From: Kezer, Doreen M
To: [redacted]
Subject: pregnant partners
Date: Thursday, June 07, 2018 10:08:00 AM
Attachments: [redacted]

Hi [redacted]–

The email that I sent you is from 2008. The email that you cite is from 2006. The 2006 email (See the highlighted area) appears more specific and may be discussing a particular protocol, in which case, if the sponsor requires collection of information on pregnant partners, the protocol should be followed and the IRB will be involved.

As stated previously, here is no general FDA policy requiring information to be collected on the partners and neonates of study subjects in FDA-regulated clinical trials.

We do not receive many questions on pregnant partners. It might be helpful for you to contact FDA's Office of Women's Health.

Kind regards,

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

From: [redacted]
Sent: Wednesday, June 06, 2018 11:32 AM
To: Kezer, Doreen M <Doreen.Kezer@fda.hhs.gov>
Cc: Less, Joanne <Joanne.Less@fda.hhs.gov>
Subject: RE: pregnant partners

Hi Doreen-thank you so much for sending this.
The information below came from the FDA questions and answers. It differs from the one you provided.
Is this one not accurate anymore?

Thanks, [redacted]

Data on Study Partners and Neonates- Informed Consent
(07/31/2006)
Question 1:

I am an IRB Chair. We would like some guidance with regard to sponsors requiring that data be collected on partners and neonates of enrolled study subjects. Sponsors are indicating that the FDA requires collection of these data, that these are not research subjects, and that research consent does not need to be obtained. We are under the belief that they would be research subjects since their data is being collected for the purposes of assessing the safety of an investigational drug. In some cases, they want to follow the partners and the neonates for several months following birth. However, isn't there a difference between FDA requiring that the sponsor attempt to obtain these data versus FDA requiring that a subject agree to the collection of these data?

Answer 1:

While there is no general FDA policy that I know of requiring information to be collected on the partners and neonates of study subjects in FDA-regulated clinical trials, I can believe that such information is required for selected studies involving products and/or procedures that have the potential to directly and/or indirectly affect these individuals. If collection of this information is required by the study protocol, it should be discussed with all individuals from whom information will be required. It also needs to be included in the written informed consent document for the study. Since, as a reviewing IRB, you would review the study informed consent as well as the protocol, you can require signatures on the written informed consent document from both the participant and that individual's partner, if it is determined that such is appropriate. If there is reason to believe that the partners of study subjects can be affected by that individual's participation in a study, it would seem to me those partners should be informed of those possibilities and have a say in the decision to participate, even if information on them is not to be collected. It would also seem that if such information is required as follow-up information for the study, those individuals are even actually participants in the study.

Since the main purpose of an IRB is human subject protection, an IRB has a right to demand whatever conditions they deem necessary to protect the rights, safety, and welfare of study participants and other individuals who will be affected. In fact, the regulations at 21 CFR 56.108(b) require that an IRB have written procedures "to ensure prompt reporting to the IRB of any unanticipated problems involving risks to human subjects or others." If a sponsor does not agree to those conditions, the study does not occur at that site.

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From: Kezer, Doreen M <Doreen.Kezer@fda.hhs.gov>
Sent: Wednesday, June 6, 2018 11:24 AM
To: [redacted]
Cc: Less, Joanne <Joanne.Less@fda.hhs.gov>
Subject: pregnant partners

Good morning [redacted] –

This is an email regarding pregnant partners that we responded to in the past. The response came from OGCP's former medical ethicist. The response appears still to be accurate.

FDA regulations, 21 CFR 50.3(g), defines human subject as, "an individual who is or becomes a participant who becomes a participant in research, weather as a recipient of the test article or as a control." In the scenario you describe neither the pregnant partner of the male subject nor the offspring of that pregnancy is receiving the test article or participating in the research as a control. Therefore, from FDA's perspective, neither the pregnant partner of a male subject nor the offspring of that pregnancy would be considered a human subject. FDA would consider the described activity as important safety surveillance activity.

That is not to imply that the pregnant partner should not be asked for her permission to provide private health information to a sponsor or submit this information to a registry. On both ethical and pragmatic (obtaining medically valid information would likely involve the pregnant woman/her medical records as a source) grounds asking for her permission would be appropriate.

FDA's industry guidance, "Establishing Pregnancy Exposure Registries" addresses this issue (as well as considerations for review by an IRB, considerations for registries involving newborn outcomes, and other related matters). Please see:
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM071639.pdf

You are probably aware that 45 CFR 46, based on its differing authority and scope, contains a different definition of human subject than FDA regulations. According to 45 CFR 46.102(f), a human subject is "a living individual about whom an investigator conducting research obtains: 1) data through interventions or interaction with the individual. or; 2) identifiable private information."

It is my understanding that under HHS regulations, if privately identifiable information is collected in a registry on the pregnant partner of a male subject and the offspring of that pregnancy then the woman and the infant are considered human subjects in the research. Consequently, informed consent would need to be obtained for this research activity unless an IRB waives this requirement under 45 CFR 46.116(d). This regulation permits an IRB to approve a consent procedure which does not include, or which alters some or all of the elements of informed consent if it finds and documents: 1) the research involves no more than minimal risk to the subjects; 2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; the research could not practicably be carried out without the waiver or alteration, and; 4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

I recommend you seeking input from OHRP if you have any questions about the applicability of the HHS regulations, 45 CFR 46. Office for Human Research Protections | HHS.gov

Although this *draft* guidance may not totally apply to your question, it might be of interest to you. (Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials).
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM603873.pdf

Additionally, it might be useful to reach out to FDA's Office of Women's Health to see if they are aware of any other FDA guidance on this subject. See their contact information on the top right side of their webpage.
Office of Women's Health

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

From: Less, Joanne
Sent: Tuesday, June 05, 2018 2:53 PM
To: [redacted]
Cc: Kezer, Doreen M <Doreen.Kezer@fda.hhs.gov>
Subject: RE: pregnant partners

Will do. I've copied Doreen. Doreen, could you see what you can find on preg partners? Thanks!

From: [redacted]

Sent: Tuesday, June 05, 2018 2:46 PM
To: Less, Joanne <Joanne.Less@fda.hhs.gov>
Subject: Re: pregnant partners

Yes thanks!

[redacted]

On Jun 5, 2018, at 2:45 PM, Less, Joanne <Joanne.Less@fda.hhs.gov> wrote:

> I'm in never-ending meetings. We've answered that before. Want me to have Doreen look for it on the Q/As we post on our website?
>
> ---
>
> **From:** [redacted]
> **Sent:** Tuesday, June 05, 2018 10:48 AM
> **To:** Less, Joanne <Joanne.Less@fda.hhs.gov>
> **Subject:** pregnant partners
>
> Hi-I wondered if you might have time for an informal chat about whether pregnant partners (not subjects) can be reasonably interpreted to fall under the definition of clinical investigation…big controversial topic with sponsors.
>
> Thanks,
> [redacted]
>
> [redacted]
>
> ---
>
> [redacted]

[redacted]