From: OC GCP Questions
To: [redacted]
Subject: IB Amendment submission time frame
Date: Wednesday, November 07, 2018 11:17:17 AM
Attachments: [redacted]

Good morning –

The regulations pertaining to providing investigators with an investigator brochure are found in 21 CFR 312.55 and 312.23(a)(5). I've pasted them into this e-mail for your convenience:

Sec. 312.55 Informing investigators.

Before the investigation begins, a sponsor (other than a sponsor-investigator) shall give [Emphasis added.] each participating clinical investigator an investigator brochure containing the information described in Sec. 312.23(a)(5).

The sponsor shall, as the overall investigation proceeds, keep each participating investigator informed of new observations discovered by or reported to the sponsor on the drug, particularly with respect to adverse effects and safe use. Such information may be distributed to investigators by means of periodically revised investigator brochures, reprints or published studies, reports or letters to clinical investigators, or other appropriate means. Important safety information is required to be relayed to investigators in accordance with Sec. 312.32.

Sec. 312.23 IND content and format.

(a) A sponsor who intends to conduct a clinical investigation subject to this part shall submit an “Investigational New Drug Application” (IND) including, in the following order:...

(5) Investigator's brochure. If required under Sec. 312.55, a copy of the investigator's brochure, containing the following information:

A brief description of the drug substance and the formulation, including the structural formula, if known.

A summary of the pharmacological and toxicological effects of the drug in animals and, to the extent known, in humans.

A summary of the pharmacokinetics and biological disposition of the drug in animals and, if known, in humans.

A summary of information relating to safety and effectiveness in humans obtained from prior clinical studies. (Reprints of published articles on such studies may be appended when useful.)

A description of possible risks and side effects to be anticipated on the basis of prior experience with the drug under investigation or with related drugs, and of precautions or special monitoring to be done as part of the investigational use of the drug.

As you can see, the sponsor is required to provide an investigator's brochure prior to beginning an investigation, and there are no conditions or exceptions listed. The brochure specifically must include summaries of information relating to the investigational drug's previous use in humans (see 21 CFR 3 12.23(a)(5)(iii) and iv), above); this suggests that "first use in man" is not the only basis for providing the brochure.

To answer your question, I don’t think the IB amendment is required to be submitted on a tighter timeline as the AR. Just to be sure, it might be best to contact the Center for Drugs directly at druginfo@fda.hhs.gov

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: Monday, November 05, 2018 3:42 PM
To: CDER DRUG INFO <DRUGINFO@fda.hhs.gov>; Industry.Biologics <Industry.Biologics@fda.hhs.gov>; OC GCP Questions <gcpquestions@fda.hhs.gov>
Subject: IB Amendment submission time frame

Hello,

I wanted to inquire about the timeframe for submitting an IB Amendment to the FDA. It appears the rules differ a bit for protocol amendments, so I wanted to check on the rules for IB amendments.

I am under the impression that an IB amendment could be submitted with the Annual Review (AR) each year, but is it not a good idea to send an IB update with the AR. Can one wait until the AR is due to submit an IB amendment, or is an IB amendment required to be submitted on some tighter timeframe.

Your assistance is much appreciated,

[redacted]