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On July 15, 2014, the U.S. Food and Drug Administration (“FDA”) released draft guidance that provides extensive commentary on FDA’s current thinking regarding the clinical trial informed consent process. Once finalized, this document, entitled “Informed Consent Information Sheet: Guidance for IRBs, Clinical Investigators, and Sponsors” (“Draft Guidance”), will replace FDA’s 1998 informed consent guidance, “A Guide to Informed Consent.” On September 26, FDA announced that it was reopening the comment period for the Draft Guidance and would accept comments through October 27. The initial comment period for the Draft Guidance closed on September 15; however, in response to a request from the Biotechnology Industry Organization, FDA decided to reopen the comment period for an additional 30 days.

Although the Draft Guidance is largely consistent with current practices, as discussed below, a number of FDA’s recommendations signal the modification or expansion of previous guidance regarding FDA’s thinking on important topics, such as:

1. Order of presentation of required disclosures
2. Providing risk information
3. Disclosures relating to FDA’s right to access subject information
4. Disclosures of potential additional costs
5. Alternative consent pathways
6. Financial conflicts of interest and informed consent
7. Recommended notifications with respect to multi-site studies in the event a single institutional review board (“IRB”) requires changes to an informed consent form (“ICF”)
8. Obtaining consent from vulnerable populations

In addition to providing specific information on FDA’s current thinking with respect to clinical trial informed consent, the publication of the Draft Guidance also supplies insight into the status of FDA’s combined efforts with the Office for Human Research Protections of the U.S. Department of Health and Human Services (“HHS”) to update the “Common Rule” and FDA’s regulations on human subject protection, and highlights...
FDA’s continued focus on manufacturers’ communication of risk information to patients and subjects.

**Updated Recommendations Relating to Informed Consent**

While the Draft Guidance largely reiterates existing best practices and brings together prior FDA interpretations of informed consent regulations into a single, comprehensive resource, several aspects of the Draft Guidance are notable.

1. **Order of presentation of required disclosures**

FDA’s updated recommendations on informing subjects that the clinical study involves research likely will require many sponsors and sites to reorganize their ICFs and update their ICF templates to incorporate FDA’s recommendations. For example, historically, many researchers have included the required statement that the clinical study involved research at the beginning of the ICF. However, FDA is now recommending that potential subjects first be informed of the care that the potential subject would receive should the subject choose not to participate in the research, followed by a disclosure that the study involves research and a description of how the subject’s treatment will differ if he or she participates in the research. In presenting this information in this order, FDA recommends that the description of the research identify those tests and procedures that are part of the standard of care but will not be performed as part of the research study, as well as any additional tests and procedures required by the protocol that are not part of the standard of care. These and other changes suggest that the time is ripe for manufacturers to reevaluate their existing form of ICF in light of the Draft Guidance.

2. **Providing risk information**

Consistent with FDA’s apparent belief that providing too much risk information may reduce an individual’s understanding of risk information, FDA recommends limiting the amount of risk information that is included in the ICF. Specifically, FDA recommends that only those risks that are serious or more likely to occur be included in the main body of the consent form. When presenting this information, FDA recommends including a discussion about whether a risk is reversible, the probability of the risk

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2 FDA notes that it may not be advisable to include, in the body of the informed consent form, the full list of procedures and tests that will be performed as part of the clinical study and that such information may be presented in an addendum, possibly in chart form, attached to the end of the informed consent form.

3 See Food and Drug Administration, Agency Information Collection Activities; Proposed Collection; Comment Request; Disclosure Regarding Additional Risks in Direct-to-Consumer Prescription Drug Television Advertisements, 79 Fed. Reg. 9,217 (Feb. 18, 2014).
based on existing data, what may be done to mitigate the most common and serious risks, and a description of reasonably foreseeable risk to others (e.g., whether radiation therapy may pose a risk to those who are in close contact with the subject following the procedure).

FDA’s focus on risk information is not surprising in light of its recent attention to risk disclosures to consumers in other contexts. For example, earlier this year, FDA sought comments regarding its proposal to study comprehension of risk information in direct-to-consumer TV drug advertising. Additionally, all six warning letters issued by the Center for Drug Evaluation and Research’s Office of Prescription Drug Promotion (“OPDP”) in 2014 included findings of inadequate presentation of risk information.

3. Disclosures relating to FDA’s right to access subject information

FDA states that ICFs should not state or imply that FDA needs permission from the subject to access the subject’s records, nor should the ICF promise or imply absolute confidentiality by FDA. As a result, sponsors and investigators may need to update their existing ICF language to ensure that it is clear that FDA does not need permission to access a subject’s medical records.

4. Disclosures of potential additional costs

The Draft Guidance provides significant new insight into FDA’s expectations regarding the information that a subject should be provided about the potential additional costs that a subject may incur by participating in the clinical study. The updated recommendations include the possibility of referring subjects to a knowledgeable financial counselor or reimbursement specialist when the additional costs may involve complex issues, such as insurance reimbursement. As sponsors and investigators are reviewing this part of their ICFs in light of the recommendations in the Draft Guidance, they also should consider evaluating whether the language regarding payment for subject injuries should be updated to address the recent changes with respect to Medicare secondary payer requirements.

4 Id.
6 Section 111 of the Medicare, Medicaid, and SCHIP Extension Act of 2007 amended the Medicare Secondary Payer statute by adding mandatory reporting requirements and penalties for noncompliance. The Centers for Medicare & Medicaid Services (“CMS”) issued guidance in 2010 stating that sponsors of clinical trials are deemed primary payers if the sponsor agrees to pay for injuries to Medicare beneficiaries that arise from the conduct of the research. The reporting obligations of research sponsors under Section 111 are detailed in CMS’s MSP Non-Group Health Plan (“NGHP”) User Guide.
5. Alternative consent pathways

The Draft Guidance discusses alternative methods of obtaining informed consent (i.e., beyond the traditional face-to-face interview and paper consent forms). FDA recognizes that as new technologies become available, alternate methods of obtaining informed consent, including methods that are not face to face, may be implemented—for example, e-mailing a consent form to a potential subject, conducting the consent interview over the phone, and executing the consent form electronically. Further, FDA encourages those interested in pursuing alternate methods of obtaining informed consent to contact FDA to discuss such proposed methods.

6. Financial conflicts of interest and informed consent

FDA recommends considering whether information related to financial relationships should be provided to subjects, based on the potential effects that the relationship might have on the clinical investigation or interactions with subjects. Specifically, FDA recommends two methods that can be used to help mitigate potential conflicts of interest: (1) including the information in the consent, and (2) using special measures to modify the consent process, such as utilizing a monitor or another individual to perform the consent. While this is consistent with some institutions’ conflict-of-interest practices, it may impact independent practitioners or institutions without adequate conflict-of-interest disclosure policies.

7. Recommended notifications with respect to multi-site studies in the event a single IRB requires changes to an ICF

FDA recognizes that for multicenter clinical investigations, certain changes to the consent form may be needed to address local and institutional requirements. However, if an IRB requires modifications to the consent form that significantly impact the rights, safety, or welfare of the subjects, FDA recommends that sponsors share this information with all investigators and IRBs. As the Draft Guidance does not provide further detail regarding what subject rights may be contemplated by this requirement, it is unclear the extent to which FDA expects consistency and uniformity across sites.

8. Obtaining consent from vulnerable populations

The final section of the Draft Guidance focuses recommendations designed to ensure that adequate consent is obtained from non-English speaking subjects, subjects with low literacy and numeracy, physically challenged subjects, subjects with impaired consent capacity, and minor subjects. Most of the guidance is simply a reiteration of previous FDA recommendations, but we have included some highlights below:

- FDA outlines a process for satisfying the informed consent requirement when appropriate consents are not available for non-English speaking individuals and time restrictions do not allow for the IRB-approved consent form to be translated prior to the consent process. As a prerequisite for this process, the IRB must
have previously approved a generic short-form informed consent in the language that the subject speaks.

- Some of the considerations recommended by FDA when obtaining consent from individuals with impaired consent capacity (partial, fluctuating, or complete) include using an independent qualified professional to assess consent capacity, establishing a waiting period in the decision-making process to allow additional time, assessing a subject’s understanding of the information through a questionnaire, and re-assessing capacity after the initiation of the investigation for subjects with progressive disorders.

- When obtaining parental permission for a child’s participation in clinical research, if the parents do not understand English, FDA recommends that a child not be used as a translator, even if the child is fluent in English and may be able to assent.

Possible Insight into Status of Common Rule Updates

FDA issued the Draft Guidance nearly three years after the HHS released its Advance Notice of Proposed Rule Making (“ANPRM”) raising the possibility of modifying the “Common Rule.” As FDA was involved in the development of the ANPRM, it is interesting that FDA decided to issue the Draft Guidance while changes to the Common Rule, which the Draft Guidance is designed to clarify, remain under consideration. As it would be unusual for FDA to expend its limited resources updating a guidance that may become obsolete before it is finalized, the publication of the Draft Guidance likely means either: (1) FDA does not believe that the changes to the Common Rule will significantly modify the regulatory requirements related to informed consent, or (2) FDA does not believe that the changes to the “Common Rule” will move forward anytime soon. Either way, it is probably safe to say that sponsors and investigators can depend on this recommendations included in the Draft Guidance to reflect FDA’s current thinking for at least the next few years.

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This Client Alert was authored by Amy K. Dow, Daniel G. Gottlieb, Bonnie I. Scott, and Ryan R. Benz. For additional information about the issues discussed in this Client Alert, please contact one of the authors or the Epstein Becker Green attorney who regularly handles your legal matters.

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