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Clinical Researcher—June 2019 (Volume 33, Issue 6)

PEER REVIEWED

Why Your Clinical Research Site Needs a Quality Management System

Seema Garg, MS, MBA, CQA, CSSGB

Most of the time when someone in charge at a research site first brings up their desire for a quality management system (QMS), the first thought that comes to many staff members' minds is "Oh no! We have to buy another expensive software product!" But does a QMS really have to come in the form of software or a full-scale program? It can, but it does not have to. A QMS can simply be a set of procedures and processes that ensures the consistency and compliance of any task being performed.

I have been auditing clinical research sites for a while, and a few of the things that I find quite amazing for almost all sites include their dependency on monitoring and their lack of a site-level QMS.

Who's in Charge?

When presented with a concerning study audit finding, most clinical research coordinators (CRCs) that I have dealt with during this process will respond to the effect that "Our monitor didn't ask us about this." It's almost as if the site staff are on a robotic cycle of answering queries and findings from sponsors, monitors, and contract research organizations (CROs), so if no one asks about something, they assume that they don't have to do it.

There is a certain lack of understanding on part of the staff that it is the site's responsibility to operate according to the regulations and protocol, and that the monitoring is simply a verification of the site's operations. The regulations require the investigator and the study staff to conduct the study according to the protocol and regulatory requirements, and the sponsor to guide and oversee the clinical site through monitoring, auditing, and other processes.{1}

However, somewhere along the way, the dependence of site staff on monitoring has become an all-inclusive check for everything they do for the study, which is not always possible, especially with risk-based monitoring models.{2} One of the reasons this may have happened is because there are no formal education or training requirements for the CRC position; most of the training comes in an on-the-job fashion and this on-the-job training has a great emphasis on being trained by the monitors during the site initiation visits.{3}

Where's the Quality?

The lack of a site-level QMS at many sites is the second thing that amazes me. Most of the clinical sites I have audited will have a standard operating procedure (SOP) for conducting informed consent, but not an overall QMS.

Most study staff think of a QMS to be the sponsor's responsibility. However, a clinical site should also have its own QMS through which the site would ensure continuity and consistency of site processes, training of study staff, maintenance of essential documents, and site readiness for an audit or an inspection.

Examples of activities that should be included in a clinical site QMS would be:

- Training SOP describing requirements for regulatory training and protocol-specific training before any staff can be assigned to a study.
- Continuity SOP describing the process of study handover from one staff member to another, and how will new staff be trained if the staff changes without a proper handover.
- Informed consent process SOP.{4}

- Good Documentation Practices (GDP) SOP describing documentation and correction process of regulated data.
- Source documents SOP describing the process of generation and maintenance of source documents.{5}
- Internal assessment SOP describing process of clinical site's own internal assessment of its studies.
- Inspection readiness SOP describing what the site would need to do to prepare and host a regulatory inspection.

Many sites don't have these SOPs, or if they do, the procedures have not been read or revised by anyone in years. It may not be possible for smaller sites to implement all these procedures at the same time; however, it is important to start somewhere and then keep going. If a clinical site implements two SOPs a year, in three to four years it would have most of the needed SOPs. If the SOPs are reviewed and revised every two to three years, they will become second nature for the site staff as a routine part of conducting all clinical research studies.

An inspection readiness SOP is the most common one that I find lacking at sites. Most site staff have not experienced a regulatory inspection and are unfamiliar with how they are handled in terms of logistics and staff conduct.

Most site staff don't consider a lack of inspection readiness as a risk because the low probability of being inspected by a regulatory agency if they are not conducting high-risk studies or are not a high-enrolling site. This attitude can be an issue in itself, as the site staff become complacent and things start to fall between the cracks.

Case Studies

1. About a year after a site has started a long-term study, the assigned CRC leaves the site without training other staff on the regulatory procedures and systems required to continue the proper conduct of the study. The new study staff starts to miss procedures like calling subjects for follow-up visits, answering data queries from data management, re-consenting subjects on revised consents, etc.

- If the site had an SOP for study continuity, it would have allowed the outgoing staff member to conduct a proper handover to a newly assigned staff member—bringing him or her up to speed on the ongoing study with minimal disruption to timelines and participants.
- Additionally, a site internal assessment procedure would have helped, as it would have required the site to audit itself at least annually to see where other procedures were lacking.

2. A site enrolls a subject and during a follow-up visit, a CRC notices a note in the subject's file from a case manager indicating that the subject cannot read. The principal investigator decides to discontinue the subject from the study upon his confirmation of being illiterate. If the site had an informed consent SOP, it would have required an assessment of the reading and comprehension capabilities of the subject during the consent process. This would have allowed the enrollment and retention of the subject with the help of a literate, legally acceptable representative serving as witness.
3. A site generates its own source documents and worksheets and the case report forms (CRFs) are provided by its sponsors. Neither the site nor the sponsor of a current study have provided space on their documents for study personnel to initial and date for the procedures being performed or entries being made on these documents. The study keeps going until a monitor makes an observation that the source documents and CRFs are not attributable. If the site had a source documentation and GDP SOP, the site staff would have been trained to make this observation themselves and correct the forms.

Conclusion

A QMS does not have to be a large system; indeed, it can be simple and flexible. Conducting research in compliance with regulations and the protocol is first and foremost the clinical research site's responsibility—sponsors, monitors, and auditors can verify compliance, but the site staff are the ones who must comply.

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PEER REVIEWED

BIMO Inspections: Recommendations for Sponsors

Mary Kay Kessinger Sobcinski, RN, BSN, MHA; Susan Wiskow, CCRP

The U.S. Food and Drug Administration's (FDA's) Bioresearch Monitoring (BIMO) program is designed to protect the rights, safety, and welfare of subjects, verify the accuracy and reliability of clinical study data, and assess study compliance with FDA regulations. BIMO inspections can be conducted by FDA at any time during a clinical study, "for cause," near the time of study closure, or during agency review of a marketing application.

At the conclusion of an inspection, FDA may issue a Form 483, which outlines specific findings that need correction. If the findings are not addressed to the agency's satisfaction, or if the findings are egregious enough, FDA may issue a Warning Letter. These actions by the agency can delay or even obviate product approval. It is therefore imperative that study sponsors and sites are always prepared for a BIMO inspection. This article presents several recommendations to help ensure successful inspections.

Background

During FDA's fiscal year 2017 (FY17), the agency's Center for Devices and Radiological Health (CDRH) division conducted 287 domestic inspections. Of these, 198 were inspections of clinical investigators or study sites, and 48 were inspections of sponsors, clinical research organizations (CROs), or monitors.{1} The most common investigator/site deficiencies were:

- Failure to follow the investigational plan/agreement or regulations, or both.
- Protocol deviations.
- Inadequate recordkeeping.
- Inadequate subject protection (informed consent issues and failure to report adverse events [AEs]).
- Inadequate accountability of the investigational product.
- Inadequate communication with the institutional review board (IRB).
- Investigational product represented as safe/effective.

The most common sponsor/CRO/monitor deficiencies were:

- Inadequate monitoring.
- Failure to bring investigators into compliance.
- Inadequate accountability for the investigational product.
- Failure to obtain FDA and/or IRB approval prior to study initiation.

It is important to note that FDA also inspects entities outside the United States (OUS). In FY17, CDRH inspected 13 investigators/sites and four sponsors/CROs/monitors and found deficiencies similar to those identified domestically.

Many sponsors erroneously assume that FDA will not inspect OUS sites, but this is a dangerous assumption. FDA expects all study sites, regardless of location, to adhere to federal study regulations, and the agency will inspect OUS sites using the same rigor as it inspects domestic sites. Sponsors need to ensure their OUS sites are as carefully monitored and prepared as their U.S. sites, and it is especially important to ensure OUS

sites that contribute a substantial portion of study data to the marketing application are well prepared.

Ultimately, study integrity and compliance are the responsibility of the sponsor, who is charged by federal regulation to ensure the compliance of the investigators and their study site staff, CROs, monitors, and all other contractors to regulations and the study protocol. Delegating responsibility to another entity does not absolve the sponsor of its oversight responsibility.

Ensuring compliance is an ongoing activity, spearheaded by robust monitoring efforts to ensure sites and sponsors are always "inspection ready." To support inspection readiness, FDA has posted the *Compliance Program Guidance Manuals* online to direct its field inspectors on inspection conduct. These publicly available manuals are valuable resources for sites and sponsors/CROs/monitors as they indicate the information that will be reviewed by inspectors and serve as a great tool for inspection preparation.

Readiness requires top-level sponsor commitment and departmental prioritization to ensure all internal and external team members are confident and well-trained, processes are adequate and adhered to, and documentation is in place in order to demonstrate compliance. Sponsors need to ensure that their own files and those of their site contractors are ready at all times for a BIMO inspection.

Sponsor Readiness

The most effective and efficient way a sponsor can help sites and contractors to be ready is by setting standards for inspection readiness. Key measures include:

- *Ongoing and robust clinical trial document generation, collection, review, and filing*.

  Everyone who has worked on a clinical study, whether at the sponsor, CRO, or site level, knows that there is an extensive and never-ending stream of study documentation required by law and good clinical practices. Managing this mountain of paperwork is daunting and, frankly, not very interesting; however, it is *critically* important.

Failure to properly manage study documentation throughout a study will result in extensive, time-consuming, and very expensive remediation measures at the time of BIMO inspection. It is cheaper, easier, and far less stressful to develop a file management system before the trial starts and to maintain it for the entire course of the study, whether on paper or electronically in a 21 CFR Part 11–compliant system (as detailed in the *Code of Federal Regulations*).

It can be difficult to convince management of the criticality of robust study file management; it's often seen as an unnecessary administrative task. However, at the end of the study, FDA cares about two things: the integrity of the study data and how well the study was conducted, including subject protection. Every aspect of the study must be carefully, thoroughly, and accurately documented to assure the agency that the trial data are accurate, that subject safety was protected, and that the study was conducted in compliance with regulations and the protocol. If it's not documented, it wasn't done.

Recommendations to help ensure robust study file management include designating and training file management personnel on using a 21 CFR Part 11–compliant electronic trial master file system (eTMF). If an eTMF is not used, develop automated trackers to manage trial documents.

- *Development and ongoing review of standard operating procedures (SOPs) that encompass all clinical trial activities, are compliant to applicable regulations for all relevant geographies, reflect best clinical practices, and outline the actual processes used by the sponsor*.

It is challenging to develop SOPs that provide enough procedural structure to ensure regulatory and clinical practice compliance and consistency across studies, while remaining flexible to avoid boxing yourself into a corner with too much detail. Sponsors must be able to produce adequate documentation during an inspection that confirms SOPs are being followed, or that the sponsor recognized an SOP needed to be modified.

If modifications were needed, the sponsor must demonstrate that appropriate revisions were made, training was conducted, SOP modifications have been evaluated for

effectiveness, and that all of these elements are documented. FDA does not necessarily judge the quality of an SOP *per se;* the agency judges if an SOP is in regulatory compliance and if documentation adequately demonstrates it is being followed. The agency also looks for evidence that shows the sponsor recognizes when an SOP is not robust enough or is ineffective, and that it makes improvements to ensure compliance.

- *Systematic review of study operations and compliance at the site level through onsite and remote monitoring; this may be done by the CRO or monitor*.

To ensure study integrity; to oversee protection of human subject health, safety, and welfare; to assess for fraud; and to ensure site compliance to regulations and the protocol, FDA mandates that a sponsor monitor its studies. Monitoring assures these key study elements are compliant and facilitates achievement of enrollment goals. Monitoring also builds important relationships with site personnel, including the investigators who are your customers, and allows you to correct mistakes that may affect the study's ultimate success and product approval. Monitoring is an excellent opportunity to ensure or correct site compliance and train sites for inspection readiness, including document organization, file review for completeness, proper inspection conduct, and how to interact collaboratively and effectively with FDA.

- *Conduct BIMO inspection training and mock inspections to ensure sponsor and site personnel are knowledgeable about the study and its current status and conduct a protocol review.*

Site training should include a review of the site's specific contributions to the study as reported to FDA, including the site-specific start/stop dates; number of subjects screened, enrolled, and treated with investigational product and/or withdrawn, including reason for withdrawal; as well as the number and type of protocol deviations and the number and type of AEs. Provide each site with a copy of its protocol deviation and AE listings from the regulatory submission for product approval to ensure the site records match what was reported to FDA, and to be able to address discrepancies during the inspection.

Train the sponsor and site teams on what to expect during the inspection, including examples of the types of questions that may be asked, how to interact with the inspector(s), and how answer questions accurately and confidently without overexplaining or providing information that is not requested, speculating, or talking just to fill periods of silence.

If the sponsor does not have prior experience with FDA inspections, it is recommended to seek assistance from a clinical research consulting firm or CRO with proven inspection success helping sponsor and sites prepare for a BIMO inspection.

Clinical Investigator Inspections

Sponsor and CRO assistance to sites during a BIMO inspection helps ensure that site personnel feel well-supported and that they are able to act with confidence, ultimately contributing to a successful inspection. While some sites do not allow sponsors to be present during an inspection, in-person sponsor or CRO support before and/or during an inspection can be very helpful, especially for studies that had a long duration, were complicated, or closed more than a few months before FDA's visit.

Several days before the inspection, if the site allows, the sponsor should go to the site and assist the study coordinators with reviewing the study files to ensure they are in good order and to re-familiarize them with the study history and file structure. During the inspection, it can be helpful to have sponsor representatives ready to assist the investigators and study coordinators with locating documents requested by the inspector, logging the requested documents on the audit log, taking notes, supporting their responses to FDA questions, and providing guidance as appropriate to the site team. Onsite support of OUS sites is especially important and helpful, as site staff in these locations may be less familiar with FDA regulations, inspection practices, and how to work with the agency during an inspection.

Key Points for Sponsors and Sites to Remember During an Inspection

- Be polite and collegial. Alert your receptionist that an FDA inspector may be coming and what to do when the inspector arrives, such as who to notify and in what order.

- Do not leave an inspector alone or allow her/him to wander around unaccompanied. Inform all staff that an inspector is on site and to keep all documents off desks, counters, printers, etc., and to be mindful of hallway, elevator, and bathroom conversations.
- During the inspection, record the inspector's questions, requests, and comments, and log the documents provided to the inspector. Only provide the requested documents and be sure they are complete and in good order before you deliver them. Make two copies of each document: one for FDA and one for you.
- Be sure you understand a question before answering it and ask for clarification if you are uncertain. Never guess, speculate, or lie. If you do not know an answer, it's acceptable to tell the inspector you'll provide the answer later.
- At the end of each day, ask for a summary of the day's activities, clarify any issues that were raised, and try to resolve them immediately. Ascertain if there are any findings that may lead to a Form 483 issuance and ask for the next day's agenda.

What if You Receive a Form 483?

Don't panic! Form 483 is an official list of "Inspectional Observations" issued after an inspection, usually at a closing meeting. Sponsors should use the Form 483 as a guide for corrective action, as the FDA inspector does not usually make specific recommendations. Your firm can and should respond to the Form 483 during the discussion with the investigator before the investigation concludes. In fact, corrective actions or procedural changes that were accomplished immediately in the presence of the investigator are regarded as positive indications of your concern and desire to voluntarily correct discrepancies.

Consider seeking outside expertise for assistance in determining appropriate corrective actions and/or for help with your response. It is critical that you respond in writing with a thorough plan of corrective actions within 15 calendar days to satisfy the requirements of the FDA. The agency will issue an acknowledgment letter to confirm receipt of your response and may ask for additional information or notify you the corrective actions are not adequate. Failure to respond or failure to respond adequately may result in escalation to a Warning Letter. If you receive a Warning Letter, you must respond in writing within 30 days.

Be aware that FDA may conduct a future (and unannounced) inspection to verify corrective actions were implemented and adequately addressed the findings; this may occur as a result of a Form 483 or Warning Letter. Within six months of an inspection, FDA issues an Establishment Inspection Report (EIR), which is a factual narration of the inspection. Form 483s and EIRs are available through the Freedom of Information Act. However, Warning Letters are published on the FDA's website on a monthly basis and are therefore easily accessible to competitors and other interested parties.

Positive Results of Sponsor/CRO BIMO Inspection Support

Presented here are several case studies of successful BIMO inspection readiness activities. The readiness activities addressed potential or identified areas of risk, and ultimately resulted in a successful FDA inspection with no findings.

Case Study 1: BIMO Inspection of a Recently Closed Study

An application for an implantable Class III device was submitted to FDA for Premarket Approval (PMA), which triggered an expected FDA BIMO inspection. The sponsor proactively identified areas of risk for the study and sites, implemented appropriate readiness activities, and had successful inspections.

Areas of Risk

- Investigator noncompliance (repeated protocol deviations, inadequate device accountability).
- Inadequate efforts to secure investigator compliance or discontinue shipment.
- Inconsistent safety event review (lack of documentation to support that all AEs were reviewed by the Clinical Events Committee [CEC] as required).

Sponsor Readiness Activities

- The CRO conducted mock BIMO preparation audits at targeted sites and at the sponsor.

- A corrective and preventive action (CAPA) program was initiated by the sponsor to address noncompliance.
- The CRO provided BIMO inspection readiness training to sponsor and site personnel.
- The CEC adjudicated all AEs as required per the protocol prior to FDA inspections.

Results

- No Form 483 or Warning Letter was issued.
- The PMA application was approved.

Case Study 2: BIMO Inspection of an Archived Study

In a more unusual case, a clinical study for an implantable Class III device was successfully conducted and closed with statistically satisfactory results. However, the sponsor decided to not proceed with a PMA application for business reasons, so all study documents were archived. Several years later, the device was acquired by another firm, which proceeded with a PMA application submission.

Areas of Risk

- The study had been closed and archived for several years. There was extensive sponsor and site staff turnover.
- Some sites had missing files.
- Some sites had closed.
- FDA expressed concern that it would not be able to view source documents and verify that case report form data were true and accurate.

Sponsor Readiness Activities

- All sites were contacted by the CRO well in advance of the PMA submission to determine which study staff were still available, the status of the study documents, and the logistics involved with retrieving them from archive.

- The CRO retrieved the files from storage and carefully categorized and reviewed each document to ensure its completeness. Spreadsheets were developed to catalogue the documents at both the sponsor and individual site levels and missing/incomplete documents were noted.
- All available site files were retrieved from storage and carefully cataloged and filed by the sites.
- FDA was notified which sites had missing or inadequate files.
- Sites were given customized webinar training to refresh them on the study and their site's study details and results.
- The CRO supported the site inspections onsite and remotely by providing requested but missing documents in real time during the inspections.

Results

- FDA acknowledged the challenges for the sites to undergo inspections years after study closure and commended the sponsor for its inspection support.
- The CRO also underwent a successful inspection.
- No Form 483s or Warning Letters were issued for the sponsor, CRO, or sites.
- The PMA application is pending.

Conclusion

FDA inspections are an important component to ensuring product and subject safety and study integrity. Undergoing an inspection is often stressful, but being well organized throughout the study, keeping sponsor and site files in pristine order, training staff on inspection conduct, conducting inspection readiness activities prior to the inspection, and maintaining your composure during an inspection will help ensure a successful outcome.

Reference

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CLINICAL RESEARCHER—JUNE 2019 (Volume 33, Issue 6)

HOME STUDY

Clinical Trial Insights and Imperatives

Why Your Clinical Research Site Needs a Quality Management System

LEARNING OBJECTIVE

After reading this article, the participant will be able to describe the purpose and elements of, and associated responsibilities for staff regarding, a site-based quality management system.

DISCLOSURE

Seema Garg, MS, MBA, CQA, CSSGB: *Nothing to disclose*

1. According to the article, which of the following can constitute a task performance–related quality management system (QMS)?

A. A panel of subject matter experts who meet monthly to review work assignments.
B. A checklist that ensures consistent pay for common duties across job roles.
C. A set of procedures and processes for ensuring consistency and compliance.
D. A regulatory authority–mandated training program for reporting non-compliance.

2. From this article's perspective, which entity holds responsibility for operating according to trial–related regulations and the protocol?

A. The patients
B. The sponsor
C. The contract research organization
D. The site

3. The article cites which of the following as a reason for site staff becoming too dependent on monitoring?

A. Financial pressures on sites has forced them to subcontract many study duties to vendors.
B. The clinical research coordinator role lacks formal education or training requirements.
C. Regulatory authorities have downplayed the legal implications of failed studies for sites.
D. Principal investigators (PIs) often feel monitors are more trustworthy than their own staff.

4. A site-based QMS can ensure continuity and consistency in which of the following areas?

A. Reconciling study budget issues with sponsors.
B. Closing study enrollment ahead of schedule.
C. Maintaining a study's essential documents.
D. Publishing a study's results in a timely manner.

5. The article cites which of the following activities to be covered in standard operating procedures (SOPs) as examples of items to be included in a site's QMS?

1. Inspection readiness
2. Informed consent process
3. Source documents
4. Patient reimbursement

A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

6. An internal assessment SOP describes what process at a site?

A. The site's internal assessment of its financial health.
B. The site's internal assessment of its studies.
C. The site's internal assessment of its inspection readiness.
D. The site's internal assessment of its reputation.

7. Which of the following SOPs does the author cite as most commonly absent at sites?

A. Training
B. Internal assessment
C. Informed consent
D. Inspection readiness

8. An SOP for study continuity allows which of the following?

A. Departing staff members to hand over a study to new staff.
B. Departing PIs to take a study protocol with them to their new site.
C. Departing sponsors to hand over investigational products to new sponsors.
D. Departing patients to continue taking a study drug at a new site.

9. What type of SOP is mentioned in relation to a subject's reading and comprehension skills?

A. Training
B. Internal assessment
C. Informed consent
D. Inspection readiness

10. A source documentation and Good Documentation Practices SOP can address which of the following challenges?

A. Ensuring informed consent documents are no longer than four pages.
B. Ensuring that a study protocol in layperson's language is available.
C. Ensuring that PIs turn in their observations in legible handwriting.
D. Ensuring source documents and case report forms are attributable.

BIMO Inspections: Recommendations for Sponsors

LEARNING OBJECTIVE

After reading this article, the participant should be able to describe the reasons for and structure of FDA BIMO inspections, and how sponsors can prepare for and follow up on them.

DISCLOSURE

Mary Kay Kessinger Sobcinski, RN, BSN, MHA; Susan Wiskow, CCRP: *Nothing to disclose*

11. Which of the following is noted as a role of the Bioresearch Monitoring (BIMO) program?

A. Verify accuracy and reliability of biological specimen collection.
B. Verify accuracy and reliability of clinical study data.
C. Verify accuracy and reliability of study blinding procedures.
D. Verify accuracy and reliability of study's published results.

12. Following a BIMO inspections, which two documents are possible for sponsors to receive from the U.S. Food and Drug Administration (FDA)?

A. Form 1572, Conflict of Interest Disclosure
B. Form 482, Notice of Disbarment
C. Form 483, Warning Letter
D. Form 3674, Study Closeout Notice

13. Which of the following is noted as a commonly discovered deficiency for an investigator or study site?

A. Inadequate accountability of the investigational product.
B. Inadequate budgetary resources for the study being conducted.
C. Inadequate review of the protocol by independent doctors.
D. Inadequate documentation of the subjects' motivations for participating.

14. What does the article say about FDA inspections of sites outside the United States (OUS)?

A. FDA only inspects OUS sites in certain problematic countries.
B. FDA will inspect OUS sites the same as domestic sites.
C. FDA currently never inspects OUS study sites due to the expense.
D. FDA inspects one OUS site for every 10 U.S. sites in a study.

15. Which online resource is available from FDA to support inspection readiness?

A. *Code of Federal Regulations*
B. *Corporate Social Responsibility Guide*
C. *Compliance Compendium*
D. *Compliance Program Guidance Manual*

16. The authors recommend developing a file management system that is compliant with which of the following?

A. ICH GCP
B. Form 483
C. 21 CFR Part 11
D. CDRH

17. Which of the following is cited as a reason for FDA mandating that sponsors monitor their studies?

A. Overseeing protection of the study's human subjects.
B. Overseeing functions of the site's institutional review board (IRB).
C. Overseeing training of the study's principal investigator (PI).
D. Overseeing vendors assigned to data safety monitoring.

18. If the site permits, what should a sponsor do in advance of a BIMO inspection?

A. Assist PI with protocol amendments review.
B. Assist IRB with meeting minutes review.
C. Assist study coordinators with study file review.
D. Assist monitors with delegation of authority review.

19. How soon should sponsors respond to a Form 483 from FDA?

A. Within two weeks.
B. Within 15 calendar days.
C. Within 30 calendar days.
D. Within two months.

20. FDA may do which of the following after a scheduled BIMO inspection?

A. Conduct an unannounced, follow-up inspection.
B. Mandate a full-scale reassignment of study staff.
C. Launch a financial investigation of the PI with the IRS.
D. Direct the sponsor to award the site new studies.