**From:** OC GCP Questions
**To:** [redacted]
**Cc:** CDER DRUG INFO
**Subject:** RE: pharmaceutical company requirements for licensed MDs
**Date:** Wednesday, October 01, 2014 12:19:00 PM

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Dear [Redacted]-

Thank you for your question, which was forwarded to my office for a response. From the limited information provided, I am not sure whether you are asking if **the sponsor company** that initiates a clinical investigation must employ licensed physicians vs. whether **the investigator** who actually conducts a clinical investigation must be a licensed physician, so I've addressed both of these questions in that order below.

The FDA regulations regarding responsibilities of sponsors and investigators who participate in FDA-regulated drug studies can be found in 21 CFR 312 subpart D (see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312&showFR=1&subpartNode=21:5.0.1.1.3.4).

Among the many responsibilities of sponsors outlined in these regulations, section 312.56(a) and (c) requires the following:

> *Sec. 312.56 Review of ongoing investigations.*
>
> *(a) The sponsor shall monitor the progress of all clinical investigations being conducted under its IND.*
>
> *(c) The sponsor shall review and evaluate the evidence relating to the safety and effectiveness of the drug as it is obtained from the investigator. The sponsors shall make such reports to FDA regarding information relevant to the safety of the drug as are required under 312.32. The sponsor shall make annual reports on the progress of the investigation in accordance with 312.33.*

Additionally, the regulations regarding IND safety reports, found at 21 CFR 312.32 (see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.32), specifically section 312.32(b) states:

> *Sec. 312.32 IND safety reporting.*
>
> *(b) Review of safety information . The sponsor must promptly review all information relevant to the safety of the drug obtained or otherwise received by the sponsor from foreign or domestic sources, including information derived from any clinical or epidemiological investigations, animal or in vitro studies, reports in the scientific literature, and unpublished scientific papers, as well as reports from foreign regulatory authorities and reports of foreign commercial marketing experience for drugs that are not marketed in the United States.*

The ICH GCP E6 Good Clinical Practice: Consolidated Guidance, (which is recognized as official FDA guidance – see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf) also addresses sponsor responsibilities. Section 5.3 of this guidance specifically states:

> *5.3 Medical Expertise*
>
> *The sponsor should designate appropriately qualified medical personnel who will be readily available to advise on trial-related medical questions or problems. If necessary, outside consultant(s) may be appointed for this purpose.*

Sections 5.4 (Trial Design) and 5.5 (Trial Management, Data Handling, Recordkeeping, and Independent Data Monitoring Committee) of this guidance also discuss sponsor responsibilities to utilize appropriately qualified individuals throughout all stages of the trial process.

While the regulations don't specifically address whether or not a physician at a sponsor company must hold an active medical license, it is clear that in order to review and evaluate the evidence relating to the safety and effectiveness of the drug as it is obtained from the investigators, the sponsor should designate qualified and appropriately trained staff to perform such tasks.

If you are asking whether an investigator must be a physician, FDA addresses this question in our guidance for sponsors, clinical investigators and IRBs titled, "Frequently Asked Questions – Statement of Investigator (Form FDA 1572)" – see http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm214282.pdf. Questions 4 and 5 in section I (General) read:

> *4. Must the investigator be a physician?*
>
> *The regulations do not require that the investigator be a physician. Sponsors are required to select only investigators qualified by training and experience as appropriate experts to investigate the drug (21 CFR 312.53(a)). In the event the clinical investigator is a non-physician, a qualified physician (or dentist, when appropriate) should be listed as a subinvestigator for the trial and should be responsible for all trial-related medical (or dental) decisions. (ICH E6 section 4.3.1; http ://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf).*
>
> *5. What are the minimum qualifications of an investigator?*
>
> *As stated in #4, the regulations require that sponsors select investigators who are qualified by training and experience*

*as appropriate experts to investigate the drug. The regulations do not specify the minimum requirements nor do the regulations specify what qualifications an investigator must have in order to be considered qualified by training and experience to conduct a clinical investigation. Sponsors have discretion in determining what qualifications, training, and experience will be needed, based on the general recognition that this would include familiarity with human subject protection (HSP) regulations (i.e., 21 CFR Parts 50 and 56) and practices as well as good clinical practice (GCP) regulations (see 21 CFR Part 312) and standards (e.g., ICH E6) for the conduct of clinical studies.*

FDA performs on-site inspections of sponsors, contract research organizations and monitors as well as clinical investigators through our Bioresearch Monitoring (BIMO) Program. BIMO inspections include an assessment of compliance with FDA's regulations governing the conduct of clinical trials. FDA has developed Compliance Program Guidance Manuals (CPGMs) for each of the BIMO inspection types. These CPGMs were developed to provide uniform guidance and specific instructions for FDA inspections of regulated entities. If you are interested in reviewing the CPGMs for FDA inspections of Sponsors, Contract Research Organizations and Monitors and Clinical Investigators, you can access these documents at http://www.fda.gov/ICECI/ComplianceManuals/ComplianceProgramManual/ucm255614.htm.

I hope this information is useful. If you need further information and/or have additional questions, please feel free to contact us at the official GCP mailbox, gcp.questions@fda.hhs.gov. You may also find it useful to access the set of redacted GCP e-mails found at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm since we find that many questions and concerns are repeated over time.

Best Regards,

Janet

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**From:** [Redacted]
**Sent:** Monday, September 22, 2014 8:58 PM
**To:** CDER DRUG INFO
**Subject:** pharmaceutical company requirements for licensed MDs

Hello

I am enquiring on whether companies that run and oversee drug development trials are required to have licensed MDs to oversee the trials/data. Specifically, if the drug development company is obligated to ensure patient safety via safety reviews of the ongoing clinical trials, do the physicians have to hold ***active medical licenses*** (and thus have proven continuing medical education and have a quality standard from the state licensing board to ensure they are properly trained physicians from an accredited medical school)?

If not, how does the FDA ensure that biopharmaceutical companies have qualified personnel overseeing the trials?

Thank you,