UC DAVIS HEALTH

Compliance Department
RESEARCH COMPLIANCE MEMORANDUM

To: UCD Health Chairs & Chief Administrator Officers
From: Nirali Patel, Compliance Manager
Kathy Olson, Research Compliance Analyst
Re: Department of Health and Human Services Final Rule & National Institutes of Health Complementary Policy
Date: January 18, 2017

Introduction

In 2000, ClinicalTrials.gov was created to establish a registry of clinical trials involving investigational drugs as a result of the Food and Drug Administration Modernization Act of 1997 (FDAMA). Subsequently, the FDA Amendments Act of 2007, Section 801 (FDAAA 801) required additional types of trials to register on the ClinicalTrials.gov website and submit certain data elements.

Recently, in September 2016, the Department of Health and Human Services (DHHS) issued a Final Rule clarifying and expanding the registration and results information submission requirements under FDAAA 801. In parallel to the Final Rule, the National Institutes for Health (NIH) issued a complementary policy outlining the requirements for registering and submitting results information to ClinicalTrials.gov. Both the Final Rule and the NIH Policy have effective dates of January 18, 2017, and will impact all new studies and some existing studies at UD Davis Health. The following is a summary of the registering and data submission requirements contained in the Final Rule and NIH Policy that impact many of our researchers.

1. Which trials must register and submit results on ClinicalTrials.gov?

Under the new rules, the studies that must register and report results on ClinicalTrials.gov are[1]:

A. Clinical trials funded in whole or in part by NIH, only when the NIH application/proposal or IRB approval is received on or after January 18, 2017[2]; and

B. Applicable Clinical Trials (ACT), which include:
- Studies initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007;
- Interventional Studies or Studies that involve a pediatric postmarket surveillance of a device[3];
- Studies involving a U.S. FDA Regulated Drug, Biologic, or Device Product;
- Studies that do not include Phase 1 (drug and biological product);

[1] Note: While not discussed in detail in this memorandum, studies that intend to publish in journals governed by the International Committee of Medical Journal Editors (ICMJE) are also required to register on ClinicTrials.gov and may have additional requirements pursuant to ICMJE guidelines. For more information, please see: http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html

[2] Trials that use NIH-supported infrastructure but receive no other NIH funds for the conduct of a specific clinical trial are not subject to the NIH Policy.

[3] *See* 42 CFR 11.22(b)(1)(i)

- Studies where the primary purpose is not device feasibility (device products); and
- Studies where any of the following apply: (1) Trial site has one or more locations in the United States, (2) trial is conducted under an FDA investigational new drug application or investigational device exemption, or (3) trial involves a drug, biologic, or device that is manufactured in the United States or its territories and is exported for research.

2. Who is responsible for complying with these rules?

A single Responsible Party must be designated to register and submit results information via the ClincalTrials.gov website. The Responsible Party is defined as:

- The sponsor of the clinical trial; or

- The principal investigator (PI), if designated by a sponsor, grantee, contractor, or awardee, so long as the PI 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 requirements for the submission of clinical trial information.

Practically, it is crucial for researchers to understand whether a trial sponsor will be complying with the requirements or if the study personnel (i.e., the Principal Investigator) are responsible for compliance.

3. What are the registration and results requirements?

Under the new rules, there are two primary categories of required activities on ClinicalTrials.gov: (A) Registration and (B) Results Submissions.

A. Registration

All eligible studies must register online at ClincalTrials.gov[4]. The studies that must register include: all ACTs with a *study start date*[5] on or after January 18, 2017; and all NIH funded studies where the NIH application/proposal or IRB approval was received on or after January 18, 2017.

Studies must register no later than 21 days after the first subject enrollment[6]. Registration information must also be updated no less than once every 12 months, although certain information may be required to be updated more frequently[7]. In addition, an expanded access registration is required if an investigational drug product studied in an applicable drug clinical trial is available through an expanded access program. Only one expanded access record will be created for each investigational drug product, although multiple applicable clinical trials can be linked to the same record if they study the same product. For more information, *See* 42 CFR 11.28 (c) of the Final Rule.

[4] *See* https://clinicaltrials.gov/ct2/manage-recs/how-register#StepsForRegistering
[5] Study Start Date is the estimated date on which the clinical trial will be open to enrollment of human subjects, or if the clinical trial has enrolled the first human subject, the actual date on which the first human subject was enrolled. *See* 42 CFR 11.10(b)(16)
[6] *See* Appendix A for registration data requirements.
[7] *See* Appendix B for submission timing requirements.

B. **Results**

In addition to meeting the registration requirements, certain studies must also input results information on the ClinicalTrials.gov website. These studies include: ACTs with a *primary completion date*[8] on or after January 18, 2017; and all NIH funded studies where the NIH application/proposal or IRB approval was received on or after January 18, 2017. Studies must generally report results within 1 year of the primary completion date[9]. Data must be updated no less than once every 12 months, although certain information may be required to be updated more frequently[10].

4. What are the possible penalties for non-compliance?

Failure to comply with the Final Rule and NIH Policy requirements may have significant implications for both researchers at the institution. Possible penalties include: criminal proceedings, civil penalties up to $10,000 per day, and the withholding or loss of DHHS and NIH funds for individual researchers and the institution.

Additional Resources:

The Final Rule: https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission.

Final Rule information, resources and training: https://prsinfo.clinicaltrials.gov

NIH Policy: https://federalregister.gov/d/2016-22379

[8] Primary Completion Date is (1) Date the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, (2) If multiple primary outcome measures, the date on which data collection is completed for all of the primary outcomes, or (3) Estimated date updated to actual primary completion date.

[9] *See* Appendix C for reporting results data requirements, and 42 CFR 11.48 for more information on when delays are allowed.

[10] *See* Appendix B for submission timing requirements.