T.W.I.S.T.
All Good Things Must End: Trial Closure and Financial Reconciliation

Presented by

Cristina Garcia-Miller, Joint Clinical Trials Office
Gabrielle Gaspard, Human Research Compliance
Kedeisha Carty and Simran Matharu, Joint Clinical Trials Office
Trial Closure
Regulatory Considerations

Cristina García-Miller
JCTO Clinical Trials Operations

June 29, 2017
jcto.weill.cornell.edu
Terminology

Closure to Enrollment
vs.
Closure
Closure to Enrollment

No more subjects can be enrolled

*Industry/External:*
Sponsor/CRO notification that the study-wide enrollment number has been reached or enrollment is closing for another reason

*Investigator Initiated Trial (IIT):*
Protocol enrollment goal has been met or enrollment permanently stopped for another reason
Closure to Enrollment

• Send notification to the study team that study is closed to enrollment
• Advise ancillary committees and/or departments, as applicable (i.e.: pharmacy, DSMB, IBC)
• Submit update to JCTO website for overall study enrollment closure and cohort/arm closure
• Remove access to consent forms and enrollment materials (i.e.: eligibility checklists, recruitment flyers)
• Update any relevant databases, including clinicaltrials.gov
Closure (Termination)

Industry/External:

- Enrollment closed;
- All subjects *off study*;
- Drug/device/equipment reconciliation
- All data queries are complete
- Regulatory binder reviewed & complete
- Close-out Visit (COV)
- Financial reconciliation
- File closure with the IRB
Closure (Termination)

*Investigator Initiated Trial (IIT)*:

- Enrollment closed;
- All subjects off study;
- Drug/device/equipment reconciliation;
- All data analysis complete;
- Regulatory binder reviewed & complete;
- Financial reconciliation, if applicable;
- Update clinicaltrials.gov;
- Submit IND/IDE closure with FDA as applicable
- File closure with the IRB
Closure (Termination)

**Investigator Initiated Multi-Center Trial (IIT):**
- Enrollment closed *(all sites)*;
- All subjects off study *(all sites)*;
- Drug/device/equipment reconciliation *(all sites)*;
- All data and specimens collected *(all sites)*;
- Regulatory documents collected *(all sites)*;
- IRB closure (termination) *(all sites)*;
- Data analysis complete;
- Financial reconciliation;
- Update clinicaltrials.gov

*Then…*
- Submit IND/IDE closure with FDA as applicable
- File WCM IRB Closure
Long-Term Storage

*Industry/External:*

- Obtain sponsor authorization;
- Notify sponsor of location of files;

*Investigator Initiated Trials (IIT):*

- As soon as IRB closure acknowledgment is received;
- All other reconciliations complete;
Long-Term Storage

Regulatory Requirement
2 years beyond marketing approval

Industry Requirement
Varies – refer to CTA
ClinicalTrials.gov
Posting Results at the Close of Your Study

Thursday, June 29th, 2017

Gabrielle Gaspard, MPH
Assistant Director, Human Research Compliance
OBJECTIVE

1. Describe the regulatory requirements for reporting results

2. Define “primary completion date” and understand how it affects the timeline for results reporting
# Posting Requirements for ClinicalTrials.gov

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scope</strong></td>
<td>Registration</td>
<td>Registration &amp; Results Reporting</td>
<td>Registration &amp; Results Reporting</td>
</tr>
<tr>
<td><strong>Phase</strong></td>
<td>All</td>
<td>Not Phase 1 or small feasibility device studies</td>
<td>All</td>
</tr>
<tr>
<td><strong>Intervention Type</strong></td>
<td>All</td>
<td>Drug, biologic, &amp; device products regulated by the FDA</td>
<td>All (e.g., including behavioral interventions)</td>
</tr>
<tr>
<td><strong>Funding Source</strong></td>
<td>Any</td>
<td>Any</td>
<td>NIH</td>
</tr>
<tr>
<td><strong>Initial Registration</strong></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>
</tr>
<tr>
<td><strong>Results Reporting</strong></td>
<td>N/A</td>
<td>Within 12 months of primary completion date</td>
<td>Within 12 months of primary completion date</td>
</tr>
</tbody>
</table>
| **Enforcement**       | Refusal to publish               | • Criminal proceedings and civil penalties (up to $10,000/day)  
• Loss of HHS funding  
• Noncompliant records Identified on ClinicalTrials.gov | • Suspension or termination of grant or contract funding  
• Can be considered in future funding decisions  
• Noncompliant records Identified on ClinicalTrials.gov |

**CMS:** Mandatory Reporting of NCT# Requirement for Qualifying Trials
Preparatory to Reporting Results

- Overall Study Status (log in to http://register.clinicaltrials.gov and enter within 30 days)
  - Completed
    - The study has concluded normally; participants are no longer receiving an intervention or being examined (that is, the last participant’s last visit has occurred)
  - Terminated
    - Study halted prematurely and will not resume; participants are no longer being examined or receiving intervention
  - Withdrawn
    - Study halted prematurely, prior to enrollment of first participant
    - Results Not Needed

- Enter the Primary Completion Date
  - The date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome (if more than one primary outcome, date is when data was collected for all primary outcomes)
  - Results for the primary outcome must be submitted within 12 months of the Primary Completion Date
# Change of Status

## Edit Study Status

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Record Verification Date:</td>
<td>Month: June  ▪ Year: 2017</td>
</tr>
<tr>
<td>* Overall Recruitment Status:</td>
<td>Completed</td>
</tr>
<tr>
<td>Tip: Day is not required for Anticipated dates.</td>
<td></td>
</tr>
<tr>
<td>* § Study Start Date:</td>
<td>Month: January  ▪ Day: [ ] ▪ Year: 2010 ▪ Type: --Select-- ▪</td>
</tr>
<tr>
<td></td>
<td>Data study is open for recruitment (Anticipated) or date first participant is enrolled (Actual).</td>
</tr>
<tr>
<td>* Primary Completion Date:</td>
<td>Month: January  ▪ Day: 12 ▪ Year: 2013 ▪ Type: Actual ▪</td>
</tr>
<tr>
<td></td>
<td>Final data collection date for primary outcome measure.</td>
</tr>
<tr>
<td>* § Study Completion Date:</td>
<td>Month: January  ▪ Day: [ ] ▪ Year: 2013 ▪ Type: Actual ▪</td>
</tr>
<tr>
<td></td>
<td>Final data collection date for study.</td>
</tr>
</tbody>
</table>

* Required

* § Required if Study Start Date is on or after January 18, 2017

[*] Conditionally required (see Definitions)
Preparatory to Reporting Results

- The remaining required results information for secondary outcome measures or additional adverse event information is due:
  - Within 12 months of the date on which the final subject was examined or received an intervention for the purposes of final collection of data for that secondary outcome measure

***There is no place on ClinicalTrials.gov to enter dates relevant to secondary outcome measures, so it must be tracked externally***
(1) Update “Overall Study Status” within 30 days of status change and...

(2) Update “Primary Completion Date,” which determines when results are required

(3) Make sure no errors, notes, or warnings are present in the record. They are designated in blue and red to alert you that changes are still needed

(4) Click “Save,” then the large green “Entry Complete” button

(5) WCM ClinicalTrials.gov Administrator will, if no notes, warnings or errors, approve the record to send to ClinicalTrials.gov

(6) ClinicalTrials.gov (“PRS”) evaluates the changes and publicly posts them to ClinicalTrials.gov

(7) The “results clock” starts ticking based on the entered Primary Completion Date

(8) The WCM ClinicalTrials.gov Administrator sends you a reminder email of when results are required
Data Elements

Participant Flow
Shows how participants were assigned to intervention(s) and how they progressed through the study

Baseline Characteristics
Table of demographic and baseline data

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)
Results Reporting: Adverse Events

- **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.

**Adverse Event reporting to the IRB is currently being revised to incorporate an option to identify affected body system for each adverse event for easy uploading to the ClinicalTrials.gov results section**
Results Overview

- Results Section page is your home base for inputting results.
- Access the 4 Results modules from here.
- Click on “edit” next to Participant Flow to edit that module.
Supplementary Results Information

- Required posting of research protocol and statistical analysis plan
  - The regulations allow for redaction of:
    - Names
    - Addresses
    - Personally identifiable information
    - Trade secrets
    - Confidential commercial information
  - Guidance from HHS on redaction is forthcoming
Enter Results Data in all required modules. WMC ClinicalTrials.gov Admin “approves” & “releases” data to ClinicalTrials.gov (“PRS”).

PRS conducts QA review of data within 30 days.

**APPROVES:**
ClinicalTrials.gov publicly posts the data.

**DOES NOT APPROVE** but publicly posts the data with problems, then **RESETS** to “in-progress”: with PRS Review Comments that must be responded to within 25 days.

Responding as soon as possible is in your best interest to stop poor quality information from being publicly posted to ClinicalTrials.gov.
## Summary: Results Reporting Timeline

<table>
<thead>
<tr>
<th>Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change “Overall Study Status” and enter Primary Completion Date</strong></td>
</tr>
<tr>
<td>Within <strong>30 days</strong> of study completion, termination, or withdrawal</td>
</tr>
<tr>
<td><strong>Enter Results for all primary outcomes</strong></td>
</tr>
<tr>
<td>Within <strong>12 months</strong> of the Primary Completion Date</td>
</tr>
<tr>
<td><strong>Respond to comments from ClinicalTrials.gov (“PRS Review Comments”)</strong></td>
</tr>
<tr>
<td>Within <strong>25 days</strong>, as soon as possible to avoid the public posting of information with issues</td>
</tr>
<tr>
<td><strong>Enter Results for each secondary outcome measure</strong></td>
</tr>
<tr>
<td>Within <strong>12 months</strong> of the date on which the final subject was examined or received an intervention for the purposes of final collection of data for each secondary outcome measure</td>
</tr>
</tbody>
</table>
For Help: Contact

Clinicaltrials.gov

- Email register@clinicaltrials.gov with your NCT #
  - The PRS Results Team provides detailed assistance in response to targeted questions about filling out the modules
  - Assist in scheduling a WebEx session with the PRS Results Team for assistance in entering results

Guidance

- The “Help” dropdown for “Results Data Entry” has resources:
  - Results Modules Guidance
  - Definitions for each data element in each section
  - Description of ClinicalTrials.gov review criteria for results
  - Example results entries for parallel, cross-over, factorial, dose escalation, and multiple period study designs

WCM Clinicaltrials.gov Administrator

- registerclinicaltrials@med.cornell.edu or call 646-962-4065
- http://researchintegrity.weill.cornell.edu/clinicaltrialsdotgov.html
Financial Reconciliation

Kedeisha Carty & Simran Matharu
Financial Analysts, Joint Clinical Trials Office - Finance

June 29, 2017
JCTO.WEILL.CORNELL.EDU
Financial Reconciliation

Financial Trackers Purpose, Creation and Responsibilities
Financial Tracking Purpose

Financial Tracking or financial reconciliations are conducted to recover all unpaid funds and to resolve all financial matters at time of study closure and/or during the life of the study, including but not limited to:

• Unpaid subject visits
• Unpaid invoiceable items
• Holdback amounts
• Payment discrepancies
Financial Tracking Purpose

Joint Clinical Trials Office Finance implemented a Financial Tracking Dashboard and centralized the Financial Trackers for the purposes of organization and streamlined communications with study teams. The Financial Tracking Dashboard and Financial Trackers are located within the JCTO SharePoint site.

https://sharepoint.weill.cornell.edu/sites/jcto/

Financial tracking allows for JCTO Finance and study teams to see visits completed, invoices sent to Sponsors, items paid, and any outstanding balances. Centralized Financial Tracking reduces the need for back and forth emailing.
Financial Tracker Creation

- Financial Trackers are created upon request from study teams via email to jctofinance@med.cornell.edu.
- Financial Trackers are created by JCTO Finance based on the fully executed Clinical Trial Agreement budget, payment terms and any associated budget or payment terms contract amendment.
- Once a Financial Tracker is created, study teams receive an email with the link to the Financial Tracker located in SharePoint.

Simran Matharu <sim2012@med.cornell.edu>

Simran Matharu has shared '1106011756'
To: Maria Enamorado

Dear Study Team,

Welcome to the Joint Clinical Trials Office – Finance SharePoint. This email serves as notification that you now have editing access to the Financial Tracker for Dr. Nanus’s Cougar Biotechnology COU-AA-206 study. Please use the financial tracker on an on-going basis by entering subject visits and invoiceable dates of completion. JCTO Finance will enter payments information and follow up with sponsors on any amounts due.

To access the JCTO SharePoint site directly go to: https://sharepoint.weill.cornell.edu/sites/jcto. Please feel free to contact jctofinance@med.cornell.edu with questions.

Thank you,

Joint Clinical Trials Office - Finance

Go to 1106011756
Financial Tracking
Study Team Responsibilities
Financial Tracking
Study Team Responsibilities

• Once a Financial Tracker is created, it is the responsibility of study teams to go into the Financial Trackers and update it with the subject ID’s and associated visit dates.

• That’s it!! JCTO Finance will handle the rest.
Financial Tracking
JCTO Finance Responsibilities

JCTO Finance is responsible for:

- Entering invoice and payment information into Financial Trackers
  - Financial Trackers will be updated by JCTO Finance by the third week of each month based upon their payment mechanisms.
- Invoice Sponsors for services rendered as agreed to in the Clinical Trial Agreement and any associated amendments.
  - Some study teams prefer to invoice for invoiceables on their own. Please let us know ahead of time to avoid duplicate invoicing and effort. JCTO Finance must be made aware of invoicing via email by copy of jctofinance@med.cornell.edu
- For all studies, regardless if a Financial Tracker exists or not, JCTO Finance invoices for initial start-up services and all IRB services.
  - Initial start-up services include but are not limited to JCTO administration, initial IRB review, Clinical Study Evaluation Committee review, and initial pharmacy services.
  - IRB services include IRB continuing review and IRB amendment review.
- Follow up with Sponsors on an on-going basis requesting status of payments for items invoiced
Trial Closeout Reconciliations

Upon notification of trial closeout:

• **Immediately notify JCTO Finance**
  • If a financial tracker exists for the study already, JCTO Finance will complete the final reconciliation
  • If a financial tracker does not exist and if you need assistance with final reconciliation, request a tracker from JCTO Finance. Please include the number of patients enrolled with your request

• **JCTO Finance will:**
  • Review and enter all payments received to date against visits and invoiceable procedures provided by the study teams
  • Work with the sponsor to determine the accurate final payment amount, accounting for any unpaid visits, overpayments, and holdback amounts
  • Invoice the sponsor for the final amount due
  • Follow up with the sponsor on final payment until it’s received
JCTO SharePoint
https://sharepoint.weill.cornell.edu/sites/jcto

<table>
<thead>
<tr>
<th>Sponsors</th>
<th>Division</th>
<th>Department</th>
<th>JTOS Assignment</th>
<th>Count</th>
<th>Protocol ID</th>
<th>Payment Mechanism</th>
<th>Invoicable Items</th>
<th>Tracker Link</th>
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<tbody>
<tr>
<td>Rigol, Inc.</td>
<td>Hematology, Oncology</td>
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<td>C935788</td>
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<td>Celgene Corporation</td>
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<td>Medicine</td>
<td>KC</td>
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<td>C935788</td>
<td>Invoice CRF Ongoing</td>
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<td>Automatic CRF Ongoing</td>
<td>Yes</td>
<td>Link</td>
</tr>
</tbody>
</table>
JCTO SharePoint

- While the above pop-ups appear to be error messages, they normally appear when opening a financial tracker through SharePoint
- Please click “Yes” or “Open in Excel”
**JCTO SharePoint**

- Enter your WCM user name and password, click OK
- Click “Edit Workbook”
Each financial tracker contains a Summary tab, Subject Visit Tracker tab(s) and Invoiceables tab(s)
The study team will use the Subject Visit Tracker tab(s) to enter Subject Study ID numbers and completed visit dates.

If any visit columns are missing or look inconsistent with the protocol, please notify JCTO Finance.

Please do not copy and paste data into the tracker, as this will break the formula and result in reference errors.
The study team will use the Invoiceable(s) tabs to enter Subject Study ID numbers and Dates of Service for applicable invoiceable items.

If any invoiceable procedure columns are missing or look inconsistent with the protocol, please notify JCTO Finance.

Please do not copy and paste data into the tracker, as this will break the formula and result in reference errors.
JCTO SharePoint

- As edits are entered into the tracker, click “Save” and the tracker will load the latest version to SharePoint

- You may see this pop-up box appear, click “X” to close and return to JCTO SharePoint
JCTO Finance Contact Information

jctofinance@med.cornell.edu
(646) 962-8215

Kedeisha Carty, Financial Analyst
Virginia Chen, Financial Analyst
Marlom Marmol, Financial Analyst
Simran Matharu, Financial Analyst
Oliver Trejo, Financial Analyst

Maria Enamorado
Assistant Director, Finance, Contracts and Business Development
Q&A

QAU Contact Information

E-mail: JCTOQAU@med.cornell.edu

-or-

evo2001@med.cornell.edu