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Human Research Report

PROTECTING RESEARCH SUBJECTS AND RESEARCHERS

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IRBs Have Newly Updated Informed Consent Procedures and Answers to IRB Questions (#1)

FDA has issued a final guidance titled "Informed Consent: Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors."

"The guidance provides the Agency's recommendations regarding informed consent and describes FDA regulatory requirements to help assure the protection of the rights and welfare of human subjects in clinical investigations.

The guidance finalizes the draft guidance entitled, 'Informed Consent Information Sheet: Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors,' issued on July 15, 2014, and supersedes FDA's guidance entitled 'A Guide to Informed Consent,' issued in September 1998" (88 Fed. Reg. 55703, August 16).

All of the details of this new 61-page FDA guidance are obviously beyond the scope of the HRR's usual emphasis on highlights of IRB regulations and immediate tips.

However, we can focus on the changes contained in this new guidance, along with newer IRB issues not fully addressed in prior documents.

We begin by excerpting key portions of the guidance's new recommendations on "coercion and undue influence."

Importance of Minimizing Coercion or Any Type of Undue Influence

"The conditions under which informed consent is sought and the relationship between the subject and the person obtaining consent should be carefully considered to minimize the possibility of coercion or undue influence (21 CFR 50.20).

According to the [past and extremely influential] BELMONT REPORT, 'Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance.

Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate[,] or improper reward or other overture in order to obtain compliance.'[20]

[FN #20: The BELMONT REPORT was written by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

The Commission, created as a result of the National Research Act of 1974, was charged with identifying the basic ethical principles that

NOTE #1: Quoted materials in this newsletter appear exactly as originally published in source documents, including any misspellings, grammatical errors, or missing words. However, we will on occasion insert words or edit text and/or formating in brackets [ ] to make the material easier to read.

NOTE #2: Emphases are added to articles by HRR by underlining or adding ***bold/italics*** to selected text, unless stated otherwise.

NOTE #3: Articles **T**o **B**e **C**ontinued in subsequent issues are marked at the end of the article with **{TBC}**.

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should underlie the conduct of biomedical and behavioral research involving human subjects and developing guidelines to assure that such research is conducted in accordance with those principles.

See BELMONT REPORT, available at https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html.]" (guidance, August, pp. 6-7; on the Web at https://www.fda.gov/media/88915/download).

Being Extra Careful When Researcher Is Patient's Physician

"For example, if an employer seeks to enroll employees in a clinical investigation sponsored or conducted by the employer, the informed consent process should contain safeguards to ensure that participation is voluntary and that the possibility of undue influence or coercion by supervisors, peers, or others is minimized.

Similarly, because of a potential conflict of interest and the nature of the physician-patient relationship,[21] when the investigator is also the prospective subject's physician, for example, the investigator should ensure that the prospective subject understands that enrollment in the clinical investigation is voluntary, and that a decision to forgo enrollment will not adversely affect their medical care, in accordance with 21 CFR 50.25 (a)(8).

[FN #21: For the purposes of this document physician means a medical doctor or other appropriate healthcare providers.]" (supra at page 7).

Many Subject Populations Are Covered, Not Just the Vulnerable Ones

"The consent process and form should emphasize that an individual's participation is truly voluntary.

Note that coercion and undue influence may be situational, and can affect any population, not just subject populations seen as vulnerable to coercion or undue influence.

For example, in a clinical investigation involving the collection of extra tissue samples during a planned surgical procedure, waiting to obtain informed consent until the prospective subject is in the preoperative area would generally fail to minimize the possibility of undue influence.

The possibility of undue influence could be addressed by first discussing the study with the prospective subject during a preoperative visit as part of the informed consent process.

The prospective subject could be told that the study will be reviewed with them again prior to the procedure and, after all questions are resolved, they will be asked to sign a consent form acknowledging their willingness to participate in the study at that time.

In addition, statements that claim investigational drugs and devices are safe or effective for the purposes for which they are being investigated are prohibited (21 CFR 312.7(a) and 21 CFR 812.7 (d))" (ibid).

Researchers Must Not Imply More Than Is Actually True

"Likewise, statements that overstate the possibility of benefit may unduly influence prospective subjects by leading them to incorrectly assume that it is known that the investigational product will be of benefit to them, influencing them to agree to participate when they might not have otherwise chosen to do so.

For example, wording that refers to the clinical investigation as a 'therapeutic trial' could contribute to a prospective subject's misunderstanding that the trial will offer a direct benefit for their disease or condition.

Furthermore, we generally recommend against including statements such as 'FDA has given permission for the clinical investigation to proceed' or 'FDA has approved the clinical investigation' in the informed consent process, because such statements may suggest to subjects that the investigation has FDA's endorsement.

In addition, these statements may not be accurate for the particular clinical investigation at issue (see, e.g., 21 CFR 312.40(b) and 21 CFR 812.2 (b)).

FDA does not consider reimbursement for reasonable travel expenses to and from the clinical trial site (e.g., airfare, gas, tolls), and associated costs, such as parking and lodging, to raise issues related to coercion or undue influence.

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