



JOHNS HOPKINS
M E D I C I N E

JOHNS HOPKINS
HEALTH SYSTEM

Clinicaltrials.gov Program Launch

What Research Teams Need to Know

Anthony Keyes, MBA, PMP
JohnsHopkinsU PRS Administrator
Institute for Clinical and Translational Research (ICTR)
akeyes1@jhmi.edu / 410.550.6259

Session Acknowledgements

- ClinicalTrials.gov Taskforce
- CTSA Presentations
- Final content reviewed by;
 - Dan Ford (Vice Dean)
 - Monica Owens (PRS Admin: SKCCC)
 - Miye Schakne (PRS Admin: JHSPH)
 - Travis Che Jarrell (RA/QA Manager: JH ACH CTRO)

Welcome to those watching via Livestream

Who requires ClinicalTrials.gov registration?

- A. WHO
- B. FDA
- C. NIH
- D. CMS

First Things First

“ClinicalTrials.gov” and “CT.gov” will be used interchangeably in this presentation for sake of brevity (the correct internet address is www.clinicaltrials.gov)

- There are 2 basic functions of ClinicalTrials.gov
 - *Registration*
 - *Results*
- There are 2 different systems
 - Public site: <https://clinicaltrials.gov/>
 - User site: Protocol Registration and Results System (PRS) <https://register.clinicaltrials.gov/>

ClinicalTrials.gov - Public Site

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. [Learn more about clinical studies](#) and [about this site](#), including relevant [history](#), [policies](#), and [laws](#).

[Find Studies](#) ▾ [About Clinical Studies](#) ▾ [Submit Studies](#) ▾ [Resources](#) ▾ [About This Site](#) ▾

ClinicalTrials.gov currently lists **209,646 studies** with locations in all 50 States and in **192 countries**.

Text Size ▾

Search for Studies

Example: "Heart attack" AND "Los Angeles"

[Advanced Search](#) | [See Studies by Topic](#)
[See Studies on Map](#)

Search Help

- [How to search](#)
- [How to find results of studies](#)
- [How to read a study record](#)

Locations of Recruiting Studies



- Non-U.S. only (54%)
- U.S. only (41%)
- Both U.S. and non-U.S. (6%)

Total N = 37,266 studies
(Data as of March 01, 2016)

- [See more trends, charts, and maps](#)

For Patients and Families

- [How to find studies](#)
- [See studies by topic](#)
- [Learn about clinical studies](#)
- [Learn more](#)

For Researchers

- [How to submit studies](#)
- [Download content for analysis](#)
- [About the results database](#)
- [Learn more](#)

For Study Record Managers

- [Why register?](#)
- [How to register your study](#)
- [FDAAA 801 requirements](#)
- [Learn more](#)

Learn More

- [Tutorials for using ClinicalTrials.gov](#)
- [Glossary of common site terms](#)
- [For the press](#)
- [Using our RSS feeds](#)

[HOME](#) [RSS FEEDS](#) [SITE MAP](#) [TERMS AND CONDITIONS](#) [DISCLAIMER](#) [CONTACT NLM HELP DESK](#)

Copyright | Privacy | Accessibility | Viewers and Players | Freedom of Information Act | USA.gov
U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health and Human Services

Protocol Registration and Results System (PRS)

ClinicalTrials.gov PRS Protocol Registration and Results System

Login

Welcome to the [ClinicalTrials.gov](#) Protocol Registration and Results System (PRS).

OMB NO: 0925-0598
EXPIRATION DATE: 11/30/2018
[Burden Statement](#)

Organization:
One-word organization name assigned by PRS (sent via email when account was created)

Username:

Password: [Forgot password](#)

Login

See [Submit Studies](#) on ClinicalTrials.gov for information on how to apply for an account, how to register your study, and how to submit results.
[Send email to ClinicalTrials.gov PRS](#) Administration

U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health & Human Services

ClinicalTrials.gov PRS Protocol Registration and Results System

[Contact ClinicalTrials.gov PRS](#)

Org: JohnsHopkinsU User: AKeyes [Logout](#)

Email: akeyes1@jhmi.edu [[Update](#)]

Help us improve: [PRS Survey](#)

Quick Links

[New Record](#)
[Admin Quick Reference](#)
[Problem Resolution Guide](#)

Records ▾ Accounts ▾ Help ▾

Record List

6/13/2016

<https://register.clinicaltrials.gov/>

6

Outline

- Overview and background of ClinicalTrials.gov
- Rationale for clinical trial registration and results reporting
- Program Highlights
- How to “register” your study
- How to submit your study “results”
- Tip and Tricks to help you

Overview and background

Year	Entity	Event
1997	Congress	<i>1st U.S. law to require trial registration (FDAMA)</i>
2000	NIH	<i>Releases ClinicalTrials.gov website</i>
2005	ICMJE	<i>Requires registration before enrollment</i>
2006	WHO	<i>All clinical trials should be registered</i>
2007	CMS	<i>PI must enroll qualifying clinical trials in ClinicalTrials.gov</i>
2007	Congress	<i>Expanded registration, submission of results and adverse events, civil penalties (FDAAA)</i>
2008	NIH	<i>Releases results database</i>
2015	CMS	<i>Mandatory Reporting of Clinical Trial Number on Claims</i>

FDMA: Food and Drug Administration Modernization Act
NIH: National Institutes of Health
ICMJE: International Committee of Medical Journal Editors

WHO: World Health Organization
CMS: Centers for Medicare & Medicaid Services
FDAAA: Food and Drug Administration Amendments Act 8

Watchful Eyes

thebmj

Research ▾

Education ▾

News & Views ▾

Campaigns

Open Access

Research

BMJ Open Clinical trial registration, reporting,



BMJ 2014;349:g7089 doi: 10.1136/bmj.g7089 (Published 10 December 2014)

Page 1 of 2

EDITORIALS

Clinical trials: what a waste

Trials that are unregistered, unfinished, unpublished, unreachable, or simply irrelevant

Watchful Eyes



Chest. 2009 Jul; 136(1): 295–303.

PMCID: PMC2821287

doi: [10.1378/chest.08-3022](https://doi.org/10.1378/chest.08-3022)

Reporting “Basic Results” in ClinicalTrials.gov

[Tony Tse](#), PhD, [Rebecca J. Williams](#), PharmD, and [Deborah A. Zarin](#), MD

[Author information](#) ► [Article notes](#) ► [Copyright and License information](#) ►

This article has been [cited by](#) other articles in PMC.

Growing awareness of selective publication of research studies (“publication bias”) and the selective reporting of outcomes in publications (“outcome reporting bias”),¹ has led policymakers to call for increased “clinical trial transparency” through the public disclosure of key information about clinical trials.² A US

Clinical Trials Site

Bridget M. Kuehn

JAMA. 2012;307(7):651-653. doi:10.1001/jama.2012.127.

Watchful Eyes

STAT

Law ignored, patients at risk

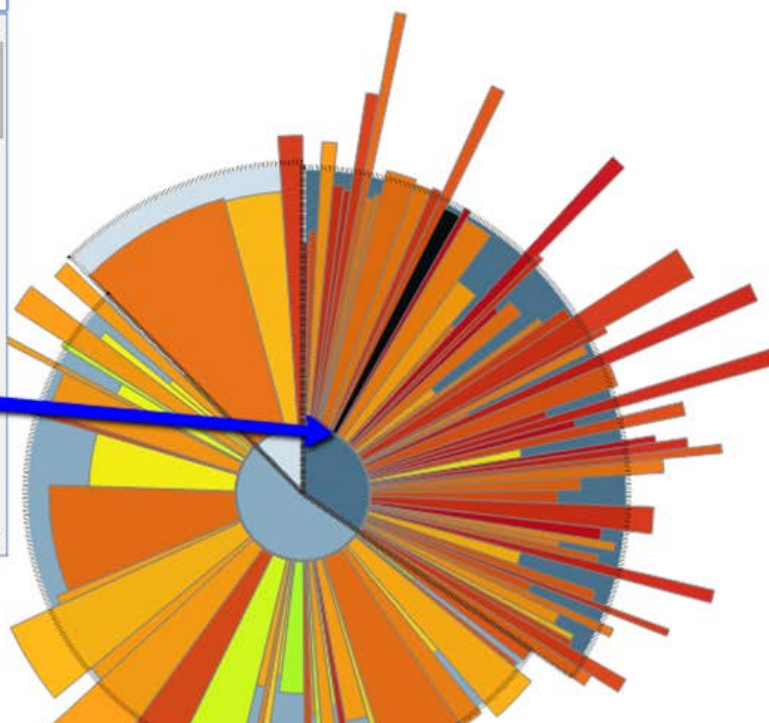
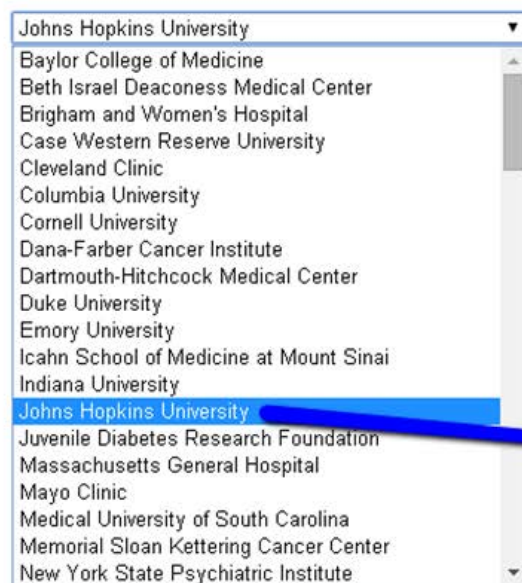
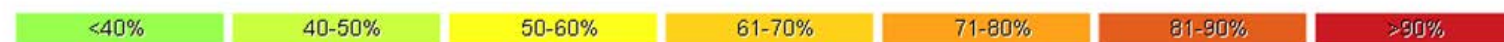
Johns Hopkins University ▼



Johns Hopkins University
Entity type: **Academic or Nonprofit**
Main location: **Baltimore, MD**
Trials that require results: **56**
% of those trials with no posted results: **54%**
% of those trials with no results or results posted late: **88%**
For late results, average days late: **368**

Watchful Eyes

Percentage of clinical trials by entity that have late or no results:



Overview and background

2016: Final Rule

- ...stay tuned

Whatever the Final Rule states Johns Hopkins will be well-positioned to respond based on the new ClinicalTrials.gov Program



Program Highlights

- **1.5 FTEs of dedicated staffing**
 - Anthony Keyes and Nidhi Atri, M.D.
- **Statistical expertise**
 - Provided by the BEAD Core
 - <http://jhcchr.org/bead/>
 - First 1-hour covered by the program
 - During this hour;
 - Most concerns can be handled
 - Additional time needed and costs can be discussed

Program Highlights

- **For the PI/Study team, assistance with...**
 - Account creation and maintenance
 - Initial registration
 - PRS reviewer comments
 - Update and results reminders
 - Results reporting
 - Changes to PI/Study team (including when a PI leaves)

Program Highlights

- **Future Capabilities**

- Effective E-mail

- Relational database sending automated reminders for
 - updates (every 6 months)
 - results reporting (1 year after Primary completion date)

- Efficiencies within eIRB

- Appropriately identify what studies meet registration and results criteria
- Update eIRB lead questions to harmonize with ClinicalTrials.gov

- Education

- Training Workshops
- Lunch and Learn
- Website

Registration: Purpose and Benefits

Registry Purpose

Fulfill ethical obligations to participants and community

Provide information to potential participants and referring clinicians

Reduce publication bias

Help editors and others understand the context of study results

Promote more efficient allocation of research funds

Help institutional review boards (IRBs) determine appropriateness of a research study

Results Reporting; Purpose and Benefits

Results Database and Purpose

Provide public record of basic study results in a standardized format

Promote fulfilling of ethical responsibility to participants; use of research results to contribute to medical knowledge

Mitigate "publication" and "outcome reporting" biases

Facilitate systematic reviews and other analyses of the research literature

Registration and Reporting Requirements

Why Register and Report?

- Commitment to research participants
- Scientific validity/transparency
- Ethical standards
- Responsible stewardship of federal funds
- Required by law (FDAAA)
- Required by NCI
- Required for journal publication (ICMJE)
- Required for CMS
- Required by WHO

Why?

What?

Who?

When?

How?

Registration and Reporting Requirements

What Trials to Register and Report?

‘Applicable Clinical Trials’ include the following:

- Trials of drugs/biologics. Controlled clinical investigations, other than phase 1 trials of drugs/biological products subject to FDA regs.
- Trials of devices. 1) Controlled trials with health outcomes of devices subject to FDA regulation (other than small feasibility studies) and 2) pediatric post-market surveillance required by FDA
- The trial has one or more sites in the U.S.
- The trial is conducted under an FDA IND or IDE application
- The trial involves a drug, biologic, or device that is **manufactured in the U.S.** or its territories and is **exported** for research

ACT Wizard: http://grants.nih.gov/clinicaltrials_fdaaa/docs/Flow_chart-ACT_only.pdf

Identifying an ACT under FDAAA http://grants.nih.gov/ClinicalTrials_fdaaa/ACTs_under_FDAAA.htm

Why?

What?

Who?

When?

How?

Registration and Reporting Requirements

Trials that are Excluded:

- (Non-serious/life-threatening) Phase 1 drug trials, including studies in which drugs are used as research tools to explore biological phenomena or disease processes
- Small clinical trials to determine the feasibility of a device or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes
- Trials that do not include drugs, biologics, devices, or clinical procedures (e.g., behavioral interventions)
- Non-interventional (observational) clinical research, such as cohort or case-control studies
- Trials that were ongoing as of September 27, 2007, and reached the Completion Date before December 26, 2007

Registration and Reporting Requirements

Who is Responsible?

Responsible Party (RP) for a clinical trial must register the trial and submit results information. An RP can be:

- ❑ The **Sponsor** of the clinical trial (as defined in 21 CFR 50.3) who initiates the study (i.e., “Johns Hopkins University”)

[Help](#) [Definitions](#)

* ‡ Responsible Party:  

...ess the Investigator has been designated as Responsible Party per FDAAA.
...nsible Party has not been entered.

* ‡ Sponsor: 

Primary organization conducting study and associated data analysis (not necessarily a funding source).

As a matter of policy the “Sponsor” should be listed as the RP

Registration and Reporting Requirements

Who is Responsible?

Responsible Party (RP) can be:

- The **Principal Investigator (PI)** of such clinical trial, assuming:
 - the PI is responsible for conducting the trial,
 - has access to and control over the data from the clinical trial,
 - has the right to publish the results of the trial, and
 - has the ability to meet all of FDAAA's requirements for the submission of clinical trial information.
- Maintains full compliance with 6-month updates

As a matter of policy the “Sponsor” should be listed as the RP
Not doing so bypasses internal review

Why?

What?

Who?

When?

How?

Registration and Reporting Requirements

When to Register?

- ICMJE requires trial registry at or **before first patient enrollment** as a condition for publication

Source: <http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>

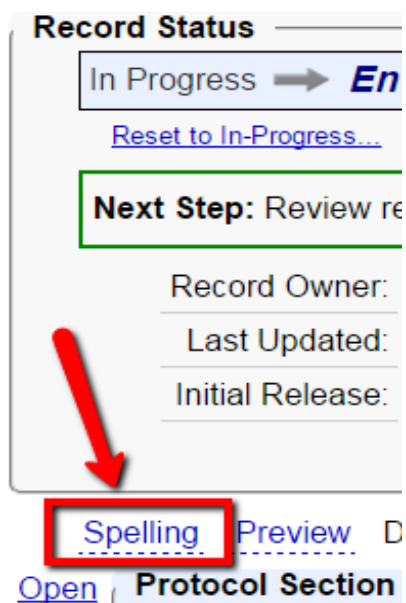
- The Responsible Party for an Applicable Clinical Trial must submit required clinical trial information through the Protocol Registration and Reporting System (PRS) no later than **21 days after enrollment of the first participant.**

Source: <https://www.clinicaltrials.gov/ct2/manage-recs/fdaaa>

Registration: Tips and Tricks

Before you submit the PRS Admin or RP should...

Check for spelling and to see that all acronyms are expanded using the “Spelling” feature



Record Status

In Progress → **En**

[Reset to In-Progress...](#)

Next Step: Review re

Record Owner:

Last Updated:

Initial Release:

Spelling Preview D

[Open](#) Protocol Section

Possible Unexpanded Acronyms

Acronyms should be expanded at least the first time used in the Protocol section and (if applicable) in the Results section.
Example: National Institutes of Health (NIH)

Data Element	Acronym	Possible Expansion(s) [Show]
Detailed Description	AI	[15]
Detailed Description	DE	[8]
Detailed Description	ID	[45]
Primary Outcome Measure	OFC	[3]

Registration: Tips and Tricks

Before you submit the PRS Admin or RP should...

- ☐ Check all Outcome Measures for accuracy and completion
- ☐ Check for any “Errors” or “Warnings”

Protocol Section

Identifiers: NCT00382850 Unique Protocol ID: 05-08-01-01

Brief Title: Clinical Trial Comparing Open and Laparoscopic Nissen Fundoplication in Children

Module Status:

Study Identification: ✓

Study Status: 2 Errors 2 Warnings

Sponsor/Collaborators: 1 Warning

Oversight: 1 Warning 1 Note

Study Description: ✓

Conditions: ✓

Study Design: 1 Error

Arms and Interventions: 1 Warning 1 Note

Outcome Measures: 14 Warnings 1 Note

Eligibility: ✓

Contacts/Locations: ✓

References:

Update Requirements

When to update a study in-process?

- While Study is In-Process:
 - RPs must update the record within 30 days of a change to:
 - Recruitment Status -or-
 - Completion Date
 - Record Verification Date must be updated every 6 months, even if no changes to the study. Failure to update ClinicalTrials.gov info can result in penalties
 - Need to update ends when the study is completed/terminated and results are entered, approved and posted

Not yet recruiting
Recruiting
Enrolling by invitation
Active, not recruiting
Completed
Suspended
Terminated (Halted Prematurely)
Withdrawn (No Participants Enrolled)

Reporting Requirements

When to submit Basic Results?

- No later than 12 months after (Primary) Completion Date.
- **Primary Completion Date** ^{FDAAA} [Required by for records first released on or after December 1, 2012]
 - Date that the final subject was examined or recv'd an intervention for purposes of final data collection for the primary outcome, whether the trial concluded per protocol or was terminated.
 - Must keep this field accurate in clinicaltrials.gov since it's how NIH determines the timeliness of basic results reporting
- **Study Completion Date**
 - Final date on which data was (or is expected to be) collected.

Source: <https://prsinfo.clinicaltrials.gov/definitions.html#PrimaryCompletionDate>

Reporting Requirements

But what if the dog ate my homework?

A Responsible Party may DELAY submission of Basic Results / Seek an Extension

Source: <https://www.clinicaltrials.gov/ct2/manage-recs/fdaaa>

Prior Publication Comment:

Medical journals have stated that reporting results to ClinicalTrials.gov in compliance with FDAAA 801 will not be considered “prior publication.” Source: <http://www.nejm.org/doi/pdf/10.1056/NEJMe078110>

Reporting Requirements

Additional Note about FDA

New Drug Applications (NDA) require certification that trial registration is up-to-date (**IND sponsor must submit an FDA Form 3674 to their IND file**)

Practical Application

How long will it take to..

- Register a Trial?
 - ClinicalTrials.gov may have comments
 - After review usually 2-5 days
- Submit Basic Results?
 - Highly variable based on study specifics
 - Tables will likely not be constructed the same way
 - ClinicalTrials.gov may have comments
 - May need statistical assistance
 - ClinicalTrials.gov will assist

Practical Application

How to Register <http://clinicaltrials.gov/ct2/manage-recs/how-register>

1. Obtain a PRS user account, and know your institutional PRS account name (“JohnsHopkinsU”)
 - Each user should have their own account (no user account sharing)
2. Identify the Responsible Party
 - The RP role is similar to the PI role in the IRB...?

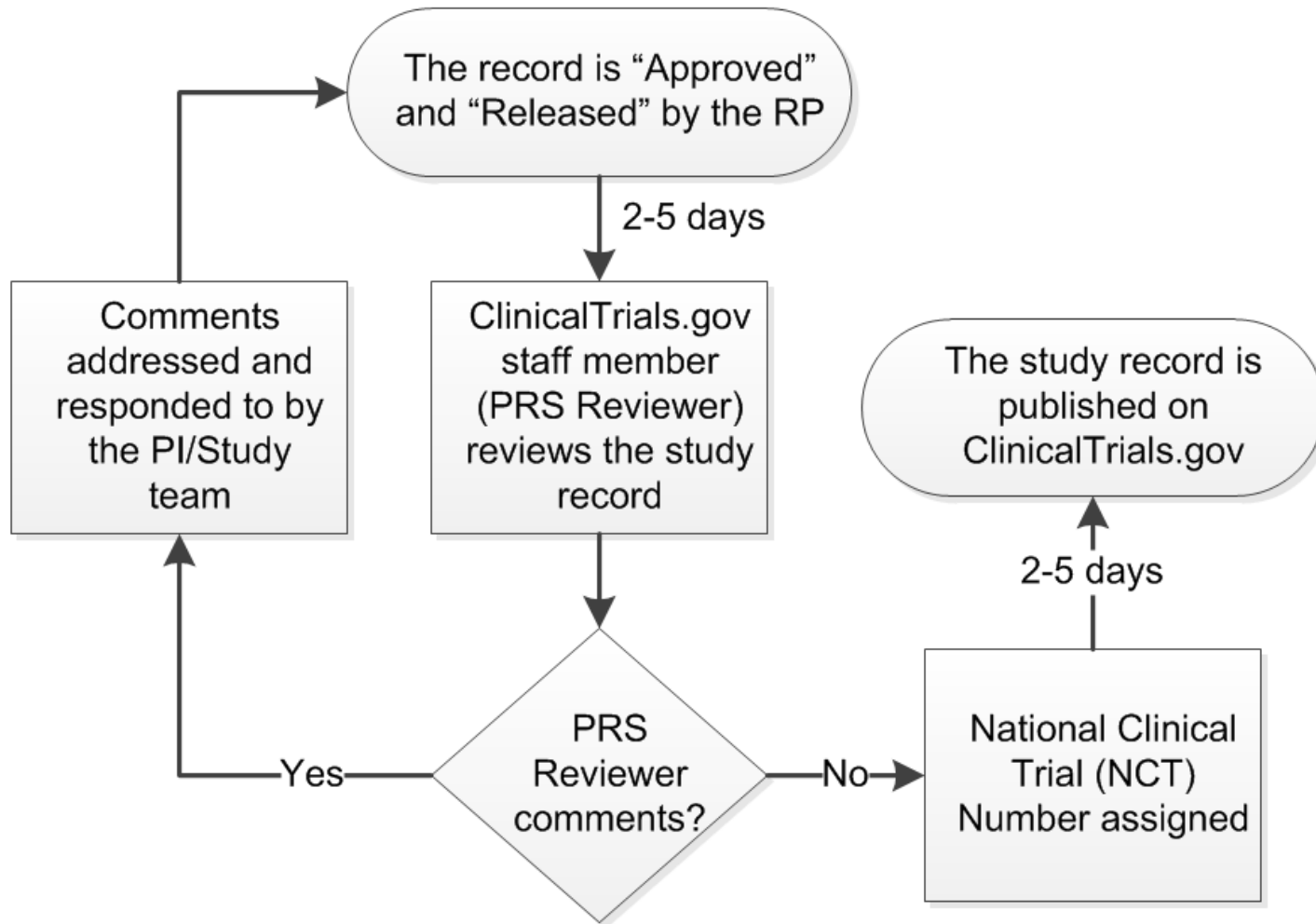
	Who can enter information/update the study?	Who can “ <i>submit</i> ” the study for review?
IRB	PI, Study team members	PI
ClinicalTrials.gov	Record owner, Responsible Party, Anyone on the Access list	Responsible Party

Practical Application

How to Register (cont.)

3. Enter the required and optional data elements
 - (webinar: <http://prsinfo.clinicaltrials.gov/webinars/module3/index.html>)
4. Preview and inspect
 - review the ClinicalTrials.gov Protocol Review Criteria document <http://prsinfo.clinicaltrials.gov/ProtocolDetailedReviewItems.pdf>
5. The RP will “Approve” and “Release” the record

Protocol Information Review Process



Practical Application: Entering Basic Results

What Info Must be Submitted?

Scientific Information (per arm)

- Participant Flow
 - Number of participants started and completed
- Baseline Characteristics
 - Number of participants analyzed
 - Age and gender
- Outcome Measures
 - Number of participants analyzed
 - Title and Description
 - Measurements (e.g., mean) and Measure of Dispersion (e.g., Std Dev)
 - Statistical analyses, as appropriate

Practical Application: Entering Basic Results

What Info Must be Submitted (cont.)?

Scientific Information (per arm)

- Adverse Events – Serious and “Other”
 - Number of Participants Affected/At Risk
 - Adverse Event Term and Organ System
- Limitations and Caveats (optional section)
- Other Administrative Information
 - Results Point of Contact
 - Certain Agreements (related to investigator’s right to publish, if not an employee of the sponsor)

Practical Application

- Summary results at the end of the trial only
 - No interim or “real time” reporting
 - No participant-level reporting
- Info targeted at *readers of the medical literature*
 - “Tables” of information; “just the facts”
 - No narrative discussion or results/conclusions
- Entering results ~ preparing a journal article (but more rigid)
- Data provider need to be familiar with the study design/analysis
 - the investigator and/or a statistician will need to be involved

Results: Tips and Tricks

- How to Submit Your Results homepage
<http://clinicaltrials.gov/ct2/manage-recs/how-report>
- Basic Results Data Elements Definitions
http://prsinfo.clinicaltrials.gov/results_definitions.html
- 10 minute webinars for each results module
<http://clinicaltrials.gov/ct2/manage-recs/present>
- Helpful Hints (with common study designs examples)
<http://prsinfo.clinicaltrials.gov/ResultsExamples.pdf>

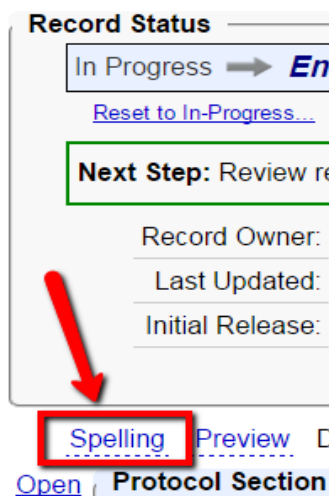
Practical Application: Top 10

Common Errors and Tips when Entering Basic Results:

1. The Enrollment # in the protocol section conflicts with the # of participants Started in the Participant Flow module
2. The Arm/Group Description should be used to provide additional details about the interventions administered *(e.g., dosage, dosage form, frequency of administration) or groups evaluated.

3. Expand all acronyms and abbreviations the first time used (and include acronym in parentheses).

Use “Spelling” feature



Record Status

In Progress → **En**

[Reset to In-Progress...](#)

Next Step: Review re

Record Owner:

Last Updated:

Initial Release:

Spelling Preview D

[Open](#) | **Protocol Section**

Possible Unexpanded Acronyms

Acronyms should be expanded at least the first time used in the Protocol section and (if applicable) in the Results section.
Example: National Institutes of Health (NIH)

Data Element	Acronym	Possible Expansion(s) [Show]
Detailed Description	AI	[15]
Detailed Description	DE	[8]
Detailed Description	ID	[45]
Primary Outcome Measure	OFC	[3]

Practical Application: Top Ten

Common Errors and Tips when Entering Basic Results:

4. Provide a brief but descriptive summary of the criteria used for the Outcome Measure/Assessment (“X” as assessed by “Y”)
5. # of Participants analyzed is not consistent with numbers provided in any of the rows in the Participant Flow Module
6. The Outcome Measure should be specific and measurable by the units of measure provided
7. Measure Title/Description (# of AEs) and Unit of Measure (# of Participants with AEs) are inconsistent
8. The time-frame provided is not specific.
9. Previous comments have not been addressed.
10. Provide brief but informative Arm/Group titles

Practical Application

- Legacy Studies -

When entering **Basic Results for legacy studies** (i.e. studies starting 2007 and earlier) with limited data accessibility or **older studies that changed significantly from the time that they were first registered**, one may attempt to punt via adding a link to the publication preceded by the following descriptive text (edit text as needed) under the “Basic Results/Limitations and Caveats” section (note: there is no guarantee this will be accepted by the clinicaltrials.gov office but it’s worked in the past for some SKCCC trials):

*“The raw study data is no longer available for this study [or] the design of this trial changed significantly from when it was first registered. The study’s publication can be accessed here:
[www.webaddresshere.com].”*

Practical Application

- Terminated Studies -

How do I submit results information if the trial is terminated (that is, stopped prematurely) and no data were collected for one or more Outcome Measures?

- If no participants were ever enrolled in the trial, set the Overall Recruitment Status to Withdrawn, and no further results information will need to be submitted.
- For a trial that was terminated after participants were enrolled, provide any available data. If no data are available for any of the Outcome Measures, specify zero ("0") for the Number of Participants Analyzed in each Arm/Group, and leave the data fields blank. Provide an explanation in the Analysis Population Description or the Limitations and Caveats module.

<https://clinicaltrials.gov/ct2/manage-recs/faq#terminated>

Practical Application

Suggested Best Practices







- **Consistent institutional identity and registration process**
 - Central registration assistance via a local PRS administrator
 - As a matter of policy the “Sponsor” should be listed as the RP
- **Maintain data during the conduct of the study**
 - RPs must update the record within 30 days of a change to:
 - Recruitment Status -or-
 - Completion Date
 - Record Verification Date must be updated at least every 6 months, even if no changes to the study (for all studies not yet completed).
- **RP must manage timelines (Calendar updates work well!)**

Practical Application

Enter your NCT number in eIRB

Current Status
Researcher Prep

Project Editor
View/Edit
Print Friendly
View Differences

Current Activities
 Submit
 Request Study Team Participation
 PI Withdraw
 Submit IND Safety Reports
 Alert PI
 Admin Changes

This can be done as an “Admin Change”

- Does not require a Change in Research
- Does not require the PI to submit

Admin Changes

Use the activity **ONLY** to update the application if the change pertains to one or more of the options provided below. All other changes require submission of a Change in Research application.

1. ☐ Change study team role and start/stop receiving study related notifications.
2. ☒ Update Clinical Trials registration information.

* Has the trial been registered?

☐ Yes ☐ No [Clear](#)

* Which trial registry site was this trial registered on?

ClinicalTrials.gov

* What is the registration number?

NCT12345678

"NCT" followed by 8 digits

Practical Application

- 1-on-1 assistance is now available at registerclinicaltrials@jhmi.edu
- Send all technical clinicaltrials.gov questions to register@clinicaltrials.gov

Results Section

[Enter Results](#) Results submission is required by FDAAA 801 for certain [applicable clinical trials](#) of drugs, biologics and devices. Note: other clinical trials may need to have results submitted based on other funder or sponsor policies.

[Delay Results](#) For applicable clinical trials subject to FDAAA 801, results submission may be delayed (in limited circumstances) with a Certification or Extension Request.

For more information see: [When Do I Need to Register and Submit Results?](#)

Need help with Results? [Contact ClinicalTrials.gov PRS](#) to request one-on-one assistance.

Further Training

- **Results Database Train-the-Trainer Workshop**
 - This workshop was developed for staff at National Institutes of Health (NIH) Clinical and Translational Science Award (CTSA) institutions who are responsible for providing ClinicalTrials.gov training and support to investigators and other staff who must submit summary results information to ClinicalTrials.gov. The workshop focuses on the data entry content and format requirements of the results database and provided hands-on tutorials on PRS data entry.
 - Two-day workshop held twice/year at NIH in Bethesda, MD
 - Workshop slides are posted on-line
<https://clinicaltrials.gov/ct2/manage-recs/present>

Summary

- Quiz!

Quiz (1 of 5)

How often should records in ClinicalTrials.gov be updated for ongoing studies?

- A. Weekly
- B. Within 30 days of a change to recruitment status or completion date
- C. Every 6 months
- D. Annually
- E. B + C

Quiz (2 of 5)

What studies need to be registered on ClinicalTrials.gov?

- A. Phase 1 trials
- B. Multi-center trials
- C. Behavioral Intervention studies
- D. Applicable clinical trials
- E. All of the above

Quiz (3 of 5)

When should basic results be reported?

- A. Within 6 months of the primary completion date
- B. Within 12 months of the primary completion date
- C. Within 6 months of the publication date
- D. Within 6 months of IRB closeout/termination
- E. Whenever I can get to it

Quiz (4 of 5)

What is true about the Responsible Party (RP)?

- A. The RP is the Principal Investigator (PI)
- B. As a matter of policy the “Sponsor” should be listed as the RP
- C. The RP is the only one who can edit information in ClinicalTrials.gov
- D. The RP releases records for review
- E. B & C
- F. B & D

Quiz (5 of 5)

Public information on ClinicalTrials.gov is written at the level of...?

- A. 5th grade reading level
- B. Members of the scientific community
- C. Readers of medical literature
- D. 12th grade reading level

Questions

- **JohnsHopkinsU (SOM, SON)** – Anthony Keyes, Nidhi Atri
registerclinicaltrials@jhmi.edu
- **Oncology (SKCCC)** – Monica Owens (Jhcccro@jhmi.edu)
- **JHSPH** – Miye Schakne (mschakne@jhsph.edu)

Thank You

It has been a tremendous pleasure and honor to launch this exciting new program

registerclinicaltrials@jhmi.edu



Select References

- ACT Wizard: http://grants.nih.gov/clinicaltrials_fdaaa/docs/Flow_chart-ACT_only.pdf
- Clinicaltrials.gov history: <https://www.clinicaltrials.gov/ct2/about-site/history>
- Clinicaltrials.gov homepage: <https://www.clinicaltrials.gov/>
- Clinicaltrials.gov FAQ: <https://clinicaltrials.gov/ct2/manage-recs/faq>
- NIH Guidance on FDAAA:
<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>
- FDA Guidance on Form FDA 3674:
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm125335.htm>
- Elaboration of Definitions of Responsible Party and Applicable Clinical Trial
<https://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf>

Select Publications

- Anderson ML, Chiswell K, Peterson ED, Tasneem A, Topping J, Califf RM. Compliance with Results Reporting at ClinicalTrials.gov. N ENGL J MED 2015; 372:1031-1039 MARCH 12, 2015 DOI: 10.1056/NEJMSa1409364. Available at. <http://www.nejm.org/doi/full/10.1056/NEJMSa1409364>
- Gopal AD, Desai NR, Tse T, Ross JS. Reporting of noninferiority trials in ClinicalTrials.gov and corresponding publications. JAMA. 2015 Mar 17;313(11):1163-
- Pillar C. Failure to Report: A STAT Investigation. STAT. 2015. Available at <http://www.statnews.com/2015/12/13/clinical-trials-investigation/>
- Williams RJ, Tse T, DiPiazza K, Zarin DA. [Terminated trials in the ClinicalTrials.gov results database: Evaluation of availability of primary outcome data and reasons for termination](#). PLoS One. 2015 May 26;10(5):e0127242. [[Full Text](#)]
- Zarin DA, Keselman A. Registering a clinical trial in ClinicalTrials.gov. Chest. 2007;131(3):909-12
- Zarin DA, Tse T. Sharing individual participant data (IPD) within the context of the trial reporting system (TRS). PLoS Med. 2016 Jan 19;13(1):e1001946. [[Full Text](#)]
- Zarin DA, Tse T, Ross JS. Trial-results reporting and academic medical centers. N Engl J Med. 2015 Jun 11;372(24):2371-2. [[Full Text](#)]

Appendixes: Overview and background

1997: Congress Passes FDAMA

- 1st U.S. law to require trial registration
- FDAMA Section 113 required NIH to create a public *information* resource on certain trials registered by FDA
- Registry designed to:
include information about federally or privately funded clinical trials conducted under investigational new drug applications (INDs) to test the effectiveness of experimental drugs for patients with serious or life-threatening diseases or conditions.

FDAMA: Food and Drug Administration Modernization Act

Source for timeline: <https://www.clinicaltrials.gov/ct2/about-site/history>

Overview and background

2000: NIH Releases ClinicalTrials.gov Web Site

- NIH National Library of Medicine (NLM) worked with FDA and others to develop ClinicalTrials.gov.
- First version of ClinicalTrials.gov published on Feb 29, 2000
- Registry primarily included NIH-funded studies

Overview and background

2000–2004: FDA Issues Guidance Documents

- 2000 - FDA issues draft guidance (provided recommendations for researchers submitting information to [ClinicalTrials.gov](https://clinicaltrials.gov)).
- 2002 - Final guidance document published
- 2004 - FDA proposed revised guidance (included new content for researchers submitting info required by the Best Pharmaceuticals for Children Act of 2002 (BPCA)).

Overview and background

2005: International Committee of Medical Journal Editors

- The ICMJE will require, as a condition of consideration for publication, registration in a public trials registry. Trials must register at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, **2005**.

<http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/>

Overview and background

2006: WHO Creates Trial Registration Policy

- World Health Organization (WHO) states that all clinical trials should be registered, and identified a minimum trial registration dataset of 20 items

2007: WHO launched the International Clinical Trials Registry Platform (ICTRP)

- Offers a **search portal** (not a registry) providing a single point of access to studies registered in various international registries
- Includes data available on [ClinicalTrials.gov](https://clinicaltrials.gov)

Overview and background

2007: Centers for Medicare & Medicaid Services (CMS)

National Coverage Determination (NCD) for Routine Costs in Clinical Trials (310.1) states:

- *Medicare covers the routine costs of qualifying clinical trials;*
- *PI must enroll qualifying clinical trials in ClinicalTrials.gov;*
- *If a research sponsor offers to pay cost-sharing/copays owed by the beneficiary, this could be a fraud and abuse problem (2009 memo)*

Overview and background

2007: Congress Passes FDAAA Expanding ClinicalTrials.gov Submission Requirements

Section 801 of FDAAA (FDAAA 801) requires:

- *More trials be registered;*
- *Additional trial registration information;*
- *Summary results, including adverse events, for certain trials.*
- *Law also included penalties for noncompliance, such as the withholding of NIH grant funding and civil monetary penalties of up to \$10,000 a day.*

FDAAA: Food and Drug Administration Amendments Act

<https://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf#page=82>

Overview and background

2007 FDAAA Cont:

- Per FDAAA 801, ClinicalTrials.gov now allows sponsors and principal investigators the ability to submit the results of clinical studies.
- Submission of adverse event information was optional when the results database was released (later required, circa Sep 2009).

Includes information about the Responsible Party, Applicable Clinical Trials, deadlines for submitting required information, and penalties.

<https://clinicaltrials.gov/ct2/manage-recs/fdaaa>

Overview and background: Role of the FDA

FDA has been given certain implementation and compliance/enforcement responsibilities related to Title VIII of FDAAA.

- Requiring a certification regarding compliance with ClinicalTrials.gov requirements to accompany IND/IDE
- Requiring the inclusion of a particular statement in the informed consent documents for "applicable clinical trials"
- Compliance and enforcement activities related to the failure to submit required clinical trial information

<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/FDAsRoleClinicalTrials.govInformation/default.htm>

Overview and background: Role of the FDA (cont.)

The following exact statement must be included in the informed consent documents of "applicable clinical trials":

“A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.” - 21CFR50.25c

Overview and background

2008: ClinicalTrials.gov Releases Results Database

Declaration of Helsinki Revision: Trial Registration and Results Dissemination

"Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject."

"Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties [i.e., researchers, authors, sponsors, editors and publishers] should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available."

Overview and background

2015: Full compliance with CMS (CR 8401)

Mandatory Reporting of Clinical Trial Number on Claims

- Trial-related claims will be returned if they do not contain the actual clinical trial identifier number (previously an 8-digit generic number, i.e., 99999999 could be used)
- Beginning January 1, 2015, without further notice, CR 8401 shall be fully implemented.

<https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/SE1344.pdf>

Overview and background

2015: NCI Issues Clinical Trial Access Policy

- Public access to results from National Cancer Institute (NCI)-supported clinical trials.
- Final results are expected to be reported in a publicly accessible manner within twelve (12) months of the trial's primary completion date, **regardless of whether the clinical trial was completed as planned or terminated earlier.**
- Policy incorporated as a Term and Condition of NCI award.

Commonly Received PRS Comments

Please remove all personal pronouns. For example, please change "we" to "the investigators" and "you" to "participants."

Please review the Intervention Descriptions. They are currently identical and this should not usually be the case. Each Intervention Description should be Intervention and Arm-specific.

Please review the entire record and expand all acronyms and abbreviations (and include acronym in parentheses) at least the first time used in **both the Protocol and Results section. The Spelling link at the top of the "Record Summary" page can be used to help locate and spell out unexpanded acronyms.**

Commonly Received PRS Comments

Outcome Measures

The Time Frame provided is not specific. The Time Frame should indicate the specific time point(s) at which the outcome measure will be assessed and for which data will be presented. (e.g., "1 year" or "up to 24 weeks", "through study completion, an average of 1 year", etc.).

The Outcome Measure describes multiple assessments with potentially different Units of Measure. Assessments with different Units of Measure (e.g., BMI in kg/m^2 , weight in kilograms, height in meters) must be presented in separate Outcome Measures. Please revise to present these assessments in separate Outcome Measures, as appropriate, or to clarify how multiple measurements will be aggregated to arrive at one reported value (e.g., Number of Participants With Abnormal Laboratory Values and/or Adverse Events That Are Related to Treatment).

The Outcome Measure Title is vague; it is unclear what will be measured and reported. In the Title field, specify the measurement that will be used (e.g., descriptive name of scale, physiological parameter, questionnaire) and, if relevant, how the collected measurement data will be aggregated. Use the Description field, for any additional information about the measurement or metric for summarizing the data. For example, an Outcome Measure Title of "Safety and Tolerability" does not sufficiently describe how quantitative data will be reported. A specific Title would instead be "Number of participants with treatment-related adverse events as assessed by CTCAE v4.0".



**Biostatistics, Epidemiology
And Data Management**

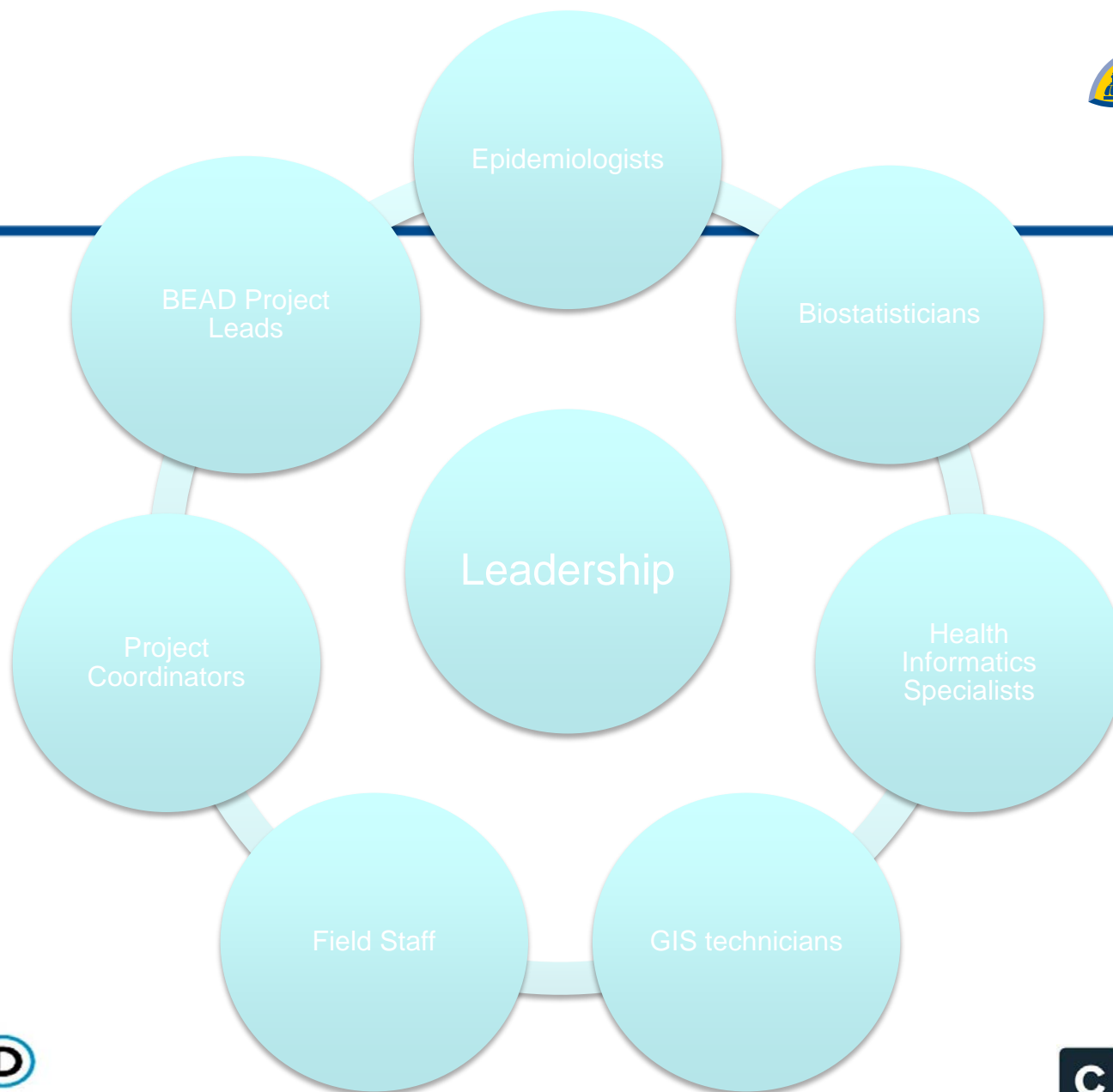
<http://jhcchr.org/bead/>

CCHR BEAD Core Mission

To provide research support services that promote, strengthen and expand the research of the Johns Hopkins University faculty so that we remain one of the top interdisciplinary research institutions, focused on improving the health and well-being of individuals, families and their communities.

Core Research Support Services

- Epidemiologic study design and approach
- Biostatistical analyses (basic, complex)
- Qualitative study design and analyses
- Database development and management
- Survey design review
- IRB submissions
- Grant submissions – review, statistical plans, power calculations, budget for services
- Research training seminars



How does the model work?

- One hour initial consultation
- Subsidized research support services for Pediatric and Bayview faculty members and their trainees
- Transition to direct-fee-for-service for value and sustainability
- Rates in line with other institutional support services

Benefits of the BEAD Model

- Conceptualization of faculty research as a developmental process
- Model of support that is service-based, responsive and efficient
- Strong focus on epidemiology and a mentored support structure
- Built on teamwork and collaboration
- Extensive grantsmanship experience (NIH, Foundation grants, PCORI)
- Breadth of content, methods, statistical expertise⁷⁸

Our Partners

- Johns Hopkins Institute for Clinical and Translational Research (ICTR)
- Johns Hopkins Biostatistics Center
- All Children's Hospital, St. Petersburg, FL
- Johns Hopkins Bloomberg School of Public Health

Tips

- Contact us early
 - Grant deadlines are similar for faculty across JHMI (September/October; May/June)
 - Faculty in need of statistical plans often also require study design assistance
- Allow plenty of time
 - Min 1 month for small database once all aspects are complete
 - Initial consults 2-4 weeks from contact date

For research support services contact:

CCHRBEAD@jhmi.edu

<http://jhcchr.org/bead/>



**Biostatistics, Epidemiology
And Data Management**