



# CTEP Clinical Oncology Research Enterprise (CORE)

7/12/17

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# Agenda

- Overview of CORE
- Enhancing safety reporting
- Improving data quality; auditing; and monitoring processes
- Streamlining regulatory compliance
  - Registration and Credentialing repository (RCR): Electronic investigator registration (1572)
  - Delegation of Tasks Log (DTL)

July 11, 2017

# Why CORE?

**Clinical Oncology Research Enterprise (CORE)** represents the development of an integrated IT solution that:

- Addresses evolving and more complex science (ex. Biomarkers, imaging, precision medicine trials, genomics and correlative studies)
- Modernizes underlying architecture and technology
- Implements scalable and configurable technology to meet new/future requirements
- Emphasis on improving data quality and control
- Enhanced regulatory compliance (CFR-11; GCP; NIST; FISMA)

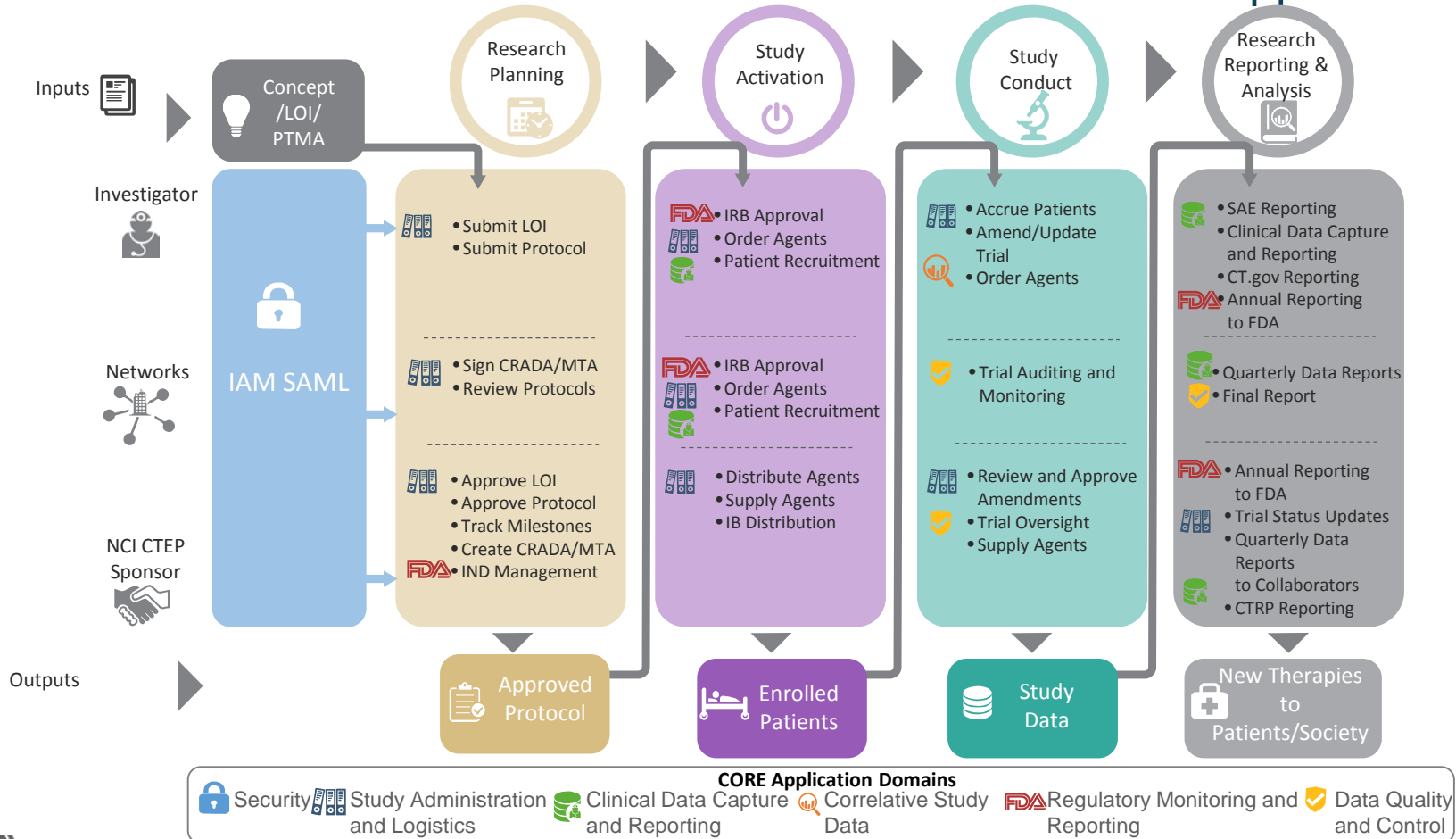
# CORE & Clinical Trials

CTEP CORE supports CTEP, other NCI staff, and the extramural community in the following clinical trial domains:

- Information Security
- Study Administration and Logistics
- Clinical Data Capture and Reporting
- Correlative Study Data
- Regulatory Monitoring and Reporting
- Data Quality and Control



# CTEP CORE – End to End Clinical Trial Process Support



# CORE – An integrated suite of tools to advance science, promote patient safety, and meet Federal regulations

## Study Admin

Study specific descriptors:  
participants, disease

Institution &  
Investigator  
Rosters

Role  
Based  
Security  
(IAM)

## Regulatory

Investigator  
Registration (RCR)

Delegation of Tasks  
Log  
(DTL)

(C)IRB Approvals

## Data Quality Suite

### Data Capture

#### Patient Enrollment

(OPEN)

Registration; randomizations;  
treatment assignment

CDMS  
(Rave)

SAE  
Reporting  
(CTEP-  
AERS)

### Data Reporting

Study  
Monitoring

Serious  
Adverse  
Event  
Review

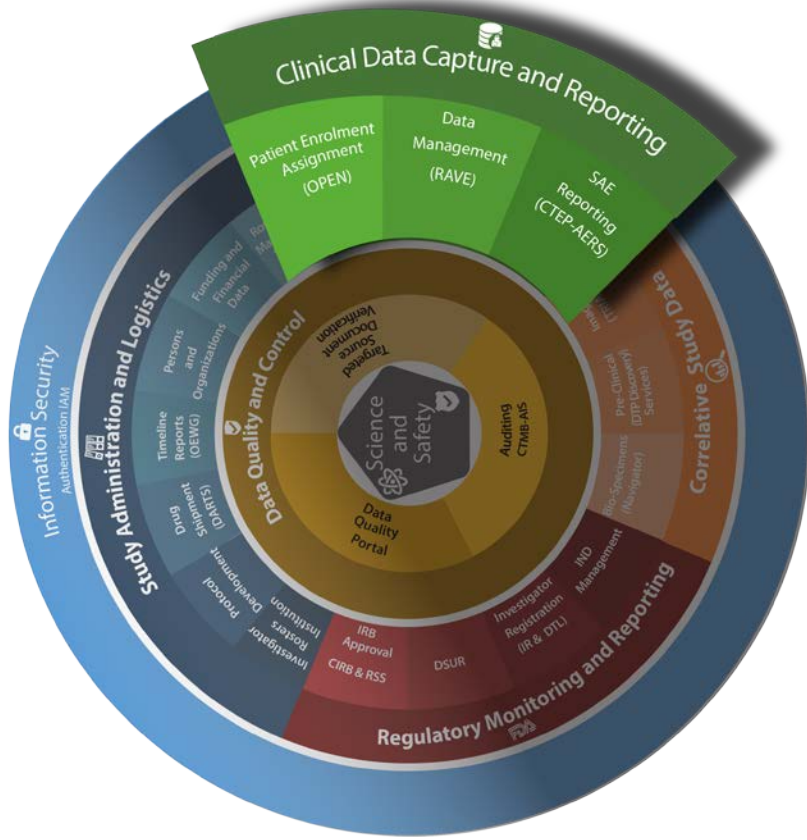
FDAAA &  
Clinical  
Trials.gov  
(CTRP)

## Correlative Science

Bio-  
Repository  
(Navigator)

Diagnostic  
Imaging  
(TRIAD)

Pre-Clinical  
Databases  
(TBD)



# CTEP-Adverse Event Reporting System (CTEP-AERS) /Rave Integration

# Goal: Promote serious and routine safety reporting into a single harmonized process by integrating CTEP-AERS and Rave

- Reduce under-reporting of Serious Adverse Events (SAEs)
- Reduce over-reporting of SAEs
- Improve timeliness of AE reporting
- Create a single source of AE data
- Eliminate need for reconciliation
- Reduce administrative burden on the entire oncology community (treating site; lead protocol organization stat & ops offices; NCI; FDA)

**Improve efficiency while promoting patient safety**



# Before

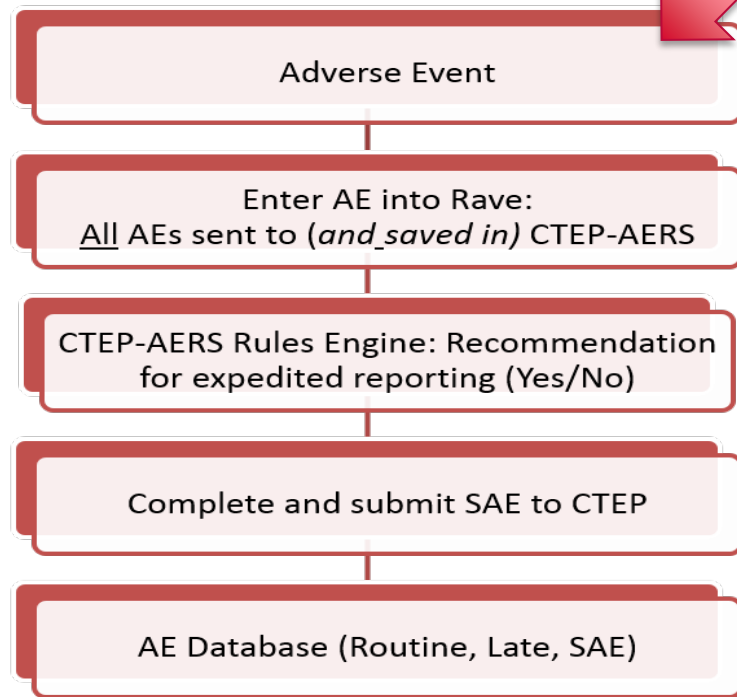
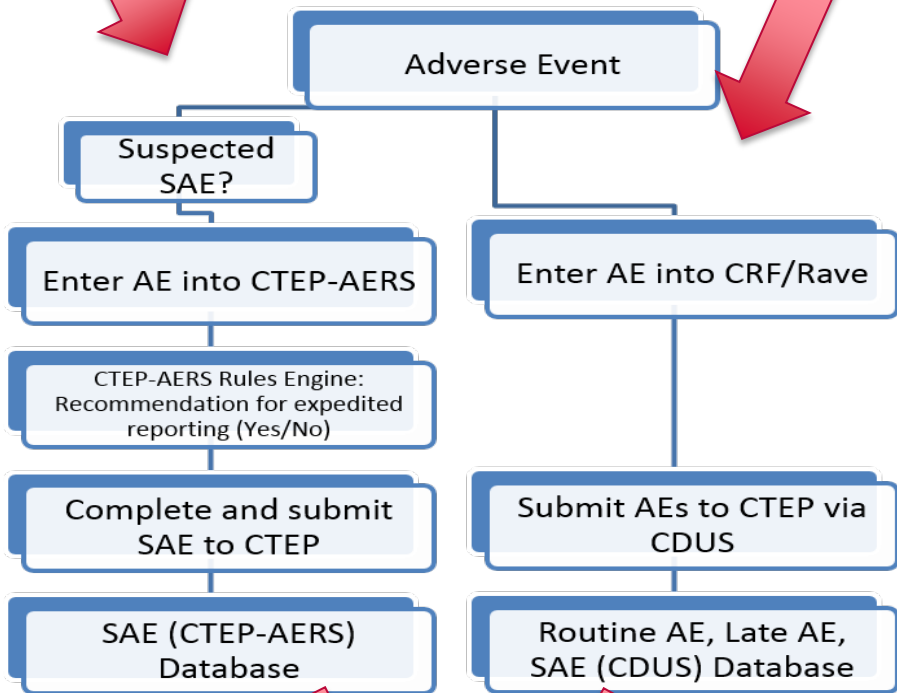
# After

Nurse 'A'  
Serious AE reporting

Nurse 'A' or 'B'  
Routine AE Reporting

Harmonized AE reporting

Nurse 'A' or 'B'



**AE Data Reconciliation**

# Rave/CTEP-AERS Status

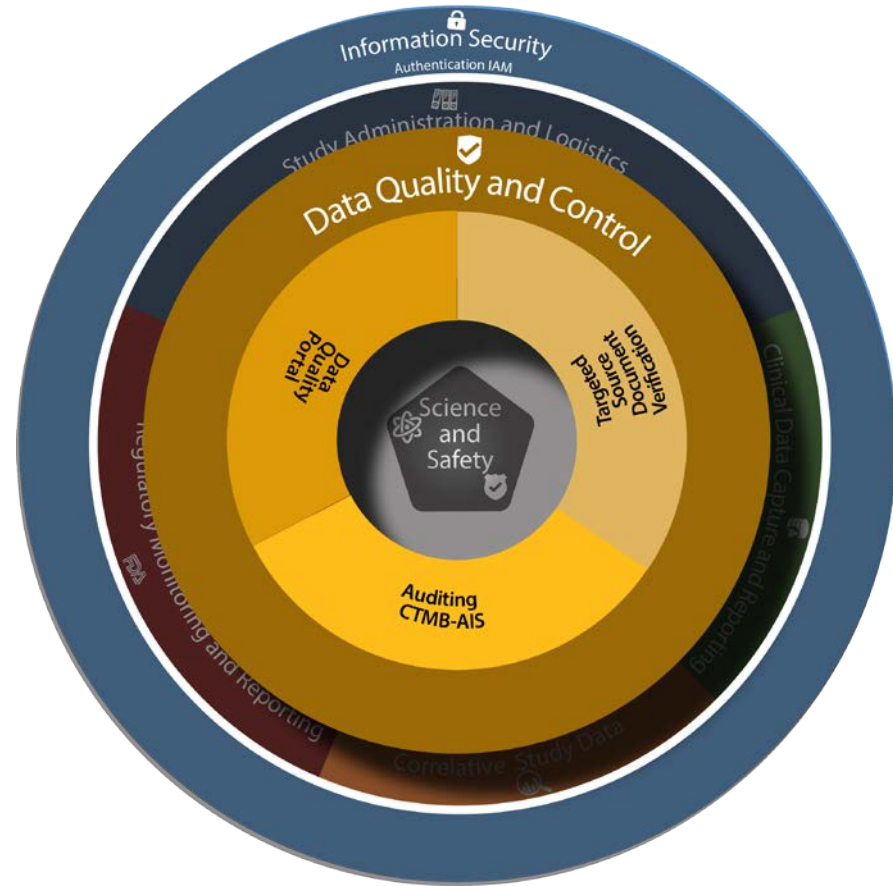
- Pilot 2016 (limited functionality):
  - 5 pilot studies
  - ~1,000 SAEs reported
- Full functionality available for new NCI-held IND studies as of Mid-March
- NCI requires use for new NCI IND studies activated after July 1, 2017
  - Several organizations have self-elected to launch for studies prior to 7/1/17
- Expanded functionality to support Network Group held IND or commercial agent studies to be available 1st quarter of 2018

*Question for CTAC: How can  
CTEP CORE better serve the  
oncology community?*

*Other questions?*

# Auditing & Monitoring

Rocio J. Paul, MSHS, CCRP  
rocio.paul@nih.gov  
July 12, 2017

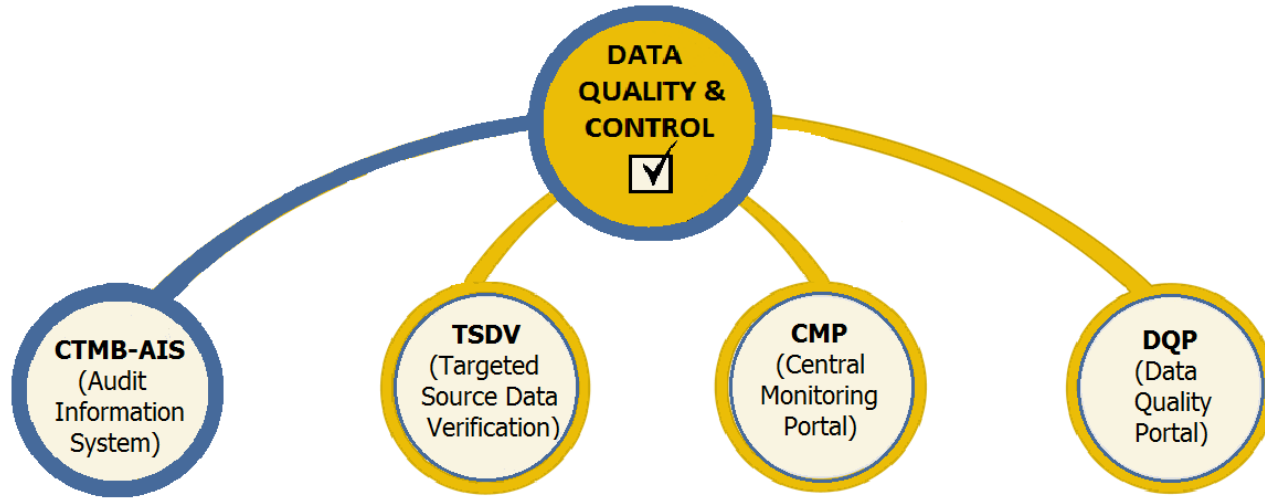


# Auditing vs. Central Monitoring

Parameter	Auditing	Central Monitoring
Frequency	Typically a retrospective review; audit scheduled every 1 to 3 years*	Continuous monitoring (intervals) of data during the conduct of the study
Patient Coverage	10 – 20 % of the total patients enrolled onto a clinical trial are reviewed	All patients or subset of patient data are reviewed
Data points reviewed	A comprehensive list of data points.* <i>Also may review data points on-site that have been monitored remotely</i>	Selected critical data points prospectively defined in the protocol's monitoring plan
Conducted by & location	Audit conducted by Lead Organization (LO); data reviewed on-site*	Monitoring conducted by Lead Organization (LO); data reviewed off-site
Tool used [New]	Targeted Source Data Verification (TSDV)	Source documents uploaded by sites into portal for verification against eCRF data
Verification of Source Data [New]	Actual source document verified at the site	The uploaded copy of source document is reviewed remotely in Rave

\* Based on NCI/CTEP CTMB Audit Guidelines.

# Enhancing the QA Program



- Database used for auditing functions (scheduling audits; site, protocol and patient selection; generating audit reports; etc.)
- Repository for all audit information (including audit findings & reports, correspondence; CAPA plans, etc) for across multiple organizations

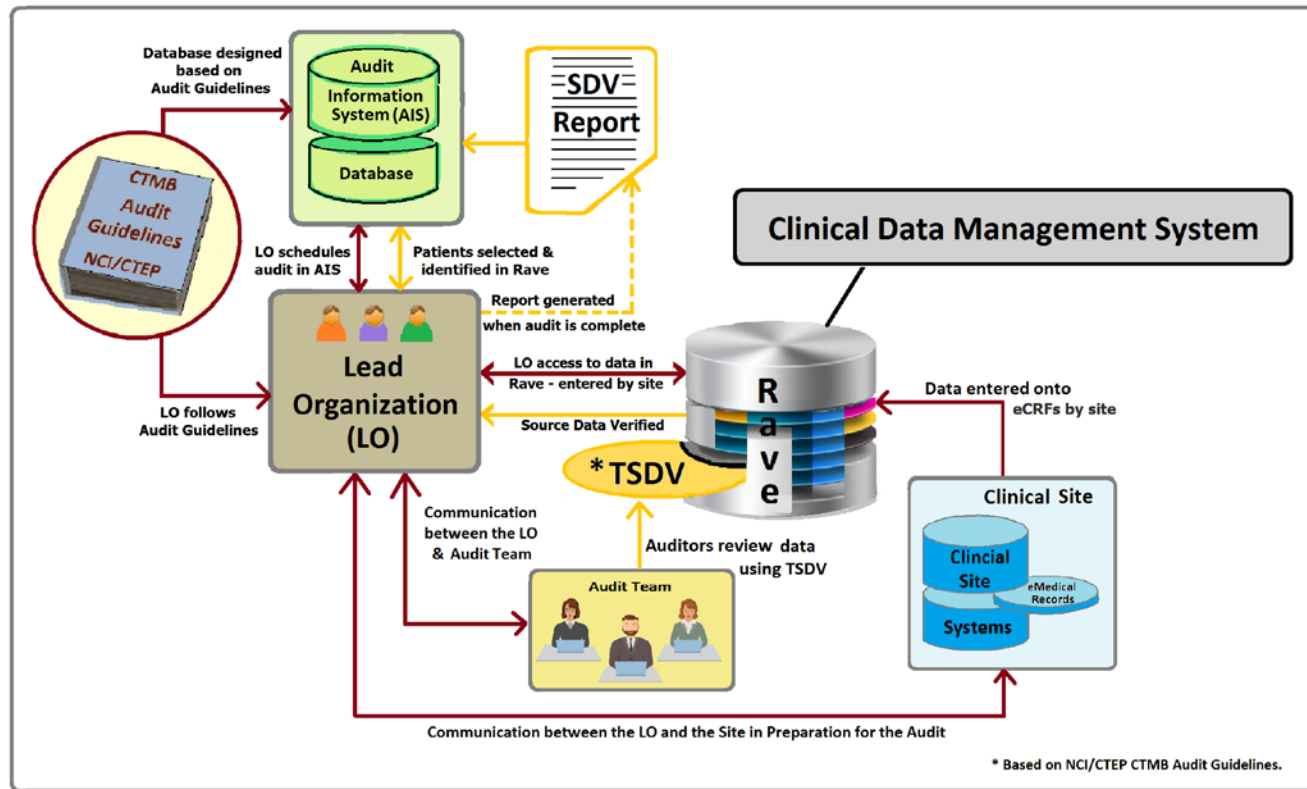
- Tool used within RAVE [Clinical Data Management System]
- Enables source data verification to be recorded

- Centralized monitoring approach to be implemented
- Mechanism allowing sites to upload source documents selected for review to a CM Portal

- Collects information from the AIS, RAVE, TSDV, CMP, others
- Generates reports of queries that are pending or delinquent; and eventually other types of reports

# Auditing Utilizing TSDV Tool

The use of the Targeted Source Data Verification (TSDV) tool enables the ability to 'record' Source Data Verification activity in Rave



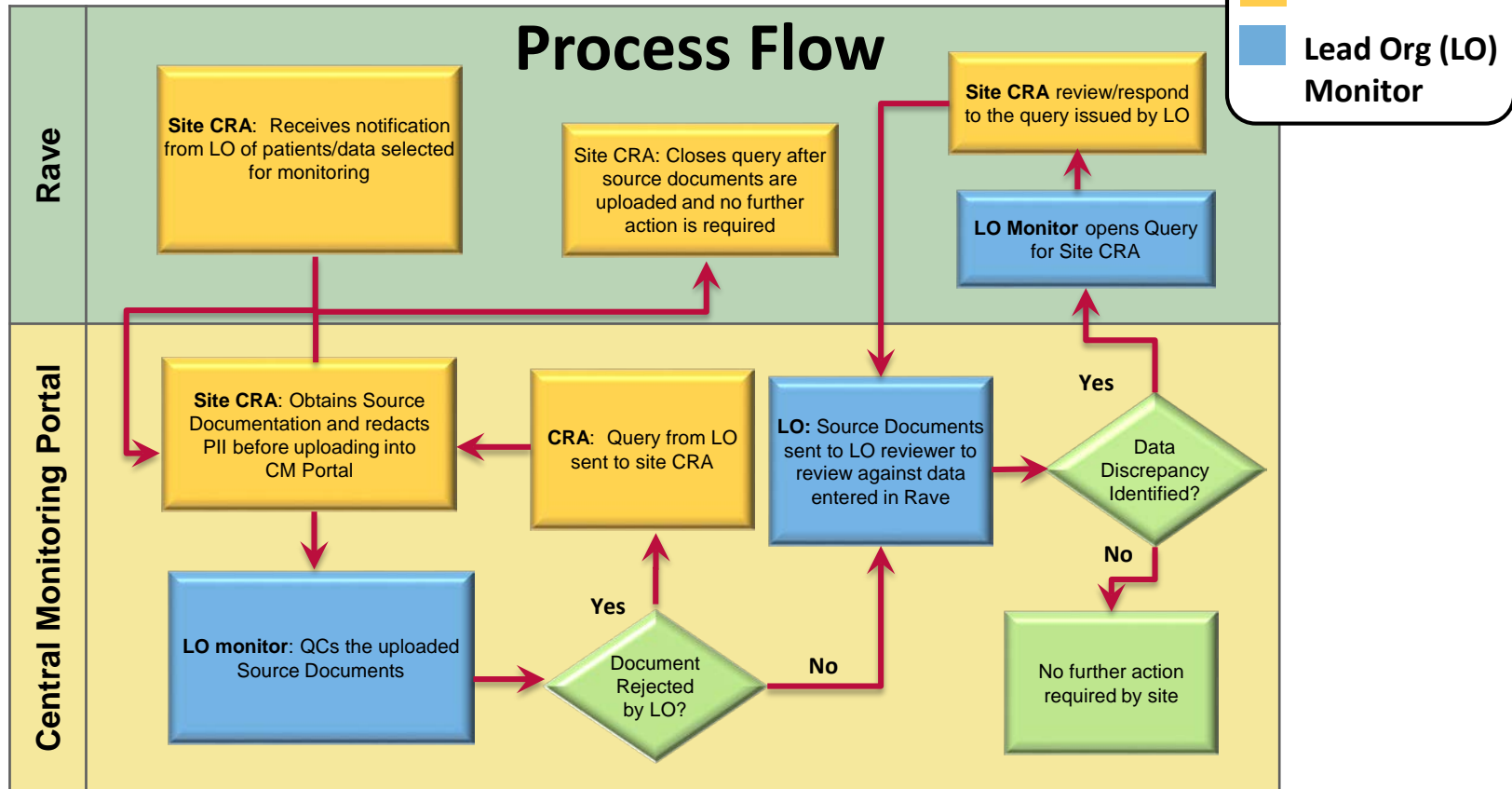
# Central Monitoring (CM)

## Augmenting the TSDV Process

- **ICH E6 (R2) - ADDENDUM of 5.18.3**  
**Extent and Nature of Monitoring (Nov 2016)**
  - The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials. ... The sponsor may choose ...combination of on-site and centralized monitoring, or ...centralized monitoring. The sponsor should document the rationale for the chosen monitoring strategy (e.g., in the monitoring plan).
  - Centralized monitoring is a remote evaluation of accumulating data, performed in a timely manner...



# Central Monitoring (CM)



# Central Monitoring (CM)

## View by Protocol & by Site

Central Monitoring > MN001 Source Document Repository

Upload New Document 4 documents are missing

Protocol: ALL Site: ALL Patient: ALL

Protocol	Site	Patient	# Documents Expected	# Documents Uploaded	# Missing Documents	# Days Document has been Missing	Actions
A081105	MN001	14602	4	4	0	0	
EAY131	MN001	14603	2	2	0	0	
NRG-GU002	MN001	14604	3	3	2	4	
S1400	MN001	14605	6	4	2	10	
A151216	MN001	14606	7	7	0	0	
E1A11	MN001	14607	8	8	0	0	

Note: The grace period for sites to upload source documents is 14 calendar days.

# Central Monitoring (CM)

## View by Protocol Data Points

Data Point	Need Review?	DOC Needed for Review	Entered?	Expected Date for SD Upload	Missing DOCs?	Uploaded DOCs?	Triage?	Data Points Reviewed?
DP1	<input checked="" type="checkbox"/>	Informed Consent	<input checked="" type="checkbox"/>	Data Entry+7	Yes	Yes	Yes	Yes
DP2	<input checked="" type="checkbox"/>	Radiology Report	<input checked="" type="checkbox"/>	Data Entry+7	Yes	No	N/A	No
DP3	<input checked="" type="checkbox"/>	Informed Consent	<input checked="" type="checkbox"/>	Data Entry+7	Yes	Yes	Yes	Yes

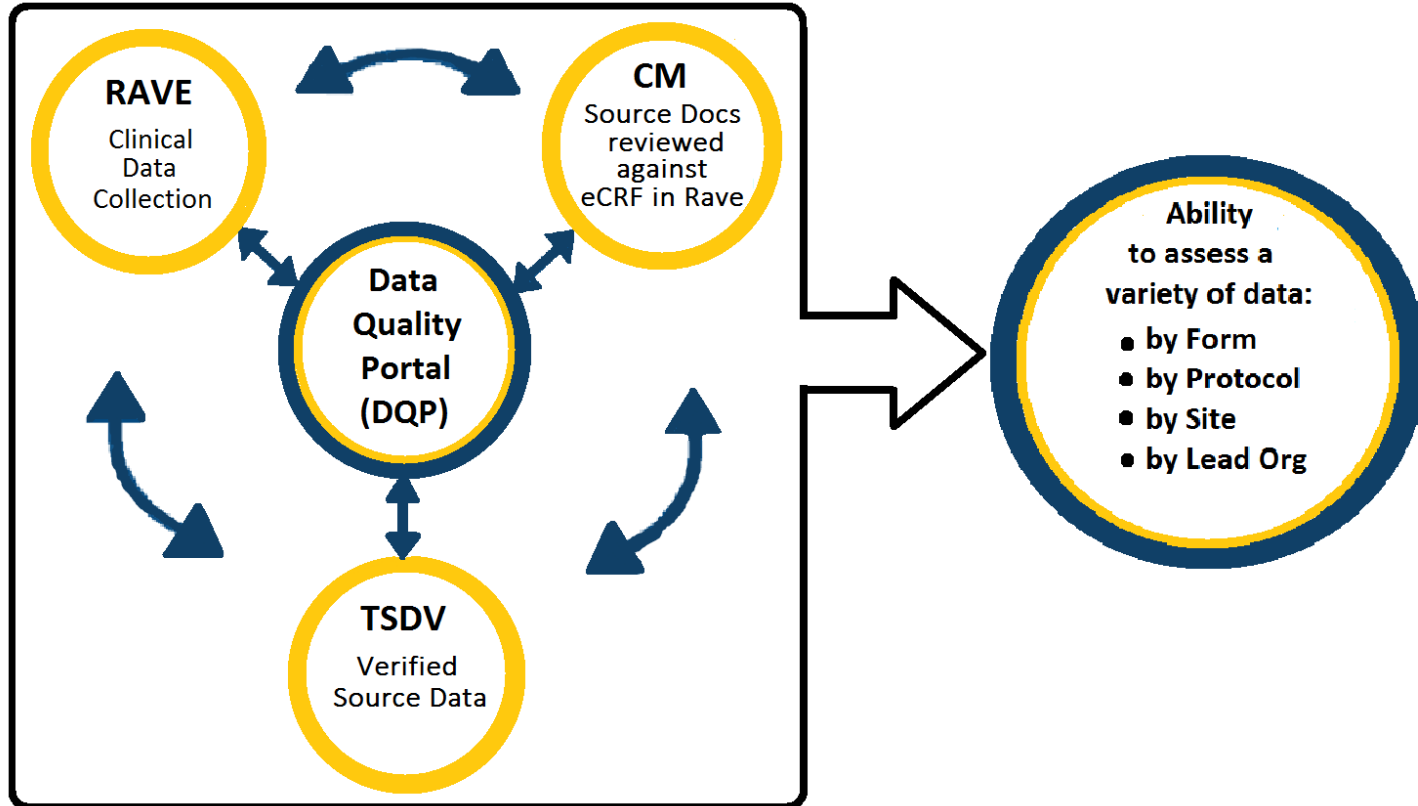
Site Ability to View Status



Lead Org Monitor Reviews; Compares SD to Data on eCRF

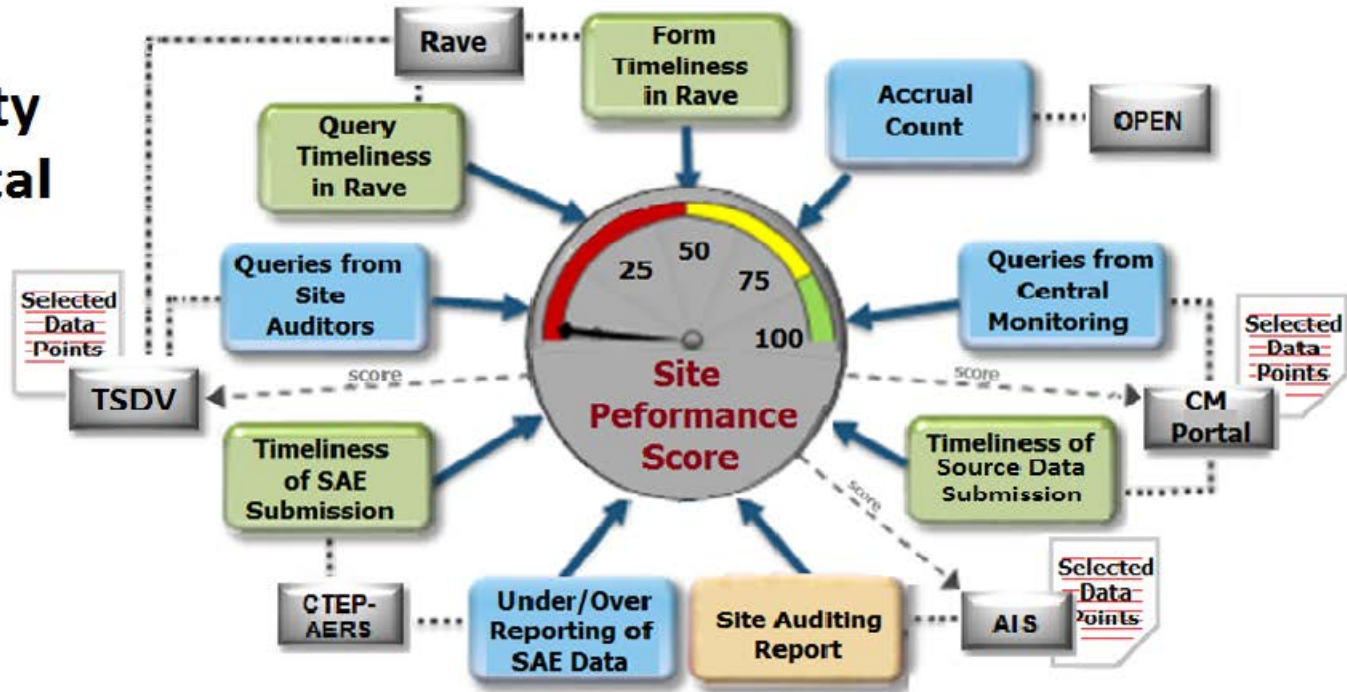


# Data Quality Portal (DQP)



# In the Future...

## Data Quality Portal



# Questions ?

# Registration and Credential Repository (RCR) and Delegation of Tasks Log (DTL)



*Matt Boron RPh*  
*boronm@mail.nih.gov*

# *Registration and Credential Repository (RCR)*

- Provides an online registration application with electronic signature
- Define specific Registration Types
- Registration Type will dictate documentation requirements



# *Registration and Credential Repository (RCR)*

- Electronic FDA Form 1572
- NCI Biosketch
- Financial Disclosure Form
- Designee Form

## *Registration and Credential Repository (RCR)*

- Requires registration in NCI IAM (Identity and Access Management) application
  - Unique profile for each individual
  - Access credentials
    - Provide access to CORE applications
    - Allows for RCR profile owners to electronically sign their registration documents
- Electronic collection of data and certificates allows for
  - sharing across NCI network
  - Control of downstream processes

# Registration and Credential Repository – Summary screen

SUMMARY
PRIMARY CONTACT INFO
FORM FDA 1572
NCI BIOSKETCH
FDF
AGENT SHIPMENT FORM
PRACTICE PREFERENCES
SUBMITTED DOCUMENTS
REVIEW AND APPROVE

### Personal Info

**CTEP Person ID**  
IVR -

**Name**  
Dr.

**Comments**

[Edit Comments](#)

### Registration Info

**Status**  
Active

**Expiration Date**  
19-NOV-2017

**Registration Coordinator**  
CTEP ID-Name

**Comments**

### Primary Contact Information

**Name**

**Address**

**Phone**

**Email**

### Group Affiliations

Group Name
Children's Oncology Group

### Practice Sites

CTEP ID	Site Name
KY027	Norton Children's Hospital
KY049	Norton Hospital Pavilion and Medical Campus

### IRBs

IRB Number	IRB Name
No Records to Display	

### Shipping Info

**Shipping Type**  
PSD

**Shipping Designee**  
A -

**Practice Site**

**Address**

### Task Access

Task	Allowed
Drug Shipment Investigator	Yes
Consenting Person	Yes
Enrolling Person	Yes
Site Protocol PI	Yes

## *Delegation of Tasks Log (DTL) - Development*

- CTEP and Lead Protocol Organizations (LPOs) collaborate during LOI / Concept / Protocol development to determine if DTL is needed
- Clinical Investigator reviews and signs the protocol and site-specific DTL
- Site/protocol activation based on completed DTL and other protocol-specific requirements (PSRs)
- DTL controls downstream system access and protocol conduct

## *Delegation of Tasks Log (DTL) - Purpose*

- Identify the Clinical Investigator (CI) and Delegation of Tasks Log Administrator (DTLA)
- Provides a complete list of investigators and sub-investigators
- Identifies individuals that can perform designated tasks on the protocol
- Track changes in task assignment over study lifecycle

# Delegation of Tasks Log (DTL) – Protocol Template

Site DTL Browser

Delegation Log > Site DTL Browser > Initiate Site Delegation Log

Site: Mercy Hospital(MN019) Protocol: A051301

**Template Information**

**Document Number:** A051301

**Document Type:** Protocol

**Document Title:** A Randomized Double-Blind Phase III Study of Ibrutinib During and Following Autologous Stem Cell Transplantation Versus Placebo in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma of the Activated B-cell Subtype

**Lead Group:** ALLIANCE

**Template Status:** Activated

**Template Revision:** 12-JUN-2017 11:02 AM

Displays DTL template information and required tasks

**Task List**

#	Task	Primary?	Required? ▾	CI Sign Required?	Registration Type	Rostered?	Training Requirements
1	DTL Administrator	Yes	Yes	Yes	IVR AP NPIVR	Yes	
2	Clinical Investigator	Yes	Yes	Yes	IVR NPIVR	Yes	
3	Enrolling Person/Treating Investigator	No	Yes	Yes	IVR NPIVR	Yes	
4	Consenting Person	No	Yes	Yes	IVR AP NPIVR	Yes	
5	HP Assessments	No	Yes	No	IVR AP NPIVR	Yes	
6	Tox Assessment	No	Yes	Yes	IVR NPIVR	Yes	
7	Eligibility Assessment	No	Yes	No	IVR AP NPIVR	Yes	
8	Rave CRA	No	Yes	No	IVR AP NPIVR	Yes	
9	OPEN Registrar	No	Yes	No	IVR AP NPIVR	Yes	
10	Study-Related Interventions	No	Yes	No	IVR AP NPIVR A	No	

Initiate DTL

# Delegation of Tasks Log (DTL) – site log

Site DTL Browser

Delegation Log > Site DTL Browser > Manage Site Delegation Log

**DTL Summary**

**Site DTL Status:** Initiated

**Site DTL Status Reason:** N/A

**Template Revision:** 12JUN2017 11:02:10 AM

**Template Status:** Activated

**Protocol Number:** A051301

**Protocol Status:** Active

**Protocol Title:** A Randomized Double-Blind Phase III Study of Ibrutinib During and Following Autologous Stem Cell Transplantation Versus Placebo in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma of the Activated B-cell Subtype

**Site:** MN019

**Site Name:** Mercy Hospital

**Site Registration Status:**

**Last Updated By:** HAASA

**Last Updated Date:** 19-JUN-2017

**Last Approved By:**

**Last Approved Date:** N/A

Assignee:  Task:  Status:   Show changes after last approval [View by Assignee](#)

**Task Assignments List for MN019, Protocol A051301**

#	Assignee Name	Task Name	Status	Start Date	End Date	Status Reason	Action
1	Tan, Annie	Clinical Investigator	Awaiting_CI_Approval				⊞ ✖
2	Horn, Amanda	DTL Administrator	Awaiting_CI_Approval				⊞ ✖
3	Tan, Annie	Consenting Person	Awaiting_CI_Approval				⊞ ✖
4	Horn, Amanda	Consenting Person	Awaiting_CI_Approval				⊞ ✖
5	Tan, Annie	Eligibility Assessment	Awaiting_CI_Approval				
6	Horn, Amanda	Eligibility Assessment	Awaiting_CI_Approval				
7	Tan, Annie	Enrolling Person/Treating Investigator	Awaiting_CI_Approval				
8	Tan, Annie	HP Assessments	Awaiting_CI_Approval				
9	Horn, Amanda	HP Assessments	Awaiting_CI_Approval				
10	Horn, Amanda	OPEN Registrar	Awaiting_CI_Approval				
11	Haas, Audrey	Rave CRA	Awaiting_CI_Approval				
12	Horn, Amanda	Rave CRA	Awaiting_CI_Approval				
13	Tan, Annie	Study-Related Interventions	Awaiting_CI_Approval				
14	Horn, Amanda	Study-Related Interventions	Awaiting_CI_Approval				
15	Tan, Annie	Tox Assessment	Awaiting_CI_Approval				

Assign Tasks

Assignee:  Task:   Show Inactive Task Assignments

**Task Assignment List**

#	Assignee Name	Tasks
<b>Awaiting_CI_Approval Task Assignments</b>		
1	Tan, Annie	<input type="button" value="Clinical Investigator"/> <input type="button" value="Consenting Person"/> <input type="button" value="Eligibility Assessment"/> <input type="button" value="Enrolling Person/Treating Investigator"/> <input type="button" value="HP Assessments"/> <input type="button" value="Study-Related Interventions"/> <input type="button" value="Tox Assessment"/>
<b>Awaiting_CI_Approval Task Assignments</b>		
2	Horn, Amanda	<input type="button" value="DTL Administrator"/> <input type="button" value="Consenting Person"/> <input type="button" value="Eligibility Assessment"/> <input type="button" value="HP Assessments"/> <input type="button" value="OPEN Registrar"/> <input type="button" value="Rave CRA"/> <input type="button" value="Study-Related Interventions"/>
<b>Awaiting_CI_Approval Task Assignments</b>		
3	Haas, Audrey	<input type="button" value="Rave CRA"/>




# Benefits of NCI Proposed Process

- Complies with FDA investigator and sub-investigator data collection requirements
- Leverages data capture across multiple NCI integrated applications to ensure only qualified investigators are participating
- Controls protocol-specific research tasks based on the DTL
- Decreases burden on investigators through use of a single NCI-specific registration packet
- Increases accuracy, efficiency, and coordination between NCI and sites



# Benefits to NCI Proposed Process

## Leveraging RCR and DTL to ensure regulatory compliance

- Active 1572 + Active DTL role  Study participation (ex. pt. registration)
- Inactive 1572 + Active DTL role  Study participation
- Active 1572 + Inactive DTL role  Study participation

*QUESTIONS?*

*Reserve slides*

# RCR/DTL Process Workflow

