Preparing for a Clinical Investigator Inspection

(Voice on phone): Jao Cardiac Center...

Inspector:
Hello, this is Inspector Al with the U.S. Food and Drug Administration. Is Dr. Jao available?

(Voice on phone):
Yes, he is. One moment, please.

Dr. Jao:
Hello, this is Dr. Jao speaking.

Inspector:
Hello, this is Inspector Al with the U.S. Food and Drug Administration. It's my understanding that you're a clinical investigator with a cardiovascular stent study sponsored by Acme Medical Device Company.

Dr. Jao:
Yes, I am.

Inspector:
I'd like to make arrangements to visit with you and your staff on Monday morning to conduct a clinical investigator inspection for the study.

Dr. Jao:
I think I can arrange that. Will you be the only one coming?

Inspector:
Yes, Dr. Jao, I'll be the only FDA employee conducting the inspection. We can be available, say around 9 a.m. Will that be good for you?

Dr. Jao:
Yes, 9 o'clock works well for me.

Narrator:
A Bioresearch Monitoring or BIMO inspection is a type of regulatory compliance inspection conducted by an employee of the United States Food and Drug Administration, or FDA. A BIMO inspection occurs at reasonable times and in a reasonable manner. Furthermore, a BIMO inspection is primarily an evidence-gathering activity In support of a marketing application.

FDA tries to complete inspections in a timely manner so FDA can make a timely decision on the marketing of the device to meet user fee performance goals and fulfill its responsibility to get new medical products to patients that need them.

FDA inspections may occur a sites located within the United States or at sites located outside the United States. The FDA Center issues inspection assignments to the FDA district office who assigns the inspection to an FDA investigator. The FDA investigator who receives the inspection assignment generally contacts the site a few days in advance of the site visit to pre-announce the inspection.
The pre-announcement helps the study site ensure that relevant study personnel and all required records will be available during the inspection.

Inspector:
Dr. Jao, in preparation for the inspection, I'd like to request that all study records are accessible, available and organized.

Dr. Jao:
I can arrange that. Would you need anything else?

Inspector:
Yes, I'll need access to a photo copier to make copies of any study-related documents.

Dr. Jao:
Is there a timeframe for the inspection?

Inspector:
Timeframe? Given the number of study subjects you have enrolled in this study, I suspect that my visit to your site will take approximately 3 to 5 days.

Dr. Jao:
In that case, I'll have my study coordinator also assist you during your visit.

Inspector:
Wonderful. Thank you, Dr. Jao, for making yourself and your staff available. I look forward to seeing you on Monday morning. Have a good day.

Dr. Jao:
Thank you, Inspector Al. We look forward to meeting with you as well. Good-bye.

Inspector:
Bye-bye.

Narrator #2
If you are a sponsor of Medical Device Research, consider the following steps to prepare all sites for an FDA inspection:

First, inform the clinicalinvestigator that the FDA may inspect their study site and to be prepared for an FDA inspection at anytime.

Ensure that the clinical investigator understands that the pre-announcement of an inspection is not an appointment to be scheduled at his or her convenience. Rather, it's a courtesy to allow the site time to collect records and notify relevant study personnel.

Additional considerations to prepare sites for an FDA inspection include informing the clinical investigator at the beginning of the study what actions to take if they receive notification of an upcoming FDA inspection.

For instance, should the sponsor, assign monitor, or Institutions Research Committee be notified?
Inform the clinical investigator and the study staff to ask sufficient questions when they receive the FDA inspection pre-announcement, so they clearly understand which study will be inspected.

Consider doing a mock FDA inspection, especially at sites where monitoring identifies regulatory departures or deviations.

[music]

Inspector: Good morning.

Receptionist: Good morning. How can I help you?

Inspector: I'm Inspector Al with the U.S. Food and Drug Administration. I have a meeting today with Dr. Jao.

Receptionist:
Do you havea government-issued form of identification?

Inspector: Yes, I do.

Receptionist: Can I see it?Thank you. You can have a seat over here. I'll inform Dr. Jao that you're here.

Inspector: Thank you.

Receptionist: You're welcome.

Dr. Jao: Hi, good morning. My name is Dr. Jao. You must be Inspector Al.

Inspector: Yes, I am. Here are my credentials.

Dr. Jao: Okay, thank you for much. I reserved a room for you to meet with me and my clinic staff and to review the study-related documents.
Can you just follow me, please?

Narrator:
At the start of inspections conducted at locations in the United States,the FDA investigator issues a Form FDA 482 or an Official Notice of Inspection to the most responsible person. This form identifies under what authority FDA may inspect the site.

Inspector: Hi, Dr. Jao. Thank you for meeting with me today.

Dr. Jao and Team: Our pleasure.

Inspector:
Great. And if you can tell me a little bit about the study, and this way I can get oriented in terms of what documents I should be looking at. That'd be very helpful.

Dr. Jao:
Okay, in this study…

Narrator:
Bioresearch Monitoring inspections are designed to monitor all aspects of the conduct, recording and reporting of FDA-regulated research.
They involve interviews with site personnel, on-site evaluation of source documents, evaluation of systems in place to protect human subjects, the quality of data, and compliance with applicable regulations.
FDA may also inspect and copy study records.

Inspector:
Did you have a series of adverse events during the course of this study?

Dr. Jao's Team:
We've had some of the adverse events that are recorded here.
Maybe, Janet, it's in that one…

Narrator:
During the inspection, the FDA investigator reviews study-related records to answer several questions. Were the rights, safety, and welfare of human research subjects protected?

Did an Independent Ethics Committee, or Institutional Review Board provide initial and continuing review and approval of the informed consent document and study protocol?

Was informed consent obtained under circumstances that provide subjects sufficient opportunity to consider whether or not to participate?

Was informed consent obtained under circumstances that minimize the possibility of coercion or undue influence?

Was information given to subjects in a language understandable to the subject?

Did the informed consent include the eight basic elements and when appropriate, the six additional elements of informed consent?

Were the informed consent documents signed and dated by the subject or their legally authorized representative prior to enrollment or before any study-related procedures?

Were the quality, reliability and integrity of data ensured?

Were study-related procedures followed?

Are expedited and periodic reports of both anticipated and unanticipated adverse events, plus device performance issues, accurate, complete and current?

Are device accountability records accurate, complete and current?

Was appropriate study monitoring completed by the sponsor?

FDA tries to answer these questions to obtain confidence in the qualityand integrity of data. FDA inspections also help to ensure human subject protections and help decision makingregarding the safety and effectiveness of medical products.

Points to consider during the inspection include:
- document any changes, deviations or exceptions to any records;
- provide information or records that are clear and responsive to questions from the investigator as appropriate;
- documentthe inspectional coverage;
- make a photo copy machine available.

During the inspection, FDA reviews study specific records such as:
- All regulatory documents such as study protocols, protocol amendments, Ethics Committee or IRB approvals and reports, device accountability records, study monitoring information, site personnel information and study subject enrollment information;

- All sponsor correspondents, such as standard operating procedures, work instructions, letters, memoranda, e-mails and monitoring visit reports.
- All study patient or study records, such as informed consent documents, Case Report Forms, clinic charts, subject diaries, laboratory reports, hospital records and adverse event records.

Inspector:
Hi Dr. Jao. Thank you for meeting with me during this closeout meeting. As we discussed duringthe time of our inspection, there were some deviations noted and I would just like to present to you the 483 today.

Narrator:
At the completion of the FDA inspection, the FDA investigator may issue a Form FDA 483, which lists significant inspection observations. Other observations may be discussed verbally with the clinical investigator at the end of the inspection. If you do not receivea Form FDA 483 or there are no significant problems, then no response is necessary.

If you receive a Form FDA 483, FDA recommends that you promptly respond to it in writing, preferably within 15 working days.

In developing your response to any Form FDA 483, consider including the following:
- an assessment of the root cause of the problem,
- any corrective actions that have been or will be taken to correct the problem,
- an evaluation of the extent of the problem to determine if the same issue is present in other study records that were not reviewed by the FDA investigator,

- a description of any preventative actions that have been or will be taken to prevent recurrence of the problem in future studies along with a timeline for their implementation.
- And finally, supporting documentation should be included with the response.

Adequate responses to FDA inspectional observations may have a favorable impact on the final classification of the inspection.

Following the inspection, the FDA investigator completes a report of the inspection referred to as an Establishment Inspection Report, or EIR.
He forwards this report, along with the Form FDA 483, if issued, and any supporting documentation or exhibits to the Bioresearch Monitoring Unit with the FDA Center.
The center evaluates the report, determines the significance of any findings to the safety and effectiveness of the device, and issues a final classification for the inspection.

These inspection findings are made publicly available through the Freedom of Information Act. FDA wants to foster the development and facilitate the marketing of innovative products that advance public health.

The agency relies on these inspections to build confidence in the design, conduct, recording and reporting of clinical research that supports the safety and effectiveness of medical devices.

It is very helpful for people to be cordial and cooperative throughout the inspection. Thank you.