From: OC GCP Questions
To: [redacted]
Subject: FW:
Date: Monday, June 25, 2018 12:39:00 PM
Attachments: [redacted]

Good afternoon –

FDA regulations require very few signatures regarding clinical trial documents - notably those required are the clinical investigator s signature on a Form FDA 1572 (for drug studies under an IND) or the investigator agreement (for device studies under an IDE) and the dated signature of study subjects on an informed consent document. Additional signatures are recommended in the ICH Good Clinical Practice (GCP) guidance (ICH E6 (R2)) which FDA does consider official guidance but which is still just guidance. In addition, investigational plans/protocols often require additional signatures. When FDA inspects a site and reviews study documents, compliance with what is specifically in regulations is what is expected for all aspects of the study, including signatures on appropriate documents. If a study sponsor or reviewing IRB requires additional signatures, lack of such signatures would be considered a failure to comply with the investigational plan/protocol or the requirements of the IRB respectively and could be so noted among an FDA investigator's inspectional observations. Therefore, if the sponsor, IRB, or local/country regulations require signatures on the source documents, then FDA would expect to find them. Otherwise, they are not required by FDA regulations. When the regulations are silent, sites and institutions have the freedom to develop you own standard operating procedures to handle a specific situation outlined in your email.

Additionally, the regulations require sponsors of clinical investigations to select only investigators qualified by training and experience to investigate the test article (see 21 CFR §§ 312.53 and 812.43). FDA considers this to include the investigator meeting any licensing requirements of the jurisdiction where the trial takes place. The regulations further require investigators to supervise the testing (for investigations of drugs, including biological products, under 21 CFR Part 312, investigators commit themselves to personally conduct or supervise the investigation; for investigations of medical devices, under 21 CFR Part 812, investigators commit themselves to supervise all testing of the device involving human subjects). Investigators may delegate a task to individuals who are qualified to perform the task, including being appropriately licensed.

FDA's "Guidance for Industry: Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects" (available at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf), includes the following information:

The investigator should ensure that any individual to whom a task is delegated is qualified by education, training, and experience (and state licensure where relevant) to perform the delegated task. Appropriate delegation is primarily an issue for tasks considered to be clinical or medical in nature, such as evaluating study subjects to assess clinical response to an investigational therapy (e.g., global assessment scales, vital signs) or providing medical care to subjects during the course of the study. Most clinical/medical tasks require formal medical training and may also have licensing or certification requirements. Licensing requirements may vary by jurisdiction (e.g., states, countries). Investigators should take such qualifications/licensing requirements into account when considering delegation of specific tasks. In all cases, a qualified physician (or dentist) should be responsible for all trial-related medical (or dental) decisions and care.

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional questions.

Kind regards,

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Office of Good Clinical Practice
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This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.

From: [redacted]
Sent: Friday, June 22, 2018 7:58 PM
To: OC GCP Questions <gcpquestions@fda.hhs.gov>
Subject: FW:

Hello FDA!

I recently monitored a site that has created the following policy regarding the requirement of signing off on all labs that the subjects have while on study. Some of the Cancer patients get multiple labs each week. They decided that they will ONLY have the Investigator physically sign and date a review of those labs that are sent to the central (not local) lab. The investigator will note if the labs are significant or not significant.

Any local lab results will , of course be reviewed, but will not be printed out and signed off as significant or not significant. I think this is a great idea. They told me some sponsors have no problem with it but other sponsors said the FDA wont like this practice. I disagree that this practice of not physically signing off on LOCAL labs would be problematic for an FDA auditor. The FDA wants evidence of physician oversight. As the treating physician, they do review all lab results upon receipt and are notified by the lab if there are any significant values. I don't think they need to sign all of these local labs. They still have oversight without having to do this added step. I know many other sites that are adopting this practice. I think its very reasonable. Please let me know if the FDA or its Inspector would have any problems with this practice.
Thanks!!!!!

Here is the text from the SOP:

"Investigator oversight is essential in the proper conduct of any clinical trial. Some sponsors have historically requested that investigators provide a wet-ink sign-off on laboratory results originating from the patient electronic medical record, indicating clinical significance of values. This has put undue burden on study staff, as this is often duplicative effort since it is standard practice for the investigators to review a subject's labs in the electronic medical record prior to treatment. Often it is not possible for study staff to obtain a physical signature on printed labs prior to treatment, so

signatures may have been obtained days or weeks later. The Cancer Center Clinical Trial Office (CCCTO) does not feel this practice improves patient safety and does not add value to the clinical trial process. Signing off on pages of labs that took place in the past is a hindrance to study investigators and takes away time from performing other meaningful safety-related tasks. Lab results generated from a central lab will continue to be reviewed and signed by investigators if required by the sponsor.

The practice of obtaining physical signatures (often long after treatment is delivered) does not improve patient safety or add value to the clinical trial process. Therefore, the study staff will not obtain investigator wet-ink signatures on laboratory results originating from the electronic medical record. As a standard practice, patient laboratory results are reviewed by the study coordinator and the subject's clinical team
Clinical Trials Office prior to treatment. These values are evaluated with the protocol to check for any necessary dose modifications, sponsor reporting, or other necessary clinical actions.

All laboratory results requiring action (i.e. dose modification and/or other intervention such as supportive medication administration, supplementation, physical therapy, diet change, fluid administration, transfusions, additional testing, etc.) will be considered "clinically significant". If no action is taken based on an out-of-range lab value, it will be considered "not clinically significant."

Treatment decisions will be based on local lab results. An investigator will only use central labs to determine treatment decisions if local labs results are unavailable.

Laboratory reports originating from a central lab will be reviewed and signed by the investigator, if required by the sponsor.