United States Senate
WASHINGTON, DC 20510

October 13, 2022

VIA ELECTRONIC TRANSMISSION

Lawrence A. Tabak, D.D.S., Ph.D.
Acting Director
National Institutes of Health
Bethesda, M.D. 20892

Acting Director Dr. Tabak:

We write to you today regarding the Department of Health and Human Services (HHS), Office of Inspector General's (OIG) recent report finding that the National Institutes of Health (NIH) failed to ensure that the results of NIH-funded intramural and extramural clinical trials are submitted to ClinicalTrials.gov, as required by federal law.[1, 2, 3] For example, HHS OIG found that, of 72 NIH-funded intramural and extramural clinical trials required to report findings in 2019 and 2020, only 37 studies complied with federal reporting requirements.[4] Moreover, NIH allowed 21 researchers who failed to comply with federal reporting requirements to begin new NIH-funded trials before submitting the results of their previous clinical trials.[5] According to HHS OIG, providers, patients, and researchers benefit the most when clinical trial results are posted online because it gives them more information on patient outcomes including adverse side-effects and other related events.[6]

Federal law and NIH policy requires the sponsor(s) of a clinical trial to report the results of its clinical trial to ClinicalTrials.gov within one year of the trial completion date.[7] NIH policy establishes an exception for NIH-funded clinical trials, which requires the sponsor to submit the results of the clinical trial to the National Library of Medicine staff.[8] NIH policy then requires the National Library of Medicine to report these findings to ClinicalTrials.gov.[9] HHS OIG found that

[1] Intramural clinical trials are carried out by NIH scientists in NIH laboratories. *See* U.S. Dept. of Health and Human Servs., Off. of Inspector Gen., *Report No. A-06-21-07000*: *The National Institutes of Health did not Ensure that All Clinical Trial Results were Reported in Accordance with Federal Requirements* 3-4 (2002), https://oig hhs.gov/oas/reports/region6/62107000.pdf.
[2] Extramural clinical trials are carried out by scientists at universities, medical centers, hospitals, and research institutions and are supported by NIH grants and contracts. *See* U.S. Dept. of Health and Human Servs., Off. of Inspector Gen., *Report No. A-06-21-07000*: *The National Institutes of Health did not Ensure that All Clinical Trial Results were Reported in Accordance with Federal Requirements* 3-4 (2002), https://oig hhs.gov/oas/reports/region6/62107000.pdf.
[3] 42 C.F.R. § 11.12. *See* U.S. Dept. of Health and Human Servs., Off. of Inspector Gen., *Report No. A-06-21-07000*: *The National Institutes of Health did not Ensure that All Clinical Trial Results were Reported in Accordance with Federal Requirements* 4 (2002), https://oig.hhs.gov/oas/reports/region6/62107000.pdf.
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[5] *Id. at 8.*
[6] *Id.*
[7] *Id.* at 5.
[8] *Id.* at 2.
[9] *Id.*

NIH did not have adequate internal policies and procedures in place to notify parties prior to non-compliance, and took limited enforcement actions after the fact.[10]

HHS OIG made a number of recommendations to NIH to improve its internal processes and procedures regarding clinical trials.[11] NIH concurred with HHS OIG, and outlined a series of steps it planned to implement including the establishment of an integrated electronic system that will allow NIH staff to monitor ClinicalTrials.gov and alert them of instances of non-compliance.[12] According to NIH, this integrated electronic system will "provide a robust and automated system for centralized tracking of registration and reporting information."[13]

The NIH is the United States' preeminent medical research institution and receives billions of dollars in federal appropriations each year. For example, in FY2022, NIH received $46.183 billion in federal appropriations.[14] When American taxpayers spend billions of dollars on federal programs, they expect accountability, transparency, and results. HHS OIG's report makes clear that the NIH must do more to hold grant recipients accountable, so that the public is able to access timely clinical trial results.

In light of these concerns, please respond to the following questions by November 3, 2022:

1. What steps, including those noted in NIH's response to the OIG report, is the NIH taking to increase accountability for grant recipients? What types of enforcement measures will be put in place?

2. Please provide the status and implementation timeline of those improvements referenced in the NIH's response to the OIG's recommendations including NIH's development of a centralized workflow and the establishment of an integrated electronic system to facilitate non-compliance alerts.

3. Since 2007, how many NIH-funded trials have failed to comply with federal and NIH reporting requirements? Will NIH commit to making these results public? If not, why not?

4. Please provide a list of the 37 grant recipients that failed to comply with federal and NIH reporting requirements in 2019 and 2020.
    a. How much taxpayer funding did NIH grant to the 37 recipients that failed to comply with reporting requirements?
    b. How much funding did NIH give to the grant recipients that have failed to comply with reporting requirements since 2007?

[10] *Id.* at 5.
[11] *Id.* at 8-9.
[12] *Id.* at 12-14.
[13] *Id.* at 12-13.
[14] Congressional Rsch. Serv., *Report No. 43341: National Institutes of Health (NIH) Funding: FY1996-FY2023* (2022).

5. What actions has NIH taken to remove oversight responsibilities from employees who intentionally opted to ignore the enforcement requirements?

6. How will NIH ensure that staff follows their enforcement obligations??

Thank you for your attention to this important matter. We look forward to your reply.

Sincerely,

Marsha Blackburn
United States Senator

Charles E. Grassley
United States Senator

Ron Johnson
United States Senator

Roger Marshall, M.D.
United States Senator

From: Everett, Chris (NIH/OD) [E]
To: Kelly, Christopher (Blackburn)
Subject: NIH Response to Sen. Blackburn Letter
Date: Wednesday, December 21, 2022 1:51:55 PM
Attachments: NIH Response to Sen. Blackburn on Clinical Trial Results_FINAL.signed.pdf

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Hi Christopher,

I hope you're doing well. Please see attached NIH's response to a letter we received from Sen. Blackburn regarding NIH's efforts to ensure that the results of NIH-funded intramural and extramural clinical trials are submitted to ClinicalTrials.gov. Please let me know if you have any further questions or concerns and I hope you have a happy holiday season and new year!

Best,
Chris

Christopher Everett, J.D.
Office of Legislative Policy & Analysis
National Institutes of Health
P: (301) 443-2202
C: (b) (6)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

December 20, 2022

The Honorable Marsha Blackburn
United States Senate
Washington, DC 20510

Dear Senator Blackburn:

Thank you for your interest in the efforts of the National Institutes of Health (NIH) to ensure that the results of NIH-funded intramural and extramural clinical trials are submitted to ClinicalTrials.gov, consistent with federal law and NIH policy. NIH is committed to ensuring that information about clinical studies and their results is shared, including studies supported by NIH. NIH has taken several steps to strengthen oversight and improve compliance with clinical trial registration and results reporting requirements, which we are pleased to share with you and your colleagues in this letter.

NIH takes seriously its responsibility to disseminate the results of the research it supports, including the results of clinical trials. NIH continues to collaborate with the U.S. Food and Drug Administration (FDA) to improve compliance with the requirements of the Food and Drug Administration Amendments Act of 2007 (FDAAA), as implemented through the Department of Health and Human Services Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11). This regulation applies to "applicable clinical trials,"[1] defined by statute and regulation to include most interventional studies of drug, biological, and device products that are regulated by FDA. Reflecting NIH's commitment to data sharing, NIH issued a complementary policy that applies to **all** NIH-funded clinical trials, including those not subject to the regulation (see NIH policy on the Dissemination of NIH-Funded Clinical Trial Information). Both 42 CFR Part 11 and the NIH policy became effective on January 18, 2017.

Since the regulation and NIH policy went into effect, NIH has instituted a number of internal procedures to strengthen our compliance infrastructure.

- For Intramural Research. NIH has taken several steps to strengthen oversight and verify compliance with clinical trial registration and results reporting requirements. The NIH Office of Intramural Research published a new chapter for the NIH Policy Manual entitled, *Clinical Trial Registration and Results Information Reporting*, to define responsibilities and procedures for registering and reporting results of NIH's intramural clinical trials and establish procedures for addressing non-compliance. The new NIH Policy Manual Chapter has prompted improvement in compliance with timely reporting of primary outcome data and has proven to be an effective tool to facilitate intramural compliance with reporting requirements.
- For Extramural Research. The NIH Office of Extramural Research implemented enhancements to internal procedures to verify compliance among NIH-funded extramural investigators, including contractors and grant recipients. Contractor compliance is mandated

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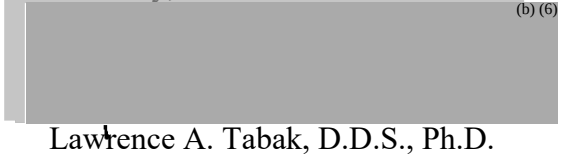
as part of the terms and conditions written into applicable research contracts and monitored by contracting officers and their contracting officer's technical representatives. For grant recipients, NIH developed a "Clinical Trials Compliance Workflow" to standardize approaches across NIH Institutes and Centers for verifying compliance with both the NIH policy and regulation. As part of the grants workflow, validations occur automatically through NIH's internal electronic Research Administration (eRA) systems at the time investigators submit annual progress reports and prior to award issuance. The eRA captures clinical trial information entered by grant recipients in a structured manner, communicates with other NIH information systems to verify clinical trial registration and reporting requirements have been met, alerts NIH staff to cases of potential non-compliance, and alerts grant recipient and NIH staff of inconsistencies across NIH information systems. The eRA Human Subjects System functionality increases grant recipient and NIH staff awareness of trials with late registration or results reporting. Additionally, NIH grants management and program staff review grant recipient annual progress reports to ensure grant recipients meet the clinical trial registration and results reporting requirements. Finally, to assist staff in carrying out their compliance responsibilities, NIH has implemented system validations at the time of award to ensure no awards will be issued without resolving delinquent registrations or results reporting.

For your awareness, the third Report on Clinical Trials, as mandated in section 2052 of the 21st Century Cures Act (P.L. 114-255), is currently being prepared for transmission to Congress in early spring of 2023. This report will include information on activities conducted by NIH and FDA to encourage compliance with section 402(j) of the PHS Act, including its implementing regulations, by responsible parties; activities undertaken to educate responsible parties about data bank registration and summary results information submission requirements; the total number of applicable clinical trials (ACTs) with complete data bank registration information registered on ClinicalTrials.gov between January 18, 2017, and September 30, 2022; and the total number of ACTs registered for which summary results information was submitted to the data bank between January 18, 2017, and September 30, 2022.

We continue to seek opportunities to improve our oversight procedures and will continue to monitor NIH-funded clinical trial results reporting and refine our procedures as needed. Thank you for your interest in NIH's oversight and stewardship of the clinical research enterprise. An identical response has been sent to each co-signer of your letter.

Sincerely,



Lawrence A. Tabak, D.D.S., Ph.D.
Performing the Duties of the NIH Director

From: Murray, Katie (NIH/OD) [E]
To: nic_pottebaum@grassley.senate.gov
Subject: NIH Response to Letter on Clinical Trial Results
Date: Tuesday, December 20, 2022 5:16:00 PM
Attachments: Letter to NIH_Final (3).pdf
NIH Response to Sen. Grassley on Clinical Trial Results_FINAL.signed.pdf

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Hi Nic,

Please find attached the NIH response to Senator Grassley's October 13, 2022 letter regarding clinical trial results on ClinicalTrials.gov.

We hope that you and the Senator find this information helpful. Please feel free to reach out to me with any questions.

Kind regards,
Katie

Katie Murray, MS
Office of Legislative Policy & Analysis
National Institutes of Health
Cell: (b) (6) | katie.murray@nih.gov

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

December 20, 2022

The Honorable Charles E. Grassley
United States Senate
Washington, DC 20510

Dear Senator Grassley:

Thank you for your interest in the efforts of the National Institutes of Health (NIH) to ensure that the results of NIH-funded intramural and extramural clinical trials are submitted to ClinicalTrials.gov, consistent with federal law and NIH policy. NIH is committed to ensuring that information about clinical studies and their results is shared, including studies supported by NIH. NIH has taken several steps to strengthen oversight and improve compliance with clinical trial registration and results reporting requirements, which we are pleased to share with you and your colleagues in this letter.

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For your awareness, the third Report on Clinical Trials, as mandated in section 2052 of the 21st Century Cures Act (P.L. 114-255), is currently being prepared for transmission to Congress in early spring of 2023. This report will include information on activities conducted by NIH and FDA to encourage compliance with section 402(j) of the PHS Act, including its implementing regulations, by responsible parties; activities undertaken to educate responsible parties about data bank registration and summary results information submission requirements; the total number of applicable clinical trials (ACTs) with complete data bank registration information registered on ClinicalTrials.gov between January 18, 2017, and September 30, 2022; and the total number of ACTs registered for which summary results information was submitted to the data bank between January 18, 2017, and September 30, 2022.

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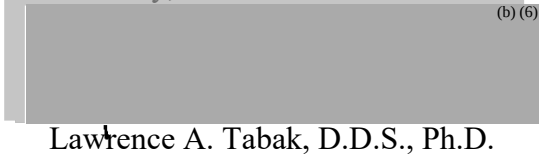

Lawrence A. Tabak, D.D.S., Ph.D.
Performing the Duties of the NIH Director

From: Murray, Katie (NIH/OD) [E]
To: McLeod, Josh (Ron Johnson)
Subject: NIH Response to Letter on Clinical Trial Results
Date: Tuesday, December 20, 2022 5:17:00 PM
Attachments: Letter to NIH_Final (3).pdf
NIH Response to Sen. Johnson on Clinical Trial Results_FINAL.signed.pdf

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Hi Josh,

Please find attached the NIH response to Senator Johnson's October 13, 2022 letter regarding clinical trial results on ClinicalTrials.gov.

We hope that you and the Senator find this information helpful. Please feel free to reach out to me with any questions.

Kind regards,
Katie

Katie Murray, MS
Office of Legislative Policy & Analysis
National Institutes of Health
Cell: (b) (6) | katie.murray@nih.gov

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

December 20, 2022

The Honorable Ron Johnson
United States Senate
Washington, DC 20510

Dear Senator Johnson:

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Sincerely,

(b) (6)

Lawrence A. Tabak, D.D.S., Ph.D.
Performing the Duties of the NIH Director

From:	Brand, Morgan (NIH/OD) [E]
To:	Pineda, Charlotte (Marshall)
Subject:	NIH Response to Sen. Marshall letter on clinical trials
Date:	Wednesday, December 21, 2022 3:00:18 PM
Attachments:	NIH Response to Sen. Marshall on Clinical Trial Results_FINAL.signed.pdf Letter to NIH_Final (3).pdf

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Hi Charlotte,

Please see the attached response to a letter signed by Sen. Marshall on clinical trials.

Best,
Morgan

Morgan S. Brand
Office of Legislative Policy & Analysis
National Institutes of Health
morgan.brand@nih.gov
D: (301) 480-8590 | C: (b) (6)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

December 20, 2022

The Honorable Roger Marshall
United States Senate
Washington, DC 20510

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Lawrence A. Tabak, D.D.S., Ph.D.
Performing the Duties of the NIH Director