From: OC GCP Questions
To: [redacted]
Subject: Question about the SMO
Date: Thursday, January 12, 2017 8:54:00 AM
Attachments: [redacted]

Good morning –

I can offer you general information on SMOs.

FDA does not have an explicit definition of SMO's in our regulations nor do we regulate SMO's as a unique entity. In general, SMO's represent groups of clinical investigators sharing common SOP's and patient data bases; they therefore fall under CI regulations. In some cases, the SMO also assumes contract responsibilities for a sponsor (i.e., taking on sponsor responsibilities under the regulations), and in rare cases, we have seen SMO's set up IRB's (which thereby fall under IRB regs).

The point here is that SMO's are a heterogeneous lot --- and are regulated according to the groups they comprise and functions they undertake. They are clearly an important and growing entity in clinical research --- and one for which we are indeed reviewing the possible need for some regulatory definition and guidance/regulations appropriate to any such definition.

The tasks that you list in your email should be documented in writing. SOPs should also in place documenting the specific tasks. If a particular site is using an SMO, the sponsor should be informed and agree. Additionally you may want to consult your legal representative at your institution to ensure the tasks that you describe are in agreement with the institutional policies and procedures.

Again, SMO's duties and responsibilities should be clearly stated and described in writing. The role of a SMO is different than the monitor. SMOs are mentioned in the guidance link below - Protecting the Rights, Safety, and Welfare of Study Subjects
www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127740.pdf It states

What are an Investigator's Responsibilities for Oversight of Other Parties Involved in the Conduct of a Clinical Trial?

a. Study staff not in the direct employ of the investigator

*The staff involved directly in the conduct of a clinical investigation may include individuals who are not in the direct employ of the clinical investigator. For example, a site management organization **(SMO)** may hire an investigator to conduct a study and provide the investigator with a study coordinator or nursing staff employed by the **SMO**. In this situation, the investigator should take steps to assure that the staff not under his/her direct employ are qualified to perform delegated tasks (see section III.A.1) and have received adequate training on carrying out the delegated tasks and on the nature of the study (see section III.A.2), or the investigator should provide such training. The investigator is responsible for supervision of the study tasks performed by this staff, even though they are not in his/her direct employ during the conduct of the study (see section III.A.3) and this responsibility exists, no matter how qualified and experienced these staff members are. In the event that the staff's performance of study-related tasks is not adequate and cannot be made satisfactory by the investigator, the investigator should document the observed deficiencies in writing to the staff's supervisor(s). Depending on the severity of the deficiencies, the clinical trial may need to be voluntarily suspended until personnel can be replaced.*

b. Parties other than Study Staff

There are often critical aspects of a study performed by parties not involved directly in patient care or contact, and not under the direct control of the clinical investigator. For example, clinical chemistry testing, radiologic assessments, and electrocardiograms are commonly done by a central independent

laboratory retained by the sponsor or the investigator. Under these arrangements, the central laboratory usually provides the test results directly to the sponsor and to the clinical investigator. Because the activities of these parties are critical to the outcome of the study, and because the sponsor retains the services of the laboratory, the sponsor is responsible for seeing that these parties are fulfilling their responsibilities for the study.

Less frequently, a study may require that clinical investigators arrange to obtain information critical to the study that cannot be obtained at the clinical investigator's facility. For example, if the study protocol requires testing with special equipment or expertise not available at the clinical investigator's facility, the investigator might make arrangements for someone outside the facility to perform the test. In this case, the results are provided directly to the clinical investigator, who then submits the information to the sponsor. Where such assessments are retained by the investigator, the investigator should take steps to ensure that the facility is adequate (e.g., has the required certifications or licenses). The investigator may also institute procedures to ensure the integrity of data and records obtained from the party providing the information (e.g., a process to ensure that records identified as coming from the party are authentic). Procedures are particularly important when assessments are crucial to the evaluation of the efficacy or safety of an intervention or to the decision to exclude subjects who would be exposed to unreasonable risk.

Additionally, Transfer of obligations to a contract research organization (CRO) is outlined in 312.52 (drugs and biologics)

(a) A sponsor may transfer responsibility for any or all of the obligations set forth in this part to a contract research organization. Any such transfer shall be described in writing. If not all obligations are transferred, the writing is required to describe each of the obligations being assumed by the contract research organization. If all obligations are transferred, a general statement that all obligations have been transferred is acceptable. Any obligation not covered by the written description shall be deemed not to have been transferred.

(b) A contract research organization that assumes any obligation of a sponsor shall comply with the specific regulations in this chapter applicable to this obligation and shall be subject to the same regulatory action as a sponsor for failure to comply with any obligation assumed under these regulations. Thus, all references to "sponsor" in this part apply to a contract research organization to the extent that it assumes one or more obligations of the sponsor.

There is a draft guidance regarding monitoring - link below - A Risk-Based Approach to Monitoring
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf

For purposes of this guidance, monitoring generally refers to the methods used by sponsors of investigational studies, or CROs delegated responsibilities for the conduct of such studies, to oversee the conduct of and reporting of data from clinical investigations, including appropriate investigator supervision of study site staff and third party contractors. The primary focus should be on the processes that are critical to protecting human subjects, maintaining the integrity of study data, and compliance with applicable regulations. The findings should be used to correct investigator and site practices that could result in inadequate human subject protection and/or poor data quality.

I hope this information is helpful.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

U.S. FOOD & DRUG ADMINISTRATION

From: [redacted]
Sent: Tuesday, January 10, 2017 2:30 PM
To: OC GCP Questions
Subject: Question about the SMO

Dear Madam, Sir,

I'm [redacted] working in a clinical research team.
We are newly exploring the role and responsibility of external SMO and having some questions about what can or cannot do with SMO. Our local SMOs are private companies providing admin services and thus are not directly hired by investigators and by hospitals.

I'm writing to you in order to seek your advice regarding the below questions related to external SMO:

1. I have consulted FDA website but could not find any guidance regulating SMOs' activities. Do you have this type of document?
2. If a sponsor uses 1 SMO for admin work at every site in a specific study. The payment is made directly from sponsor to SMO based on an agreement between sponsor, investigator, hospital and SMO. It is considered as a study setup. Do you see any conflict of interest and/or any risk of data bias?
3. To ensure site admin tasks, which qualification we can expect from SMO? Is biology-related field graduation acceptable?
4. Is a direct contact with a patient for collecting AE/SAE information considered as admin task?
5. Can SMO complete the medical notes during a consultation? An investigator will sign off after reviewing the notes.

We hope that with the involvement of SMO in our studies, we can ensure a better patient follow-up and protocol compliance. Therefore, your advice is important to our further consideration.

Thank you in advance for your kind response,
Regards,
[redacted]