From: OC GCP Questions
To: [redacted]
Subject: additional checks for AEs and ConMeds.
Date: Wednesday, November 22, 2017 10:03:00 AM
Attachments: [redacted]

Good morning --

The terms "protocol deviation" and "protocol violation" are not defined in FDA's regulations, but are often used somewhat interchangeably. FDA's Compliance Program Guidance Manual (CPGM) chapter on clinical investigator (CI) inspections contains the following description of the term:

A protocol deviation/violation is generally an unplanned excursion from the protocol that is not implemented or intended as a systematic change. A protocol deviation could be a limited prospective exception to the protocol (e.g. agreement between sponsor and investigator to enroll a single subject who does not meet all inclusion/exclusion criteria). Like protocol amendments, deviations initiated by the clinical investigator must be reviewed and approved by the IRB and the sponsor prior to implementation, unless the change is necessary to eliminate apparent immediate hazards to the human subjects (21 CFR 312.66), or to protect the life or physical well-being of the subject (21 CFR 812.35(a)(2)), and generally communicated to FDA. “Protocol deviation” is also used to refer to any other, unplanned, instance(s) of protocol noncompliance. For example, situations in which the investigator failed to perform tests or examinations as required by the protocol or failures on the part of study subjects to complete scheduled visits as required by the protocol, would be considered protocol deviations.

It appears that the scenario you describe would probably not be cited as a protocol violation if an inspection occurred at your site. You should communicate with the sponsor to see if the protocol should be amended to include what you are really doing at each visit for the concomitant meds.

Please see the link below to FDA’s Compliance Program Guidance Manuals. You will find these very informative.

Clinical Trials and Human Subject Protection > Bioresearch Monitoring Program (BIMO)

Kind regards,

Doreen M. Kezer, MSN
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Office of Good Clinical Practice
Office of the Commissioner, FDA

U.S. FOOD & DRUG ADMINISTRATION

From: [redacted]
Sent: Saturday, November 18, 2017 7:29 PM
To: OC GCP Questions <gcp.questions@fda.hhs.gov>
Subject: additional checks for AEs and ConMeds.

To: Office of Good Clinical Practice/GCP questions;

Given the table below, as you can see checking/assessing for AEs and ConMeds are X'd at V2 ,4,5,7,8,10,11. Is it a protocol violation, if at V1,V3,V6,V9, the study coordinator were to ask if there were any changes to the meds the subject is taking or if the subject feels any different than last visit ("any untoward medical occurrence") or has any changes in their baseline medical conditions?

Per protocol, at visit 1 they ***are required*** to determine if the subject is taking HTN meds and how many for Inc/Ex criteria, and record those in source and eCRFs. It is not checked on the events schedule, so is that a Protocol Violation?

A coordinator states this is a protocol violation: I had suggested that if the subject comes in at any time its a good idea to ask and make sure there are no changes in medications that would be cause to drop the subject from the study (no changes to baseline HTN medications are allowed per protocol) or to check if there are any changes to or new medical conditions (the study subjects are taking a double-blind IP).

Again, would this constitute a protocol violation?

Thank you for your consideration of this question

Cheers, [redacted]

Appendix 1 Schedule of Events

Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11
Vital Signs	X	X	X	X	X	X	X	X	X	X	X
Brief PE & weight	X				X			X		X	
Complete PE & weight		X									
Adverse Events		X		X	X		X	X		X	X
Concomitant Medication		X		X	X		X	X		X	X