FDA FINALIZES ITS INFORMED CONSENT GUIDANCE FOR IRBS, CLINICAL INVESTIGATORS AND SPONSORS

On August 15, 2023, the U.S. Food and Drug Administration ("FDA") finalized "*Informed Consent: Guidance for IRBs, Clinical Investigators, and Sponsors*" ("Final Guidance"), following the FDA's earlier issuance of draft guidance on the subject in July 2014. The Final Guidance reflects the FDA's recommendations on informed consent and the regulatory requirements in place to protect human subjects' rights and welfare in clinical investigations.

ELEMENTS OF INFORMED CONSENT

Informed consent is a process by which a prospective participant in a clinical investigation (often referred to as a subject), or their legally authorized representative, is provided with information to allow the subject or their representative to make an informed decision about participation in the clinical investigation prior to enrollment. The Final Guidance notes that "obtaining documentation of a subject's informed consent is only part of the consent process," and compliance with the FDA's informed consent requirements necessitates more than execution of a consent form. Through the informed consent process, a subject should be provided with an adequate level of information regarding the clinical investigation and opportunities to ask questions about participation in the investigation. The subject's voluntary agreement to participate should then be obtained and documented prior to enrollment. Informed consent also requires disclosure of any additional information that arises during the course of the clinical investigation, to ensure subjects are able to make an informed decision regarding continued participation.

Situational factors should be considered and accounted for to ensure that the informed consent process is conducted with minimal potential for coercion or undue influence. The Final Guidance provides examples of potentially coercive or unduly influenced informed consent processes, such as an employer enrolling employees in a clinical investigation sponsored by the employer, or seeking consent for tissue collection in the preoperative area immediately prior to the performance of a surgical procedure. The Final Guidance clarifies that reimbursement of reasonable travel expenses and associated costs do not constitute coercion or undue influence.

Informed consent includes the following basic elements:

1. *Description of clinical investigation.* The statement should clearly denote that the clinical investigation involves research to make subjects aware that the purpose of participation is primarily to contribute to research rather than to their own medical treatment. The Final Guidance recommends discussing the care that the subject would receive if they did not participate in the clinical investigation, followed by information about the care they would receive if participating in the investigation. Such information should include a description of the investigational product being researched, the procedures that the subject will participate in and the expected duration of the investigation (including any follow-up).

2. *Risks and discomforts.* There should be a description of foreseeable risks and discomforts caused by any tests, interventions or procedures required by the clinical investigation protocol. There should be a particular emphasis on activities that involve potentially significant risks, such as the risk of new or exacerbated disease or death. This may also include privacy risks – for example, the possibility of unintended disclosure of the subject's private information.

3. *Benefits*. Potential benefits include benefits directly impacting the subject, as well as the broader societal benefits of the research. Where there is no anticipated benefit directly to the subject, that should be clearly communicated. Any reimbursements that will be provided to subjects should not be identified as a benefit of participation.

4. *Alternative procedures or treatments*. Informed consent must disclose, appropriate alternatives that might be advantageous to the subject. This should include a description of the currently medically recognized standard of care treatment and any alternative therapies (including the foreseeable risks or discomforts and potential benefits of such therapies). Where appropriate, the subject should be referred to another provider to fully discuss treatment alternatives.

5. *Confidentiality*. The consent process must describe how the confidentiality of records identifying the subject will be maintained and

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identify all entities (e.g., study sponsor, regulatory agencies, etc.) who may gain access to the records relating to the clinical investigation. Subjects must be made aware that the FDA may inspect records related to the investigation without the subject's permission or authorization. The FDA also noted that the role of the Institutional Review Board ("IRB") in privacy goes well beyond simply reviewing the informed consent form. The IRB should require and review the data management plan to assess privacy risks.

6. *Compensation and medical treatment in event of injury.* For clinical investigations involving more than minimal risk, informed consent should describe compensation and medical treatment available should an injury occur. The consent process should clearly state if no compensation will be made available to subjects; however, any language that is exculpatory is prohibited. Therefore, it is permissible to say that no plans exist for compensating subjects who are injured; it is not permissible to state that any right to seek legal redress has been waived.

7. *Contacts.* The consent process must provide information on how a subject would contact an individual for questions about the clinical investigation and the subjects' rights, and whom to contact if a research-related injury to the subject occurs. If contact information changes during the course of the clinical investigation, updated contact information must be provided to subjects.

8. *Voluntary participation.* Subjects should be informed that they may decline to take part in the clinical investigation or may stop participation at any time without penalty or loss of benefits to which they would otherwise be entitled.

The FDA also discussed additional elements that should be included in informed consent when the IRB determines the information is material to a subject's decision to participate including:

1. Unforeseeable risks;
2. Involuntary termination of subject participation;
3. Additional costs to the subject;
4. Consequences of subject's decision to withdraw;
5. Providing significant new findings to subjects; and
6. Number of subjects.

The informed consent form, as well as all consent discussions, must be provided in language that is understandable to the subject or legally authorized representative and cannot include exculpatory language. The Final Guidance provides examples of prohibited language, such as statements that the subject waives their right to take legal action for any injury suffered in the course of the clinical investigation.

DOCUMENTATION OF INFORMED CONSENT

With limited exceptions, informed consent must be documented by a signed and dated written consent form. The FDA acknowledges that informed consent has typically been obtained and documented in a face-to-face interview using paper consent forms, but that technologies are available that may serve as an alternative in the informed consent process. The FDA counsels entities interested in pursuing alternative methods to discuss such plans with their IRB. The FDA notes that methods other than a face-to-face discussion may be acceptable if those methods allow for an adequate exchange of information and documentation and ensure that the signer of the consent form is the person who plans to enroll as a subject in the clinical investigation or is a legally authorized representative of the subject. Electronic signatures are permitted but must comply with applicable regulations (including 21 CFR Part 11).

RESPONSIBILITIES FOR INFORMED CONSENT

In addition to outlining the informed consent requirements and exceptions as discussed above, the Final Guidance also provides information regarding the responsibilities of IRBs, clinical investigators and sponsors in the informed consent process. These entities share responsibility of regulatory compliance as it relates to the form and process for informed consent.

The Final Guidance explains that the IRB must review all materials used for informed consent, which includes considering the wording and language of such materials that are provided to subjects, as well as the consent process to be used by the investigator. As a clinical investigation evolves or changes, the IRB may also decide to require new information relating to the clinical investigation to be provided to subjects and is charged with the responsibility of determining whether subjects must be informed of certain financial arrangements or

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interests associated with the clinical investigation. Ultimately, the IRB must review and approve these materials to ensure subjects' rights and welfare are meaningfully protected.

Clinical investigators must provide the IRB, for review and approval, information on the consent process, including who will conduct the consent discussion, as well as any revised consent forms to reflect new information that may affect a subject's participation in a clinical investigation. The Final Guidance also outlines how clinical investigators may delegate the required consent discussion with subjects and what to consider when disclosing financial relationships to subjects.

Additionally, the FDA provides guidance to sponsors on model consent forms and the responsibility of working with the clinical investigator on modifying consent forms to address local and institutional requirements, if necessary. Sponsors should also ensure the informed consent form includes information on sponsor personnel activities.

Lastly, the FDA outlines its own responsibilities related to the review of informed consent forms regarding investigational new drugs, biologics and medical devices.

FAQS

The Final Guidance incorporates sixteen frequently asked questions ("FAQs") to provide answers to the FDA's regulations on the protection of subjects generally, which include considerations and processes for enrolling children and non-English speaking subjects in clinical investigations, as well as those subjects with low literacy and numeracy, and physical and sensory disabilities. Additionally, the FAQs provide information on individuals who may serve as legally authorized representatives to consent on behalf of a subject, guidance on consent obtained through electronic methods, how data is handled when a subject withdraws from a clinical investigation and informed consent to review subjects' medical records.

PRACTICAL TAKEAWAYS

- Entities subject to these informed consent requirements should consult the FDA's Final Guidance to ensure compliance with best practices for obtaining and maintaining informed consent in clinical investigations. The FAQs are helpful for inquiries regarding FDA regulations for the protection of human subjects.
- The FDA Guidance clarifies several issues related to the information that must be provided to potential subjects, and the detail necessary for IRB review. Education of principal investigators and IRB members regarding the FDA Guidance may be beneficial.
- Informed consent guidance continues to be modernized as the FDA provides guidance on how new technologies can be incorporated into the informed consent process.

CONCLUSION

This Final Guidance finalizes the FDA's draft guidance entitled "*Informed Consent Information Sheet*," issued in July 2014, and supersedes the FDA's guidance entitled "*A Guide to Informed Consent*," issued in September 1998.

If you have any questions on the Final Guidance or would like help with advertising and promotion of drugs, biologics or medical devices, please contact:

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