National Institute of Allergy and Infectious Diseases

DAIDS Monitoring Processes

Cross-Network Site Coordinators Working Group

07 Oct 2019

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Agenda

- Overview of The Monitoring Operations Branch
- DAIDS Monitoring Activities
- DAIDS Monitoring Model
- Process Changes
  - Site Visits Findings
  - Site Visits Work Orders
- Best Practices Review

Monitoring Operations Branch (MOB) Functions

Manage and oversee DAIDS-wide CRS monitoring activities to support DAIDS sponsored research and to fulfill the monitoring obligation of the sponsor

Coordinate with all DAIDS programs to align monitoring resources requirements for existing and upcoming work

Direct the monitoring activities of clinical investigations in compliance with 21 CFR 312.56 and ICH Good Clinical Practices section 5.18

Develop tools and processes to strengthen and enhance site compliance to ICH GCP E6 R2, DAIDS Policies

Develop and execute the clinical site monitoring contract. Provide technical oversight of the monitoring contract.

Develop and implement tools to support risk-based monitoring, and to evaluate the efficiency and effectiveness of new monitoring strategies

HIV/AIDS Networks: Clinical Research Sites

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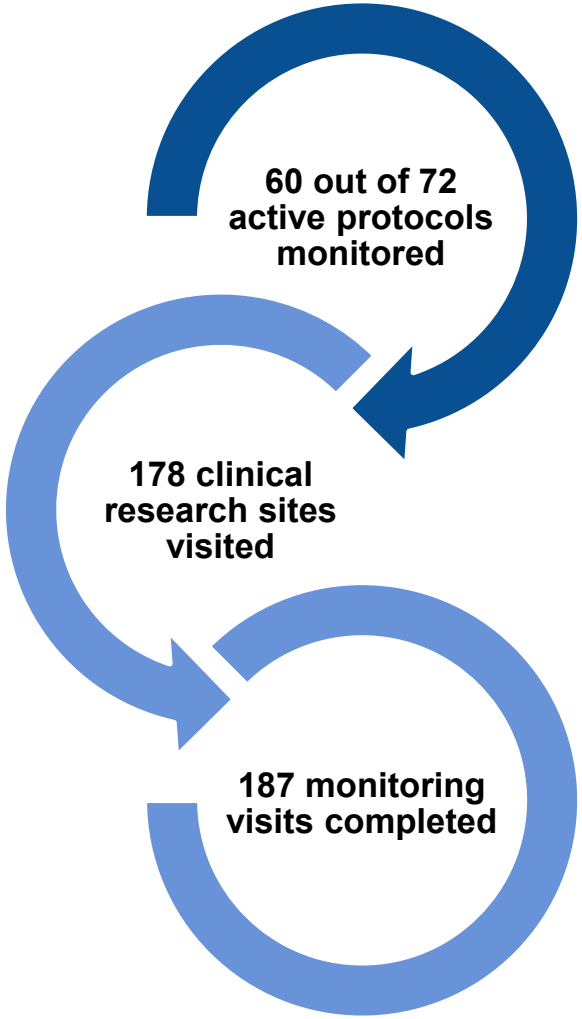
Scope of Monitoring Activities

2Q 2019 SNAPSHOT



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DAIDS Site Monitoring Model

Monitor Responsibilities

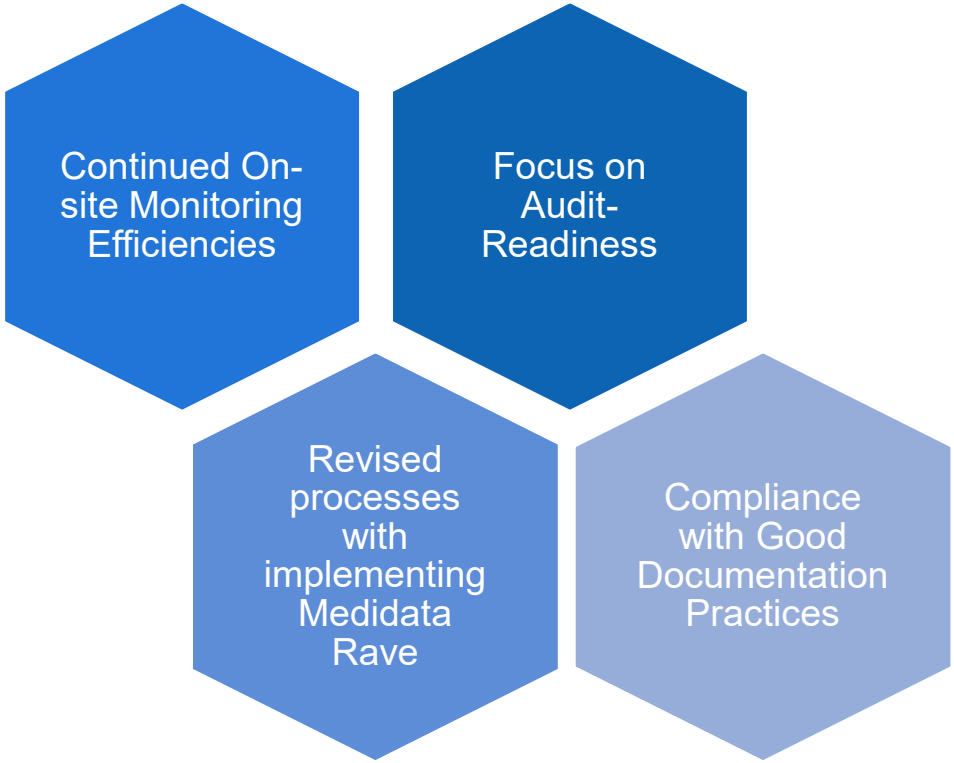
- Verifies, observes and reports findings
- Objective assessment of GCP/ICH compliance, compliance with local/national regulations, SOPs, and protocol
- Detects implementation and process issues on-site which may not be readily apparent via study data
- Offers insight & suggestions to site personnel, based on protocol and regulatory guidelines

PO Responsibilities

- Performs site management
- Reviews & interprets observations noted in Site Monitoring Reports (SMR)
- Identifies significant findings requiring resolution & follow-up, assesses corrective action plan developed by sites, and provides helpful guidance as necessary
- Follows-up on critical events identified by the Monitoring Contractor or through other sources

DAIDS Monitoring Process Improvements

Why did MOB implement recent process changes?



SITE VISIT FINDINGS

Documentation of Visit Findings

Record Review Tools (RRT) Part B

- Monitors complete these tools for each participant reviewed during the monitoring visit
- RRT Part B is used to document record review-related findings (protocol and PID specific)
- Observations noted during the monitor's record review are reviewed with applicable site staff

Process Change - Visit Findings Documentation

PREVIOUS PROCESS

- Monitor prepared Record Review Tool Part B forms while on site so they were ready for signature at end of visit.
- The site staff signed this form at the conclusion of the visit and a copy of each RRT was left on site.
- For very busy sites participating in multiple Networks and protocols, this resulted in the need to make numerous copies of RRT Part B.

REVISED PROCESS

- The site staff signatures are no longer required for the RRT Part B.
- Copies of RRT Part B form are no longer left on site.

Documentation of Visit Findings

Process that remains the same:

- Monitors review significant observations with site staff at the visit debrief meeting.
- Monitors provide written findings after the visit (within 15 business days) through the visit report.
  - The record review summary in the site monitoring report provides detail of observations noted during the monitoring visit.
- If an observation is found or revised by PPD post-visit, then a “Change in Record Review Tool (RRT) Notification Form” will be sent to the site by email.

Advantages of the Process Improvement

Optimizes monitoring time on-site during quarterly visits by allowing monitors to focus on data review and ensuring reported trial data are accurate, complete, and verifiable from source documents at your site.

Increased focus on data review and on the conduct of the trial, allows monitoring to detect any process gaps at the site.

Removes duplication of documentation. Following the visit, the monitor enters the RRT data in to the visit report system. This generates the Record Review Summary, which summarizes all record review findings. This is reviewed and approved by monitor's manager.

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CHANGES TO THE WORK ORDER

Review: Scheduling of Visits

- During the monitoring visit, the monitors propose visit dates for the next quarterly visit at the site.
- This is to manage scheduling at the site and to coordinate monitoring schedules.
- If there are changes to the proposed date, there may be flexibility to make change if communicated prior to the visit confirmation.
- If there is a scheduling conflict which places the ability to complete a visit in any particular quarter at risk, this will be escalated to MOB for discussion of contingencies.

Review: Pre-Visit Letter Notification

The Pre-Visit Letter (PVL) Email Notification is received upon site visit confirmation.

CRS Leader, CRS Coordinator, Pharmacist of Record (if any pharmacy assignments exist in the site visit), CTU PI, CTU Coordinator, ICC users will receive email notifications generated from the system notifying them of the availability of PVL and site visit reports.

Included in the notification is a quick link to access the site visit documents in order to view all relevant documents associated with the site visit.

ANNOUNCED WORK ORDERS CHANGE

With the April 2019 update release of NIAID CRMS, the Announced Work Order was updated to incorporate changes which allowed for accurate reporting of what the site monitor will review during scheduled monitoring visits.

Announced Work Order Process

PREVIOUS PROCESS

- CRS staff receives the Announced WO (AWO) with the pre-visit letter.
- The Pre-Visit Letter is sent to the site no less than fifteen (15) business days prior to the start of the visit.
- The AWO captures 50% of PIDs anticipated to be reviewed during a monitoring visit.
- Sites can view the “Full Work Order” on the start date of the visit. The FWO starts showing up to the site staff on the midnight (12:00 AM EST) of the visit start date.
- The FWO remained accessible through the NCRMS CSM by both site staff and the monitoring team.

REVISED PROCESS

- CRS staff receives the announced WO (AWO) with the pre-visit letter.
- The Pre-Visit Letter is sent to the site no less than fifteen (15) business days prior to the start of the visit.
- The AWO captures 50% of PIDs anticipated to be reviewed for non-TSDV studies. For TSDV studies, the work order will only lists the protocols that will be reviewed during the monitoring visit.
- Sites can view the “Full Work Order” on the start date of the visit. The FWO starts showing up to the site staff on the midnight (12:00 AM EST) of the visit start date.
- The FWO remained accessible through the NCRMS CSM by both site staff and the monitoring team.

Rationale for Changes to the Announced Work Order

With the implementation of Medidata Rave, all enrolled PIDs for which data has been entered in the database would populate the AWO.

Subsequently, the AWO no longer accurately reflected the data your site monitor(s) could review for these protocols during one monitoring visit.

The changes to the AWO ensures that the AWO adheres to good documentation practices and accurately reflects what a monitor will review while on site, focusing on ongoing protocols.

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Site Access to View Pending Review & Verification eCRFs in Medidata RAVE

The Revised Announced Work Order Memorandum dated May 2, 2019 indicated that there are several reports in Medidata RAVE that could be used to assess the status of eCRFs as a tool to aid sites.

These included the Page Status Report, the Comprehensive Page Status Report and the Page Status V2.0 Report.

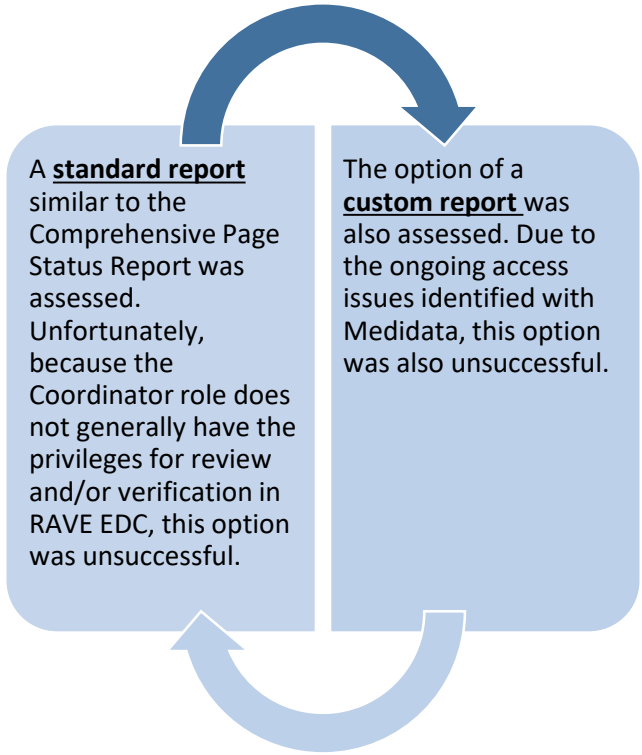
The Comprehensive Page Status report was highlighted as a report that could be used to identify participants and study visits that require verification using the "Page Requiring Action" section of the report.

Subsequent to the release of the memo, the DMCs alerted DAIDS of technical issues and concerns surrounding access to this report. Site access to the report was consequently revoked to remove this risk.

Medidata RAVE: Solutions Explored

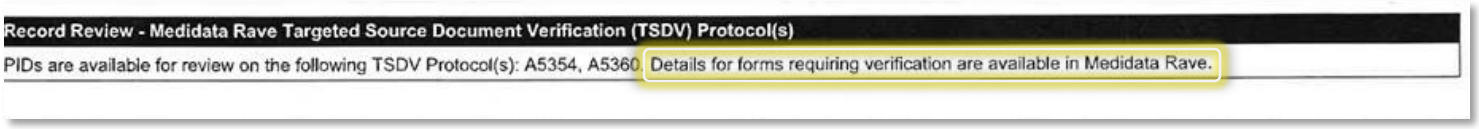
Since identifying the access issue with the Comprehensive Page Status report, both DMCs and the MOB have explored several options and work-arounds with Medidata to provide site users a separate report that would provide details of eCRFs and PIDs pending verification in RAVE EDC.

Solutions Explored



Site Access to View Pending Verification in Medidata RAVE: WO Language

- The Work Orders include language indicating that details for forms pending verification is available in Medidata Rave.



- OCSO MOB is actively working with NIAID CRMS to update the report to remove this language.

Announced Work Order Process

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- The AWO captures 50% of PIDs anticipated to be reviewed for non-TSDV studies.
  - **For TSDV studies, the work order will only lists the protocols that will be reviewed during the monitoring visit.**
- Sites can view the "Full Work Order" on the start date of the visit. The FWO starts showing up to the site staff on the midnight (12:00 AM EST) of the visit start date.
- The FWO remained accessible through the NCRMS CSM by both site staff and the monitoring team.

Let's Talk Best Practices

Before the Visit

Review the Announced and full WO

Review the database to ensure that all data entry is up to date and queries answered.

Prepare documents for the protocol(s) that will be reviewed: Source Documents, Regulatory File, Pharmacy File, Laboratory Specimens /Documentation

During the Visit

Set the Day's/visit Agenda with your monitor (confirm monitoring PIDs).

Additional PIDs may be requested during the monitoring visit. Set a process.

Review queries & set daily debriefs as needed to address questions.

The final debrief of the visit will be a **summary** of what was accomplished, significant observations /findings, outstanding issues for follow-up, and when next visit is to occur.

Review your calendar, confirm availabilities for the next visit.

After the Visit

Review the Site Monitoring Report.

The opportunity to correct discrepancies or challenge findings still exists after monitoring report is released. If there is an error in the report that is found, immediately contact your DAIDS Program Officer for follow-up.

Address issues (specific and systemic). Review and address database queries.

Begin preparing for next visit

Let's Review

The purpose of monitoring is to ensure that:

a) the rights and well-being of participants are protected;

b) reported trial data are accurate, complete, and verifiable from source documents; and

c) conduct of the trial is in compliance with the currently approved protocol/amendment(s), GCP, and applicable regulatory requirement(s) (ICH/E6: GCP Sponsor Obligations: 5.18.1)

As DAIDS strives to improve the effectiveness and efficiency of monitoring, current approaches, systems, and processes are continually evaluated to ensure compliance with good clinical practices and regulations.

Common vital goal is the success of research trials by **ensuring the safety of our study participants and integrity of study data**.

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Questions

OCSOMOB@niaid.nih.gov