ClinicalTrials.gov Training

Outline

- ClinicalTrials.gov Overview
- Purpose, Impact, and Reputational Implications
- ClinicalTrials.gov Regulations and Definitions
- Registering and Maintaining A ClinicalTrials.gov Record
- Results Modules
- Institutional Resources
ClinicalTrials.gov Overview

- Service of the NIH National Library of Medicine that acts as a public registry and results database of clinical studies of human participants.

- Requirements to publicly register/post results apply to WCM investigator-initiated studies only.

- If multi-site, one registration functions as ClinicalTrials.gov registration and results record for all sites.
• Public registration and reporting of clinical trial results on ClinicalTrials.gov is required for:
  o Intervventional studies:
    — Evaluating FDA-regulated products ("Applicable Clinical Trials"); or
    — That are (partially or wholly) NIH-funded and meet NIH’s clinical trial definition; or
    — That meet The International Committee of Medical Journal Editors (ICMJE) clinical trial definition (registration only); or
    — That are qualifying clinical trials rendering claims for items and services to the Center for Medicare & Medicaid Services (CMS)
  — Note: Some funding entities require registration and results reporting (e.g., PCORI; Bill & Melinda Gates Foundation). Be sure to check the terms of your award!
The Importance of ClinicalTrials.gov

The Outcome of My Clinical Trial Is a Mystery

As a kid, I enrolled in a study whose results were never published—meaning I’ll live the rest of my life with a heart implant, but may never know how well it actually works.

Q: Isn’t it administratively burdensome to have a definition of clinical trial that requires so many studies involving human participants to report their results?

A: Results Reporting should not be considered a burden. Reporting results is an essential part of the scientific method; it is an integral component of the scientific process.

"...the days of deciding whether or not summary results are worth reporting are over...The time to decide whether a trial is worth doing is before the trial is started, not after participants have been put at risk."


In 1999, GSK received Paxil approval for treating depression in adults.

After conducting several pediatric trials for Paxil, GSK hired a consulting company to write a journal article selectively presenting results.

Article:

– Claimed that Paxil worked better than placebo in treating depression in children and adolescents.
– De-emphasized side effects like suicidal thoughts and actions.
– Did not disclose two other studies that did not show Paxil to be efficacious in children and adolescents.

Doctors prescribed off-label in reliance on this selectively published data.

In 2015, an article was published in BMJ after researchers re-examined the data concluding Paxil was ineffective and unsafe in the study.

GSK fined by the government; black box warning put on Paxil.

ClinicalTrials.gov regulatory requirements remove the “option” to report results selectively.
Spotlight on Noncompliance

Where Are the Results of These Five Clinical Trials of Antidepressant Drugs?

By Till B¨uchner, PhD
January 28, 2020

AllTrials tracker site names clinical trial non-reporters

Organizations that fail to report the results of their clinical trials are to be named on a new website set up by the AllTrials campaign group. The new FDAAA Trials Tracker site went live this week and - as its name suggests - seeks to highlight the failings of the FDA Amendments Act 2007 law which required...
WCM ClinicalTrials.gov Records with Late Results

- **Last 5 Years**: 91% reduction in late results records
- **Last Year**: 41% reduction in late results records

January 2017 to January 2022

ClinicalTrials.gov Regulations & Definitions
**ClinicalTrials.gov Reporting Requirement**

<table>
<thead>
<tr>
<th>Requirement</th>
<th>ICMJE Policy</th>
<th>FDAAA 801 (Applicable to Older Studies)</th>
<th>HHS Final Rule (42CFR11) (Applicable to Older Studies)</th>
<th>NIH Policy on Dissemination of NIH-Funded Clinical Trial Information (Applicable to Newer Studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective Date</td>
<td>2005</td>
<td>September 27, 2007</td>
<td>January 18, 2017</td>
<td>January 18, 2017</td>
</tr>
<tr>
<td>Scope</td>
<td>Registration</td>
<td>Registration &amp; Results Reporting</td>
<td>Registration &amp; Results Reporting</td>
<td></td>
</tr>
<tr>
<td>Phase</td>
<td>All</td>
<td>Not Phase 0 or Phase 1 studies or small feasibility device studies</td>
<td>All</td>
<td></td>
</tr>
<tr>
<td>Intervention Type</td>
<td>All</td>
<td>Approved/licensed/cleared drug, biologic, &amp; device products regulated by the FDA</td>
<td>Most drug, biologic, &amp; device products regulated by the FDA</td>
<td>All (e.g., including psychological or behavioral interventions)</td>
</tr>
<tr>
<td>Funding Source</td>
<td>Any</td>
<td>Any</td>
<td>NIH</td>
<td></td>
</tr>
<tr>
<td>Initial Registration</td>
<td>Prior to enrollment of first participant</td>
<td>Not later than 21 days after enrollment of first participant</td>
<td>Not later than 21 days after enrollment of first participant</td>
<td></td>
</tr>
<tr>
<td>Results Reporting</td>
<td>N/A</td>
<td>Within 12 months of primary completion date (for primary outcome measures)</td>
<td>Within 12 months of study completion date (for secondary outcome measures)</td>
<td></td>
</tr>
<tr>
<td>Document Upload with Results</td>
<td>N/A</td>
<td>N/A</td>
<td>Protocol Document Statistical Analysis Plan</td>
<td>Protocol Document Statistical Analysis Plan</td>
</tr>
<tr>
<td>ICF Statement</td>
<td>N/A</td>
<td>Required</td>
<td>Required</td>
<td></td>
</tr>
<tr>
<td>Consequences of Noncompliance</td>
<td>• Refusal to publish in ICMJE journals</td>
<td>• Criminal proceedings and/or civil monetary penalties (up to $12,103/day – adjusted for inflation)</td>
<td>• Suspension or termination of grant or contract funding</td>
<td>• Can be considered in future funding decisions</td>
</tr>
</tbody>
</table>

**WCM policy requires registration prior to enrollment of the first participant.**

---

Phase 1 studies that are NIH funded don't have to be registered or have results publicly posted on ClinicalTrials.gov.

**True**  **A**

**False**  **B**
Phase 1 studies that are NIH funded don't have to be registered or have results publicly posted on ClinicalTrials.gov.

A  B

True  False

Start the presentation to see the content. Still no live content? Install the app or get help at Polls.com/app.
A consequence of failing to register on ClinicalTrials.gov prior to enrollment of the first participant is being unable to publish in ICMJE member journals.

True
False

Poll locked. Responses not accepted.
A consequence of failing to register on ClinicalTrials.gov prior to enrollment of the first participant is being unable to publish in ICMJE member journals.
Publicly Posting the Informed Consent

A Revised Common Rule Requirement Impacting ClinicalTrials.gov for Clinical Trials Conducted or Supported by A Common Rule Agency and Initially Approved on or after January 21, 2019

Out of Compliance with §46.116(h)

If a clinical trial informed consent form is posted before the study is closed to recruitment, §46.116(h) is not satisfied.

Clinical trial closed to recruitment*

Subject recruitment begins

Last study visit by any enrolled subject as required by the protocol

In Compliance with §46.116(h)

Per §46.116(h)(3), one IRB-approved informed consent form used to enroll subjects must be posted.

Only forms posted (1) after a study is closed to recruitment, and (2) where 60 or fewer days have passed since the last study visit satisfy the regulatory requirement.

Out of Compliance with §46.116(h)

If a clinical trial informed consent form is posted 61 or more days after the last study visit, §46.116(h) is not satisfied.

60 days after last study visit by any enrolled subject as required by the protocol

*The clinical trial can be closed to recruitment at any time up to and including 60 days after the last study visit by any enrolled subject as required by the protocol, and this timeline will accurately represent posting requirements.

Source: Hartsmith, Lauren. (2019). Clinical Trial Informed Consent Posting for Studies Subject to the Revised Common Rule (i.e., the 2018 Requirements) [Powerpoint Slides]

Required ClinicalTrials.gov Statement in The Informed Consent

<table>
<thead>
<tr>
<th>ICMJE Clinical Trials</th>
<th>FDAAA 801</th>
<th>HHS Final Rule</th>
<th>NIH-funded Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>• N/A – No ClinicalTrials.gov statement is needed in the ICF.</td>
<td>• Requires an exact, unaltered statement in the informed consent form for all sites recruiting subjects.</td>
<td>• At WCM, the required statement is already included in the ICF template provided by the WCM IRB.</td>
<td>• If multi-site study, coordinate to ensure it’s included in ICF at other sites.</td>
</tr>
<tr>
<td>• Requires an exact, unaltered statement in the informed consent form for all sites recruiting subjects.</td>
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<td>• Requires an exact, unaltered statement in the informed consent form for all sites recruiting subjects.</td>
<td>• At WCM, the required statement is already included in the ICF template provided by the WCM IRB.</td>
<td>• “A description of this clinical trial will be available on <a href="http://www.ClinicalTrials.gov">http://www.ClinicalTrials.gov</a>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.”</td>
</tr>
</tbody>
</table>

Source: Hartsmith, Lauren. (2019). Clinical Trial Informed Consent Posting for Studies Subject to the Revised Common Rule (i.e., the 2018 Requirements) [Powerpoint Slides]
Data Sharing Statement

“IPD Sharing Statement”

- Refers to sharing of de-identified individual participant data with others not affiliated with the research project.

- Applies to all clinical trials enrolling on or after Jan 1, 2019.

- Answer to “IPD Sharing Statement” in initial ClinicalTrials.gov registration must say “No” or “Yes” at time of initial registration. (Can be changed later if needed.)
  - “Undecided” is an option in the system, but selecting it doesn’t meet the requirement.

- Statement in ClinicalTrials.gov registration must match the data sharing statement submitted with the results manuscript at the time of publication.

Data Sharing Statement

“IPD Sharing Statement” Examples

<table>
<thead>
<tr>
<th>Example 1</th>
<th>Example 2</th>
<th>Example 3</th>
<th>Example 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Will individual participant data be available including data elements?</td>
<td>Yes</td>
<td>Yes</td>
<td>Individual participant data that underlie the results reported in this article, along with the tables, figures, and appendices.</td>
</tr>
<tr>
<td>What data in particular will be shared?</td>
<td>All of the individual participant data collected during the trial, other than data elements</td>
<td>Individual participant data that underlie the results reported in this article, along with the tables, figures, and appendices.</td>
<td>Not available</td>
</tr>
<tr>
<td>When will data be available, start and end dates?</td>
<td>Immediately following publication: No end date.</td>
<td>Beginning, 3 months and ending 5 years following article publication.</td>
<td>Beginning, 3 months and ending 36 months following article publication.</td>
</tr>
<tr>
<td>With others?</td>
<td>None who wish to access the data.</td>
<td>Researchers who provide a methodologically sound proposal.</td>
<td>Investigators whose proposed use of the data has been approved by the independent review committee (known as the “interim” or “reviewing” committee) identified for this purpose.</td>
</tr>
<tr>
<td>For what types of analysis?</td>
<td>Any purpose.</td>
<td>For analyses done in the approved proposal.</td>
<td>For individual participant data meta-analysis.</td>
</tr>
<tr>
<td>By what mechanisms will data be made available?</td>
<td>Data are available in deidentified at least to be included.</td>
<td>Data should be deidentified and made available to investigators submitting a request.</td>
<td>Proposals may be submitted up to 36 months following publication.</td>
</tr>
</tbody>
</table>

© These examples are meant for sharing purposes, but not all data sharing requests.
Dissemination Plan

- Required to be uploaded in NIH FORMS-G.

- Describes how the awardee will ensure:
  - Registration, updates, and results posting will occur as required.
  - ICF statement will be included in the ICF.

- OSRA (grantsandcontracts@med.cornell.edu) provides template text at the following link:
  https://research.weill.cornell.edu/sites/default/files/wcm_clinicaltrials.gov_dissemination_plan_v1.0_4.06.18.docx

- More information:

Clinical Trial
Regulatory Definitions
Knowing When Registration is Required
Clinical Trial Definition

- Any research study that:
  - Prospectively assigns human participants or groups of humans
  - To one or more health-related interventions
  - To evaluate the effects on health outcomes.

- Health-related interventions include any intervention used to modify a biomedical or health-related outcome:
  - Examples of health-related interventions: drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes.
  - Health outcomes include any biomedical or health-related measures obtained in patients or participants.
Clinical Trial Definition

• Unsure of whether the ICMJE clinical trial definition is met?
  o Err on the side of caution and register your study; or
  o Consult the editorial office of the journal you wish to publish the study in.

List of ICMJE member journals:
http://www.icmje.org/journals-following-the-icmje-recommendations/

• Note: ICMJE does not consider the summary results posted on ClinicalTrials.gov to be prior publication.

Applicable Clinical Trial (ACT)

HHS Final Rule (42CFR11)

ACT if the answer is “Yes” to 1 through 4.

1. Interventional; **AND**

2. ANY of the following applies:
   o At least one study facility in the U.S. or U.S. territory; **OR**
   o Study is conducted under an IND or IDE; **OR**
   o Study involves a drug, device, or biologic manufactured in the U.S. (or U.S. territory) and exported for study in another country; **AND**

3. Evaluates at least one FDA-regulated drug, device, or biological product; **AND**

4. Not a:
   o Phase 0 or Phase 1 study of a drug or biological product; **OR**
   o Device feasibility study
Clinical Trial Definition

• A research study in which:

1. One or more human subjects are prospectively assigned
   - NIH Clarification: Single arm trials still qualify as prospectively assigned as long as assignment is pre-defined in the protocol.

2. To one or more interventions (which may include placebo or other control)
   - NIH Clarification: Measurements are used to collect data, while interventions are used to modify health-related endpoints.

3. To evaluate the effects of those interventions

4. On health-related biomedical or behavioral outcomes
   - NIH Clarification: Pre-specified goal(s) or condition(s) that reflect the effect of the intervention(s) on subjects’ biomedical or behavioral status or quality of life.
     - E.g., Positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and/or information retention);
     - Positive or negative changes to health behaviors, disease processes, or quality of life.
     - Positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression)

If an interventional trial evaluating an FDA-regulated product doesn't have an IND or IDE associated with it, then it doesn't have to be registered or have results posted on ClinicalTrials.gov.

True
False
If an interventional trial evaluating an FDA-regulated product doesn't have an IND or IDE associated with it, then it doesn't have to be registered or have results posted on ClinicalTrials.gov.
Preliminary Info on Registration

PRS: http://register.clinicaltrials.gov
Who & When

- WCM PI must be ClinicalTrials.gov record owner or formally name a WCM designee via email at registerclinicaltrials@med.cornell.edu.

- PI and research coordinator receive courtesy “Action Required” notice from Human Research Compliance prompting PI to register on ClinicalTrials.gov.
  - Supplemental to SASP (Study Activation Status Page) in WRG

- Can register to obtain NCT # once an IRB protocol # is assigned to your protocol.

- Receiving a National Clinical Trials (NCT) # means registration has been successful.

Registering and Maintaining A ClinicalTrials.gov Record
Staying Compliant

• Courtesy Action Required E-mails from Human Research Compliance:
  
  o With resources, prompting PI/designee to:
    
    ➤ Register prior to enrollment of the first participant.
    
    ➤ Update the study record at least once every 12 months.
      • Certain elements require proactive updates within 30 days after a change in status.
    
    ➤ Enter results no later than 12 months after the primary completion date (for primary outcome measures) and 12 months after the study completion date (for secondary outcome measures).
      • Internal WCM deadline is earlier to allow for timely completion of internal QC process and statistical analyses entry.
    
    ➤ Respond to PRS Review Comments either in 1 week (if registration) or 2 weeks (if results).
  
• Noncompliance with associated deadlines for updates, results, and response to PRS trigger hold on IRB approvals for any mid-process submissions by the PI across protocols.

Deadlines for Proactive Updating

- Study Start Date: 30 calendar days after the first subject is enrolled (if the first human subject was not enrolled at the time of registration).
- Intervention Name(s): 30 calendar days after a proprietary name is established.
- Availability of Expanded Access: 30 calendar days after expanded access becomes available (if available after registration), and 30 calendar days after an NCT number is assigned to a newly created expanded access record.
- Expanded Access Status: 30 calendar days after a change in the availability of expanded access.
- Expanded Access Type: 30 calendar days after a change in the type(s) of available expanded access.
- Overall Recruitment Status: 30 calendar days after a change in overall recruitment status.
- Individual Site Status: 30 calendar days after a change in status of any individual site.
- Human Subjects Protection Review Board Status: 30 calendar days after a change in status.
- Primary Completion Date: 30 calendar days after the clinical trial results are submitted.
- Enrollment: At the time the primary completion date is changed to “actual,” the actual number of participants enrolled must be submitted.
- Study Completion Date: 30 calendar days after the clinical trial results are submitted.
- Responsible Party: 30 calendar days after a change in the responsible party or the official title of the responsible party.
- Responsible Party Contact Information: 30 calendar days after a change in the responsible party or the contact information for the responsible party.
- Device Product Not Approved or Cleared by U.S. FDA: 15 calendar days after a change in approval or clearance status has occurred.
- Device Product Not Approved or Cleared by U.S. FDA: 15 calendar days after a change in approval or clearance status has occurred.
- Record Verification Date: Any time the responsibility party reviews the complete set of submitted clinical trial information for accuracy and completeness or within 30 days of any change in the status of any clinical trial information.
### Overall Recruitment Status in the Study Status Section

- Enter within 30 days of change in status:
  - **Not Yet Recruiting**
    - Participants are not yet being recruited.
  - **Recruiting**
    - Participants are currently being recruited, whether or not any participants have yet been enrolled.
  - **Enrolling by invitation**
    - Participants are being (or will be) selected from a predetermined population.
  - **Active, not recruiting**
    - Study is continuing, meaning participants are receiving an intervention or being examined, but new participants are not currently being recruited or enrolled.

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### Overall Recruitment Status in the Study Status Section

- Enter within 30 days of change in status:
  - **Completed**
    - Study has concluded normally; participants no longer receiving intervention or being examined (i.e., last participant’s last visit has occurred).
  - **Suspended**
    - Study halted prematurely, but potentially will resume.
  - **Terminated**
    - Study halted prematurely and will not resume; participants no longer receiving intervention or being examined.
  - **Withdrawn**
    - Study halted prematurely, prior to enrollment* of first participant.

Determining the Federal Deadline for Results
Entering the Primary and Study Completion Date in the Study Status Section

**PRIMARY COMPLETION DATE**
Determines results due date for primary outcome measures.

- ✔ Date final participant was examined or received intervention for purposes of final data collection for all **primary outcome measures**.

**STUDY COMPLETION DATE**
Determines results due date for secondary outcome measures.

- ✔ Date final participant was examined or received intervention for purposes of final data collection for all:
  - ✔ (1) primary outcome measures,
  - ✔ (2) **secondary outcome measures**, and
  - ✔ (3) adverse events*.

*Last participant’s last visit.

These dates are not:
- ✗ The date the protocol was closed with the IRB.
- ✔ The date of publication.
- ✗ The date of the start of data analysis.

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**Example: Study Status Section**
Not Yet Recruiting

- ✔ Record Verification Date: Month: December, Year: 2016
- ✔ Overall Recruitment Status: Not yet recruiting
- ✗ § Study Start Date: Month: January, Day: , Year: 2017, Type: Anticipated
  - Tip: Day is not required for Anticipated dates.
- ✔ Primary Completion Date: Month: October, Day: , Year: 2019, Type: Anticipated
  - Final data collection date for primary outcome measures.
- ✔ § Study Completion Date: Month: November, Day: , Year: 2019, Type: Anticipated
  - Final data collection date for study.

- Recruitment status, taking into account all sites, is “Not Yet Recruiting.”
- First subject will likely enroll in Jan 2017, so date is set to “anticipated.”
- Last subject’s last visit for data collection of **primary** outcome measures is anticipated to occur in Oct 2019.
- Last subject’s last visit for data collection of **secondary** outcome measures is anticipated to occur in Nov 2019.
Example: Study Status Section

Recruiting

- Recruitment status, taking into account all sites, is “Recruiting.”
- First subject enrolled on Jan 25, 2017, so date is set to actual.
- Last subject’s last visit for data collection of primary outcome measures is anticipated to occur in Oct 2019.
- Last subject’s last visit for data collection of secondary outcome measures is anticipated to occur in Nov 2019.

Example: Study Status Section

Active, not recruiting

- Subjects are still receiving intervention or being examined, but the study is no longer recruiting.
- Last subject’s last visit for data collection of primary outcome measures occurred on Oct 19, 2019, so the date is set to “actual.”
- Last subject’s last visit for data collection of secondary outcome measures is anticipated to occur in Nov 2019 so the date is set to “anticipated.”
• Recruitment status, taking into account all sites, is “Completed.” (IRB protocol will still be open while data analysis occurs.)
• Last subject’s last visit for data collection of secondary outcome measures occurred Nov 25, 2019, so the date is set to “actual.”
Which of these most accurately explains the meaning of the Primary Completion Date?

- The date the protocol was closed with the IRB.
- The date the last participant’s test results are received for analysis of the primary outcome measure(s).
- The date that data analysis for the primary outcome measure(s) is completed.
- The date the last participant was examined or received an intervention for final collection of data for the primary outcome measure(s).
- None of the above

Poll locked. Responses not accepted.

Start the presentation to see live content. Did I miss live content? Install the app or get help at PollFish.com/app

Which of these most accurately explains the meaning of the Primary Completion Date?

- The date the protocol was closed with the IRB.
- The date the last participant’s test results are received for analysis of the primary outcome measure(s).
- The date that data analysis for the primary outcome measure(s) is completed.
- The date the last participant was examined or received an intervention for final collection of data for the primary outcome measure(s).
- None of the above

Poll locked. Responses not accepted.

Start the presentation to see live content. Did I miss live content? Install the app or get help at PollFish.com/app
When poll is active, respond at PollEv.com/laurenwcm
Text LAURENWCM to 22333 once to join

Which of these most accurately explains the meaning of the Study Completion Date?

- The date of publication.
- The date the last participant was examined or received an intervention for final collection of data for the primary and secondary outcome measures and adverse events. (Last subject’s last visit.)
- The date the protocol was closed with the IRB.
- The date the last participant was examined or received an intervention for final collection of data for the primary outcome measure(s).
- None of the above

Poll locked. Responses not accepted.
Registration Requirements

- Unique Protocol ID must be the IRB protocol number.
- Secondary ID must be the NIH grant number, if applicable.

<table>
<thead>
<tr>
<th>Study Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unique Protocol ID: 19-07023411</td>
</tr>
<tr>
<td>Brief Title: Trial to Test the Safety and Effectiveness of SH234 for Asthma</td>
</tr>
<tr>
<td>Official Title: A Phase II Trial to Test the Safety and Efficacy of SH234</td>
</tr>
<tr>
<td>Secondary IDs: R01GM067654 [U.S. NIH Grant/Contract Award Number]</td>
</tr>
</tbody>
</table>

- Sponsor/Collaborators section must:
  o Indicate “Responsible Party” as “Sponsor.” WCM account name will auto-populate.
  o List collaborating organizations providing support: funding, design, data analysis or reporting.
Registration Requirements

- Contacts/Locations section should list:
  - Central Contact w/Backup.
  - WCM Principal Investigator as a Study Official.
  - All sites that will recruit participants w/Site PI and contacts.

<table>
<thead>
<tr>
<th>Contacts/Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Contact Person: FirstName1 LastName1, NP</td>
</tr>
<tr>
<td>Telephone: 646-962-9200</td>
</tr>
<tr>
<td>Email: <a href="mailto:CWD@med.cornell.edu">CWD@med.cornell.edu</a></td>
</tr>
<tr>
<td>Central Contact Backup: FirstName2 LastName2, BS</td>
</tr>
<tr>
<td>Telephone: 646-962-9245</td>
</tr>
<tr>
<td>Email: <a href="mailto:CWD@med.cornell.edu">CWD@med.cornell.edu</a></td>
</tr>
<tr>
<td>Study Officials: FirstName3 LastName3, MD</td>
</tr>
<tr>
<td>Study Principal Investigator</td>
</tr>
<tr>
<td>Well Cornell Medicine</td>
</tr>
</tbody>
</table>

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<tr>
<th>Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States, New York</td>
</tr>
<tr>
<td>Well Cornell Medicine</td>
</tr>
<tr>
<td>New York, New York, United States, 10065</td>
</tr>
<tr>
<td>Contact: FirstName4 LastName4, BA</td>
</tr>
<tr>
<td>Telephone: 646-962-4065</td>
</tr>
<tr>
<td>Email: <a href="mailto:CWD@med.cornell.edu">CWD@med.cornell.edu</a></td>
</tr>
<tr>
<td>Contact: FirstName5 LastName5, NP</td>
</tr>
<tr>
<td>Telephone: 645-962-7569</td>
</tr>
<tr>
<td>Email: <a href="mailto:CWD@med.cornell.edu">CWD@med.cornell.edu</a></td>
</tr>
<tr>
<td>Principal Investigator: FirstName3 LastName3, MD</td>
</tr>
<tr>
<td>Brooklyn Methodist Hospital - NewYork-Presbyterian</td>
</tr>
<tr>
<td>Brooklyn, New York, United States, 11215</td>
</tr>
<tr>
<td>Contact: FirstName6 LastName6, MD</td>
</tr>
<tr>
<td>Telephone: 718-790-3542</td>
</tr>
<tr>
<td>Email: <a href="mailto:CWD@nyc.org">CWD@nyc.org</a></td>
</tr>
<tr>
<td>Contact: FirstName7 LastName7, MD</td>
</tr>
<tr>
<td>Telephone: 718-790-3547</td>
</tr>
<tr>
<td>Email: <a href="mailto:CWD@nyc.org">CWD@nyc.org</a></td>
</tr>
<tr>
<td>Principal Investigator: FirstName6 LastName6, MD</td>
</tr>
</tbody>
</table>

Oversight Section

- Refer to definitions and linked ACT Checklist for these sections.
- If this is “Yes”, the IND/IDE # is required with serial #.
- Answer “Yes” if using a data monitoring committee.
- Neither of these questions is required. Can leave unanswered.

For “Human Subjects Protections Review,” provide the IRB information outlined in the WCM ClinicalTrials.gov Requirements for Posting.
Study Description Section

* Brief Summary:
  The purpose of this study is to assess the safety and efficacy of Remuvelor of treatment of Condition A.

- Describe the study hypothesis in terms understandable to the lay public.
- Can be adapted from the informed consent.
- Omit any and all personal pronouns, (e.g. we, you).

Detailed Description:
Avoid duplicating information that will be entered elsewhere, such as Eligibility Criteria or Outcome Measures

- Optional and can be left blank.
- Does not have to be in lay language. Can be adapted from the background or aims section of the protocol, but do not copy and paste the entire protocol.
- No promotional language permitted.
- Where applicable, explain uncertainties or exploratory nature of study.
- If there are any parts of the trial that the public cannot know about while the study is ongoing without affecting scientific integrity, such as deception research or inclusion/exclusion criteria which could be easily faked in order to join a study (e.g. pain levels in order to have access to a controlled substance), it would be good to explain here, e.g. “Some inclusion/exclusion criteria are purposely omitted at this time to preserve scientific integrity. They will be included after the trial is complete.”

Conditions Section

- Enter each study condition, one per line.
- Use Search MeSH link to verify the correct condition term.
- If no conditions, enter focus of study.

Enter keywords that will help patients find this study when searching at the public ClinicalTrials.gov site.

No need to repeat a Condition or Focus of Study as a Keyword.
Study Design Section

- Study Type: Interventional
- Primary Purpose: Treatment
- Study Phase: Phase 2
- Intervventional Study Model: Parallel
- Number of Arms: 2
- Allocation: Randomized
- Enrollment: Number of Subjects: 100

Check the “definitions” link

Can enter target enrollment.

Arms & Interventions Section: Arms

- Arm Title: Remuverol
  - Arm Type: Experimental
  - Arm Description: Participants receive Remuverol 15 mg tablet orally twice daily for 24 weeks.

- Arm Title: Placebo
  - Arm Type: Placebo Comparator
  - Arm Description: Participants receive Remuverol placebo tablet matching Remuverol orally twice daily for 24 weeks.

Add Arm

- Manually add each arm.
- Be sure # of arms matches # specified in the protocol and the Study Design section.

Avoid titling the arm as Intervention 1 or Arm 1. Arm title must be sufficiently descriptive.
List placebo as a drug intervention.

The preferred format is to include *all* interventions that were pre-specified to be administered as part of the protocol, even if a particular intervention is not "of interest."

Errors must be fixed to move on.
Click edit to resolve these Errors.

- For multi-arm studies, user must link arms and interventions in Cross-Reference to proceed.
- Cross-Reference tables will not exist for single arm studies.
Outcome Measures

- Include all PRIMARY and SECONDARY outcome measures, as pre-specified in the protocol.

  - Listing tertiary or exploratory outcomes is not required.

- Outcome measures must be specific and indicate what is being measured and how it is being measured.

  - Outcome measure titles, descriptions and time frames should help provide context for the data that will ultimately be publicly posted on the site.

Outcome Measures: Title

- Include the metric (i.e., scale, score, number, percentage)

  - How can the title be written to explain the meaning of the data in the example data table shown here?

    | ArmGroup Title | ArmGroup Description | Safety, as measured by number of subjects with at least 1 adverse event |
    |----------------|----------------------|---------------------------------------------------------------|
    | Cetuximab 250 mg/m² IV every 2 wk | 50 mg/m² IV every 2 wk | 3 |
    | Cetuximab 275 mg/m² IV every 2 wk | 50 mg/m² IV every 2 wk | 5 |
    | Cetuximab 300 mg/m² IV every 2 wk | 50 mg/m² IV every 2 wk | 13 |

  - How can the title be written to explain the meaning of the data in the example data table shown here?

    - To determine the maximum tolerated dose of Cetuximab in patients with lung adenocarcinoma.

    - Maximum Tolerated Dose of Cetuximab in patients with lung adenocarcinoma.
Outcome Measures: Title

- List outcomes separately.
  - All-cause mortality, hospitalizations, and ER visits.
  - Number of deaths.
  - Number of hospitalizations.
  - Number of ER visits.
- Exception: If a composite score of multiple measures will be used.
  - Example: Count of participants who experience any of the following: All-cause mortality, hospitalizations, or ER visits.

Outcome Measures: Time Frame

- Be specific. E.g., # of minutes, weeks, months a subject is assessed for the outcome measure.
  - Baseline, Week 2
  - During hospitalization, approximately 5 days
  - Post-intervention, Week 12
- If multiple time points are included:
  - ClinicalTrials.gov assumes change is being assessed. Must include “Change” in the Outcome Measure Title.
    - Example:
      - Title: Change in Severity of Depression as Measured by the Hamilton Depression Scale
        - Description: Total score of Hamilton Depression Scale ranges from 0 (no depression) to 60 (worst depression possible). If reporting a score on a graph, please include the unabbreviated scale title, the reference and maximum values, and whether higher scores mean a better or worse outcome.
        - Time Frame: Baseline, 12 weeks
  - If not measuring change, each time point must be listed as a separate Outcome Measure.
Outcome Measures: Description

• If using a scale as method of measurement for an outcome measure, the description must include:
  
  o Expanded scale acronym, if acronym is used in title.
  
  o Low and high scores of the scale with meaning of high score.
    – Example
      
      | Title | Change in Severity of Depression as Measured by the Hamilton Depression Scale |
      |-------|------------------------------------------------------------------------------|
      | Description | Total score of Hamilton Depression Scale ranges from 0 (no depression) to 60 (worst depression possible). If reporting a change on a scale, please include the individualized scale title, the reference and maximum values, and whether higher scores mean a better or worse outcome. |
      | Time Frame | Relative, 12 weeks |

• If scale isn’t linear (e.g., logarithmic), this should be mentioned.

When poll is active, respond at PollEv.com/laurenwcm
Text LAURENWCM to 22333 once to join

What's wrong with this example?

- The title doesn’t indicate how pain is being measured.
- The title doesn’t omit verbs.
- The title doesn’t indicate that change is being assessed.
- The description doesn’t include the range of scores for a scale used to measure pain or what the scores mean.
- All of the above.
What's wrong with this example?

The title doesn't indicate how pain is being measured.

The title doesn't omit verbs.

The title doesn't indicate that change is being assessed.

The description doesn't include the range of scores for a scale used to measure pain or what the scores mean.

All of the above.
Outcome Measures: Example 1

Corrected

<table>
<thead>
<tr>
<th>Title:</th>
<th>To determine the effect of Remuverol on pain in adults with Condition A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description:</td>
<td></td>
</tr>
<tr>
<td>Time Frame:</td>
<td>Baseline, 12 weeks</td>
</tr>
</tbody>
</table>

Outcome Measure

<table>
<thead>
<tr>
<th>Title:</th>
<th>Change from baseline in pain, as measured by the Visual Analog Scale (VAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description:</td>
<td>Scores are measured on a 100 mm VAS. The VAS ranges from 0 to 100 with 0 indicating no pain and higher scores indicating greater pain.</td>
</tr>
<tr>
<td>Time Frame:</td>
<td>Baseline, 12 weeks</td>
</tr>
</tbody>
</table>

Title must omit verbs and include the name of the scale that will be used to assess change in pain.

Since there are 2 time points, the word “change” must be in the corrected title.

The description must include the range of the scale and what the scores mean.

What's wrong with this example?

- The title doesn’t omit verbs.
- The title doesn’t include the metric by which safety will be measured.
- The time frame isn’t specific enough.
- The description doesn’t define which adverse events are going to be included in the count.
- All of the above
Poll locked. Responses not accepted.

What's wrong with this example?

The title doesn't omit verbs.

The title doesn't include the metric by which safety will be measured.

The time frame isn't specific enough.

The description doesn't define which adverse events are going to be included in the count.

All of the above

Start the presentation to see live content. Still no live content? Installing the app or get help at PollKit.com/app.

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Poll locked. Responses not accepted.

What's wrong with this example?

The title doesn't omit verbs.

The title doesn't include the metric by which safety will be measured.

The time frame isn't specific enough.

The description doesn't define which adverse events are going to be included in the count.

All of the above

Start the presentation to see live content. Still no live content? Installing the app or get help at PollKit.com/app.

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Outcome Measures: Example 2

Corrected

The title must omit verbs and include the metric by which adverse events will be measured.

The Time Frame must include the specific point in time at which the outcome measure will be assessed.

The Description must define “adverse events.”

Eligibility Section

Use Inclusion / Exclusion Criteria with colon followed by dashed list format. No paragraphs.

Make sure that all criteria you post are appropriate for the public to see. Match informed consent more than protocol, if something might need to be masked from participants. If necessary, use Detailed Description field to flag that the eligibility criteria are deliberately incomplete to preserve the scientific integrity of the study.
References Section

- Studies available in PubMed are linked automatically if the NCT# was included in the publication. Others need to be added manually.

- Indicate if the reference provided reports results from this study. (Note: This doesn’t remove the requirement to post summary results in the results modules on ClinicalTrials.gov.)

Release to ClinicalTrials.gov

- **After saving any edits to a record:**
  - Update the “Record Verification” date in “Study Status” section to current month and year.
  - Click the green “Entry Complete” button.

"Entry Complete" releases record for WCM internal QC review.

Internal QC Review

ClinicalTrials.gov/PRS QC Review

CT.gov/PRS identified issues - record return to PI/designee for edits.

Record publicly posted w/NCT # assigned.

Internally identified issues - record return to PI/designee for edits.
Results Modules

Participant Flow
Baseline Characteristics
Outcome Measures
Adverse Events
Protocol and SAP Document Upload

Know Before You Go

• As of January 2020, any ClinicalTrials.gov results record for a study with an FDA-regulated product will be made permanently public upon first submission, even if ClinicalTrials.gov identifies major issues during its QC review.
• Once any results record is publicly posted to ClinicalTrials.gov, it’s permanently publicly archived along with any subsequent changes made to the record.
• Partner with the WCM ClinicalTrials.gov Administrator to ensure:
  o Consistency: Make sure one part of the ClinicalTrials.gov record doesn’t contradict other parts of the ClinicalTrials.gov record.
  o Context: Be sure you’re providing information that would effectively communicate the results of the study to someone unfamiliar with the research.
  o Timeliness: Federal estimates are 10 – 50 hours for results entry. Plan ahead and take advantage of the institutional resources available to you (E.g., Results sheet, scheduled 1:1 guidance, Webex call with ClinicalTrials.gov, etc.)
• Human Research Compliance conducts dual-layer internal QC review before a record is publicly released:
  o Review by ClinicalTrials.gov administrator
  o Review by biostatistician with biostatistician entry of statistical analyses.
Participant Flow

- Shows how participants were assigned to intervention(s) and how they progressed through the study.
  - Arranged by arm/group and according to "period," meaning stages of the clinical study. E.g., Double-Blind Period; Open-Label Period.
    - If only one period, the period title will default to "Overall Study."
    - Each period must include at least 2 milestones to convey key events:
      - MILESTONE: # of subjects who STARTED the period.
      - Should add up across all arms to actual # of subjects enrolled as indicated in Study Design section.
      - MILESTONE: # of subjects who COMPLETED the period.
    - If not all subjects completed the period, indicate # not completed and choose from dropdown list of "Reason Not Completed."
      - E.g., AE; physician decision; withdrawal by subject; other.
  - Use comments field and footnotes to explain discrepancies.

![Participant Flow Diagram]

Source: Results: Participant Flow Module; Rebecca J. Williams, PharmD, MPH; Assistant Director; ClinicalTrials.gov. NLM (September 2014)
Baseline Characteristics

- Table of demographic and baseline data for the overall trial population and for each arm or comparison group. Age, sex, race and ethnicity are required.
  - **Age** can be represented continuously (mean or median), categorically (<=18 years; >18 and <65 years; >65 years), or customized.
    - Choose only 1. Avoid choosing customized option unless the study design necessitates it.
  - **Sex/Gender** can be displayed using Sex: Female, Male or Sex/Gender, Customized.
    - Avoid choosing customized option unless the study design necessitates it.
  - **Race and Ethnicity** entered using:
    - NIH Office of Management and Budget (OMB) Classification Categories; or
    - Race and Ethnicity, Customized; or
    - Race and Ethnicity Not Collected
  - **Region of Enrollment**

**Baseline Measure Title** (i.e., name of measure).

- **Baseline Measure Type:**
  - Count of Participants - Mean
  - Median - Least Squares Mean
  - Geometric Mean - Geometric Least Squares Mean
  - Number - Count of Units

- **Measure of Dispersion:**
  - N/A (only if measure type is Number, Count of Participants, or Count of Units)
  - Standard Deviation
  - Inter-Quartile Range
  - Full Range

- **Unit of Measure** – should correspond to Baseline Measure Title (for age, Unit of Measure would be years).

- **Tip 1:** Use “Baseline Analysis Population Description” to explain any discrepancies between number of participants analyzed vs. the number represented in each arm/group.
- **Tip 2:** Don’t enter “0” unless the value of a data point is actually “0.” Enter “NA” for data “not available” and provide an explanation as to why the data isn’t available.
- **Tip 3:** The regulations don’t allow researchers to indicate the data was never analyzed. Analyzing available data is required.
Baseline Characteristics

- Summarizes results data for all measures assessed and describes statistical tests (e.g., p-value) or other parameters derived from the outcome data (e.g., odds ratio).

Outcome Measures and Statistical Analysis

- Summarizes results data for all measures assessed and describes statistical tests (e.g., p-value) or other parameters derived from the outcome data (e.g., odds ratio).

- Arm/Group Title - Number of Participants Analyzed
- Outcome Measure Title - Unit of Measure
- Measure Type (prim./secondary) - Data
- Measure of Dispersion/Precision (E.g., Standard Deviation)

- Statistical analyses are entered by the biostatistician named in the protocol document.
- If no statistician is named in the protocol document, one is assigned at the completion of the internal QC process to enter statistical analyses.
### Outcome Measures for Terminated Studies

<table>
<thead>
<tr>
<th>If &quot;0&quot; Subjects Analyzed</th>
<th>If Some, but Not All Subjects Analyzed</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Indicate “0” for “Number of Participants Analyzed” in each Arm/Group for which no data were collected.</td>
<td>• Indicate “Number of Participants Analyzed” in each Arm/Group.</td>
</tr>
<tr>
<td>• In “Analysis Population Description” state the specific reason no data were collected, i.e., “No data were collected for this secondary outcome measure because no subjects completed 12 weeks of the study and thus were not assessed.”</td>
<td>• In “Analysis Population Description” state the specific reason data were not collected from some subjects, i.e., “No data were collected from x number of subjects because those subjects didn’t complete the questionnaire for this outcome measure.”</td>
</tr>
<tr>
<td>• Submit all available data in Participant Flow, Baseline Characteristics, and Adverse Event Modules.</td>
<td></td>
</tr>
<tr>
<td>• Note: Analysis is required even for terminated studies. The regulations don’t allow for analysis not to be performed because the trial was terminated.</td>
<td></td>
</tr>
</tbody>
</table>

### Adverse Events

- Tables showing # of subjects experiencing serious and other adverse events that were collected during the course of the study.

- Need to specify classification system used (e.g., MedDRA 10.0, CTCAE 5.0).

- All-Cause Mortality
  - All deaths due to any cause that occurred during the study.

- Serious Adverse Events
  - All SAEs collected during the study, whether or not they were anticipated or considered to be attributed or associated with the intervention.

- Other (Not Including Serious) Adverse Events
  - Non-serious adverse events collected during the study, whether or not they were anticipated. Option to set frequency threshold to 5% to only report non-serious AEs if exceeded a frequency of 5% within any arm.
Adverse Events

**Organ Systems**

- Blood and Lymphatic System Disorders
- Cardiac Disorders
- Congenital, Familial and Genetic Disorders
- Ear and Labyrinth Disorders
- Endocrine Disorders
- Eye Disorders
- Gastrointestinal Disorders
- Hepatobiliary Disorders
- Immune System Disorders
- Infections and Infestations
- Injury, Poisoning and Procedural Complications
- Investigations
- Metabolism and Nutrition Disorders
- Musculoskeletal and Connective Tissue Disorders

**Definition:** High level categories used to group AE terms by body or organ system (If multiple systems affected, select “General Disorders”):

- Neoplasm Benign, Malignant and Unspecified (Including Cysts and Polyps)
- Nervous System Disorders
- Pregnancy, Puerperium and Perinatal Conditions
- Product Issues
- Psychiatric Disorders
- Renal and Urinary Disorders
- Reproductive System and Breast Disorders
- Respiratory, Thoracic and Mediastinal Disorders
- Skin and Subcutaneous Tissue Disorders
- Social Circumstances
- Surgical and Medical Procedures
- Vascular Disorders

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Adverse Events for Terminated Studies

- If 0 of subjects “at risk” (i.e., evaluated) for a given adverse event:
  - In “Adverse Event Description” indicate the reason for the difference in # of subjects enrolled vs. # of subjects “at risk.”
Adverse Events

Protocol and SAP Document Upload

- At time of results posting, upload of a PDF/A required for:
  - IRB-approved protocol document, including:
    - NCT #
    - List of amendments to the document (w/approval dates) affecting all trial sites.
    - Objective(s), design, and methods.
    - Relevant scientific background and statistical considerations.
  - IRB-approved Statistical Analysis Plan (SAP)
    - Can be part of the protocol document.
- Redaction of the following required:
  - Protected Health Information (PHI)
  - Personally Identifiable Information (PII)
  - Trade secrets/confidential commercial information
    - Must not redact info otherwise required to be disclosed by the regulations.
- Cannot upload eIRB application or IRB application as a protocol document to the public site.
Institutional Resources

WCM ClinicalTrials.gov Resources

- CT.gov Institutional Policy
- CT.gov Decision Tree: Interactive Qualtrics tool that helps investigators determine if study needs to be registered.
- Requirement for Posting checklist: Checklist to ensure all elements are entered correctly prior to releasing a record.
- Registration and Results Resource Guides: 1-pagers with links to help modules, data element definitions etc.
- Regulatory Resource Guide: 1-pager with all relevant regulatory requirement for registration and posting.
- When to Update your CT.gov Record: 1-pager with all reasons and timelines to update a record.
- Simplified Result Preparation template: Excel spreadsheet for data gathering prior to posting results. Also, helps facilitate meetings with biostatisticians.
- Protocol and SAP Upload Guidance: Info on upload of protocol and SAP at time of results entry; includes required format and info, what and how to redact, remove metadata, etc.
- Tailored WebEx call with CT.gov: Arranged for complicated results entry cases.
- Dissemination Plan template: Template language to be included in NIH Form F.
- Biostatistician Results Entry Assistance (statistical analyses)
- Guidance and Trainings (Group or 1:1) Available Upon Request
- Website: https://research.well.cornell.edu/clinicaltrialsgov
- Email: registerclinicaltrials@bmed.cornell.edu
- Phone: Available via scheduled Zoom or MS Teams call.