ClinicalTrials.gov for Researchers and Support Staff

Elli Gourna Paleoudis, MS, PhD
Manager, Investigator Initiated Research Program
HMH ClinicalTrials.gov Administrator
Office of Research Administration at the HMH Research Institute

Assistant Professor | Medical Sciences Department, Hackensack Meridian School of Medicine

Hackensack Meridian *Health*
KEEP GETTING BETTER

Overview

- Defining Applicable Clinical Trials
- Registration requirements
- Regulations
- Violations and Penalties
- Responsible party
- ClinicalTrials.gov at HMH

Applicable Clinical Trial (ACT)

Definition as per the Final Rule (42 CFR 11.10) :

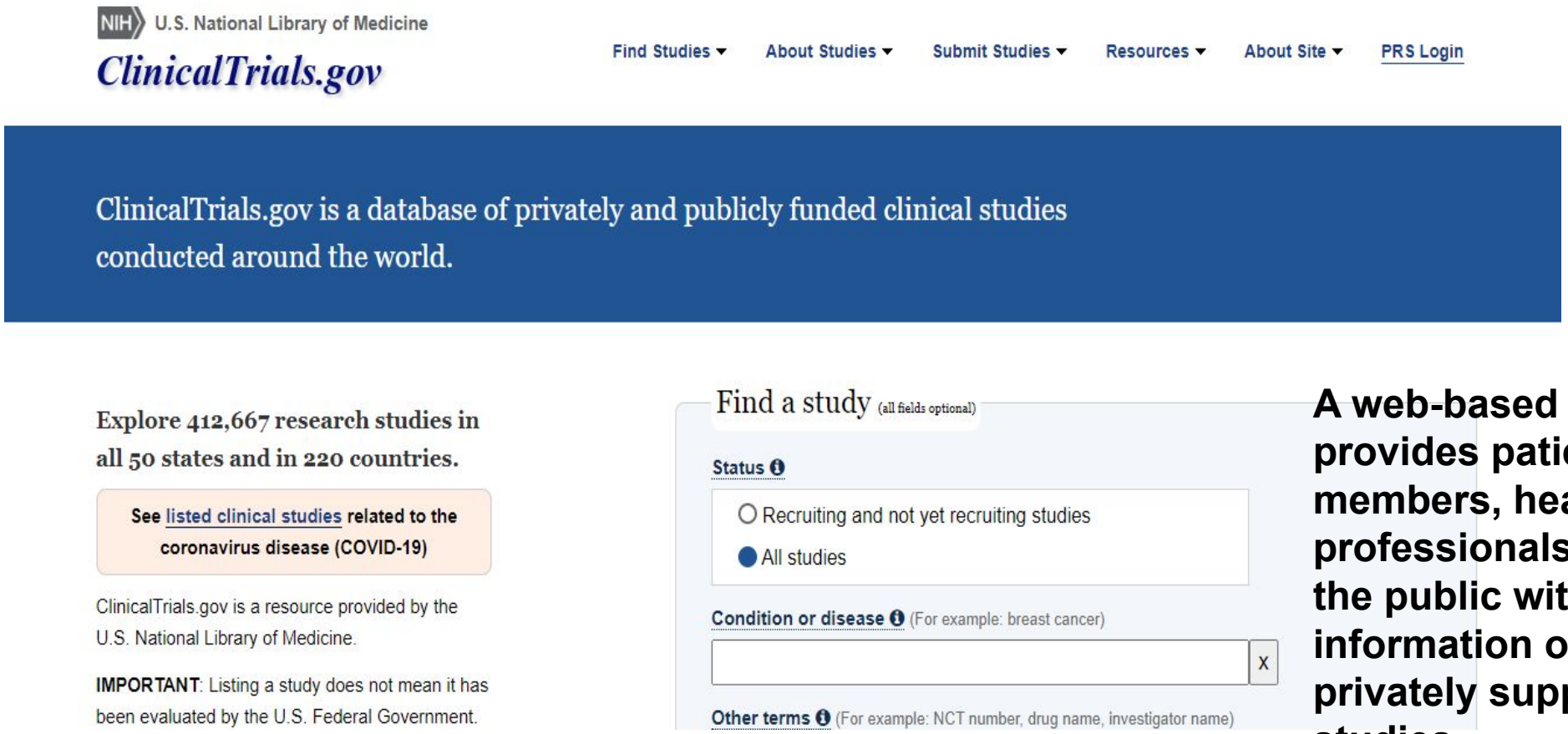
- Trials of drugs/biologics: Controlled clinical investigations (excluding Phase 1 trials) of any U.S. Food and Drug Administration (FDA)-regulated drug or biological product for any disease or condition
- Certain studies of FDA-regulated medical devices (excluding small feasibility and certain clinical trials to test prototype devices), but including FDA-required pediatric postmarket surveillances of a device product
- Trial has one or more sites in the U.S.
- Trial is conducted under an FDA IND/IDE application
- Trial involves a drug, biologic or device that is manufactured in the U.S. or its territories and exported for research

https://clinicaltrials.gov/ct2/manage-recs/fdaaa#WhichTrialsMustBeRegistered

Why register an ACT?

- Fulfill ethical obligation to participants and the research 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
- Serve as a resource for review boards
- Required for journal publication

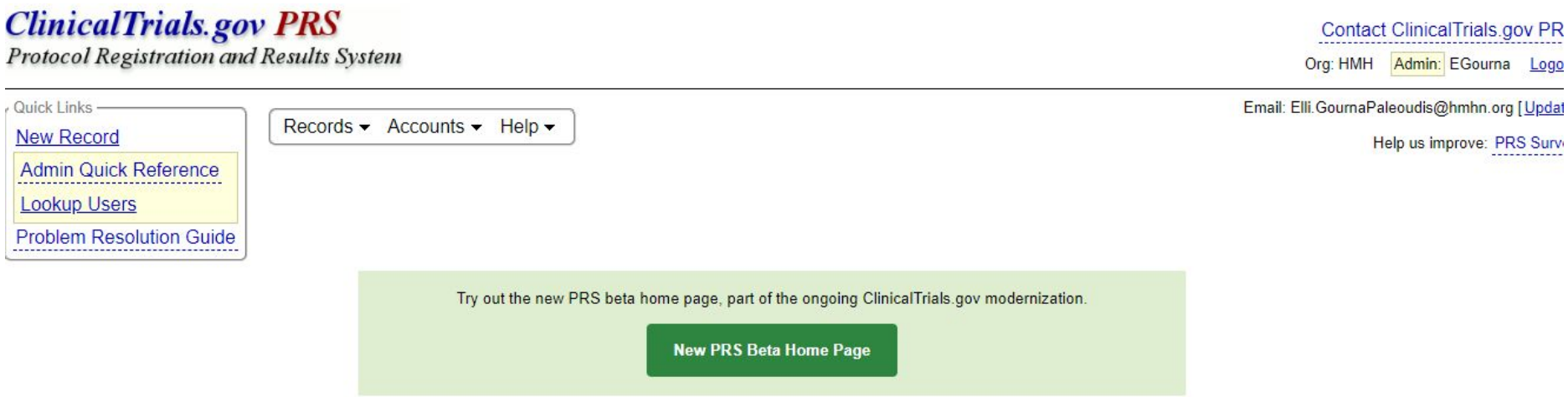
ClinicalTrials.gov



A web-based resource that provides patients, their family members, health care professionals, researchers, and the public with easy access to information on publicly and privately supported clinical studies

Hackensack Meridian *Health*
KEEP GETTING BETTER

PRS System



Protocol Registration and Results System (PRS)

For institutions to register a clinical study or submit results information for a registered study.

Hackensack Meridian *Health*
KEEP GETTING BETTER

Relevant Regulations on CT Registration and Results Reporting

Body/Name	Date	Scope
Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11) Revised Common Rule	effective in 2017 effective in 2019	Clinical trials of a FDA-regulated drug, biological, or device product other than Phase 1 (drug/biological products) or small feasibility studies (device products)
NIH Policy on the Dissemination of NIH-funded Clinical Trial Information	effective in 2017	CT funded by the NIH (in whole or partially)
International Committee of Medical Journal Editors (ICMJE) Policy	2004/2005	All interventional studies, including Phase 1 studies; defines criteria for "acceptable registries"

HHS Final Rule under FDAAA
Final Rule (42 CFR Part 11)

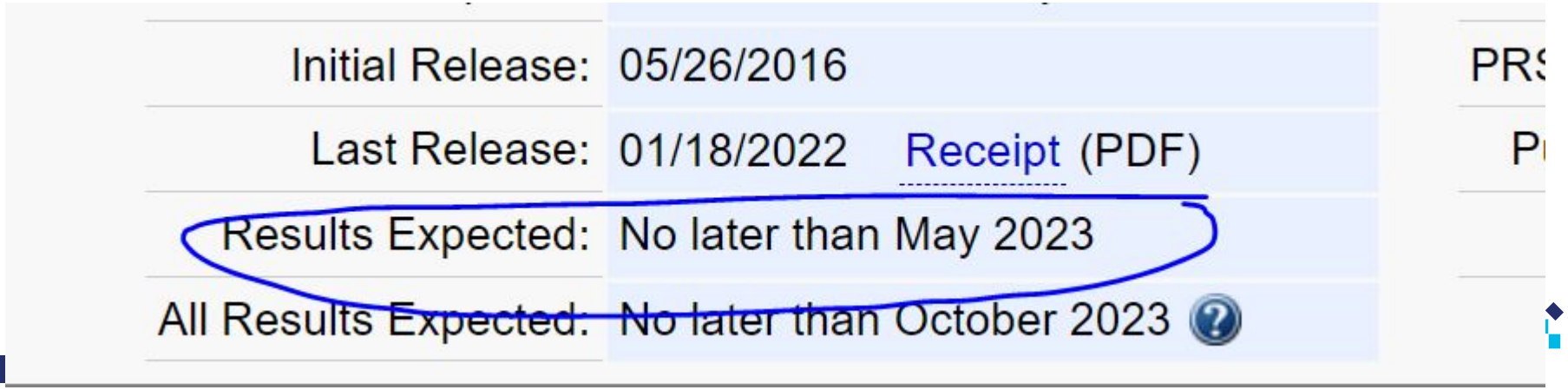
- Applies to Applicable Clinical Trials (ACTs)
- Registration must be within 21 days of first enrollment
- Record must be verified at least annually

Study updates that need to be reflected on CT.gov within **30 days**

- Study start date
- Intervention name(s)
- Availability of expanded access
- Expanded access status
- Overall recruitment status
- Explanation for change in status
- Actual enrollment data
- Individual site status
- IRB status
- Completion date
- Responsible party
- Official title
- Contact information

HHS Final Rule under FDAAA
Final Rule (42 CFR Part 11)

- Record must be updated within 30 days of the applicable date
- Comments must be responded to within 15 calendar days (registration) or 25 calendar days (results)
- Results are due 365 days from primary completion date
- Requires submission of full protocol and statistical analysis plan with submission of results information



Additional requirements for NIH or federally funded studies

- All clinical trials need to be registered (even if not ACT)
- Study has to be registered within 21 days of enrollment
- Results need to be posted and will be made available within 30 days from submission (with or without comments)
- Baseline race and ethnicity race needed to be reported
- Informed consent form needs to be uploaded once recruitment is completed (no later than 60 days after the last study visit by any subject)

Violations

1. Failure to submit required clinical trial information
2. Submission of false or misleading clinical trial information
3. Failure to submit primary and secondary outcomes

Penalties for noncompliance

1. Civil monetary penalties up to $13,237 (as of July 2022) per study, per day
2. Civil or criminal judicial actions
3. Withhold current or future funding (for NIH studies)

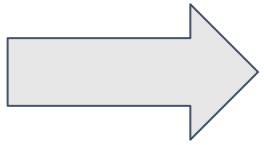
FDA Enforcement Plan

Pre-Notice Letter

30 days to correct and then review again if issues not addressed

Notice of Noncompliance

30 days to correct



- **Civil money penalties, injunction, and/or criminal prosecution.**
- **Other applicable penalties**
- **Note added to the CT record**

Who is responsible for registering, maintaining and reporting?

Responsible party : *The person responsible for submitting information about a clinical study to ClinicalTrials.gov and updating that information. Usually the study sponsor or investigator.*

1. For sponsored trials, the sponsor (e.g. industry)
2. For Investigator initiated trials, the investigator or the institution (as the sponsor, “Grantee Organization”)

ClinicalTrials.gov at HMH

Hackensack Meridian *Health*
KEEP GETTING BETTER

ClinicalTrials.gov at HMH

1. HMH Policy (*Investigator Initiated Program Policy No. 2 - Investigator Initiated Clinical Trials and Clinical Trial Registration*)
   - Can be found in PolicyStat, effect date: Nov 2021
   -
2. Available assistance (as needed) for:
   - initial registration
   - ongoing maintenance
   - result reporting
   -
3. Enforcement Plan to promote compliance

1. Education for administrators and investigators

HMH CT.gov Policy

Policy Title: Investigator Initiated Program Policy No. 2 - Investigator Initiated Clinical Trials and Clinical Trial Registration

Includes:

1. Important definitions
2. CT decision tree
3. Outlining procedures for registration, record maintenance and result reporting

Available assistance

Assistance is available for registration/maintenance/result reporting BUT it it the PI's/Study Team's responsibility to reach out to the HMH CT.gov Administrator(s)

Important timepoints (1/2)

1. Registration prior to enrollment
2. Respond to PRS Review Comments within 15 calendar days (registration) –OR- 25 calendar days (results)
3. Verify the record at least once a year

Important timepoints (2/2)

4. Update the record within 30 calendar days from any of the following changes:
   - Study start date
   - Intervention name(s)
   - Availability of expanded access
   - Expanded access status
   - Overall recruitment status
   - Explanation for change in status
   - Actual enrollment data
   - Individual site status
   - IRB status
   - Completion date
   - Responsible party
   - Official title
   - Contact information
5. Report the results within 356 days from the primary completion date

Enforcement Plan to promote compliance

- Tracking tools
- Reminders to the study team
  - Record owner
  - PI
  - Local leadership (Director/Department Chair)
- Escalation plan including Research Institute and Compliance leadership

Enforcement Plan

Email Reminder	Record Owner	PI / Central Contact(s)	Divisional Director/ Department Chair	VP of Research and Reg. Affairs	President, Academics, Research and Innovation	Corporate Compliance
Step 1 - 90 days before applicable deadline	✓	✓				✓
Step 2 - 60 days before applicable deadline	✓	✓				✓
Step 3 - 30 days before applicable deadline	✓	✓	✓			✓
Step 4 - 7 days before applicable deadline	✓	✓	✓	✓		✓
Step 5 - on applicable deadline	✓	✓	✓	✓	✓	✓

What do you need to do if you are conducting a clinical trial:

1. Complete the **pre-registration** form and indicate that your study is/might be an applicable clinical trial.
2. During **IRB submission**, complete the respective sections and indicate that your study is/might be an applicable clinical trial
3. Use the correct **protocol template**.
4. Include appropriate language in the **ICF**.
5. Once study is IRB approved and prior to patient enrollment, reach out to the HMH CT.gov Administrator to get assistance.
6. Ensure record is maintained as outlined above.
7. Post results once the study is completed.

When registering a trial:

- PI is aware of CT.gov requirements
- Clinical research study falls under the definition of ACT
- PI information including contact info is correct
- Appropriate access is given to PI proxy and CT.gov record owner
- Registration reflects IRB/FDA approved protocol
- Stated outcomes are measurable
- Each outcome is presented separately
- Stated timepoints are specific and not generic
- Record is updated each time an IRB/FDA amendment is approved
- Spelling and abbreviations are reviewed before record is marked as complete

When reviewing a registered trial/ CT.gov record:

- All applicable changes take place within 30 days
- Study status reflect the IRB status
- If any protocol changes have been made, the record has been updated as well (reminder: the protocol will have to be submitted once the study closes and consistency must be maintained)
- Record verification date is updated
- PI and CT.gov record information (including contact information) remains correct

When closing a trial:

- CT.gov record is updated to reflect study closure
- Actual end date and actual enrollment are being updated
- Data on race and ethnicity is included even if not part of the study outcomes
- Results are ready to be uploaded within 300 days of study completion to ensure compliance
- Results are finalized no later than 365 days of study completion
- Protocol (and ICF if applicable) are uploaded

Key takeaways

- There are specific requirements if one is planning on conducting a clinical trial
- If in doubt, please reach out for help.
- Assistance is available at HMH but it is the PI's/team's responsibility to reach out for help.
- HMH CT.gov Program includes:
  - Education
  - Policy
  - Ongoing support
  - Enforcement plan
  - Leadership engagement
- **Significant consequences for non compliance (monetary and other penalties)**

Decision Tool: Does Your Human Subjects Research Study Meet the NIH Definition of a Clinical Trial?

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

Clinicaltrials.gov Information for HMH

More information about clinicaltrials.gov, including a decision tree and a link to the PRS system, can be found on the ORA website:

https://www.hackensackmeridianhealth.org/en/Research/office-of-research-administration/researcher-resources/protocol-development

Thank you!

Do not hesitate to contact us for questions or clarifications.

The H*M*H Research Institute

Hackensack Meridian *Health*
KEEP GETTING BETTER