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## New FDA Informed Consent Guidance for ClinicalTrials.gov Requirement

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In the Federal Register (FR) of January 4, 2011 (76 FR 256), FDA published a final regulation (21 CFR § 50.25(c)) amending the current informed consent regulations to require that informed consent documents and processes for applicable drug (including biological products) and device clinical trials include a specific statement that clinical trial information will be entered in a databank. The databank referred to in this final rule is the clinical trial registry databank maintained by the National Institutes of Health/National Library of Medicine (NIH/NLM).

For applicable clinical trials initiated on or after March 7, 2012, informed consent documents must include a specific statement that refers to the trial's description on [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov). This rule will not be applied retroactively, and it will not be necessary for currently enrolled subjects to be asked to re-consent using a consent form containing this wording.

Under the new regulation at 21 CFR 50.25(c), the following statement must be reproduced word-for-word in informed consent documents for applicable clinical trials:

*"A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."*

### What is an "applicable clinical trial"?

FDA provided a definition of "applicable clinical trial" in 42 U.S.C. § 282(j)(1)(A). "Applicable clinical trials" generally include controlled interventional studies (with one or more arms) of drugs, biological products, or devices that are subject to FDA regulation, meaning that the trial has one or more sites in the United States, involves a drug, biologic, or device that is manufactured in the United States (or its territories), or is conducted under an investigational new drug application (IND) or investigational device exemption (IDE).

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## FDA Informed Consent Guidance (cont)

### *Applicable clinical device trials:*

The trial is an “applicable clinical device trial” if: (I) the trial prospectively compares a device-based intervention subject to FDA regulation against a control in human subjects; or (II) the trial is a pediatric post-market surveillance trial.

A device trial is not an applicable clinical device trial when it is a small feasibility trial or a study of prototype devices with a primary measure of feasibility rather than health outcomes. Further, a device trial is not an applicable device clinical trial when the trial includes only de-identified human specimens (e.g., in vitro testing) and does not include “human subjects” (a requirement to be considered an applicable clinical trial).

### *Applicable clinical drug trials:*

The trial is an “applicable clinical drug trial” if the trial is a controlled clinical investigation, other than a phase I clinical investigation, required to comply with FDA regulations. More specifically, a “clinical investigation” is “any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects.”

Uncontrolled (e.g., observational) clinical investigations of drugs or devices are not considered “applicable clinical trials.”

### Who must decide whether it is an “applicable clinical trial?”

According to the FDA, trial sponsors and investigators have the responsibility of determining whether or not a trial is an “applicable clinical trial.”

If a clinical trial is not subject to the rule, then consent forms need not inform subjects about the ClinicalTrials.gov website.

### Resources:

Review the FDA Guidance document: <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM291085.pdf>.

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## Dos and Don'ts in Drafting Informed Consent forms

Adapted with permission from:

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DO Simplify, simplify, simplify. Some sources include Stanford University's Glossary of Lay Terms

(<http://humansubjects.stanford.edu/general/glossary.html>) and the University of Michigan's IRB

Simplification Guide to Medical Terms

(<http://www.med.umich.edu/irbmed/guidance/guide.htm>). The NCI issued a useful report on

simplification: National Cancer Institute.

Simplification of Informed Consent Documents

(<http://www.cancer.gov/clinicaltrials/education/simplification-of-informed-consent-docs>)

DON'T use jargon.

DO use a serif font, such as Times or New York, and make it at least 12 points (bigger if you are

enrolling elderly or others who might have difficulty seeing)!

DON'T right-justify text... this unevenly spaces out words and is harder on the eyes.

DON'T use redundant language.

DO use sentences that have one subject or topic/focus (you cannot supplant good writing ...).

DON'T use run-on sentences.

DO use paragraphs that narrowly address the topic of the section heading; short paragraphs with very specific subjects are good, especially when introduced with a specific heading.

DON'T ever say "I understand that..." This language can be deleted with no loss of meaning. Any assertions about understanding are problematic, in that subjects cannot be charged with knowing what they do not understand. This also just adds to the all-too-common perception of subjects that consent forms are meant to protect the institution, NOT facilitate informed decisions.

DO increase the use of 'white space'.

DON'T use passive language; replace "study doctor" by "we"; and when discussing what potential subjects can expect in the study, "you."

DO say "take part" or "be" instead of "participate."

DON'T unnecessarily repeat technical matters; try to figure out how to be efficient with the goal of enabling potential subjects to follow along. You don't want their eyes to glaze over.

DO think about how you would verbally tell an 8<sup>th</sup> grade student what it is you are doing. Consent forms are supposed to be written at a 6<sup>th</sup> to 8<sup>th</sup> grade level, and this can be quite challenging to achieve (but it is doable). If you have an 8<sup>th</sup> grader, let them read your form. More importantly, getting the prose to sound normal, as if you were saying it,

may help people follow along and ultimately understand.

DON'T isolate the risks by treatment arm, as it may yield unnecessary repetition and it risks unblinding subjects if some risks are unique to a blinded intervention.

DO try to put the risks in context, such as by categorizing as expected but minor, less frequent but severe, rare but serious, including possible death. Of course, if there's one that's likely and serious, that might be first in the list.

DON'T obfuscate important information by burying it in . . . noise.

DON'T use limited-disclosure "Screening Consents." These risk seriously undermining a voluntary informed consent

- \* Subjects may commit to a course of action; they "buy in" to a study, without knowing what's involved

- \* They may treat screening activities as a 'sunk cost' that binds them to continuing ("throwing good money after bad")

- \* They may feel an obligation of reciprocity to the investigators who dedicated time and effort to the screening



## Consent form Readability Resources

Wendy Charles

Those who write consent forms face a persistent challenge with communicating complex terms and concepts in a manner that subjects can understand.

My favorite is an excellent program for assisting readability called Program for Readability in Science and Medicine (PRISM). The website includes a tool kit and online training: [http://www.grouphealthresearch.org/capabilities/readability/readability\\_home.html](http://www.grouphealthresearch.org/capabilities/readability/readability_home.html). The toolkit features sample consent form sections and shows the grade level for each sample.

Seattle Children's Hospital features a language resource text that provides sample language for multiple types of procedures written at an 8<sup>th</sup> grade reading level. Another is a glossary that includes substitutions for medical terms. Go to

<http://www.seattlechildrens.org/research/forms-policies/irb/assent-consent-forms/> for these resources.

For assessing readability, consider using a website that calculates reading level using a few indices of grade level: <http://www.ist.rit.edu/~jxs/services/TestReadability.html>. Copy and paste sections of the consent form in the website to calculate reading level for that text. (The entered text is not saved or stored on the website.)

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