Preparing for Close-Out of Studies and Sites

Presented by:

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Learning Objectives

• Discuss planning for trial close-out, and identify critical activities that make for timely and efficient close-out.

• Define roles and responsibilities, regulatory obligations, documentation requirements, and other processes to consider at the end of a study.

• Review lessons learned in the close-out of other CTN studies.
Why It Matters

• Regulatory obligation
• Resources invested
• Ability to answer research question
• Contribution to generalizable knowledge and improved care
• It’s our job
Key Personnel Involved

Research Site (RA, RC, Medical Staff, PI)

Regional Research & Training Center (RRTC) (Local QA, PM, PD, LI)

Clinical Coordinating Center (CCC) and Data and Statistics Center (DSC) (Protocol Specialist, CCC Monitor, Medical Monitor, Safety Monitor, Data Manager, Statistician)

Other External Partners (Vendors, Central Laboratory, Central Pharmacy, Suppliers, Regulatory Entities)
Timeline from Development to Study Start

Protocol Reviews:
- PRB, DSMB, Lead Node IRB Approval
- Site Selection
- Other Regulatory Submission(s)

Revise eCRFs at DM meeting
Then, revise Ops Manual as needed (recruitment materials, logs et. al.)
Selected Sites Hiring Staff

Initiation Visits (Node QA/CCC)
Site Endorsements
Start Enrollment

Dev’t
Protocol Approval
Trial Dev & Logist.
DM Meeting
Nat’l Training
Study Start

CCTN Concept Approval
CTN Number assigned
Initial Budget/revise as needed
Timeline Development

Other Study Docs in Dev’t:
eCRFs, Ops Manual, QA Plan, SOPs
Training Dev & Planning
Meds, Labs, and Supplies Contracts
Sites to submit for IRB Approval

Training Doc Form
Delegation Log
Regulatory Training/Document Collection
Supplies/Meds to sites

Timeline from Study Start to Close-Out

- **Study Start**
- **End of Enrollment**
- **Last Pt Last Visit**
- **Database Lock**
  - 2 months after LPLV*
- **Final Report**
  - 4 months after database lock
- **Primary Paper**
  - 6 months after database lock
- **Data Share**
  - 18 months after database lock

*LPLV – Last Participant Last Visit*
Components of Site Close-Out

- Monitoring Visits
- Study Personnel
- Medication, Supplies & Equipment
- Storage & Record Retention
- Data Cleaning
- Safety & Regulatory

CTN Site Close-Out Checklist

NIDA Protocol CTN-0054

SITE CLOSE-OUT PREPARATION CHECKLIST

SITE NAME: ____________________________
NODE NAME: __________________________

Date report submitted: __________________

December 19, 2014
Version 1.0

NIDA Protocol CTN-0054
Site Close-Out Preparation Checklist

December 19, 2014
Version 1.0

1. CTN 0054 – Site Close-out Preparation Checklist
2. Safety
3. General Regulatory
4. Site Regulatory Files/Binders and CCC Trial Master File
5. Confirmation of Analysis of All Primary Specimen Sample
6. Investigational Product:
7. Supplies and Equipment:
8. Shipping Instructions
9. Data Cleaning Activities
10. Close-Out Monitoring
11. Departures of Study Personnel:
12. Further Close-Out Questions
13. Storage Location of Study Records

Page 1 of 10
Safety and Regulatory

Adverse Event Reporting

- All AEs/SAEs that require reporting must be entered in AdvantageEDC and reported to the IRB, as appropriate.

- AEs must be resolved prior to site closure:
  - Resolved without sequelae
  - Resolved with sequelae
  - Resolved by convention
Safety and Regulatory

Protocol Deviation (PD) Reporting

• All PDs in AdvantageEDC must be complete and resolved prior to site closure

• PDs that require IRB reporting must have a corresponding date of report

• NIDA CCC Protocol Specialist will consult with the Lead Node to perform PD “cleaning” prior to close-out and may request edits
Safety and Regulatory

• Regulatory Binder/Files must be complete and copies of all required documents uploaded to the Regulatory Tracking System (RTS)

  IRB-approved protocols
  IRB-approved consent forms*
  Protocol Signature Pages *
  Form FDA 1572 / IA*
  Final Staff Delegation Log (signed by PI)*
  HSP and GCP Training Certifications*
  CVs (for anyone listed on the 1572/IA)
  Licenses, if applicable*
  Financial Disclosure Certification (IND trials)*
  Training Documentation Form*
  IRB approval letters*
  Copies of other participant agreement documents (HIPAA auth, CA Bill of Rights, W-9, ROIs, etc)
  IRB Notification of Study Closure*
  Active FWA
  DEA Registrations*
  Site Visit Log
  SOPs

* Required to be submitted to the CCC via RTS
Safety and Regulatory

• Prior to close-out, a NIDA CCC Protocol Specialist will provide a RTS audit report of documents housed in the system

• Any action items should be resolved prior to site close-out
Sample RTS Audit Report – Site Documents

<table>
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<tr>
<th>RTS Doc</th>
<th>Doc Status</th>
<th>Version#</th>
<th>Doc Date</th>
<th>Expiration Date</th>
<th>Doc Note to File</th>
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<td>S-Federalwide Assurance (FWA)</td>
<td>In RTS Field</td>
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<td>Missing in RTS</td>
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<tr>
<td>S-IRB Notification Acknowledging Site Closeout</td>
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<td></td>
<td></td>
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<td>S-IRB Notification of Site Closeout</td>
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<tr>
<td>S-Protocol Signature Page</td>
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<td></td>
<td>Version 2 PSP</td>
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<td>Version 3 PSP</td>
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<tr>
<td>S-Protocol Signature Page</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Version 4 PSP</td>
</tr>
<tr>
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<td>On File in RTS</td>
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<td>9/25/2013</td>
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<td>S-Site Staff Signature &amp; Delegation Log-Final</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
Safety and Regulatory

• For IND trials, the original, signed copy of all Form FDA 1572s must be mailed to the CCC (or the IND holder if other than the sponsor)

• For non-IND trials, the Investigator Agreement should be signed, dated, and mailed to the CCC
Safety and Regulatory

- Some tasks may not be completed until after database lock has occurred
  - Final Staff Delegation Log with PI signature
  - IRB acknowledgement of study closure
  - Final Site Close-Out Checklist

(These tasks will be listed as action items on the site visit report)
QA & MONITORING
Close-Out Monitoring Visits

• Sites participating in trials within the CTN typically have 2 close-out visits
  – Local QA (RRTC)
  – NIDA CCC (Emmes)

• Items covered during close-out visit:
  – Action items from the last monitoring visit
  – Data integrity/query resolution
  – Roles and responsibilities
  – Record storage requirements
  – Disposition of supplies / study medication
  – Regulatory requirements
  – Publications
  – Review of close-out presentation
Close-Out Monitoring Visits (cont.)

- Close-Out visit may not occur until last participant last visit has occurred
- Ideally, the final local QA monitoring visit will occur before the CCC close-out visit, but this is not required
- CCC close-out visits can either be done on-site or remotely by conference call
- At a minimum, the Site PI and a SC/RA must be present
- NIDA CCC will provide Close-Out Memo
Close-Out of Study Personnel

- Updated CTN Research Staff Information Forms should be sent to the DSC Help Desk for any staff no longer participating in the study.

- Staff members that continue to perform study functions (i.e., those that use AdvantageEDC for data cleaning purposes or RTS for regulatory uploads) should not send this form until after database lock.

- Staff Information Form can be found on Livelink:

  LiveLink: [https://Livelink.nida.nih.gov](https://Livelink.nida.nih.gov)

  Or contact the DSC Help Desk: nidadsc2help@emmes.com
Break for Questions

Use the chat to post questions or comments...
MEDICATION, SUPPLIES, & EQUIPMENT
Medication

• Determine who has Disposition Authority
  – Should be indicated in the Site Close-Out Checklist
  – Is generally the same source that provided the medication

• If study Investigational Product is being returned to the central pharmacy, they or the CCC will provide detailed instructions

• Final drug reconciliation is a key process at close-out
Supplies & Equipment

• Work with CCC to maintain a low supply inventory toward the end of the study
• Consider who provisioned the supplies and equipment, namely who ‘owns’ it, then ask when is it returned and how?
  – This information is indicated on the Site Close-Out Checklist
Supplies & Equipment (cont.)

• Items that may be donated:
  – Urine collection and testing supplies, pregnancy tests
  – Lab kits, needles, shipping boxes/gel packs

• Items that must be destroyed:
  – Prescription labels, medication wallet cards, waybills
  – Any expired supplies that are not returned

• Items that must be returned:
  – Genetics kits- to NIDA repository

• Contact Node regarding:
  – Gloves, band aids, equipment (e.g., refrigerator), office supplies, computers...
DATA CLEANING ACTIVITIES
Data Cleaning Activities

• Data Managers (Data and Statistics Center (DSC) at Emmes)
  – Generate data quality reports, missing form and value reports and integrity checks throughout the study and at close-out

• It’s vital to maintain complete and accurate data throughout the trial

• Can check data completion via Missing Forms and Missing Values Reports
Data Cleaning Activities (cont.)

- Complete all exception requests (out of range items, missing value or missing form exceptions) as needed
- End of Study Forms submitted and signed by PI
- Access the Monitoring Discrepancy reports in EDC frequently and resolve all data discrepancies
- Be responsive to requests from the DSC!
RECORDS RETENTION & STORAGE
Records Retention & Storage

- Sites should establish procedures for the archiving of research records, in compliance with state, local, institutional, and IRB regulations.
- At minimum, study records for CTN studies must be maintained for 3 years after database lock.

CTN Policies and Procedures Section 8.3
Records Retention & Storage (cont.)

- RRTC prepares clear, written documentation of the location and the retrieval process for research records for a given site and informs the Lead Team and the CCC at study close-out
  - Must include a contact person
  - Must notify if storage location changes
  - Must notify prior to the destruction of any protocol related records
WRAPPING IT UP!
In Summary

• Preparation for an efficient close-out begins before the study starts
• Careful and timely execution of all trial-related duties throughout the implementation phase will aid the close-out process
• Appropriate site staff (including the PI) must be available through (and beyond) database lock
• Utilize available tools and resources
• If you do not know, please ask for help
References


• Reference any Institutional/Local IRB Policies and Procedures
Alternatively, questions can be directed to the presenter(s) by sending an email to CTNtraining@emmes.com.
A copy of this presentation will be available electronically.

http://ctnndisseminationlibrary.org

The CTN DISSEMINATION LIBRARY is a digital repository of resources created by and about NIDA’s National Drug Abuse Treatment Clinical Trials Network (CTN). It provides CTN members and the public with a single point of access to research findings and other materials that are approved for dissemination throughout the CTN and to the larger community of providers, researchers and policy-makers.

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About the CTN
- Protocols (Studies) in the CTN
- CTN Nodes & Community Treatment Programs (CTPs)
- CTN International Activities
- NIDA’s CTN web site
- ATTC’s Blending Product site
- NIDA Data Share
- CTN Directory (2014)

New in the Library
- Blending Initiative Motivational Interviewing CME/CE & Patient Simulating
- The newest NIDA/SAMHSA-ATTC Blending Team Product has just been released. It combines a CME course and interactive online Patient Simulation to provide practical guidance for physicians, nurses and other practitioners in effective DBT techniques. Check it out!
All participants are encouraged to complete the post webinar survey, which will be issued directly following this webinar session. This is the primary collective tool for rating your experience with this training and for communicating the interests and needs of CTN members and associates.

Next topic...

**Family Involvement in Substance Use Disorder and Mental Health Treatment and Research**

Wednesday, May 27, 2015

1:00 – 2:00 pm ET
THANK YOU FOR YOUR PARTICIPATION