What’s New in GCP?
FDA, OHRP Issue Joint Electronic Informed Consent Guidance

The FDA and the Department of Health and Human Services’ Office for Human Research Protections (OHRP) issued joint guidance Dec. 15 on the use of electronic informed consent (eIC).

The final guidance replaces a draft FDA-only question and answer guidance released in March 2015. The final guidance adds two new questions:

- What methods may be used to verify the identity of the subject who will be electronically signing an eIC for FDA-regulated clinical investigations?
- What eIC materials should the investigator submit to the institutional review board?

The guidance noted that if a study is conducted or supported by HHS and involves an FDA-regulated product, “the study is subject to both 45 C.F.R. Part 46 and 21 C.F.R. Parts 50 and 56, meaning that both sets of regulations must be followed. Where the regulations differ, the regulations that offer the greater protection to human subjects should be followed.” The FDA also noted that research not subject to 21 C.F.R. Parts 50 and 56 “is also not generally subject to 21 C.F.R. Part 11, the FDA regulations regarding electronic records and electronic signatures.”

The final guidance added, “electronic informed consent may be used to either supplement or replace paper-based informed consent processes in order to best address the subject’s needs throughout the course of the study. For example, some subjects may prefer one method over another. Other subjects may have difficulty navigating or using electronic systems because of, for example, a lack of familiarity with electronic systems, poor eyesight, or impaired motor skills. In such cases, the eIC process may not be appropriate for these subjects. Therefore, subjects should have the option to use paper-based or electronic informed consent methods completely or partially throughout the informed consent process. Moreover, in some circumstances, it may be appropriate for investigators or study personnel to assist subjects in using the eIC technology. For example, study personnel may help the subject navigate the consent by clicking on links for the subject.”

The guidance provides recommendations on procedures that may be followed when using electronic informed consent to help ensure the protection of the rights, safety and welfare of human subjects; aid the subject’s comprehension of the information presented during the eIC process; ensure that appropriate documentation of consent is obtained when electronic systems and processes that may employ multiple electronic media are used to obtain informed consent; and ensure the quality and integrity of eIC data included in FDA applications and made available to FDA during inspections.

The final guidance answers questions on how to present information in the eIC to the subject; how and where to conduct the eIC process; how and when questions from subjects should be answered; steps that may be taken to aid subject understanding; how to convey additional information to the subject during the research; how to use electronic signatures to document eIC; how to verify the identity of the subjects who will be electronically signing the informed consent; how to use electronic informed consent for pediatric studies; how to provide copies of the eIC to the subject; steps that may be taken to ensure privacy, security and confidentiality of the eIC information; how to obtain Health Insurance Portability and Accountability Act authorizations for research electronically; what eIC materials the investigator should submit to the IRB; what the IRB’s responsibilities are in the eIC process;
the eIC documentation required for FDA submission with applications; steps to ensure that eIC materials are archived appropriately for FDA-regulated clinical investigations; and what eIC materials or documents FDA will require during an inspection.

New Questions Detailed

On the new question of what eIC materials an investigator should submit to an IRB, the guidance said the investigator should submit copies of all forms — both electronic and paper — as well as informational materials, including any videos and web-based presentations, which the subject will receive and view during the eIC process.

The guidance noted, “the investigator must obtain IRB approval for any subsequent modifications to the study-related information, whether electronic or in hard copy (45 C.F.R. §46.109 and 21 C.F.R. §56.109). OHRP and FDA recommend that an investigator discuss plans for using eIC with the IRB before finalizing development of the eIC to ensure that the IRB agrees that such a format may be used for the applicable research for obtaining informed consent.”

The final guidance adds that IRBs must maintain and retain copies of materials that have been reviewed in accordance with 45 C.F.R. §46.115 and 21 C.F.R. §56.115. IRBs also should review optional questions or methods used to gauge subject comprehension of key study elements, as well as the usability of the eIC materials, to ensure they are easy to navigate. "If the program uses hyperlinks to convey study-related information, IRBs should review the contents to which subjects are referred in order to determine if the study-related information that has been supplied is accurate and appropriate,” the guidance said.

“Because web sites are often modified over time, IRBs must maintain the version of the web site information that contains the study-related information that the IRB reviews and approves, either electronically or as a hard copy (45 C.F.R. §46.115 and 21 C.F.R. §56.115).”

As to what methods may be used to verify the identity of a subject who electronically signs an informed consent document, the guidance said the “FDA regulations do not specify any particular method for verifying the identity of an individual and accepts many different methods. For example, verifying someone’s identity can be done by using information from some form of official identification, such as a birth certificate, government-issued passport, or a driver’s license. In addition, use of security questions to confirm an individual’s identity can also be considered,” the guidance said.

The final guidance notes that, “whether part or all of the eIC process takes place on-site or remotely, the responsibility for obtaining informed consent remains with the investigator and the study personnel to which responsibility has been appropriately delegated. The investigator cannot delegate authority to obtain informed consent to the electronic system.”

In addition, if any or all of the consent process takes place remotely and is not personally witnessed by study personnel, the electronic system must include a method to ensure that the person electronically signing the informed consent is the subject who will be participating in the research study or is the subject’s legally authorized representative (LAR) (21 C.F.R. §11.100(b)). Methods to do that include verification of a state-issued identification or other identifying documents or use of personal questions, biometric methods, or visual methods.

OHRP noted that, for research under its sole jurisdiction, “it may not be possible or necessary for all types of research covered by 45 C.F.R. Part 46 to verify that the person signing the informed consent is the subject or the subject’s LAR who will be participating in the research study. OHRP encourages investigators to apply a risk-based approach to the consideration of subject identity. For example, social behavioral minimal risk research will
not typically warrant such verification. In addition, informed consent may be waived for minimal risk research meeting the requirements of 45 C.F.R. §46.116(d).”

**Other Guidance Changes Noted**

The final guidance also states that the eIC process must provide sufficient opportunity for the subject to consider whether to participate (45 C.F.R. §46.116 and 21 C.F.R. §50.20). In addition, “the eIC process must provide sufficient opportunity for the subject to consider whether to continue participation (45 C.F.R. §46.116 and 21 C.F.R. §50.20).” In cases where the eIC is updated or amended, “the subject or the subject’s LAR must sign the amended eIC before the subject continues in the study (45 C.F.R. §46.117(a) and 21 C.F.R. §50.27). OHRP and FDA regulations permit the flexibility of using electronic and paper informed consent methods independently or in combination throughout the course of the study. Thus, amendments to the eIC do not need to be electronic in nature and can instead rely on more traditional means, such as paper-based amendments or postal mail, for conveying and transmitting the information to the subject.”

OHRP added that it permits electronic signatures if such signatures are legally valid within the jurisdiction where the research is to be conducted.

The guidance also said that electronic signatures based on biometrics must be designed to ensure they cannot be used by anyone other than their genuine owners (21 C.F.R. §11.200(b)). “Therefore, suitable biometrics should be uniquely identified with the individual and should not change with time. In addition, electronic signatures based upon biometrics are accepted, provided they meet the requirements found in 21 C.F.R. Part 11 (i.e., they must contain pertinent information associated with the signing (21 C.F.R. §11.50(a)); they are subject to the same controls as electronic records and must be included as part of any human readable form of the electronic record (21 C.F.R. §11.50(b)); and they must be linked to their respective electronic records (21 C.F.R. §11.70).”

The agencies noted IRBs, investigators and sponsors also should consider how the electronic signature is created and whether the informed consent or permission document can be produced in hard copy for review by the subject upon request. “IRBs, investigators and sponsors may rely on a statement from the vendor of the electronic system used for obtaining the electronic signature that describes how the signature is created and that the system meets the relevant requirements contained in 21 C.F.R. Part 11,” the guidance said.

For pediatric studies, the new guidance adds that “parental permission may be obtained and documented using the same eIC procedures as would be used for informed consent” and that, “when approving an eIC assent process, an IRB should consider whether the capability of a child to assent may be affected by the method used to obtain and/or document child assent.”

And for FDA-regulated trials, the guidance said that, “depending on the method of identity verification used to satisfy the regulations in 21 C.F.R. Part 11 for electronic signatures in FDA-regulated clinical investigations, a child may lack the documentation necessary to verify their identity for the purposes of preventing fraudulent use of electronic signatures (e.g., driver’s license). If so, depending on the clinical investigation, it may be reasonable for the parent to initially document the child’s assent, which can then be verified when the investigator first sees the child.”

The final guidance added that the copy of the eIC provided to the subject can be paper or electronic and may be provided on an electronic storage device or via email. If the copy includes one or more hyperlinks to information on the Internet, the hyperlinks should be maintained and information should be accessible until study completion. In addition, if the eIC uses hyperlinks or other web sites or podcasts to convey information specifically related
to the research, the information in these hyperlinks should be included in any printed paper copy.

For FDA-regulated trials, the guidance also added that “the electronic system that supports the eIC must be secure with restricted access (21 C.F.R. §11.10 and 21 C.F.R. §11.30) and should include methods to ensure confidentiality regarding the subject’s identity, study participation, and personal information after informed consent has been obtained.”


Other Recent Developments in the Guide to Good Clinical Practice
CIOMS Revises Ethical Research Guidelines
NIH Pushes Back Implementation Of Single IRB Policy to September 2017
Checklist Released for Determining Whether a Study Must Be Registered in ClinicalTrials.gov