From: OC GCP Questions
To: [redacted]
Subject: Commercial Drug That is Subject of Sponsor"s IND Study Belongs to Another Company
Date: Tuesday, June 10, 2014 2:08:12 PM
Attachments: Clinical trials_ Reporting Adverse Events in a Study involving a Marketed Drug.pdf

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Good afternoon [Redacted] –

I reached back to the folks in CDER again and this is what they provided --

We did some research and found the following --

Under 21 CFR 314.80:

The requirements of paragraphs (c)(1)(i) and (c)(1)(ii) of this section, concerning the submission of postmarketing 15-day Alert reports, shall also apply to any person other than the applicant (nonapplicant) whose name appears on the label of an approved drug product as a manufacturer, packer, or distributor.

But here, it states that these regs apply to a nonapplicant whose name appears on the label (not to an unrelated entity).

And in the "Safety Reporting Requirements forINDs and BA/BE Studies" guidance, it only states that the IND holder must submit a report adverse reactions (even for the active comparator) in an IND safety report. It doesn't say anything about sending the info to the sponsor of the comparator.

There is a 2008 email from Carolyn Hommel (see attached above) that might be helpful to you. You can read the full question and response for the full context, but the last paragraph of the email response states: There are no regulatory requirements for the study sponsor to provide a copy of the report of the serious adverse experience to a pharmaceutical company that owns a marketed product used during the trial, however, there is no prohibition to doing so.

For additional questions, please contact CDER's Office of Medical Policy at CDEROMP@fda.hhs.gov as this office wrote and finalized the reporting rule.

Kind regards,

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

From: [Redacted]
Sent: Monday, June 09, 2014 11:15 AM
To: OC GCP Questions
Subject: Re: Commercial Drug That is Subject of Sponsor's IND Study Belongs to Another Company

Hi Doreen,

Since the study below is under an IND and it is a question regarding a drug regulation, will CDRH be capable of providing the most appropriate answer regarding the drug product?

Thanks,

[redacted]

From: OC GCP Questions <gcp.questions@fda.hhs.gov>
Date: Mon, 9 Jun 2014 10:55
To: [Redacted]
Subject: Commercial Drug That is Subject of Sponsor's IND Study Belongs to Another Company

Good morning –

I forwarded your question to the Center for Devices (CDRH), If you have not hear back from them, please contact them directly at DICE@fda.hhs.gov.

Kind regards,

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

From: [Redacted]
Sent: Sunday, June 08, 2014 5:38 PM
To: OC GCP Questions
Subject: RE: Commercial Drug That is Subject of Sponsor's IND Study Belongs to Another Company

Dear FDA Representative,

[redacted]Device Company is the applicant of the "IND;" however, they are not the applicant as referenced in 21 CFR **314** in that [redacted] has no NDA or ANDA. The response was not clear regarding reporting under **314**.

Again, this is strictly a medical device company who will conduct a study of their drug-delivery device. [redacted] Device Company will use commercially available drug manufactured and sold by other drug companies for testing in their device. So again, our question is related to the requirement specific to 21 CFR 312.32(c)**(4).**

Since the [redacted] Device Company:

- is not one of the manufacturers of the commercially available drug product,
- does not hold the NDA or ANDAs for the product, and
- is looking to revise labeling of the device and not labeling of various manufacturers' drug product…

Question 1 - Is [redacted] in compliance with the regulations if they report solely to the IND as required by 21 CFR 312.32(c)(1)-(3) since [under 21 CFR 312(c)(4)], the sponsor [redacted] is not one of the approved-drug NDA or ANDA applicants (i.e., [redacted] Device Company does not have any application under Sec. 314.50)?

In your email, you noted "it appears the reports might also need to be submitted to the manufacturer of the product."
Question 2 - Considering the facts above, is it a regulatory requirement that [redacted] submit reports to each manufacturer of the drug product that will be used in the study or is [redacted] in compliance with regulation if they choose not to inform the manufacturers, while reporting solely to the IND?

Thank you,
[Redacted]

From: OC GCP Questions [mailto:gcp.questions@fda.hhs.gov]
Sent: Thursday, June 05, 2014 8:42 AM
To: [redacted]
Subject: Commercial Drug That is Subject of Sponsor's IND Study Belongs to Another Company

Good morning –

Sorry for the delay in responding. We had to consult with the Center for Drugs (CDER). Although we feel that we don't have enough information to specifically answer your question, it appears that "ACME Device Company" would be the applicant if they submit the IND and therefore safety reporting is required under 312.32(c) and it appears the reports might also need to be submitted to the manufacturer of the product. Whether the study is under IND or IDE it would be best to discuss the reporting requirements with the regulatory project manager that will be or is overseeing the study.

Additionally since you have mentioned both a device and investigational product, it might be helpful to discuss this issue with FDA's Office of Combination Products. Please see their web page below specifically the phone number and email address at the bottom of the page.

Office of Special Medical Programs > Office of Combination Products

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

Kind regards,

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

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: Thursday, May 29, 2014 7:24 PM
To: OC GCP Questions
Subject: Commercial Drug That is Subject of Sponsor's IND Study Belongs to Another Company

Dear FDA Representative,

After reviewing Part 312 and the guidance "Safety Reporting Requirements for INDs and BA/BE Studies," I still have a question:

Scenario: The sponsor, [redacted] Device Company, will perform a study using their cleared device with a commercially available drug.

- The device is not cleared for use with this particular drug, and the drug is not approved for use with this device.
- The plan is to perform a study so the device can be labeled for use with such drug.
- This study will be under IND.
- The commercial drug product for use in the study will be several dosages/formulations and will come from 2 or 3 drug manufacturers.

For the study, [redacted] Device Company will comply with:

- 21 CFR 312.32(b) for review of all info from the study
- 21 CFR 312.32(c)(1)-(3) for reporting (i.e., IND safety reports)

My question is specific to the requirements of 21 CFR 312.32(c)(4), which requires the sponsor submit safety information from the clinical study as prescribed by the relevant postmarketing safety reporting requirements (i.e., 314.80). Part 314.80 discusses requirements of the "applicant," who is defined as having an approved application under Sec. 314.50 or, in the case of a 505(b)(2) application, an effective approved application. [redacted] Device Company does not meet the definition of applicant. Ultimately, is [redacted] supposed to review/submit under 314 or should they submit the info to the drug manufacturer(s) for follow up (i.e. review and submission)?

In a similar scenario but under IDE rather than IND, the advice was as follows:

> **From:** OC GCP Questions **Sent:** Monday, September 10, 2012 7:14 AM **To:** [redacted]
> **Subject:** RE: Adverse Event Reporting Procedure for Marketed Drugs being used in IDE and non-IDE Device Trials
> Dear [redacted]:
> We have inquired with staff from the Center for Devices and Radiological Health (CDRH) regarding your questions relating to adverse event reporting associated with approved drug products that are used in a device trial. Their advisement is as follows:
> If the sponsor of an device trial (IDE or non-IDE) becomes aware of an AE associated with the use of a marketed drug product in that trial, FDA recommends

that the sponsor forward the AE report to the applicant of the marketed drug product so that the applicant can evaluate the report and determine whether it is reportable under the drug postmarketing AE reporting regulations (21 CFR 314.80 for products marketed under an NDA or ANDA and 310.305 for prescription drugs marketed without an approved application). The sponsor conducting the trial is not required to submit the report directly to FDA.

Your prompt response is greatly appreciated.

Kind Regards,

[Redacted]