FDA recently updated its informed consent guidance in the form of an Information Sheet. The new document reflects the Agency’s current thinking on the informed consent process utilized in FDA-regulated clinical trials. No changes have occurred to the regulation addressing the informed consent process (21 CFR 50.20); however, it is important to understand FDA’s perspective and the potential impact this could mean to clinical trial sponsors and investigators.

The primary issues addressed in the Information Sheet are:

1. informed consent form (ICF) content,
2. anticipated interactions between the sponsor, site, Institutional Review Board (IRB), and the FDA, and
3. the informed consent process.

What might these issues mean for your organization? The major changes are outlined below:

**IRB vs FDA Consent Form Review**
The Agency states that, although it may request a copy of the consent for review, the IRB of record is the final authority on these required documents and, if requested by the IRB, sponsors should utilize IRB-standardized formats. IRBs are required to track document revisions (date stamping is recommended, but not required).

This differs for studies conducted under an IND, as they have different requirements that those conducted under an IDE. In an IND study, the IRB of record is considered the final authority on ICF content and a copy of the ICF isn’t required during the initial IND submission to FDA. In an IDE study; however, the ICF is a required part of the submission and any substantive changes to the ICF that are requested by an IRB must also be approved by FDA.

**The Consent Process**
As specified in 21 CFR 50.20, all investigational trials involving human subjects are required to obtain informed consent from research subjects prior to engaging in any study-specific activities with that subject. Informed consent documents must contain each of the 8 elements specified in 21 CFR 50.25(a), basic elements of informed consent, all of the applicable 6 additional elements specified in 21 CFR 25.50(b), and any additional
elements of informed consent. The study's informed consent document must be updated to reflect any “substantive” changes (i.e. from protocol revision, interim analyses or otherwise) and the subject must be reconsented using the new form as soon as possible.

FDA states that it views informed consent as a “process”, and not as a series of static events, and wants PIs/IRBs/Sponsors to view it the same way. FDA will be paying close attention to the time taken to revise the consent and obtain new consent from clinical subjects, as well as Investigator/site notes about consent. Investigators/PI should be keeping close tabs on the IFC process and making a habit of writing notes to document their efforts.

21 CFR 50.20 – General Requirements for Informed Consent

In this section, FDA specifies its opinion on specific phrasing and procedures utilized in the informed consent process. This is the Agency’s current thinking on the process – these items are not codified in the CFR.

The Agency cautions/does not prefer usage of the following language:

- “I understand”, in relation to the subject’s signature, preferring “I am satisfied with the explanation”
- “FDA has given permission/approved” the IFC, since, predominantly, they do not
- “The IRB has approved recruitment”, as it may lead subjects to think their consideration is unnecessary

For non-English speaking subjects, FDA cautions use of “short forms” (i.e. forms written in the subject’s native language that state the consent has been explained in their language). Instead, Sponsors/Investigators should have the English form translated, certified, and create a note-to-file that delineates the steps taken. In the long-term, this process is more transparent and provides a clearer record of what actually happened.

Illiterate subjects, who often sign by making their “mark”, should be videotaped to avoid any presumptions of foul play. Since the subject cannot read the full consent form, it is appropriate for these subjects to sign a short form stating that the consent (i.e. the “long” form) was explained in its entirety to their satisfaction.

When the subject uses an authorized representative (i.e. in the assent of children or the consent of subjects who are unable to provide informed consent), it is highly recommended that the Investigator employ an unbiased third party as a witness.

Informed Consent Document Content

FDA provides explanations of the meanings behind the 8 basic elements of informed consent (21 CFR 50.25(a)) and the 6 additional elements of informed consent (21 CFR 50.25(b)). The Agency’s primary intention is to highlight areas pertinent to clinical research subject’s rights, primarily statements designed to transparently explain the trial to the subject. None are particularly new interpretations of the required elements of informed consent, which have not changed, but are worth reading as a refresher to what the agency means by each of the elements.

It is important to pay attention to FDA’s interpretation of costs to the subject. Since the clinical trials industry has evolved to become integrated with subject’s insurance,
sponsors/sites should be careful on how this section is phrased, being careful to not take liberties with or make assumptions about how medical insurance will reimburse subjects for trial costs. Subjects should be advised to review their policy and confirming reimbursement first prior to signing an informed consent.