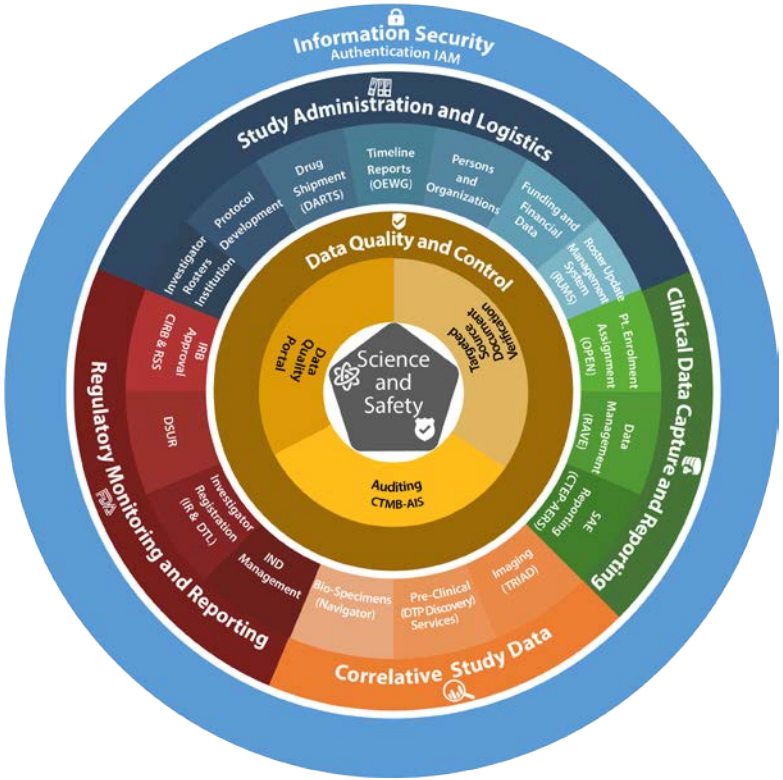

CTEP Clinical Oncology Research Enterprise (CORE)

7/12/17

Michael Montello, PharmD, MBA

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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)

Why CORE?

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

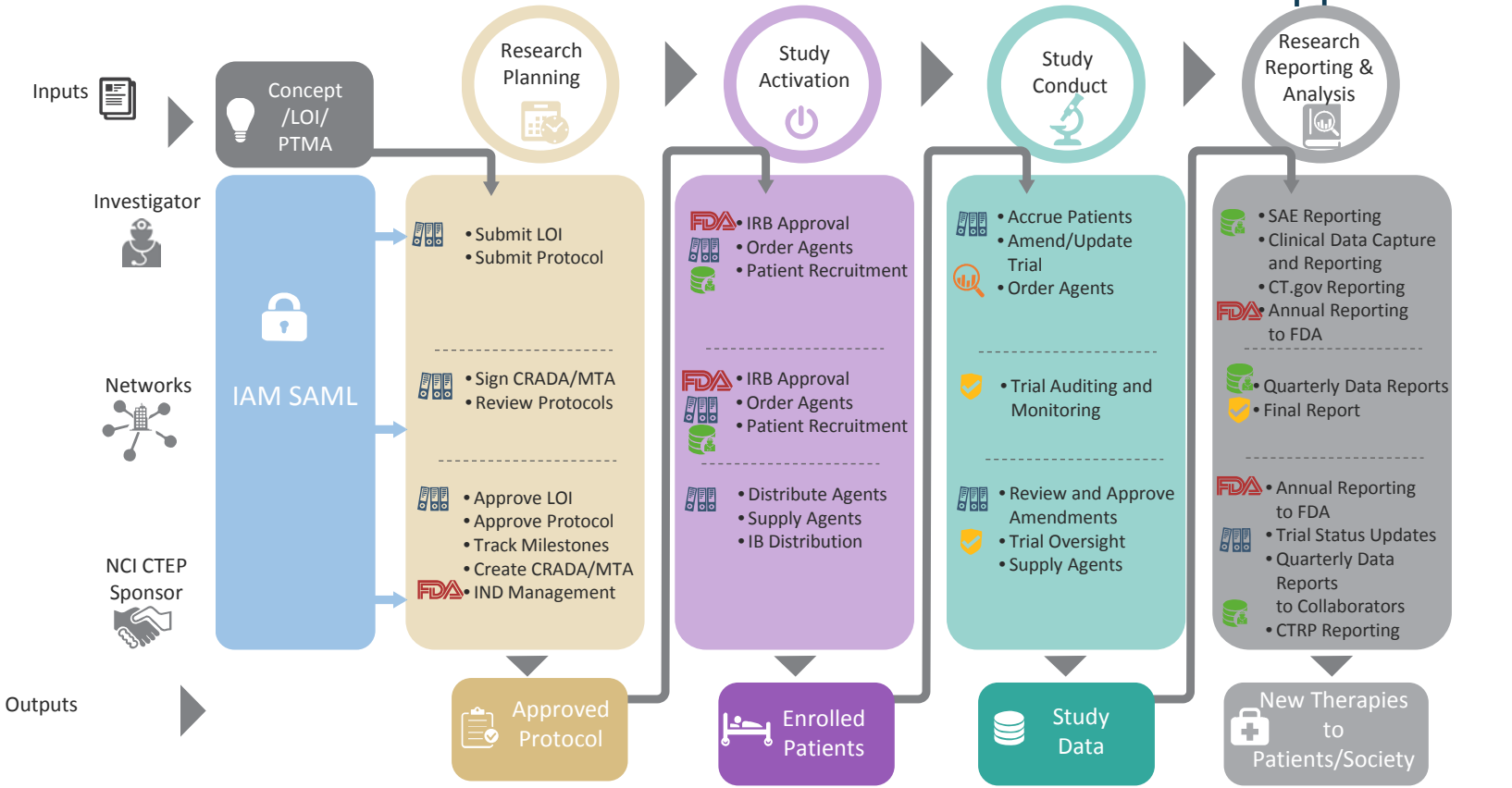
- Addresses evolving and more complex science (ex. Biomarkers, imaging, precision medicine trials, genomics and correlative studies)
- Modernizes underlying architecture and technology
- Implements scalable and configurable technology to meet new/future requirements
- Emphasis on improving data quality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

CORE & Clinical Trials

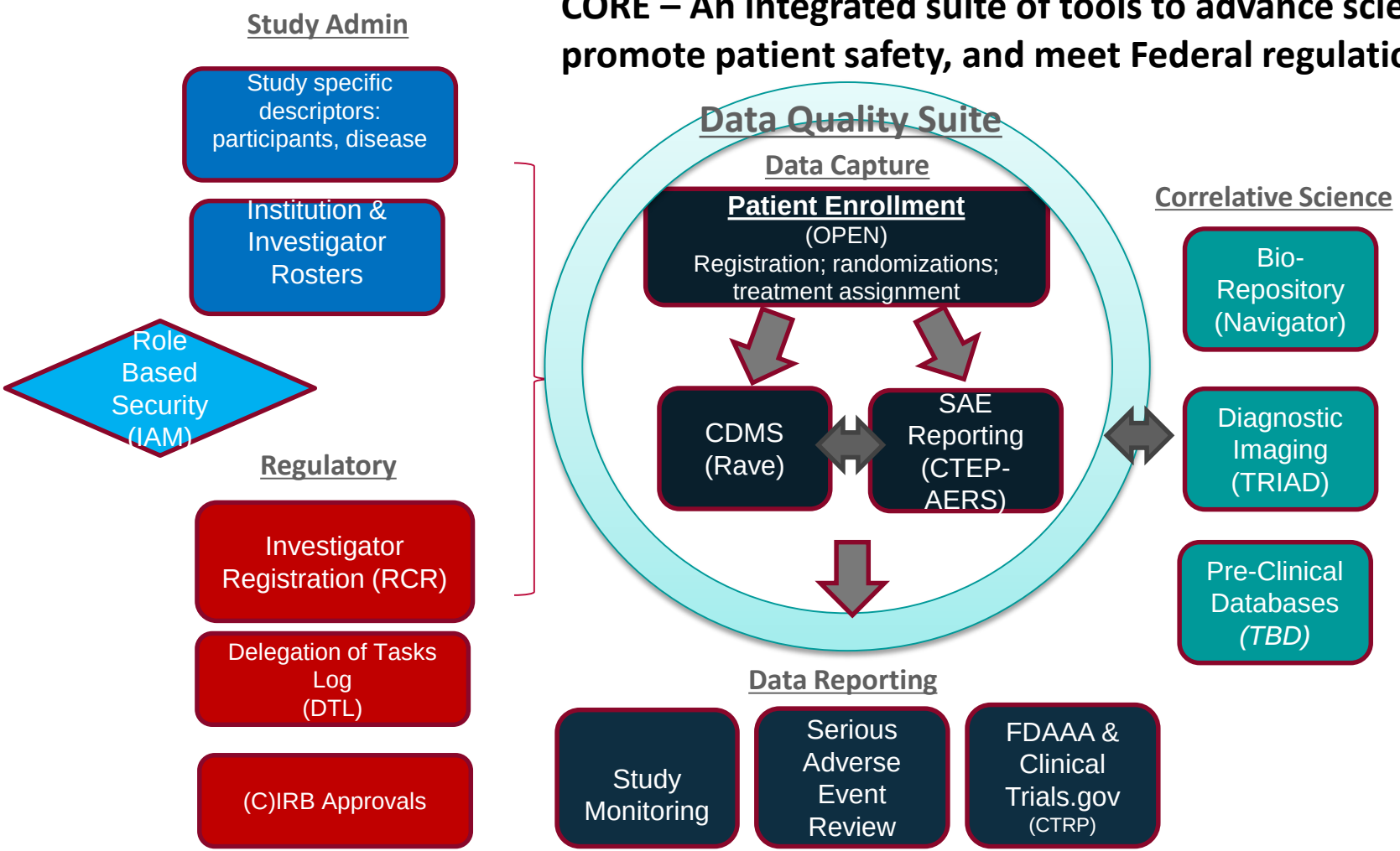
CTEP CORE supports CTEP, other NCI staff, and the extramural community in the following clinical trial domains:

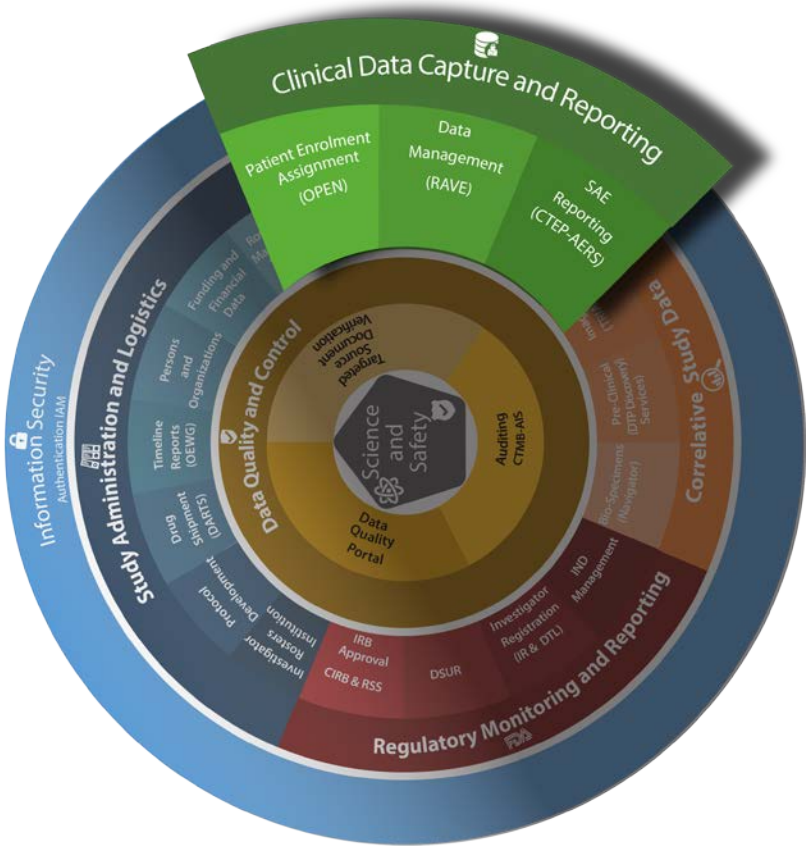
- Information Security
- Study Administration and Logistics
- Clinical Data Capture and Reporting
- Correlative Study Data
- Regulatory Monitoring and Reporting
- Data Quality and Control

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





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

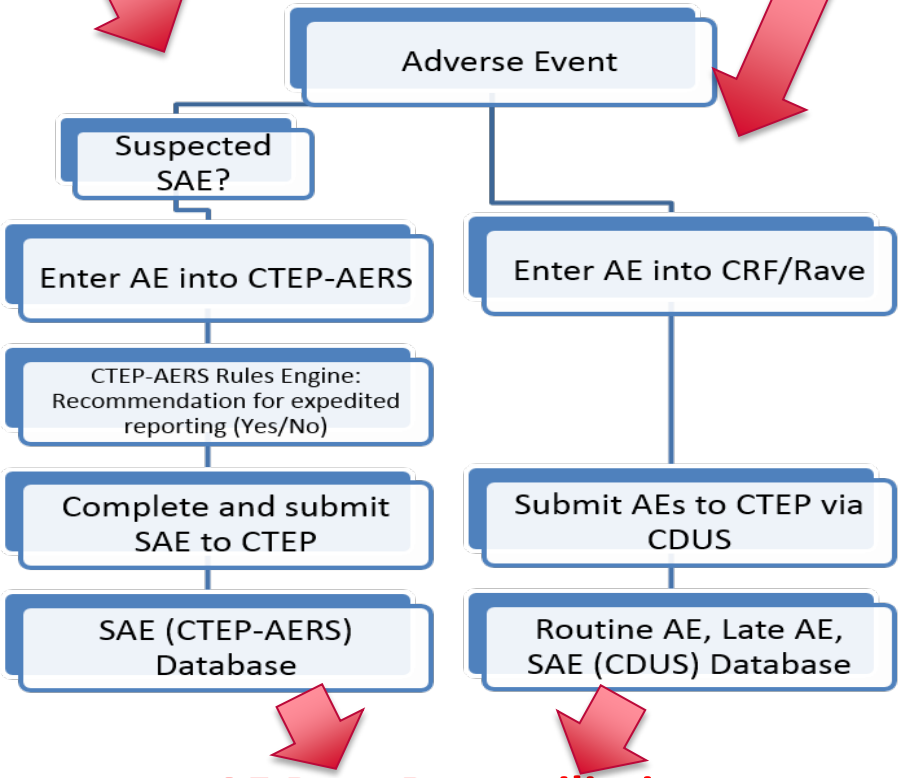
- Reduce under-reporting of Serious Adverse Events (SAEs)
- Reduce over-reporting of SAEs
- Improve timeliness of AE reporting
- Create a single source of AE data
- Eliminate need for reconciliation
- Reduce administrative burden on the entire oncology community (treating site; lead protocol organization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

Improve efficiency while promoting patient safety

Before

Nurse 'A'
Serious AE reporting

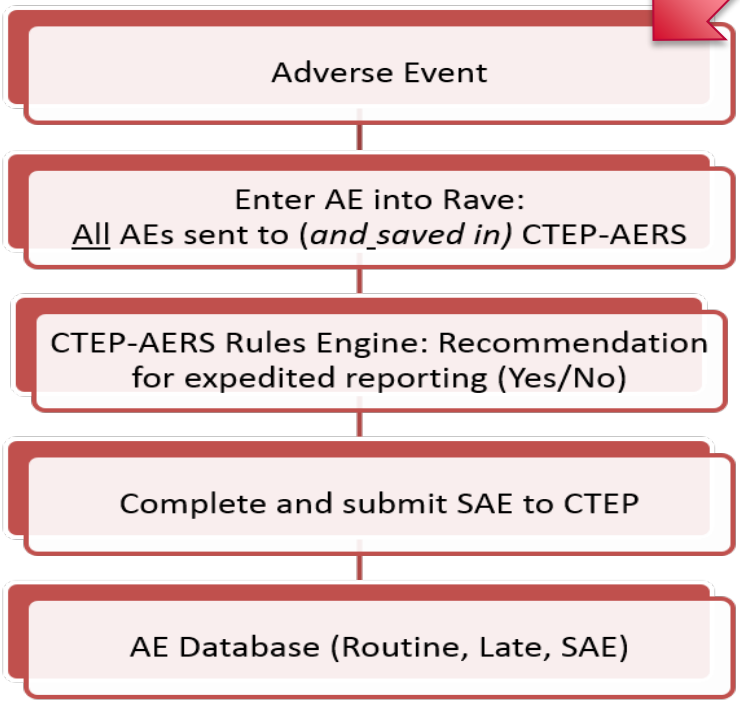
Nurse 'A' or 'B'
Routine AE Reporting



After

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

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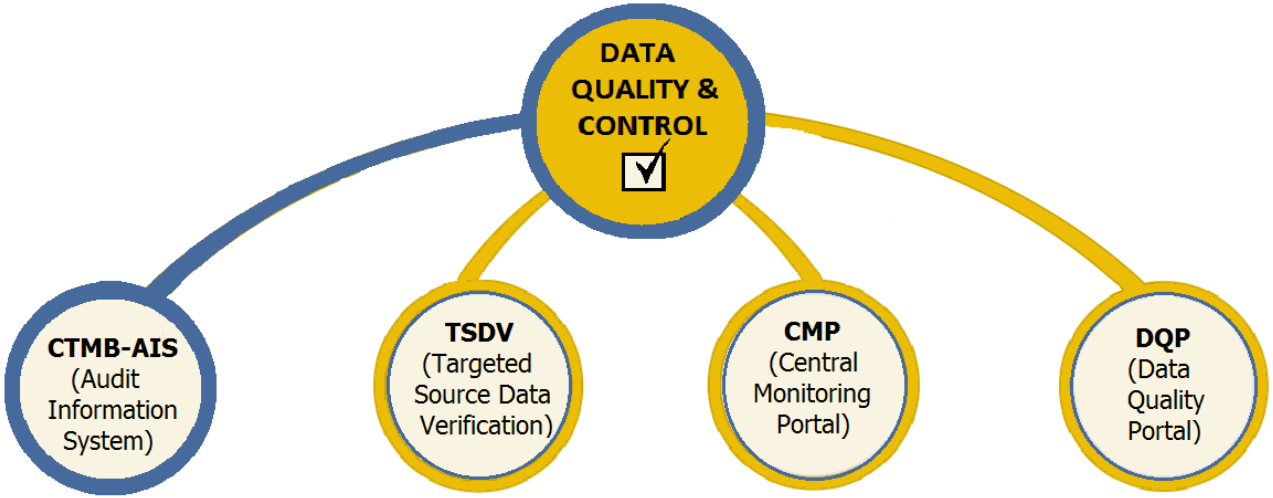
July 12, 2017

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.* *Also may review data points on-site that have been monitored remotely*	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

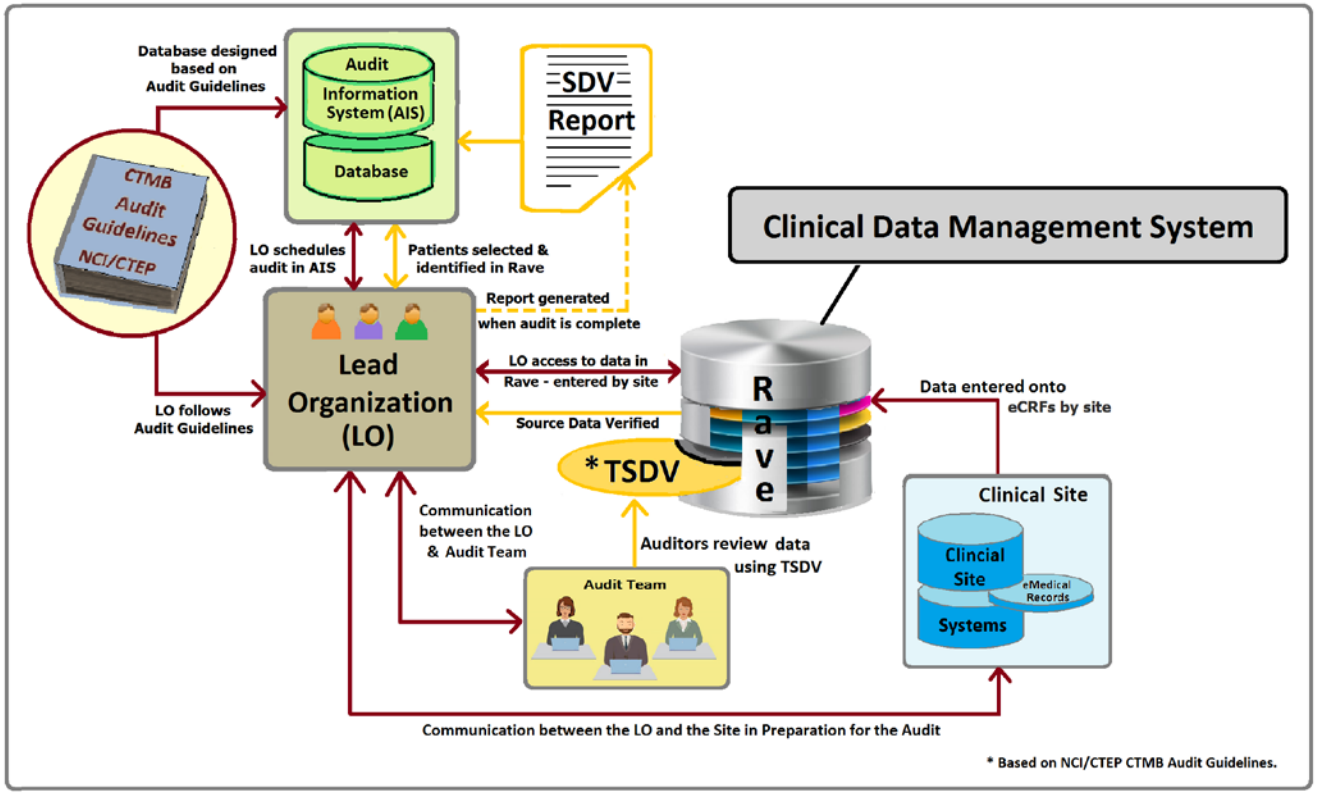
- Tool used within RAVE [Clinical Data Management System]
- Enables source data verification to be recorded

- 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

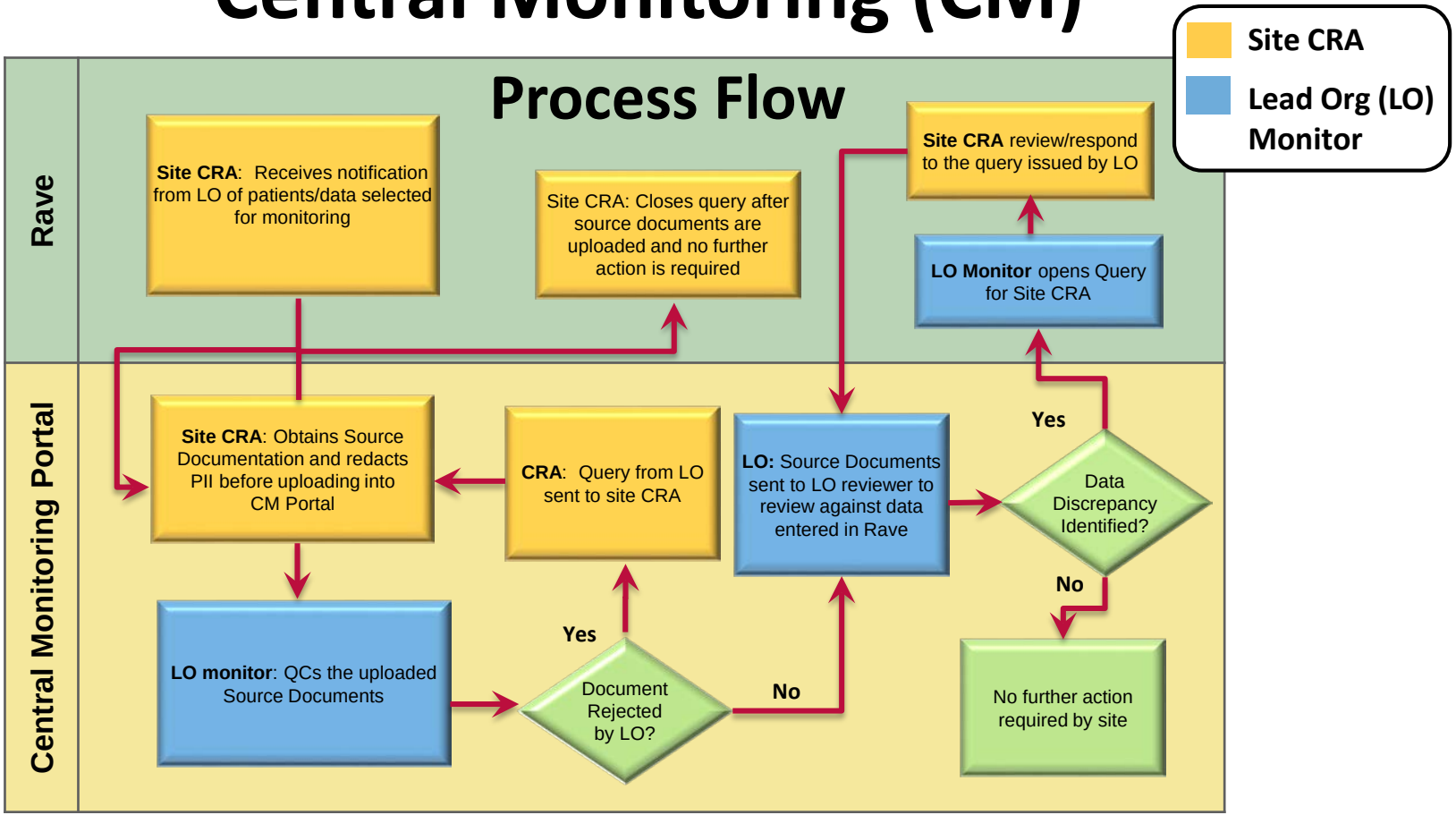
The use of the **T**argeted **S**ource **D**ata **V**erification (TSDV) tool enables the ability to 'record' Source Data Verification activity in Rave



Central Monitoring (CM)
Augmenting the TSDV Process

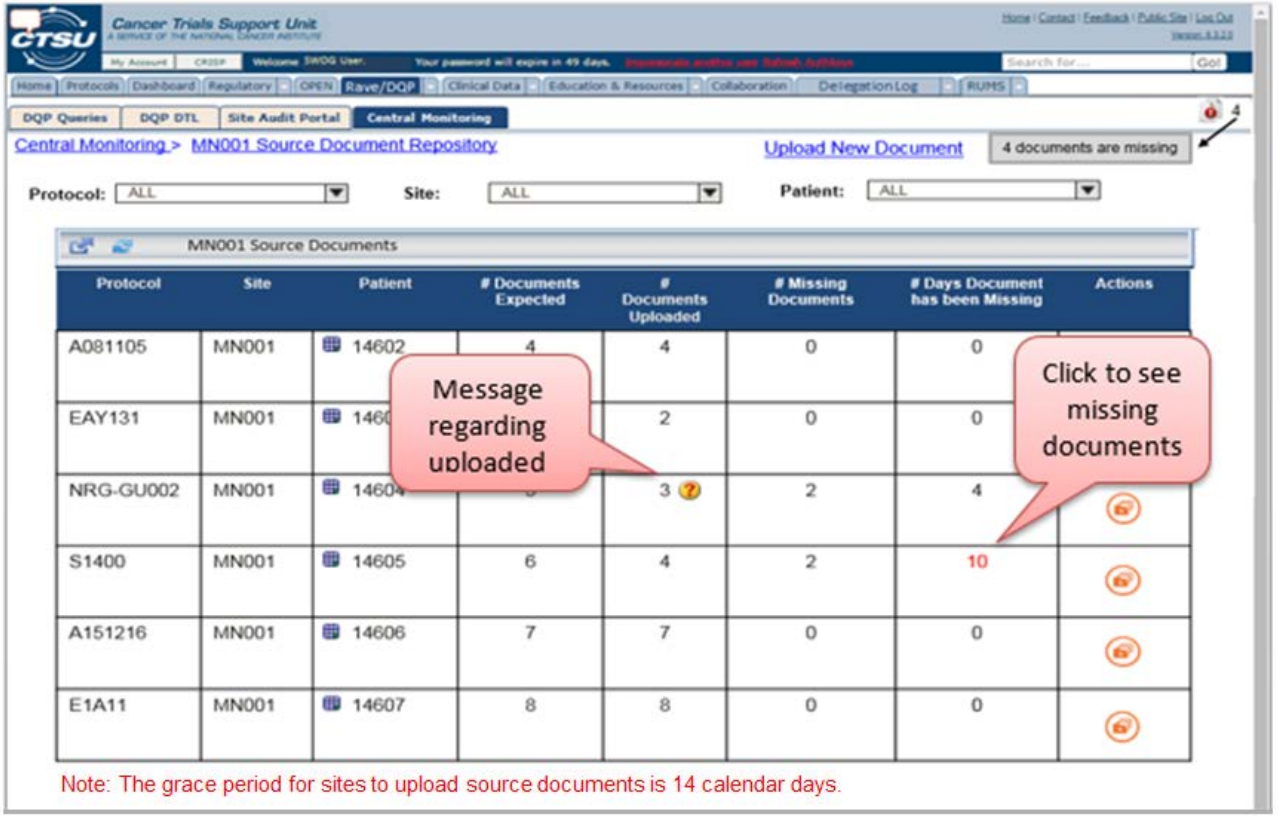
- **ICH E6 (R2) - ADDENDUM of 5.18.3**
  Extent and Nature of Monitoring (Nov 2016)
  - The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials. ... The sponsor may choose ...combination of on-site and centralized monitoring, or ...centralized monitoring. 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)



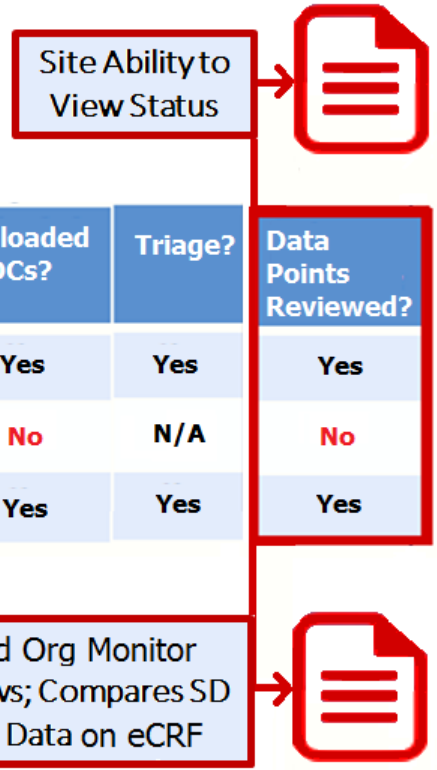
Central Monitoring (CM)

View by Protocol & by Site



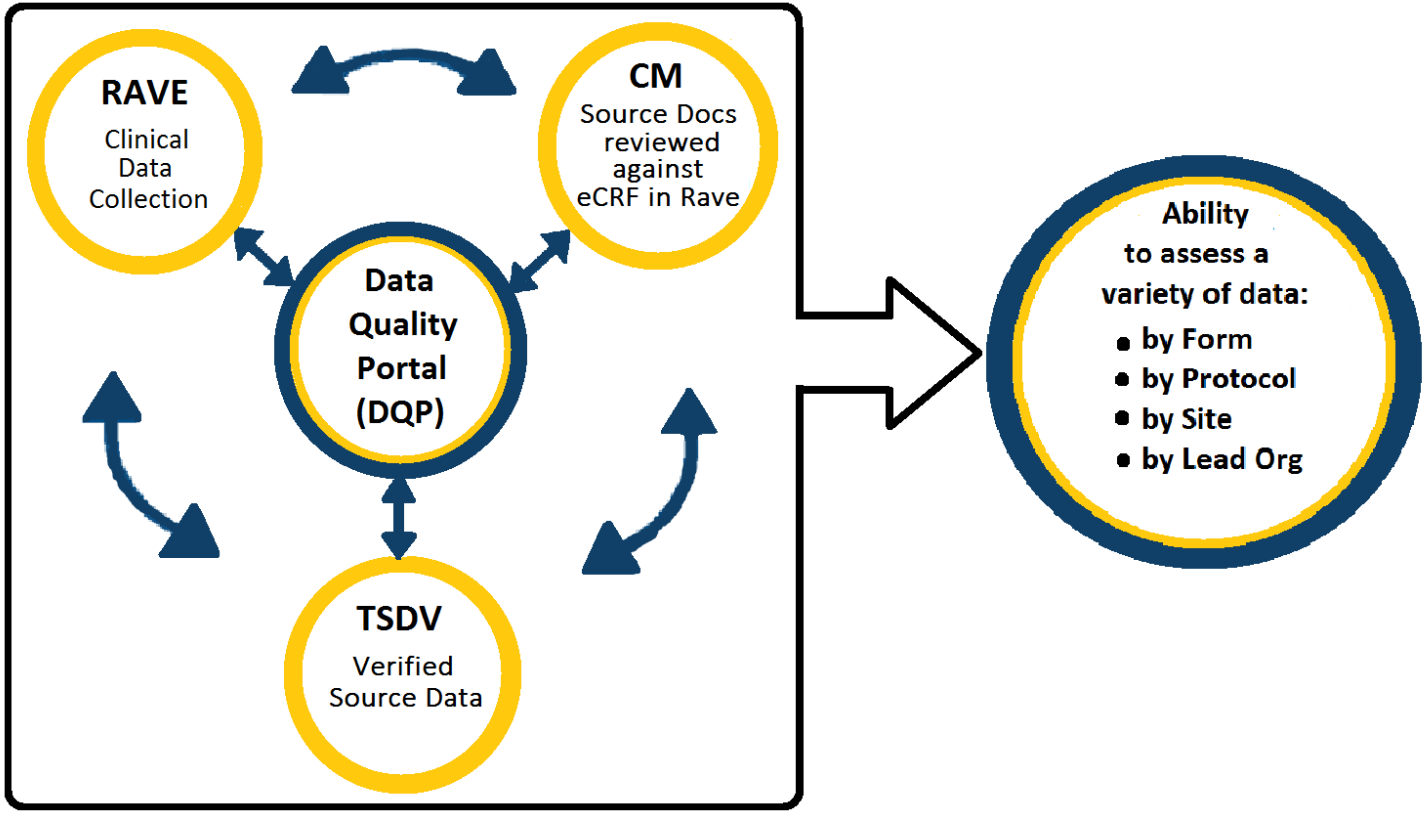
Central Monitoring (CM)

View by Protocol Data Points

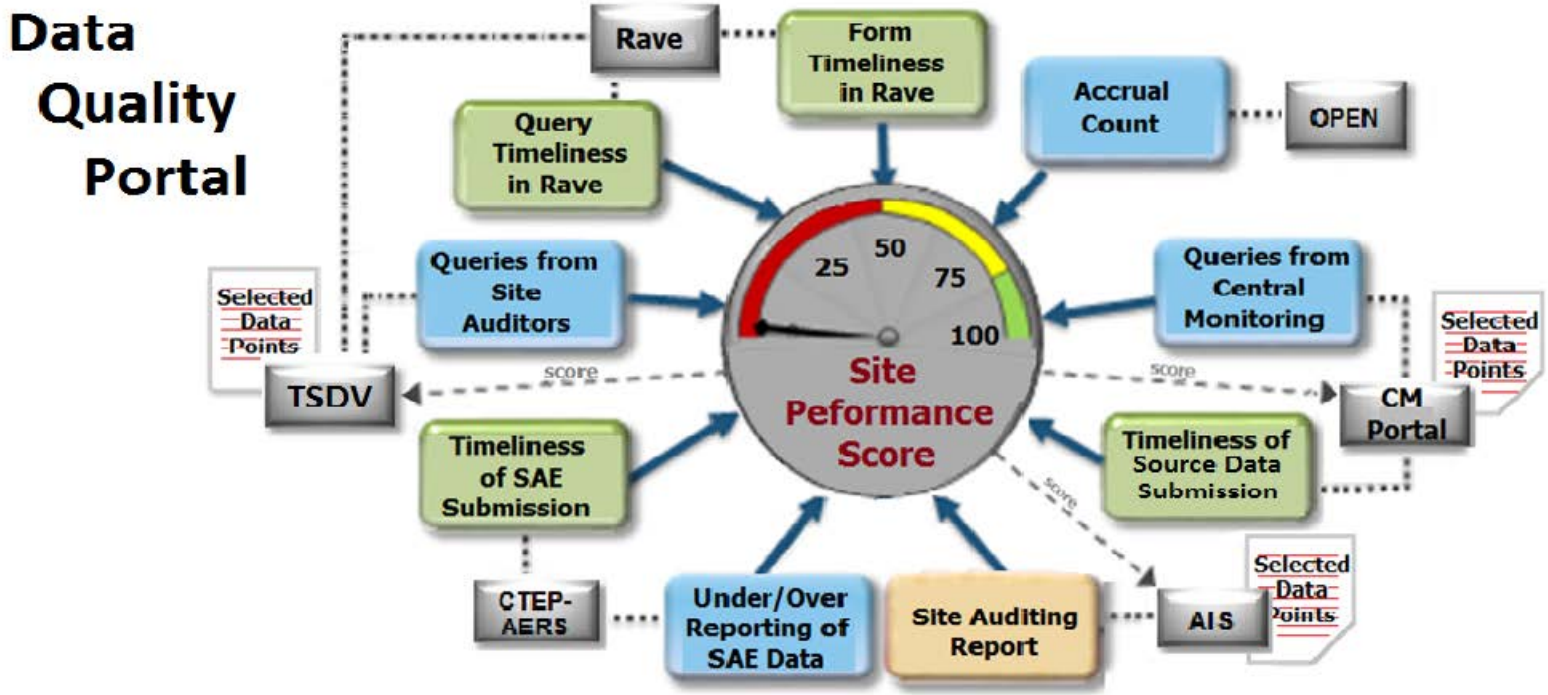


Data Point	Need Review?	DOC Needed for Review	Entered?	Expected Date for SD Upload	Missing DOCs?	Uploaded DOCs?	Triage?	Data Points Reviewed?
DP1	☑	Informed Consent	☑	Data Entry+7	Yes	Yes	Yes	Yes
DP2	☑	Radiology Report	☑	Data Entry+7	Yes	No	N/A	No
DP3	☑	Informed Consent	☑	Data Entry+7	Yes	Yes	Yes	Yes

Data Quality Portal (DQP)



In the Future…



Questions ?

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

Matt Boron RPh

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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)

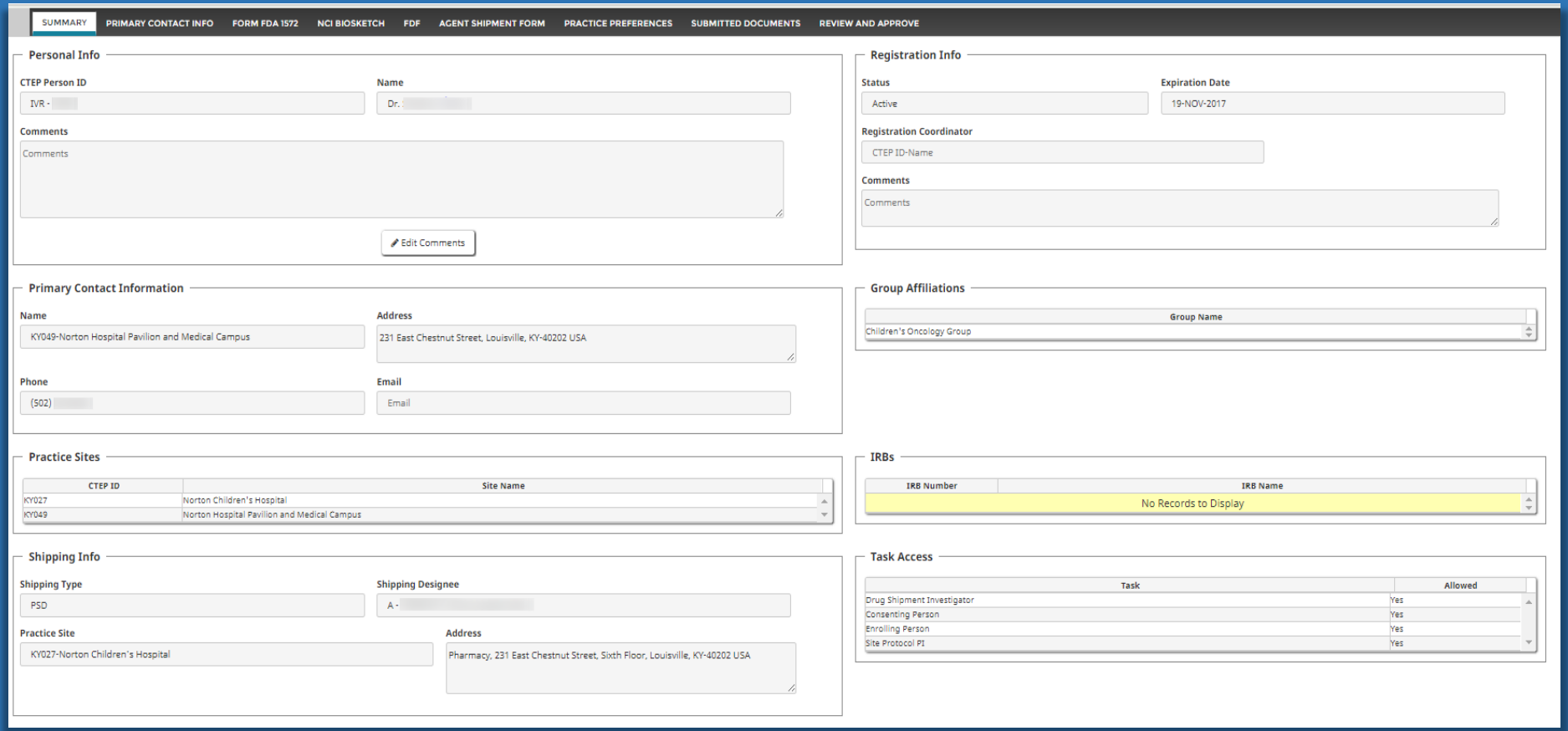
- Electronic FDA Form 1572
- NCI Biosketch
- Financial Disclosure Form
- Designee Form

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



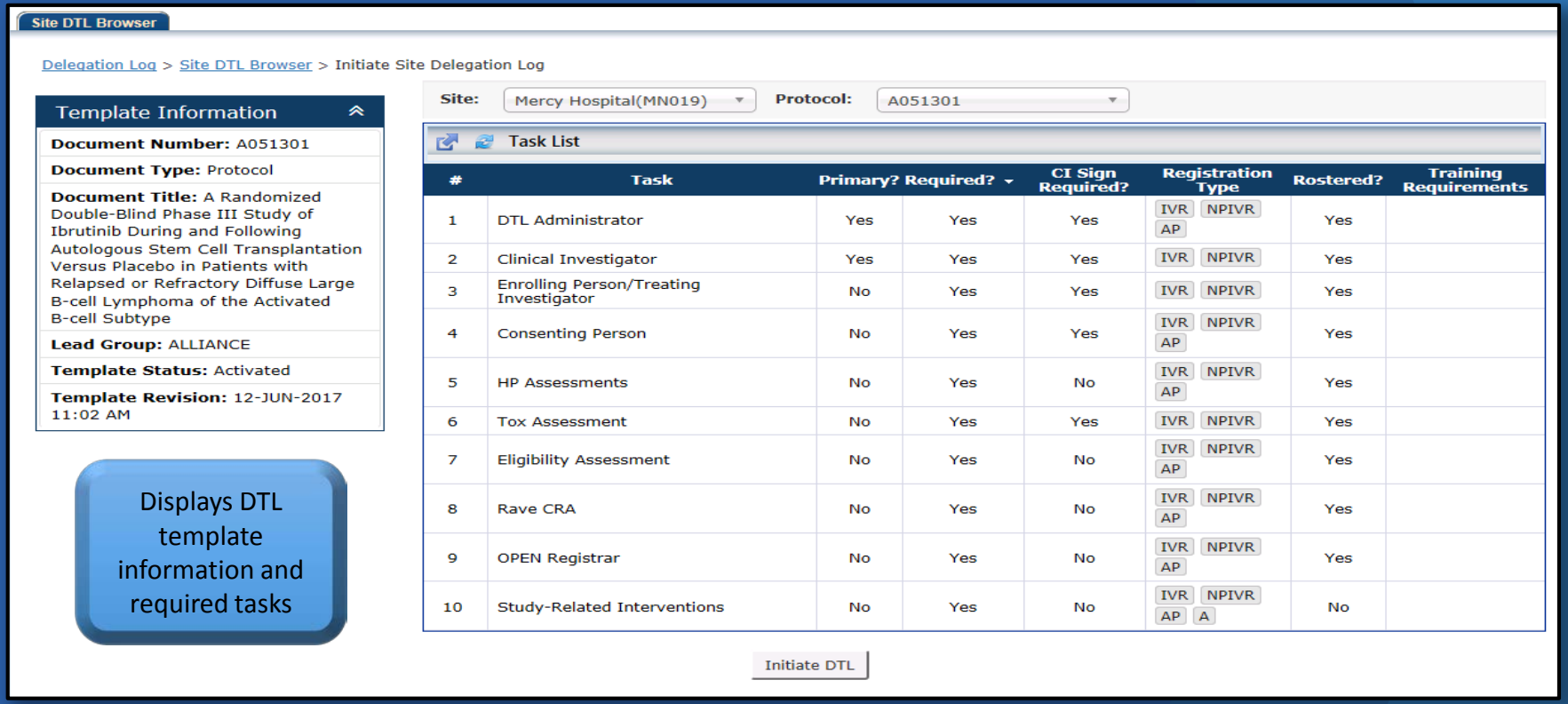
Delegation of Tasks Log (DTL) - Development

- 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

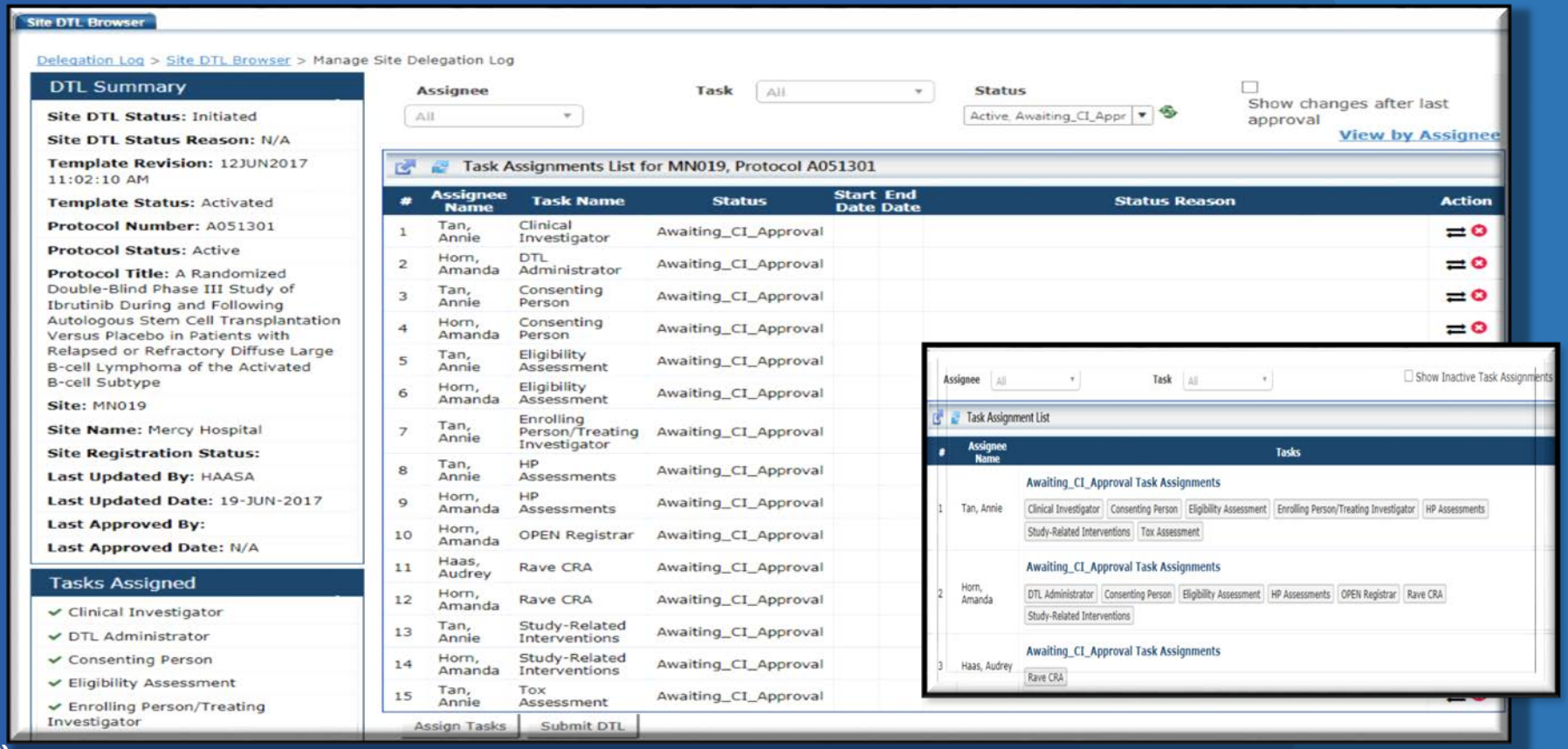
- Identify the Clinical Investigator (CI) and Delegation of Tasks Log Administrator (DTLA)
- Provides a complete list of investigators and sub-investigators
- Identifies individuals that can perform designated tasks on the protocol
- Track changes in task assignment over study lifecycle

Delegation of Tasks Log (DTL) – Protocol Template



Displays DTL template information and required tasks

Delegation of Tasks Log (DTL) – site log

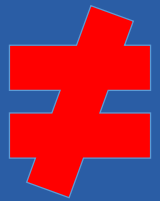


Benefits of NCI Proposed Process

- 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