From: OC GCP Questions
To: [redacted]
Subject: RE: Informed Consent Signature Reqiurement 3
Date: Tuesday, August 18, 2015 1:01:00 PM

Hi [redacted],

IND-exempt does not mean the study is outside FDA's jurisdiction; the study still must comply with Parts 50 (informed consent) and 56 (IRB approval), per 312.2(b)(iv), and is therefore considered to be FDA-regulated. FDA may inspect the investigator, sponsor, or IRB of record.

Best regards,

Sheila

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

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From: [redacted]
Sent: Friday, August 14, 2015 12:02 PM
To: OC GCP Questions
Subject: RE: Informed Consent Signature Reqiurement

Hi Sheila,

Thanks for the information. Just one last question. Since this study is IND exempt would it fall under the umbrella of being FDA regulated? In other words, would the FDA ever have anything to do with a study that is IND exempt?

Thanks,
[redacted]

From: OC GCP Questions [mailto:gcp.questions@fda.hhs.gov]
Sent: Friday, August 14, 2015 8:45 AM
To: [redacted]
Subject: RE: Informed Consent Signature Reqiurement

Dear [redacted],

As I noted in my previous response, from the information provided, it appears that FDA's regulatory requirements were met. IRBs, however, may have additional requirements that must also be met. From the limited information provided, it appears that the process for obtaining consent may not have been in compliance with internal SOPs. It is difficult for us to provide an opinion outside of the FDA inspectional process because of the many other considerations that go into making an assessment of noncompliance, as well as an assessment of whether or not that noncompliance was serious. Please discuss the informed consent policy regarding compliance with ICH guidelines and this occurrence with your IRB.

Best regards,

Sheila

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

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From: [redacted]
Sent: Thursday, August 13, 2015 8:06 PM
To: OC GCP Questions
Subject: RE: Informed Consent Signature Reqiurement

HI Sheila,

This is a continuation to the email below… Both the Physician and the research coordinator were present during the discussion with the interpreter. The RC is on the delegation of authority to "administer informed consent".

Our internal Informed Consent policy states the following… A signature by the person conducting the consent discussion is required only if the research needs to comply with International Conference on Harmonization (ICH) guidelines. This particular study is **IND exempt** so would it need to comply with ICH guidelines?

After further investigation the approved IRB application has a question that asks who will discuss and obtain consent from patients. PI, Attending/Physicians, study staff, and mid-level providers were all marked.

We are now being accused of serious non-compliance. Any guidance would be appreciated.

Best regards,
[redacted]

From: OC GCP Questions [mailto:gcp.questions@fda.hhs.gov]
Sent: Thursday, July 16, 2015 9:25 AM
To: [redacted]
Subject: RE: Informed Consent Signature Reqiurement

Dear [redacted],

From the information provided in your email, it appears that the initial consent process was completed except for a missing signature from the physician on the English version of the consent form, since the consent discussion took place and the subject has agreed to participate in writing, and all the other forms been signed. The physician did, however, document in writing on 6/30 that the consent process had taken place.

From the information provided, it appears that FDA's regulatory requirements were met, although the IRB's internal processes for obtaining consent were not. It is not clear from your email whether it was the physician or the research coordinator who obtained consent (along with the interpreter), and also whether the short form was in the subject's language or also in English. FDA's regulations require that the witness sign both the short form and a copy of the summary, and the person who obtains consent also must sign the summary:

50.27(b)(2) A *short form* written consent document stating that the elements of informed consent required by 50.25 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

Since it is a requirement of the IRB that a clinically licensed person sign the English version of the informed consent (IC) document, the blood draw prior to this being done may possibly be viewed as a deviation from the IRB's process. Here are some items for

the IRB to consider:

1. If the English version of the informed consent (long form) is used as the consent summary, should the SOP be revised to reflect FDA's regulatory requirement for the person actually obtaining the consent to sign a copy of the summary? Should the English long form subsequently be translated into the language of the subject? To satisfy the IRB's requirement, a clinically licensed person could sign the summary also, in addition to the person obtaining consent, if the clinical person was not the one obtaining consent.
2. Should the physician be re-trained on informed consent processes for this institution?
3. The IRB may wish to reconsider whether this subject should be allowed to participate in the study, given that the documentation appears to indicate consent was given and the physician's failure to sign the English version of the IC was a deviation from the IRB's requirements.

FDA's current guidance document on informed consent may be helpful. It can be found at http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm

FDA also has a draft informed consent guidance, which is a revision of the one noted above. When finalized, this will replace the current guidance. The draft guidance can be found at http://www.fda.gov/RegulatoryInformation/Guidances/ucm404975.htm

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

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From: [redacted]
Sent: Friday, July 10, 2015 12:28 AM
To: OC GCP Questions
Subject: Informed Consent Signature Reqiurement

Hello,

A non-English speaking patient signed an *short form* on June 30th and there is a clinic note by the treating MD documenting the consent/trial discussion and patient's desire to participate. A certified interpreter was used to consent the patient and the required signatures on a short form were obtained per 21 CFR 50.27(b)(2).. The treating MD signed a consent process form on June 30th further

documenting this discussion. He did not sign the English version consent. The research coordinator signed the English version consent, as did the non-English speaking patient per the IRB of records requirements, on 6/30 as the "Name of the person obtaining consent" the IRB of record requires the person obtaining consent be a clinically licensed person who signs on that line of the English version consent.

The IRB of record signatory requirements are as follows:

1. Translated Short Form Consent: Patient and Interpreter sign
2. English version HIPPA Authorization: Patient signs
3. English version consent: Patient and PI sign
4. Interpretation Certification Form: Interpreter signs

The IRB <u>does not</u> require that the English version consent get translated to the patients native language at any point during their participation in the clinical trial.

The pre-treatment research blood was drawn after the patient and interpreter signed the short form, after the Dr. documented in the clinic note and documented on a separate consent process form. The institution is now stating that the lab draw is an issue because the consent process was not complete prior to the draw due to the PIs signature not being on the English version consent. They are stating that the patient should be denied access to the clinical trial because of the "missing" signature. Could you please provide guidance.

Thank you in advance for your help with this!

[redacted]