From: Shah, Vibhakar J <Vibhakar.Shah@fda.hhs.gov>
Sent: Monday, May 8, 2017 9:33 AM
To:
Subject: Inquiry_Questions on GMP regulations for owners/sponsors of investigational products

Dear XXXXXXX,
This email responds to your recent inquiry to FDA. Your inquiry was routed to the Office of Policy for Pharmaceutical Quality for a response. Our response is below. Note that the questions below are excerpted and summarized from your email, which is also reproduced as a reference at the end.

Question:

I am seeking clarity on:

A. the GMP responsibilities of a US-based organization who does no manufacturing or testing but rather contracts manufacturing and testing of their investigational drug product (clinical trial in USA only).

B. which of these oversight/controls that an Owner/Sponsor of investigational drug products must have in place if they contract all manufacturing and testing. In other words, could an investigational drug product owner/sponsor (who does no manufacturing/testing) be cited for failing to do the following:

1. "evaluate, qualify, audit, and monitor their contract facilities"
2. "owners' quality units …ensur[es] that the products are manufactured in accordance with CGMP
3. "oversee the contract facility's manufacturing activities"
4. "oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products."
5. "… the quality control unit of a contracting firm must approve or reject drug products produced by contractors."
6. "The responsibility to approve release of a drug product for distribution must rest with the owner of the drug product."

C. Also, two of the above quotes use the term "quality [control] unit" when referring to the Owner organization activities. Can you verify that the Owner/sponsor could be cited for failing to have a quality [control] unit.

FDA Response:

GMP responsibilities question:

Whether an IND owner/sponsor manufactures an investigational new drug in-house or gets it manufactured by a contract manufacturer/facility, as noted on page 6 of the *Guidance for Industry: CGMP for Phase 1 Investigational Drugs - July 2008*, both the IND owner/sponsor as well as the contract manufacturer are responsible for assuring that the (phase 1) investigational new drug is manufactured in compliance with *current good manufacturing practice* (CGMP) to meet the statutory requirement of the FDCA (Food Drug & Cosmetic Act)[1]. However, as the owner, the IND sponsor bears the ultimate responsibility for assuring the consistent quality of (and thereby safety of) the investigational drug product(s) for clinical studies [see sections III and IV of the Guidance for Industry – Contract Manufacturing Arrangements for Drugs: Quality Agreements (November 2016)].

Oversight/controls question:

Based on your reading of the Guidance for Industry – Contract Manufacturing Arrangements for Drugs: Quality Agreements (November 2016), the points you have summarized and referred to as "a candidate list of oversight/controls" in your email, are a part of shared and necessary responsibilities that need be clearly delineated and established as a part of the quality agreement between the IND owner/sponsor and the contract manufacturer/facility. The determination of the terms and condition of a quality agreement with regard to who is responsible for what is a business decision, to be made between the IND owner/sponsor and the Contract manufacturer/facility, and not by the FDA. That said, it will not be unreasonable to expect the following: (i) the IND owner/sponsor to be responsible for establishing appropriate procedures for the responsibilities in points #1, #2, #3, #5 and #6, and the some oversight responsibility under point #4; and (ii) the contact manufacturer to be responsible for establishing appropriate procedures for the "control" responsibilities in the point #4. Additionally, note that assigning quality control or other activities to either the IND owner/sponsor or contract manufacturer/facility in the quality agreement does not relieve either party from compliance with applicable CGMP requirements. As a result, failure to establish appropriate control procedures [as applicable to the IND sponsor or the contract manufacturer/facility for fulfilling the role-based responsibilities (e.g., the responsibilities in points 1-6 above)], would be considered noncompliance with CGMP and thereby violation of the statutory (but not regulatory) requirement under the FDCA, and for that the IND owner/sponsor could be cited.

Quality [control] unit establishment and activities question:

Failure to establish its own quality unit and appropriate control procedures relevant to the quality unit activities [see section IV.B.1.a. of the Quality Agreement Guidance mention above] would be considered noncompliance with CGMP, and thereby violation of the statutory (but not regulatory) requirement under the FDCA, and for that the IND sponsor/owner could be cited.

[1] Section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351 (a)(2)(B))

Please let me know if you need further clarification on this topic. If, however, you have a new question unrelated to this inquiry, please send it to CDER-OPQ-Inquiries@fda.hhs.gov

Regards,

- Vibhakar Shah

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