1.8 FTE
- Monitor >2,000 records across 4 PRS accounts
  - SOM, SON
  - SKCCC
  - JHSPH
  - All Children’s

- Regularly assist other AMCs to develop programs
- Maintain 99% compliance and one of the top success rates of all academic sites
ClinicalTrials.gov – Public Site

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Public Site
https://clinicaltrials.gov

Public Beta Site
https://beta.clinicaltrials.gov/
ClinicalTrials.gov - PRS

Protocol Registration & Results System (PRS) https://register.clinicaltrials.gov

PRS Beta Site https://register.clinicaltrials.gov/v2/
Why a ClinicalTrials.gov Program?

1.) Commitment to participants, scientific validity/transparency, responsible stewardship

2.) Avoid non-compliance penalties
   — Civil or criminal judicial actions
   — Civil monetary penalties up to $12,462 per study, per day
   — Withholding of current or future funding
   — Reputational risk (also upside!)

3.) Faculty support
   — Steep learning curve (institutional efficiency)*
   — Changing regulations and modernization

Registration

• **Due prior to enrollment**
  - Any research study meeting the definition of a clinical trial
    - International Committee for Medical Journal Editors (ICMJE)
    - Food and Drug Administration Amendments Act (FDAAA)
    - National Institutes of Health (NIH)
  - Any research study with funding from an agency that requires registration
  - Any research from a foundation that requires registration as a term or condition of the grant/award
Results Reporting

- Due **12 months after primary completion date*** – Need to start 3-4 months early
- Results reporting reminders are sent to PI/Study team
- Assistance with results reporting
- Assistance with PRS reviewer comments (25 calendar days)
- Changes to PI/Study team (including when a PI leaves)
- Direct services at $50 per hour (optional)

* Final data collection date for primary outcome measure.
Record Maintenance

- If your record has an NCT number but isn’t approved in the IRB.
- If the study has an Overall Status of **Withdrawn**, the number enrolled/consented is 0, and an explanation must be entered.
- If the Overall Study status is **Terminated**, the number enrolled is entered and an explanation is required.
- If the Overall Study status is **Completed**, the Primary and Study completion dates (final data collection) are changed to actual dates and the actual enrollment number is provided.
Record Transfer

- Obtain email of PI to maintain communication, and follow up regarding the transfer
- PI provides transferring organization the contact information of the receiving organization PRS administrator
- Transferring organization confirms via email from the receiving organization or responsible party that the record will be accepted
- The email to Register@ClinicalTrials.gov should include:
  - Confirmation the record will be accepted at the receiving organization
  - Organization name
  - New username of the PI
  - NCT record number
Departing Faculty

• UMB is considering instituting a Checklist for departing faculty
• Each clinical trial needs action
  1. Will the study/grant be closed?
  2. Will the study/grant be transferred to a new PI at UMB?
  3. Will the study/grant be transferred to the new institution?

• Data from clinical trials are property of UMB and not the PI
  —Cannot be taken
  —If taken must be returned immediately
  —Refusal to return may involve legal action
Violations and Enforcement

Anthony Keyes, MBA, PMP
Program Administrator, Clinical Research Operations
FDAAA 801 Violations

• Applies to Applicable Clinical Trials (ACT)
• Notices are sent to the Responsible Party
  — Pre-Notice Letters are not identified as an FDAAA 801 Violation and not identified in ClinicalTrials.gov
  — Notice of Noncompliance Letters are identified as an FDAAA 801 Violation in ClinicalTrials.gov

FDA Enforcement

- FDA has sent 53 Pre-Notice Letters
- FDA has sent 4 Notice of Noncompliance Letters

<table>
<thead>
<tr>
<th>Responsible Party/Submitter</th>
<th>NCT Number</th>
<th>Notice of Noncompliance</th>
<th>Response Letter (if any)</th>
<th>Civil Money Penalty Amount (if any)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocugen</td>
<td>NCT03705340</td>
<td>4/15/2022</td>
<td>08/01/2022</td>
<td></td>
</tr>
<tr>
<td>Petrikovets, Andrey M.D.</td>
<td>NCT03052816</td>
<td>8/31/2021</td>
<td>12/20/2021</td>
<td></td>
</tr>
<tr>
<td>Accuitis Inc.</td>
<td>NCT03064438</td>
<td>7/26/2021</td>
<td>05/26/2022</td>
<td></td>
</tr>
<tr>
<td>Acceleron Pharma, Inc.</td>
<td>NCT01727336</td>
<td>4/27/2021</td>
<td>12/13/2021</td>
<td></td>
</tr>
</tbody>
</table>

- FDA has, so far, not issued any civil monetary penalties

https://www.fda.gov/science-research/fdas-role-clinicaltrialsgov-information/clinicaltrialsgov-notices-noncompliance-and-civil-money-penalty-actions#:~:text=FDA%20has%20the%20authority%20to,or%20misleading%20clinical%20trial%20information
FDA/NIH Enforcement

• August 2022 Office of Inspector General (OIG) Report
  “NIH did not ensure that all NIH-funded Intramural and Extramural clinical trials complied with Federal reporting requirements”

• FDA and NIH are working together to identify and target noncompliance

• NIH has sent >300 Noncompliance Letters

https://oig.hhs.gov/oas/reports/region6/62107000.asp
FDAAA 2007 is a law that requires certain clinical trials to report results. After a long wait, it effectively came into force for all trials due after January 2018. The FDA are not publicly tracking compliance. So we are, here.

Trials reported

13174 out of 17257

Percent reported

76.3%

US Govt could have imposed fines of at least

$46,920,219,765

Fines claimed by US Govt

$0

https://fdaaa.trialstracker.net/)
Congress demands that FDA and NIH sanction sponsors that fail to report clinical trial results

FDA is petitioned to boost enforcement of trial sponsors that fail to register studies or report results

NIH waste far over $100 million in medical research funding every year – new study

https://www.transparimed.org/single-post/fdaaa-pallone
https://www.transparimed.org/single-post/nih-research-waste
## Summary of Requirements

<table>
<thead>
<tr>
<th>Entity</th>
<th>Registration</th>
<th>Results Reporting</th>
<th>Penalties</th>
</tr>
</thead>
</table>
| Health and Human Services (HHS)             | Within 21 days of enrollment      | Within 365 days of primary completion date for ACTs                               | • $13,237/study/day  
• Criminal proceedings  
• Loss of grant funding |
| National Institutes of Health (NIH)         | Within 21 days of enrollment      | Within 365 days of primary completion date for clinical trials receiving NIH funding | Loss of grant funding (to include the institution)                |
| National Cancer Institute (NCI)            | Within 21 days of enrollment      | Within 365 days of primary completion date of NCI-supported clinical trials (in a peer-reviewed journal and/or ClinicalTrials.gov) | Loss of grant funding                                            |
| Veterans Health Administration (VHA)        | Prior to release of funding. Prior to enrollment | Within 365 days of primary completion date                                      | Loss of grant funding                                            |
## Summary of Requirements

<table>
<thead>
<tr>
<th>Entity</th>
<th>Registration</th>
<th>Results Reporting</th>
<th>Penalties</th>
</tr>
</thead>
</table>
| **Centers for Medicare & Medicaid Services** (CMS)  | All qualifying clinical trials                    | Study-specific                              | • Coverage denial  
• Costs and fraud investigations                      |
| **Patient-Centered Outcomes Research Institute** (PCORI) | All Clinical studies (including observational)   | Expected of all PCORI Clinical studies – 500 word abstract published on PCORI website | • Loss of grant funding |
| **International Committee of Medical Journal Editors** (ICMJE) | Prior to enrollment                              |                                             | Ineligibility to publish                           |
| **Department of Defense** (DoD)                     | Prior to enrollment. Prior to release of funding. | Study-specific                              | • Withholding or recovery of award funds            |
Using the Checklist

• Developed a Quality Review Checklist

<table>
<thead>
<tr>
<th></th>
<th>Pre-checklist</th>
<th>Post-checklist</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Registration, N</strong></td>
<td>107</td>
<td>104</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Success rate (%)</td>
<td>44.86</td>
<td>79.81</td>
<td></td>
</tr>
<tr>
<td>Submission cycles, mean (SD)</td>
<td>1.74 (0.78)</td>
<td>1.22 (0.46)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total days in review, mean (SD)</td>
<td>18.90 (26.72)</td>
<td>2.12 (3.85)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Results—Overall, N</strong></td>
<td>44</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Success rate (%)</td>
<td>11.36</td>
<td>40.91</td>
<td>0.010</td>
</tr>
<tr>
<td>Submission cycles, mean (SD)</td>
<td>2.23 (0.68)</td>
<td>1.64 (0.58)</td>
<td>0.0011</td>
</tr>
<tr>
<td>Total days in review, mean (SD)</td>
<td>115.80 (129.33)</td>
<td>39.27 (19.84)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

ClinicalTrials.gov at UMB
# Communication Process at UMB

<table>
<thead>
<tr>
<th>Communication</th>
<th>PI</th>
<th>Auditing and Monitoring (OAC)</th>
<th>Chair/Dean /IO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Email/CICERO</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Email/CICERO #2</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Email/CICERO #3</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

**Escalation**

![Escalation Arrow](image-url)
• OAC monitors compliance
• OAC will send periodic e-mails to PIs with non-compliant or soon to be non-compliant issues
• Problem records will impact future HRPO review
• Continuing Review will be delayed/denied with annual verification
• Appropriate handoff for new PIs (data, reporting obligations)
• Use the checklist to increase quality and decrease time in review
Continued Success

• Registering Records
  — Keep them updated!
    ▪ Within 30 days of changes
    ▪ Annually

• Departing faculty
  — Nationwide the biggest barrier
  — Communicate!

• Transferring Records
  — Register@ClinicalTrials.gov
ClinicalTrials.gov Taskforce

- 650 members, 220 Academic Centers
- Monthly Meetings (NLM, FDA, OHRP, NCI, NCATS)
- Many best practices developed
- Active listserv
- Revamping website to be ADA accessible
- Ongoing initiatives (i.e., dashboard for CTSA PIs, train the trainer, follow-up survey*)


https://ctrrtaskforce.org/
Co-Leads: Sarah White, MRCT; Tony Keyes, JHU
Questions

- https://ictr.johnshopkins.edu/service/study-conduct/rcss/
- akeyes1@jhmi.edu

- https://ictr.johnshopkins.edu/service/regulatory/ct-gov/
- registerclinicaltrials@jhmi.edu