FDA Issues Draft Guidance on Use of Electronic Informed Consent in Clinical Trials

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On March 9, 2015, the U.S. Food and Drug Administration (FDA) released a draft guidance, Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers, that provides recommendations for clinical investigators, clinical trial sponsors and institutional review boards (IRBs) on the use of electronic informed consent (eIC) in FDA-regulated clinical trials of medical products, including drugs and biological products, medical devices and combinations of those products for human use. For purposes of the draft guidance, the FDA describes eIC as “using electronic systems and processes that may employ multiple electronic media (e.g., text, graphics, audio, video, podcasts and interactive Web sites, biological recognition devices, and card readers) to convey information related to the study and to obtain and document informed consent.”

In the draft guidance, the FDA articulates a flexible approach to obtaining and documenting informed consent that appreciates the tangible benefits that technological advancements may bring to the consent process. Electronic systems and media may be deployed to facilitate subjects’ understanding of the information conveyed during and in completing the informed consent process, onsite and in-person, remotely, or both.

The eIC draft guidance was developed as part of the FDA’s joint effort with the U.S. Department of Health and Human Services’ (HHS’s) Office for Human Research Protections (OHRP) to modernize and harmonize the agencies’ requirements and guidance for research involving human subjects. The draft guidance was also developed in response to the clinical research community’s growing interest in using electronic media to convey information more meaningfully and to enhance the informed consent process.

The FDA’s draft guidance provides recommendations regarding four interlocking considerations in designing and implementing an eIC process: (1) the need and methods for protecting human subjects, (2) facilitating and improving people’s understanding of the information being conveyed during the electronic consent process to ensure that their decision to enroll as subjects in a clinical trial is informed, (3) ensuring appropriate documentation of eIC, and (4) ensuring the quality and integrity of data collected when consent is obtained through an electronic process.

The FDA noted in the draft guidance that eIC’s implementation would likely have several benefits for both subjects and investigators, including the following:

- The ability of a subject to complete the eIC process outside of the research site by using interactive media and electronic signature processes
- A subject’s potentially enhanced ability to understand and retain information provided via an interactive process
- The research team’s ability to rapidly notify subjects of any amendments or other information that may affect a subject’s willingness to continue to participate in the study
- The promotion of timely eIC data collection and entry, and other administrative simplifications for
The FDA notes that eIC must still contain all of the elements of informed consent currently required by FDA regulations. The draft guidance recommends several steps to help address potential issues that may arise from use of the eIC process and to help ensure that the eIC process maintains the same level of subject protections as found in the traditional consent process. The FDA suggests that investigators and IRBs address, at minimum, the following considerations to respond to potential particular challenges of using an eIC:

- **Subject Identity:** An in-person informed consent process provides research team members ample opportunities to confirm and document the identity of the individual enrolling in the clinical trial. Use of eIC can complicate the identification verification process, since the eIC process can occur remotely and involve the potential participant navigating the informed consent process without any in-person interaction with the research team. The draft guidance, therefore, recommends that remote eIC processes include a “method to ensure that the person signing the informed consent is the subject (or the subject’s legally authorized representative) who will be participating in the research study.” When electronic signatures are used to evidence consent, IRBs should ensure compliance with applicable requirements in FDA’s electronic records/electronic signature regulations at 21 C.F.R. Part 11.

- **Data Integrity:** The draft guidance recommends that any remote eIC process electronically document “all interactive responses by subjects, witnesses, or other involved parties” using software systems that prevent a potential subject’s responses from being altered.

- **Interactive Process:** As with traditional informed consent, eIC is not only a form; it is a process. Any eIC process conducted onsite or remotely should include an opportunity for subjects to ask questions and receive answers prior to providing their consent to participate in the study. The eIC process also should be easy to navigate, appropriate for the intended audience, and designed to minimize the possibility of coercion or undue influence on a subject’s study participation. Interactive computer programs utilized in the eIC process may be enhanced by including questions at the end of each section that assess the subject’s understanding of the eIC materials, although use of such comprehension quizzes and assessments raises additional compliance and legal concerns that should be considered in connection with their potential use.

- **Data Privacy and Security:** Since copies of the consent document must be presented to the subject under the FDA’s and OHRP’s informed consent regulations, the draft guidance contemplates providing electronic copies to the subjects when eIC is employed. The draft guidance notes that the electronic copy should include a transcript of any audiovisual presentations, and that subjects should be informed of the risks of storing or viewing an electronic copy of the consent document on a personal electronic device, including the inability to permanently remove the copy or prevent the information from being hacked. The draft guidance also sketches some broad data security and use requirements for the systems that support and retain the eIC data. The draft guidance notes that the Health Insurance Portability and Accountability Act (HIPAA) generally permits e-signatures in lieu of in-person signatures, provided the subject’s signature meets the requirements for electronic signatures under the Electronic Signatures in Global Commerce Act (P.L. 106-229). The draft guidance indicates that e-signatures in the eIC context would also be acceptable, provided that they met the foregoing and the FDA’s regulations at 21 C.F.R. Part 11.

The draft guidance does not, however, provide recommendations on the use of electronic media and processes for subject recruitment. This exclusion is notable in view of the FDA’s position that the informed consent process begins at recruitment. The OHRP also requires IRB oversight of any recruitment materials, and therefore electronic media and processes intended for use in connection with subject recruitment will require IRB oversight.

The FDA notes that it has been working alongside OHRP seeking to harmonize regulatory requirements and guidance for clinical research involving human subjects, including this guidance. The OHRP has also requested comments on whether it should adopt the positions and recommendations discussed in the draft guidance for all human subject research studies to which the HHS protection of human subjects regulations at 45 C.F.R. Part 46 (Common Rule) apply. The HHS Federal Register notice indicates that the OHRP specifically requests comments on whether the OHRP and the FDA should issue a joint guidance on eIC, and whether the FDA’s draft guidance would be appropriate and applicable for research governed by the Common Rule. For example, the Common Rule governs certain types of research, such as social or behavioral studies that are less likely to be subject to FDA oversight. In the event that commenters think that different requirements and/or protections should be adopted for research regulated under the Common Rule, OHRP requests that commenters provide specific examples of how the OHRP’s approach should differ from the FDA’s draft guidance.

**Further Considerations**
The draft guidance is significant in that it appears to support researchers’ and sponsors’ interest in harnessing technology to ease administrative burdens and better inform subjects of the potential risks and benefits of research participation. The draft guidance, however, leaves unanswered a number of questions that stakeholders may face in implementing and utilizing eIC processes. For example, while the draft guidance explains that an IRB must review eIC materials, it does not provide guidance regarding how an IRB should review such materials, or what specifically an IRB should review. Moreover, while the draft guidance raises the possibility of subjects taking quizzes to confirm comprehension of disclosed information, it does not address how investigators should respond if a subject incorrectly answers a question (or questions) regarding such information. Thus, IRBs will likely have an important and active role in navigating how best to incorporate eIC tools on a going-forward basis.

Stakeholders interested in commenting on the draft guidance should submit comments to the FDA by May 8, 2015. Stakeholders interested in responding to OHRP’s request for comments should submit comments to HHS by May 7, 2015.

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