Recent Changes to ClinicalTrials.gov

What every PI and Research Team Member Should Know

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Objectives

- Provide an overview of the history, aims, and expansion of ClinicalTrials.gov
- Briefly describe the registration, updating, and results reporting processes, the underlying regulatory requirements, and the consequences for noncompliance (eg potential daily fines and funding interruptions)
- Review the recent changes to ClinicalTrials.gov and the PRS (Protocol Registration and Results System)
- Compare the 'modernized' to the 'classic' versions of the public website ClinicalTrials.gov and the PRS

ClinicalTrials.gov

- ClinicalTrials.gov is a **website** and **online database** of clinical research studies and information about their results.
- The purpose of ClinicalTrials.gov is to provide information about clinical research studies to the public, researchers, and health care professionals.
- The NLM maintains CTgov but the U.S. government does not review or approve the safety and science of all studies listed on this website.
- ClinicalTrials.gov:
  - Relies on sponsors or investigators to submit and update information about studies
  - Lists up-to-date information on clinical research studies and their results with new studies added almost every day
  - Includes studies that take place in all 50 states and over 200 countries
  - Supports laws, regulations, and policies that require sponsors and investigators to publicly share information about clinical trials, including results

Two Aims of ClinicalTrials.gov

ClinicalTrials.gov
PRS Protocol Registration & Results System
register.clinicaltrials.gov

1 **Collect and disseminate** complete, accurate, and timely information about clinical studies submitted by study sponsors and principal investigators.

ClinicalTrials.gov

2 **Facilitate information use** to help patients, clinicians, and researchers find studies of interest for participation or research.

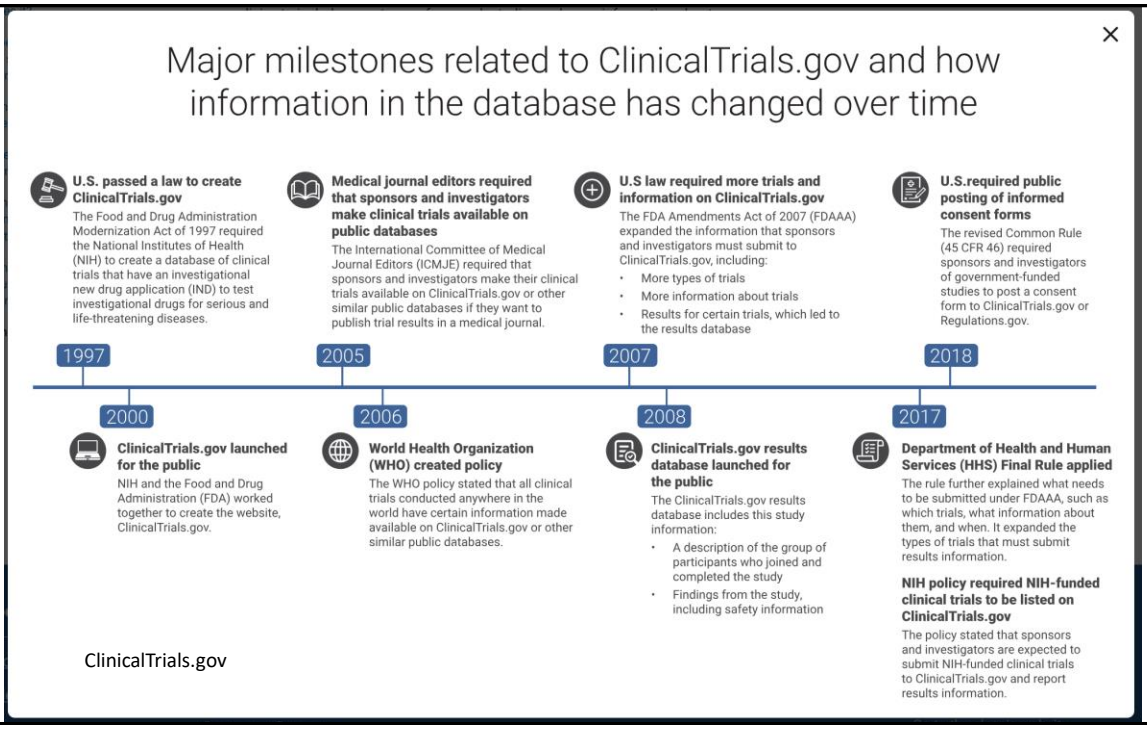
NIH National Library of Medicine

ClinicalTrials.gov

ClinicalTrials.gov Primary Users

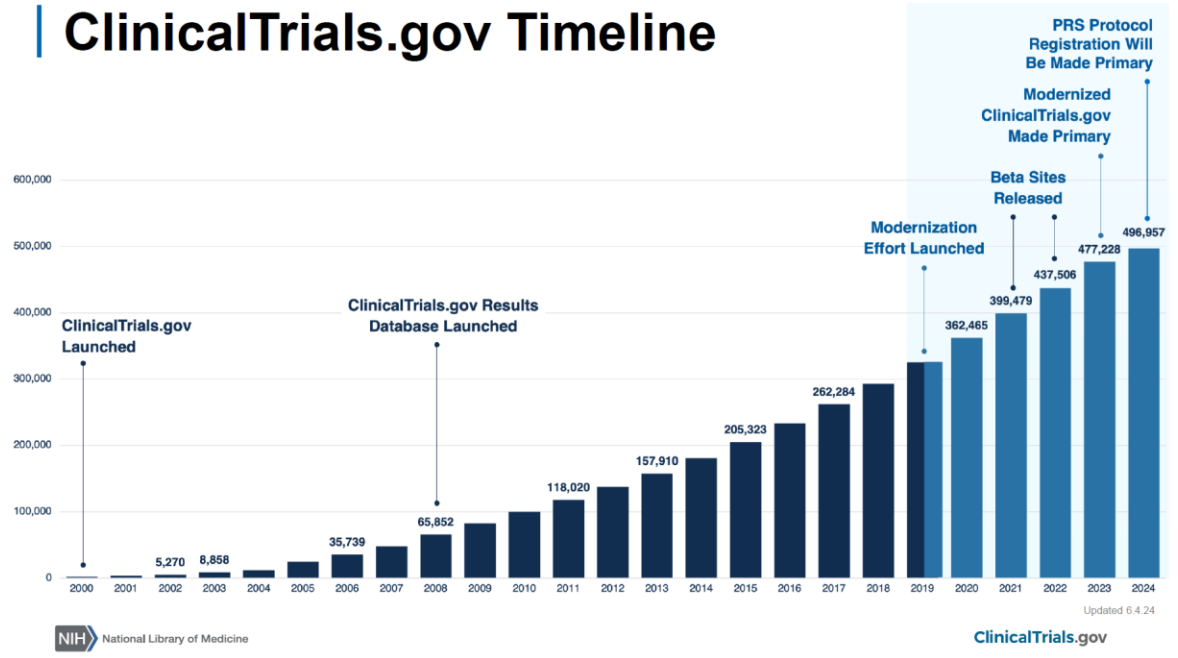
Why was ClinicalTrials.gov created?

- ClinicalTrials.gov was created as part of the 1997 FDAMA (Food and Drug Administration Modernization Act of 1997). This federal law required the National Institutes of Health (NIH) to create a database of clinical trials that have an investigational new drug (IND) application to test investigational drugs for serious or life-threatening diseases.
  - NLM of the NIH created ClinicalTrials.gov which was launched the end of Feb 2000.
- Since then, ClinicalTrials.gov has expanded based on other laws, regulations, and policies to include more types of research studies and more information about these studies.
  - Subsequent changes to the law via FDAAA (the Food and Drug Administration Amendments Act of 2007) to its 'Final Rule' in 2017 provide a legal definition of Applicable Clinical Trials (**ACTs**) for which the law applies and details about registration, maintenance, and results reporting to remain in compliance with the law.
  - These laws, regulations, and policies ensure that information about ongoing and completed studies and their results are publicly available for people to consider joining and to inform investigators and future research.
- With a public registry for clinical trials in place to meet legal requirements, other entities have taken advantage of the ClinicalTrials.gov platform for their own purpose.



Additional milestones

- **2007** Centers for Medicare & Medicaid Services (CMS) require qualifying clinical trials registered to the public database.
- **2015** CMS mandates National Clinical Trial (NCT) numbers are reported on all claims.
- **2019** The revised Common Rule (45 CFR 46.116(h)) requires that any clinical trial conducted or supported by a Common Rule department or agency, must post one informed consent form that was used on the study in enrolling participants on a publicly available Federal website within a specific time frame. ClinicalTrials.gov and Regulations.gov are the currently approved federal websites.
- **2019** ICMJE required the description of an Individual Participant Data (**IPD**) Sharing Plan at registration to ClinicalTrials.gov to encourage researchers to share and leverage data from participant volunteers.
- The result of layering additional requirements with differing expectations on a framework not designed with their compliance in mind can create confusion, frustration, and reactivity toward compliance. It also buries the bigger picture of why the database was established in the first place, *as a participant-centered resource*.



What clinical studies can be registered in ClinicalTrials.gov?

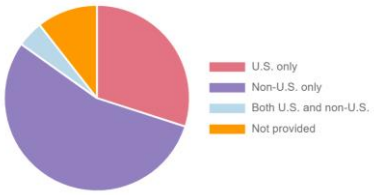
- ClinicalTrials.gov lists studies that involve people, have health-related research questions, and follow ethics review and other health authority rules and laws. The ClinicalTrials.gov database includes:
  - Interventional studies/Clinical trials: research studies in which researchers assign participants to get one or more interventions (such as a drug, behavior, or medical device) to investigate what happens in people.
  - Observational studies: research studies in which researchers collect information from participants or look at data that was already collected. The data may be about participants' health, habits, or environments. In observational studies, researchers do not assign participants to get an intervention. If there is an intervention, participants were already using it as part of their regular health care or daily life.
  - Expanded access: a possible way for a patient with a serious illness who is unable to take part in a clinical trial to get an intervention, such as a drug or medical device, that isn't approved for treatment. More about expanded access on the FDA's website.

Locations of registered studies

The chart below shows the distribution of locations for all studies registered on ClinicalTrials.gov.

Percentage of registered studies by location (as of 2024-09-05)

Total of 507,934 studies



Types of registered studies

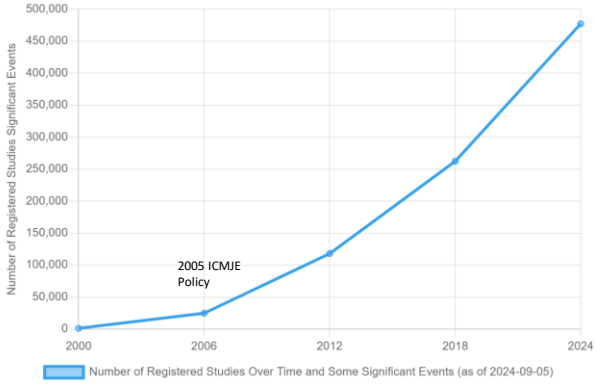
The table below shows the number and types of studies that are registered and have results posted on ClinicalTrials.gov.

Study and Intervention Type (as of 2024-09-05)		Number of Registered Studies and Percentage of Total	Number of Studies With Posted Results and Percentage of Total***
Total		507,934	65,996
Interventional		389,200 (77%)	62,328 (94%)
Type of Intervention*	Drug or biologic	196,094	45,907
	Behavioral, other	146,060	14,101
	Surgical procedure	40,503	3,181
	Device**	52,827	9,322
Observational		116,893 (23%)	3,668 (6%)
Expanded Access		951	N/A

https://clinicaltrials.gov/about-site/trends-charts

Number of registered studies over time

The graph and table below show the total number of studies posted on ClinicalTrials.gov since 2000, based on the First Posted date. The first version of ClinicalTrials.gov was made available to the public on February 29, 2000.



Key:

ICMJE: Indicates when the International Committee of Medical Journal Editors (ICMJE) began requiring trial registration as a condition of publication (September 2005)

https://clinicaltrials.gov/about-site/trends-charts

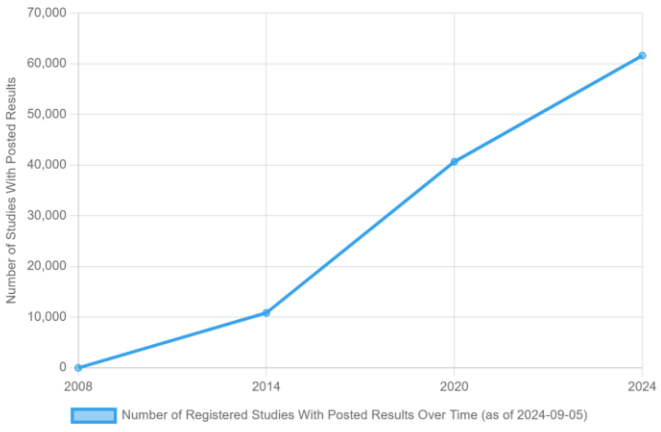
ICMJE Role in promoting data sharing

Data sharing required by ICMJE

- As of July 1, 2018 manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statement.
- Clinical trials that begin enrolling participants on or after January 1, 2019 must include a data sharing plan in the trial's registration.
  - If the data sharing plan changes after registration this should be reflected in the statement submitted and published with the manuscript and updated in the registry record.
- Data sharing statements must indicate the following:
  - whether individual de-identified participant data (including data dictionaries) will be shared ("undecided" is not an acceptable answer)
  - what data in particular will be shared; whether additional, related documents will be available (e.g., study protocol, statistical analysis plan, etc.)
  - when the data will become available and for how long; by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism).

Number of registered studies with posted results over time

The graph and table below show the number of registered studies with results posted on ClinicalTrials.gov, based on the Results First Posted date. ClinicalTrials.gov launched its results database in September 2008, at which time sponsors or investigators could begin submitting results for their registered studies. The results database was first developed to accommodate the results submission requirements outlined in FDAAA. See Which trials must have results submitted? and When to submit results on the FDAAA 801 page for more information.



https://clinicaltrials.gov/about-site/trends-charts

Final Rule for FDAAA 801 Issue

- In September 2016, the U.S. Department of Health and Human Services issued a Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11) that **clarifies and expands the regulatory requirements and procedures for submitting registration and summary results information of clinical trials on ClinicalTrials.gov, in accordance with Section 801 of the Food and Drug Administrations Amendments Act (FDAAA) of 2007 known as FDAAA 801**.
- The final rule is intended to make it clear to sponsors, investigators, and the public which trials must be submitted, when they must be submitted, and whether compliance has been achieved.
  - For example, the final rule clarifies the definition of an **Applicable Clinical Trial (ACT)** and provides structured criteria for determining which studies meet the definition.
- The final rule also expands the FDAAA 801 requirements by requiring the submission of results information for trials of unapproved products.
  - The regulation became effective on **January 18, 2017** and responsible parties were expected to be in compliance as of **April 18, 2017**.

Final NIH Policy on the Dissemination of NIH-funded Clinical Trial Information Issued

- In September 2016, NIH issued a final policy to promote broad and responsible dissemination of information from NIH-funded clinical trials through ClinicalTrials.gov.
- Under this policy, **every clinical trial funded in whole or in part by NIH is expected to be registered on ClinicalTrials.gov and have summary results information submitted and posted in a timely manner, whether subject to FDAAA 801 or not.**
- This policy is effective for *intramural and extramural* applications for funding, including grants, other transactions, and contracts **submitted on or after January 18, 2017**.

Why is trial registration Important?

The registration of all interventional trials is considered to be a scientific, ethical and moral responsibility.

- There is a need to ensure that decisions about health care are informed by all of the available evidence
- It is difficult to make informed decisions if publication bias and selective reporting are present
- The Declaration of Helsinki states that "**Every clinical trial** must be registered in a publicly accessible database before recruitment of the first subject".
- Improving awareness of similar or identical trials will make it possible for researchers and funding agencies to avoid unnecessary duplication
- Describing clinical trials in progress can make it easier to identify gaps in clinical trials research
- Making researchers and potential participants aware of recruiting trials may facilitate recruitment
- Enabling researchers and health care practitioners to identify trials in which they may have an interest could result in more effective collaboration among researchers. The type of collaboration may include prospective meta-analysis
- Registries checking data as part of the registration process may lead to improvements in the quality of clinical trials by making it possible to identify potential problems (such as problematic randomization methods) early in the research process

Benefits of Registration and Results Reporting

- Help patients and the public know what trials are planned or ongoing into which they might want to enroll
  - Support enrollment
- Help give ethics review boards considering approval of new studies a view of similar work and data relevant to the research they are considering.
  - Identify unmet research needs
- Facilitate complete reporting
- Prevent and avoid unnecessary duplication of research effort
- Honor commitment to participants that their contributions will advance science
- Contribute to increased public trust in clinical research
- Prevent selective publication and selective reporting of research outcomes
  - Mitigate positive results publication bias
- Advance stewardship and accountability
- Evaluate research integrity
- Support evidence-based medicine

Clinical Trials.gov Promotes Transparency and Scientific Integrity

Transparency promotes access to the evidence or data used to support empirical research claims and assesses how they relate to broader claims and to evaluate whether they have been interpreted or analyzed correctly.

Public disclosure of study descriptions, designs, eligibility criteria, outcome measures, full protocol and statistical analysis plans, clinical results, and soon lay summaries.

Scientific integrity deals with best practices or rules of professional practice of researchers, stemming from a 2007 OECD (Organization for Economic Co-operation and Development), and is set in the context of the replication crisis and the fight against scientific misconduct.

Replication crisis is the finding that many scientific studies are difficult or impossible to replicate or reproduce. It most severely affects the social sciences and medicine

Scientific misconduct is the violation of the standard codes of scholarly conduct and ethical behavior in the publication of professional scientific research.

Mandatory CTgov Registration

CTgov registration is required when any of the following conditions are met:

- The International Committee of Medical Journal Editors' (ICMJE) Uniform Requirements for Manuscripts Submitted to Biomedical Journals [2005 policy] require ClinicalTrials.gov registration prior to enrollment of the first participant as a condition of consideration for publication.
- The Food and Drug Administration (FDA) requires registration for all Applicable Clinical Trials (ACTs) on ClinicalTrials.gov within 21 days of the first participant's enrollment.
  - ACTs are clinical trials of FDA-regulated drug, biologic, or device products
  - Use the ACT Checklist for help in determining whether a study is an ACT
- NIH funded Clinical trials including BESH trials that are funded in whole or in part by the NIH
- Centers for Medicare and Medicaid Services (CMS) requires registration for qualifying trials that evaluate a therapeutic item or service that falls within the Medicare benefit category

ICMJE Definition of a Clinical Trial

- In June 2007, the ICMJE adopted the WHO's definition of clinical trial:

  "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events."
- Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration.
- Those who are uncertain whether their trial meets the expanded ICMJE definition should err on the side of registration if they wish to seek publication in an ICMJE journal.
- If researchers or others have questions about the need to register a specific study, they should err on the side of registration or consult the editorial office of the journal they wish to publish the study in.

www.ICMJE.org

Instructions: Answer the following questions to evaluate whether the study is an applicable clinical trial (ACT). Use the accompanying "Elaboration" for additional information to help answer the questions.

Question	Yes	No
1. Is the study interventional (a clinical trial)? *Study Type* data element is "Interventional"	☐	☐
2. Do ANY of the following apply (is the answer "Yes" to at least one of the following sub-questions: 2a, 2b, OR 2c)?	☐	☐
a. Is at least one study facility located in the United States or a U.S. territory? *Facility Location – Country* data element is "United States," "American Samoa," "Guam," "Northern Mariana Islands," "Puerto Rico," "U.S. Virgin Islands," or other U.S. territory.		
b. Is the study conducted under a U.S. FDA Investigational New Drug application (IND) or Investigational Device Exemption (IDE)? *U.S. Food and Drug Administration IND or IDE Number* data element is "Yes."		
c. Does the study involve a drug, biological, or device product that is manufactured in and exported from the U.S. (or a U.S. territory) for study in another country? *Product Manufactured in and Exported from the U.S.* data element is "Yes."		
3. Does the study evaluate at least one drug, biological, or device product regulated by the United States Food and Drug Administration (U.S. FDA)? *Studies a U.S. FDA-regulated Device Product* data element is "Yes" and/or *Studies a U.S. FDA-regulated Drug Product* data element is "Yes."	☐	☐
4. Is the study other than a Phase 1 trial of a drug and/or biological product or is the study other than a device feasibility study? For drug product trials, *Study Phase* data element is NOT "Phase 1" and for device product trials, *Primary Purpose* is NOT "Device Feasibility."	☐	☐

If "Yes" is answered to all 4 questions, and the study was initiated on or after January 18, 2017, the trial would meet the definition of an ACT that is required to be registered under 42 CFR 11.22.

https://cdn.clinicaltrials.gov/documents/ACT_Checklist.pdf

NIH Clinical Trial Definition

A research study[1] in which one or more human subjects[2] are prospectively assigned[3] to one or more interventions[4] (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.[5]

[1]See Common Rule definition of ***research*** at 45 CFR 46.102(d).

[2]See Common Rule definition of ***human subject*** at 45 CFR 46.102(f).

[3]The term "***prospectively assigned***" refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

https://grants.nih.gov/policy/clinical-trials/definition.htm

[4]An ***intervention*** is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints.

- *Examples include*: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and diagnostic strategies.

[5]***Health-related biomedical or behavioral outcome*** is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life.

- *Examples include*: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and positive or negative changes to quality of life.

Based on the NIH Definition, Ask 4 questions to determine if a study is a CT

1. **Does the study involve human participants?**
2. **Are the participants prospectively assigned to an intervention?**
3. **Is the study designed to evaluate the effect of the intervention on the participants?**
4. **Is the effect being evaluated a health-related biomedical or behavioral outcome?**

If the answer to all four questions is "yes," then the clinical study would be considered a clinical trial according to the NIH definition, even if it:

- is studying healthy participants
- does not have a comparison group (e.g., placebo or control)
- is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- is utilizing a behavioral intervention
- only one aim or sub-aim of the study meets the clinical trial definition

- Clinical studies that are not considered trials are those:
  - intended solely to refine measures
  - that involve secondary research with biological specimens or health information

https://grants.nih.gov/ct-decision/index.htm

ClinicalTrials.gov Records require the following maintenance

ClinicalTrials.gov records are dynamic and require routine maintenance to remain compliant. The OHRA assists the PI and Study Teams to maintain accurate records.

- Register the study on CTgov before IRB approval per HRPP policies
- Update of Anticipated Study Start Date to Actual Start Date (date of first participant consent) within 30 days
- Update of Study Status Changes within 30 days
- Update of Anticipated Enrollment to Actual Enrollment at Closed to Accrual
- Update of ClinicalTrials.gov records to reflect applicable institutional study changes including protocol amendments, change of Principal Investigator, participating site additions or withdrawal, and funding/collaborator changes as required within 30 days of change
- Upload of a consent form that was used to consent participants any time after the trial is closed to recruitment, but no later than 60 days after the last study visit by any subject (for federally funded studies, as applicable)
- At least annual Record Verification if there have been no other Study Changes*
- Update of Anticipated Primary and Study Completion Dates to Actual Completion Dates
- Submission of Results within 10 months of the Primary Completion Date
- Submission of remaining results (secondary and ancillary) within 1 year of Study Completion Date, if different than Primary Completion Date

** Update Record verification date to the month/year each time the record is entered.*

When to Transfer a ClinicalTrials.gov Record

- If the study is ongoing and will continue at the new Institution, **the ClinicalTrials.gov record should be transferred to the new Institution**. Example: An awardee or Principal Investigator (PI) of a federally funded grant is transferring to a new Institution and the grant will be transferring with the PI.
- If the study is completed, and will not continue at the new Institution, **the record should be completed in the PRS account of the Institution where the research took place** (otherwise it would appear that the new Institution was the sponsor of the study even though it was not associated with the study.)
  - This means allowing the departing PI to retain access in the departed Institution's PRS account until such records are completed.

Recent Changes in ClinicalTrials.gov

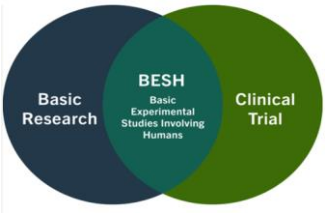
- Longer times for NLM registration and results review
- BESH clinical trials (NIH funded)
- Multiple time frames for primary outcome measures
- Increased specificity of outcome measure descriptions
- Expansion of IPD sharing section
- Enhanced harmonization of ClinicalTrials.gov information and data with:
  - NIH information and reports
  - Manuscripts submitted for journal review
- Increased enforcement and consequences for noncompliance
  - Journal 'creep'
- The home institution for the PI (BUMC or BMC) is the Responsible Party/RP unless there is an IND/IDE held by the PI
- ClinicalTrials.gov and PRS Modernization Initiative

BESH Definition

- Basic experimental studies involving humans (BESH) are studies that meet both the federal definition of basic research and the NIH definition of a clinical trial:

  - ***Federal definition of basic research***
    A systematic study directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications towards processes or products in mind. (32 CFR 272.3)
  - ***NIH definition of a Clinical Trial***
    A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.
    - A 'yes' response to each of the four NIH CT questions

https://grants.nih.gov/policy/clinical-trials/besh.htm



Key Characteristics of BESH

The study uses an experimental manipulation/intervention to understand a basic phenomenon

- Basic research uses a range of probes or experimental manipulations to perturb a physiological process (including cognitive and perceptual processes) . Under the NIH definition of a clinical trial, most experimental manipulations involving humans are considered to be interventions.

The intervention/experimental manipulation is not intended to change the health status of the participants

- The NIH definition of clinical trial defines intervention as " a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints."

For BESH studies, interventions include a wide range of probes, tasks, or other procedures to control, isolate, and/or manipulate a study variable (typically the independent variable).

- For example, evaluating the effect of the intervention on the participants in BESH often takes the form of *observing the effect of the manipulation on a physiological, psychological, or social process (including cognitive and perceptual processes).*

Intervention vs Measurement

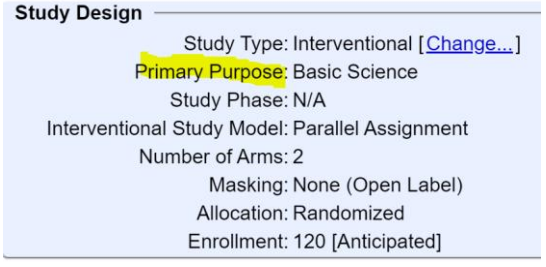
Sometimes the same specific task or test could represent either an "intervention" or a "measurement" depending on how it is used, what is being measured, and why. Because of this, there cannot be a list of tests that are always measurements, or always interventions.

The context of how a task is used is important in determining whether it is being used as an intervention or a measurement.

If the task or test is being used to purposefully change or manipulate something about the participant and is being used to explore a concept – ***the task or test is probably an intervention.***

Think of the intervention as the independent variable in a study.

On CTgov, whether the clinical research study is a CT or BESH is not specified



Study Design

Study Type:	Interventional [Change...]
Primary Purpose:	Basic Science
Study Phase:	N/A
Interventional Study Model:	Parallel Assignment
Number of Arms:	2
Masking:	None (Open Label)
Allocation:	Randomized
Enrollment:	120 [Anticipated]

Primary Purpose
Definition: The main objective of the intervention(s) being evaluated by the clinical trial.

Options for 'Primary Purpose' in the PRS Study Design Section

- **Treatment**: One or more interventions are being evaluated for treating a disease, syndrome, or condition.
- **Prevention**: One or more interventions are being assessed for preventing the development of a specific disease or health condition.
- **Diagnostic**: One or more interventions are being evaluated for identifying a disease or health condition.
- **Supportive Care**: One or more interventions are evaluated for maximizing comfort, minimizing side effects, or mitigating against a decline in the participant's health or function.
- **Screening**: One or more interventions are assessed or examined for identifying a condition, or risk factors for a condition, in people who are not yet known to have the condition or risk factor.
- **Health Services Research**: One or more interventions for evaluating the delivery, processes, management, organization, or financing of healthcare.
- **Basic Science**: One or more interventions for examining the basic mechanism of action (for example, physiology or biomechanics of an intervention).
- **Device Feasibility**: An intervention of a device product is being evaluated in a small clinical trial (generally fewer than 10 participants) to determine the feasibility of the product; or a clinical trial to test a prototype device for feasibility and not health outcomes. Such studies are conducted to confirm the design and operating specifications of a device before beginning a full clinical trial.
- **Other**: None of the other options applies.

Multiple Time Frames for Primary Outcome Measures

Outcome Measures

Primary Outcome Measure:
1. Anxiety symptoms

Change in anxiety symptoms using the Mental Health Assessment Inventory (MHAI) anxiety subscore

[Time Frame: Baseline, 3 months, 6 months. 9 months, 12 months]

More Specificty of Outcome Measure Descriptions

Outcome Measures

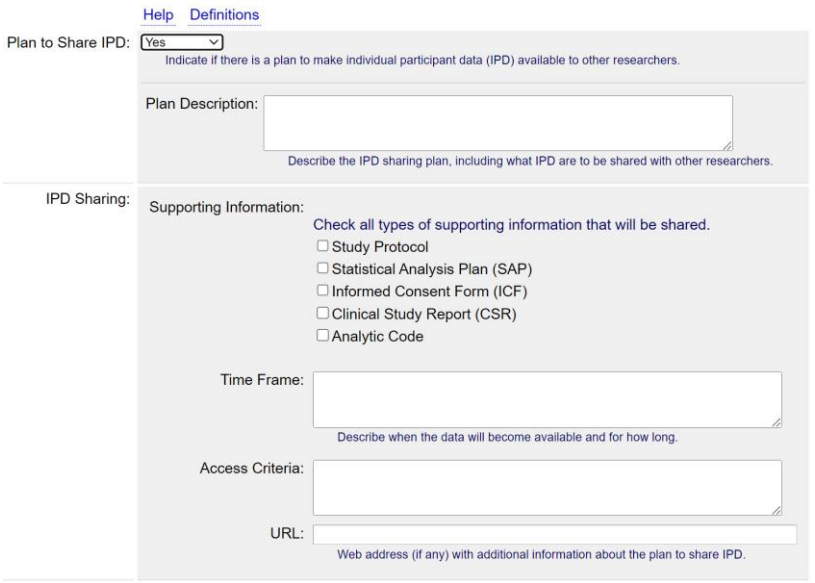
Primary Outcome Measure:
1. Anxiety symptoms

Anxiety will be assessed using the Mental Health Assessment Inventory (MHAI). It is a 12-item instrument with potential responses from 0 to 4, where 0= None and 4= 3 or more times daily.

Scores can range from 0 to 48. Higher scores are associated with greater anxiety.

[Time Frame: Baseline, 3 months, 6 months. 9 months, 12 months]

Expansion of IPD Data Section



Enhanced Focus on Harmonization of ClinicalTrials.gov Information

- ClinicalTrials.gov data are linked with the NIH databases so discrepancies such as with NIH Assist and RPPRs are identified and reported to the project officers (PO) who contacts the PI to the adjudicate any errors.
  - The RP/PRS Administrator will assist with harmonizing the discrepant information
- Manuscripts related to studies registered on ClinicalTrials.gov list the NCT# soand reviewers are instructed by the editor to compare the information in the manuscripts (eg methods, eligibility criteria, sample size, and results with the information on ClinicalTrials.gov
  - Authors are contacted if discrepancies are identified
  - The RP/PRS Administrator will assist with harmonizing the discrepant information

Increased Enforcement and Consequences for Noncompliance

- Unable to have manuscripts published in journals that subscribe to ICMJE policies if the clinical trial was not registered on CTgov prior to enrollment of any participant
  - 'Journal creep' is occurring where some journals are sending back manuscripts even if the research does meet the ICMJE definition of a clinical trial [eg some even for observational studies)
  - When in doubt register your clinical research study on CTgov to avoid publication issues
- Potential legal consequences for responsible parties and their institution if they do not comply with the requirements to submit registration and results information on ACTs, described in 42 CFR 11.66
  - Potential legal consequences include civil or criminal judicial actions, civil monetary penalty actions, and grant funding actions
  - FDA is issuing many more pre-notices for noncompliance warning letters
  - In 2024, fines for late FDAAA are $14,262/day
- For NIH funded studies, grant funds can be withheld for a specific study or for the institution
- The institution/organization can be featured in published articles on CTgov noncompliance and there are many watchdog groups and websites to identify noncompliant records.

The PI's Home Institution is the Responsible Party (RP) for studies that do not have an IND or IDE

- The RP is responsible for submitting all information in the PRS including record registration, updating, and if required submitting results.
- For ACTs- Regulations (42 CFR Part 11)
  - The final rule specifies that there must be one (and only one) responsible party for purposes of submitting information about an applicable clinical trial. The sponsor of an applicable clinical trial will be considered the responsible party, unless and until the sponsor designates a qualified principal investigator as the responsible party. This final rule specifies the approach for determining who will be considered the sponsor of an applicable clinical trial under various conditions, what qualifies a principal investigator to be designated a responsible party by a sponsor, and how responsibility reverts to the sponsor if a designated principal investigator is unable to fulfill the requirements for submitting information to ClinicalTrials.gov unless and until the sponsor designates another principal investigator as the responsible party (42 CFR Part 11). For more information, see 81 FR 64982.

ClinicalTrials.gov BMC/BUMC HRPP Policies

6.6.9 Registering, Updating, and Posting Requirements for Clinical Trials (Revised 10/20/23

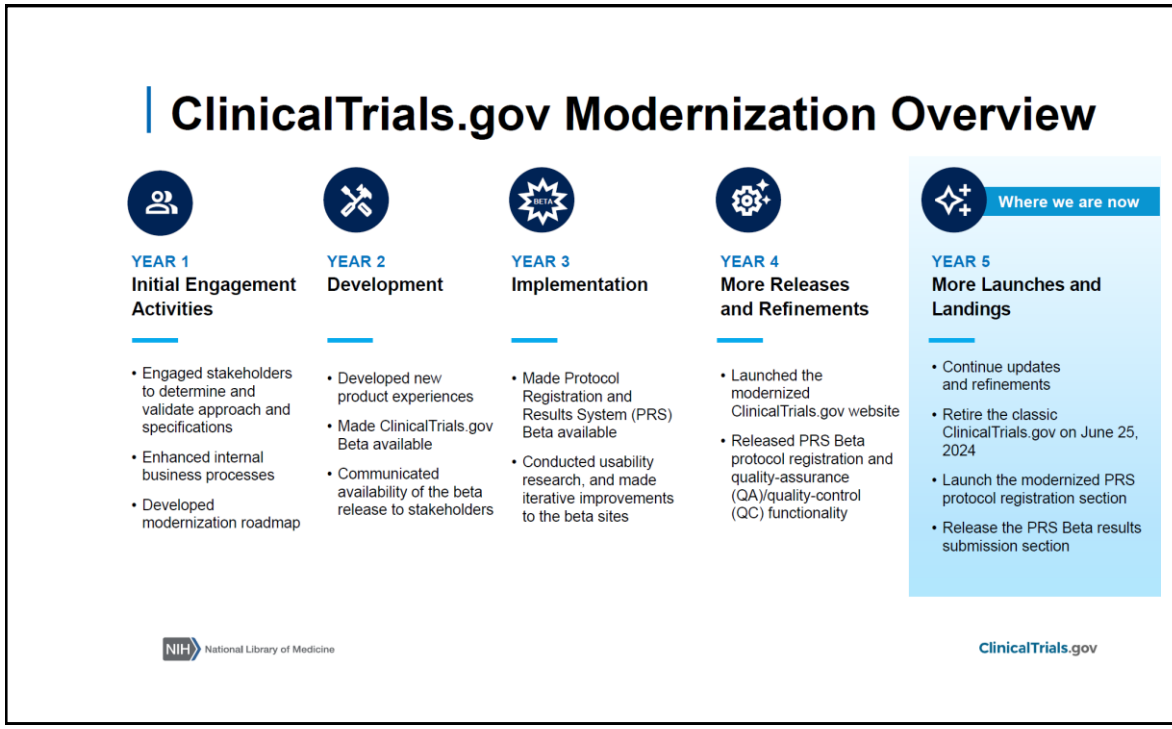
- All studies meeting the definition of a clinical trial according to the International Committee of Medical Journal Editors (see Section 13) must be registered on ClinicalTrials.gov before final IRB approval is issued. NIH-funded Basic Experimental Studies Involving Humans (BESH) that meet both the federal definition of basic research and the NIH definition of a clinical trial must also be registered on ClinicalTrials.gov before final IRB approval is issued.
- For all studies meeting the definition of a clinical trial, IRB approval will be issued only after the NCT number (assigned at registration on ClinicalTrials.gov) is communicated to the IRB as documentation that the trial has been registered. The responsible party must comply with all applicable updating and posting requirements (see http://www.bumc.bu.edu/ohra/clinicaltrials-gov/).
- For clinical trials that involve an IND or IDE held by the Principal Investigator at Boston Medical Center or Boston University Medical Campus, the Principal Investigator is the responsible party, regardless of how the clinical trial is funded.
- For clinical trials that are initiated by an external sponsor and do not involve an IND or IDE held by the Principal Investigator at Boston Medical Center or Boston University Medical Campus, the responsible party is the sponsor of the clinical study, as defined in 42 CFR 11.10(a).

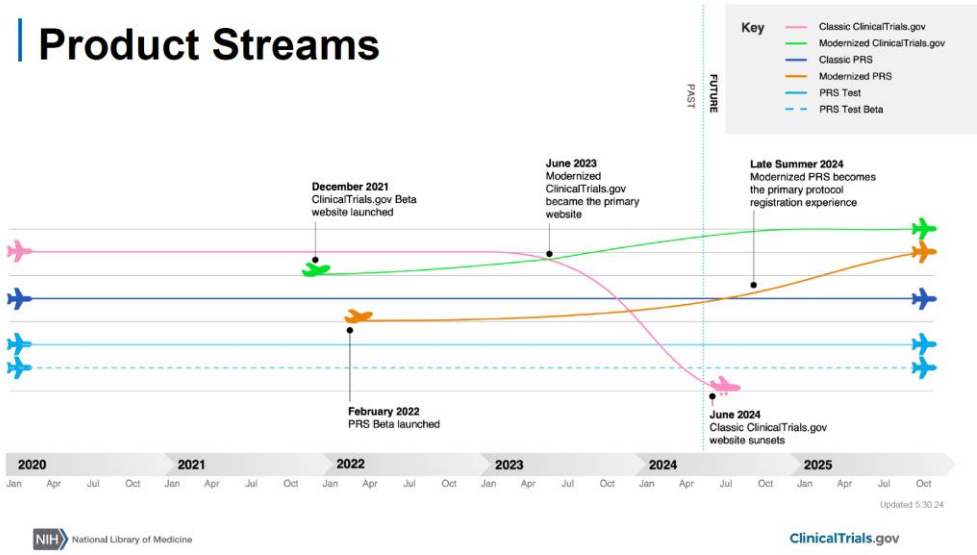
ClinicalTrials.gov BMC/BUMC HRPP Policies *(cont)*

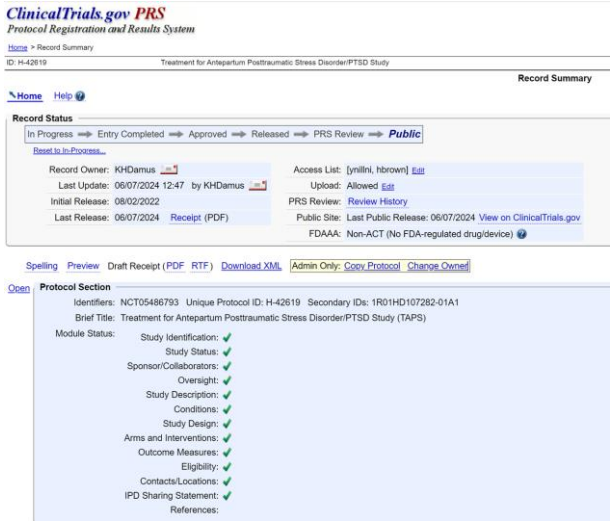
- For all other clinical trials that are initiated by the Principal Investigator at Boston Medical Center or Boston University Medical Campus, the responsible party is the home institution of the Principal Investigator (Boston Medical Center or Boston University).
- Boston Medical Center and Boston University Medical Campus will register a study on ClinicalTrials.gov if the Principal Investigator is the sponsor of the study, and/or if Boston Medical Center or Boston University Medical Campus is the prime awardee of the external funding, or if Boston Medical Center or Boston University Medical Campus is determined to be the main site in a multi-site study.
- If results are required to be posted, the initial submission of results must occur **no later than 10 months** after the actual primary completion date, to allow time for results review by ClinicalTrials.gov.
- For clinical trials supported by a Federal department or agency that are approved on or after January 21, 2019, if the Principal Investigator at Boston Medical Center or Boston University Medical Campus is the responsible party, the PI must ensure that one blank IRB-approved informed consent form used to enroll subjects is posted on ClinicalTrials.gov after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.
- If Boston Medical Center or Boston University Medical Campus registers a study on ClinicalTrals.gov and the Principal Investigator departs the institution while the record is still active, the Principal Investigator must contact the PRS Administrator prior to departure to discuss plans for the record, as described in Section 6.6.8.

ClinicalTrials.gov and PRS Modernization Initiative 2019-2024

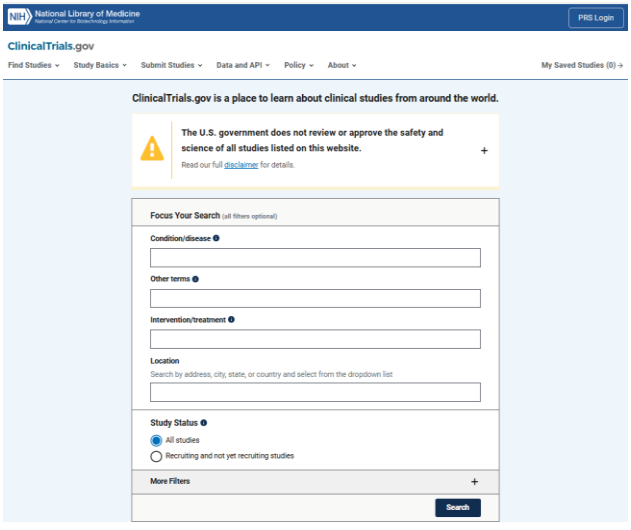
- The National Library of Medicine (NLM) began an effort to modernize ClinicalTrials.gov in 2019, with the aim to deliver an improved user experience on an updated platform that will accommodate growth and enhance efficiency.
- Details about the Modernization Initiative and resources can be viewed at https://clinicaltrials.gov/about-site/modernization







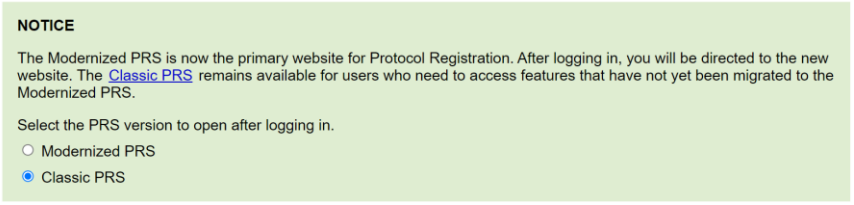
Classic version of PRS (register.clinicaltrials.gov)



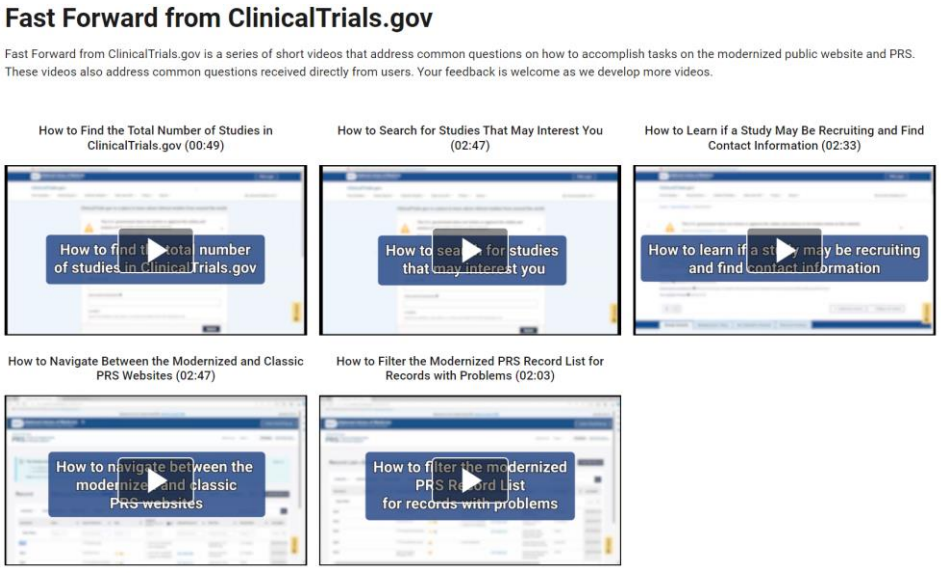
Modernized version of ClinicalTrials.gov

The Modernized PRS (as of September 2024)

- There are major problems accessing and using the Modernized PRS
- It is often difficult to login; depending on the time of day, access can take minutes to hours
- Many of the PRS features are still not available so one needs to still use the Classic PRS
  - Records with Results, Delayed Results, and Study Documents can only be opened in classic PRS
- Errors appear on the Modernized and Classic PRS such as discrepancies in information
- Using features migrated to the Modernized PRS takes on average 30% longer than if using the Classic PRS
- To facilitate logging into the PRS and to perform features that have not yet been migrated to the Modernized PRS at PRS login there is now an option to select which version of the PRS to use; for efficiency and fewer errors, continue to use the Classic PRS



ClinicalTrials.gov Demonstration Videos



www.nlm.nih.gov/oet/ed/ct/demo_videos.html

Primary registries in the WHO registry network International Clinical Trials Platform (ICTRP)*

There are 17 primary registries of ICTRP, the first one, the ISRCTN of England was initiated in 2000 and the most recent being Lebanese registry, in 2019.

- Australian New Zealand Clinical Trials Registry (ANZCTR)
- Brazilian Clinical Trials Registry (ReBec)
- Chinese Clinical Trial Registry (ChiCTR)
- Clinical Research Information Service (CRiS), Republic of Korea
- Clinical Trials Registry - India (CTRI)
- Cuban Public Registry of Clinical Trials (RPCEC)
- EU Clinical Trials Register (EU-CTR)
- German Clinical Trials Register (DRKS)
- Iranian Registry of Clinical Trials (IRCT)
- International Standard Randomised Controlled Trial Number (ISRCTN)
- International Traditional Medicine Clinical Trial Registry (ITMCTR)
- Japan Registry of Clinical Trials (jRCT)
- Lebanese Clinical Trials Registry (LBCTR)
- Thai Clinical Trials Registry (TCTR)
- Pan African Clinical Trial Registry (PACTR)
- Peruvian Clinical Trial Registry (REPEC)
- Sri Lanka Clinical Trials Registry (SLCTR)

*Primary Registries in the WHO Registry Network meet specific criteria for content, quality and validity, accessibility, unique identification, technical capacity and administration. Primary Registries meet the requirements of the ICMJE.

AYU-40-141.pdf (nih.gov)

ClinicalTrials.gov Resources

- **Contact the BMC/BUMC PRS Administrator**
  - **Karla Damus- damusk@bu.edu or 617 956 2506**
- **Visit the 3 web pages on the OHRA website about CTgov**
  - **What, Why, Which Studies, When**
  - **Who, How, Consent Form Posting, Legal Requirements**
  - **Guidance and Helpful Tips** (eg schedule a CTgov Zoom training, links, updates, etc)
- **CR Times article about CTgov**
- **Access to this ClinicalTrials.gov CRS** at the **CRS Library** on the CRRO website
- **Find out about the modernization effort**
  - https://clinicaltrials.gov/about-site/modernization
- **Review the latest questions about the Modernization Effort** Modernization Transition Top Questions
- **Stay up to date with the Hot Off the PRS! e-bulletin**
  - https://bit.ly/33qcZBb
- **Contact clinicaltrials.gov**
  - Register@clinicaltrials.gov

Thank you!!

- Matt Ogrodnik, Director OHRA
- Jami Wood, BMC Research Compliance Officer
- Jamie Merrill, Director BMC/BUMC IRB
- Mary-Tara Roth, Director CRRO
- All the PIs and research team members
- All the IRB analysts
- Zoey, RA

Questions?