Stem Cell Research Oversight (SCRO)

Regulatory Services for Clinical Trials

ClinicalTrials.gov, FDA INDs and IDEs

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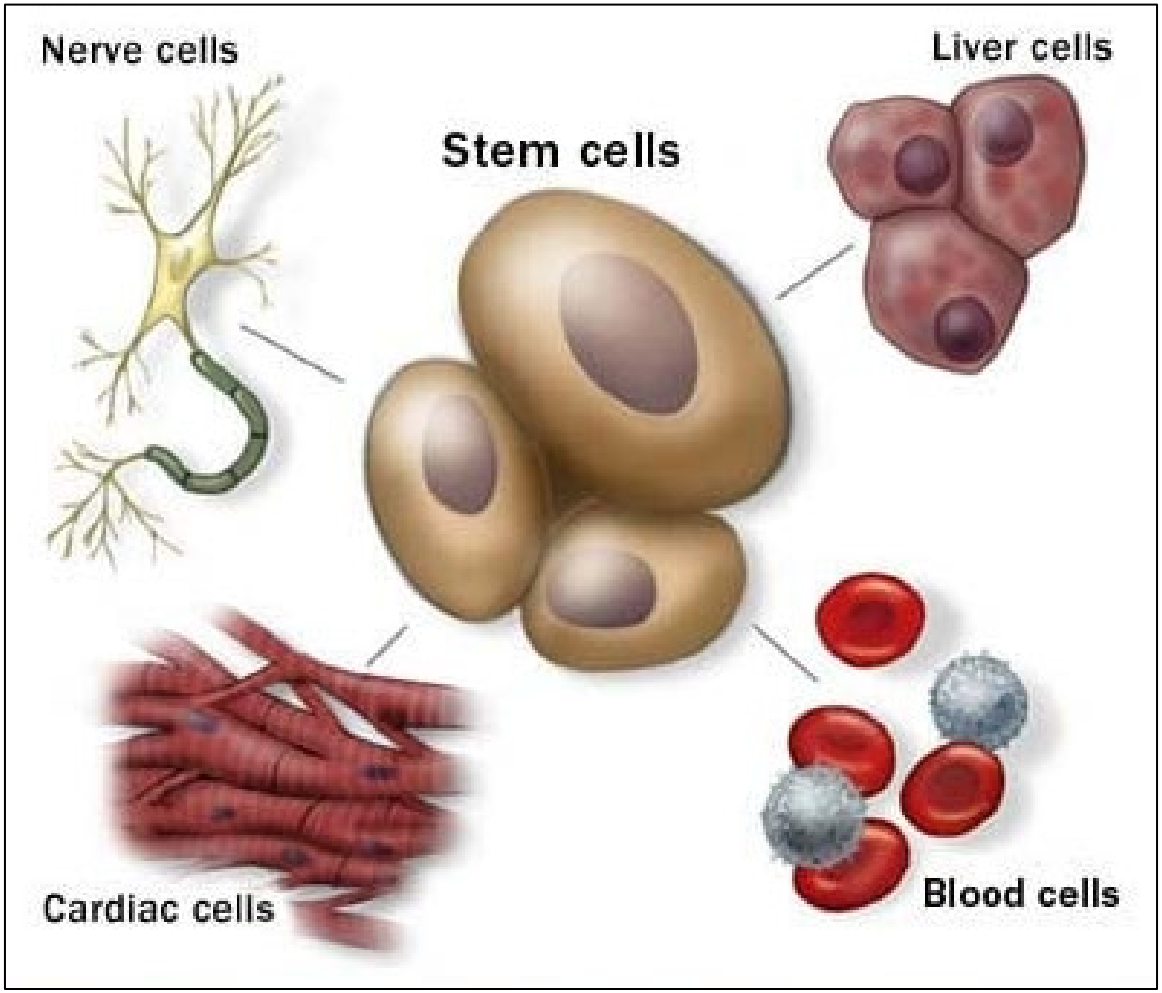
Clinical Trials Resource Center (CTRC)

The University of Texas Health Science Center at Houston

Stem Cell Research Oversight (SCRO)

Stem cells are the body's raw materials — they are cells from which all other cells with specialized functions are generated



From https://www.mayoclinic.org/tests-procedures/bone-marrow-transplant/in-depth/stem-cells/art-20048117

There are many different types of stem cells.

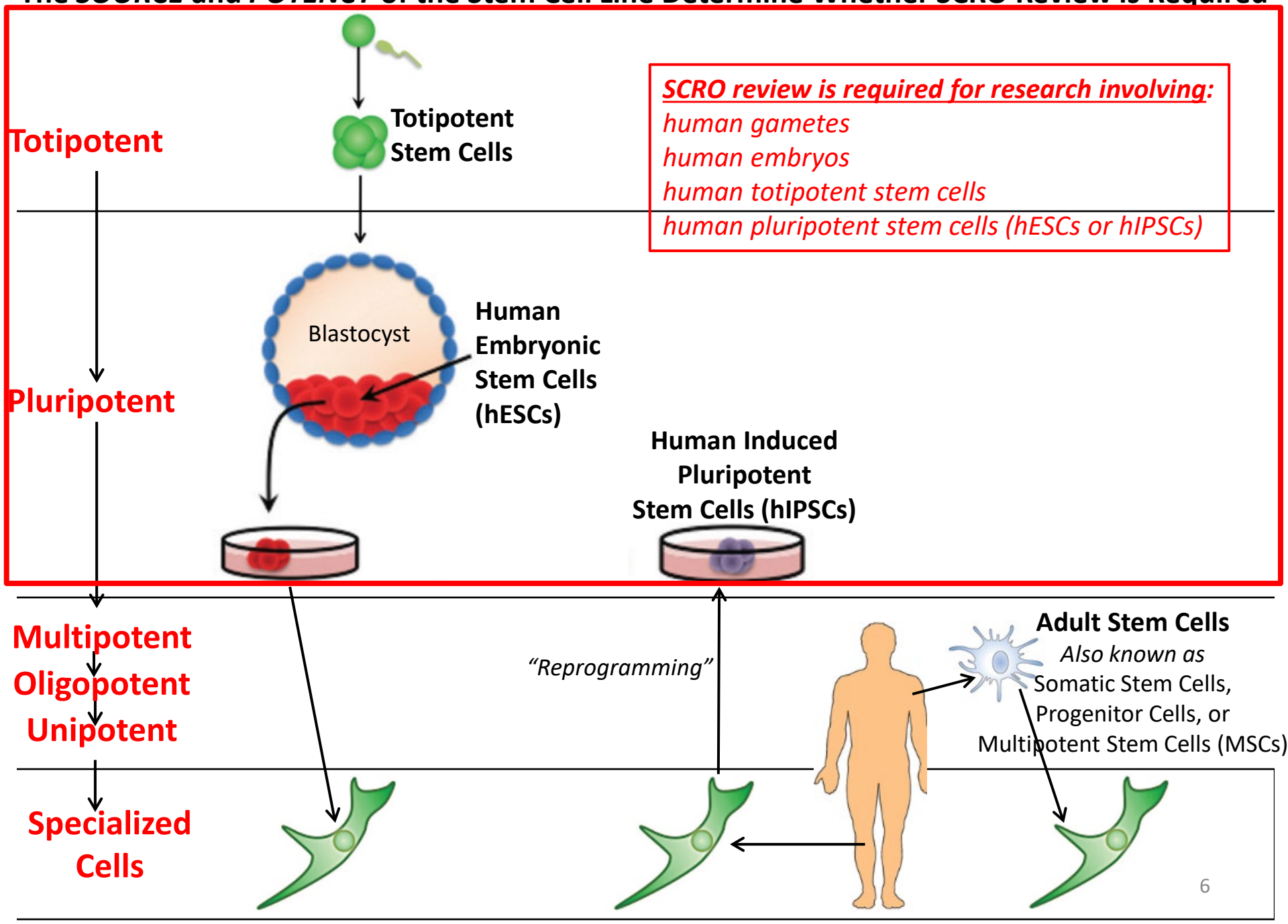
SCRO Committee review is only required for certain human stem cell types.

HOOP 200 – Review of Research

H. Human Stem Cell Research Oversight (SCRO) Committee

All research involving human embryonic stem cells (hESCs) or human induced pluripotent stem cells (hIPSCs) conducted at the university by its employees and/or involving use of its facilities or resources must be reviewed and approved by the Human Stem Cell Research Oversight (SCRO) Committee before it is initiated. Some research involving hESCs or hIPSCs may require additional approval by the AWC, IBC and/or CPHS. For more information on the application process, please contact the SCRO office at scro@uth.tmc.edu.

The *SOURCE* and *POTENCY* of the Stem Cell Line Determine Whether SCRO Review is Required



SCRO Review is Required for Research Involving the Following (or their Derivatives)

	Generation for Research Purposes	Research Use
human embryonic stem cells (hESCs)	**YES**	**YES**
human induced pluripotent stem cells (hIPSCs)	*No*	**YES**
human totipotent stem cells	**YES**	**YES**
human gametes	**YES**	**YES**
human embryos	**YES**	**YES**
human adult stem cells (non-neural)	*N/A*	*No*
human neural stem cells, of any source	*depends on source*	**YES**

Reach out to Elizabeth Gendel to discuss whether SCRO review is required for your project.
Elizabeth.M.Gendel@uth.tmc.edu

To Avoid Delays in Release of Grant Funds:

- Ensure Review and Approval (R&A) Form Submitted to SPA Correctly Indicates Stem Cell Involvement and Correctly Indicates Stem Cell Types
- Ensure Project is Submitted to SCRO Well Before Grant Funding is Received

R&A Form within UTSTART

INSTITUTIONAL COMPLIANCE

Yes ☐ No ☑ * Does project involve human subjects (or material or data from human subjects)?

Yes ☑ No ☐ * Does project involve stem cells?

* type(s):
embryonic ☐ iPSC ☐ adult ☐

Yes ☐ No ☑ * Does project involve vertebrate animals?

Yes ☐ No ☑ * Does project involve biological agents, infectious agents, or recombinant or synthetic nucleic acid?

Yes ☐ No ☑ * Does project involve radioactive materials?

Yes ☐ No ☑ * Does project involve toxic or physically dangerous chemicals or carbon or silica based nanochemistry?

Stem Cell Research Oversight (SCRO) Website

https://inside.uth.edu/scro/

- SCRO Application
- Document “SCRO Policy and Procedures”
- Document “Guidelines for SCRO Review”

Levels of SCRO Review and Timelines

- **Expedited Review** **(about 1 week turnaround time)**
  - *In vitro* work with hESC lines that are approved by NIH or previously approved by UTHealth SCRO
  - *In vitro* work with hIPSC lines
  - Introduction of hESCs (NIH- or UTHealth SCRO-approved) or hIPSCs to animals if:
    - *Cells are transplanted to postnatal animals and there is no likelihood of contributing to the central nervous system or germ line (e.g., the development of a teratoma to evaluate pluripotency).*
- **Full Committee Review** **(about 2-week to 2-month turnaround time, but new technology or new ethical issues may take longer)**
  - Generation of brain organoids
  - Transplantation of hESCs or hIPSCs to animals if:
    - *There is a likelihood of transplanted cells contributing to the central nervous system or germ line.*
  - Transplantation of hESCs or hIPSCs to humans
  - Any work with hESCs that are not NIH approved or previously approved by UTHealth SCRO
    - Lines listed on NIH Registry are eligible for use in NIH-supported research: https://grants.nih.gov/stem_cells/registry/current.htm
  - Derivation of hESCs
  - Creation of embryos, gametes, or totipotent cells

Stem Cell Research Oversight (SCRO) Contact Information

- *SCRO Office*
  - SCRO@uth.tmc.edu
  - *(*713) 500-3587

- *Elizabeth Gendel*
  - Elizabeth.M.Gendel@uth.tmc.edu
  - (713) 500-3587

Regulatory Services for Clinical Trials

FDA INDs and IDEs

ClinicalTrials.gov

Regulatory Services for Clinical Trials

- **IRB submissions (full board) are reviewed to determine:**
  - If a study must be registered at ClinicalTrials.gov
  - If a study of a drug, biological product, or device might need to receive FDA approval before it begins *(that is, if an IND or IDE is needed)*

- **Either the Clinical Trials Resource Center (CTRC) or CPHS will notify your study team if *ClinicalTrials.gov registration* or an *IND or IDE application* are required**

- **In general, CTRC can assist with:**
  - ClinicalTrials.gov Registration, Updates, and Results Entry
  - INDs and IDEs – Regulatory Analysis, Requesting an IND or IDE Determination from FDA, Initial IND or IDE Applications, IND and IDE Reports
  - Resources for Study Initiation and Management

Clinical Trials Resource Center (CTRC)

website - https://www.uth.edu/ctrc/
email - clinicaltrials@uth.tmc.edu

Sujatha Sridhar, MBBS - Associate Vice President, Research Compliance

Elizabeth Gendel, PhD - 713-500-3587, Elizabeth.M.Gendel@uth.tmc.edu

Shwetha Pazhoor, MS - 713-500-3578, Shwetha.Pazhoor@uth.tmc.edu

Jessica Martinez Alvarado, MPH - 713-500-3551, Jessica.L.Martinez@uth.tmc.edu

Clinical Research Newsletter and Forum

Contact CTRC at clinicaltrials@uth.tmc.edu to be Added to the Weekly Clinical Research Coordinator Newsletter

Clinical Coordinator Forum

12-1pm, 4th Wednesday of the Month

https://www.uth.edu/ctrc/training/clinical-coordinator-forum

FDA INDs and IDEs

An IND or IDE Application Must be Submitted to FDA for Certain Studies of Drugs or Devices

- **Investigational New Drug (IND)** application
  - A request for authorization from the FDA to administer an investigational **drug** or **biological product** to humans

21 CFR Part 312
https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application

- An **Investigational Device Exemption (IDE)** application
  - A request to allow an investigational **medical device** to be used in a clinical study to collect safety and effectiveness data

21 CFR Part 812
https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/investigational-device-exemption-ide

If an IND or IDE is required,
then IND/IDE *and* IRB approval must be in place before study begins.

During Initial IRB Review . . .

- The IRB assesses whether “drugs” or “devices” (*as defined by FDA*) are being applied to study participants as part of the study protocol.

- The IRB determines whether an IND or IDE is needed for the study.

FDA INDs and IDEs
Helpful Tip

- **To avoid delays with study start-up, consider ASAP whether your study involves something FDA views as a "drug" or "device" and whether an IND or IDE might be required**
  - If the product is not FDA approved, or if the product is being used off label in the study, then an IND or IDE might be required.
  - FDA defines "drug" or "medical device" as a product "*intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease*" or "*intended to affect the structure or any function of the body*"
    - FDA considers INTENDED USE when determining if a test article meets the FDA definition of "drug" or "device."

Examples of Unexpected Products that Might be Used as "Drugs" or "Devices" in a Study

FDA considers INTENDED USE when determining if a test article meets the FDA definition

In addition to prescription and OTC drugs and biological products and medical devices commonly used in medical practice, other products might also be regulated as "drugs" or "devices" in a study:

- **Supplements**
- **Vitamins**
- **Botanicals**
- **Food**
- **Essential Oils/Aromatherapy**
- **Human Tissue Products**
- ***in vitro* Diagnostics**
- **Digital Health Products**
  - **Software**
  - **Algorithms**
  - **Artificial Intelligence**
  - **Machine Learning**
  - **Virtual Reality**
  - **Mobile Apps**

UTHealth CPHS Policies re: IRB Review of Drug and Device Studies

- Drugs and Biological Products
  - https://www.uth.edu/cphs/policies/drugs-agents-biologics.htm

- Devices
  - https://www.uth.edu/cphs/policies/investigationaldevice.htm

IRB Submissions Involving a Drug or Device
Helpful Tips

- In iRIS:
  - Select “Yes” for Drugs if the protocol assigns a drug to study participants
  - Select “Yes” for Devices if the study will develop and/or assess a device
  - Complete ALL items in the Drug and Device sections of the iRIS app
- Submit Package Inserts for all Drugs assigned by the protocol
- Submit Instructions for Use (IFUs) for all Devices assessed in the study

Contact Elizabeth Gendel for guidance - Elizabeth.M.Gendel@uth.tmc.edu - (713) 500-3587

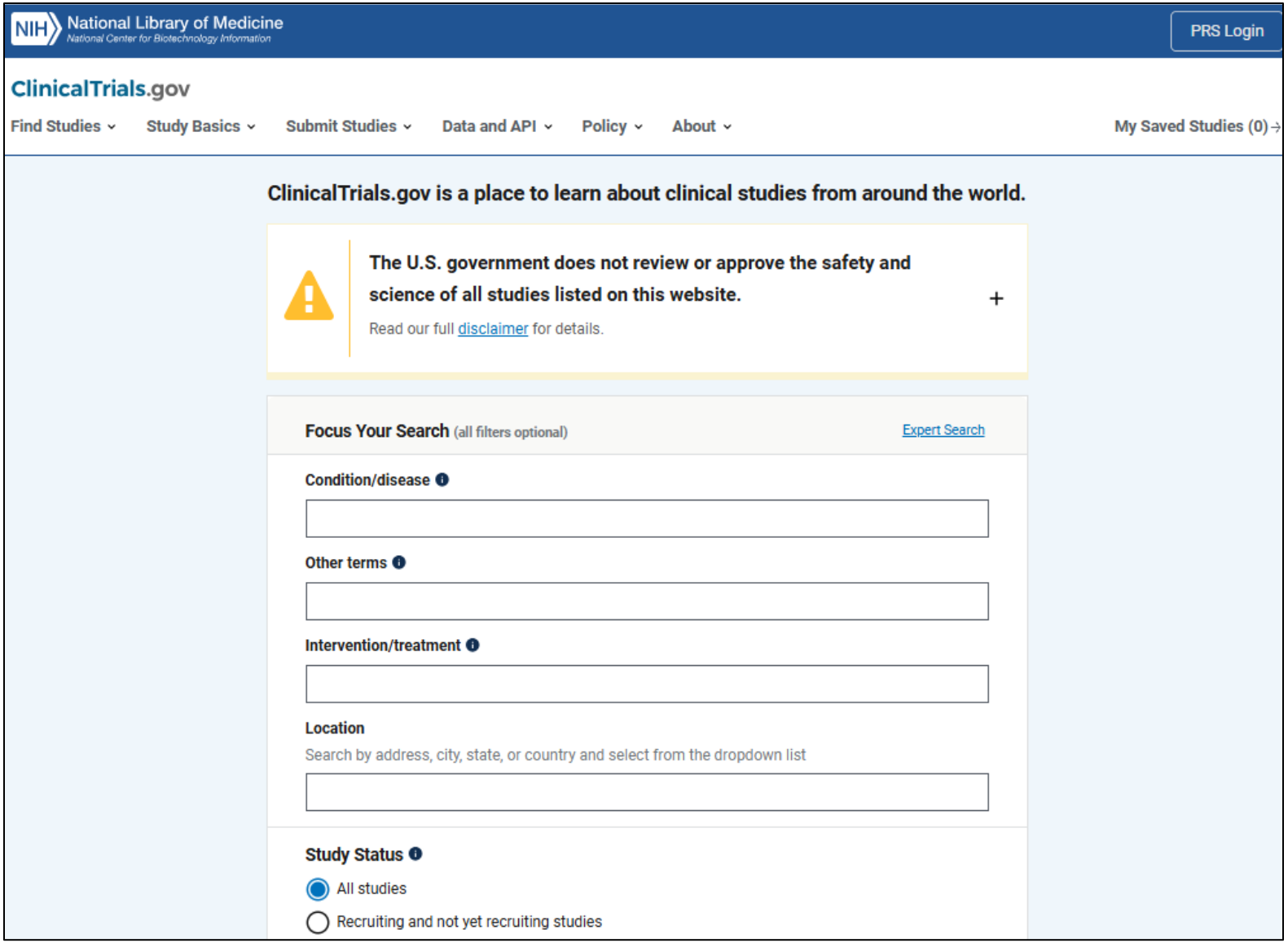
FDA INDs and IDEs
Reporting

- **For studies conducted under an FDA IND or IDE held by the UTHealth PI, the UTHealth PI is responsible for submitting various reports to FDA, per the regulations:**
  - Annual Reports
  - Safety Reports
  - Protocol Amendments
  - Changes to Investigators
  - Changes to the Study Product
  - New Pharmacology-Toxicology or New Clinical Information
  - Withdrawal of the IND or IDE

There are specific requirements for what to submit and how to submit to FDA, with major differences between submissions for INDs (drugs) and IDEs (devices).
Elizabeth Gendel and Jessica Martinez Alvarado of CTRC Can Assist

ClinicalTrials.gov

ClinicalTrials.gov is a Public Database of Clinical Trials



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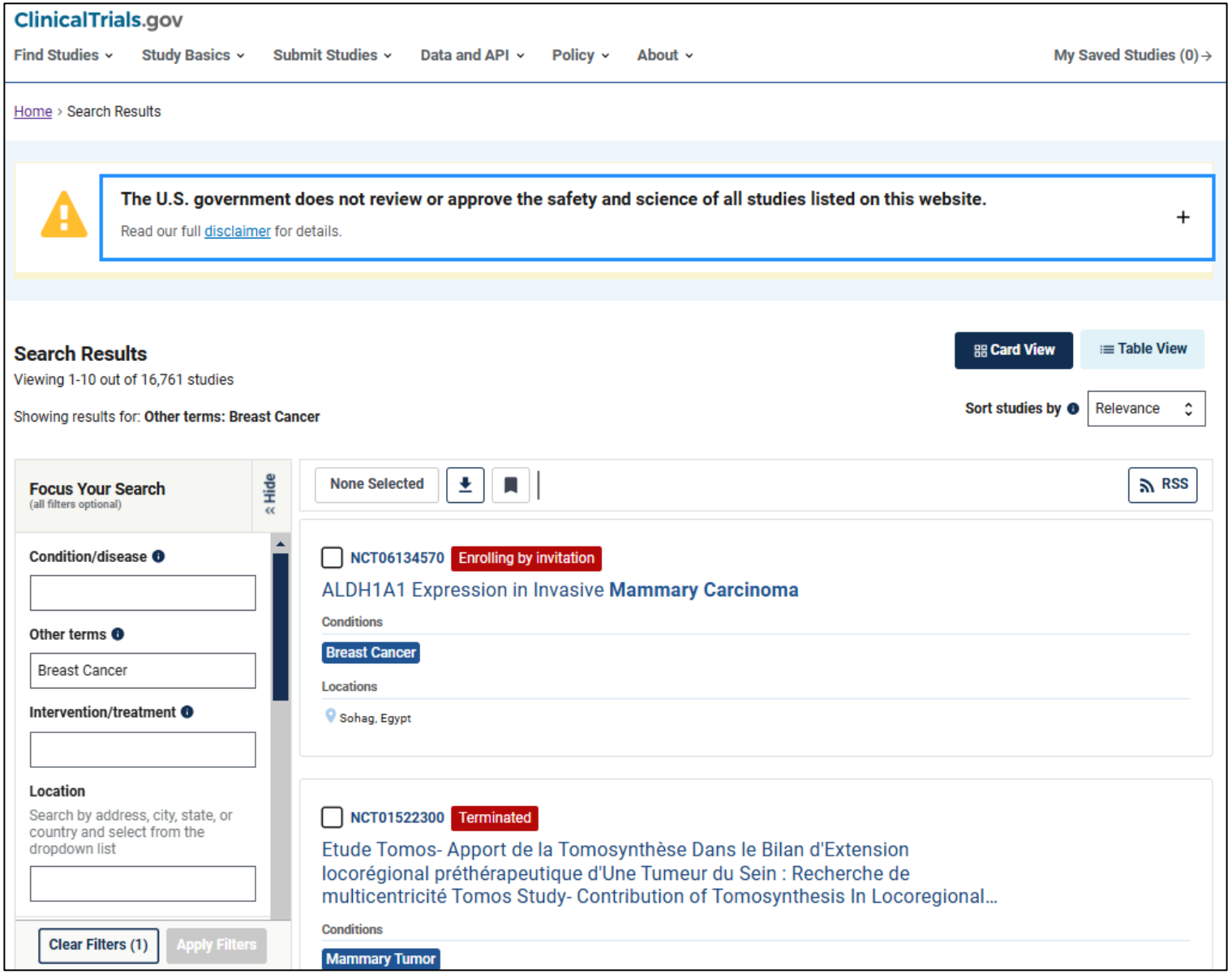


Once a Trial is Registered, it is Assigned an NCT

NCT # stands for National Clinical Trial #

NCT00000000

ClinicalTrials.gov Record Life Cycle

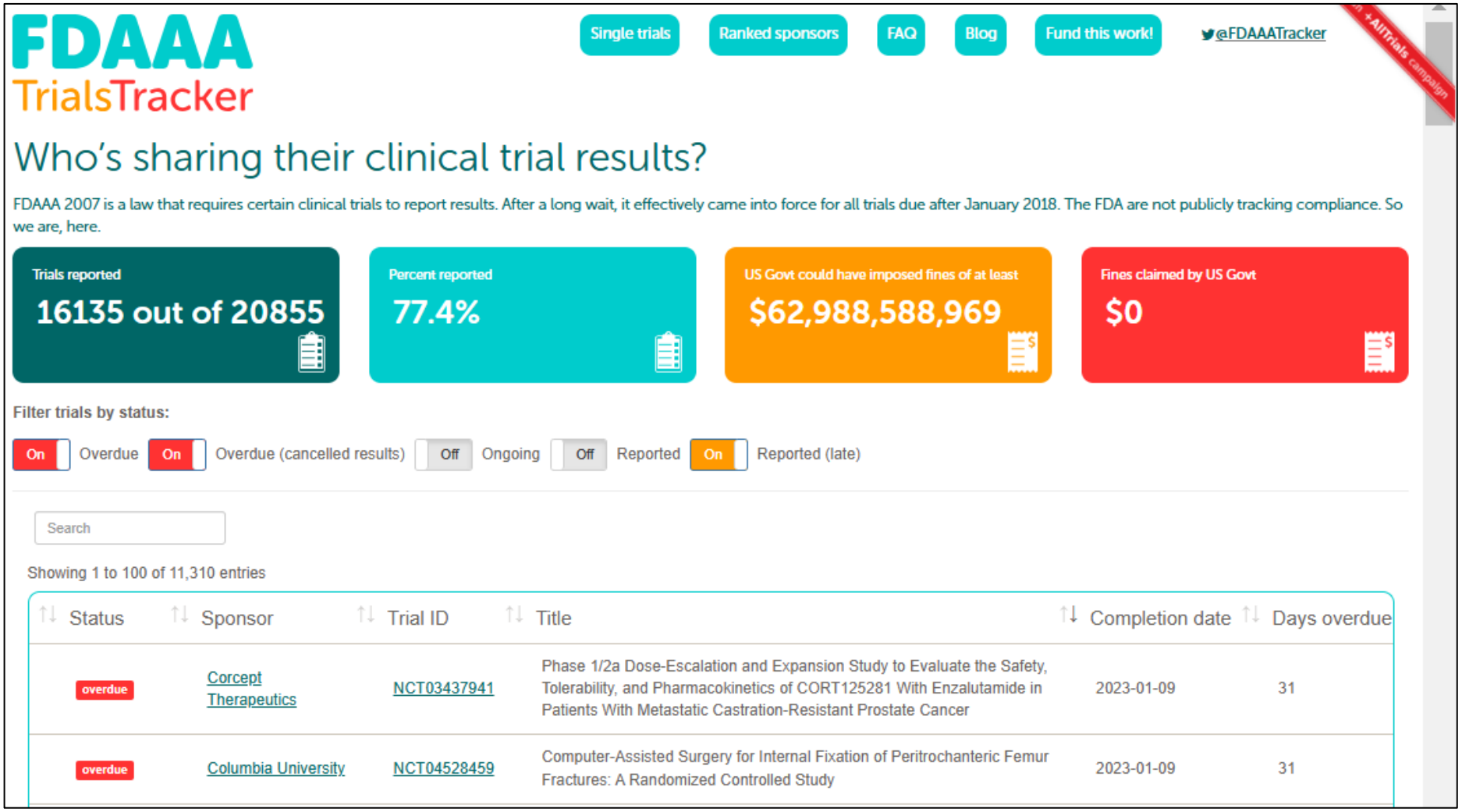
- **REGISTER**
  - *before enrollment begins*
- **UPDATE RECORD**
  - *At least once per year until data collection is completed*
- **ENTER RESULTS**
  - *1 year after the date that last piece of primary outcome data was collected*

Why Register and Report Results at ClinicalTrials.gov?

- It's the **Law**! **FDA** issues Non-Compliance Letters and Fines
- **NIH** funding can be terminated or withheld
- It can affect the ability to publish in a medical **journals**
  - ICMJE = International Committee of Medical Journal Editors
- An NCT # is required by **CMS** for claims for research-related procedures
- **To Avoid Public Shaming** for Late Results: https://fdaaa.trialstracker.net/
- Required per UTHealth's **HOOP 186**
- Can serve as a **recruiting** tool

Public Shaming Website for Late Results

https://fdaaa.trialstracker.net/



UTHealth's ClinicalTrials.gov Policy and Procedures

https://www.uth.edu/ctrc/regulatory/clinicaltrials.gov-registration.htm

PURPOSE:

- Ensure Compliance with Law and NIH Policy
- Avoid Consequences of Non-Compliance
  - *FDA Letters of Non-Compliance and Fines*
  - *Withholding or Termination of NIH or other Federal Funding*
  - *NIH Withholds Funding from Entire Institution*
  - *NIH Sends Letter to Institutional Official*
  - *Journals Won't Publish Reports of the Trial*
  - *CMS consequences (an NCT # is required by CMS for claims for research-related procedures)*
  - *Institution Receives Lower Ranking in National Report of Results Entry Compliance*
  - *Public Shaming*

UTHealth's ClinicalTrials.gov Policy and Procedures

https://www.uth.edu/ctrc/regulatory/clinicaltrials.gov-registration.htm

- **Policy**
  - What needs to happen, by who, and by when
  - Responsibilities of UTHealth PIs
- **Procedures**
  - How responsibilities will be met
  - How CTRC can help
  - How noncompliance will be handled

The Clinical Trials Resource Center (CTRC) Assists with ClinicalTrials.gov

CTRC - clinicaltrials@uth.tmc.edu

Elizabeth Gendel, PhD - 713-500-3587, Elizabeth.M.Gendel@uth.tmc.edu

Shwetha Pazhoor, MS - 713-500-3578, Shwetha.Pazhoor@uth.tmc.edu

Jessica Martinez Alvarado, MPH - 713-500-3551, Jessica.L.Martinez@uth.tmc.edu

Find Guidance on the CTRC ClinicalTrials.gov website:

https://www.uth.edu/ctrc/regulatory/clinicaltrials.gov-registration.htm

ClinicalTrials.gov Process at UTHealth

- **DETERMINATION - During initial IRB review, Elizabeth Gendel reviews studies that go to the full-board IRB to determine if the study must be registered at ClinicalTrials.gov**
  - *Note that expedited studies are not reviewed, but be aware that some expedited studies must be registered*
- **REGISTRATION - Shwetha Pazhoor notifies study teams if a full-board study must be registered, and provides assistance**
- **UPDATES - Jessica Martinez Alvarado reaches out about updates, and provides assistance**
- **RESULTS ENTRY - Jessica Martinez Alvarado and Elizabeth Gendel reach out about results entry, and provide assistance**

Which Studies are Required to Be Registered at ClinicalTrials.gov?

- In general, all "Clinical Trials," defined as:
  - **A research study in which human subject(s) are assigned to an intervention to evaluate the effect of the intervention on a health-related outcome**
    - Interventional = Subjects assigned to an intervention as part of a study protocol (*and not as part of routine medical care*)

Because expedited studies are not reviewed for registration needs, study teams will need to consider whether an expedited study needs to be registered.

Contact Elizabeth Gendel for guidance: 713-500-3587, Elizabeth.M.Gendel@uth.tmc.edu

To Help You Keep Track of ClinicalTrials.gov Deadlines, Keep this Guidance PDF on Hand

Download from CTRC website at this link: https://www.uth.edu/ctrc/regulatory/clinicaltrials.gov-registration.htm

ClinicalTrials.gov DUE DATES

https://register.clinicaltrials.gov/

1. **Registration:** no later than 21 days after enrollment of first participant (per the law and NIH); at or before time of first patient enrollment (per ICMJE journals)

2. **Updates:** at least once per year until the record is closed out; update as soon as changes are made, especially "Recruitment Status" and "Primary Completion Date"

3. **ICF Upload (federally-supported clinical trials):** after trial is closed to recruitment and no later than 60 days after the last study visit by any subject

4. **Results Entry and Protocol Upload:** no later than 1 year after the "Primary Completion Date," which is defined as "*the date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical study concluded according to the pre-specified protocol or was terminated*"; contact CTRC at the time of the Primary Completion Date

For assistance with any of the above, please contact CTRC at clinicaltrials@uth.tmc.edu.

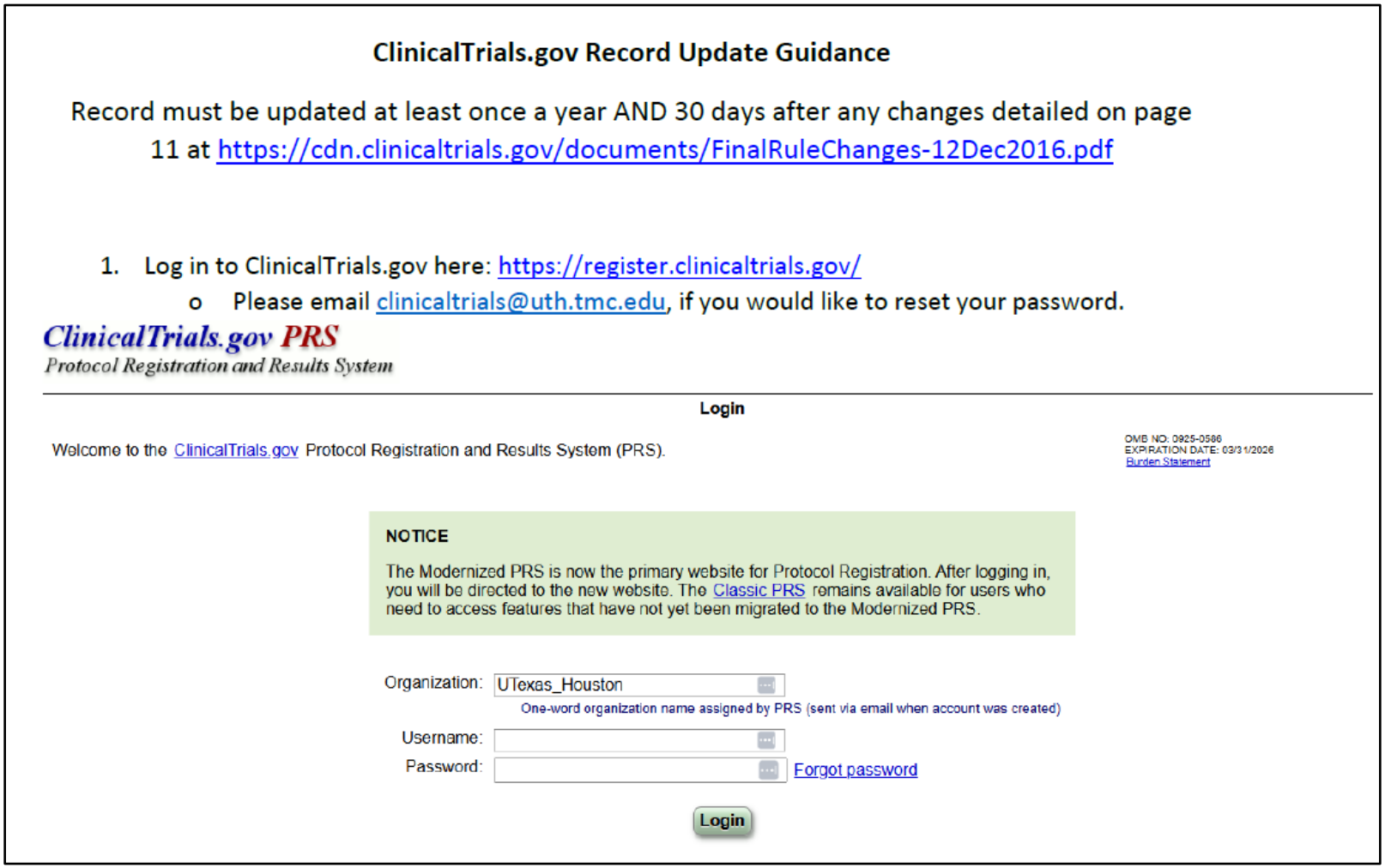
PDF Guidance –
How to Update ClinicalTrials.gov Records

Download from CTRC website at this link: https://www.uth.edu/ctrc/regulatory/ClinicalTrialsgov%20Update%20Guidance_12_05_2024.pdf

ClinicalTrials.gov Record Update Guidance

Record must be updated at least once a year AND 30 days after any changes detailed on page 11 at https://cdn.clinicaltrials.gov/documents/FinalRuleChanges-12Dec2016.pdf

1. Log in to ClinicalTrials.gov here: https://register.clinicaltrials.gov/
   - Please email clinicaltrials@uth.tmc.edu, if you would like to reset your password.



Protocol Must Clearly List Primary and Secondary Outcome Measures, *with Timepoints for Each Outcome Measure*

See guidance PDF at this link, as well as guidance within the Complex Protocol Template at this link,
and contact Elizabeth Gendel for further guidance

- Study objectives are distinct from study outcome measures
- Outcome measures (also called endpoints) are specific measurements or observations used to assess the effect of the study intervention
  - *e.g., specific laboratory tests, clinical assessments, psychological assessments, patient-reported outcomes*
- Timepoint = time at which data will be recorded or samples will be obtained
- General formula for an outcome measure:
  - [*Thing being measured*] as assessed by [*type of assessment*] at [*timepoint(s)*]
  - *Examples:*
    - *Quality of life as assessed by the SF-36 survey at baseline and 1 year*
    - *Systolic blood pressure as assessed by blood pressure cuff at baseline, week 1, month 1*
    - *Pain as assessed by a visual analogue scale (VAS) at baseline and day 30*
    - *Cognitive impairment as assessed by the Montreal Cognitive Assessment (MoCA) at baseline and 6 months*
    - *Tumor size as assessed by MRI at baseline and 1 year*
    - *Number of participants with disease progression as assessed by MRI at baseline and 1 year*

THANK YOU!

- **Elizabeth Massey Gendel, PhD**
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