

UMB Session IV: June 6, 2023



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JHU ClinicalTrials.gov Program



• 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

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ClinicalTrials.gov - PRS

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INSTITUTE for CLINICAL & TRANSLATIONAL RESEARCH

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- If the study has an Overall Status of **Withdrawn**, the number enrolled/consented is 0, and an explanation must be entered.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



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Anthony Keyes, MBA, PMP Program Administrator, Clinical Research Operations



FDAAA 801 Violations

- Applies to Applicable Clinical Trials (ACT)
- Notices are is 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

Responsible Party/Submitter	NCT Number	Notice of Noncompliance	Response Letter (if any)	Civil Money Penalty Amount (if any)
Ocugen	NCT03785340	4/15/2022	08/01/2022	
Petrikovets, Andrey M.D.	NCT03052816	<u>8/31/2021</u>	<u>12/20/2021</u>	
Accuitis Inc.	NCT03064438	7/26/2021	05/26/2022	
Acceleron Pharma, Inc.	NCT01727336	<u>4/27/2021</u>	<u>12/13/2021</u>	

• 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

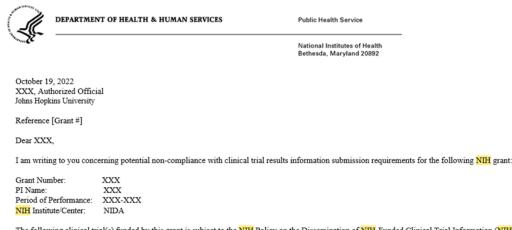


FDA/NIH Enforcement

• August 2022 Office of Inspector General (OIG) Report

"NIH did not ensure that all NIHfunded 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



The following clinical trial(s) funded by this grant is subject to the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information (NIH policy), NIH Grants Policy Statement, Section 4.1.3.1.

> NCTXXXXXXXX [Study Title] Primary Completion Date: XX/XX/XX

Compliance with the NIH policy is a term and condition of this grant award; however, NIDA has been unable to verify that results information has been submitted to ClincialTrials.gov for the clinical trial(s) funded by the above-referenced grant. The standard timeline for submission of results information is not later than one year after the trial's primary completion date. Similar requirements apply if the above-referenced clinical trial is also an "applicable clinical trial" subject to the requirements of Section 801 of the Food and Drug Administration Amendments Act of 2007, including its implementing regulations in 42 CFR part 11.



FDAAA TrialsTracker

FDAAA TrialsTracker

Who's sharing their clinical trial results?

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.

Ranked sponsors

Blog

Fund this work!

FAQ

All Has call

GFDAAATracker

Trials reported	Percent reported	US Govt could have imposed fines of at least	Fines claimed by US Govt
13174 out of 17257	76.3%	\$46,920,219,765	\$0 \$
Filter trials by status:	Off Ongoing Off Reported Off Reported (I	ate)	
Search Showing 1 to 100 of 36,750 entries		https://fdaaa.trialstracker.net/	JOHNS HOPKINS INSTITUTE for CLINICAL & TRANSLATIONAL RESEARCH

2023 Articles

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.statnews.com/pharmalot/2023/02/27/fda-petition-clinical-trials-transparency-nih/ INSTITUTE for CLINICAL & TRANSLATIONAL RESEARCH

https://www.transparimed.org/single-post/nih-research-waste

Summary of Requirements

Entity	Registration	Results Reporting	Penalties
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
<u>National Institutes</u> <u>of Health</u> (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/ <u>or</u> 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

Entity	Registration	Results Reporting	Penalties
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

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

CLINICALTRIALS.GOV JHU RECORD REVIEW

PROTOCOL ID	RECORD OWNER	REVIEWER	Regist Updat Result (add Result)	e status	D pACT/ACT
DATE RELEASED	COMMENTS DATE	REPLY DATE		DATE PUBLIS	HED
GENERAL REVIEW ITEMS				NOTES	
 All Warnings (if need All parenthetical cita All acronyms have b Spell-check complet Free-text fields are b 	is IRB PI: ord Owner is up-to-date d in IRB "Clinical Trials Inform ded) ations have been removed een expanded on their first u	ise on to report, and do r			
PROTOCOL SECTION					
 Brief Title does not i Official title should r 	s the IRB number (JHU Policy nclude study type (e.g., Phas natch what is in the IRB (or g de NIH grant numbers (verify	e J, Randomized) rant application if ap	plicable)		
 Overall Status match Study start date veri Completion Dates A 	Date is the current month/ye nes IRB/CRMS fied with CRMS enrollment d ctual/Anticipated have been tcomes are the same the prir	late evaluated for accura		es are identical	
SPONSOR/COLLABORATOR		nformation" section	included as	s Collaborators	5

All sources of support identified in IRB "Support Information" section included as Colla

 $\hfill\square$ Full Name used and if not recognized. "Recognize" is selected

Tetteh, O., Nuamah, P., Keyes, A. Addressing the quality of submissions to ClinicalTrials.gov for registration and results posting: The use of a checklist. *Society of Clinical Trials.* Published online August 5, 2020. https://doi.org/10.1177/1740774520942746



ClinicalTrials.gov at UMB



Communication Process at UMB

Communication	PI	Auditing and Monitoring (OAC)	Chair/Dean /IO
Email/CICERO			
Email/CICERO #2			
Email/CICERO #3			\checkmark



Escalation



- OAC monitors compliance
- OAC will send periodic e-mails to PIs with non-compliant or soon to be non-compliant issues



UMB HRPO

- 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*)

*Mayo-Wilson, E., Heyward, J., Keyes, A. *et al.* Clinical trial registration and reporting: a survey of academic organizations in the United States. *BMC Med* 16, 60 (2018) <u>doi:10.1186/s12916-018-1042-6</u>

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

