16th Edition
August 2021

MOB Report

OFFICE OF CLINICAL SITE OVERSIGHT

SCORE for Winning Site Performance!

On January 24th, DAIDS launched the Site Clinical Operations and Research Essentials (SCORE) Manual to align with the timing of the new Clinical Trial Units grant cycle. The manual was developed over the course of a year with input from various stakeholders, including the HIV/AIDS Networks and site personnel. It describes the operational requirements for Clinical Research Sites implementing DAIDS-sponsored clinical research within the DAIDS Clinical Trials Networks. The manual was designed as part of DAIDS' policy restructuring, to consolidate these requirements in a central location, to promote efficiency and to facilitate compliance with ICH/GCP and applicable regulations.

The Manual covers a breadth of topics with the following 18 sections:

- Introduction to DAIDS Systems
- Investigator Responsibilities
- CRS Personnel Qualifications, Training, and Responsibilities
- Site Activation Process
- Pharmacy Requirements
- Electronic Systems
- CRS Facility Requirements (Clinic, Laboratory and Additional Locations)
- Laboratory Requirements
- Screening, Enrollment/Randomization, and Unblinding of Participants
- Protocol Compliance
- Quality Management
- DAIDS Protocol Registration and IRB/EC Communications
- Informed Consent of Participants
- Essential Documents
- Site Visits
- Premature Termination or Suspension of a Clinical Trial
- Clinical Research Site Inspection Readiness
- Source Documentation

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NIH National Institute of Allergy and Infectious Diseases

SCORE for Winning Site Performance!

Continued

These 18 sections include appendices, optional templates, forms/ logs, guidelines and tools to further assist sites in optimizing clinical research operations at their institution. There are also FAQs on the SCORE Manual web page which provide clarification on the topics covered in the manual. These FAQs will continue to be updated.

Accompanying release of the SCORE Manual were some DAIDS policy changes. A new SCORE Manual Policy was introduced, which requires all CRS staff to comply with the requirements outlined in the SCORE Manual, while several other DAIDS policies were obsoleted. The requirements from the obsoleted policies [e.g., Delegation of Duties Log Policy, Source Documentation, Clinical Quality Management Plans, Requirements for On-Site Monitoring, Requirements for Manual of Operational Procedures (MOP), and Enrolling Children in Clinical Research; Clinical Site Requirements] are now specified in the manual.

Monitors will be confirming adherence to the SCORE Manual, applicable regulations and other requirements that may be more stringent at individual institutions.

DAIDS hopes that the manual will be used as a tool for on-boarding new research personnel, as well as an ongoing resource for current site staff.

The DAIDS SCORE Manual Launch sessions, including the recording and presentation slides are available on the HANC website on the DAIDS Resources and Announcements page, along with the consolidated Q&A from both sessions.

QUESTIONS?

CRS staff should direct any questions related to the SCORE Manual to their DAIDS Program Officer.

Obsoletion of the Critical Events Policy

As communicated by the DAIDS Protection of Participants, Evaluation and Policy Branch, the DAIDS Clinical Research policy on Critical Events was obsoleted on May 14th, 2021. This included the policy titled "Identification and Classification of Critical Events: Site Responsibilities Policy" and its associated "Critical Events Manual". Obsoleting this particular policy is part of an overall restructuring of DAIDS' external-facing clinical research policies: new policies are being developed, existing policies are being updated and certain policies are being obsoleted. One of the outputs of this reassessment and restructuring is the SCORE Manual (see related article).

So what does obsoletion of the Critical Events policy mean for sites?

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Obsoletion of the Critical Events Policy

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The underlying regulations which require reporting of critical events still exist and must be followed by sites. By definition these events are significant in nature: unanticipated problems involving risks to participants or others, serious or continuing noncompliance, suspension/termination of IRB/EC approval, and suspected research misconduct. Thus, these events must be reported in an expedited manner.

Some examples include:

- Significant study-related trends or non-compliance with protocol and/or DAIDS policies/procedures, ICH GCP or other applicable regulations.
- Informed Consent and Enrollment Violations (initial or subsequent)
- Significant issues with investigational product and/or failure to follow PAB policies/procedures
- Newly identified lapse in IRB/EC approval
- Safety issues such as unreported Serious Adverse Event/Expedited Adverse Event/death.

To fulfill DAIDS' oversight responsibilities as Sponsor, the monitors will continue to follow established procedures regarding these significant events. Sites will now see these documented in the site visit reports as Significant Events.

The monitors assess documentation and the sites' action surrounding the recorded significant events. If the significant event is adequately documented, and reported to the appropriate parties, this is noted as such in the monitoring visit report. For undocumented/unreported significant events identified during a monitoring visit, these are reported via the monitor to the DAIDS Program Officer, and to PAB personnel for any pharmacy-related significant events. Sites should report undocumented/unreported significant events as per their institutional requirements.

To ensure that obsoletion of the Critical Events policy does not result in any process gaps at sites for DAIDS studies, documents utilized at sites which referenced the Critical Events Policy should be modified accordingly to reference the specific regulations. For guidance, sites may wish to reference the key regulations which were previously listed in the DAIDS Critical Events Policy pertaining to site's responsibilities:

- HHS regulations for the protection of human subjects in research
- OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks toSubjects or Others and Adverse Events
- FDA Regulations on IRBs
- FDA Regulations on INDs
- ICH E6(R2)
- NIAID Research Misconduct SOP
- PHS Policies on Research Misconduct at 42 CFR 93
- Guidance for Clinical Investigators, Sponsors, and IRBs. Adverse event reporting to IRBs
- OHRP Guidance on Continuing Review of Research
- SCORE Manual

Remote Source Document Verification (SDV): Where We Are

We continue to experience the effects of the COVID-19 public health emergency, even though imposed restrictions are lessening, and more on-site visits are being performed. At the end of the most recent quarter (2Q 2021), 74% of all completed visits were onsite relative to remote source document verification (rSDV) as indicated in Figure 1 . However, it is anticipated that to maintain adequate Sponsor oversight of DAIDS sponsored/ supported clinical trials there will be a need for a hybrid of on-site visits and rSDV for the foreseeable future.

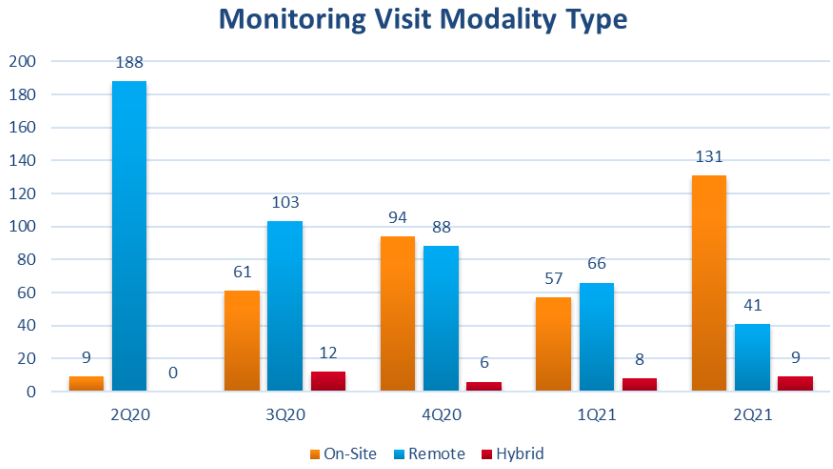


Figure 1: Percentage of on-site versus rSDV during the period 2Q 2020 to 2Q 2021

Table 1: Estimated Database Lock Dates by protocol

Protocol ID	Database Lock Dates
HVT 133	24-Aug-2021
A5369	1-Sep-2021
HVTN 115	1-Sep-2021
IMPAACT 2008	1-Sep-2021
HVTN 123	3-Nov-2021
IMPAACT 2010	1-Dec-2021
MTN-034	21-Jan-2022
MTN-043	28-Feb-2022
A5312	1-Jun-2022
A5372	1-Jun-2022
IMPAACT 2014	1-Jun-2022
MTN-042	29-Jul-2022

For many sites, rSDV is now in place as an alternative or a complement to on-site visits. We greatly appreciate all the efforts of sites in setting up a secured platform and obtaining IRB/EC approval to conduct rSDV. On DAIDS' part, we have implemented a monitoring strategy to prioritize monitoring, based on Database Lock (DBL) dates within the subsequent 12 months as noted in Table 1. This is with the expectation that it will lessen the burden on sites by focusing on a specific number of studies to upload source documents and other preparatory activities prior to each monitoring visit. The specific studies to be monitored will be reflected in the Pre-Visit Letter and Work Order received from your PPD site monitor. It should be noted that adequate monitoring will continue as feasible for protocols with upcoming DBL dates scheduled for beyond 12 months.

Since the implementation of rSDV we have received several questions from sites, and a list of these Frequently Asked Questions is now available on the HANC website on the DAIDS Resources and Announcements page .

CRS staff should direct additional questions related to rSDV to their PPD monitors and DAIDS Program Officer.

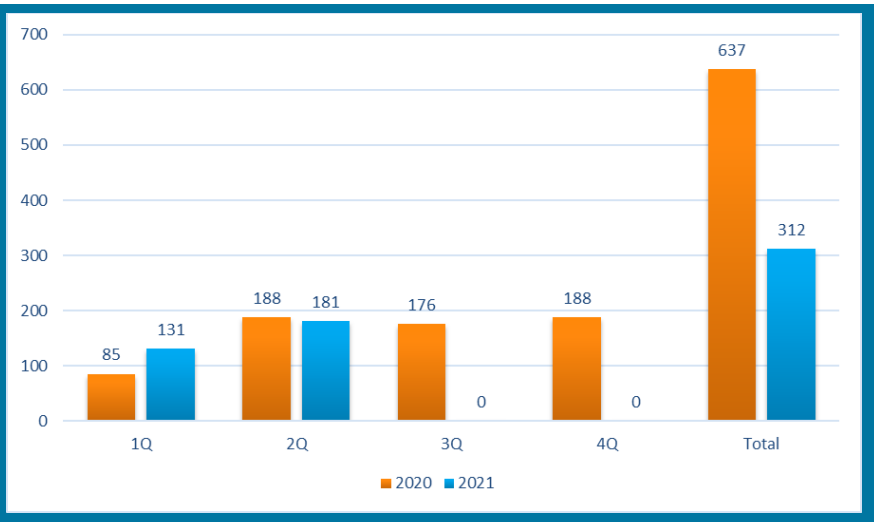
Monitoring Metrics

Year to Date Monitoring Metrics

February, March	1Q
April, May, June	2Q
July, August, September	3Q
October, November, December, January	4Q

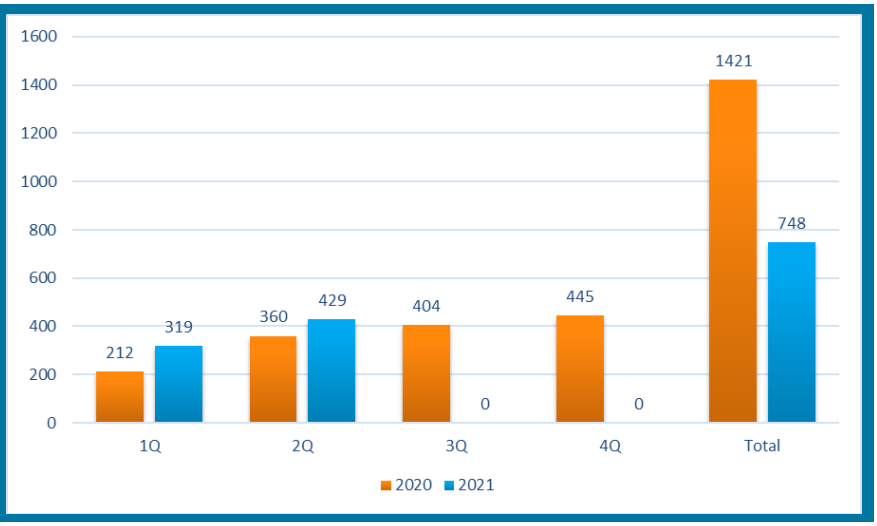
Monitoring Visits

Any time a monitor travels to a site to conduct monitoring.

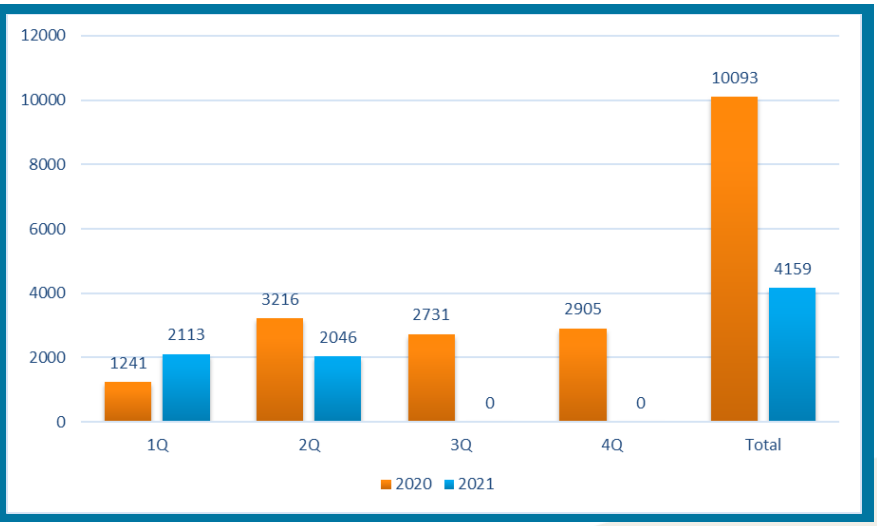


Monitoring Trips

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



Records Reviewed



Monitoring Metrics

Year to Date Monitoring Metrics

February, March	1Q
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July, August, September	3Q
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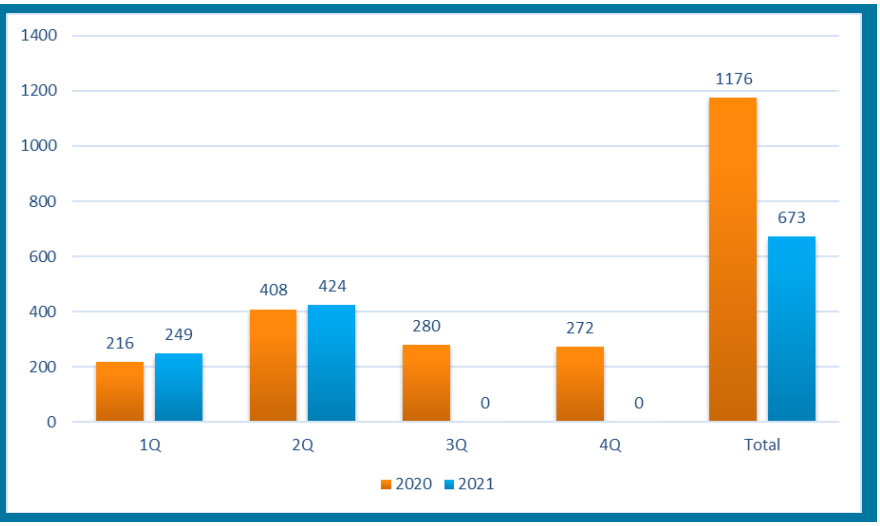
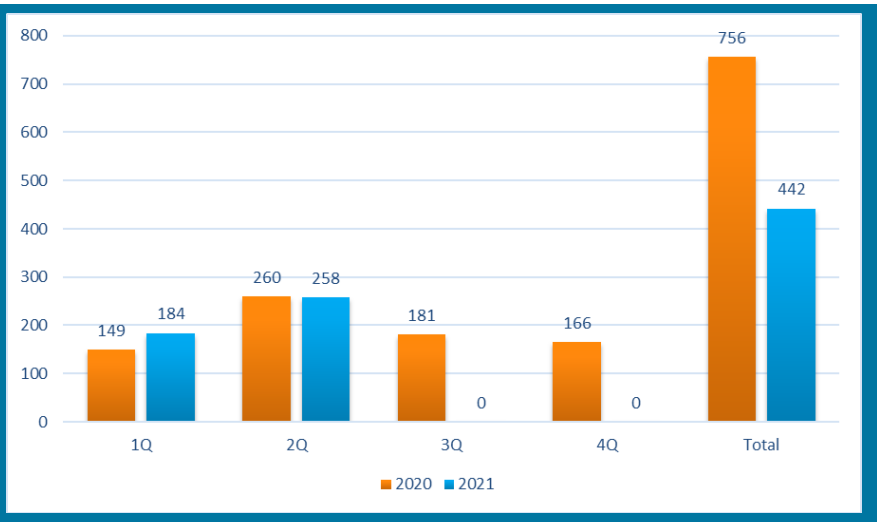
Pharmacy Assessments



Regulatory Files Reviewed



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