NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information

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Purpose

Summary

The National Institutes of Health (NIH) is issuing this policy to promote broad and responsible dissemination of information from NIH-funded clinical trials through ClinicalTrials.gov. The policy establishes the expectation that all investigators conducting clinical trials funded in whole or in part by the NIH will ensure that these trials are registered at ClinicalTrials.gov, and that results information of these trials is submitted to ClinicalTrials.gov. The policy is complementary to the statutory and regulatory reporting requirements. These are section 402(j) of the Public Health Service Act, as amended by Title VIII of the Food and Drug Administration (FDA) Amendments Act of 2007 (FDAAA), and the regulation Clinical Trial Registration and Results Information Submission, at 42 CFR Part 11. Hereafter, we refer to section 402(j) as the statute and 42 CFR Part 11 as the rule or regulation. This policy as well as the rule were posted in the Federal Register.

Supplemental Information

On November 19, 2014, and in tandem with the publication of the Notice of Proposed Rulemaking (NPRM) on Clinical Trial Registration and Results Submission, the NIH issued a complementary draft policy for public comment on the Dissemination of NIH-funded Clinical Trial Information[1,2]. The draft policy proposed that all NIH-funded awardees and investigators conducting clinical trials, funded in whole or in part by the NIH, regardless of study phase, type of intervention, or whether they are subject to the statutory registration and results information submission requirements, would be expected to ensure that those clinical trials are registered and results information is submitted to ClinicalTrials.gov. It further stated that submission of the same type of registration and results information would be expected and in the same timeframes as the trials subject to the statute, and that this information would be made publicly available through the ClinicalTrials.gov website. The NIH received approximately 240 public comments on its proposed policy. The comments came from a range of stakeholders including researchers, academic/research institutions, medical practitioners, patients, patient/disease advocacy groups, scientific/professional societies and associations, device manufacturers, trade associations, not-for-profit non-governmental organizations, and the general public[3]. The NIH appreciated the public interest in the proposed policy and the time made and effort taken by stakeholders to provide comments. The NIH carefully considered those comments in the development of the final policy. In the next section, we provide an overview of the comments on the proposed policy. Because those in compliance with the policy would be expected to follow specific provisions of the rule, a number of commenters on the policy reiterated comments that they submitted to the docket in response to the NPRM[4]. Since these comments are discussed at length in the preamble of the rule, we are limiting the discussion of comments here primarily to those that identified issues specific to the policy, such as its scope, applicability, and impact on NIH-funded awardees and investigators.

Overview of the Public Comments

A significant majority of the public comments were supportive of the proposed NIH policy and of its application to the full range of NIH-funded clinical trials. Most commenters appreciated the impetus behind the policy and agreed that it was important to provide ways other than journal publication for clinical trial results to be disseminated and made publicly available to researchers, health care providers, and patient communities. They recognized that increased availability of information from NIH-funded clinical trials would help researchers by informing the design and development of their future

studies, address the needs of patients and healthcare providers seeking information about NIH-funded trials, and serve the public's interest by preventing duplication of unsafe and unsuccessful trials and mitigating publication bias. They also agreed that improving the availability of clinical trial information will strengthen the public's trust in biomedical research as well as assure volunteers that their participation in clinical trials has advanced knowledge on human health and disease. A number of commenters also suggested that the policy is particularly appropriate because NIH-funded clinical trials are supported by public funding, and recipients of those funds have a special obligation to ensure that the nation's investment is maximized.

A number of comments from academic investigators and stakeholder organizations were supportive of the policy and its goals. Others, however, disagreed with the policy, suggesting that it was ill-advised and/or unnecessary. These commenters suggested that the benefit of greater transparency was outweighed by the burden and cost of the policy to those who conduct clinical trials and that the NIH had not made a sufficient case for the policy or that it was not evidence-based. Some commenters suggested that the NIH should simply encourage investigators to be more transparent or that the NIH's public access policy made the policy unnecessary since it requires NIH-funded investigators to make their published articles publicly available through PubMed Central.

Scope and Applicability of the Policy. Although the majority of commenters fully supported the scope of the policy, i.e., that it should apply to NIH-funded clinical trials of FDA-regulated drugs regardless of phase, small feasibility studies of devices, and trials of interventions not regulated by FDA, including surgical and behavioral interventions, there were comments suggesting that the scope was too narrow, or conversely, too broad.

One commenter suggested that the policy ought to encompass more detailed summary results, such as Clinical Study Reports, as well as de-identified individual patient-level data. One commenter suggested that the NIH should consider extending the policy to preclinical in vivo (laboratory) animal studies because the arguments for the registration and required reporting of preclinical in vivo (laboratory) animal studies are similar to those of human clinical trials. Some commenters suggested that the policy should be retroactive and apply to clinical trials that are underway as of the policy's effective date as well as those that have already been completed as of the effective date.

On the other hand, there were other comments suggesting that the policy should not apply to phase 1 or so called phase 0 trials, pilot trials designed to examine the feasibility of an approach, trials mounted by an investigator at a small organization, or trials that are unable to enroll a statistically significant number of participants. One suggested that even pilot trials that reach their enrollment target should not be expected to submit results information because the results might be more misleading than helpful. Another proposed that reporting on phase 1 clinical trials should be limited to adverse events information because these trials are designed to assess safety rather than efficacy, and reporting non-safety outcomes could be misleading. Another suggested that clinical trials not covered under the statute should not submit adverse event information unless a regulatory authority or equivalent body has first performed an analysis of the event in order to prevent public misunderstanding. Another commenter suggested that submission of data from early phase research could divert limited research resources and time from phase 3 studies. Another suggested that only information about phase 3 clinical trials should be included in ClinicalTrials.gov because information

about early stage trials could confound, rather than enhance, public understanding of human health and could, thereby, inadvertently adversely affect patient safety.

One commenter suggested that the policy should apply only to the registration of clinical trials, not the submission of results information. This commenter asserted that registration information was sufficient because any interested party could follow up with an investigator to learn more about the trial and because submission of registration information takes a fraction of the time needed to submit results information.

There were a few commenters who took issue with the application of the policy to trials that are only partially funded by the NIH. They asserted that the policy would entail the disclosure of confidential commercial information and that the NIH's authority to do so is limited to a trial that is wholly NIH-funded and involves a product with research and development costs wholly government-funded. A few other commenters suggested that the policy should exclude clinical trials that use NIH-supported infrastructure, but involve no NIH funds.

NIH Definition of Clinical Trial. Some commenters addressed the NIH definition of clinical trial, which is key to determining the policy's applicability. There was support for the breadth of the definition, i.e., encompassing all interventional studies with biomedical outcomes (e.g., pharmacokinetic and behavioral outcomes, as well as health-related outcomes). One commenter, however, thought more elaboration on the definition was needed to clarify the meaning of "health-related

biomedical or behavioral outcomes." They thought that without such specificity, the definition might be interpreted to exclude studies that contain valuable information for public health research, science, and clinical medicine. Commenters believed that addressing this issue would be vital to ensure a common understanding that the NIH policy applies to all clinical trials involving a biomedical or behavioral intervention. Another suggested that a study involving only one participant should not be considered a clinical trial since a trial with a sample size of one would not provide any valid data to share with the public.

Some commenters noted that the wording of the NIH definition was not identical to the wording of the definition of clinical trial in the proposed rule or to how other organizations, e.g., the World Health Organization (WHO), International Committee of Medical Journal Editors (ICMJE), and Centers for Medicare & Medicaid Services (CMS), use the term. They were concerned that investigators would have difficulty understanding their obligations under the policy and under the rule and in meeting requirements of others. They called for reconciliation of any actual or apparent differences in the definitions.

A commenter urged the NIH to issue guidance to help determine whether a study is a clinical trial under the definition and to clarify how disagreements in the matter would be resolved and communicated.

Results Information Submission Timeline. A few commenters raised concerns about the proposed rule's timeline for reporting results information, asserting that 12 months after the primary completion date of the clinical trial (i.e., the date of final data collection for the primary outcome measure) is too soon, particularly for NIH-funded academic investigators. These commenters suggested that academic investigators will have more difficulty meeting the timeframe because they must also spend time teaching, fulfilling clinical care responsibilities, and writing grant applications. Another commenter suggested that a 12-month timeframe would also be more challenging for academic investigators because, unlike industry investigators, they generally cannot count on support from a central administrative service to help them carry out their reporting responsibilities. Decentralization of information in academic centers would also present a particular challenge to those covered by the NIH policy, according to another commenter, who also suggested that the mobility of new investigators may make it difficult to meet timelines. These commenters urged the NIH to allow a longer submission timeframe, e.g., 18 or 24 months. A few noted that providing more time would also give investigators time to prepare journal publications, and one also expressed concern about the possibility that journal editors will begin to consider submission of results information to ClinicalTrials.gov as prior publication, which could thwart journal publication altogether.

Structured Results Data Elements. A few commenters suggested that the data submission structure, which is determined by the provisions of the statute, does not work well for clinical trial types that will be covered only the policy, e.g., phase 1 trials of drugs/biologics, small feasibility device studies, trials of social and behavioral interventions, or those with non-standard designs. These commenters thought that other fields would need to be added to the ClinicalTrials.gov to enable investigators to report data elements for those trials appropriately and accurately. They also suggested increasing the character limit on data fields to allow for more careful and nuanced explanations. Commenters also suggested that if the ClinicalTrials.gov cannot accommodate these types of trials, investigators should be exempted from the policy. One commenter requested that an additional data element should be included to allow an investigator to indicate that the trial's hypothesis had been confirmed.

Protecting Privacy. One commenter raised a concern about the policy's impact on the privacy of clinical trial participants suggesting that it might be easy to re-identify participants in many NIH-funded pilot studies with small sample sizes. The commenter pointed to the five percent threshold for non-serious adverse events and site location information as the data elements creating the vulnerability. The commenter urged the NIH to allow an investigator to obtain a waiver from results information submission where participant privacy was at risk.

Compliance Issues. The proposed policy noted that compliance with the policy would be a term and condition of award and that non-compliance may provide a basis for enforcement actions, including termination. A few commenters discussed the importance of compliance. One suggested that the NIH should take compliance records into account when considering future applications for funding. They suggested that such an approach could be more effective than terminating funding of a current grant since most of the research may already be completed. Another thought that making compliance a term and condition of award was important and that it would incentivize good behavior and help change attitudes about the value of enhancing availability of clinical trial information.

Other commenters raised concerns about the costs that will be incurred by NIH-funded academic institutions to ensure that clinical investigators are following the policy. They suggested institutions will need to provide more administrative support and other resources to help investigators comply and that this would be difficult given the indirect cost cap of 26 percent. Commenters urged the NIH to allow the time and effort required for ClinicalTrials.gov compliance to be included as a direct

cost on NIH grants. Another commenter suggested that the increased results information submissions brought on by the NIH policy will stretch the NIH's capabilities and that it will be important for the NIH to ensure that sufficient resources are available to manage high volume data uploads and customer service requests.

Overview of Final NIH Policy

The NIH considered all the comments received on the proposed policy as well as those that were submitted in response to the NPRM. There was overwhelming support for both the proposed policy and the NPRM, particularly among concerned citizens, scientific societies, medical practitioners, and individual scientists. There were also concerns expressed, particularly in the comments from academic commenters. We appreciate those concerns and understand that the policy will create additional work for many investigators. However, we believe that the work should not be seen as a burden, but, rather, an inherent part of an investigator's commitment to the advancement of science. The benefits will, in the long run, accrue to the investigators as well as to the public, patients, and the enterprise as a whole because transparency will improve future research designs and maximize the public's investment – and their trust – in research. Equally important, it will help investigators fulfill the ethical obligation they have to clinical trial participants, namely to ensure that the findings from their participation contribute to generalizable knowledge and the advancement of public health.

As we noted in the preamble to the proposed policy, a fundamental premise of all NIH-funded research is that the results of such work must be disseminated in order to contribute to the general body of scientific knowledge and, ultimately, to the public health. The NIH awardees have always been expected to make the results of their activities available to the research community and to the public at large because it is intrinsic to the scientific process. In research involving human beings, moreover, scientists also have an ethical obligation to ensure that the burden and risk that volunteers

assume by participating in research comes to something, at the very least by ensuring that others are aware of the study and that its findings contribute to the advancement of human health.

We disagree with commenters who suggested that there is no need for coverage of certain types of trials, such as early exploratory trials, small trials, trials assessing only safety, or trials that terminate before reaching enrollment targets. The benefits of transparency and the need to fulfill the ethical obligation to participants is as relevant to these types of trials as to any other type. We were also not persuaded that the timeframe for results information submission should be longer for academic investigators because of their competing responsibilities or that they should be allowed more time to publish their results in a journal. The timeframe of 12 months from the primary completion date should provide enough time for investigators to organize their data and submit results information. We are also confident that academic institutions can develop central support services as necessary to assist investigators should they need it. We also believe that 12 months represents an appropriate balance between investigators' interests and the interests of the public in having access to the results of a publicly funded trial. In addition, it will be possible to delay results information submission for up to two years beyond the initial deadline with a certification that regulatory approval of the trial product is being sought.

Some commenters suggested that a policy on clinical trial information dissemination is not needed because it duplicates other NIH policies. This policy is certainly in keeping with our principles, longstanding expectations, and other policies as well as the more recent broad policy call for scientific agencies to increase public access to scientific data [5]. However, it does not duplicate any other NIH policy, nor does any other NIH policy accomplish what this one will.

Some commenters also contended that this policy is not necessary because the results of clinical trials will be published or because they can be obtained via direct requests to the trial's principal investigator. In fact, research has shown that the results of a significant portion of clinical trials are not published or published in a timely manner. For example, a 2012 study of NIH-funded clinical trials found that after a median of 51 months following trial completion, 32 percent were unpublished [6]. A more recent study of the trial publication rate among 51 U.S. academic medical centers found that 43 percent of their clinical trials were unpublished two years after the trial was completed [7]. While the ability to seek results information from the original investigator is useful to facilitate collaborations, to access individual-level data, and to gain insights from those who conducted the trial, it is not a surefire way to increase access to trial results nor is it efficient or transparent, particularly for the public.

We believe that the public availability of clinical trial results information will be beneficial to all parties in the long run, including those who are covered by this policy. All investigators stand to benefit from this policy. For example, science may progress more quickly because investigators will be able to learn from trials to which they otherwise would not have had access because they were unpublished. In addition, the public availability of results information helps investigators design trials and Institutional Review Boards (IRBs) review proposed trials, by allowing them to weigh the proposed study's risks

and benefits against a more complete evidence base than is currently available through the scientific literature [8]. Submission and posting of results information will also help investigators avoid repeating trials on interventions that have been found to be unsafe or unsuccessful while also providing access to information that may help verify findings.

For all of these reasons, we have not changed the essential contours of the policy. In terms of scope, the policy still applies to all NIH-funded awardees and investigators conducting clinical trials funded in whole or in part by the NIH regardless of study phase, type of intervention, or whether they are subject to the statute and to the rule. It clarifies that the policy is an expectation, that applicants and offerors 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 their plan through the terms and conditions of the award. The required plan can be a brief statement explaining whether the applicant/offeror intends to register and submit results information to ClinicalTrials.gov as outlined in the policy or to meet the expectations in another manner. It is important to remember that an NIH-funded clinical trial that meets the definition of an applicable clinical trial is subject to the regulation and, therefore, register and submission of results information to ClinicalTrials.gov is a requirement.

The policy applies to both the extramural and intramural programs. For the NIH extramural program, the policy applies to applications for funding including for grants, other transactions, and contracts submitted on or after the policy's effective date that request support for the conduct of a clinical trial that is initiated on or after the policy's effective date. This means that the policy does not apply to clinical trials in ongoing, non-competing awards, but that it will apply if the grantee submits a competing renewal application that includes a new clinical trial, i.e., a clinical trial initiated on or after the effective date of the policy. For the intramural program, the policy applies to clinical trials initiated on or after the policy's effective date. The policy's effective date is January 18, 2017. The policy clarifies that a clinical trial that uses NIH-supported infrastructure, but does not receive NIH funds to support its conduct, is not subject to the policy.

The policy outlines the responsibilities for NIH-funded investigators according to whether the trial is covered by the policy only or also the rule. For those covered by the policy only, NIH-funded awardees and investigators will be expected to submit the same registration and results information in the same timeframes as those subject to the statute and rule. The timeline for registration is not later than 21 calendar days after the enrollment of the first participant. The standard timeline for results information is not later than one year after the trial's primary completion date, but the policy also allows for delayed submission of results information in certain circumstances for up to two additional years for trials of products regulated by the FDA that are unapproved, unlicensed, or uncleared or for trials of products for which approval of a new use is being sought.

Although the policy does not apply to NIH-funded clinical trials initiated before the effective date, we encourage all ongoing NIH-funded clinical trials to follow it. It is also critical for investigators conducting NIH-funded applicable clinical trials that are subject to the statute and rule to be sure they are in compliance with those requirements.

The policy continues to use the NIH definition of "clinical trial" as proposed in the draft policy to determine which research studies are covered by the policy. This definition was developed in 2014 to reflect the NIH research mission and the scope of clinical trials within the NIH portfolio. With regard to the concern expressed by a public commenter that the phrase "health-related biomedical or behavioral outcomes" might be too narrow, we note that the definition considers biomedical and behavioral outcomes to be health-related outcomes in interventional studies that meet the other components of the definition. Also, regarding the concern that the wording of the definitions of clinical trial in this policy and the rule differ, this is so mainly in reference to outcomes, i.e., the NIH definition explicitly references behavioral outcomes whereas the definition in the rule encompasses them within the term "health related." These distinctions are not significant in terms of defining what is covered by the NIH policy. All NIH-funded clinical trials, whether they are assessing biomedical or behavioral outcomes or whether they are employing an FDA regulated product, are covered by the policy. An NIH-funded clinical trial assessing a behavioral intervention that is not regulated by the FDA would meet both definitions of clinical trial, and, thereby, be covered by the policy. However, such a trial would not be subject to the rule because it does not meet the rule's definition of "applicable clinical trial." Guidance available on the NIH's website can help awardees and investigators understand whether a research study is a clinical trial for purposes of the NIH policy (see first website listed below). Questions should be directed to the NIH program staff. To understand whether an NIH-funded clinical trial is also subject to the statute and the rule, awardees and investigators should look to the rule's definition of "applicable clinical trial."

NIH-funded awardees and investigators will be expected to follow the provisions of the rule in terms of when they register their trials, what information they provide as part of the registration process, when they submit their results information, and what results information is submitted. All of the alternate approaches in the rule will also be available to those covered by the policy, e.g., for delayed posting of device registration information, delayed submission of results information for trials involving unapproved products or products for which a new use is sought, extensions for good cause, and waivers that might

be needed for privacy or national security reasons.

With regard to the concern that ClinicalTrials.gov is not set up to accept NIH-funded trials that are small or exploratory in nature or involve behavioral interventions, it is important to note that the ClinicalTrials.gov does accommodate the submission of all trial types and that a variety of study and trial types have been entered into ClinicalTrials.gov since its inception. In addition, ClinicalTrials.gov

has resources available to assist investigators in navigating the registration and results information submission processes. These resources will continue to be updated over time to be responsive to investigators' needs and the evolving clinical research enterprise. Therefore, it should not be necessary for a clinical investigator of an NIH-funded clinical trial to seek an exemption from the policy for reasons related to the capacity of ClinicalTrials.gov to accommodate all types of clinical trials.

Registration and results information submission to ClinicalTrials.gov complements publication of trial results in peer-reviewed scientific journals. Information submitted to ClinicalTrials.gov is displayed in a structured way and includes a complete list of all pre-specified outcome measures and all adverse events. Journal articles, on the other hand, typically focus on a select set of outcome measures and adverse events and include background and discussion of the implications of the results. Information submitted to ClinicalTrials.gov undergoes a quality control review whereas journal articles will be peer reviewed. With regard to the concern that submission of results could make journal publication more difficult or impossible, the ICMJE has stated that submission of summary results to ClinicalTrials.gov will not be considered prior publication and will, thus, not interfere with journal publication [9]. We encourage all NIH-funded investigators to publish the results of their studies in peer-reviewed journals.

We have no doubt that this policy will be beneficial for the research community as well as the public generally, but we recognize that adhering to it will be a new obligation. We will provide additional guidance to facilitate implementation and help awardees and investigators understand the policy as well as the tasks described in the rule that they will be expected to undertake. In terms of the costs of complying with the policy, grantees are permitted to charge the salaries of administrative and clerical staff as a direct cost [10]. Such staff could assist investigators in meeting their responsibilities under the policy. In addition, administrative costs can be covered through indirect cost recovery.

We intend for this policy to benefit all communities who seek information about NIH-funded clinical trials, and we are confident that the benefits of transparency will become evident soon after the policy is implemented. We plan to evaluate the implementation and impact of the policy from the perspective of those who comply with it as well as from the perspective of ClinicalTrials.gov users, including patients, providers, and investigators.

We look forward to engaging with NIH-funded investigators and awardees as they work to meet the expectations of this important public policy. Information to assist applicants, offerors, and investigators is available at the following websites. The NIH will continue to add guidance materials to these sites as the policy's implementation continues.

http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials
https://clinicaltrials.gov/ct2/manage-recs
https://grants.nih.gov/clinicaltrials_fdaaa/faq.htm

The NIH policy is set forth below.

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NIH Policy on Dissemination of NIH-Funded Clinical Trial Information

Purpose

The National Institutes of Health (NIH) Policy on Dissemination of NIH-funded Clinical Trial Information establishes the expectation that all NIH-funded awardees and investigators conducting clinical trials, funded in whole or in part by the NIH, will ensure that their NIH-funded clinical trials are registered at, and that summary results information is submitted to, ClinicalTrials.gov for public posting1 The purpose of the policy is to promote broad and responsible dissemination of information from NIH-funded clinical trials through ClinicalTrials.gov. Disseminating this information supports the NIH mission to advance the translation of research results into knowledge, products, and procedures that improve human health.

This policy is complementary to requirements in the Clinical Trial Registration and Results Information Submission regulation at 42 CFR Part 11, hereinafter referred to as the regulation 2. Clinical trials that are subject to the regulation are, in general, clinical trials of drug, biological, and device products regulated by the Food and Drug Administration (FDA), except phase 1 trials of drug and biological products and small feasibility studies of device products. A pediatric post-market surveillance study of a device product required by the FDA is also subject to the regulation. Clinical trials subject to the regulation are generally called "applicable clinical trials." Applicable clinical trials are required to be registered in ClinicalTrials.gov not later than 21 calendar days after the enrollment of the first participant. Results information from those trials generally must be submitted not later than one year after the trial's primary completion date. Submission of results information can be delayed in certain circumstances for up to two additional years for trials of products regulated by the FDA that are unapproved, unlicensed, or uncleared or for trials of products for which approval, licensure, or clearance of a new use is being sought.

Scope and Applicability

This policy applies to all NIH-funded clinical trials regardless of study phase, type of intervention, or whether they are subject to the regulation. For example, NIH-funded phase 1 clinical trials of an FDA-regulated product are covered by this policy as are clinical trials studying interventions not regulated by the FDA, such as behavioral interventions. As such, the policy encompasses all NIH-funded clinical trials, including applicable clinical trials subject to the regulation. All NIH-funded clinical trials will be expected to register and submit results information to ClinicalTrials.gov.

This policy applies to clinical trials funded in whole or in part through the NIH extramural and intramural programs. For the NIH extramural program, the policy applies to applications for funding including for grants, other transactions, and contracts submitted on or after the policy's effective date that request support for the conduct of a clinical trial that is initiated on or

after the policy's effective date. For the NIH intramural program, the policy applies to clinical trials initiated on or after the policy's effective date.

This policy does not apply to a clinical trial that uses NIH-supported infrastructure but does not receive NIH funds to support its conduct.

Responsibilities

As part of their applications or proposals, applicants and offerors seeking NIH funding will be required to submit a plan for the dissemination of NIH-funded clinical trial information that will address how the expectations of this policy will be met. NIH-funded awardees and investigators conducting clinical trials funded in whole or in part by the NIH will be required to comply with all terms and conditions of award, including following their plan for the dissemination of NIH-funded clinical trial information.

Consistent with those terms and conditions, the responsibilities of such awardees and investigators will fall within one of the three categories. The category depends on whether, under the regulation, the clinical trial is also an "applicable clinical trial" and the awardee or investigator is the "responsible party."

1. If the NIH-funded clinical trial is an applicable clinical trial under the regulation and the awardee or investigator is the responsible party, the awardee or investigator will ensure that all regulatory requirements are met.

2. If the NIH-funded clinical trial is an applicable clinical trial under the regulation but the awardee or investigator is not the responsible party, the awardee or investigator will coordinate with the responsible party to ensure that all regulatory requirements are met.

3. If the NIH-funded clinical trial is not an applicable clinical trial under the regulation, the awardee or investigator will be responsible for carrying out the tasks and meeting the timelines described in regulation. Such tasks include registering the clinical trial in ClinicalTrials.gov and submitting results information to ClinicalTrials.gov.

In addition, informed consent documents for clinical trials within all three categories are to include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov.

Each NIH-funded clinical trial should have only one entry in ClinicalTrials.gov that contains its registration and results information. Awardees and investigators need not and should not create a separate record of the applicable clinical trial to comply with this policy.

The NIH will publicly post registration information and results information in ClinicalTrials.gov.

Definitions

Clinical Trial. For purposes of this policy, a "clinical trial" means "a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes."3 This definition encompasses phase 1 trials of FDA-regulated drug and biological products, small feasibility studies of FDA-regulated device products, and studies of any intervention not regulated by the FDA, e.g., behavioral interventions. This definition of "clinical trial"4 is broader than the term "applicable clinical trial" as defined in the regulation.5

Responsible Party. In the policy, the awardee or the investigator is responsible for meeting the expectations of this policy. In the regulation, a "responsible party" means, in part, "with respect to a clinical trial, the sponsor of the clinical trial, as defined in 21 CFR 50.3 (or any successor regulation); or the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, 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 under [42 CFR Part 11] for the submission of clinical trial information."6

Primary Completion Date. In the policy, this term has the same meaning as the term "primary completion date" in the regulation, which is "the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated."7

Registration Information. In the policy, this term has the same meaning as the term "registration information" in the regulation. In the regulation, registration information consists of descriptive information, recruitment information, location and contact information, and administrative data.8

Results Information. In the policy, this term has the same meaning as the term "results information" in the regulation. In the regulation, results information includes participant flow, demographic and baseline characteristics, outcomes and statistical analyses, adverse events, the protocol and statistical analysis plan, and administrative information.9

Compliance

If the clinical trial is NIH-funded in whole or in part, expectations for clinical trial registration and summary results submission will be included in the terms and conditions of the award. Failure to comply with the terms and conditions of the NIH award may provide a basis for enforcement actions, including termination, consistent with 45 CFR 75.371 and/or other authorities, as appropriate. If the NIH-funded clinical trial is also an applicable clinical trial, non-compliance with the requirements specified in 42 USC 282(j) and 42 CFR Part 11 may also lead to the actions described in 42 CFR 11.66.

Effective Date

This policy is effective January 18, 2017.

Footnotes

1. ClinicalTrials.gov is operated by the National Library of Medicine within the NIH.
2. The Clinical Trial Registration and Results Information Submission regulation at 42 CFR Part 11 was issued in the Federal Register in September 2016. The regulation implements section 402(j) of the Public Health Service Act.
3. Further information about this definition is available from the NIH Office of Science Policy at http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials.
4. Note that the regulation also includes a definition of "clinical trial." That definition is "a clinical investigation or 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" (see 42 CFR 11.10 (a)). For the purposes of this policy, the regulatory definition and the definition in this policy are treated as synonymous.
5. In the regulation, applicable clinical trial is defined as an applicable device clinical trial or an applicable drug clinical trial. The regulation defines an applicable device clinical trial to mean, in part, "a prospective clinical study of health outcomes comparing an intervention with a device product subject to section 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360(k), 21 U.S.C. 360e, 21 U.S.C. 360j(m)) against a control in human subjects (other than a small clinical trial to determine the feasibility of a device product, or a clinical trial to test prototype device products where the primary outcome measure relates to feasibility and not to health outcomes)." The regulation defines an applicable drug clinical trial to mean, in part, "a controlled clinical investigation, other than a phase 1 clinical investigation, of a drug product subject to section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or a biological product subject to section 351 of the Public Health Service Act (42 U.S.C. 262), where "clinical investigation" has the meaning given in 21 CFR 312.3 (or any successor regulation) and "phase 1" has the meaning given in 21 CFR 312.21 (or any successor regulation).
6. See 42 CFR 11.10 (a) and 42 CFR 11.4.
7. See the complete definition at 42 CFR 11.10 (a).
8. See 42 CFR 11.10 (b) and 42 CFR 11.28 for the specific data elements.
9. See 42 CFR 11.28 for complete results information and specific data elements.

Inquiries

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