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Readable Informed Consent Forms Are Not Optional

By Norman M. Goldfarb

Informed consent requires that potential clinical trial subjects be fully-informed and capable of making a rational decision about participation in a clinical study. There is substantial evidence that the current informed consent process does not lead to fully- or even well-informed subjects. For example, a survey of 1,900 subjects at 16 U.S. research institutions revealed that 53% were not even aware they were part of a clinical study.[1]

Informed consent is a process that begins when a potential subject learns of a study and ends some time after the study concludes. The central elements of this process include:

- The informed consent form
- The investigator's explanation of the study
- The discussion between the investigator and the potential subject

A good informed consent form serves multiple purposes in the informed consent process, including:

- In theory, potential subjects read it carefully prior to giving consent.
- It is an important reference document for subjects, since they probably do not remember all the information delivered prior to giving informed consent.
- It reduces subject anxiety, because they know they do not have to remember everything.
- It improves subject adherence and retention because subjects are less likely to get confused or feel misled.
- It is the principle source of information for investigators in determining WHAT information to communicate to potential subjects and HOW to communicate that information. It discourages investigators from delivering information that contradicts the informed consent form.

The Current Trend

The clinical research industry is aware that the informed consent process, as practiced by thousands of investigators with millions of potential subjects, is far from perfect. In 2004, FDA inspections found informed consent deficiencies (codes 02 and 03) at 24% of sites, and the FDA inspected only the documents, not the actual experiences.[2] (The inspected sites may not have been representative of the entire site population, but they probably were not isolated cases, either.) Enrollment and cost pressures, lack of training, and the practicalities of conducting clinical research in a real-world setting contribute to the difficulties. Unfortunately, the informed consent process is probably not perfectible for any but the simplest clinical studies.

Prompted in part by the threat of litigation, informed consent forms grow longer and longer, and include more and more legally-motivated text. An industry consensus is growing that many informed consent forms are now too long, too complex, and include too much arcane vocabulary for potential subjects to digest. Ten-page informed consent forms are now common, with the longest, most difficult documents often reserved for potential subjects with the most serious illnesses and therefore the least ability to understand them. The trend

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may have reached its logical conclusion: informed consent forms that include every detail, but that are so long and complex that they defeat their own purpose.

High school graduates typically read simple texts at 200 to 225 words per minute.[3] Marginal readers read the same material at 160 words per minute.[4] The average ten-page informed consent form has 2,500 words. Because of its complexity, reading speeds may be halved. It therefore takes high school graduates about 23 minutes to read the document, and marginal readers about 31 minutes. Research indicates that people are unlikely to completely read standard educational documents over four pages long (5 minutes), so it is unrealistic to expect potential subjects to read ten-page, highly-complex documents word for word.[5]

Expanding informed consent forms are forcing the informed consent process to go full circle, back to the days before written informed consent forms, when potential subjects relied primarily on verbal explanations by the investigator. The burden is thus growing on the investigator to provide the information that potential subjects actually want, in a simplified, understandable format. As mentioned before, the informed consent form is a vital resource for the investigator as well.

The Threat of Litigation

All of the 35 clinical research litigations that a leading clinical research defense firm has seen since 1980 include a claim of inadequate informed consent, generally the absence of information that appears important in hindsight.[6] However, adding every conceivable piece of information to the informed consent form creates a document of such size and unreadability that the plaintiff's attorney can then ask the court, "Do you really expect anyone to read and understand all of this material?" The counter-argument may not convince a jury, but it is very straightforward: "Yes, we do; my client included all of the material because we believe in the principle of informed consent." The question of length is thus a question of balance. How much information is enough and how much is too much? The answer to this question requires a rigorous cost/benefit analysis that is yet to be performed.

> "There's a real disconnect between what the subjects understand to be going on and what the consent form says." – Alan Milstein of Sherman, Silverstein, Kohl, Rose & Podolsky[7]

The question of readability is another matter, one that is possible to address. First, however, it is necessary to ask whether improving readability is worthwhile. The research literature on the subject suggests that it may not be; there is minimal persuasive evidence that improving readability improves subject comprehension.[8,9]

The lack of evidence is probably due to:

- Defects in other parts of the informed consent process, such as subject assumptions, inadequate time to read the document, and the potential subject's trust in the physician-investigator
- Flaws in research methodologies such as inaccurate measures of readability, lack of correlation between readability measures and comprehension, how and when comprehension was measured, and the reading level of the study population

It would be hard to argue that readability has zero impact on comprehension, or that no effort is worthwhile. It would also be hard to argue that a readable informed consent form does not better serve the purposes stated at the beginning of this paper. As informed consent forms grow in length, readability becomes ever more important. With readable informed consent forms as the foundation, we can then address the other obstacles in the process.

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From the perspective of potential legal liability, readability is clearly important: An unreadable informed consent form, by definition, does not contribute to informed consent. If the plaintiff's attorney proves that his/her client has an eighth-grade reading level and proves that the informed consent form is written at a twelfth-grade reading level, that document contributes little or nothing to informed consent. Neither of these proofs is difficult to make. Furthermore, the plaintiff's attorney can easily argue that the investigator was negligent and simply did not care about the welfare of the plaintiff. If the investigator had cared, he/she would have done more to make the informed consent form readable.

How readable are today's informed consent forms? An analysis of 107 informed consent forms at the Emory University Winship Cancer Center showed a mean reading level of grade 11.9 +/- 1.53. None of the documents were at or below the eighth-grade reading level; 1.8% were at or below the ninth-grade level; and 10.5% were below the 10th-grade level.[10]

The average American has 12.5 years of education, but many people read three to five grade levels below their self-reported educational attainment.[11,12] People who participate in clinical trials may not be as educated as is commonly believed; 28% do not have a high school diploma, compared to the 16% of the general population.[13,14] Target populations for specific clinical trials may have particularly poor reading skills. For example, one study measured the reading level of a Medicaid population at about sixth grade.[11]

It is no surprise that a recent Harris Survey showed that only 61% of clinical trial participants strongly agreed with the statement that their informed consent form was easy to read and understand.[15] As a result:

- Only 83% strongly agreed with the statement that their participation was voluntary.
- Only 65% strongly agreed with the statement that they were made aware of the risks.
- Only 63% strongly agreed with the statement that they could choose other treatment options, including no treatment at all.
- 48% agreed or strongly agreed with the statement that they participated to get the best possible treatment.

Readability of the informed consent form was a relatively small issue in the Diaz case, settled for $3.8 million with only dignitary damages, i.e., no physical injury.[16] It may have played a more significant role in cases that have been settled out of court. It is only a matter of time before readability of the informed consent form becomes a determining issue in a case for physical injury. If the court determines that the informed consent form was not readable by the subject, that the investigator made little or no effort to make it more readable, and that the investigator made little or no effort to determine whether the subject was even capable of reading the document, the plaintiff's signature on the informed consent form becomes largely meaningless. The defense is then left with the assertion that the investigator verbally explained the study to the subject. This defense is inherently weak for several reasons:

- Unless the informed consent meeting was electronically recorded, it is probably the word of a sympathetic subject against the word of an unsympathetic defendant.*
- The investigator's verbal explanation probably covered only the high points. If the case hinges on the communication of one specific point, e.g., an unlikely side effect, whose memory will get the benefit of the doubt?
- The person who explained the study to the subject was probably a nurse or study coordinator, who may not be available or interested in testifying for the defense.

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- An unreadable informed consent form opens the door for the investigator to say anything he/she wants, opening the door wider to claims of coercion and undue influence.

* Videotaping or audiotaping the informed consent meeting would answer this question, but it is also likely to reveal omissions and errors. It will make many subjects uncomfortable.

The investigator's and his/her institution's defense is clearly weakened by defective informed consent. The Institutional Review Board (IRB) is legally obligated to ensure that the elements of informed consent are "provided to each subject." [17] Providing them in unreadable form does not meet this requirement. Readability is certainly a minimum standard that a court could impose on an IRB, especially when the IRB does not follow its own rules.[18] An argument by the IRB that it ignored its regulatory duty because of inadequate resources is unlikely to persuade a jury assessing liability in a personal injury case.

The sponsor is not a party to the informed consent, but is exposed to financial liability through indemnification. It also has indirect responsibility for adequate informed consent,[19] and juries are free to assess damages as they see fit. The learned intermediate doctrine protects the sponsor if it provides adequate information to the investigator. It has been an effective defense so far, [6] but is vulnerable when the sponsor writes or approves the informed consent form. Since exculpatory ("don't blame me") language is prohibited from informed consent forms,[20] a document that appears to be written by the sponsor's attorneys to avoid liability rather than to inform the subject may be problematic. State law may also bear on the question of sponsor negligence.[21] In Kansas, Rhode Island, and South Carolina, the age of consent is sixteen. Many sixteen-year olds have only reached tenth grade, and are especially sympathetic plaintiffs.

The Floodgates Open

Once such a case sets the precedent, the litigation floodgates will open. The industry will then recognize the risk and attempt to convert tens-of-thousands of informed consent forms overnight. Investigators may have to obtain fresh informed consent from millions of subjects. To make the crisis even worse, the industry currently does not have the methodology or expertise ready to deal with such a crisis.

The most popular measure of readability is the Flesch-Kincaid Grade Level Formula. The U.S. government uses the Flesch-Kincaid formula as its standard. A version is incorporated in Microsoft Word. Dr. Rudolf Flesch developed the first version in the 1940's. J. P. Kincaid modified the test based on work with Navy inductees' understanding of their training manuals. The formula calculates reading grade level = (.39 x ASL) + (11.8 x ASW) – 15.59. (ASL = average number of words per sentence and ASW = average number of syllables per word).[21] Sentence complexity contributes to the calculation only indirectly through sentence length. Short obscure words such as "stent" do not factor in at all. People who have not read a million words in their entire lives are unlikely to be familiar with very rare words (<1/million words in general usage) such as "detrimental", "hygiene" and "jeopardize".[9]

Assuming an informed consent form is to be rewritten for readability, who is going to do the rewriting? Doctors? Scientists? Technical medical writers? Have you seen their writing?

FDA regulations and ICH guidelines both require that "the information that is given to the subject or the representative shall be in language understandable to the subject or the representative." [22,23] This requirement is for every subject, not just the average subject. The regulations and guidelines require that ALL of the information must be understandable. The investigator may explain part of the informed consent form language to make it understandable, but it is hard to imagine them consistently explaining entire page-long lists

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of potential side effects. The regulations and guidelines do not, however, require that subjects actually understand the information. This distinction is fortunate for the industry because the literature suggests that comprehension less than 70% is common.[8] What percentage of comprehension would the reader consider adequate for his/her child? The absence of a clear regulatory rule leaves it to the courts to decide what percentage is required for informed consent. Should the issue come to public attention, and given the heavy seas currently sailed by the FDA, the Agency is unlikely to steadfastly defend its benevolent neglect of the regulatory requirements.

The consensus in the industry is that informed consent forms should be written at the eighth- or ninth-grade reading level. This consensus, however, is mostly honored in the breach. For example, university recommendations for informed consent reading levels range from fifth to tenth grade, with their own templates averaging three grades higher.[10] In other words, the regulations are largely ignored. How many investigative sites could pass a by-the-book FDA inspection for eighth- or ninth-grade informed consent reading levels?

The average adult in the United States reads at about the eighth-grade level[5], so half the population reads at a lower level. If we write at an eighth-grade level, do we screen-out potential subjects who read at the fourth-grade level? And, by the way, are we going to test subject literacy?

What To Do

Fortunately, the industry can take positive steps now to meet regulatory requirements, minimize the risk of litigation, and fulfill its ethical obligations:

- Ensure that all informed consent forms are written at a reading level no higher than eighth grade, according to the Flesch-Kincaid formula. This good-faith effort will have some protective benefit in litigation.
- Require training and certification of investigators, at least in the informed consent process.
- Develop the tools, methodology and expertise to create and validate readable informed consent forms.
- Develop, validate and use standardized subject comprehension quizzes. As a side benefit, anticipation of the quiz will improve attentiveness.
- For subjects with reading levels below that required by the informed consent form, obtain consent as if they are illiterate. Note, however, that potential subjects are unlikely to comprehend 100% of an informed consent form that is read to them verbatim.
- Develop templates for, and examples of, readable and validated informed consent forms.
- Develop the tools, methodology and expertise to write readable informed consent forms, which also involves word-choice, grammar, formatting and organization.
- Validate the usefulness of multimedia tools in the informed consent process.
- Communicate the legal risks to investigators, sites and sponsors of a defective informed consent process.
- Incorporate research about informed consent into a significant percentage of clinical studies. This research needs to consider readability as just one factor in the subject's decision to participate in a study.
- Ask the FDA for realistic and practical guidance on implementation of the regulations. For example, it does not make sense for readability requirements

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apply to every subject. The FDA should make it clear that readability weaknesses in the informed consent form must be supplemented with verbal explanations.

Readability is far from a complete solution to the problem of informed consent form comprehension. Length, organization, word-choice, level of abstraction, visual presentation, and numerous other factors also play important roles. Although not sufficient for comprehension, readability is, however, necessary, and a good place to start.

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