Stem Cell Research Oversight (SCRO)

Regulatory Services for Clinical Trials

ClinicalTrials.gov, FDA INDs and IDEs

Elizabeth Massey Gendel, PhD

Assistant Director, Research Compliance

Vice Chair, Stem Cell Research Oversight Committee (SCRO)

Clinical Trials Resource Center (CTRC)

The University of Texas Health Science Center at Houston

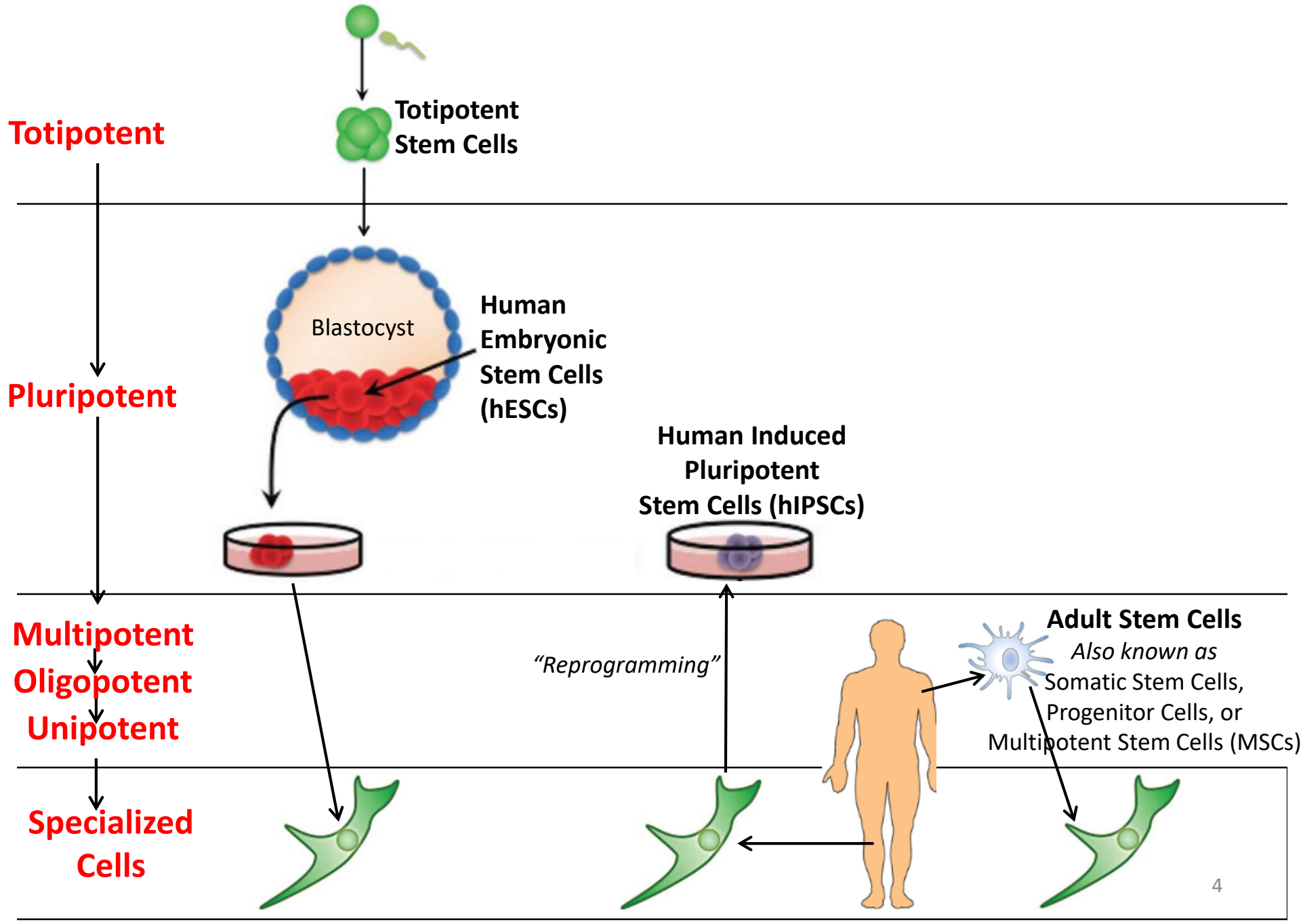
Stem Cell Research Oversight (SCRO)

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



Types of Research for Which Stem Cell Research Oversight (SCRO) Review is Required

	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**

Stem Cell Research Oversight (SCRO) Website

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

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

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

ClinicalTrials.gov

FDA INDs and IDEs

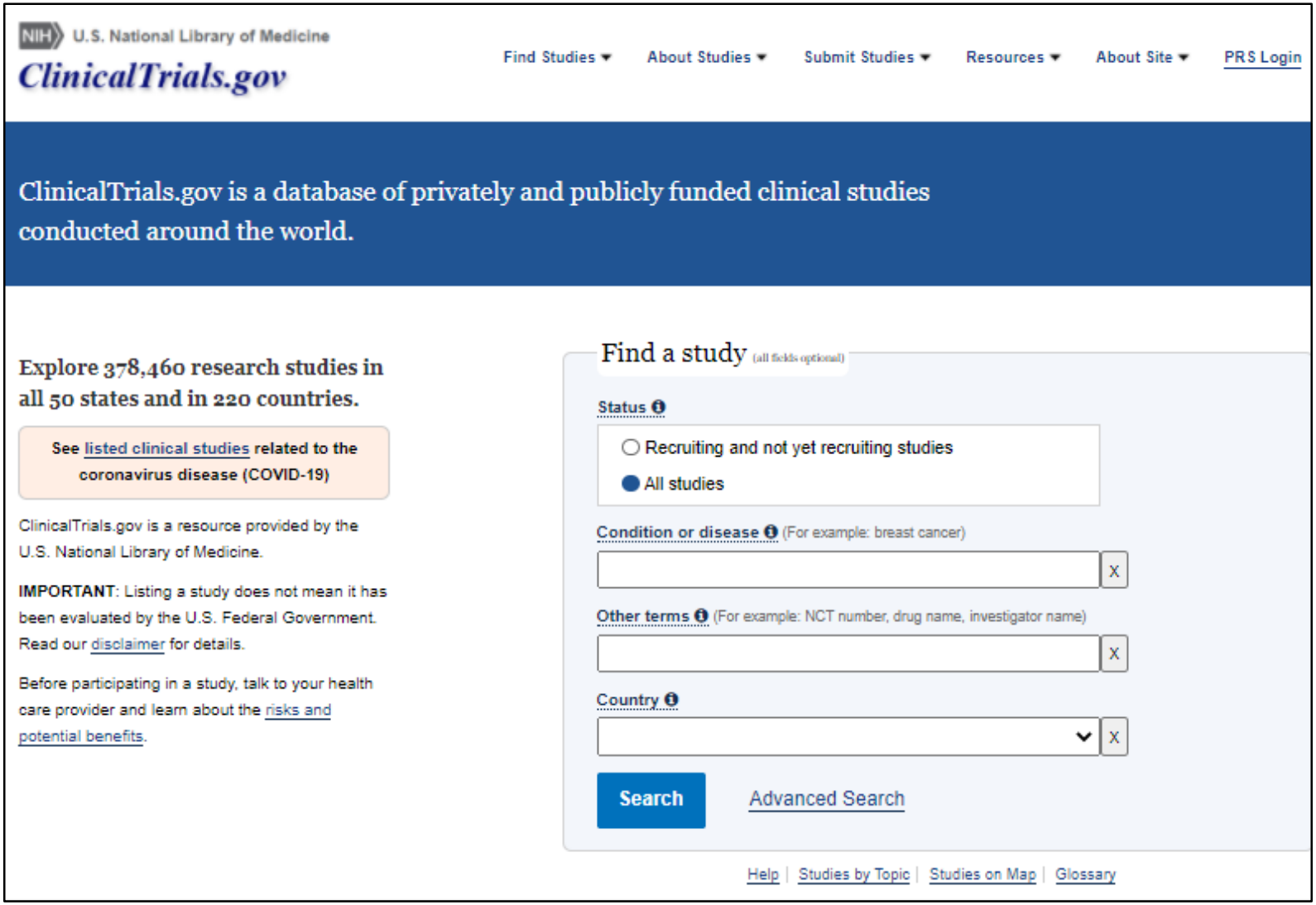
Regulatory Services for Clinical Trials

- **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 any of the above are required**

- **CTRC can assist with:**
  - Registration, Updates, and Results Entry at ClinicalTrials.gov
  - Preparation and Submission of Application to FDA for Approval to Study an Investigational Drug or Device *(that is, an IND or IDE application)*

ClinicalTrials.gov is a Public Database of Clinical Trials



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*

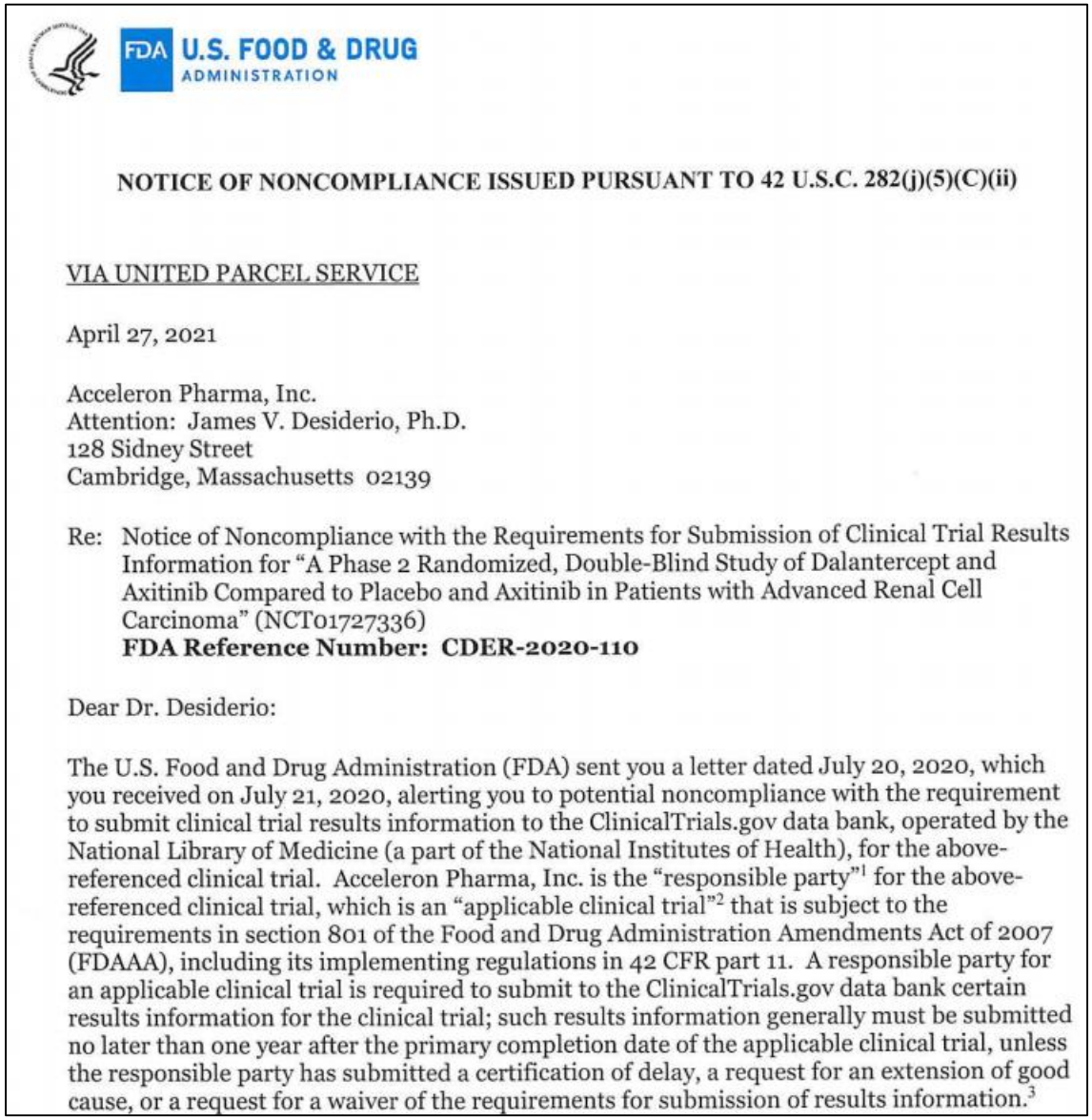
Why Register and Report Results at ClinicalTrials.gov?

- It's the **law**! *enforceable by 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

FDA Fines for Late ClinicalTrials.gov Results

- FDA fines of **$10,000** plus **$10,000 per day thereafter**
- FDA performs audits of ClinicalTrials.gov records

On 4/28/21, FDA Issued the First **Notice of Noncompliance**



U.S. FOOD & DRUG ADMINISTRATION

NOTICE OF NONCOMPLIANCE ISSUED PURSUANT TO 42 U.S.C. 282(j)(5)(C)(ii)

VIA UNITED PARCEL SERVICE

April 27, 2021

Acceleron Pharma, Inc.
Attention: James V. Desiderio, Ph.D.
128 Sidney Street
Cambridge, Massachusetts 02139

Re: Notice of Noncompliance with the Requirements for Submission of Clinical Trial Results Information for "A Phase 2 Randomized, Double-Blind Study of Dalantercept and Axitinib Compared to Placebo and Axitinib in Patients with Advanced Renal Cell Carcinoma" (NCT01727336)
FDA Reference Number: CDER-2020-110

Dear Dr. Desiderio:

The U.S. Food and Drug Administration (FDA) sent you a letter dated July 20, 2020, which you received on July 21, 2020, alerting you to potential noncompliance with the requirement to submit clinical trial results information to the ClinicalTrials.gov data bank, operated by the National Library of Medicine (a part of the National Institutes of Health), for the above-referenced clinical trial. Acceleron Pharma, Inc. is the "responsible party"[1] for the above-referenced clinical trial, which is an "applicable clinical trial"[2] that is subject to the requirements in section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), including its implementing regulations in 42 CFR part 11. A responsible party for an applicable clinical trial is required to submit to the ClinicalTrials.gov data bank certain results information for the clinical trial; such results information generally must be submitted no later than one year after the primary completion date of the applicable clinical trial, unless the responsible party has submitted a certification of delay, a request for an extension of good cause, or a request for a waiver of the requirements for submission of results information.[3]

Link to FDA Letter

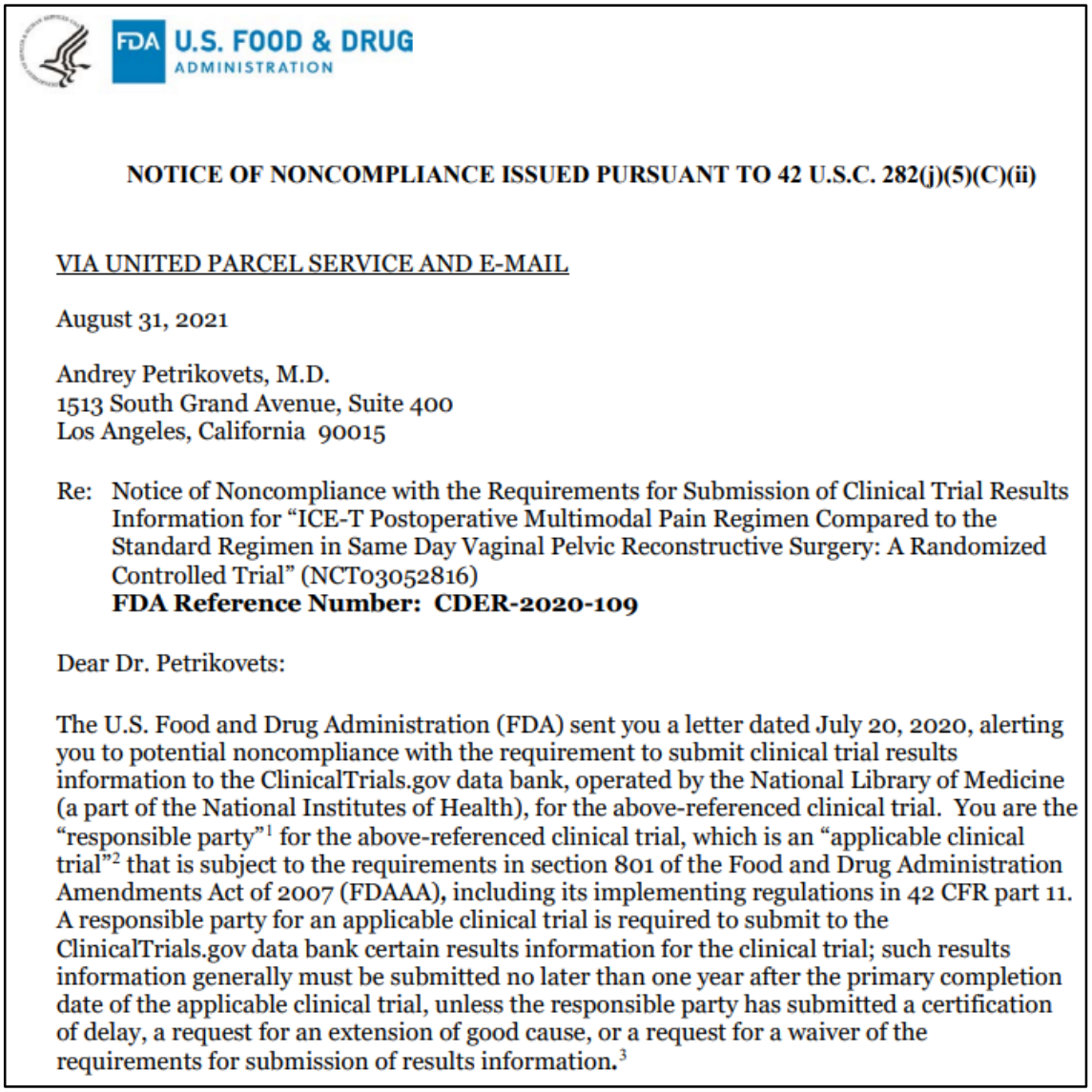
Link to FDA announcement

Link to Science article

Link to CenterWatch WCG article

Link to all Notices of Noncompliance

On 8/31/21, FDA Issued the First **Notice of Noncompliance** ***to an Individual Investigator***



FDA U.S. FOOD & DRUG ADMINISTRATION

NOTICE OF NONCOMPLIANCE ISSUED PURSUANT TO 42 U.S.C. 282(j)(5)(C)(ii)

VIA UNITED PARCEL SERVICE AND E-MAIL

August 31, 2021

Andrey Petrikovets, M.D.
1513 South Grand Avenue, Suite 400
Los Angeles, California 90015

Re: Notice of Noncompliance with the Requirements for Submission of Clinical Trial Results Information for "ICE-T Postoperative Multimodal Pain Regimen Compared to the Standard Regimen in Same Day Vaginal Pelvic Reconstructive Surgery: A Randomized Controlled Trial" (NCT03052816)
FDA Reference Number: CDER-2020-109

Dear Dr. Petrikovets:

The U.S. Food and Drug Administration (FDA) sent you a letter dated July 20, 2020, alerting you to potential noncompliance with the requirement to submit clinical trial results information to the ClinicalTrials.gov data bank, operated by the National Library of Medicine (a part of the National Institutes of Health), for the above-referenced clinical trial. You are the "responsible party"[1] for the above-referenced clinical trial, which is an "applicable clinical trial"[2] that is subject to the requirements in section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), including its implementing regulations in 42 CFR part 11. A responsible party for an applicable clinical trial is required to submit to the ClinicalTrials.gov data bank certain results information for the clinical trial; such results information generally must be submitted no later than one year after the primary completion date of the applicable clinical trial, unless the responsible party has submitted a certification of delay, a request for an extension of good cause, or a request for a waiver of the requirements for submission of results information.[3]

Link to FDA Letter

Link to STAT article

Link to all Notices of Noncompliance

Effects on Federal Funding

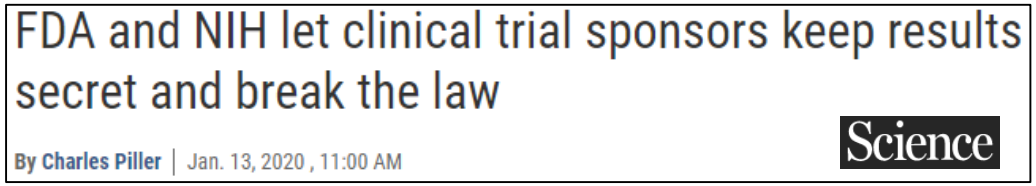
- Federal grant funding can be withheld
- Suspension or termination of NIH funding
- May affect future NIH funding decisions
- Enforcement by NIH at the institutional level

  "NIH will withhold clinical trial funding to grantee institutions if the agency is unable to verify adequate registration and results reporting from all trials funded at that institution."

  JAMA: Toward a New Era of Trust and Transparency in Clinical Trials - Kathy Hudson, Michael Lauer, Francis Collins

  http://jamanetwork.com/journals/jama/fullarticle/2553888?guestAccessKey=554e0981-9434-45f2-b122-d0e673cd1182

Steady Stream of Public Shaming


FDA and NIH let clinical trial sponsors keep results secret and break the law

By Charles Piller | Jan. 13, 2020 , 11:00 AM

Science


The New York Times

OPINION

Biden Made a Promise to Scientists. He Can Still Keep It.

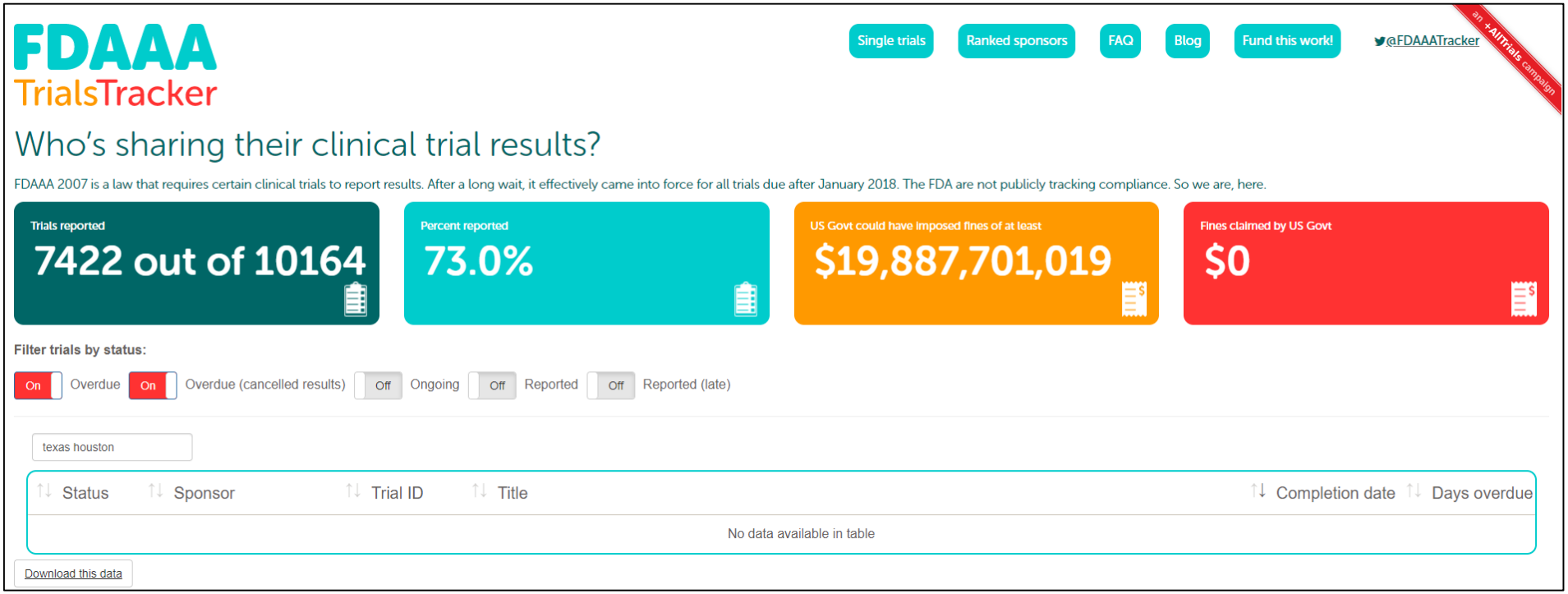
Researchers who receive federal help consistently fail to report their results to the public. The government should hold them accountable.

April 8, 2021

- Robert Califf et al., NEJM report (2015)
- Charles Piller, STAT report (2015)
- Harlan Krumholz, BMJ report (2016)
- Ben Goldacre, first TrialsTracker report (2016)
- Charles Piller/Talia Bronshtein, STAT report (2018)
- Holly Fernandez Lynch, STAT editorial (2018)
- Ben Goldacre of University of Oxford, FDAAA TrialsTracker site launched (2018)
  - Open letter to FDA
  - BMJ unreported trial of the week
- TranspariMED and UAEM report (2019)
  - Nature report on TranspariMED/UAEM findings (2019)
- John P.A. Ioannidis of Stanford, Annals of Internal Medicine report (2019)
  - Harlan Krumholz of Yale, Annals of Internal Medicine editorial (2019)
- Charles Piller, Science report (2020)
- Charles Piller, NY Times editorial (2021)
- TranspariMED and UAEM report #2 (2021)
- Reshma Ramachandran, JAMA report (2021)

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*
  - *Loss of NIH and other federal funding*
  - *Inability to publish in ICMJE journal*
  - *Public shaming*
  - *CMS consequences (an NCT # is required by CMS for claims for research-related procedures)*

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 noncompliance will be handled
  - How CTRC can help

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

- CTRC, led by Sujatha Sridhar, MBBS
  - 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, MPH** - 713-500-3551, Jessica.L.Martinez@uth.tmc.edu

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

ClinicalTrials.gov Process at UTHealth

- **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*
- **Shwetha Pazhoor notifies study teams if a full-board study must be registered, and provides assistance**
- **Jessica Martinez reaches out about updates, and provides assistance**
- **Elizabeth Gendel reaches out about results entry, and provides assistance**

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

THANK YOU!

- **Elizabeth Massey Gendel, PhD**
  - Elizabeth.M.Gendel@uth.tmc.edu
  - (713) 500-3587
- **Clinical Trials Resource Center (CTRC)**
  - clinicaltrials@uth.tmc.edu
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  - https://inside.uth.edu/scro/