MOB Report

Office Of Clinical Site Oversight

National Institute of Allergy and Infectious Diseases (NIAID)

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Obtaining Informed Consent: Overview and Tips Part 2

By Katie Tayloe, MS., CCRP, Clinical Team Manager- PPD

This article is a continuation of the article "Obtaining Informed Consent: Overview and Tips" by Greg Lessing, published in the Fifth (5th) Edition of the Office of Clinical Site Oversight (OCSO) MOB Newsletter in April 2016. The previous article contained several tips for sites to follow when obtaining Informed Consent (IC) in DAIDS sponsored clinical trials. For Part 2 of this article, an analysis was performed of all IC issues noted in PPD Monitoring Reports for DAIDS sponsored clinical trials from July 2015 through June 2016 to determine the areas of IC where findings are most often cited. Table 1 contains the results of this analysis.

In this issue...

Table 1: Number of IC issues cited per category for DAIDS sponsored clinical trials from July '15 through June '16

Category of IC Finding	Number of Issues Cited	Percentage (%) of Total (rounded)
Failure to Record Time of Consent	126	41%
Failure to Provide Updated Consent at Next Visit	62	20%
Failure to Document the IC Process	41	13%
Issues With Recording Initials	14	5%
IC Process Conducted by Undelegated Staff	15	5%
Signature Date Issues	13	4%
Outdated Version of Informed Consent Form (ICF) Provided to Participant	11	4%
Other	8	3%
IC Given After Procedures Were Conducted	4	1%
Staff Unable to Locate Original Signed ICF	3	1%
Participant Signature	4	1%
Staff Signature	4	1%

As evidenced by the data in Table 1, there were three specific categories of IC findings noted most often 1) Failure to Record Time of Consent; 2) Failure to Provide Updated Consent at Next Visit; and 3) Failure to Document the IC Process. The following are additional tips and guidance to avoid these three areas of IC findings.

Continued on page 2

Failure to Document the IC Process
As noted in the previous article, lack of source documenting the IC process is a frequent audit finding. The Declaration of Helsinki states, "After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing." This statement suggests verbally informing a participant of their involvement in a research trial and ensuring comprehension is just as important as obtaining a signed ICF.

The only way for a monitor or auditor to confirm requirements pertaining to the IC discussion outlined in International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP) Section 4.8 and the DAIDS Policy on Source Documentation: DWD-POL-CL-04.00 and DWD-POL-CL-04.00A1 (Appendix 1) were followed is by the presence of written documentation outlining the IC discussion with each participant. The IC process must be thoroughly documented at the time of initial consent, as well as each time a subsequent consent is signed by a participant during the trial to serve as evidence that the participant was provided with and understood the information needed to make an informed decision on whether to participate, or continue participating, in a clinical trial.

The previous article contained several tips for ensuring the IC process is appropriately documented such as creating a standard IC Checklist to be completed and placed in a participant's record each time an ICF is signed. The IC Checklist should include specific aspects of the IC process including that the participant understood the information and was provided a copy of the signed ICF. It should also include a place to record the date and time of consent, a description of the discussion to ensure it was not coercive, and confirmation the information was provided in a language understood by the participant. Site staff should also capture documentation that the participant was provided ample opportunity to review the ICF and have their questions answered by trained, delegated site staff. When preparing for a participant's first visit (such as at screening) or a visit during which an updated ICF must be signed, include a blank IC Checklist in the information taken to the visit as a reminder for site staff to conduct and document the IC process appropriately.

Failure to Record Time of Consent
A participant must provide consent to participate in a clinical trial, or continue participating in a clinical trial, before any study-related procedures are performed. The most direct way to document this requirement has been met, is by recording the date and time the IC discussion was completed and the participant signed the ICF. Recording the time of consent is especially vital when study-specific procedures are completed the same day the ICF is signed. To verify sequence of events, the monitor or auditor will compare the time of consent to other times recorded in the source documentation such as when laboratory samples were obtained or a physical exam was conducted.

As noted above, including a place to record the date and time of consent on an IC Checklist will ensure site personnel have a reminder to document that the ICF was signed prior to conducting study-specific procedures. The date and time of consent should be recorded for the initial ICF, as well as for subsequent ICFs that may be presented to the participant during the trial.

Failure to Provide Updated Consent at Next Visit
Throughout the life of a clinical trial, new information is gathered which can necessitate changes to the protocol. The DAIDS study management team, the Food and Drug Administration (FDA), and a site's Institutional Review Board (IRB)/Ethics Committee (EC) may be involved in determining whether trial participants must be informed of a change to the protocol and whether the ICF should be updated accordingly. Regardless of the specific changes, a participant should be informed of any new updates as soon as possible and should be presented with a revised ICF at the very next study visit following IRB/EC approval of the revised ICF.

Continued on page 3

As with an initial ICF, it is important for site personnel to thoroughly explain the new information outlined in a revised ICF so that the participant can make an informed decision on whether to continue his or her involvement in a clinical trial. When IRB/EC approval is received for an updated ICF, applicable study personnel should be notified immediately that a revised ICF is available, and must be given to each participant. One tip is to place a blank hard copy of the approved ICF, along with an IC Checklist, in each participant's record to remind study personnel to provide it to the participants at their next study visits.

IC is a process, not just a form, and it continues throughout each participant's trial-related experience. It is an ongoing agreement and mutual commitment between researchers and participants and is a main component in conducting ethical clinical trials. Performing and documenting the IC discussion, as well as ensuring the ICF is signed appropriately, are the responsibility of site personnel. Following the tips presented in both parts of this article can help to reduce the number of monitoring visit findings related to the IC process by at least 75%, based on the findings noted in Table 1. This will help to further demonstrate that all DAIDS sponsored trials are being conducted per the applicable policies and regulations. ■

Tips for Monitoring Visits

By Erica Lazarus MBCHB DipHIVMan DCH. Soweto HVTN CRS

1. Be Prepared

- As soon as the next monitoring visit is scheduled (often a preliminary date is provided during the debriefing meeting of the current visit), inform relevant stakeholders including clinic staff, regulatory personnel, pharmacy, and laboratory so they can "save the date" and schedule their own preparation time. You may want to send a calendar invitation as a reminder to assist with planning so that each team can avoid scheduling conflicts.

- Having the same allocated monitor(s) during a trial is helpful for continuity and understanding of expectations from both sides, but this is often not possible. Whenever there is a change in monitor, consider informing the new monitor of your site's working hours to prevent unhappiness around failure of the site to remain open late enough to complete monitoring or site staff having to work unnecessary and unplanned overtime.

- While reviewing announced files is no substitute for ongoing and consistent QA/QC processes per site CQMP, it is still a valuable opportunity to pick up errors and address them, often with more thoroughness and thought than corrections made under the pressure inherent in monitoring visits and in response to monitor found citations. For this reason, it is recommended that review of announced files begin as soon as possible after receipt of the announced work order. This will also allow some breathing room to review unannounced files upon arrival of the monitor

- Ensure a suitable space is set aside for the monitors to use during the visit. If you are working at a site prone to electricity outages, have a back-up plan in place for lighting rooms with poor natural light.

- A monitoring file is recommended. This file should include up-to-date copies of delegation log, site signature log, FDA 1572 or IoR, source doc. table or other SOP to guide the monitor on which documents are or are not source, and general notes to file, as well as monitoring visit logs for signature by the monitor(s) and site staff representative on each day of the visit.

Continued on page 4

2. During the Visit

- Allocate a designated site staff contact person through whom the monitor can direct all requests and queries. Usually this is a study coordinator, investigator or senior research nurse who is very familiar with all site processes and site staff's handwriting. This ensures that findings requiring resolution are channelled to the appropriate person and that queries around processes which simply require an explanation are handled accordingly. It also prevents junior site staff from making inappropriate corrections as a reflex response to perceived pressure from the monitor, which could inadvertently result in even more citations! It is beneficial to regularly remind all staff that queries from a monitor or QA officer, are not always instructions to make a correction or change – often times they are just inquiries around processes for which the monitor requires clarification or explanation.

- The frequency and mode of contact should be negotiated at the start of the visit: some monitors may want the contact person to come by twice a day - first thing in the morning to determine which files are required and later in the day to discuss queries, others may prefer a single daily contact for query resolution with ad hoc calls for any additional requests.

- Site staff are just as prone to "recall bias" as our participants, so try as far as possible to resolve all findings before the end of the monitoring visit so that there are no outstanding items to be addressed after the visit is completed.

3. Prevention is Better Than Cure ("the more you write, the more they cite")

In ensuring adequate documentation there is a fine balance between documenting essential details without writing so much as to cause apparent inconsistencies. Careful preparation of source documents is helpful. Tips:

- Avoiding duplication: have one source for each required data collection item. For example, if the AE log is source, ensure that the template includes all required information so that no other progress notes are required. Discourage staff from entering the same data in 2 different places e.g. entering the blood pressure onto the vital signs template and then noting it again in a progress note.

- Limit free-hand writing – rather create templates which provide clear guidance for staff completion. ■

The Goal is...

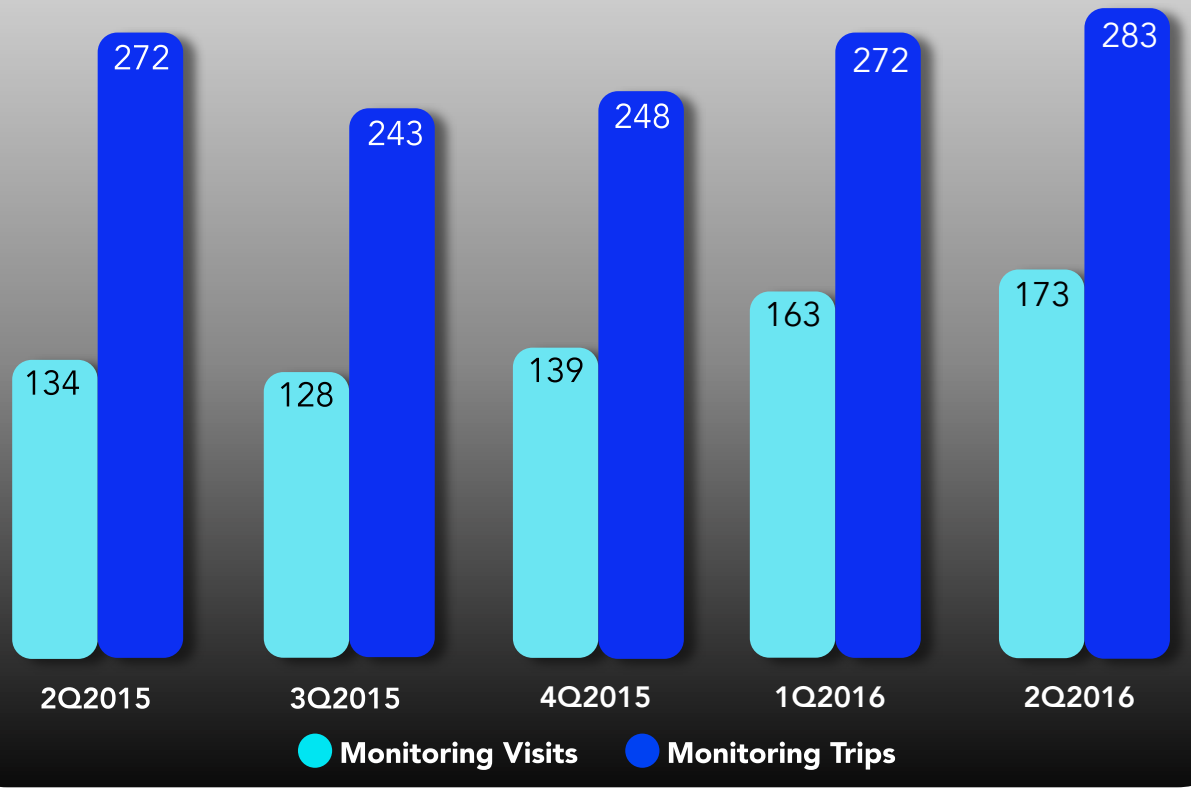
"Always Be Audit Ready!"

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 737 Monitoring Visits and 1,318 Monitoring Trips.



Record Review 2015

(Running Total)

1Q	2Q	3Q	4Q
2,102	4,356	6,296	8,812

Record Review 2016

(Running Total)

1Q	2Q	3Q	4Q
2,197	4,268	?	?

Pharmacy Assessment 2015

(Running Total)

1Q	2Q	3Q	4Q
351	782	1,162	1,602

Pharmacy Assessment 2016

(Running Total)

1Q	2Q	3Q	4Q
457	1,001	?	?

Manager and Monitor Spotlight: North America

Virginia (Jenny) Scott has an Associate's Degree in Nursing and a Bachelor's Degree in Psychology from the University of North Carolina in Wilmington. Jenny began her career at Pharmaceutical Product Development (PPD) in 1998 as a Clinical Research Associate and joined the Clinical Site Monitoring Group (CSMG) in 1999. Jenny started as a Clinical Team Manager in 2001, and as a manager, she leads the Global Pharmacy Services (GPS) team. This team conducts specialized pharmacy assessments for DAIDS. Jenny enjoys her family especially her three grandchildren, traveling and gardening.

Michael Scott has a Bachelor's Degree in Psychology and an Associate Degree in Nursing. He worked as a staff nurse and research clinician in HIV/AIDS prior to joining Pharmaceutical Product Development (PPD) in December 2004, as a Clinical Research Associate (CRA) within the Government Group. He has worked on both Network and Non-Network Protocols. He spends his free time volunteering in his community and with family and friends. He's a member of the Association of Nurse's in AIDS Care (ANAC) and is a Certified CRA (CCRA). He enjoys working with his peers and training new CRAs to the project.