**From:** OC GCP Questions
**To:** [redacted]
**Subject:** Unblinding of randomization
**Date:** Friday, November 21, 2014 11:22:08 AM

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Good morning –

You are correct. There is no way of documenting that the sponsor employee did not open and read the email and therefore become unblinded. It is best to contact the FDA review division (e.g. the assigned FDA Project Manager for the IND and discuss what actions need to take place for the situation you describe. I cannot be assured that FDA would not see that the situation would comprise the study data. There is the potential that information may unintentionally be revealed that could break the blind for study staff. If you or the sponsor do discuss the situation with FDA, it is best to document all that discussed to ensure the integrity of the study data.

As you probably know, The ICH E-6 Good Clinical Practice Consolidated Guidance, an FDA official guidance, addresses Randomization Procedures and Unblinding in Section 4.7

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

*4.7 Randomization Procedures and Unblinding*

*The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product(s).*

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:** Thursday, November 20, 2014 7:23 PM
**To:** OC GCP Questions
**Subject:** Unblinding of randomization

Hello,

We have encountered an unusual situation in a blinded study today and we would greatly appreciate the FDA's guidance on how to proceed.

As a CRO we were assigned to rescue a blinded vaccine study with comparator products. The original

CRO was responsible for creating and maintaining the randomization codes that were used for dosing all subjects and there were individual sealed envelopes used for emergency unblinding situation. There is an unblinded pharmacist at the research facility who assigns the treatments . A copy of the randomization list and sealed enveoples are on stie.

We have not been given access to the codes since we signed the TORO with the Sponsor.

We have an unblinded monitor who conducts drug accountability and confirms the codes envelope remains sealed. This unblinded CRA reports to the Director of Operations who is also unblinded. The Director reviews the unblinded monitors reports and maintains all collected unblinded drug accountability documents.

We have a blinded monitor who conducts the source data verification for the study visit data and interacts with the blinded site staff. The blinded CRA reports to a blinded Project Manager assigned to the study. The blinded PM reviews all blinded monitoring reports.

There is no exchange of unblinded study information between the Director of Operations and the PM. The PM does not have access to any unblinded reports or documents.

The study has concluded. We are currently in the process of locking the database but it is not locked. A blinded Sponsor employee requested via email that the randomization codes be sent from the original CRO to our unblinded Director of Operations. Instead of complying with these instructions the original CRO sent the Sponsor the randomization codes in an attachment.

Only the unblinded Director of Operations at our CRO has received the email with the codes. Our blinded staff continue to remain blinded.

The Sponsor employee who received the email has stated they did not open the attachment. We are concerned that there is no way to verify this and that the FDA may feel that the employee must be considered unblinded from this point on. If the Sponsor employee recuses themselves from any further involvement or analysis of any study data, is this acceptable? Do you have any other advice or guidance on how you would like this to be addressed?

Thank you for your assistance with this matter.

Take care,
[redacted]