MOB Report

Edition 25 ▪ July 2026

Office of Clinical Site Oversight

Follow-up Letter Reminder

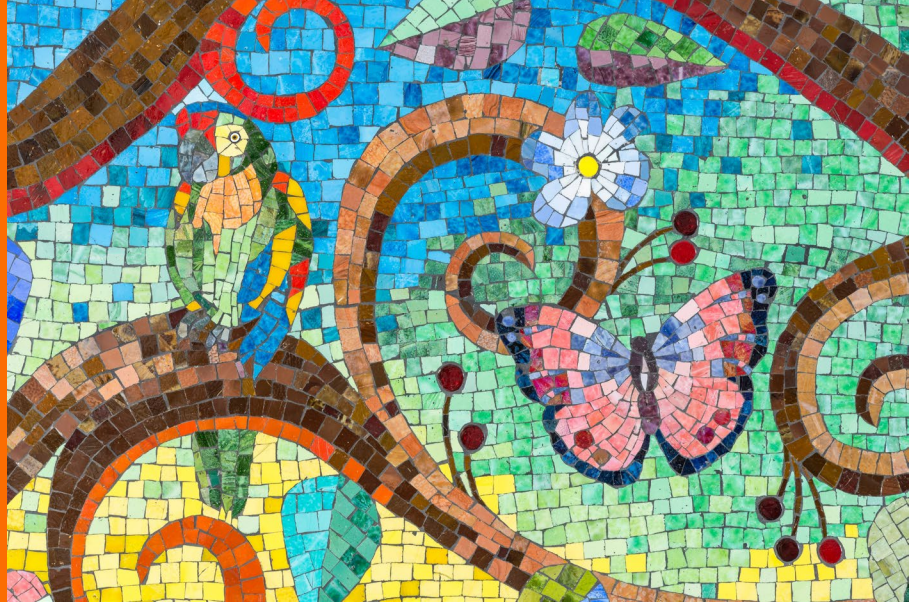
This is a gentle reminder that sites will begin receiving follow-up letters starting in 2027. This transition, previously communicated to sites, is intended to streamline post-monitoring-visit communications while continuing to clearly document observations, required follow-up actions, and any requested responses.

Following applicable monitoring visits, sites will receive a follow-up letter in place of a monitoring report. The follow-up letter will serve as the official communication of monitoring findings, including any required corrective or preventive actions. As with the current monitoring process, sites are expected to address all observations identified during the monitoring visit and respond to any issue resolution requests from their Program Officer (PO), as applicable. Sites are encouraged to review these letters carefully and provide all requested responses promptly.

If you have any questions about this upcoming change, please contact your PO.

In This Issue

Best Practices for Section 4 of FDA Form 1572



The FDA Form 1572 is a key regulatory document reviewed during monitoring visits. In accordance with applicable country regulations, CRAs may request documentation such as CLIA certificates to verify the quality and regulatory compliance of laboratory testing facilities.

What to Include

When completing Section 4 of the1572 titled, "Name and address of any clinical laboratory facilities to be used in the study," list only those laboratories or testing facilities that directly contribute to the clinical trial. This includes facilities performing protocol-required analyses or generating data that support study endpoints, such as efficacy or pharmacokinetic (PK) data.

Ensure that the full name and complete address of each applicable laboratory or facility are accurately documented.

Acceptable Facilities TO List

- Diagnostic Laboratories (e.g. specimens including bloodwork, sputum, urine etc.)
- Imaging Centers
- Cardiology Laboratories
- Central/non-local Laboratories

Facilities to NOT List

- Specimen Repositories*
- Satellite or Contract Repositories*

***Note:** Specimen, satellite, or contract repositories may be excluded if the primary laboratory maintains traceable documentation of sample handling and analysis.

Centralized Monitoring

DAIDS Launches Centralized Monitoring Pilot to Strengthen Clinical Trial Oversight

On June 1, 2026, the Division of AIDS (DAIDS), Office of Clinical Site Oversight (OCSO), officially launched its Centralized Monitoring (CM) Pilot to strengthen participant safety, enhance data quality, and advance risk-based quality management practices across its global clinical research network.

What Is Centralized Monitoring?

Centralized monitoring is a remote, data-driven approach to study oversight in which data are extracted from the Electronic Data Capture (EDC) system and reviewed at both the protocol and site level, and across all participating sites. Rather than relying solely on scheduled remote and on-site visits, centralized monitoring allows potential concerns to be detected on a continuous, routine basis — enabling timely clarification, resolution, and quality improvement.

It is important to note that **centralized monitoring does not replace routine monitoring visits**. Instead, it adds an additional layer of data-driven oversight that complements existing on-site and remote monitoring activities.

Why is DAIDS Implementing Centralized Monitoring?

This initiative is not happening in a vacuum. It is directly aligned with evolving regulatory expectations for Risk-Based Quality Management (RBQM) specifically ICH E6(R2), adopted by the FDA in March 2018, and the more recent ICH E6(R3), adopted in September 2025. Both guidelines encourage sponsors to proactively identify and manage risks that could affect participant safety or the reliability of clinical trial data.

Periodic site visits alone are no longer sufficient to meet these regulatory standards. Centralized monitoring fills that gap by enabling continuous data review as required by ICH E6.

The Pilot: Four Studies, Across Three Networks

The CM Pilot is being conducted by DAIDS's monitoring contractor, PPD, and is currently implemented across four selected DAIDS-sponsored studies:

- **A5300B/I2003B/PHOENIx** – Protecting Households On Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients (PHOENIx MDR-TB)
- **A5409 (RAD-TB)** – A Phase 2 adaptive, dose-ranging trial of novel regimens for treatment of pulmonary tuberculosis

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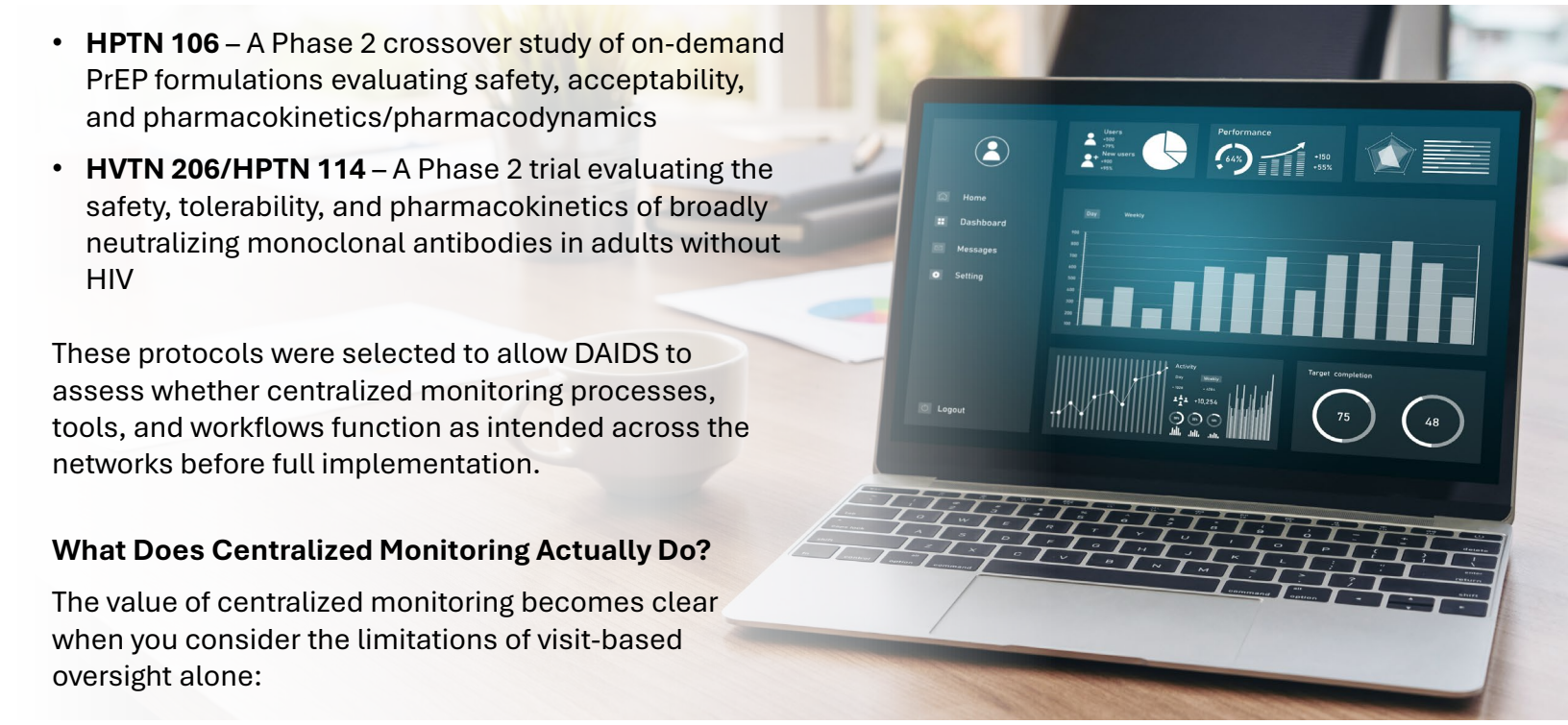
Centralized Monitoring *continued*



- **HPTN 106** – A Phase 2 crossover study of on-demand PrEP formulations evaluating safety, acceptability, and pharmacokinetics/pharmacodynamics
- **HVTN 206/HPTN 114** – A Phase 2 trial evaluating the safety, tolerability, and pharmacokinetics of broadly neutralizing monoclonal antibodies in adults without HIV

These protocols were selected to allow DAIDS to assess whether centralized monitoring processes, tools, and workflows function as intended across the networks before full implementation.

What Does Centralized Monitoring Actually Do?

The value of centralized monitoring becomes clear when you consider the limitations of visit-based oversight alone:

Area	The Challenge Without CM	How CM Helps
Data Review	Adverse event trends may be missed between quarterly visits	Continuous review flags safety signals immediately
Risk Identification	A spike in protocol deviations may go unnoticed until the next visit	Trends are detected without delay, enabling early mitigation
Data Integrity	Discrepancies in participant data can persist for months	Discrepancies are caught and addressed promptly
Resource Allocation	Frequent travel increases cost and staff burden	Remote review does not require physical presence onsite
Issue Resolution	Corrections may wait weeks for a monitoring report to be finalized	Corrective action can begin immediately upon identification

What Sites in the Pilot Can Expect

For sites participating in one of the four pilot protocols, your assigned PPD Clinical Research Associate (CRA) may reach out regarding findings identified through monthly centralized monitoring analysis.

A **finding is not necessarily an indication that something went wrong**. Findings are data signals identified through routine review that require CRA assessment. The CRA will evaluate each signal and, when appropriate, seek site input to determine whether any action is needed.

If follow-up is required, the CRA may:

- Seek clarification or request data correction
- Recommend steps to strengthen quality measures
- Ask the site to develop a Corrective and Preventive Action (CAPA) plan in cases of significant or recurring concerns

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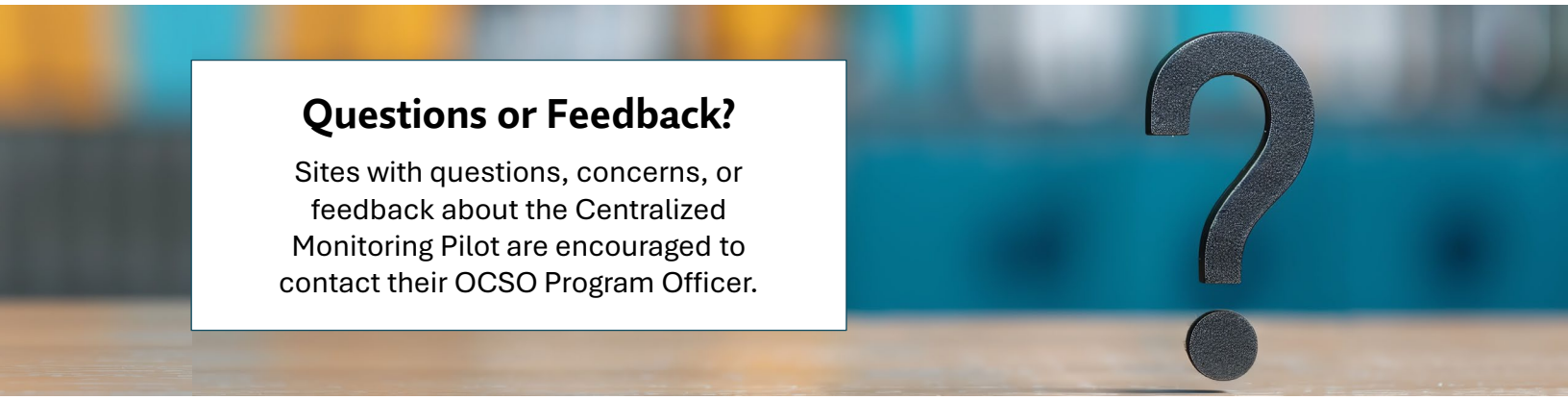
Centralized Monitoring *continued*

Most communications will be handled by email, though some may require a phone discussion or be addressed during a monitoring visit. Program Officers will be included in relevant communications, and sites may be asked to upload supporting documentation through a DAIDS-approved secure platform.

Why This Matters for All Sites

Even if your site is not participating in one of the four pilot protocols, this initiative signals an important direction for the entire DAIDS Clinical Trial Units Network. The lessons learned will help DAIDS evaluate centralized monitoring processes, tools, and workflows before considering broader implementation across additional studies.

The success of this initiative depends on the continued partnership between the DAIDS, the protocol teams, the CRAs, and the clinical research sites. Together, we are building a stronger, more proactive quality framework that supports excellence in clinical research.



Questions or Feedback?

Sites with questions, concerns, or feedback about the Centralized Monitoring Pilot are encouraged to contact their OCSO Program Officer.

Direct Data Entry Statements in DAIDS Protocols:
References in Interim Site Monitoring Visit Reports (ISMRs)

Background

The identification of data entered directly into data acquisition tools as source data has gained importance following the release of the ICH E6 (R3) requirement, specifically Section B.14.2. In response to this regulatory update, the DAIDS Regulatory Affairs Branch (RAB) provided guidance to the four networks—ACTG, HVTN, HPTN, and IMPAACT. Each network was instructed to ensure that their protocols include a statement addressing the possibility of direct data entry into the database for the protocol.

Protocol Review and Monitoring Procedures

CRAs from PPD have been directed to review the current Institutional Review Board (IRB) or Ethics Committee (EC) approved version of the protocol for references regarding direct data entry when starting record review. This review determines whether the protocol allows or prohibits direct data entry. With this protocol guidance, CRAs examine source documents during site monitoring visits.

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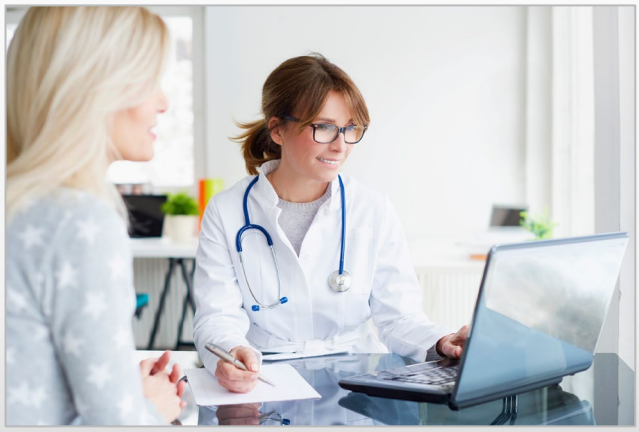
Direct Data Entry Statements in DAIDS Protocols:
References in Interim Site Monitoring Visit Reports (ISMRs) *Continued*

Reporting in Interim Site Monitoring Reports (ISMRs)

In the "Summary of Debriefing" section of each ISMR, CRAs are required to indicate whether direct data entry is permissible according to the protocol. If direct data entry is not allowed by the protocol or by a specific case report form, but such entry has occurred, the CRA records this instance as a protocol deviation, using the A72 code in the ISMR.

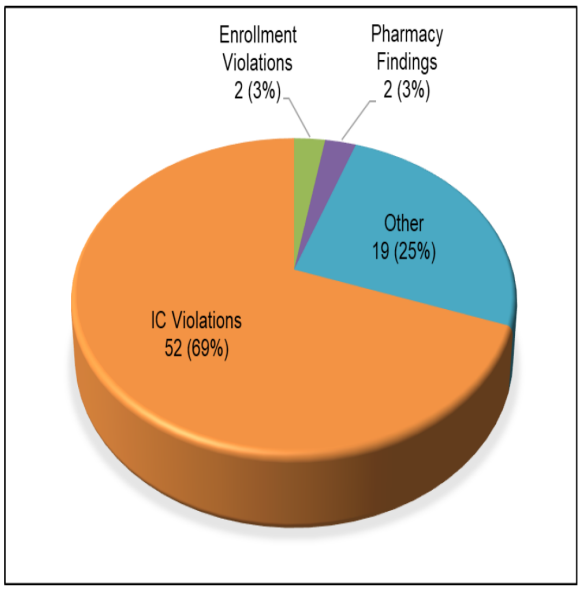
Additionally, if a protocol has not been updated yet to address direct data entry and remains silent on whether it is allowed, any occurrence of direct data entry at a site is also documented by the CRA using the A72 code.

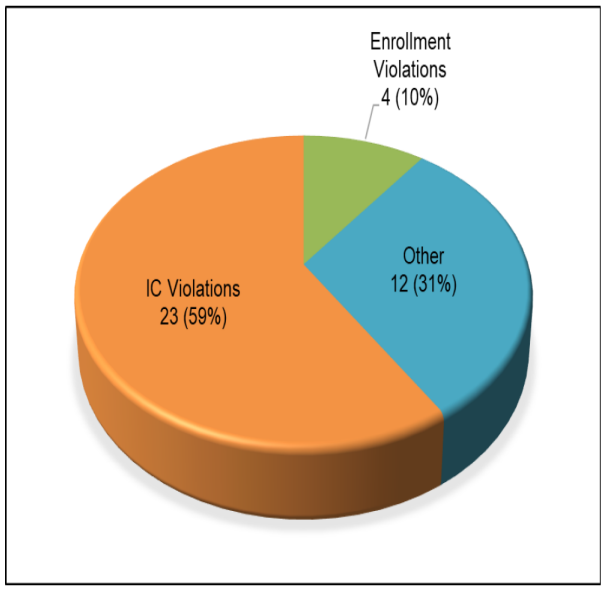


Informed Consent Form (ICF) Violations

Between 01-Nov-2025 and 31-Jan-2026, monitoring visits identified 75 Significant Events (SEs), 52 of which were related to informed consent (IC) violations. During the subsequent period (01-Feb-2026 to 30-Apr-2026), both measures decreased: the total number of SEs fell by 48%, from 75 to 39, while IC-related SEs declined by 56%, from 52 to 23. This represents a positive trend and reflects the sites continued efforts of sites to strengthen informed consent practices.

01-Nov-2025 to 31-Jan-2026 vs. 01-Feb-2026 to 30-Apr- 2026





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Informed Consent Form (ICF) Violations *Continued*

However, despite this improvement, informed consent violations remain the most frequently reported category of SEs. A review of the findings from both reporting periods identified several recurring themes that may serve as areas of focus for continued quality improvement:

Use of Unapproved or Outdated Consent Forms

Participants were not always consented using the most current approved version of the informed consent form (ICF) and/or consent forms were used before all required approvals, or implementation requirements were met.

Examples

- Participant signed an ICF before the protocol version was implemented.
- Use of previous version of the ICF when a newer approved version is available.

Consent Obtained by Unauthorized Personnel

Consent was obtained by staff who were not appropriately documented on study delegation records or regulatory documentation.

Examples

- Staff member obtaining consent was not listed on the Delegation of Duties (DoD) log.
- Staff member obtaining consent was not listed on the Form FDA 1572.

Consent Documentation Inaccuracies

Incomplete or inconsistent consent documentation continued to be observed.

Examples

- Missing staff, participant, or parent signatures.
- Missing participant initials.
- Inconsistencies in participant or parent initials across consent forms.

Consent Process Requirements Not Fully Documented or Followed

Required elements of the informed consent process were not consistently documented or completed.

Examples

- No documentation that a copy of the signed ICF was offered to the participant.
- Participant assent was not obtained in accordance with applicable requirements.
- No documentation noting that participant comprehension was assessed.

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Informed Consent Form (ICF) VIOLATIONS *Continued*

As a reminder, a few simple practices can go a long way toward preventing informed consent findings such as:

- ✓ Verifying that the most current approved ICF is being used before each consent discussion.
- ✓ Confirming that staff obtaining consent are appropriately trained, delegated, and listed on required regulatory documents.
- ✓ Reviewing completed consent forms for accuracy and completeness before filing them.
- ✓ Using consent checklists and routine self-reviews to identify and correct issues early.
- ✓ Incorporating periodic staff training and refresher sessions on informed consent requirements.

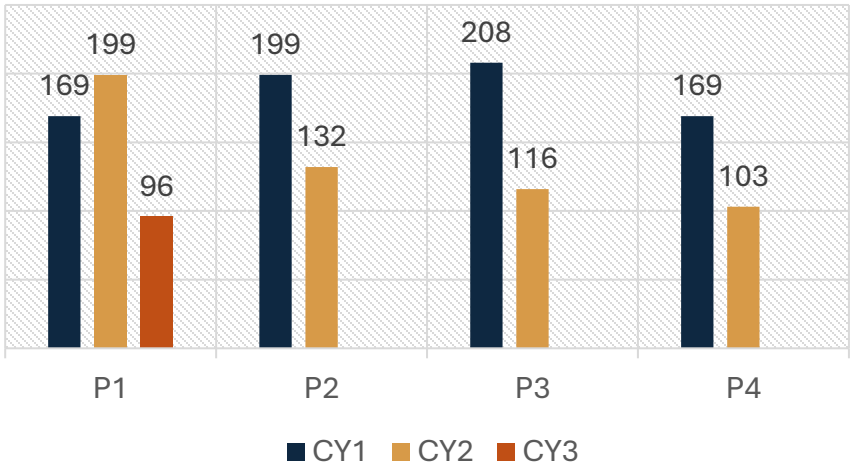
- ✓ Conducting a two-person review of the signed informed consent form before the participant leaves the site.

The decrease in informed consent violations this quarter is a positive step, and we appreciate the ongoing efforts of site teams to support compliant consent processes and protect participant rights, safety, and welfare.

Year to Date Monitoring Metrics

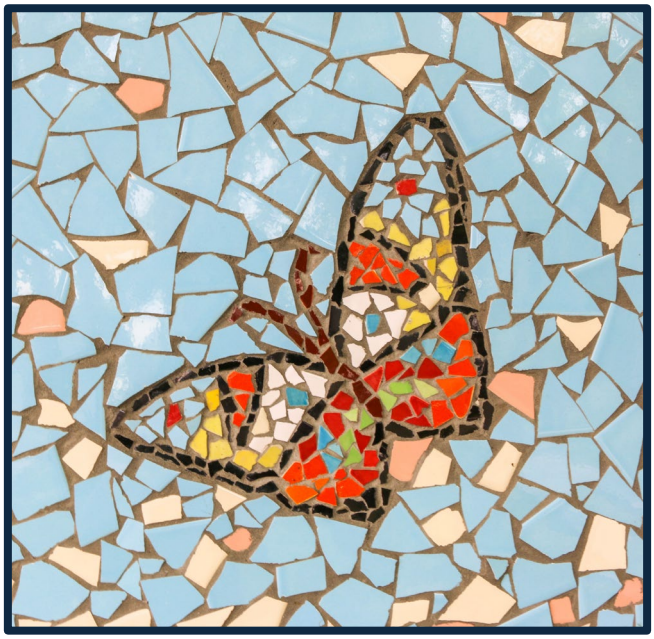
Visits

Anytime monitoring is conducted during a site visit



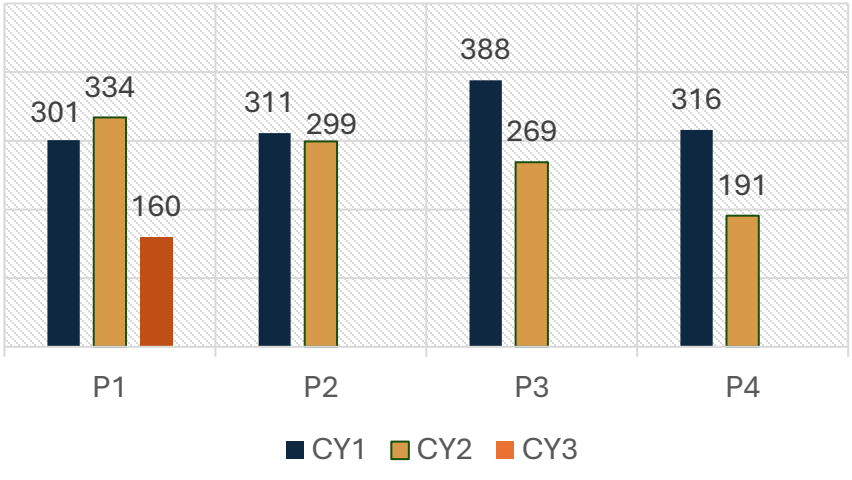
Reporting Periods	
February, March, April	P1
May, June, July	P2
August, September, October	P3
November, December, January	P4

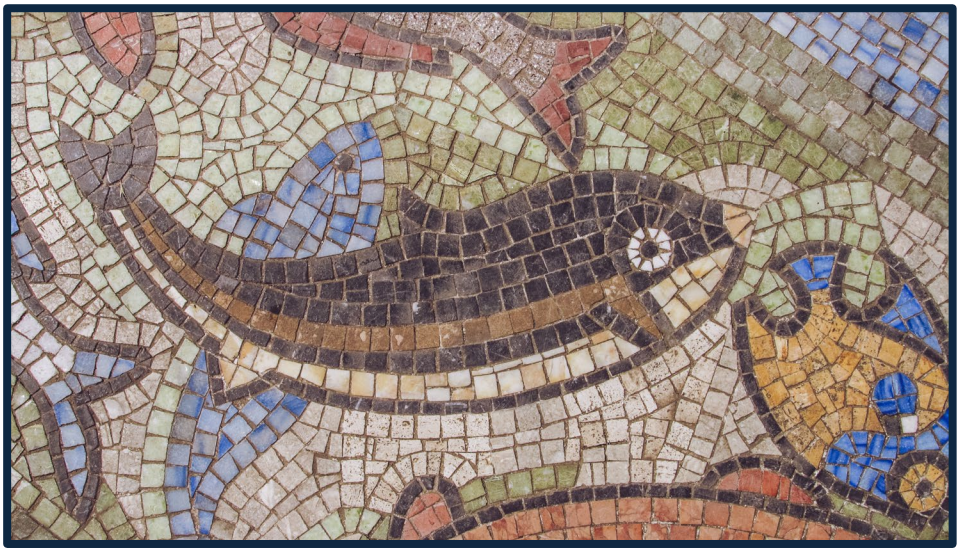
Contract Years	
February 1, 2024- January 31, 2025	CY1
February 1, 2025- January 31, 2026	CY2
February 1, 2026- January 31, 2027	CY3



Trips

Total number of CRAs conducting monitoring during site visit





Year to Date Monitoring Metrics

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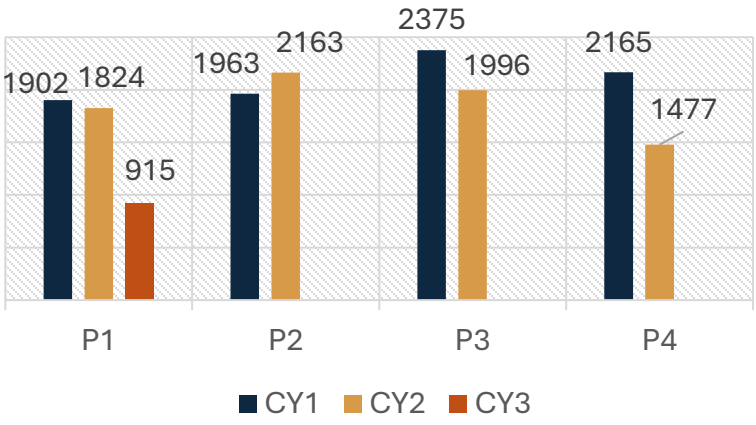
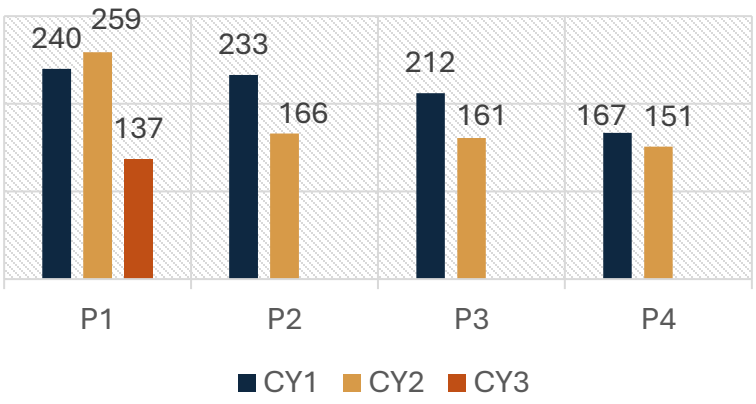
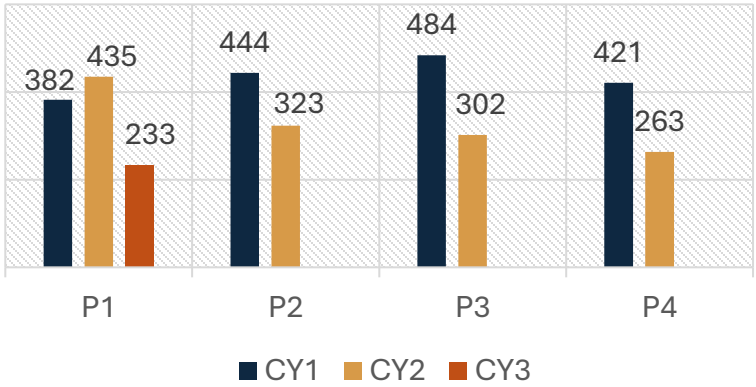
Records Reviewed



Regulatory File Reviews



Pharmacy Assessments



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