MOB Report

Office Of Clinical Site Oversight (OCSO)

National Institute of Allergy and Infectious Diseases (NIAID)

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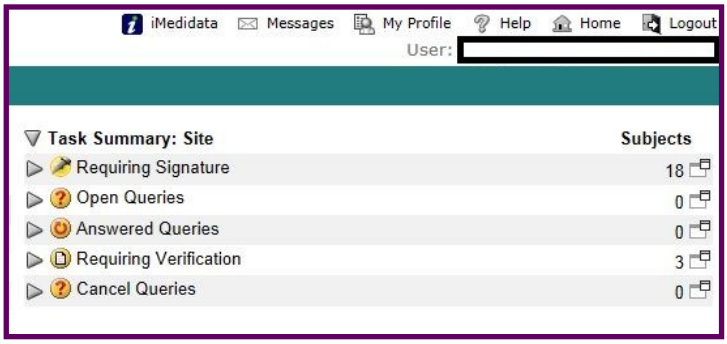
In this issue

iMedidata RAVE

By: Nguyen Tang, PPD CRA

Does your site have an upcoming monitoring visit? Are you feeling lost with where to start with the new iMedidata system? From my eight years of cumulative experience across multiple sites as both a coordinator and a monitor, the following are the most important tips to share that enabled me to confidently navigate through Medidata and better prepare my sites for monitoring visits.

We'll begin with the Task Summary panel located on the right side of your protocol home page. This will be your best friend for each protocol in iMedidata. As more protocols begin to utilize this new system and with so many pages for each participant, things can start to feel overwhelming as you try to navigate and keep track of every item. This panel will simplify things by indicating any items that require your attention from opened queries, to pages that require your signature. Not only this, but you can go directly to these pending items by simply clicking on them instead of having to search around.



In addition to utilizing this panel, one of the most important, but often overlooked tips is to ensure that you log into iMedidata frequently to evaluate your pending workload. This will strengthen your capabilities to address any outstanding queries prior to the monitoring visit. This is especially important for the site if the DMC has to request any additional supporting documents to clarify data entered. As we all know, the process of requesting medical records from other institutions usually takes longer than anticipated. So the sooner these requests are identified, the sooner the site staff can request and receive these records prior to the monitor's arrival. In doing this, you will also keep your query count down and free up your calendar to address other circumstances that may arise, such as a participant coming for an unscheduled visit while the monitor is on site. Although this may seem like a minor and burdensome process, it carries grave consequences as it is directly correlated to the safety and welfare of your participants. By actively ensuring all information is up-to-date on a regular interval, you are providing data management with the ability to identify and track trends across all correlating studies in real time.

Clinical research is a dynamic field. There will always be new processes and new systems that will be developed to better aid us in searching for better treatment options for everyone. Eventually the Data Management Centers will transition all new protocols to the Medidata system, which will help streamline data collection and sharing of data.

Evaluation of Inclusion and Exclusion Criteria:

An Overview of Enrollment Violations Reported and tips for monitoring

Factors that allow someone to participate in a clinical trial are inclusion criteria. Those that exclude or disallow participation are exclusion criteria. These criteria are meant to ensure participants safety during a clinical study and provide data of participant eligibility for the study, therefore minimizing withdrawal and ensuring that primary end-points of a study can be reached.

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Evaluation of inclusion and exclusion criteria is a key process that must be conducted by trained and experienced personnel and documented following ALCOA-C (Attributable, Legible, Contemporaneous, Original, Accurate and Complete) principles.

Failure to adhere to inclusion/exclusion criteria may be considered a failure to ensure the rights, safety, and welfare of the enrolled participant and may impact study outcomes or data integrity.

In DAIDS sponsored clinical trials, the site's evaluation of inclusion/exclusion criteria is routinely reviewed by Monitors during monitoring visits. Violations related to inclusion/exclusion criteria are reported as Critical Events, in accordance with the DAIDS Critical Events Policy and the PPD/NIAID NCSM PWI "Identification and Sponsor Notification of Critical Events ". This Project Work Instruction is aligned with International Conference on Harmonisation (ICH) guidelines and the applicable sections of the Code of Federal Regulations (CFR). Evaluation and monitoring of inclusion/exclusion criteria must also be aligned with local regulations and applicable policies.

During the last three quarters, a number of enrollment violations have been reported.

In this article, the enrollment violations reported in DAIDS sponsored clinical trials from July 2016 through March 2017 (3Q2016 to 1Q2017) will be reviewed to determine the processes involved in the evaluation of inclusion/ exclusion criteria where the findings were reported.

Table I details the number of Enrollment Violations reported per Category for DAIDS sponsored clinical trials from July 2016 through March 2017

Table I. Number of Enrollment Violations reported per Category for DAIDS sponsored clinical trials from July 2016 through March 2017

Category of Enrollment Violations	Total per Category
Participant confirmed by monitor to be ineligible by evaluations being performed outside protocol-defined screening period ("window")	10
Participant confirmed by monitor to be ineligible per inclusion or exclusion criteria	8
Unable to verify eligibility due to inadequate or missing documentation.	7
Total	25

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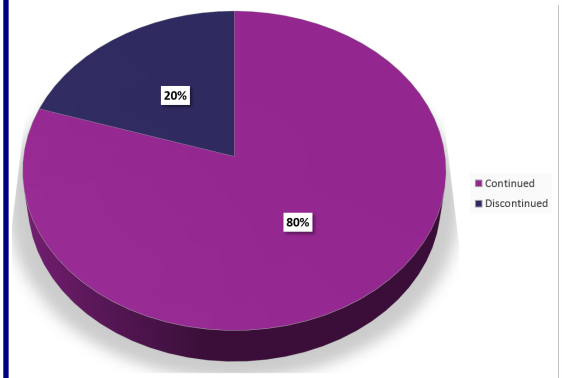
All of these Enrollment Violations were reported to DAIDS and to the respective Institutional Review Boards (IRBs). Five violations lead to participant discontinuation from study treatment (20% of total Enrollment Violations – Graphic 1).

Based on the information above, it is important to point out the impact of Enrollment Violations on participants' continuation and data integrity. Since Enrollment Violations are Critical Events, the monitor will recommend corrective and preventive actions, and notify the sponsor as per the Critical Events communication process.

The following is further information regarding Enrollment Violation categories with tips and guidelines to avoid recurrences.

Graphic 1:
Participant confirmed by monitor to be ineligible per inclusion or exclusion



Participant confirmed by monitor to be ineligible per inclusion or exclusion criteria.

Site staff should remember to verify all inclusion and exclusion criteria against the protocol to ensure participant's eligibility is confirmed, even though the data have been previously collected and evaluated.

In some cases, a participant was enrolled using available information at the site; however, further source documentation was later obtained from other departments of the same institution, with discrepant information that met an exclusion criterion. During monitoring visits, monitors must review all available data and discuss with site personnel the sources where the information is being collected for enrollment purposes.

Tips for site to follow-up:

- Site must ensure all available source documentation is obtained prior to enrolling a participant. If a participant was evaluated in other departments or an external institution, the site must consider collecting further information from external sources when possible, especially from departments that can provide significant information related to inclusion/exclusion criteria.
- Site personnel responsible for evaluation of inclusion/exclusion criteria must be trained and capable of interpreting study lab values or other clinical results in order to ensure correct verification.
- It is also important to ensure that site personnel are aware, in a timely manner, of new protocol updates and their effective date for implementation.

Participant confirmed by monitor to be ineligible by evaluations being performed outside protocol-defined screening period ("window").

In order to facilitate the verification of validity of evaluations and lab reports during monitoring, monitors verify key dates such as a screening date, an enrollment date, a study drug assignment date, and other dates on hand.

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Monitors ensure there is evidence that lab reports and evaluations were evaluated within protocol defined specified time period. They verify that lab reports are signed and dated by the reviewing personnel. Further details of lab report review can also be documented in the medical records.

Tips for site to follow-up:

- Site must carefully verify that evaluations are contemporaneous and valid for criteria evaluation. If enrollment does not occur within the period of validity of the laboratory results, instructions in the protocol should be followed.
- Depending on site laboratory systems the lab reports can potentially be set up to automatically generate exclusion flags to indicate an exclusion value according to the exclusion criteria set by the sponsor for a specific protocol.

Unable to verify eligibility due to inadequate or missing documentation.

Sites must ensure all information related to inclusion/exclusion criteria from a participant is consistent among all source documentation. Medical records and other study reports/forms are often completed by different site personnel during a study visit.

To verify the consistency of source documentation, the monitor identifies the documents where criteria can be reviewed/validated, and compares these documents to each other.

Tips for site follow-up:

- Personnel must identify all source documentation where each inclusion/exclusion criteria can be verified, in compliance with DAIDS Source Documentation Requirements Appendix 1 DWD-POL-CL-04.00A1. In addition, this documentation must be available during eligibility evaluation and for monitoring/audit/inspection purposes. This tip also applies for all other study procedures.
- In order to avoid discrepancies, site personnel should verify information previously recorded by other personnel through the sites' internal quality assurance and quality control process. If there are discrepancies between two or more source documents, clarification should be provided from the personnel who collected the information before continuing with the enrollment process.

A general suggestion to prevent enrollment violations is that the Investigator of Record (IOR) or other qualified site personnel performs a quality check of all inclusion and exclusion criteria before enrolling a participant. This quality check is performed and documented in the medical record and can be verified by the monitor.

Evaluation of inclusion/exclusion criteria is not only a checklist to be completed; but it is an evaluation process that needs to be carefully performed by all personnel involved in order to ensure participants safety and the quality of the information collected.

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In Case You Missed It

New DAIDS Requirement: Protocol Signature Page (PSP)

The Division of AIDS has implemented a new regulatory requirement, a **PSP,** to document the commitment of the Investigator of Record (IOR) to conduct the trial as agreed to by the sponsor and in compliance with the following; United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/ Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements and institutional policies.

DAIDS/PPD Survey

Thank you for participating in the recent PPD survey. The response rate was great and we appreciate your time and effort. We are reviewing the results and compiling an analysis. We take concerns highlighted by the survey very seriously. Information on plans and processes to address these concerns are forthcoming.

DAIDS announces 3 New courses available at https://daidslearningportal.niaid.nih.gov

Monitoring 101 is designed to help you understand the purpose and processes that are part of DAIDS monitoring activities. While the idea of monitoring visits may cause anxiety at a site, the visit is meant to be a collaborative effort to ensure your site is always ready for any potential regulatory agency inspection. This course includes interactive exercises to verify your level of understanding.

FDA/EMA Inspections Awareness is designed to help you understand the processes associated with both FDA and EMA inspections and to provide guidance for preparation before, during, and after an inspection using interactive exercises, knowledge checks, and references. Additionally, it covers both Routine and For-Cause inspections by both regulatory agencies.

Introduction to Quality Management course provides site staff with a basic understanding of quality management and how to apply quality practices to clinical research activities. After completing this course, you will be able to define key terms related to quality management; understand regulations and guidelines related to quality management; demonstrate an application of tools and techniques; and review best practices for communicating quality measurements and outcomes at your site.

Monitoring Metrics

Overview of Monitoring Metrics—February and March 2017

Monitoring Trips and Visits

119 Monitoring Visits

Monitoring Visits: Any time a monitor travels to a site to conduct monitoring.

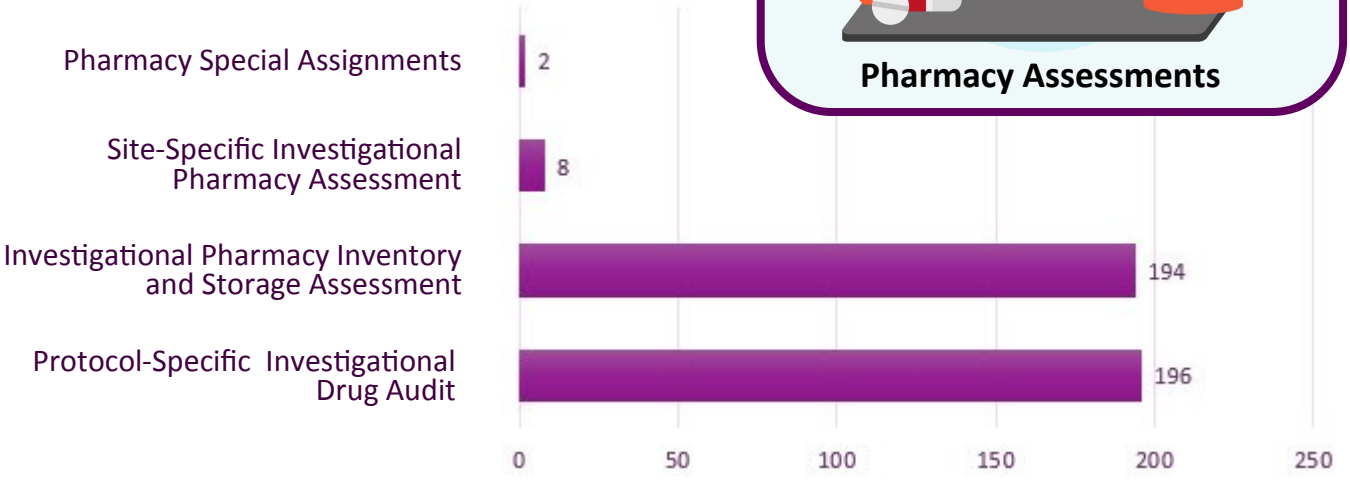
207 Monitoring Trips

Monitoring Trips: Includes the total number of monitors traveling to a site to conduct a site monitoring visit.

1526 Records Reviewed

400

Pharmacy Assessments



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Manager and Monitor Spotlight: North America

Karen Hufham received her Bachelor's Degree in Nursing and Post-Graduate Certificate in Project Management from the University of North Carolina at Wilmington. Karen's early nursing career included hospital, nursing home, and private practice management positions. She came to PPD as a CRA on the DAIDS contract in 2004. In 2006, Karen moved to the CTM role and has been the PPD IT Liaison during the three contract periods for the development and maintenance of the NCRMS. She has also expanded her career at PPD to include industry trial management, but remains on the current contract as the North American functional lead. Family and friends are very important in Karen's life, and she enjoys spending time with two daughters and two granddaughters, and two four-legged fur-babies.

Jamie Culp has a Bachelor's Degree in Kinesiology and completed his coursework towards a Master's Degree in Exercise and Nutritional Science prior to embarking on a professional volleyball playing and college coaching career. He began working in the pharmaceutical research industry as a Clinical Data Manager for 1.5 years at PPD's Phase I Clinic in Austin, Texas. He was brought on as a CRA with the CSMG in 2005 and has been a part of the government group ever since. He initially focused on prevention (HVTN and HPTN networks) but has also worked on ACTG and IMPAACT networks over the last several years. He spends his free time working out at the gym, enjoying the outdoors, traveling, volunteering with Special Olympics, and spending precious time with family and friends.

Nikki Cortez has a Bachelor's Degree in Business Administration from Georgetown University and a Master's Degree in Early Childhood Education. Prior to entering the world of research, she taught first grade at a charter school in Brooklyn, New York. Following her move from New York to Philadelphia in 2011, she began working as a Clinical Research Coordinator in Women's Health at the University of Pennsylvania (UPenn). She joined the Compliance Team as an Auditor at UPenn in 2015 and became an Institutional Review Board (IRB) member as well. In August of 2016 Nikki started at PPD in the Government Group as a CRA on the CSSM (now NCSM) contract. In her free time she enjoys taking long walks with her dog, running outdoors, and visiting her family in New York.