From: OC GCP Questions
To: [redacted]
Subject: Signing off on a Revised ICF
Date: Monday, March 21, 2016 9:09:48 AM

Good morning –

Changes to an informed consent form can occur for various reasons (e.g., protocol changes, when new information is available about risks to subjects posed by the investigational article, administrative changes with respect to whom the subject should contact regarding the subject's rights). The IRB is responsible for determining the significance of the changes and whether they affect the rights, safety, and welfare of study subjects. The IRB would also be expected to weigh in on whether currently enrolled subjects need to be informed about the changes right away, or whether the information can be provided to the subjects at their next scheduled visit.

If a study had an informed consent document revised during the course of the study and at some point there is a bioresearch monitoring (BIMO) inspection of the study, the sites would be expected to show that they provided the new information to all study subjects. This can be documented by "re-consenting" with the new informed consent (with the changes highlighted for subject convenience) or with a separate statement of the changes that the subject signs and dates.

Additionally protocol amendments must receive IRB review and approval before they are implemented, unless an immediate change is necessary to eliminate an apparent hazard to the subjects (21 CFR 56.108(a)(4)). Those subjects who are presently enrolled and actively participating in the study should be informed of the change if it might relate to the subjects' willingness to continue their participation in the study (21 CFR 50.25(b)(5)). FDA does not require reconsenting of subjects that have completed their active participation in the study, or of subjects who are still actively participating when the change will not affect their participation, for example when the change will be implemented only for subsequently enrolled subjects.

A few guidances that might be helpful to you -

Also - A Guide to Informed Consent - Information Sheets
www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm

And - A draft 2014 guidance on Informed Consent -
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM405006.pdf

A “protocol deviation” is a failure to adhere to the clinical trial protocol contained in the application - for example, failure to follow the protocol contained in an investigational new drug (IND) application. Another example -- if the sponsor wishes to require a signature on one or more study documents, it would be considered a protocol deviation if these documents were not signed.

Protocol deviations are discussed in the “Guidance for Industry - E6 Good Clinical Practice: Consolidated Guidance”
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

Under IRB procedures in this E6 guidance document, it states the IRB's procedures should specify “that no deviations from, or changes of, the protocol should be initiated without prior written IRB/IEC approval/favorable opinion of an appropriate amendment, except when necessary to eliminate immediate hazards to the subjects or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change of monitor(s), telephone number(s))”, and that the “investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.” Further, it states the “investigator may implement a deviation from, or a change in, the protocol to eliminate an immediate hazard(s) to trial subjects . . .”

Please see FDA's Clinical Investigator Compliance Program at:
http://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/UCM133773.pdf

Please see Section F, Part III. It discusses the informed consent process.

You should probably produce a note-to-file explaining why the subject did not sign the new approved ICD at his first visit after the form was approved and steps that you will take in the future to prevent this from happening again (A corrective action plan)

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: Saturday, March 19, 2016 7:46 AM
To: OC GCP Questions
Subject: Signing off on a Revised ICF

Good day. If a subject was consented to a trial under the original version of a consent that was IRB approved and a new version of the consent was recently approved because of a protocol amendment. Is it a protocol deviation if the subject did not sign the revised ICF at their next scheduled?

Example: Subject signed the original version of the ICF on Day 0 (Screening and Enrollment) on February 1, 2016. The revised ICF was approved on February 10, 2016 and the site was in receipt of it on February 12, 2016. Day 14 study visit occurred on February 15, 2016 (The subject did not sign the revised ICF; however, it was available and the site was in receipt of it). On Day 28, February 28, 2016, the subject signed the revised ICF.

I look forward to hearing from you.

Kind regards,
[redacted]

[redacted]