

Department of Health and Human Services

**OFFICE OF  
INSPECTOR GENERAL**

**THE NATIONAL INSTITUTES OF  
HEALTH DID NOT ENSURE THAT  
ALL CLINICAL TRIAL RESULTS  
WERE REPORTED IN  
ACCORDANCE WITH FEDERAL  
REQUIREMENTS**

*Inquiries about this report may be addressed to the Office of Public Affairs at  
[Public.Affairs@oig.hhs.gov](mailto:Public.Affairs@oig.hhs.gov).*



**Amy J. Frontz**  
Deputy Inspector General  
for Audit Services

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# ***Office of Inspector General***

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# Report in Brief

Date: August 2022  
Report No. A-06-21-07000



## Why OIG Did This Audit

The National Institutes of Health (NIH) provides funding for clinical trials carried out by NIH scientists in NIH laboratories on its campuses (Intramural) and through awards to the community of scientists at universities, medical centers, hospitals, and research institutions throughout the United States and abroad (Extramural). NIH is responsible for ensuring that NIH-funded Intramural and Extramural clinical trials are reported on ClinicalTrials.gov. Our preliminary review of data from ClinicalTrials.gov showed that most NIH-funded clinical trials that were completed in calendar year 2018 did not have their results posted.

Our objective was to determine whether NIH ensured that NIH-funded Intramural and Extramural clinical trials complied with Federal reporting requirements.

## How OIG Did This Audit

We reviewed all 72 NIH-funded Intramural and Extramural clinical trials for which Federal law and NIH policy required the results to be reported in calendar year 2019 or 2020. To determine whether responsible parties complied with reporting requirements, we compared the date the results should have been submitted with the date they were submitted. We also determined whether NIH posted the clinical trial results submitted by the responsible parties to ClinicalTrials.gov within 30 days of the submission date.

## The National Institutes of Health Did Not Ensure That All Clinical Trial Results Were Reported in Accordance With Federal Requirements

### What OIG Found

NIH did not ensure that all NIH-funded Intramural and Extramural clinical trials complied with Federal reporting requirements for responsible parties to submit the results of clinical trials to ClinicalTrials.gov. The Table summarizes the number of clinical trials requiring results to be submitted in 2019 or 2020 that were submitted on time, late, or not submitted at all.

**Table: Summary of Clinical Trials Requiring Results To Be Submitted in 2019 or 2020**

	Intramural	Extramural	Total
Submitted on Time	20	15	35
Submitted Late	11	1	12
Results Not Submitted	5	20	25
Subtotal of Noncompliance	16	21	37
<b>Total</b>	<b>36</b>	<b>36</b>	<b>72</b>

The noncompliance with Federal reporting requirements occurred because NIH did not have adequate procedures for ensuring that responsible parties submitted the results of clinical trials, took limited enforcement action when there was noncompliance, and continued to fund new research of responsible parties that had not submitted the results of their completed clinical trials. For the 47 NIH-funded clinical trials in which the responsible party submitted their results (35 submitted on time and 12 submitted late) NIH complied with the Federal reporting requirements to post the results to ClinicalTrials.gov.

### What OIG Recommends

We recommend that NIH (1) improve its procedures to ensure that responsible parties of NIH-funded clinical trials comply with requirements to submit results to ClinicalTrials.gov in a timely manner, (2) take enforcement actions against responsible parties that are late in submitting trial results or do not submit results, and (3) work with the responsible parties to understand their challenges related to ClinicalTrials.gov and implement procedures to address the challenges.

In written comments on our draft report, NIH concurred with our recommendations and described the actions it has taken or plans to take to address them. For example, NIH stated it has begun to implement improvements to its internal procedures and activities to enhance its ability to take compliance action against responsible parties out of compliance.

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## INTRODUCTION

### WHY WE DID THIS AUDIT

The National Institutes of Health (NIH) provides funding for clinical trials carried out by NIH scientists in NIH laboratories on its campuses (Intramural) and through awards to the extramural community of scientists at universities, medical centers, hospitals, and research institutions throughout the United States and abroad (Extramural). A clinical trial is a research study that evaluates the effect of an intervention on study participants. An intervention may be a medical product, such as a drug or device; a procedure; or changes to participants' behavior, such as diet.<sup>1</sup> Clinical trials are vital to human medical advances because they help determine whether interventions are safe and effective.

NIH is responsible for ensuring that NIH-funded Intramural and Extramural clinical trials are reported on the public website ClinicalTrials.gov. Posting the results of clinical trials on ClinicalTrials.gov provides the public information that is available for understanding the safety and effectiveness of interventions. We conducted this audit because our preliminary review of data from ClinicalTrials.gov showed that the results of most NIH-funded clinical trials that were completed in calendar year 2018 were not posted.

### OBJECTIVE

Our objective was to determine whether NIH ensured that NIH-funded Intramural and Extramural clinical trials complied with Federal reporting requirements.

### BACKGROUND

#### The National Institutes of Health

According to its website, NIH is the nation's medical research agency – making important discoveries that improve health and save lives. NIH comprises 27 Institutes and Centers, each with a specific research agenda, one of which is the National Library of Medicine. Among its other responsibilities, the National Library of Medicine developed, maintains, and operates the ClinicalTrials.gov registry and results databank on behalf of NIH. The Office of Intramural Research oversees clinical trials conducted by intramural researchers within the Institutes and Centers. The NIH Office of Extramural Research supports the entire NIH extramural research community, as well as the 24 NIH Institutes and Centers that award grants to research institutions, by providing policy, guidance, systems, and other technical support. The Office of Policy for Extramural Research Administration, within the Office of Extramural Research, ensures NIH-funded projects are conducted in accordance with the approved application,

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<sup>1</sup> 42 CFR § 11.10(a) defines clinical trials as a “clinical study in which human subject(s) are prospectively assigned, according to a protocol, to one or more interventions (or no intervention) to evaluate the effect(s) of the intervention(s) on biomedical or health-related outcomes.”

budget, and the terms and conditions of award and inform NIH of any problems or concerns regarding compliance.

### **Submitting and Posting Clinical Trial Results to ClinicalTrials.gov**

ClinicalTrials.gov is a publicly accessible registry and results database of publicly and privately supported clinical studies of human participants maintained by the National Library of Medicine. Federal law requires the responsible party of an “Applicable Clinical Trial” to submit the results of its clinical trial to ClinicalTrials.gov within 1 year of the earlier of the estimated or actual completion date.<sup>2, 3</sup> NIH policy established an expectation for the submission of results of all NIH-funded clinical trials and requires the investigator or the awardee to perform the duties of the responsible party for all NIH-funded clinical trials. The policy clarifies that award applicants are required to submit a plan outlining how they will meet the policy's expectations, and, that upon receipt of an award, an awardee will be obligated to adhere to its plan through the terms and conditions of the award.<sup>4</sup> Federal law and NIH policy require NIH to ensure that the responsible party of NIH-funded clinical trials complies with the submission requirements.<sup>5, 6</sup> The National Library of Medicine staff reviews the submissions for apparent errors, deficiencies, or inconsistencies and notifies the responsible parties of any it finds. After its review is complete, the National Library of Medicine staff posts the results of the clinical trial on ClinicalTrials.gov for the public to view. Federal law requires NIH to post the results within 30 days of the submission date.<sup>7</sup>

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<sup>2</sup> 42 CFR § 11.10. The responsible party is defined as the sponsor of the clinical trial or the principal investigator if designated by the sponsor, grantee, or awardee, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements of the responsible party in the law and regulation. The sponsor initiates but does not actually conduct the clinical trial. 42 U.S.C. § 282(j)(1)(A)(ix); 42 CFR § 11.4(c).

<sup>3</sup> An applicable clinical trial is a clinical trial of a drug, biologic, or device product regulated by the Food and Drug Administration initiated after Sept. 27, 2007, or ongoing as of Dec. 26, 2007; phase 1 clinical trials are not included (42 U.S.C. § 282(j)(1)(A)(i); 42 CFR § 11.22(a)).

<sup>4</sup> NOT-OD-16-149, “NIH Policy on Dissemination of NIH-Funded Clinical Trial Information.” Available online at <https://grants.nih.gov/grants/guide/notice-files/not-od-16-149.html>. Accessed Aug. 5, 2022. The policy incorporates the definition of the responsible party and the reporting timeframes from the law and regulation.

<sup>5</sup> The head of the grant-making agency must verify that the responsible party for an applicable clinical trial that is funded in whole or in part by a grant from that agency has submitted the results of its clinical trial before releasing any remaining funding for the grant or a future grant for the same grantee. Upon verification that the responsible party has not submitted the results, the awarding agency must provide a 30-day notice to the grantee to correct the non-compliance (42 U.S.C. § 282(j)(5)(A)).

<sup>6</sup> Throughout this report, we have used the term “responsible party” for applicable clinical trials as defined in 42 CFR part 11 and when referring to the investigator or awardee for clinical trials that fall under the scope of the NIH policy.

<sup>7</sup> With limited exceptions, 42 CFR § 11.52 requires NIH to publicly post the clinical trial results of applicable clinical trials on ClinicalTrials.gov not later than 30 calendar days after the responsible party has submitted them.

Each trial record on the ClinicalTrials.gov website includes, among other information submitted by the responsible party, the trial's purpose, recruitment status, and eligibility criteria.<sup>8</sup> The results information must include a summary of, among other information, the number of participants starting and completing the trial, baseline characteristics of the study population, outcome measures and statistical analysis, and adverse events.<sup>9</sup> Posting clinical trial results on ClinicalTrials.gov helps researchers focus on areas in need of study and avoids unnecessary duplication of studies, improves future research designs, increases public trust in research, enhances patient access to and understanding of the results of clinical trials, and ultimately advances the development of clinical interventions.

### **Office of Intramural Research**

Approximately 10 percent of NIH funds supports research activities, including clinical trials, that are carried out by NIH scientists in NIH laboratories. The NIH Office of Intramural Research is responsible for oversight and coordination of this intramural research, as well as for training, policy development, and laboratory safety within NIH laboratories and clinics. The Office of Intramural Research evaluates all clinical trial proposals with a review group composed of qualified and experienced professionals.

To ensure that Intramural clinical trials comply with Federal reporting requirements, the Office of Protocol Services within the Office of Intramural Research begins sending notifications that contain the reporting requirements to the responsible parties approximately 6 months before the deadline for submitting the trial results to ClinicalTrials.gov and every other month as the deadline approaches. The Office of Protocol Services also monitors trials for noncompliance and sends notices to the responsible parties that have not submitted the results of their trial to ClinicalTrials.gov requesting compliance.

### **Office of Extramural Research**

More than 80 percent of the amount appropriated to NIH is awarded through awards to the extramural community. The extramural community comprises scientists at universities, medical centers, hospitals, and research institutions throughout the United States and abroad. (In this report, we refer to these entities, collectively, as institutions.) With NIH support, the extramural community conducts the vast majority of the research that leads to improvement in the prevention, detection, diagnosis, and treatment of disease and disability. NIH's Office of Extramural Research provides leadership, oversight, tools, and guidance to administer the NIH grants management operations. All grants and contracts undergo a peer review process in

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<sup>8</sup> Recruitment status indicates whether the trial is recruiting participants. Statuses include not yet recruiting; recruiting; active, not recruiting; suspended; terminated; completed; withdrawn; or unknown.

<sup>9</sup> 42 CFR § 11.28 and 42 CFR § 11.48 define the required registration and results information, respectively, that the responsible party must submit to ClinicalTrials.gov.



which a panel of experts evaluates proposed research based on merit, availability of funds, and other considerations.<sup>10</sup>

To ensure that extramural clinical trials comply with Federal reporting requirements, the NIH Funding Institute's or Center's Office of Grants Management sends notices of noncompliance to the responsible parties that have not submitted the results of their trial to ClinicalTrials.gov. If the responsible parties are not responsive, the Office of Policy for Extramural Research Administration, within the Office of Extramural Research, sends out a second notice of noncompliance. However, these notices are sent out only after the required reporting timeframe has passed.

## **HOW WE CONDUCTED THIS AUDIT**

We reviewed all 72 NIH-funded Intramural and Extramural clinical trials (36 of each) for which NIH policy required the results to be reported in calendar year 2019 or 2020. To determine whether responsible parties complied with NIH policy for reporting the results of their clinical trials, we compared the date the results should have been submitted with the date the responsible party submitted them.<sup>11</sup> We also determined whether NIH posted the trial results to ClinicalTrials.gov within 30 days of the submission date as required by Federal law.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Appendix A contains the details of our audit scope and methodology.

## **FINDINGS**

NIH did not ensure that all NIH-funded Intramural and Extramural clinical trials complied with Federal reporting requirements for responsible parties to submit the results of clinical trials to ClinicalTrials.gov. Of the 72 NIH-funded clinical trials we reviewed, NIH ensured that responsible parties associated with 35 clinical trials (20 Intramural-funded and 15 Extramural-funded) complied with Federal reporting requirements. However, NIH did not ensure that responsible parties associated with 37 clinical trials (16 Intramural-funded and 21 Extramural-funded) complied with Federal reporting requirements. Specifically, responsible parties for the

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<sup>10</sup> 42 CFR part 52h.

<sup>11</sup> 42 CFR § 11.44(b) allows responsible parties to delay submission of results in certain circumstances and 42 CFR § 11.54 allows responsible parties to request, and NIH to grant, waivers to submission requirements. In addition to the flexibilities allowed in the CFR, NIH policy NOT-OD-19-126 (issued July 24, 2019 and effective during our audit period) allowed flexibilities in enforcement for certain clinical trials. NIH did not grant any waivers, extensions, or exceptions (or employ any other flexibilities) for the clinical trials in our audit scope.

37 clinical trials that did not comply with Federal reporting requirements either did not submit their results (5 Intramural-funded and 20 Extramural-funded) or submitted them late (11 Intramural-funded and 1 Extramural-funded).

NIH complied with the Federal reporting requirement to post clinical trial results to ClinicalTrials.gov within 30 days of the submission date for the 47 NIH-funded clinical trials in which responsible parties submitted their results (35 submitted on time and 12 submitted late). NIH posted these results in an average of 14 days. NIH was not able to post the results of the remaining 25 clinical trials because the results were not submitted by the responsible parties.

NIH did not have adequate procedures for ensuring that responsible parties submitted the results of clinical trials, took limited enforcement action when there was noncompliance, and continued to fund new research of responsible parties that had not submitted the results of their completed clinical trials. NIH officials explained that they were aware that some responsible parties faced challenges with submitting the results of their clinical trials to ClinicalTrials.gov. The NIH Office of Intramural Research began analyzing its procedures during our audit and drafted a new chapter for the *NIH Policy Manual*, Chapter 3007, Clinical Trials Registration and Results Information Reporting (Chapter 3007), related to the Intramural Research Program. The new chapter was finalized in January 2022 and designed to improve responsible parties' compliance with clinical trial registration and results information reporting.<sup>12</sup> The chapter defines the roles and responsibilities of key officials and includes the consequences responsible parties face when they do not comply.

## **NIH DID NOT ENSURE THAT ALL CLINICAL TRIAL RESULTS WERE REPORTED IN ACCORDANCE WITH FEDERAL REQUIREMENTS**

### **NIH Did Not Always Ensure Responsible Parties Submitted Clinical Trial Results**

Federal law and NIH policy require the responsible party to submit the results of its clinical trials to ClinicalTrials.gov within 1 year of the earlier of the estimated or actual completion date. Federal law and NIH policy also require NIH to ensure that the responsible party complies with the submission requirements.

NIH did not ensure that responsible parties submitted the results of 37 NIH-funded clinical trials in accordance with Federal reporting requirements. Of the 72 NIH-funded clinical trials we reviewed (36 Intramural-funded and 36 Extramural-funded), the responsible parties associated with 35 trials (20 Intramural and 15 Extramural) complied with Federal reporting requirements. Of the 37 clinical trials for which the responsible party did not submit results in accordance with Federal reporting requirements, responsible parties submitted the results of 12 trials (11 Intramural and 1 Extramural); responsible parties did not submit the results of 25 trials (5

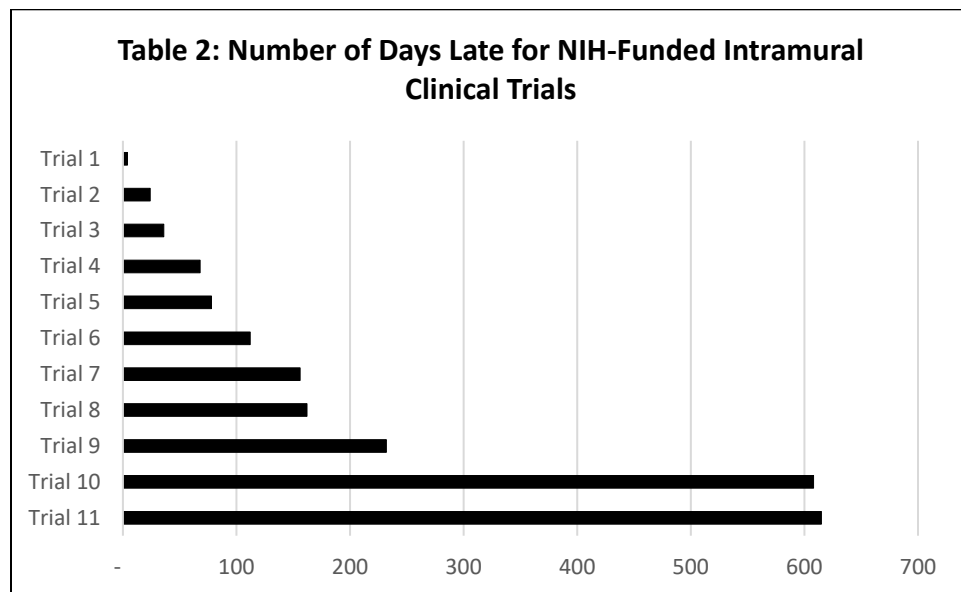
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<sup>12</sup> *NIH Policy Manual*, Chapter 3007. Effective Jan. 14, 2022. Available online at <https://policymanual.nih.gov/3007>. Accessed Aug. 5, 2022.

Intramural and 20 Extramural).<sup>13</sup> Table 1 summarizes the number of clinical trials requiring results to be submitted in 2019 or 2020 that were submitted on time, late, or not submitted at all.

	<b>Intramural</b>	<b>Extramural</b>	<b>Total</b>
Submitted on Time	20	15	35
Submitted Late	11	1	12
Results Not Submitted	5	20	25
Subtotal of Noncompliance	16	21	37
<b>Total</b>	<b>36</b>	<b>36</b>	<b>72</b>

Of the 16 responsible parties associated with the Intramural clinical trials that had submitted the results of their clinical trials late (11), or not submitted them (5), 15 responsible parties received a notice of noncompliance from the Office of Protocol Services. Table 2 summarizes the number of days the Intramural clinical trial results were late.



<sup>13</sup> On Feb. 17, and Apr. 9, 2021, we queried ClinicalTrials.gov to obtain lists of clinical trials for which the results were required to be reported during 2019 and 2020, respectively. We ran a subsequent query on Feb. 28, 2022, that showed 14 of the 25 responsible parties that were previously out of compliance had submitted the results of their clinical trials and 1 responsible party that withdrew its clinical trial. Because no participants were recruited, the one responsible party is no longer required to submit results.

Of the 21 responsible parties associated with the Extramural clinical trials that had submitted the results of their clinical trials late (1), or not submitted them (20), only 1 responsible party received a notice of noncompliance from the Office of Policy for Extramural Research Administration. That institution's responsible party submitted the results of the clinical trial 299 days late.

### **NIH Posted Clinical Trial Results When Submitted**

Federal law requires NIH to post the results of clinical trials on ClinicalTrials.gov within 30 days of the submission date. NIH complied with this requirement. For the 47 clinical trials for which responsible parties submitted results (35 submitted on time and 12 submitted late), NIH posted all 47 clinical trial results within 30 days of the submission date on ClinicalTrials.gov. NIH posted these results in an average of 14 days.

### **NIH Did Not Have Adequate Procedures To Ensure That Responsible Parties for NIH-Funded Intramural and Extramural Clinical Trials Complied With Federal Reporting Requirements**

#### *Procedures For Notifying Responsible Parties Prior to Noncompliance*

Although the Office of Protocol Services within the Office of Intramural Research has procedures in place to send notification letters to responsible parties to remind them that they are required to submit the results of their trials, the notifications alone did not ensure that responsible parties complied with Federal reporting requirements. Sending notifications can assist with and encourage compliance, but responsible parties reported experiencing challenges with reporting clinical trial results in the required format. These challenges included (1) identifying how to report clinical trial results using the ClinicalTrials.gov format, because the data format used when submitting a proposal for a clinical trial is not the same format used when submitting the results, (2) the system for reporting results in ClinicalTrials.gov is not user friendly, and (3) some ClinicalTrials.gov data fields can be overwritten when additional data is added to those fields.

NIH officials were aware of the challenges and that some responsible parties were not complying with reporting requirements but had not previously taken steps to improve compliance. To further ensure that clinical trials comply with Federal reporting requirements, the Office of Intramural Research began analyzing its procedures during our audit and issued a new chapter in the *NIH Policy Manual*, Chapter 3007, in January 2022. The new chapter was designed to improve responsible parties' compliance with clinical trial registration and results information reporting.

The NIH Funding Institute's or Center's Office of Grants Management and the Office of Policy for Extramural Research Administration do not have procedures for sending notices to responsible parties about reporting requirements in advance of the reporting deadline. However, the terms and conditions of the award refers recipients of NIH grants to the NIH Grants Policy Statement, which contains information about the reporting requirements.

## *Procedures For Enforcing Requirements After Noncompliance*

While the Office of Protocol Services within the Office of Intramural Research has procedures in place to identify clinical trials for which results were not submitted and to send notices of noncompliance to the responsible parties, the notifications were not always effective at gaining compliance, and NIH's Office of Intramural Research did not take any additional enforcement actions against responsible parties that failed to submit clinical trial results. The new chapter in the *NIH Policy Manual*, Chapter 3007, includes consequences for when responsible parties do not comply. These consequences include, among other things, notifications to NIH leadership of the noncompliance, withholding approval for future clinical trials, documentation of the noncompliance in the responsible party's annual performance evaluation, and disciplinary actions ranging from a letter of reprimand to removal from Federal service.

The Office of Extramural Research has procedures in place to identify clinical trials for which results were not submitted and to send notices of noncompliance to the responsible parties; however, it did not always follow them. NIH may delay funding subsequent budget years of an award due to noncompliance with results reporting requirements. Even though NIH may restrict funding to responsible parties until the results are submitted or restrict funding for new awards, an Office of Extramural Research official stated that the office does not take these enforcement actions because it would result in halting funding to the entire institution; instead, NIH prefers to work closely with University staff to ensure that they input their results in ClinicalTrials.gov.

Not only did NIH take limited enforcement actions in connection with Intramural and Extramural clinical trials that were out of compliance, NIH continued to fund new clinical trials of responsible parties that had not submitted the results of their clinical trials. Of the 37 responsible parties that had not complied with Federal reporting requirements, 21 responsible parties (11 Intramural and 10 Extramural) began a new NIH-funded clinical trial before submitting the late results of their previous clinical trials to ClinicalTrials.gov.

### **The Benefits of Clinical Trials May Not Be Fully Realized When Federal Reporting Requirements Are Not Met**

The results of clinical trials, whether positive or negative, improve the design of future research and ultimately advance the development of clinical interventions. When the results of clinical trials are not submitted to ClinicalTrials.gov in a timely manner, information about those results, including information on adverse events that occurred during the clinical trials, is not available to health care providers, patients, or researchers.

## **RECOMMENDATIONS**

We recommend that the National Institutes of Health:

- improve its procedures to ensure that responsible parties of NIH-funded clinical trials comply with requirements to submit results to ClinicalTrials.gov in a timely manner,
- take enforcement actions against responsible parties that are late in submitting trial results or do not submit results, and
- work with the responsible parties to understand the challenges they face when submitting their results to ClinicalTrials.gov and implement procedures to address the challenges.

### **NATIONAL INSTITUTES OF HEALTH COMMENTS**

In written comments on our draft report, NIH concurred with our recommendations and described actions it has taken or plans to take to address them. NIH stated that it has already begun to implement a series of improvements to enhance its internal procedures to work with responsible parties to ensure that they are complying with requirements to register studies and submit results to ClinicalTrials.gov. Further, NIH indicated that it is implementing activities that will enhance NIH's ability to take compliance actions against responsible parties that are late in submitting trial results or do not submit results. NIH also mentioned that it has invested substantially in making ClinicalTrials.gov an accessible and usable resource for the community. In addition, NIH stated that it has implemented significant improvements related to working with responsible parties to understand the challenges they face in submitting their results to ClinicalTrials.gov and that it has implemented procedures to address the challenges. Lastly, NIH suggested a minor revision to the language in our third recommendation, which we made.

NIH also provided technical comments on our draft report, which we addressed as appropriate.

NIH's comments, excluding the technical comments, are included as Appendix B.

## **APPENDIX A: AUDIT SCOPE AND METHODOLOGY**

### **SCOPE**

We reviewed all 72 NIH-funded Intramural and Extramural clinical trials (36 of each) for which NIH policy required the results to be reported in calendar year 2019 or 2020.

We limited our review of NIH's internal controls to the design, implementation, and operating effectiveness of its policies and procedures related to reporting the results of NIH-funded clinical trials on ClinicalTrials.gov.

We conducted our audit work from December 2020 to March 2022.

### **METHODOLOGY**

To accomplish our objective, we:

- reviewed applicable Federal laws and requirements;
- reviewed applicable NIH policies and procedures;
- interviewed NIH officials to gain an understanding of NIH's policies and procedures related to reporting the results of NIH-funded clinical trials on ClinicalTrials.gov;
- obtained an understanding of the data elements maintained in NIH's information systems that were relevant to our audit objective;
- obtained data files on clinical trials, for which the results were required to be reported in calendar year 2019 or 2020, that included the relevant data elements;
- obtained and reviewed information about enforcement actions taken against responsible parties that were out of compliance;
- obtained and reviewed information about notices of non-compliance;
- reviewed data files on clinical trials and determined whether the trials complied with Federal reporting requirements; and
- discussed the results of our audit with NIH officials.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions

based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.



## APPENDIX B: NATIONAL INSTITUTES OF HEALTH COMMENTS

### **GENERAL COMMENTS OF THE NATIONAL INSTITUTES OF HEALTH (NIH) ON THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) OFFICE OF INSPECTOR GENERAL (OIG) DRAFT REPORT ENTITLED: "THE NATIONAL INSTITUTES OF HEALTH DID NOT ENSURE THAT ALL CLINICAL TRIAL RESULTS WERE REPORTED IN ACCORDANCE WITH FEDERAL REQUIREMENTS, A-06-21-07000"**

The National Institutes of Health (NIH) appreciates the review conducted by OIG and the opportunity to provide clarifications on this draft report. The Acting Director of the National Institutes of Health (NIH), Acting Principal Deputy Director, and the 27 Institutes and Centers (ICs) are united in their commitment to ensure broad and responsible dissemination of information from NIH-funded clinical trials through ClinicalTrials.gov. NIH respectfully submits the following general comments.

#### **OIG Recommendation 1:**

We recommend that the National Institutes of Health improve its procedures to ensure that responsible parties of NIH-funded clinical trials comply with requirements to submit results to ClinicalTrials.gov in a timely manner.

#### **NIH Response:**

NIH concurs with the OIG's recommendation.

NIH has already begun to implement a series of improvements to enhance its internal procedures to work with responsible parties to ensure they are complying with requirements to register studies and submit results to ClinicalTrials.gov. Notable improvements related to Recommendation 1 include:

- **Development of a Centralized Workflow for Verifying Extramural Compliance.** NIH has worked in close collaboration with partners in the HHS Office of General Counsel and the Food and Drug Administration to standardize the NIH approach across ICs for verifying extramural grant recipient compliance with both the NIH Policy and FDAAA. This "Clinical Trials Compliance Workflow" and associated systems controls, is expected to provide a robust and automated system for centralized tracking of registration and reporting information, enabling NIH to take action upon the earliest notification of a potential violation.
- **Introduction of New Forms to Enable Better Tracking.** NIH launched the PHS Human Subjects and Clinical Trials Information Form for grant applications to collect comprehensive information about NIH-funded clinical trials at the time of award. This new form allows NIH funded awardees to provide updates in Research Performance Progress Reports (RPPR) and enables NIH Institutes, Centers, and Offices (ICOs) to track compliance activities. The form is aligned with ClinicalTrials.gov and captures ClinicalTrials.gov identifiers, including National Clinical Trial number (NCTs) and other fields that are mapped to the ClinicalTrials.gov record to support NIH's Clinical Trials Compliance Workflow.
- **Strengthening Intramural Reporting Systems.** The Intramural Research Program (IRP) developed and published NIH Policy Manual Chapter 3007, "[Clinical Trial](#)

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Registration and Results Information Reporting" that clearly establishes responsibilities and procedures for registration and results information reporting of IRP-conducted or supported clinical trials to ClinicalTrials.gov. The policy outlines processes and procedures for researchers and IC leadership, and establishes consequences in the event of noncompliance.

NIH will provide a status update with an implementation timeline at the Management Decision.

**OIG Recommendation 2:**

We recommend that the National Institutes of Health take enforcement actions against responsible parties that are late in submitting trial results, or do not submit results.

**NIH Response:**

NIH concurs with the OIG's recommendations.

The following activities will enhance NIH's ability to take compliance actions against responsible parties that are late in submitting trial results, or do not submit results. Specifically pertaining to the Clinical Trials Compliance Workflow:

- **Integrated Electronic Systems to Facilitate Non-Compliance Alerts.** The electronic Research Administration (eRA) Human Subjects System (HSS), a comprehensive electronic system that captures clinical trial information entered by the extramural recipient in a structured manner, will communicate with other NIH systems to allow NIH staff to monitor ClinicalTrials.gov results reporting requirements and be alerted to cases of potential non-compliance. HSS checks its data against ClinicalTrials.gov and alerts extramural recipients and NIH staff of inconsistencies in the two databases.
- **Validating and Taking Compliance Action Prior to Subsequent Awards.** Submitted RPPR for extramural grants will be assessed to ensure they meet the clinical trial registration and reporting requirements and that subsequent awards are not issued until the noncompliance is resolved. These validations apply to all RPPRs and non-competing continuation (Type 5) awards involving NIH-funded clinical trials. Validations occur automatically by eRA systems at the time of RPPR submission and support the process for identifying and acting upon non-compliance with the clinical trial registration and reporting requirements prior to award, as a part of the Clinical Trial Compliance Workflow.
- **Strengthening Intramural Compliance and Enforcement Procedures.** For intramural studies, since the implementation of NIH Policy MC 3007 in January 2022, all intramural responsible parties required to submit results have completed the reporting. When internal notices of possible noncompliance have been issued, the responsible parties submitted results information within 30 days of receipt of the notification, consistent with MC 3007. The IRP's experience to date with MC 3007 suggests the new

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policy is an effective tool to facilitate intramural enforcement and compliance reporting requirements.

NIH will provide a status update with an implementation timeline at the Management Decision.

**OIG Recommendation 3:**

We recommend that the National Institutes of Health work with the responsible parties to fully understand the challenges they face when submitting their results to ClinicalTrials.gov and implement procedures to address the challenges.

**NIH Response:**

NIH concurs with the OIG's recommendation.

NIH suggests removing "fully" as the scope of users and invested parties is vast and diverse (both NIH-supported and non-NIH supported) and thus fully understanding the challenges may extend beyond our mission. An alternate suggestion is to recommend NIH "continue to work with stakeholders to improve the user experience when submitting results to ClinicalTrials.gov."

NIH has invested substantially in making ClinicalTrials.gov an accessible and usable resource for the community and plans to continue working with various stakeholders to better understand challenges and the user experience with submitting results. NIH has implemented significant improvements to work with responsible parties to understand the challenges they face in submitting their results to ClinicalTrials.gov and implement procedures to address the challenges. For example:

- **Forum for Responsible Parties to Provide User Experience to NIH.** NIH regularly conducts training and outreach to educate investigators, administrators, and staff on ClinicalTrials.gov registration and reporting requirements. Through virtual seminars and workshops, NIH works to provide both virtual and in person opportunities to engage in a discussion about how to work with the Protocol Registration and Results System (PRS) but also provides a forum to provide feedback on areas of improvement to the system.
- **ClinicalTrials.gov Improvements and Redesign.** NLM has taken steps to improve the user interface based on extensive usability studies. NLM has been leading a modernization effort of the ClinicalTrials.gov website and its information submission system. NLM recently released its new beta ClinicalTrials.gov website and submission system. The effort builds on substantial stakeholder engagement including a request for information, public webinars, and a user-centered design approach intended to help ensure that modernization is responsive to user needs. The final redesign will feature a modern look and feel and provide updated technology to support users. In particular, the redesigned submission system will have functionality that supports more intuitive use and features that allow data submitters to more easily identify trials that are subject to reporting requirements and with approaching deadlines. The beta sites will function in

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parallel to the current systems to allow for usability testing and iterative improvements and to enable features and functions to be added without disrupting the current user experience. The modernization effort will make the submission of high-quality study information more intuitive, which in turn, will also benefit the end users of the data. NIH anticipates that the needs of ClinicalTrials.gov user community will continue to evolve with our changing scientific landscape and will continue to work to stay abreast of their needs to make this resource maximally useful.

NIH will provide a status update with an implementation timeline at the Management Decision.