Why conduct facility inspections? If you think about the reasons for conducting the inspection, it will guide HOW you should inspect. Field auditors – what do we inspect? Application. Harvest. Planting for some types of studies. In about 10 years of working as QA for a sponsor company, I don't honestly remember seeing other types of audits. If there were other types reported, it was really rare and always in conjunction with something else (ie harvest/shipping). It's logical because we all tend to think about inspecting the most important critical events. But there are other activities that are important in the overall compliance at a field site. They're just harder to inspect and that's partly because of scheduling. For example, you don't necessarily know when test material will be received and logged in or when samples will be shipped. Also, everyone is trying to find ways to cut costs, so it's really unlikely that you have the option of doing an "extra" audit for those activities. And somehow, it just doesn't feel like you're hitting the important events if there isn't an application or harvest involved.

Because it is expected! Facility inspections fill in that gap. When a sponsor places a trial at a field site, they are placing a trust in the field site that the study will be conducted in compliance with GLP. The way that they can have that confidence is by conducting a facility inspection to assess the entire operation at the site. The EPA will do the same thing when they conduct a facility inspection. By the way, the EPA will not consider reliable for purposes of supporting an application for a research or marketing permit any data developed by a testing facility that refuses to permit inspection in accordance with this part.(160.15) So if you are the QA for a field facility, it makes sense to do a facility inspection to head off any compliance issues before sponsors or the EPA are the ones to find issues. It's relatively easy if you are a full time or in-house QA. That leaves the facilities that use contract QA. I think it's worth paying to have a facility inspection done. Either way, your regular QA person can't really inspect the QAU.// Is there anyone whose site has never been inspected by the EPA? Has your site been doing business for less than 3 years? Is there anyone here who has never had a facility inspection done by any sponsor? Are you a brand new facility?

Get Ready. Facility inspections should be scheduled in advance. EPA generally gives a facility 10 days to 2 weeks advance notice, sponsors about the same if possible. If you're inspecting a facility using a checklist, it's a nice courtesy to attach a copy of that checklist to a confirmation email that gives the time and date of the inspection. Make it clear in your email whether you will need documents just to review or to have copies for your records. When you list the documents you need to have for your records, note whether you want these in advance or at the time of the inspection. This will always include a (Sanitized) Copy of Master Schedule, SOP Index including QA SOPs, Facility Floor Plan, Organization Chart at minimum. Also, list the documentation you will want to review. It should include SOPs, CV/Training Records, Job Descriptions, Equipment Logs, Facility Logs.

Beginning the Inspection. I know inspectors who arrive the night before and ask to review SOPs in their hotel rooms the night before the inspection. Or you can skim the SOPs on the spot. It doesn't matter what order you use, these are the two basic parts to an inspection. I prefer to do the tour first then review the documentation. Should you use a checklist or not? Depends on your preference. The checklist is a good tool to make sure you cover all areas in the inspection. But if you use a checklist, don't rely exclusively on it for gathering information about compliance. EPA inspectors don't use a checklist. They do have an SOP that guides how to conduct the inspection. I'll give you the reference for that at the end of my presentation.
During the tour, you'll be able to answer a lot of your questions from a checklist and gather information about the general operations of the site.

Focus on GLPs. (Almost) Everyone has had some experience with facility inspections. Whether you're doing the inspecting or being inspected – and whether it's facility QA, sponsor QA or EPA, the

inspection should essentially be the same. The focus is on the compliance system and the facility itself. It's not a study audit.

Subpart B Organization and Personnel. This part also includes the requirements for all of the functions of the QAU. You should review Org Chart, Master Schedule, CV/Training Records to verify that all personnel involved in the conduct of regulatory studies have the education, training, and experience to adequately perform their assigned functions, and that there are sufficient numbers of personnel for the timely and proper conduct of the ongoing studies. "Sufficient numbers" is subjective – but can be determined by asking the right questions: are functions being performed and data reported in a timely manner?// Is the org chart up to date? Does it show all personnel involved in GLP studies, the lines of reporting including QA. How is the QA informed about studies – what is the communication process for setting up inspections? Does QA have a copy of protocols? What and how often does QA inspect? What is the QA process for reporting audits? How are SOP or protocol deviations documented and reported? EPA can't review the inspection reports, but sponsors can review those that pertain to their studies//Is the MS up to date and does it contain all of the elements listed in 160.35 (B)1? Is it sortable by Test substance? Who maintains MS? How often is MS printed / archived, and does this comply with what the facility SOP says? Does QA have access to a copy. It's not a function of the QA to maintain the MS.// Are training records up to date? Archived for former employees? Are signatures and initials on file so that data can be attributed?// Are job descriptions available? Is there documentation that study personnel clearly understand their assigned functions?

Subpart C Facilities. A lot of this portion of the inspection can be covered during the tour. Determine if there is adequate space for the conduct of the study and maintaining separation of multiple test plots in the field? Are there adequate field history and maintenance chemical records? How are the plots identified? Are there separate areas for test substance receipt and storage to prevent contamination or mix up? Separate areas for sample storage, test substance mixing / calibration? Is the facility housekeeping adequate? Are facility records such as sample shipment logs up to date? Is there an archive? Is there adequate security for the site to protect the samples and data generated for the study?

Subpart D Equipment. Are there logs for all equipment? Do they contain records of routine and non routine maintenance? What is the frequency of archiving the records? Are computer programs used for the collection of data validated? Are validation records archived? Is equipment calibrated according to the requirements of the facility SOP or protocols? Protocol takes precedence over a facility SOP – so if the procedure is given in a protocol, do you have an SOP deviation, and if so how should this be documented?

Subpart E Test Facility Operation. Are there sufficient SOPs for the conduct of trials at the field site, including:

Test system care and maintenance

Receipt, identification, storage, handling, and mixing of the test, control, and reference substances.

Test system observations.

Collection and identification of specimens.

Data handling, storage and retrieval.

Maintenance and calibration of equipment.

Placement, and identification of test systems.

And an area I think has growing importance. How to handle failures of equipment, what to do in case of disaster, and how to handle business closure. These don't all have to be in separate SOPs but they should all be covered.

Are SOPs approved by facility management? How often are they reviewed? How is review documented? How are they distributed to multiple sites? How are historical SOPs handled? This is one of those areas where I don't really like checklists, because I think QA inspectors tend to get dragged into the checkbox mentality and check off whether or not a million different SOPs are in place rather than thinking about whether or not there are sufficent SOPs to conduct trials and protect data. As I mentioned earlier, I know some inspectors read every SOP in great detail prior to or during inspections. Have you heard the term "SOP Drift?" It refers to that tendency to read SOPs once a year – then think you know what's required for the rest of the time and you drift from the SOP. For an internal facility inspection, this is an excellent time for the QA to really review those SOPs to see if they're being followed. For external inspectors, my philosophy is that the SOPs should reflect the procedures conducted at the site, and that reviewing representative or key SOPs is sufficient.
EPA's SOP states that: It is not necessary for the inspector to review all SOPs in effect at the facility. However, they should verify that written SOPs exist and are of adequate scope and detail, should review several of the key SOPs, and should be alert to any deviations from SOPs which may have occurred during the conduct of an ongoing study, and ascertain that these changes were properly authorized.

Subpart F Test, Control, and Reference Substances. How are test substances received, stored, handled, and disposed? Is there adequate documentation of TS distribution? Are there procedures in place to prevent contamination of the TS? Is the test substance storage area secure/kept locked/access limited/with proper signage? If there is an expiration date assigned to the test substance, are all applications made prior to this date? Is there documentation of test substance characterization prior to trial initiation? If characterization wasn't conducted at the field facility (and it usually isn't), where are the records being retained? EPA inspectors will expect to see this documentation, so field facilities will usually need to request it from the sponsor company for the inspection. So, how do sponsors in the room expect field facilities to maintain additives (not maintenance chemicals)? GLP or not? How are the PI's doing it?

Subpart G Protocol / Conduct of Study. Is there a fully signed copy of the protocol and all amendments at the field site? For EPA inspections, you may have to request certain amendments because sponsors may consider this confidential information, but EPA expects to see it all.
It's a good idea to review the data notebook for an ongoing study, if possible. Check to see if all data being collected as required by the protocol. Is data being recorded promptly, legibly? Are corrections being made according to GLP regulations – crossed out with a single line, signed and dated, with an explanation of why the change is being made? Is it being signed and dated at the time of collection? Are applications being made at the correct intervals, samples being taken when required? If not, are deviations being handled properly – are explanations being documented? Or is the PFI overlooking activities because they don't have sufficient numbers of personnel for the timely and proper conduct of the ongoing studies.

Subpart J Record Storage & Retrieval. Are reports (field summary reports) being written at field sites? If so, are copies being archived? Is study data (or a copy of the data) archived at the site if required by study protocols or facility SOPs? In any case, facility records should be archived, along with equipment logs. Is there adequate protection of the records? Limited access to the archives? Fire/Flood protection? Are records indexed and easy to retrieve on request?

Conclude the Inspection. Paraphrasing the EPA SOP, the GLP inspection report which gives the findings from the inspection, should outline the specific areas which were reviewed as part of the inspection, and whether or not deficiencies were found. The inspector should particularly identify any GLP deficiencies which are serious enough to affect the integrity and/or reliability of data generated at the facility. All deficiencies, inconsistencies or irregularities must be properly documented. I believe that any findings should be discussed with facility personnel prior writing the report to clarify misunderstandings, so there should be no surprises or "gotcha" moments.

The exit interview should be conducted with appropriate facility personnel present who can address findings, either immediately or with follow up actions. Distribution of the final facility inspection report will depend on the SOP of the inspector. EPA will cover findings, but the final inspection report is usually not available for months. Let's take a minute to think about how inspections in general should be reported. For a Critical event inspection, the GLP requirement is that the report must be sent to the study director and study director's management. That's AT A MINIMUM. There are additional or alternate distribution requirements by some sponsor or management companies. I send them by email to all the required parties and print a copy of the "sent" email that I attach to my copy of the audit report. How should facility inspection reports be distributed?

Keys to Successful Inspections. There are some keys to successful facility inspections, whether you are the inspector or you are being inspected. The first is being prepared. If you're the inspector, list the documents you need or will need to review. If you are part of the facility being inspected, have those documents copied or ready to review. It makes the process faster – and starts the inspection on the right path. Why irritate the inspector before they even get started? Second, communication is highly important in this business. Never be afraid to ask questions. And How you state your findings is often just as important as the findings themselves. If you are respectful and have reasonable explanations for your findings, the information will be accepted more readily and hopefully used to improve facility compliance. Finally, keep in mind the difference between what is required for GLP compliance and what is your company's preference. If you're inspecting a contract facility, they probably do work for a number of different sponsors and management companies. In your inspection report, stick to listing any compliance findings, as long as they are actual GLP issues or discrepancies from the facility's SOPs. It's also reasonable to make suggestions for improvement, but these should be clearly distinguished from compliance findings.

EPA Facility Inspection SOP. I mentioned earlier that the EPA uses an SOP to guide their inspections. There isn't enough time in this sessions to cover all of the details, but if you go to the website, the 21 page SOP is posted at:

http://www.epa.gov/compliance/resources/policies/ monitoring/fifra/sop/glp-c-01.pdf