From:	OC GCP Questions
To:	[redacted]
Cc:	CDER DRUG INFO; OC GCP Questions; CDRH Small Manu. Assistance
Subject:	RE: [redacted] clinical trial
Date:	Monday, July 07, 2014 9:32:10 AM

Dear [redacted],

Thank you for your question. The option of using the short form is a valid option for the scenario you describe. In accordance with the regulations at 21 CFR 50.27(b), unless waived as described in 56.109(c), the consent form may be either [emphasis added] of the following:

> "(1) A written consent document that embodies the elements of informed consent required by 50.25. This form may be read to the subject or the subject's legally authorized representative, but, in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed."
>
> "(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."

The informed consent documentation requirements [21 CFR 50.27] permit the use of either a written consent document that embodies the elements of informed consent or a short form stating that the elements of informed consent have been presented orally to the subject. Whichever document is used, a copy must be given to the person signing the document.

When a short form consent document is to be used [21 CFR 50.27(b)(2)], the IRB should review and approve the written summary of the full information to be presented orally to the subjects. A witness is required to attest to the adequacy of the consent process and to the subject's voluntary consent. Therefore, the witness must be present (physically or by some other means, for example by phone or video conference) during the entire consent interview, not just for signing the documents. FDA recommends that an impartial third party, not otherwise connected with the clinical investigation (for example, clinical staff not involved in the research or a patient advocate), serve as the witness. The subject or the subject's legally authorized representative must sign and date the short form. The witness must sign both the short form and a copy of the summary, and the person actually obtaining the consent must sign a copy of the summary. The subject or the representative must be given a copy of the summary as well as a copy of the short form.

Your statement that you plan to follow up the use of the short form with the long form raises a potential issue I want to make certain you understand. FDA expects that the short form process should contain all required and applicable elements of consent including additional information as required by the IRB at the time of study approval, regardless of how informed consent is documented. Said another way, the short form process, including the information presented orally, is to be the same quantity and quality of information as when a long form is used. Therefore, it is not expected that the short form process of informed consent needs to be supplemented by the long form documentation.

Assuming the protocol does not preclude the use of a legally authorized representative, FDA regulations allow for a legally authorized representative to provide consent for a potential subject when the potential subject is unable to provide consent for themselves. As stated by OHRP in response to your question, prior to implementing a process that involves legally authorized representatives your IRB would need to determine whether potential subjects would have the capacity to consent for themselves.

You are correct that you need to follow the laws of the State of [redacted] with respect to who can serve as a legally authorized representative and whether there is a priority for determining who can

serve as a legally authorized representative. FDA regulations define legally authorized representative as "an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research." [21 CFR 50.3(l)] FDA interprets "applicable law" as the State or local law where the trial is conducted. You may want to seek legal counsel on this matter. However with respect to the logistics of obtaining and documenting informed consent from legally authorized representatives in the situation where they may not be accompanying the potential subject, you may want to consider the option of using electronic means to facilitate the process if possible. FDA does find it acceptable to send the informed consent document to the legally authorized representative by facsimile and conduct the consent interview by telephone when the legally authorized representative can read the consent as it is discussed. If the legally authorized representative agrees, he/she can sign the consent and return the signed document to the clinical investigator by facsimile.

Additional guidance on informed consent can be found at
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm and
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm#Informed%20Consent%20Process

I hope you find this information is helpful to you. If further assistance is needed, please feel free to contact us once again at the official GCP mailbox, gcp.questions@fda.hhs.gov.

v/r

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From: [redacted]
Sent: Tuesday, June 24, 2014 2:10 PM
To: CDER DRUG INFO; CDRH Small Manu. Assistance; OHRP@hhs.gov
Subject: [redacted] clinical trial

I was wondering if I could get some feedback from you on the issue listed below.

Our cath lab physicians are considering participation in our first [redacted] clinical trial (hopefully to open this fall). [redacted] is a life-threatening type of heart attack that requires urgent treatment. The study sponsor is NOT conducting this trial under the "emergency research exception from informed consent" regulations (21 CFR 50.24)… therefore, informed consent is required.

My questions/concerns relate to HOW to obtain and document valid research informed consent in this setting?

I've also talked to the study sponsor (a company named [redacted]) in some detail about how other study sites have approached the issue. I expected a discussion about use of Legally Authorized Representatives, but apparently most study sites are using a "short form" to obtain consent directly from the patient prior to the cath lab procedure. They follow-up with a full length consent form after the fact to ensure patient agrees to continued participation and follow-up.

I don't believe there is any hard data on whether [redacted] patients present alone or with family. Anecdotally, I believe patients often have a family member present. If we went the LAR route, that's where I could use guidance about who is authorized to give research consent and if there is a priority order. I assume I would need to follow [redacted] state law, I believe a spouse has priority over an adult child for example. So what if a patient is accompanied to the ER by his son instead of the wife? There are so many scenarios.

This particular study is a randomized trial of patients undergoing a PCI stenting procedure in the cath lab (the PCI is routine care). The patient is randomized to receive an investigational stent (study group) or commercially available stent (control group). Post-procedure, a sub-set of study patients will be required to have an MRI at Day 5 and a repeat Angiogram/IVUS (diagnostic cath lab procedure) at Month 13. Both of those assessments are done for research purposes only.

These trials can present a considerable ethical challenge because the potential subjects are in extreme pain and often medicated.

We would very much appreciate any assistance you can offer in how best to handle this issue.

Thanks so much.
[redacted]