Dissemination of NIH-Funded Clinical Trial Information (Final Policy)

Promotes broad and responsible dissemination of information from NIH-funded clinical trials through *ClinicalTrials.gov.*

Updated last **October 24, 2016**
for the 09/21/2016 Final Policy.

WHAT IT DOES

The Policy on the Dissemination of NIH-Funded Clinical Trial Information, (noticed via Federal Register 64922), creates the expectation that all NIH-funded clinical trial awardees and research investigators will make their research and results publicly available on ClinicalTrials.gov

The policy complements the requirements established in 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), the "statute", and the "Clinical Trial Registration and Results Information Submission regulation at 42 CFR part 11, the "regulation" (see background below).

This policy applies to all NIH-funded clinical trials, whether funded in whole or in part by the NIH and regardless of study phase, type of intervention, or whether they are also subject to the requirements of the "statute" or the "regulation."

The policy adopts a broader definition of "clinical trial" than the one adopted by "the regulation." The NIH policy defines a clinical trial as "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." As a result, the NIH policy applies to "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," which are not covered by the "regulation."

The awardee or the investigator are responsible for meeting the following responsibilities created by the policy:

- Applicants seeking NIH funding will be required to submit a plan for the dissemination of NIH-funded clinical trial information.
- NIH-funded awardees and investigators conducting clinical trials will be required to comply with all terms and conditions, including the plan for the dissemination of NIH-funded clinical trial information. Given that this policy is directly linked to the obligations created by the "regulation," the responsibilities of awardees and investigators can be divided into three categories depending on whether the clinical trial is also an "applicable clinical trial" under the "regulation:"
  - If the NIH-funded clinical trial falls under the "regulation" and the awardee or investigator is the responsible party, they will ensure compliance with all regulatory requirements.
  - If the NIH-funded clinical trial falls under the "regulation" and the awardee or investigator is not the responsible party, they will coordinate with the responsible party to ensure compliance with all regulatory requirements.
  - If the NIH-funded clinical trial does not fall under the "regulation," the awardee or investigator will be responsible for the regulatory requirements, which include registering the trial and submitting results information at ClinicalTrials.gov.
- In all the three cases mentioned above, the informed consent documents for all clinical trials should include a specific statement relating to the clinical trial information published at ClinicalTrials.gov

Compliance with the policy will be part of the terms and conditions to accept a funding award from the NIH. Failure to comply will result in enforcement action, including termination of the award. If the clinical trial also falls under the scope of the "regulation," non-compliance will also lead to the actions described therein (42 CFR 11.66).

This policy will change how research information is shared and accessed. While information about clinical trials is often published in

scientific journals, not all relevant information about clinical trials is made available through scientific publications. Potential benefits to enhancing the broad dissemination of clinical trials information includes:

- Advancing the translation of research results into knowledge, products and procedures that improve human health, further supporting the mission of the NIH;
- Contributing to the creation of generalizable knowledge and the advancement of public health;
- Ensuring that the risks and burdens taken by research participants can be used to advance further research;
- Supporting the design of future clinical trials;
- Preventing the duplication of costly and risky experimentation;
- Helping Institutional Review Boards to review trials more accurately and efficiently by allowing them to weigh risks and benefits against a larger evidence base;
- Allowing research participants to become more involved with the research process by having access to the online profile for the experiment; and
- Maximizing the public's investment and strengthening trust in biomedical research.

Potential costs and risks from the policy could include:

- Compliance costs for awardees and investigators. However, grantees will be allowed to include the salaries of staff supporting investigators to meet the responsibilities set forth in this policy as a direct cost; and
- Potential concerns for the privacy of research participants, especially in clinical trials with small samples where the potential for re-identification is greater.

The NIH is expected to provide additional guidance to facilitate the implementation and help awardees and investigators understand the policy and the responsibilities that they will be expected to undertake. The agency is also planning to evaluate the implementation and impact of the policy from the perspective of all the involved stakeholders –responsible parties, patients, providers and investigators.

RELEVANT SCIENCE

In a clinical trial, participants receive specific interventions, such as medical products, drugs, devices, procedures or behavioral changes such as diet, according to a research protocol created by the investigators. Clinical trials may compare new medical treatments to ones that are already available, to a placebo that contains no active ingredients, or to lack of intervention. Clinical trials can also compare two available medical treatments. When a new product or approach is being investigated, the purpose of the clinical trial is to determine its safety and efficacy by measuring certain outcomes in the participants. For example, investigators may give a drug or treatment to participants who have high blood pressure to see whether their blood pressure decreases.

Clinical trials used in drug development are sometimes described by phase. These phases are defined by the Food and Drug Administration (FDA):

- Phase I: Researchers test an experimental drug or treatment in a small group of people for the first time. The researchers evaluate the treatment's safety, determine a safe dosage range, and identify side effects.
- Phase II: The experimental drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.
- Phase III: The experimental study drug or treatment is given to large groups of people. Researchers confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.
- Phase IV: Post-marketing studies, which are conducted after a treatment is approved for use by the FDA, provide additional information, including the treatment or drug's risks, benefits and best use.

A placebo is a treatment given to a study population that lacks the active ingredient. The placebo should appear to be identical to

the drug. The purpose of the placebo is to allow investigators to compare the effects of a drug independently of the placebo effect, which is a psychological effect that shows a participant will improve because s/he is aware of treatment. Having a placebo arm of a clinical trial allows investigators to determine the effects caused specifically by the active ingredient of the drug.

RELEVANT EXPERTS

Arti K. Rai, JD, Elvin R. Latty Professor of Law & Co-Director of the Duke Law Center for Innovation Policy

BACKGROUND

Section 402(j) of the Public Health Service Act as amended by Title VIII of the FDAAA (Federal Drug Administration Amendment Act) (the statute) requires that any trial that meets the FDAAA 801 definition of an applicable clinical trial initiated after September 27, 2007 must register on clinicaltrials.gov. However, the following trials are excluded from the requirements of the statute:

- Phase I clinical trials of drugs or biological products subject to FDA regulation;
- Phase I trials in which investigational drugs are used as research tools;
- Small clinical trials to determine feasibility of a device;
- Trials studying behavioral interventions; and
- Non-interventional clinical research.

NIH press releases for the November 19, 2014 and September 16, 2016 actions are also available.

ENDORSEMENTS & OPPOSITION

Endorsements:

- Association of Academic Health Science Librarians (AAHSL), Medical Library Association (MLA), and Cancer Libraries section of MLA, stated:
  - "The proposed regulations will provide patients with more information to make necessary health care decisions, including critical information about the safety of products and treatment options. Clinicians will have access to results information about efficacy, adverse effects, and safety; and biomedical researchers will have information on research design, safety, and scientific results that can inform future protocols and discoveries. We also support timely, easily understood, and accurate reporting of all clinical trials, especially those supported by federal funding, regardless of agency and phase of the clinical trial."
- Committee on Strategies for Responsible Sharing of Clinical Trial Data, Board on Health Science Policy, Institute of Medicine, stated in its publication, Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk:
  - "Responsible sharing of clinical trial data is in the public interest. It maximizes the contributions made by clinical trial participants to scientific knowledge that benefits future patients and society as a whole. Results from many clinical trials are not published in peer-reviewed journals in a timely manner. Even when findings are published, large amounts of data remain unanalyzed. Data sharing makes data from clinical trials available to other investigators for secondary uses, which include carrying out additional analyses, analyzing unpublished data, reproducing published findings, and conducting exploratory analyses to generate new research hypotheses."

Opposition:

- Joseph R. Haywood, PhD, President, Federation of American Societies for Experimental Biology (FASEB), stated: "The proposed rule will enhance the utility of the ClinicalTrials.gov website by expanding the requirements for trial registration and the amount of data submitted per trial. However, if not implemented with appropriate financial and staffing resources, the proposed

substantial changes could result in large volumes of data with low utility for both the scientific community and the public. Therefore, FASEB strongly recommends that HHS either (A) delay finalization of the rule until the concerns listed below have been addressed, or (B) amend the NPRM to include a transition period during which additional resources would be provided to facilitate registration, reporting, and enhance the ability to address emerging system problems in real time. A gradual roll-out would allow HHS to remain flexible and treat this period as a time to rapidly improve ClinicalTrials.gov rather than focus on enforcement."

- The Endocrine Society asserts: "The administrative burden placed on the clinical researchers in order to implement the draft policy activities would require significant percent effort allocation which is currently neither accommodated by current grant budget structure nor necessarily in accordance with university policy regarding effort requirements."

STATUS

The National Institutes of Health issued this Final Policy on September 21st, 2016, which is effective January 18, 2017.

RELATED POLICIES

This policy is complementary to the following existing regulation:

- Section 402(j) of the Public Health Service Act as amended by Title VIII of the FDAAA (Federal Drug Administration Amendment Act), the "statute."
- 42 CFR part 11, Clinical Trials Registration and Results Information Submission, the "regulation."

POLICY HISTORY

The NIH noticed the Initial Draft of the Policy November 21, 2014.

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RECOMMENDED CITATION

Duke SciPol, "Dissemination of NIH-Funded Clinical Trial Information (Final Policy)" available at http:/scipol.duke.edu/content/dissemination-nih-funded-clinical-trial-information-final-policy (10/24/2016).