From: OC GCP Questions
To: [redacted]
Subject: Double blind randomized phase I trial
Date: Wednesday, October 18, 2017 9:27:22 AM
Attachments: [redacted]

Good morning –

When we speak of double-blinded studies we mean that both the study subject and the clinical investigator (CI) are blinded to the assignment of the product. (A single-blinded study meaning study subjects do not know what they receive but the CI does.) Since the sponsor will be looking at adverse events as well as trends in the data across the study, someone at the sponsor will definitely be unblinded. When there are possibilities of severe or frequent adverse events or the disease or condition is serious or life-threatening, the sponsor will often have an independent body - data monitoring committee (DMC)/data safety monitoring board (DSMB)- that will periodically assess the data. This is often the case when the sponsor wants to consider stopping a study early either because high toxicity is revealed or the product shows such success that they do not want to wait to be able to provide it for others with the disease/condition. In those cases, the sponsor is technically blinded as they leave the unblinded analysis to the DMC/DSMB and receive periodic feedback from them based on safety concerns.

Any combination of blinding is possible if it is spelled out in the study protocol. It seems that a rationale for whatever scheme is chosen would be there as well so the reviewing IRBs understand why it is being imposed on the study.

I might be best for this question to be referred to the appropriate review division (who would be most familiar with drug study designs for the specific indication and could give advice about the impact of unblinding at any stage of the investigation).

Unblinding can compromise the integrity of a study. Sponsors often use blinding and randomization to help minimize bias in the conduct of a study. Prematurely breaking the blind in a study has the potential to bias the study and would not be in keeping with Good Clinical Practice. FDA's various guidance documents repeatedly warn (generally) against inadvertently breaking the blind of a study; it sort of goes without saying that intentionally doing so is a poor practice, particularly if breaking the blind is not specified in the study protocol.

If you would like to report serious noncompliance for an FDA-regulated drug study, you can report this information to CDER-OSI-GCPReferrals@fda.hhs.gov

You may also want to ask the Center for Drugs (CDER) 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

U.S. FOOD & DRUG ADMINISTRATION

From: [redacted]
Sent: Monday, October 16, 2017 5:07 PM
To: OC GCP Questions
Subject: Double blind randomized phase I trial

Hello,

I would like to know if it is ok for a Sponsor of an investigational drug to have a physician randomize out of order to make sure a specific patient got drug and not placebo.

Kind regards,
[redacted]