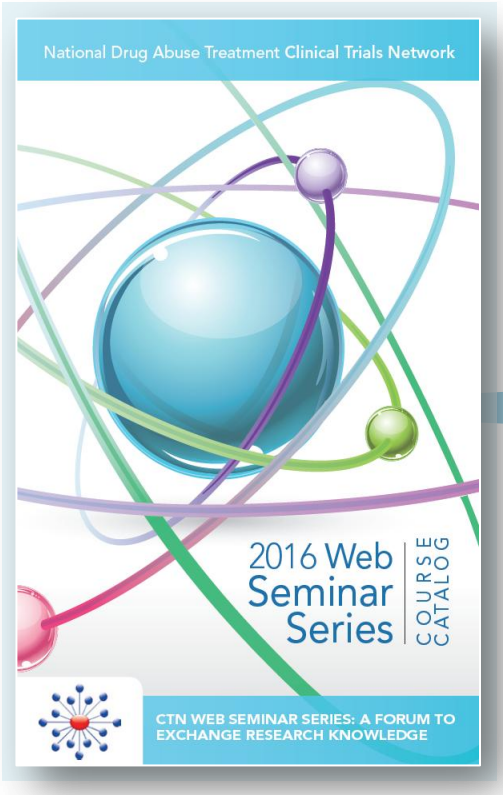

CTN INVESTIGATOR TOOLBOX – AN ORIENTATION

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CTN WEB SEMINAR SERIES:
A FORUM TO EXCHANGE RESEARCH KNOWLEDGE

Produced by: CTN Training

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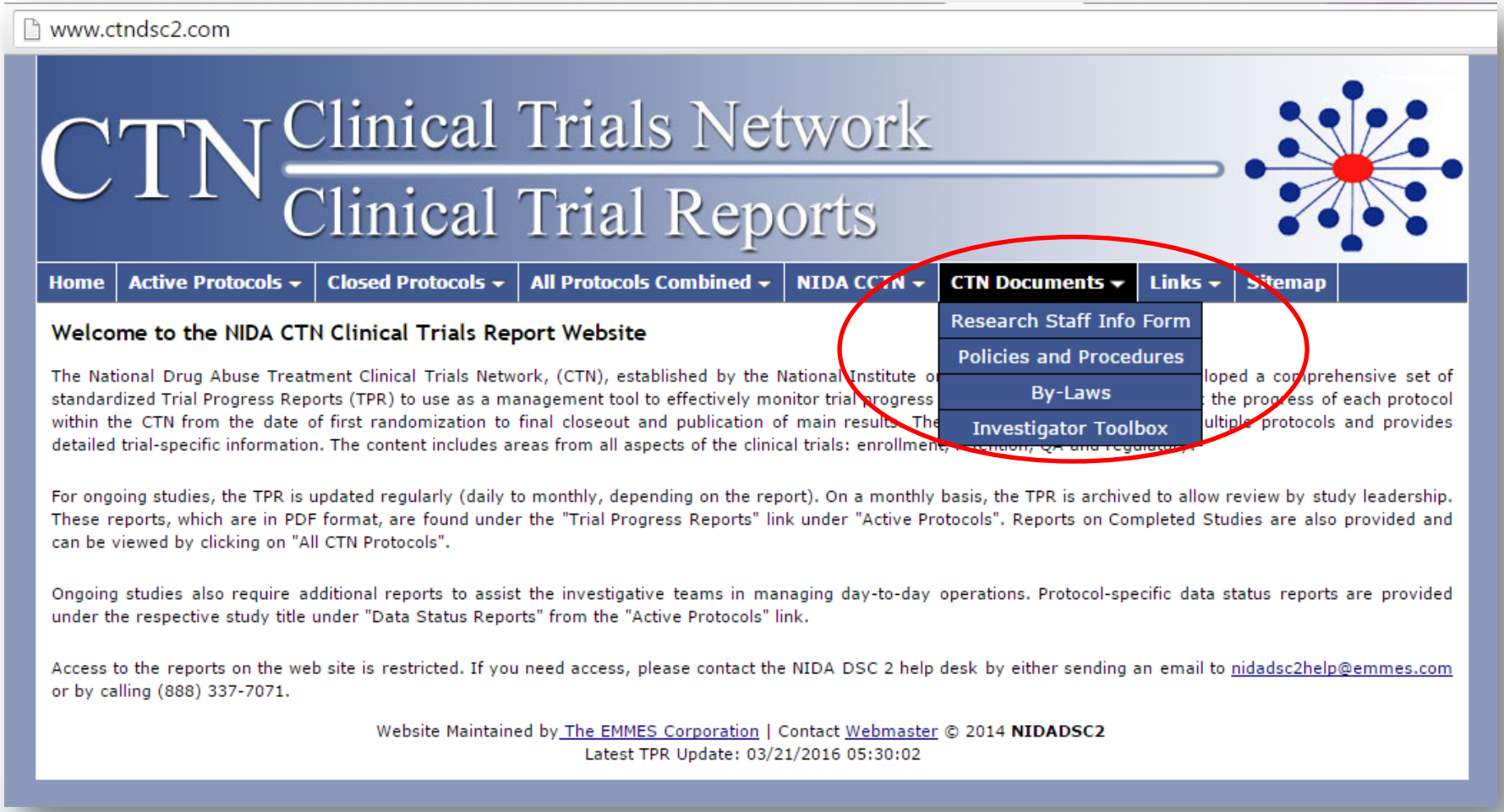
Learning Objectives

- Identify the location of the CTN Policies and Procedures, Bylaws, and the Investigator Toolbox.
- Describe the structure and some of the main tools and documents within each section of the Toolbox.
- Understand the ways in which the Toolbox can be used as a resource for those involved in developing, implementing and managing clinical trials.

Investigator Toolbox Development and Origin

- CTN Policies and Procedures Guide V6.0 – recently updated: http://www.ctndsc2.com/
  - Reminder - CTN studies must comply with all federal policies and the P&P provides highlights
- Current ByLaws: http://www.ctndsc2.com/
  - Inclusion of new definitions and new CTN structure
- Request for Applications (RFA) number: RFA-DA-15-008 (The NDAT CTN UG1): http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-15-008.html

TPR Website – Investigator Toolbox Location



Investigator Toolbox Development and Origin

- The Toolbox provides elaboration and details on the CTN Policies & Procedures document sections.
- This website is dynamic, with new documents, updates, and resources added frequently.
- Suggestions from users are always welcome.

The Clinical Trials Network Investigator Toolbox

- The Clinical Trials Network (CTN) Investigator Toolbox is a resource designed to provide guidance to both new and experienced investigators that are conducting studies within the NIDA (National Institute on Drug Abuse) CTN.
- The Toolbox provides templates and examples for key documents and in-depth step-by-step guidance on the integral tasks associated with developing, implementing, and publishing a NIDA CTN clinical research study.

Investigator Toolbox Location

Investigator Toolbox Sections

Investigator Toolbox Sections

Protocol Concept

- Protocol Concept Introduction
- Design and Analysis SIG input on early-phase trials in the CTN
- Research Development Committee (RDC)- CTN concept submission and review process and procedures

Concept Submission Procedures

Research Development Committee
CTN Concept Submission and Review Process and Procedures

General Guidelines for CTN Concepts

- The RDC reviews all CTN study concepts including those that are submitted investigators or special interest groups as investigator-initiated concepts and those that are in response to specific CTN requests for concepts.
- All CTN study concepts should be no more than 3 pages long separate title page and references), with Arial 11 font and not less than 0.5" marg
- Concepts proposing ancillary studies need to be accompanied by a letter/e-mail from the Lead Investigator(s) of the primary/parent protocol indicating that the ancillary concept has been reviewed and approved by the Lead Team.
- Concepts proposing ancillary genetics studies need to follow the specific guidelines developed jointly by the CCTN and the NIDA Genetics Consortium.
- CTN study concepts should be submitted to the RDC Chair Dennis Donovan, ddonovan@u.washington.edu) with a copy to the CCTN RDC currently Dr. Geetha Subramaniam, subramaniamga@nida.nih.gov).
- Concepts are reviewed using current NIH categories (Overall Impact, Significance, Investigators, Innovation, Approach, and Environment). Consideration is also given to the Lead Node and participating Node/CTP budgets.
- http://grants.nih.gov/grants/peer_review_process.htm#scoring2
- Additionally, concepts are considered with respect to feasibility, stage of science and readiness for multisite trials, and suitability and potential sustainability of the interventions for use in community-based treatment programs (CTPs); involvement of CTP representatives in the concept development and study design is strongly encouraged.

Protocol Development

- Protocol Template
- Management of Key Study Documents
- Protocol Review Board/DSMB
- Registering a CTN Study on ClinicalTrials.gov
- Important Study Responsibilities
- Multicenter Trial Start Up and Timeline
  - Pre-Implementation Calculator
  - Protocol Timeline/Milestone Calculator

Important Study Responsibilities

Important Study Responsibilities
CTN Investigator Toolbox Website

Important Study Responsibilities

Study Lead Team (Lead Node, CCC, DSC, and NIDA CCTN) Responsibilities

- Overall study management and ensuring human subject protection.
- Oversight of all the research sites participating in the study.
- Meet regularly with the participating sites to review study performance and discuss overall timeline, recruitment, retention, training needs, summary of site visits, data issues, participant safety, preparation for and participation in DSMB review meetings, and review/oversight of other reports and study related activities.

Node Implementation Responsibilities

- Provide ongoing local help, quality assurance ("monitoring") and support throughout the planning, execution, and wrap-up for the trial.
- Responsible for study management and oversight at their participating site(s).

The Coordinating Centers (Clinical Coordinating Center [CCC] and Data and Statistics Center [DSC])

- Act as agents of NIDA by providing electronic data support, pharmacovigilance, regulatory monitoring/guidance and document collection, help desk support, clinical site monitoring (remotely and on site), obtain and distribute designated clinical study supplies (including study medication)/laboratory support and other study specific support as necessary, research staff with general and protocol specific training, and specialty assistance throughout the planning, execution, close out and reporting of trial activity.

Safety/Pharmacovigilance Responsibilities

- The study LI is responsible for distributing data safety monitoring plans, procedures, and training regarding proper assessment and reporting of adverse events in conjunction with the Pharmacovigilance team at Emmes.
- Each participating Node PI is responsible for the safety of study participants. Each RRTC/CTP for each study site must appoint an appropriate individual to assess, report to all necessary parties, and resolve adverse events

CTN Protocol Timeline/Milestone Calculator

		CTN00XX - *title of protocol*		Draft revision Oct 31 2013
		CTN Protocol Milestone	**Expected Date Completed**	**Actual Date Completed**
	Protocol Development	Concept approved for protocol development		*X*
		Submit protocol to NIDA, including DSMP and informed consent	*X* + 4 *mo*	
		Full protocol reviewed and approved by NIDA (8 months after concept approval)	*X* + 8 *mo*	
		Budget finalized (8 months after concept approval)	*X* + 8 *mo*	
	Trial Preparation	Protocol approved by NIDA for implementation		*Y*
		Site selection completed (3 months after protocol approved for implementation)	*Y* + 3 *mo*	
		All data systems and databases in production (4 months after protocol approved for implementation)	*Y* + 4 mo.	
		Regulatory steps completed (includes IRB , IND, DEA, CoC, etc) 6 months after protocol approved for implementation	*Y* +6 *mo*	
		Training Completed (6 months after protocol approved for implementation)	*Y* + 6 *mo*	
		First site endorsed (7 months after protocol approved for implementation)	*Y* + 7 *mo*	
	Trial Conduct	First participant randomized (7 months after protocol approved for implementation)	*Y* + 7 *mo*	
		Last participant randomized (based on sample size and randomization rate)	§	
		Trial completed (last participant completes last follow-up) (based on sample size and randomization rate)	§	
		Database locked (2 months after last follow-up)	§	*Z*
	n	Trial raw data submitted to Lead Investigator (2 weeks after database lock)	*Z* + 2 *weeks*	
		Final Study Report submitted to NIDA	*Z* + 4 *mo*	

Pre-Implementation

- Training
- Site Selection
- Regulatory
  - Forms- samples, instructions, templates
  - Certificate of Confidentiality (CoC)
  - CTN Regulatory Binder requirements
  - CTN Guidelines for Defining IRB Involvement
- Assessments

CLIA document (example)

CENTERS FOR MEDICARE & MEDICAID SERVICES

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS

CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS

LABORATORIES
123 MAIN STREET
NEW CITY, IA 025321

CLIA ID NUMBER

[redacted]

EFFECTIVE DATE

03/15/2015

LABORATORY DIRECTOR

[redacted]

EXPIRATION DATE

03/14/2017

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.

This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

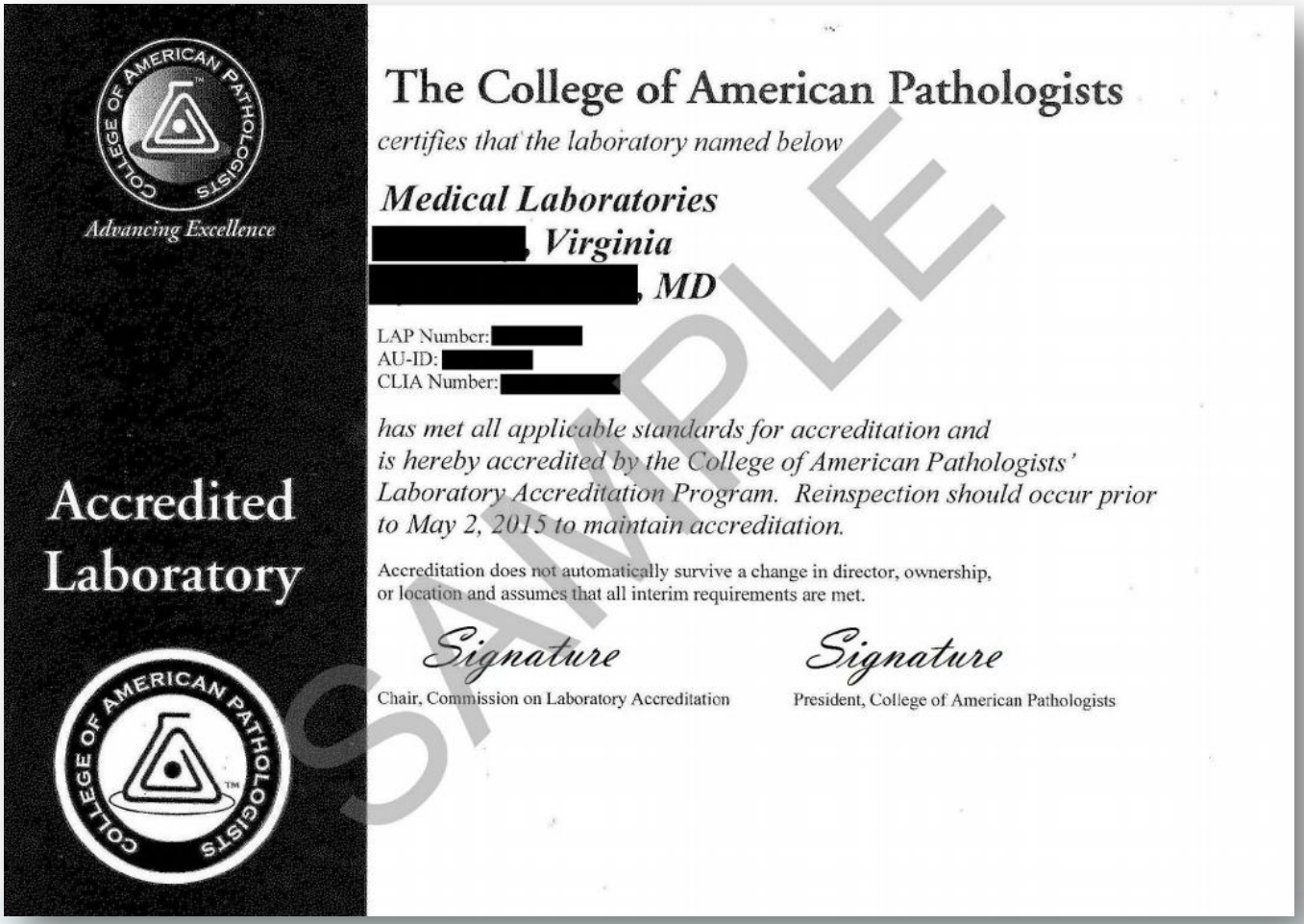
CMS

Karen W. Dyer, Acting Director
Division of Laboratory Services
Survey and Certification Group
Center for Clinical Standards and Quality

154 Certs2_021715

SAMPLE

CAP document (example)



Advancing Excellence

Accredited Laboratory

The College of American Pathologists

certifies that the laboratory named below

Medical Laboratories

[redacted], Virginia

[redacted], MD

LAP Number: [redacted]
AU-ID: [redacted]
CLIA Number: [redacted]

has met all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to May 2, 2015 to maintain accreditation.

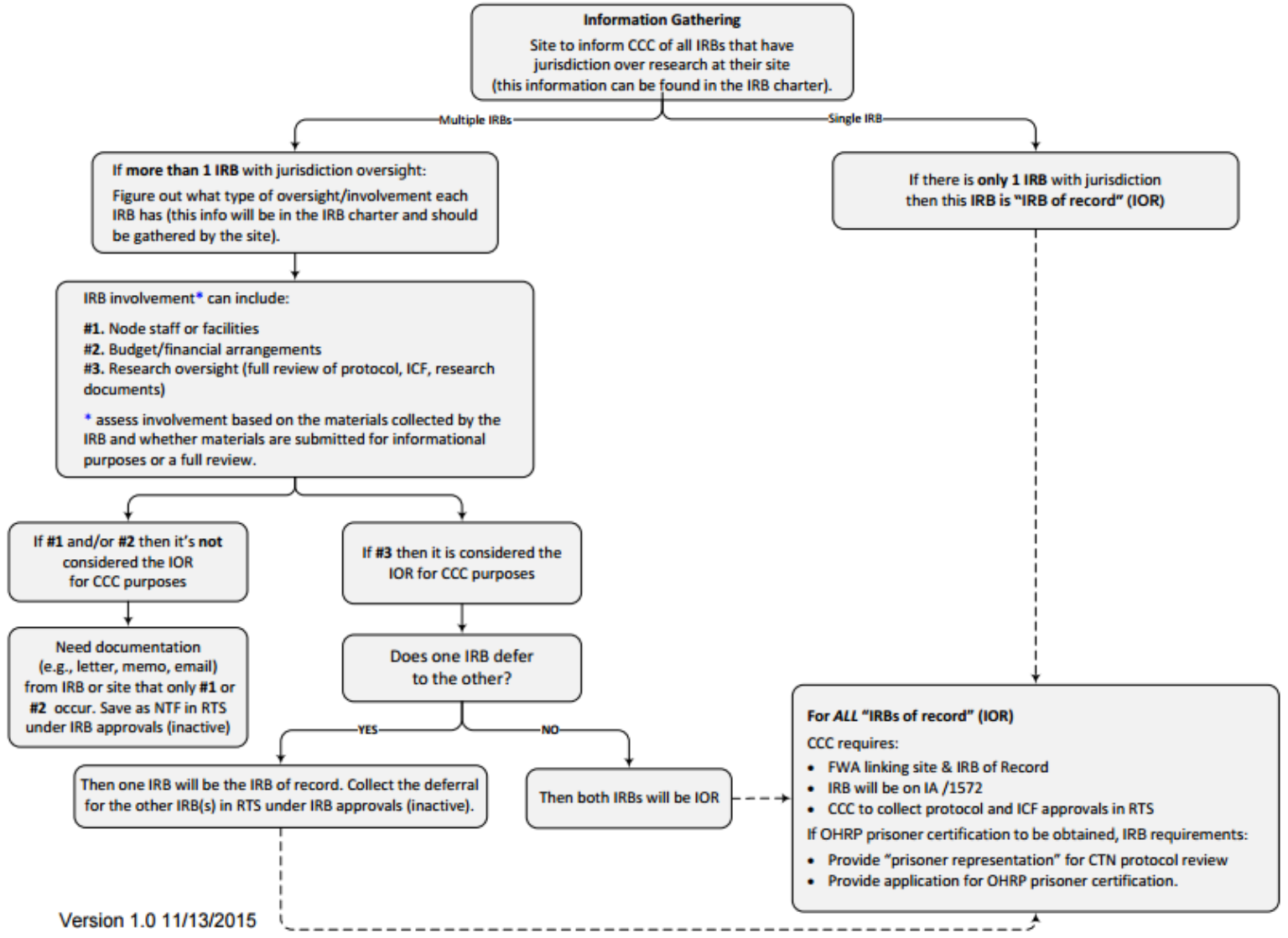
Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

Signature
Chair, Commission on Laboratory Accreditation

Signature
President, College of American Pathologists

SAMPLE

NIDA CCC Guidelines for Defining IRB Involvement and Required Documentation in CTN Trials



Implementation

- CTN Follow-up and Offsite Assessments
- Site Initiation Preparation and Endorsement

Site Initiation Preparation and Endorsement

Site Readiness Checklist

Node Name: _____

CTP Name: _____

Completed by: _____

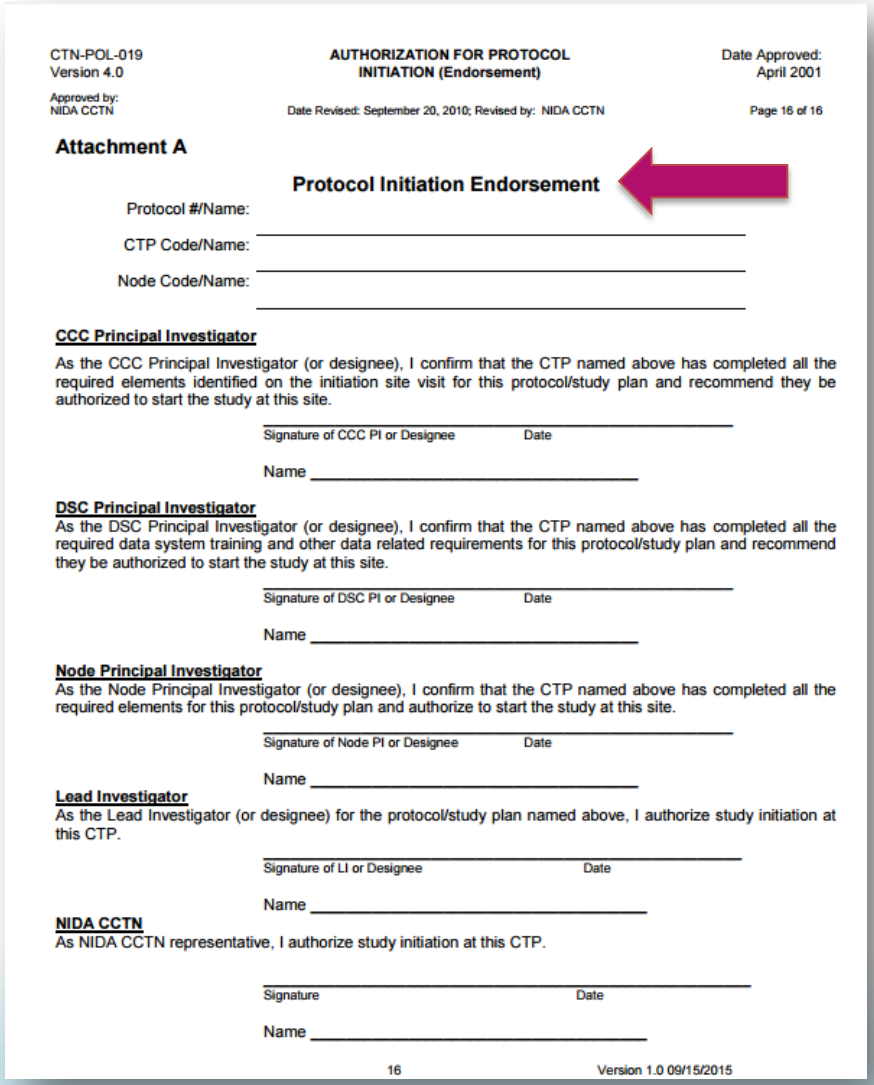
Date Submitted: _____ *(date format: mm/dd/yyyy)*

Regulatory Documents

Activity/Task	Completed?	Date *mm/dd/yyyy*	Comments
Funding secured (budget and necessary contracts in place)	☐		
IRB/IEC application prepared and submitted to IRB/IEC as required (state IRB name/s in Comments Box).	☐		
IRB/IEC study approval/s	☐		
Regulatory Binder/Files are completely assembled and on-site (in the section below indicate as documents are filed and submitted, as required).	☐		
Supply of IRB-approved consents, quizzes, HIPAA Authorizations, and other IRB-required documents duplicated and on-hand	☐		

Name of Document	Binder Tab Number	Submitted to the CCC via	Emailed to the Lead Node	Completed?	Date *mm/dd/yyyy*	Comments
Copy of the IRB Approved Protocols - Version 4.0 (parent protocol) and 4.0-G (genetics protocol) on file	2.1	N/R		☐		
Main Study Protocol v4.0 Signature Page	2.2	RTS	**Required** ☐	☐		

Site Initiation Preparation and Endorsement



CTN-POL-019
Version 4.0

AUTHORIZATION FOR PROTOCOL INITIATION (Endorsement)

Date Approved: April 2001

Approved by: NIDA CCTN

Date Revised: September 20, 2010; Revised by: NIDA CCTN

Page 16 of 16

Attachment A

Protocol Initiation Endorsement

Protocol #/Name: _____

CTP Code/Name: _____

Node Code/Name: _____

CCC Principal Investigator

As the CCC Principal Investigator (or designee), I confirm that the CTP named above has completed all the required elements identified on the initiation site visit for this protocol/study plan and recommend they be authorized to start the study at this site.

_____
Signature of CCC PI or Designee Date

Name _____

DSC Principal Investigator

As the DSC Principal Investigator (or designee), I confirm that the CTP named above has completed all the required data system training and other data related requirements for this protocol/study plan and recommend they be authorized to start the study at this site.

_____
Signature of DSC PI or Designee Date

Name _____

Node Principal Investigator

As the Node Principal Investigator (or designee), I confirm that the CTP named above has completed all the required elements for this protocol/study plan and authorize to start the study at this site.

_____
Signature of Node PI or Designee Date

Name _____

Lead Investigator

As the Lead Investigator (or designee) for the protocol/study plan named above, I authorize study initiation at this CTP.

_____
Signature of LI or Designee Date

Name _____

NIDA CCTN

As NIDA CCTN representative, I authorize study initiation at this CTP.

_____
Signature Date

Name _____

16 Version 1.0 09/15/2015

Study Termination
Final Study Report Preparation

Final Study Report Preparation

Introduction and Purpose

Lead investigators will submit a final study report to NIDA CCTN within four months of database lock.

In general, the Final Study Report should include sufficient detail to allow an understanding of the study, but will focus on the data collected in the study, utilizing the planned analysis described in the protocol and Statistical Analysis plan to address the primary outcome analyses. While the data tables may generate additional length, it is expected that the text portion of the Final Study Report will be approximately 20 pages. The following sections should be included.

1. **Descriptive Information**
   - CTN number and CTN title of the protocol. Version number and date of the last protocol
   - The name, node, and mailing address of the lead investigator and each co-investigator
   - The specific community treatment programs or sites where the study was performed
   - Dates for enrollment of the first participant and final evaluations of the last participant
   - Date of the Final Study Report, along with signature
   - Brief executive summary of the goals and results presented
2. **Rationale and Aims of the Study** (short description from the protocol)
3. **Clinical Trial Design** (short description from the protocol)
4. **Statistical Analysis**
   - Primary analysis only, per the original protocol and a statement of the conclusions drawn from this analysis.
   - Primary outcome analyses may include sensitivity of the primary outcome to missing data and investigation of site effects and interactions, consistent with the primary analysis approach defined in the protocol and/or statistical analysis plan.
   - Primary analysis by sex/gender and race/ethnicity per NIH Policies.
   - Results from any interim analysis, and any modifications made.

Investigator Toolbox Next Steps

- Add more materials and examples.
- Obtain feedback on existing content and ideas for new tools, documents, and materials – direct comments to the Toolbox support team at:

CTNtoolbox@emmes.com

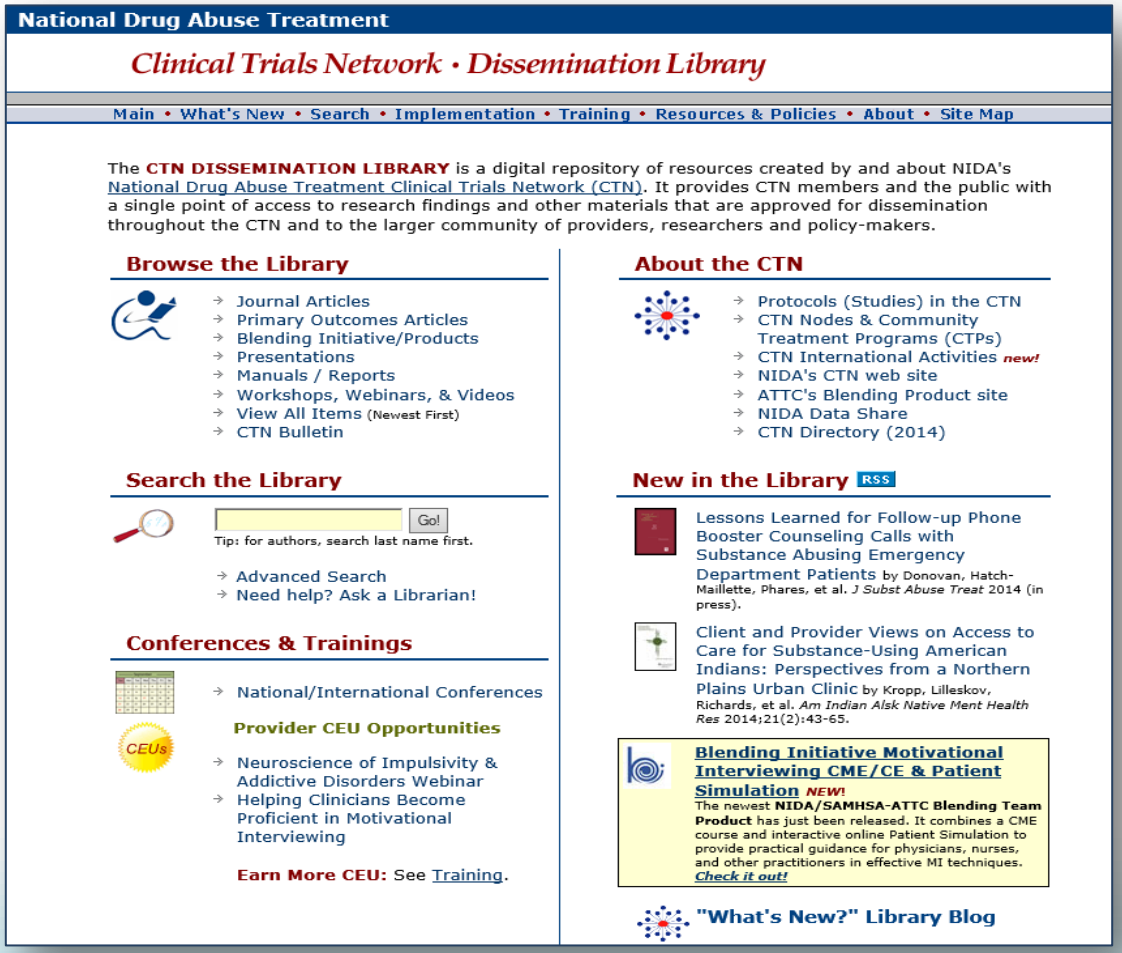
- Share materials developed by others (e.g., site tools that may be relevant for other study sites).
- Alternatively, contact Dee Blumberg directly at dblumberg@emmes.com.

Questions / Comments

Alternatively, questions can be directed to the presenter(s) by sending an email to CTNtraining@emmes.com.

http://ctndisseminationlibrary.org/ctntraining.htm

A recording of this presentation will be available electronically.



Next Topic…

CTN-0044 WEB-TX: A Review of the Primary and Secondary Outcomes

Wednesday, May 25, 2016

at 1:00 pm ET

THANK YOU FOR YOUR PARTICIPATION