

## Public Comments on FDA's Proposed Amendment Should Serve as a Reminder to Keep Informed Consent Documents Simple

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### Introduction

In December 2009, the U.S. Food and Drug Administration (FDA) released a proposed rule that would amend the informed consent requirements for drug, biologic, and device clinical investigations.<sup>1</sup> Consistent with President Barack Obama's current policy on open government and transparency,<sup>2</sup> the FDA's proposed amendment would require informed consent documents and procedures to disclose to clinical trial participants that their de-identified clinical trial results will be published in the National Institutes of Health/National Library of Medicine Clinical Trials database.<sup>3</sup> The FDA claims this proposed rule will serve to: (1) increase transparency and greater public awareness of the existence the clinical trials database; (2) provide greater accountability of clinical trial investigators for outcomes and adverse events; (3) increase public confidence in the validity of the research process; and (4) encourage physicians and patients to obtain information from the database to make educated treatment decisions.<sup>4</sup>

After releasing its proposed amendment, the FDA allowed opportunity for public response and received numerous comments<sup>5</sup> before the expiration of the March 1, 2010 submission deadline.<sup>6</sup> Even though the submission deadline expired almost nine months ago, the FDA still has not issued a final rule on this proposed amendment.<sup>7</sup>

Several of the public comments focused on issues beyond the substantive nature of the proposed amendment. These comments highlight the recent research industry-wide plea to simplify informed consent documents. Some commentators complained the proposed amendment contains highly technical and confusing language written at an 18.4 grade level, which is equivalent to the reading level of a college graduate with 2.4 years of post-graduate education.<sup>8</sup> Because studies have shown that nearly half of the adult population in the U.S. cannot read higher than an eighth grade level,<sup>9</sup> it should come as no surprise

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<sup>1</sup> 74 Fed. Reg. 68750–68756 (Dec. 29, 2009). The current FDA requirements for informed consent documents are outlined in 21 C.F.R § 50.25(a).

<sup>2</sup> The White House, Office of the Press, *Memorandum for the Heads of Executive Departments and Agencies: Transparency and Open Government*, Jan. 21, 2009, [http://www.whitehouse.gov/the\\_press\\_office/TransparencyandOpenGovernment/](http://www.whitehouse.gov/the_press_office/TransparencyandOpenGovernment/).

<sup>3</sup> 74 Fed. Reg. 68750, *supra* note 1, at 68750.

<sup>4</sup> *Id.* at 68754.

<sup>5</sup> Ninety-two public responses and comments were submitted. These are available for review through <http://www.regulations.gov/search/Regs/home.html#home>.

<sup>6</sup> 74 Fed. Reg. 68750, *supra* note 1, at 68754.

<sup>7</sup> *See id.*

<sup>8</sup> *Id.*

<sup>9</sup> Nat'l Ctr. for Education Statistics, *National Assessment of Adult Literacy: Key Findings*, 2003, [http://nces.ed.gov/naal/kf\\_demographics.asp#2](http://nces.ed.gov/naal/kf_demographics.asp#2).

that many research participants may not understand the information disclosed to them.<sup>10</sup> The fact that participants may not understand the language in consent documents is contrary to the spirit behind the FDA's general regulations governing informed consent<sup>11</sup> and the U.S. Department of Health and Human Services' (HHS) federal policy for the protection of human research subjects, otherwise known as the Common Rule.<sup>12</sup> Both the FDA regulations and the Common Rule expressly state:

The information that is given to the subject or representative shall be in a language understandable to the subject or representative.<sup>13</sup>

Thus, both of these federal requirements make it clear that consent documents must be easy to understand. The public comments to the FDA's proposed amendment should serve as a reminder to the clinical research industry of the need to ensure their informed consent documents are plain and simple and reader friendly. And, for all intents and purposes, clinical health care providers should heed this reminder, as well. Otherwise, there may be some doubt whether researchers and practitioners actually obtain adequate informed consent.

### What is Informed Consent?

In the clinical health care setting, informed consent is the process by which a fully informed patient can make choices about his or her health care.<sup>14</sup> The concept of informed consent is rooted in medical ethics and stems from a patient's legal and ethical rights to direct what happens to his or her body and the physician's ethical duty to involve the patient in his or her health care decisions.<sup>15</sup>

Informed consent in the health care setting involves more than simply obtaining a patient's signature on a written consent document.<sup>16</sup> It is a process of communication and information exchange between the patient and physician that results in the patient's agreement and authorization to undergo a specific medical treatment or procedure.<sup>17</sup>

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<sup>10</sup> Laura M. Beskow, *Developing a Simplified Consent Form for Biobanking*, PloS One, Oct. 8, 2010, <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0013302>; E. Beardsley, *et al.*, *Longer Consent Forms for Clinical Trials Compromise patient Understanding: So Why are They Lengthening?*, J. CLIN. ONCOL. 25: e13-14, <http://jco.ascopubs.org/content/25/9/e13.full.pdf>.

<sup>11</sup> 21 C.F.R § 50.20.

<sup>12</sup> The Common Rule is found in 45 C.F.R. Pt. 46, Subpart A; *see* U.S. Dep't of Health and Human Servs., *Office for Human Research Protections (OHRP): Federal Policy for the Protection of Human Subjects*, <http://www.hhs.gov/ohrp/policy/common.html>. The HHS regulations incorporate the Common Rule as Subpart A of 45 C.F.R. 46. Statutory authority for the HHS Human Subject Protection regulations derives from 5 U.S.C. § 301; 42 U.S.C. § 300v-1(b); and 42 U.S.C. § 289.

<sup>13</sup> 21 C.F.R § 50.20; 45 C.F.R. § 46.116.

<sup>14</sup> Kelly A. Edwards, *Informed Consent: Ethics in Medicine*, Univ. of Washington School of Med., available at <http://www.depts.washington.edu/bioethx/topics/consent.html>.

<sup>15</sup> *Id.*

<sup>16</sup> Am. Med. Ass'n, *Informed Consent*, available through <http://www.ama-assn.org>.

<sup>17</sup> *Id.*

In the clinical research industry, there are specific regulations that govern informed consent requirements, namely the FDA regulations<sup>18</sup> and the Common Rule.<sup>19</sup> As with informed consent criteria in the healthcare industry, these informed consent regulations are based on ethical principles, but are relevant to the protection of human research subjects.<sup>20</sup> The ethical principles form the bases of certain relevant codes of ethics, including The Belmont Report,<sup>21</sup> the Nuremberg Code,<sup>22</sup> the National Research Act,<sup>23</sup> and the Declaration of Helsinki.<sup>24</sup> These codes of ethics identify specific standards: (1) for educating participants so they can make autonomous decisions, (2) for protecting participants from unethical practices, (3) for allowing subjects to voluntarily participate in and withdraw from clinical trials, (4) for requiring disclosure of the risks and benefits of participating in clinical research, and (5) for protecting participants from harm.<sup>25</sup>

The FDA has issued guidance to the research industry, advising that informed consent should be more than just a signature on a form; it should be a process of information exchange.<sup>26</sup> Rather than serving as an endpoint, the consent document itself should be the basis for a meaningful communication exchange between the investigator and research subject, allowing for verbal instructions, question and answer sessions, and some method to measure participant understanding.<sup>27</sup> While a research participant is required to sign and date consent forms,<sup>28</sup> if the consent forms contain highly technical language and are not easily understandable, then it becomes questionable as to whether the participant truly understands the risks and benefits and the scope of the clinical trial in which he or she has supposedly agreed to participate.

### What Does it Take to Simplify an Informed Consent Document?

Over the past decade, there have been continuing calls for consent forms to be simplified in the research industry.<sup>29</sup> Despite this push, however, studies show that consent documents have generally increased in length over time.<sup>30</sup> Although nearly half of the

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<sup>18</sup> 21 C.F.R. § 50.20.

<sup>19</sup> 45 C.F.R. § 46.116.

<sup>20</sup> 74 Fed. Reg. 68750, *supra* note 1, at 68750.

<sup>21</sup> Nat'l Comm'n for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, Apr. 18, 1979, available at <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>.

<sup>22</sup> *Trials of War Criminals before the Nuremberg Military Tribunals Under Control Council Law No. 10*, U.S. Government Printing Office, 1949, Vol. 2, p. 181-182.

<sup>23</sup> Nat'l Research Act, Title II, Pub. L. No. 93-348, July 12, 1974.

<sup>24</sup> World Medical Ass'n, *Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects*, available at <http://wma.net/e/policy/b3.htm>.

<sup>25</sup> 74 Fed. Reg. 68750, *supra* note 1, at 68750-51.

<sup>26</sup> U.S. Food and Drug Adm'n, *A Guide to Informed Consent—Information Sheet*, <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm> (last accessed on Nov. 17, 2010).

<sup>27</sup> *Id.*

<sup>28</sup> *Id.*

<sup>29</sup> Beskow, *supra* note 10 and accompanying Reference Nos. 6-8; Nat'l Cancer Inst., *Simplification of Informed Consent Documents*, 1998, <http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs>; Ass'n of American Med. Colleges, *Informed Consent Documents Group: Keep it Simple*, Oct. 2007, [https://www.aamc.org/newsroom/reporter/oct07/89326/oct07\\_informedconsent.html](https://www.aamc.org/newsroom/reporter/oct07/89326/oct07_informedconsent.html).

<sup>30</sup> Beskow, *supra* note 10 and accompanying Reference Nos. 9-13.

adults in the U.S. have achieved only an eighth grade reading level, studies show that only a few consent documents are actually written at less than a tenth grade level.<sup>31</sup> The results of these studies give all the more reason to press for simplified consent documents.

The language in any consent document should be simple, easily readable, and written in language at or below the eighth grade level.<sup>32</sup> This can be accomplished by following a few basic principles for plain language writing, such as choosing common, every day words, writing in first person and in active voice, keeping sentences short with one idea per paragraph, using clear organization and format with descriptive headings and ensuring adequate spacing and margins.<sup>33</sup>

Krell Clinical Communications, L.L.C. (Krell), one of the public entities that complained of the highly technical and confusing language in the FDA's proposed amendment, suggested an alternative to the proposed amendment that encompasses the basic principles of plain language writing.<sup>34</sup> For purposes of comparison, the FDA's proposed amendment notifying research participants that clinical trial information will be submitted to the clinical trial registry databank states, in part:

Information, that does not include personally identifiable information, concerning this clinical trial has been or will be submitted, at the appropriate and required time, to the government-operated clinical trial registry data bank, which contains registration, results, and other information about registered clinical trials. This data bank can be accessed by you and the general public at [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov). Federal law requires clinical trial information for certain clinical trials to be submitted to the data bank.<sup>35</sup>

Whereas, Krell's suggested alternative states:

This study is or will be listed in an online registry. U.S. law requires this. A registry is a place where information is collected. You can see this registry at the website [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov). The U.S. government runs this website. You and anyone else can visit this website at anytime. You can get information about this study and other studies on the website. Your personal information will NOT be shown on the website.<sup>36</sup>

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<sup>31</sup> Beskow, *supra* note 10 and accompanying Reference Nos. 9-12, 15-18.

<sup>32</sup> See generally Ass'n of American Med. Colleges, *Universal Use of Short and Readable Informed Consent Documents: How Do We Get There?*, Aug. 2007, available at <http://www.aamc.org>.

<sup>33</sup> Beskow, *supra* note 10; see also J.R. Ridpath, *et al.*, *PRISM Readability Toolkit*, Seattle Group Health Research Institute, 2007, available at [http://www.grouphealthresearch.org/capabilities/readability/readability\\_home.html](http://www.grouphealthresearch.org/capabilities/readability/readability_home.html).

<sup>34</sup> Robert Krell, *Alternative to FDA's Proposed language for Informed Consent Documents*, Krell Clinical Communications, available through [www.krellclinical.com](http://www.krellclinical.com).

<sup>35</sup> 74 Fed. Reg. 68750, *supra* note 1, at 68756

<sup>36</sup> Krell, *supra* note 34.

After comparing the FDA's proposed amendment with Krell's alternative suggestion, Krell's proposed language is clear, simple, unambiguous, and reader friendly while encompassing all relevant points. Krell's proposed alternative language epitomizes the difference that plain and simple language can make.

### Conclusion

The public comments submitted in response to the FDA's proposed amendment to the informed consent rule have highlighted the need to simplify informed consent documents and make them clear, simple, unambiguous and reader friendly. This can be achieved by following the basic principles of plain language writing as exemplified in the Krell sample quoted above. Not only the clinical researchers, but practitioners in the health care industry, should heed these basic principles to ensure their research participants and patients, respectively, are giving adequate informed consent.

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