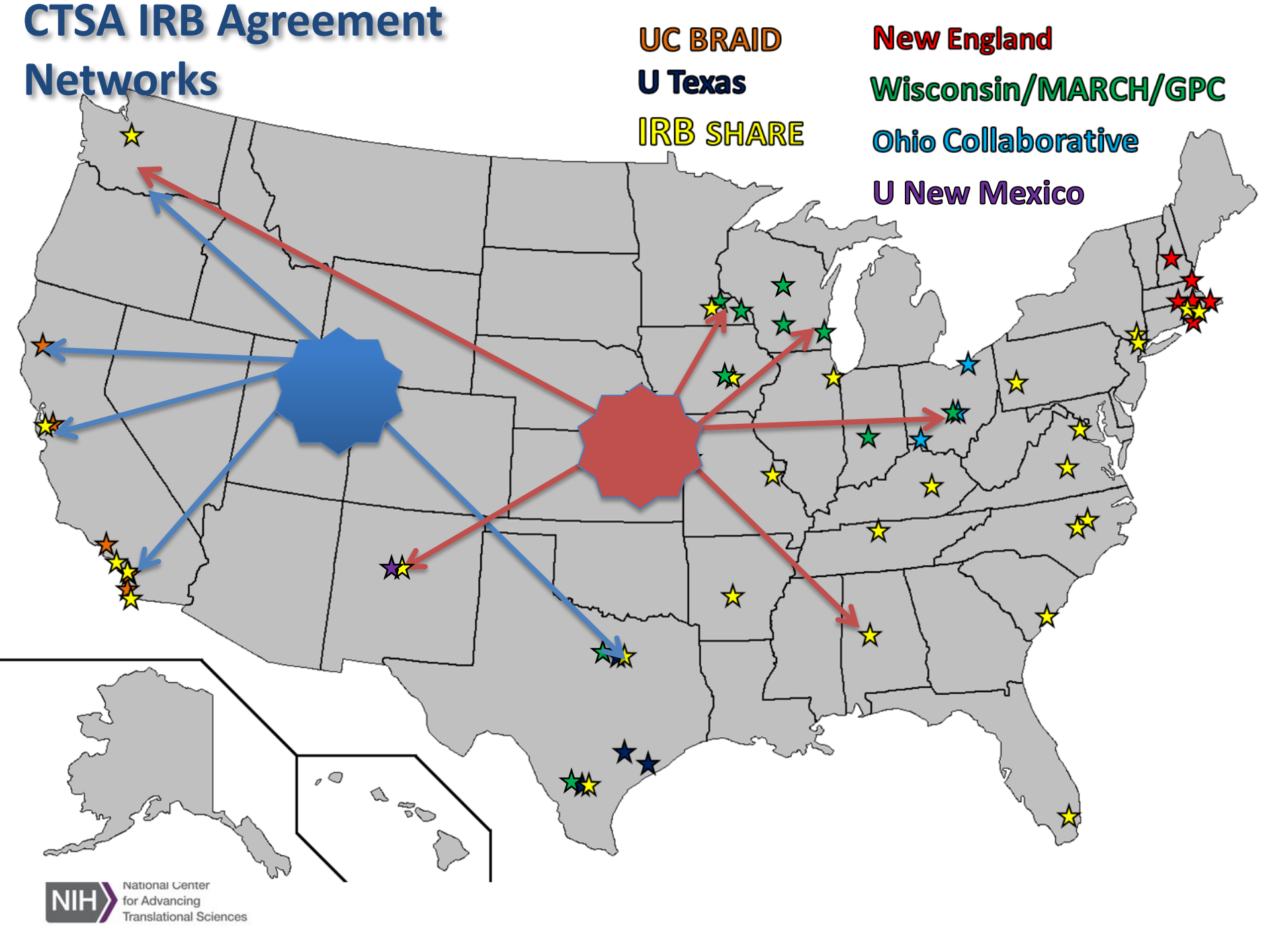
CTSA IRB Agreement Networks



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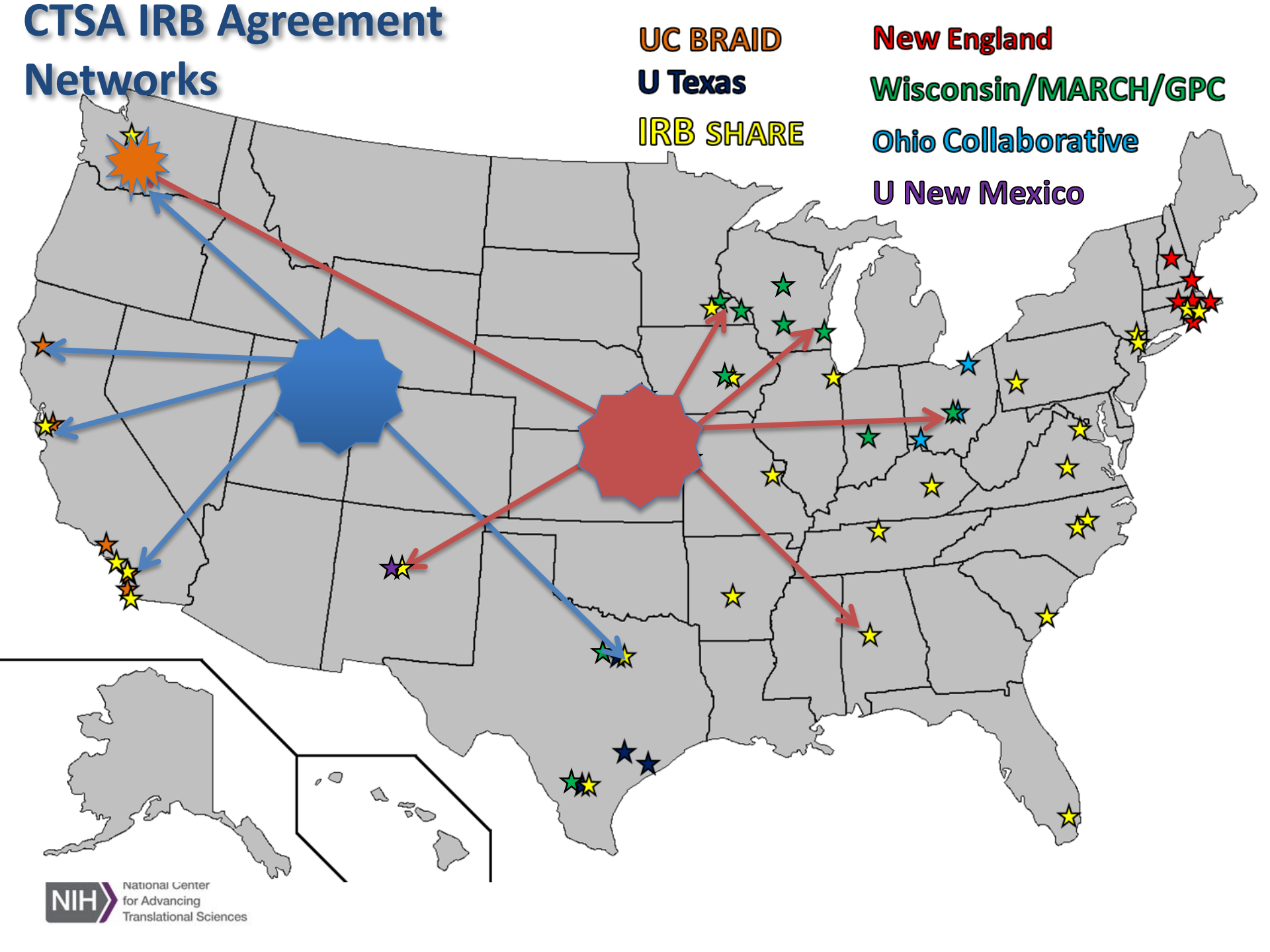
CTSA IRB Agreement Networks



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CTSA – IRB Reliance Project: Toward a National IRB System

Principal Investigator	Alan I. Green, Dartmouth
Sr. Reliance Advisor	Barbara Bierer, Harvard
Regulatory Leads	Sabune Winkler, Harvard Nichelle Cobb, Medical College of Wisconsin
Informatics Lead	Amarenda Das, Dartmouth
Critical contributions and support	CTSA investigators and their teams

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Toward a National CTSA IRB – Specific Aims

Initiative launched February 2014

- Create a national IRB reliance agreement, building on the expertise of existing regional IRB models.
- Identify and build the informatics infrastructure to support a national IRB reliance model.
- Implement and utilize the new IRB reliance national model to support multi-site clinical trials.
- Identify a low-risk multi-center clinical trial to demonstrate feasibility of national IRB reliance model.
- Evaluate the processes developed and the infrastructure created.

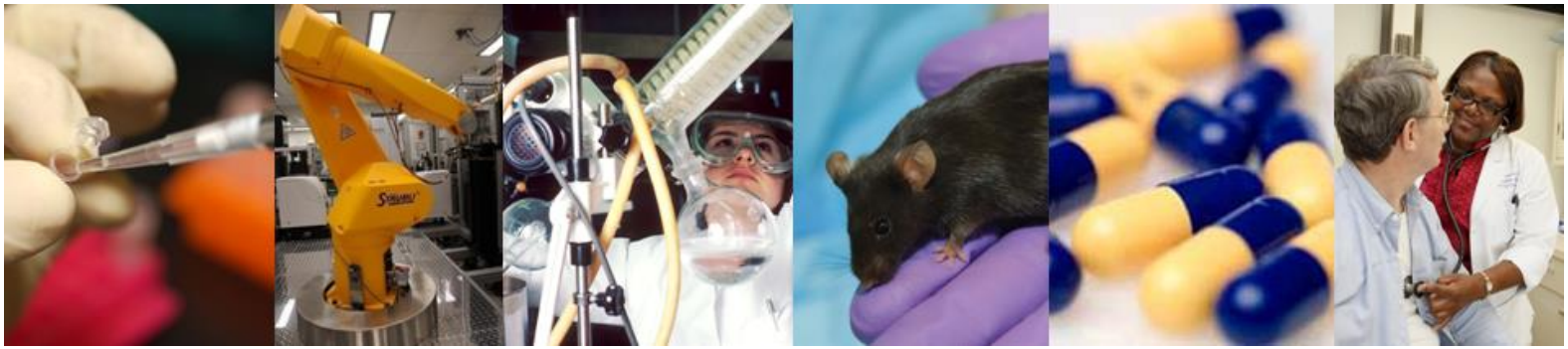
Nature of Initiative

- Starting with CTSA sites, but expected to expand beyond these institutions
- Based on reliance model
  - Similar to “NeuroNext-type”
  - Distinct from “commercial” central IRB models, as well as “IRBShare-type” model
  - Respecting the legal autonomy of each participating institution, reliance is determined in a case-by-case basis
  - Supported by the Agreement, ceding IRB review, and serving as Reviewing IRB is voluntary
  - Can be used for any multi-site, human subjects research involving institutions that have signed the Agreement

Components of a National CTSA IRB Initiative

Governance	• Provide leadership for effort and support to sites • Identify resources needed to support • Help to ensure sustainability
Workflows	• Application process • Communicating determinations
IT solutions	• To facilitate workflow and documentation • Harmonized across CTSA hubs if possible
Communication and Web-based access	• Information about initiative and joining the agreement • SOPs and other supporting documents
Best practices and harmonization	• Requirements for IRBs of record, particularly for larger studies • Universal consent form template • Reportable event requirements

Implementation and Proposed Solutions



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Determining Eligibility to Use the Agreement

Proposed Solution: Institutions must meet some minimum requirements to be eligible to use the agreement, including:

- Having a current Federalwide Assurance (FWA)
- "Unchecking the box"
- Ability to assure a certain level of HRPP standards:
  - Accreditation or OHRP's Quality Assurance Program
  - Quality assurance program ability to conduct study audits
- Following Standard Operating Procedures (SOPs) developed in support of agreement

Communication

- Develop a centralized system for communicating and reviewing requests to cede review/serve as Reviewing IRB
- Require institutional Lead Regulatory Contact (LRC) for Reviewing IRB and Relying Institution that
  - serve as resources for process
  - ensure communication across institutions and with study teams
  - can make decisions regarding accepting or ceding IRB review responsibilities
- Require identification of a Lead Study Team that would be responsible for most communication with the Reviewing IRB and disseminating information to and collecting information from participating study teams

Addressing "Local Context" Issues

Proposed Solution:

- LRCs at Relying Institutions provide "local context" information to the Reviewing IRB, such as:
  - State Law
  - Other institutional requirements that affect the study for a particular site (e.g., local populations, limited consent form language)

Division of Responsibilities

Relying Institutions required to:

- Manage their study teams' conflicts of interest (COI) and communicate relevant COIs and management plans to the Reviewing IRB
- Ensure that:
  - their study teams are trained
  - their study teams conduct the research in compliance with applicable federal regulations and IRB determinations
  - institutionally-required ancillary reviews are completed

Division of Responsibilities

Proposed Solution:

- ***Reviewing IRB*** required to:
  - Oversee studies across their lifespan (i.e., conduct review of new application, continuing review, changes, and reportable events)
  - Serve as HIPAA Privacy Boards
  - Conduct grant congruency reviews

- ***Study teams*** required to:
  - Comply with the policies of the Reviewing IRB

Pilot Multi-Center Study

- CARRA: Childhood Arthritis & Rheumatology Research Alliance
  - National Network of Rheumatology researchers
    - 63 sites
    - Serves as a registry for clinical trials
  - PI: Laura Schanberg (Duke University)
  - Proposal: extend the registry capabilities to include a biorepository utilizing sites connected to ongoing CTSA Reliance project
- 12 sites selected
- Duke University currently reviewing IRB Reliance agreement
  - May act as IRB of record for pilot
- Proposal was presented at CARRA meeting in Austin on April 17, 2015 for approval

Collaboration with Other Single IRB Initiatives

- NCATS IRB Reliance Initiative is coordinating with PCORnet investigators so that:
  - Reliance agreements will use same template to the extent possible
  - SOPs and informatics solutions will be broadly useful
- NCATS and NCATS IRB Reliance Initiative are communicating with CTTI central IRB group
- National harmonization will be important to minimize burden on institutions

Take-Home Messages

- Build network capacity
  - Reliance on a single IRB for multi-site trials
  - Streamlined subcontracting
  - Innovative tools to support research participant recruitment
- The CTSA program seeks to
  - support NIH activities
  - partner with a broad range of stakeholders
  - harmonize with other research initiatives