1. PURPOSE:
This Standard Operating Procedure (SOP) describes the process for reporting clinical trials results with ClinicalTrials.gov.

Please refer to “SOP-401: Registration of Clinical Trials in ClinicalTrials.gov” regarding the creation of an account and registration of a clinical trial on ClinicalTrials.gov.

2. SCOPE:
This SOP will provide instruction and promote consistency among all departments within University Hospitals Cleveland Medical Center regarding the requirement of registering applicable clinical trials with ClinicalTrials.gov. The U.S. Food and Drug Administration (FDA) is the government agency that requires registration of clinical trials. Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801 or US Public Law 110-85) passed on September 27, 2007 requires mandatory registration and results reporting for certain clinical trials of drugs, biologics, and devices of all applicable clinical trials initiated on or before September 27, 2007, and is ongoing as of December 27, 2007. This legislation coupled with the Final Rule for Clinical Trials Registration and Results Information Submission creates the regulatory requirements and procedures for ClinicalTrials.gov.

The International Committee of Medical Journal Editors (ICMJE) member journals require, as a condition of consideration for publication in their journals, registration in a public trials registry. The ICMJE does not advocate one particular registry, but its member journals require authors to register their trial in a registry that meets several criteria.

According to the Food and Drug Administration Amendments Act of 2007:
- Penalties may include civil monetary penalties up to $10,000 fine for failing to submit or for submitting fraudulent information to ClinicalTrials.gov.
- After notification of noncompliance, the fine may go up to $10,000 per day until resolved.
- For federally funded grants, penalties may include the withholding or recovery of grant funds.

REQUIREMENTS:
Ultimately the results of all interventional studies need to be submitted in ClinicalTrials.gov.

(1) FDA Regulated Research Requirements:
FDAAA requires registration of ‘Applicable Trials’. An ‘Applicable Trial’ is defined as:
- Interventional studies;
- Studies involving drugs, biologics, or medical devices regulated by FDA;
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- Studies that require an IND or IDE;
- Studies that one or more of the following applies:
  - at least one site in the US or one of its territories, or
  - the product is manufactured in and exported from the US or one of its territories.
- Clinical trials must be submitted for registration with ClinicalTrials.gov within 21 days after the enrollment of the first patient.

For more information regarding ‘Applicable Trials’, see Elaboration of Definitions of Responsible Party and Applicable Clinical Trials

(2) ICMJE Requirements:
ICMJE requires registration of any human research project that prospectively assigns human subjects to intervention or comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome.

(3) Medicare Requirements:
Effective January 1, 2015, all Medicare qualifying trials, including some Phase 1 and device feasibility trials, are required to be registered into the ClinicalTrials.gov database. NCT numbers are required on clinical research related claims in order to receive payment. Patients should not be enrolled on a trial unless the NCT registration number is in place. See http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/MM8401.pdf

(4) NIH Funding:
The National Institutes of Health (NIH) Policy on Dissemination of NIH-Funded Clinical Trial Information applies to all clinical trials funded by NIH, regardless of whether they are subject to the FDAAA 801 and the Final Rule effective January 18, 2017. The Policy is effective for competing applications and contract proposals submitted on or after January 18, 2017, and states that all NIH-funded awardees and investigators conducting clinical trials will register and report the results of their clinical trial in ClinicalTrials.gov.

3. RESPONSIBLE INDIVIDUALS:
(1) FDA Regulated Research Requirements:
According to federal law, the ‘Responsible Party’ is responsible for reporting results to ClinicalTrials.gov and is defined as:
- The IND/IDE holder of the trial
- For studies not conducted under an IND/IDE
  - The study sponsor or the grantee institution,
  - Principal Investigator, if there is no external funding agreement

Situations in which Institution/PI is the Responsible Party
For trials being conducted under a funding agreement, grant (e.g. NIH awards) or department/internal funding, the funding recipient is considered the Responsible Party. Because the PI is in best position to understand the research protocol study results and adverse events, the institution will designate the Principal Investigator to assume the role of the Responsible Party.

In situations where UH serves as the primary site for a clinical trial and the institution is determined to be the “Responsible Party,” the Institution will designate this responsibility to the Principal Investigator.

**Situations in which Institution/PI is NOT the Responsible Party**

For most industry sponsored trials, the sponsor will be the Responsible Party, and, as such, the institution and PI will NOT have to manage submissions or results reporting to ClinicalTrials.gov. Similarly, for multi-center trials, or trials sponsored by other academic sites only the lead site (Overall PI) typically bears responsibility for ClinicalTrials.gov reporting; site PIs typically do not have to do additional reporting.

**What are the criteria for designating the Principal Investigator as the “Responsible Party” for reporting results?**

According to federal law, the Principal Investigator can serve as a Responsible Party if that individual:

- 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

**(2) ICMJE Requirements**

Anyone involved in the clinical trial could register the trial, in practice this responsibility usually falls with the individual submitting the publication to the ICMJE journal, which is usually the Principal Investigator.

**(3) Medicare Requirements:**

In order to ensure proper research billing compliance, it is the responsibility of department research personnel to communicate the NCT number to their Research Finance Specialist (RFS) during administrative study start-up and prior to any patient enrollment on the trial. It is the responsibility of the RFS to associate the appropriate NCT number with study related claims and assure this communication to the appropriate parties in revenue cycle management.

**(4) NIH Requirements:**

The trial’s “Responsible Party” is responsible for two basic elements of compliance:

- The registration of the ACTs in ClinicalTrials.gov, and
- The reporting of summary results information (including adverse events)

All NIH grantees, regardless of whether or not they are the “Responsible Party” under FDAAA are responsible for:
• Certification in the grant application and progress report forms that the Responsible Party has made all required submissions to ClinicalTrials.gov for ACTs funded in whole or in part by the NIH.

4. DEFINITIONS:
Please see “[Section 7. REFERENCES]” for complete definitions of any additional terms not listed below.

CCCC: Case Comprehensive Cancer Center

NCT Number: National Clinical Trial (NCT) number, another term for the ClinicalTrials.gov registry number unique to each record. The format for the ClinicalTrials.gov registry number is “NCT” followed by an 8-digit number, (e.g., NCT00000419).

PRS (Protocol Registration and Results System): A quality control and reviewing body to ensure all aspects of a clinical trial are entered according to federal regulations.

Primary Completion Date (PCD): The primary completion date is the date when the final subject was examined and/or received an intervention for the purposes of final collection of data for the pre-specified primary outcome (as per protocol), regardless of whether the clinical trial was completed (recruiting and data collection was completed per protocol), or terminated (recruiting or enrolling participants was halted prematurely and will not resume).

5. POLICY STATEMENT:
All applicable clinical trials must have results reported in ClinicalTrials.gov. The primary completion date (PCD) determines the time frame for results reporting.

The Responsible Party has one year (12 months) from the PCD to enter trial results. If a results submission is delayed, the Responsible Party must submit an extension request to ClinicalTrials.gov. Please see https://www.clinicaltrials.gov/ct2/manage-recs/fdaaa for information regarding delays and extension requests.

Updating Your Registered Study
Once a trial is registered, both the FDA and ICMJE require that registrations be updated as follows:

FDA updating requirements:
- Information must be updated at least once every 12 months
- If changes affect human subjects via a protocol amendment, the information must be updated within 30 days of the IRB’s approval
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- The registry must be updated within 30 days of any changes in recruitment status or completion of the study (PCD)*
- The registry must be updated within 15 days of change in approval or clearance status of drugs and devices not previously approved by FDA

ClinicalTrials.gov notifies the Responsible Party (or designee) account of which trials are due for updates.

**ICMJE** requires updating study information every 6 months.

For the most up-to-date information or to cross reference the requirements for ClinicalTrials.gov please visit: [https://clinicaltrials.gov/ct2/manage-recs/faq](https://clinicaltrials.gov/ct2/manage-recs/faq)

*Once a study is closed to accrual, the Responsible Party or designee will then monitor the patient status (on treatment, off treatment, off study), to determine the PCD. This date can be entered in ClinicalTrials.gov as “anticipated” and updated as the study moves forward. Once the date is set as “actual” then the Responsible Party has one year from that date to enter results.

6. PROCEDURES:

**Results Reporting in ClinicalTrials.gov**

6.1.1 Please be aware that because results are specific to each study, the procedures for results reporting are generic in order to be inclusive of all studies

6.2 Helpful Tips:

6.2.1 Be aware of fields marked with the following:

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>*</td>
<td>Required by ClinicalTrials.gov</td>
</tr>
<tr>
<td>FDAAA</td>
<td>Required to comply with US Public Law 110-85, Section 801</td>
</tr>
</tbody>
</table>

6.2.2 The system offers the option to save data if you do not have time to complete the entire process.

6.2.3 Verify that all outcome measures in the ClinicalTrials.gov registration are correct before beginning the results reporting. These outcomes will automatically be copied to the results section.

6.3 Results Modules: there are nine modules of data to be completed.

6.3.1 **Participant Flow**: Recruitment details, pre-assignment details, arm/group information, type of units assigned, and periods.

6.3.2 **Baseline Characteristics**: Arm/group information, baseline analysis population information, and baseline measure information.

6.3.3 **Outcome Measures**: Outcome measure information, statistical analysis, statistical analysis overview, comparison group selection, type of statistical test, statistical test of hypothesis, method of estimation, and other statistical
6.3.4 **Adverse Event Information**: The following tables must be completed: (1) All-Cause Mortality, (2) Serious Adverse Events, (3) Other (Not Including Serious) Adverse Events. Additionally, time frame, adverse event reporting description, source vocabulary name for table default, collection approach for table default, arm/group information, adverse events, total number affected by all-cause mortality, total number at risk for all-cause mortality, total number affected by any serious adverse event, total number at risk for serious adverse events, frequency threshold for reporting other (not including serious) adverse events, total number affected by any other (not including serious) adverse event above the frequency threshold, total number at risk for other (not including serious) adverse events, adverse event term, organ system, adverse event term additional description, source vocabulary name, collection approach, and adverse event data.

6.3.5 **Limits and Caveats**: Overall limitations and caveats.

6.3.6 **Certain Agreements**: Are all PIs employees of sponsor, results disclosure restriction on PIs, and PI disclosure restriction type.

6.3.7 **Results Point of Contact**: Name or official title, organization name, phone, extension, and email.

6.3.8 **Delayed Results (Optional)**: Delay results type, intervention name(s), FDA application number(s), requested submission date, and explanation.

6.3.9 **Document Upload Information**: Document type (study protocol, statistical analysis plan (SAP), informed consent form (ICF), or study protocol with SAP or ICF), document date, subtitle, and document.

6.4 Submitting Results

6.4.1 The PRS team at ClinicalTrials.gov will review the submission and post comments for corrections/clarifications. Depending on the nature of corrections, these can be done by the Responsible Party or designee as necessary. Once the review process is complete, ClinicalTrials.gov will send notification to the Responsible Party or designee that the submission of study results has been approved and will be published on the public ClinicalTrials.gov website within two business days.

6.4.2 Secondary outcome results, if not reported at initial results submission, are reported when the data have been analyzed. Results must be reported within one year after the final patient has been given treatment unless an extension has been approved by the ClinicalTrials.gov PRS. Anticipated posting dates must be included at the time of the primary outcome results entry.

6.4.3 If corrections or clarifications are requested by the ClinicalTrials.gov team, the
Responsible Party [see Section 3 “Responsible Individuals”] must respond within 15 days for any registration related information and within 25 days for any results information.

6.5 Cancer studies have their own account, should be registered and have results reported as Case Comprehensive Cancer Center (CCCC) rather than University Hospitals Cleveland Medical Center. There is a centralized registration coordinator who acts as the Responsible Party designee. The registration coordinator will work with the Responsible Party and study team to report results on Cancer studies. Contact your Department Administrator for more information on registering Cancer studies.

6.6 Once the results of the study are released by the Responsible Party, it will be reviewed by personnel at ClinicalTrials.gov within 30 days. Any comments are posted on the Responsible Party’s account at ClinicalTrials.gov and an email will be sent to the Responsible Party. Corrections to trial results can be made, as needed, and the trial can be re-released. If there are no review comments the results are released to the public website within 2 business days following completion of the review period.

7. REFERENCES

- NIH Guidance on Clinical Trials Registration in ClinicalTrials.gov - http://grants.nih.gov/clinicaltrials_fdaaa/
- ClinicalTrials.gov public website - http://clinicaltrials.gov
- ClinicalTrials.gov registration site - https://register.clinicaltrials.gov
- Registration at ClinicalTrials.gov: Fact Sheet - http://prsinfo.clinicaltrials.gov/
- How to Submit Your Results - https://www.clinicaltrials.gov/ct2/manage-recs/how-report
- Protocol Data Element Definitions - http://prsinfo.clinicaltrials.gov/definitions.html
- UHCMC Research SOP SC-401- Registration of Clinical Trials in ClinicalTrials.gov

8. FORMS OR ATTACHMENTS

None
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APPROVALS

Approved by Dr. Grace McComsey, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center–August 7, 2018