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Topic: Don't Forget the Consent Process!

Overview of the Topic

IRBs are known to spend a lot of time dissecting, revising and rewording consent forms, and making sure that the required elements of consent are all adequately covered in the document. The required and additional elements of consent appear in 45 CFR 46.116 (a) and (b). However, there is a preface to those requirements which sometimes takes a back seat, but is just as important as the content requirements.

The first sentence in the preface simply states that "no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative" (with the exceptions of a waiver). This requirement is straight forward and emphasizes consent as a pillar of human research protection.

The second sentence starts the discussion of the consent process. Initially it requires that "An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate…" This requires that the potential subject have adequate time to read the consent form and contemplate whether they want to participate or not. This should include the opportunity to ask questions about the research. The length and complexity of the consent form affects the time needed as does the literacy and the education level of the subject population. With some long and complex forms, and seriousness of the research, investigators may often allow the potential participant to take the consent form home, read it, think about, discuss it with their family, and come back if interested in participating. Also, the person should not be pressured to participate in the research. That leads into the second part of the sentence, that the circumstances of the consent process must "minimize the possibility of coercion or undue influence." The involvement of a subject must be completely voluntary with no written or verbal language to coerce the subject into participating.

The third concept in the preface paragraph is that "The information that is given to the subject or the representative shall be in language understandable to the subject or the representative." Obviously this would require a translation of the consent form into the subject's language when the investigator can purposely include, or predict that the subject population may include, non-English speaking persons. IRBs often require someone fluent in the language in question to read the consent form to confirm the accuracy of the translation, or require a back translation. But again, the consent process goes beyond the consent form. If the subject had questions, can they ask them and have them answered in their language? If they call the investigator or designee listed in the consent form with questions, can they speak to someone in their language? Depending on the research, this may not always be possible and the IRB should discuss and decide when and if such language requirements are necessary.

The last sentence in the preface does speak to the content of the consent document, although the requirement applies to the consent process also, and what is said to the subject. "No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence." This is a tough one. There are two prominent issues that arise in this area. One is payment for research related injuries. While for most clinical trials sponsors usually pay for research related injuries, this is not the case for investigator initiated studies at most universities and hospital where the organizations do not want to assume such liability. The second issue is benefit from commercialization of donated specimen. This issue was brought to the public's attention (as well as investigators, administrators and IRBs) by the 2010 book *The Immortal Life of Henrietta Lacks* by Rebecca Skloot (Crown Publishers, New York). Ms. Lacks' cells were taken from her without consent or knowledge while she was hospitalized. The cells produced a cell line know as HeLa cells which launched a medical revolution and a multimillion dollar industry. Neither Ms. Lacks nor her surviving family received any compensation. Here are OHRP's current examples of acceptable and exculpatory language:

Examples of Exculpatory Language:

- I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

Examples of Acceptable Language

- This hospital makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge.

- Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

While there are examples of exculpatory language related to commercialization compensation in the 1996 guidance, a draft guidance issued in 2011 states that "OHRP and FDA have concluded that language in an informed consent form is not exculpatory if it informs subjects that, by agreeing to allow the use of their biospecimens for research purposes, they are giving up any legal right to be compensated for the use of the biospecimens." That draft guidance provides no examples of exculpatory language related to compensation for commercialization of donated tissues. The draft guidance has not been finalized so stayed tuned for the final resolution of this issue.

FDA information sheets provide guidance for another consent process requirement. If someone other than the investigator conducts the informed consent process and obtains informed consent from a subject or the subject's representative, the investigator must formally and prospectively designate in writing in the protocol or the application for IRB approval, the individual(s) who will have this responsibility. This is particularly important when the research or subject population requires specific expertise, for example if the research involves dealing with end of life issues in a hospice, the person obtaining consent should have expertise dealing with people who are facing death. Researchers or staff who obtain consent should be trained in the consent process, knowledgeable about the research, competent to answer questions, and experienced in dealing with the subject population, when appropriate.

In summary, do not stop reviewing the consent form, but remember also to consider the issues related to the consent process. They are just as important to adequate informed consent.

References:

- "Exculpatory Language" in Informed Consent, November 15, 1996, Office for Protection from Research Risks (OPRR; now OHRP).
- Draft Guidance on Exculpatory Language in Informed Consent, August 19, 2011, OHRP and FDA
- FDA Information Sheets: Frequently Asked Questions: Informed Consent Process

Questions for the IRB to Consider

Questions your IRB may ask about the consent process:

1. Does the consent process allow for adequate time for the subject to consider participating or not?
2. Does the consent process minimize the possibility of coercion or undue influence and allow voluntary participation?
3. Is the language of the consent and consent process appropriate for the subject population?
4. Does the consent process or consent form include any exculpatory language?
5. Has the investigator designated who will obtain consent? Are those persons adequately trained and experienced?

IRB Decision: Is the consent process adequate to allow for approval of the research?

Case Studies

Case 1. An investigator is conducting a minimal risk survey and comes upon a person who wants to participate in the survey but cannot read and thus read and sign the consent form. The project was approved with signed consent only and the investigator will lose the subject if she does not enroll him. **What should the investigator do?**

Case 2. A consent form contains the following statement: If you suffer a research-related injury, neither the institution nor the investigator can assume financial responsibility or liability for the expenses of treatment for such injury. **Would you consider this language exculpatory?**

Case 3. An investigator hands a potential subject a consent form, tells them about the study, and asks them if they want to participate. The potential subject asks if they can take the consent form home and think about it. The investigator says no, they have to decide immediately or they cannot participate. **Would you allow this as part of the consent process? Under what conditions would you allow or not allow such a process?**

Case 4. An investigator proposed a study involving a survey of prisoners with life sentences. He designates himself and his undergraduate research assistant to obtain consent. **What requirements would you have of the researcher or student?**

Prospective Thinking: Of the type of research in your organization's research portfolio, what type of projects require more scrutiny and requirements regarding the consent process? List the considerations and requirements for each major type of research area.