**From:** OC GCP Questions
**To:** [redacted]
**Subject:** [redacted] (the order of ICF)
**Date:** Thursday, December 03, 2015 9:00:00 AM

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Dear [redacted],

FDA's regulations (21 CFR 50) do not require an investigator signature on the consent form, although this may be a requirement of the IRB/IEC or local laws/regulations.

ICH E6 4.8.8 states "Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion". ICH E6 4.8.3 states "Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial."

The informed consent process allows for discussion of the research study with the subject. If the subject chooses to participate in the research study, they then are asked to sign the consent form. It is possible that the presentation of a consent form that has already been signed by the investigator to a subject could be viewed as "unduly influencing" the subject, even if this was not intended by the investigator. Although not directly addressed in FDA's regulations or guidances, such as FDA's Guide to Informed Consent (http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm ) or ICH E6, subjects are usually given an unsigned consent form to minimize any unintended influence on their decision. If a signature by another party (e.g., investigator, witness, etc.) is a requirement of the local consent process, it is generally obtained after the subject signs the consent form.

You can find the report on the findings of the Pilot EMA-FDA GCP Initiative (September 2009-March 2011) at http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/08/WC500109777.pdf

I hope this information is helpful to you. If you need further assistance, please feel free to contact the GCP mailbox at gcp.questions@fda.hhs.gov .

Best regards,

Sheila

Sheila Brown, RN, MS
Policy Analyst, Office of Good Clinical Practice
Office of Special Medical Programs, Food and Drug Administration



-----Original Message-----
From: [redacted]
Sent: Tuesday, November 24, 2015 8:31 PM
To: OC GCP Questions
Subject: [redacted] (the order of ICF)

Dear Sir/Madam

My name is [redacted], working for clinical quality assurance department of [redacted].
There is a clinical investigator site inspected by the FDA, in [redacted] this year.
The inspector pointed out that the PI should not sign off ICF before the subject signs the ICF.

So I would like to confirm whether who signs off ICF first is important for a Global study (under the ICH-GCP guidelines).
(ICH-GCP 4.8.8: Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, "and by" the person who conducted the informed consent discussion.) Also, the ICH-GCP uses the phrase "and by". Does it mean PI should sign off ICF after the subject signed the ICF?

Also, there is a clinical investigator site inspected by the EMA, in [redacted] two years ago.
The EMA also pointed out the act of PI's signing off ICF first was inadequate and called this behavior a silent presser to the subject.

I have heard the FDA and the EMA conducted the Pilot EMA-FDA GCP Initiative.
Could you tell me if the FDA and the EMA had any discussion related to the process of how to get ICF, including in what order it should be signed?

I greatly appreciate your cooperation in advance.
Best regards,

[redacted]