From: OC GCP Questions
To: [redacted]
Subject: IND Safety Reporting
Date: Thursday, April 24, 2014 4:11:37 PM

Good afternoon –

Please see CDER OMP's answer to your questions below.

Kind regards,

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

From: CDER OMP
Sent: Thursday, April 24, 2014 1:36 PM
To: OC GCP Questions
Subject: RE: IND Safety Reporting

Sponsors are responsible for notifying FDA and all participating investigators in an IND safety report of any findings from clinical studies, whether or not conducted under an IND, and whether or not conducted by the sponsor, that suggest a significant risk in humans (21 CFR 312.32(c)(1)(ii)), among other expedited reporting requirements.

The sponsor's 15 day clock begins when the sponsor determines that the information qualifies for reporting. The *Safety Reporting Requirements for INDs and BA/BE Studies* guidance contains the following information regarding reporting time frames:

- The time frame for submitting an IND safety report to FDA and all participating investigators is no later than 15 calendar days after the sponsor determines that the suspected adverse reaction or other information qualifies for reporting (21 CFR 312.32(c)(1)). The language in the IND safety reporting regulations was modified to describe the reporting time frame applicable to aggregate reports (§ 312.32(c)(1)(i)(B) and (C)) and increases in rates of occurrence of serious suspected adverse reactions (§ 312.32(c)(1)(iv)), which generally require more than one occurrence to make the determination that the event meets the criteria for reporting. Thus, the date of initial receipt of the first event could be well before it was determined that the event must be reported… FDA expects that events that are interpretable as single cases (i.e., uncommon and known to be strongly associated with drug exposure) should be reported to FDA within 15 days from initial receipt. For events that require more than one occurrence to assess causality and events evaluated in the aggregate, the time clock starts when the sponsor determines that the events qualify for expedited reporting…

As a general rule, FDA will consider a drug firm responsible for information known to its employees

(including the employees of a division or separately incorporated subsidiary of the firm), and companies should adopt procedures to ensure that employees will expeditiously bring important information to the attention of company officials (52 FR 8798 at 8816). In the case described by the inquirer, the US sponsor is considered to receive the safety information when the foreign owner learns of it. The US sponsor and its foreign owner should adopt procedures to ensure the expeditious transmission of safety information from one to the other.

The information provided in response to this inquiry does not address any product or trial specific considerations. Follow up questions regarding specific products or trials should be directed to the appropriate FDA review division by the sponsor.

From: OC GCP Questions
Sent: Tuesday, April 15, 2014 9:04 AM
To: CDER OMP
Subject: IND Safety Reporting

CDER OMP –
Can you assist with answering the question (bottom of email) regarding safety reporting?

Thank you!

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: Monday, April 14, 2014 1:22 PM
To: OC GCP Questions
Subject: IND Safety Reporting

Dear Sir/Madame:

I am a Regulatory Affairs consultant with a question regarding how the IND regulations for expedited safety reports apply to U.S. IND clinical trial Sponsors who are small entities owned by foreign small entities who also conduct non-IND clinical trials. It is acknowledged that FDA comments in this informal email exchange are not binding.

- A small business IND Sponsor is U.S. based, and owned by a separate, foreign, non-English speaking entity which is concurrently conducting a non-IND clinical trial of the same drug in a foreign country.
- The U.S. IND sponsor provides investigational drug for the foreign entity's non-IND

clinical trial; otherwise, the two entities operate separately.

- The U.S. IND sponsor and the foreign entity periodically exchange safety updates.
- Due to various communication challenges, delays occur in transmission of information from the foreign owner to the small business U.S. IND sponsor.

- The U.S. IND sponsor takes guidance from the FDA Small Entity Compliance Guide for Safety Reporting Requirements for INDs:
  "*For IND safety reporting, the Agency recognizes that a sponsor or sponsor-investigator may not have access to the complete safety data maintained by a commercial sponsor, but sponsors and sponsor-investigators are required to evaluate all safety information that is available to them to determine whether the information qualifies for reporting (21 CFR 312.32). For example, sponsors and sponsor-investigators should examine reports in the scientific literature and perform literature searches to actively seek new safety information about the drug under investigation. To protect human subjects, the Agency recommends that entities that provide drug to or receive drug from other entities share safety information with each other.*"

Please comment to the extent possible:

- **Does the U.S. IND Sponsor's 15 day clock (for reporting an IND safety report), begin <u>when it receives</u> information about an event from the foreign entity who is conducting the non-IND foreign clinical trial? Or does the U.S. IND sponsor's 15 day clock begin when its foreign owner receives (who is not the IND Sponsor) learns of an adverse event that may be reportable?**

Thank you in advance for any guidance you may offer.

Best regards,

[Redacted]