From: OC GCP Questions
To: [redacted]
Subject: Certified Letters to Study Subjects Lost to Follow-up
Date: Thursday, June 19, 2014 3:16:42 PM

Good afternoon –

As stated in the FDA Information Sheet Guidance, "Recruiting Study Subjects" (available at http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm), "FDA requires that an Institutional Review Board (IRB) review and have authority to approve, require modifications in, or disapprove all research activities covered by the IRB regulations [21 CFR 56.109(a)]. An IRB is required to ensure that appropriate safeguards exist to protect the rights and welfare of research subjects [21 CFR 56.107(a) and 56.111]. In fulfilling these responsibilities, an IRB is expected to review all the research documents and activities that bear directly on the rights and welfare of the subjects of proposed research."

In determining which written communications with already enrolled subjects require IRB review and approval prior to use, the IRB should consider whether such communications would bear directly on the rights and welfare of the subject. Written communications that clearly have no effect on the conduct of the research, its underlying science or methodology, associated risks and benefits, or the potential willingness of subjects to continue participation would not require prior review and approval by the IRB.

Based on these criteria, it would seem that certified letters to subjects who do not return for study visits would not require IRB review and approval prior to use, provided no new information is included. So, for example, IRB review and approval would not be necessary for a written communication that simply reminds a subject of his/her next appointment, including communications that provide reminders that are consistent with the written informed consent and protocol, such as the need to fast prior to the appointment. However, a letter that included information on study results (new information) or solicited interest in another research project (recruitment) would require IRB review and approval prior to use. Additionally, written communications providing results notifications (new information) would also require IRB review and approval prior to use.

In conclusion, an IRB may wish to consider developing policies and procedures that address which communications with subjects, as part of ongoing research, require IRB review and approval and which do not.

ICH GCP E6 Good Clinical Practice: Consolidated Guidance, (which is recognized as official FDA guidance), section 3.1.2 states--

3.1.2 The IRB/IEC should obtain the following documents

Trial protocol(s)/amendment(s), written informed consent form(s) and consent form updates that the investigator proposes for use in the trial, subject recruitment procedures (e.g., advertisements), written information to be provided to subjects, Investigator's Brochure (IB), available safety information, information about payments and compensation available to subjects, the investigator's current curriculum vitae and/or other documentation evidencing qualifications, and any other documents that the IRB/IEC may require to fulfil its responsibilities.

IRBs typically outline in written procedures which documents they require to be submitted in order for the IRB to fulfill its regulatory obligations. Such written procedures may address the IRB's policies and procedures on submission and review of "generic materials". Because each IRB may have differing requirements, it is best that the site discuss and understand what each IRB requires and adhere to the reviewing IRB's requirements.

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: [redacted]
Sent: Wednesday, June 18, 2014 6:03 PM
To: OC GCP Questions
Subject: Certified Letters to Study Subjects Lost to Follow-up

Hello:
Some sponsors require sites to send certified letters to subjects who do not return for study visits. Do these letters have to be approved by the ethics committee?
Thanks in advance for your assistance,
[redacted]