Office Of Clinical Site Oversight
National Institute of Allergy and Infectious Diseases (NIAID)

MOB Report

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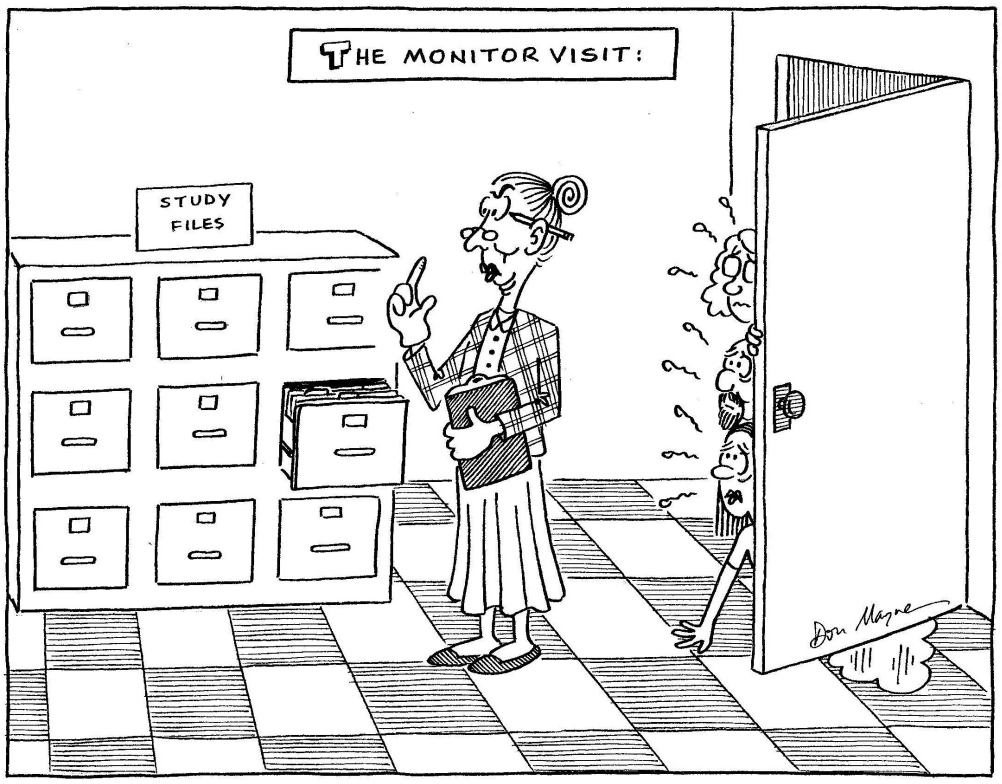

Are Your Files Clean?

Contrary to the stereotypical notion that this cartoon pokes fun at, monitoring visits can be a source of information and are essential for ethical studies. After all, a study that fails to produce verifiable data has put subjects at risk for no benefit. Worse, future patients may be harmed from reliance on false or misleading data.

By making sure that research files are in order at all times (and not commingled with medical records), a coordinator can save lots of headaches and frantic scurrying before the monitor's visit. "Squeaky clean" files can also help with annual preparation of the IRB continuing review application.

Monitoring visits should include a review of the IRB correspondence file for each study. A log of documents sent to the IRB and responses received is often helpful.

(Of course, IRB coordinators have been known to exhibit the same reactions when the FDA announces an intended IRB visit!) ■

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FDA is Comin' to Town....

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CRS Pharmacies, Pharmacy Establishment Plans (PEP), and Global Pharmacy Services (GPS) Baseline Assessments

by Scharla G. Estep, M.S., RPh Senior Pharmacist, Pharmaceutical Affairs Branch

You may recall the wording "Complete and submit a PEP by the pharmacist of record (POR) for each pharmacy affiliated with the CRS to the DAIDS Pharmaceutical Affairs Branch (PAB)?" It was a part of every letter sent from an OCSO Program Officer (PO) to a CTU PI and CRS staff in 2014. In addition, each time PAB learns a new pharmacy is going to be used by a site participating in a DAIDS Network study, a PEP will be sent to the PoR for that pharmacy (to complete and submit). The good thing is, once a DAIDS PAB PEP has been reviewed and approved for a specific pharmacy (physical location), it is good for the remainder of the grant cycle (although additional storage/equipment or Chain of Custody modules may be needed if not previously submitted and approved). Unfortunately – the PEP only provides operational information and PAB has to create their own visualization of what the pharmacy itself looks like in which study product is being managed.

You may ask doesn't PAB see the monitoring reports, because if the CRS is conducting a DAIDS sponsored protocol involving study product, that CRS pharmacy is already being visited by Pharmaceutical Product Development (PPD) monitors? However, as you also should know, during that visit the monitor(s) conduct protocol specific pharmacy assessments at that CRS. The visits are typically 4 hours long and really do not give PAB a visual picture of the pharmacy itself.

PAB in collaboration with the Monitoring Operations Branch (MOB) began requesting pharmacy centered baseline assessments separate from the routine (protocol centered) monitoring visits. These pharmacy specific assessments are conducted to provide an actual visual assessment of a pharmacy (for example: the layout of the pharmacy and storage areas, the space, the workflow, and the areas in which study product is stored and prepared, including but not limited to refrigerators and freezers). Because the GPS team at PPD is composed of monitors who are pharmacists or have more expertise in pharmacy, the detail provided in reports from GPS visits provides a snapshot in time of the pharmacy, which can be used as a point of reference for multiple users. The reports are uploaded in the DAIDS Clinical Site Monitoring (CSM) by Pharmacy ID rather than by CRS ID so that all CRS Leaders/Coordinators with which a pharmacy is associated will see the same baseline report without focus on any one specific CRS.

Although GPS visits have been taking place for some time, a recent change was made to the NIAID Clinical Research Management System (NCRMS), CSM Module to better align the entire baseline GPS pharmacy process with other monitoring visits. The GPS visits will now be requested by PAB through the DAIDS CSM Module. Upon review by the GPS monitor, the monitor communicates with the PoR to determine a visit date and then plans the visit. Once planned, an automatically generated email will be sent to all the network CRS PoR(s) associated with a Pharmacy. This email will contain a link to both the Pre-Visit Letter (PVL) and the Announced Work Order. It is critical that the PoR view the PVL prior to acknowledging successful receipt. By acknowledging the PVL, the PoR is confirming their presence for the full duration of the GPS visit. Once the visit is completed a final GPS baseline report will be issued. The PoR will be required to read and acknowledge the pharmacy report as well as respond to any queries from PAB as they do with routine monitoring visits.

Once the final baseline pharmacy report is released, everyone at a CRS who has access to monitoring reports will be able to view the GPS baseline report for the pharmacy(ies) associated to their CRS via the DAIDS CSM. Keeping these reports in the DAIDS CSM will provide a historical visual view of pharmacy operations (including study product storage capabilities).

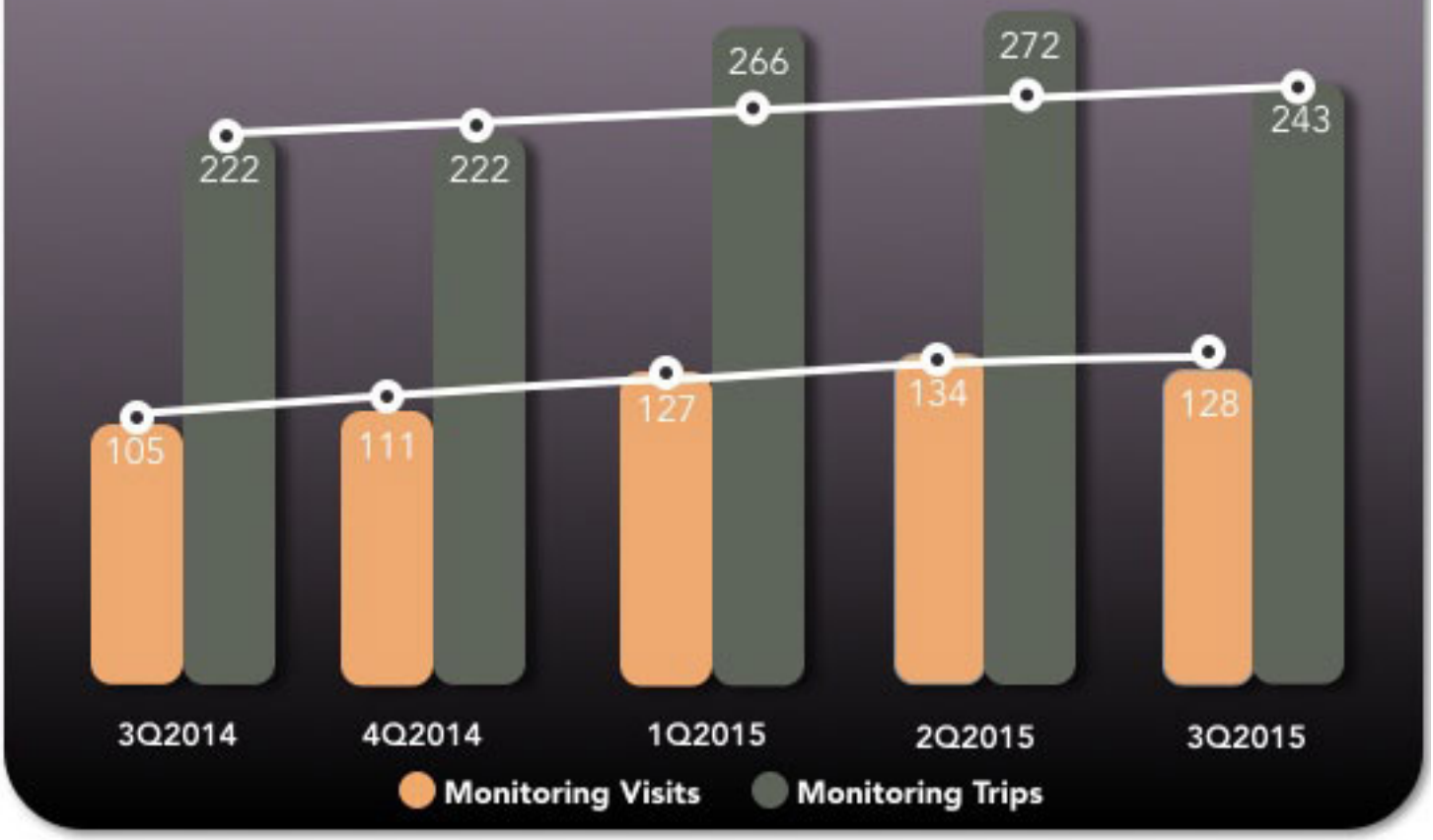
To ensure all PoRs are trained on using the NIAID CRMS, DAIDS CSM, a refresher training will be offered a couple of times in the next several months. ■

Monitoring Metrics

Overview of Monitoring Visits and Trips to Date

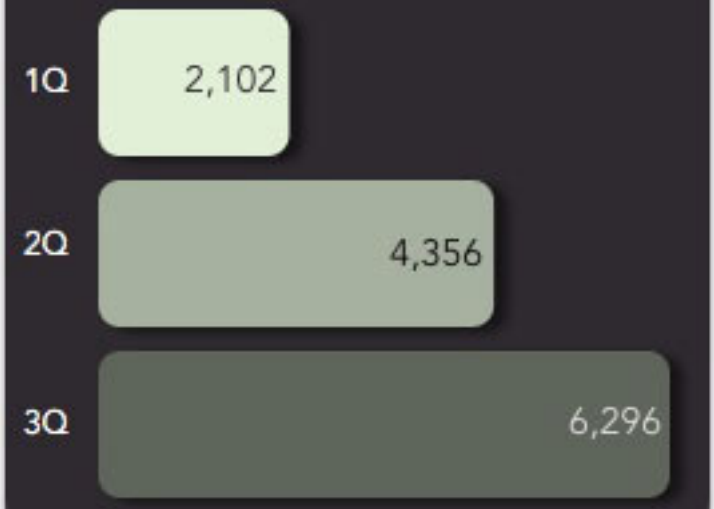
Monitoring Trips and Visits

Over the past 5 quarters, OCSO has conducted a total of 605 Monitoring Visits and 1,225 Monitoring Trips.



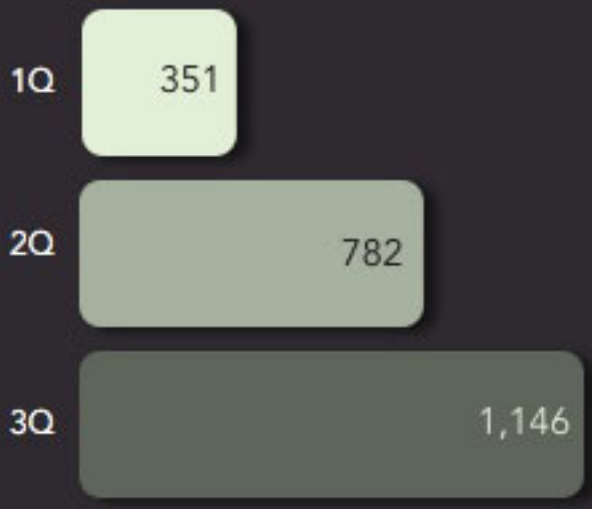
Record Review FY15

(Running Total)



Pharmacy Assessment FY15

(Running Total)



Accessing the DAIDS Adverse Experience Reporting System (DAERS)

All clinical research sites (CRSs) must have access to DAERS before a study begins in order to report expedited adverse events (EAEs) to DAIDS during the course of a study. At a minimum, each CRS must have two (2) staff members who, amongst themselves, have a combination of DAERS "reporter" and "submitter" roles.

A "reporter" is any CRS staff member whom the Investigator of Record (IoR) has authorized to initiate EAE reports using the DAERS system. A "submitter" is any study physician who will submit and electronically sign EAE reports in DAERS.

The following steps should be taken by CRS staff to obtain access to DAERS:

1. The CRS Leader or CRS Coordinator requests access for CRS staff using the Site Enrollment Module in DAERS for all protocols with EAE reportability to DAIDS. They must provide the user's name, contact information (e-mail, phone, and fax) and DAERS role (i.e., "reporter" or "submitter") for each protocol.
2. Selected staff must complete the on-line DAERS training (i.e., DAERS – New User Introductory Webinar) on the DAIDS Learning Portal at **https://www.daidslearningportal.com/**.
3. Selected staff must send a certificate documenting training completion to NIAID CRMS Support at **CRMSsupport@niaid.nih.gov**.
4. "Submitters" must
   a. Mail a signed, original, hard copy study physician Attestation and Agreement for Electronic Signatures form to the DAIDS RSC Safety Office, and (see **http://rsc.tech-res.com/safetyandpharmacovigilance/expeditedreportingdaers.aspx**)
   b. Be study physicians listed on either the FDA 1572 form or DAIDS Investigator of Record Agreement (IoRA) form. Note: These documents must be submitted to the DAIDS Protocol Registration Office at the DAIDS RSC during protocol registration. ■

For questions concerning DAERS access and training, please contact:

NIAID CRMS Support

Phone: +1 (240) 778-2517
Email: **CRMSsupport@niaid.nih.gov**

For questions concerning the attestation form and EAE reporting, please contact:

DAIDS RSC Safety Office

Phone: +1 (800) 537-9979 (US toll free) or +1 (301) 897-1709
Email: **DAIDSRSCSafetyOffice@tech-res.com**
Fax: +1 (800) 275-7619 (US toll free) or +1 (301) 897-1710
Mail: DAIDS RSC Safety Office
6500 Rock Spring Drive, Suite 650
Bethesda, MD 20817 (USA)

Decoding the Monitoring Codes: A72 versus A17 versus A16

by Veronica Sims, Physician Assistant (PA), Certified Clinical Research Associate (CCRA), Clinical Team Manager (CTM), PPD

During my ten years at PPD as a Clinical Research Associate (CRA) and a CTM, I have had the privilege of interacting with many individuals around the world. Answering questions and working in collaboration with Clinical Research Sites (CRSs) conducting DAIDS protocols is a part of my job that I find rewarding.

One of the most common questions that CRAs receive from CRSs is: **How do you know which Monitoring Code to use for items that are identified during a monitoring visit?**

Monitors utilize a standardized coding system to categorize the items and issues that they find during record review. These codes are designed to make sure that all parties understand what the finding is, the severity of the finding, and what area of the record review is affected. Three monitoring codes that seem to cause the most confusion are: A72 – Procedural Inadequate or Discrepant Source Documentation, A17 – Transcription Error, and A16 – Other.

Let's start with brief description of each of these monitoring codes.

A72 – Procedural Inadequate/Discrepant Source Documentation:

This monitoring code is used when information entered on the Case Report Form (CRF) cannot be verified in the Source Document, when the Source Document is inadequate, or the information in the Source Document is discrepant. The DAIDS Source Documentation Standard Operating Procedure (SOP) contains the requirements for Source Documentation.

Decoding the Monitoring Codes, cont.

All sites should have access to the DAIDS Clinical Research Policies and Standard Procedure Documents.

An example of an A72 would be: the monitor notes that Allegra 180 milligrams (mg) starting on 12/Sep/2015 is captured on the Concomitant Medications CRF, but there is no documentation regarding Allegra 180 mg or the start date present in the Source Document. In this case, the monitor cannot verify the information captured on the CRF using the information present in the Source Document.

A17 – Transcription Errors:

This monitoring code is used when the data entered on a CRF is incorrect because it differs from the information found in the Source Document.

An example of an A17 would be: the monitor notes that the hemoglobin on the laboratory results found in the Source Document for Week 10 is 12.3, but the hemoglobin result is captured on the Week 10 Laboratory CRF as 13.2.

In this case, the monitor can see that the information was transcribed from the Source Document onto the CRF incorrectly. An A17 finding always reflects that the issue noted was regarding the CRF.

A16 – Other:

This monitoring code is used when there are implementation issues or when an observation does not fit a specific code, but requires notation. DAIDS Program Officers often rely on the A16 findings noted in the Site Monitoring Reports to keep them informed of some of the otherwise non-reportable or non-problematic items noted by monitors.

An example of an A16 would be: the monitor notes that a participant has transferred from Site A to Site B. Site A and Site B are participating in the same protocol, but they are not affiliated with each other in any other way. When a monitor notes this as an A16, it does not signal that there is a problem. The A16 is noted to ensure that the information is accurately captured in the Site Monitoring Report. Monitors are expected to capture this type of information.

***Scenarios*:**

So, how would you fare as a monitor? Here is a list of findings taken directly from Site Monitoring Reports that you can use as a fun way to test your knowledge of the A72, A17, and A16 monitoring codes:

1. The time of the last food and drink intake captured on the Pharmacokinetics CRF is not verifiable in the Source Document.

Answer: This one requires asking a few questions and thinking critically as a monitor. It is an A72 if the CRF is not being used as Source Document because there is a data point captured on the CRF that cannot be verified in the Source Document.

If the CRF is being used as Source Document, the monitor will check to see if the CRF is signed and dated. If the CRF is not signed and dated, then this is still an A72 as the data point is not attributable.

If the CRF is being used as Source Document and has been properly signed and dated, then there is no finding.

2. The CRFs were not completed for Study Visit 008 at the time of the monitoring visit. Study Visit 008 occurred 14 days prior to the monitoring visit.

Answer: This is a situation that requires an understanding of what monitors have been tasked with documenting versus what might be required on the part of the site.

This would be an A16. PPD monitors have been tasked by the DAIDS to capture any occurrences where a study visit has been completed, but the CRFs are incomplete. The timeframe as set forth by the DAIDS, Network or Data Management Center for CRF completion is not taken into consideration when making this observation. The use of this observation in this case is for informational purposes only and should not have a negative impact unless an excessive amount of time has transpired between the completed visit and completion of the CRFs.

3. Per the Source Document, a participant used Ibuprofen from 02/Oct/2015 until 07/Oct/2015; however, this is not captured on the Concomitant Medications Record CRF. Ibuprofen is not prohibited by the protocol.

Answer: This situation requires more knowledge about what is required by the protocol regarding Concomitant Medications. It is an A17 if Ibuprofen is a reportable medication per the protocol because there is a data point that is present in the Source Document that has not been captured on the appropriate CRF as required.

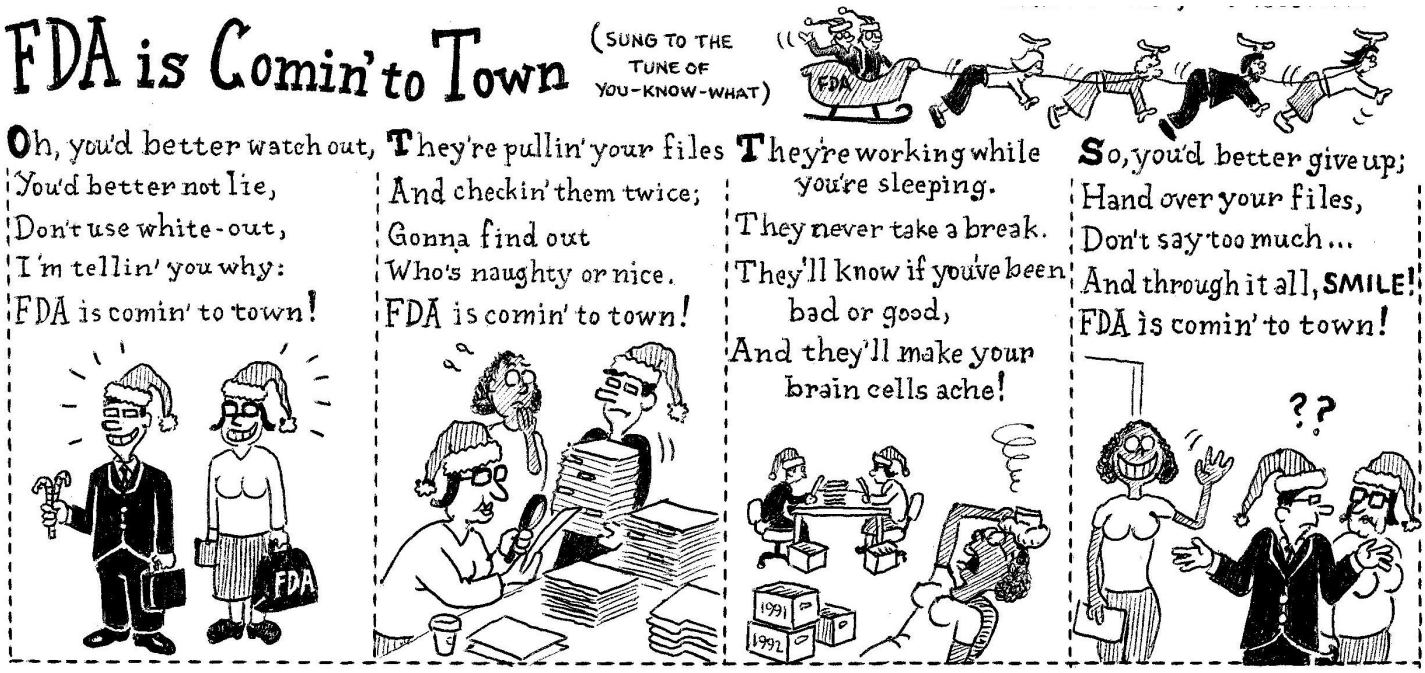
If Ibuprofen is not a reportable medication per the protocol, then there is no finding.

Hopefully this short exercise enhanced your understanding of the three monitoring codes that can be a source of confusion. Open communication between all of us involved in the conduct of DAIDS protocols is essential to achieving our common goals of reliable, usable data and safe, well-informed participants. ■

Where in the World are PPD Monitors?

United States	16	Brazil	2	Peru	2	South Africa	26
Kenya	7	Malawi	2	Uganda	4	France	1
Thailand	5	India	3	Vietnam	1	China	1

For Your Enjoyment! Happy Holidays!



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