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Assessing readability and comprehension of informed consent materials for medical device research: A survey of informed consents from FDA's Center for Devices and Radiological Health☆

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ABSTRACT

Legally effective informed consent has been a long-standing requirement for FDA-regulated clinical studies. However, informed consent forms (ICFs) are often thought to be too long, too complex, and too difficult for participants to understand. In this article, investigators from the FDAs Center for Devices and Radiological Health (CDRH) surveyed 399 ICFs from approved investigational device exemption (IDE) applications for fiscal years 2015 and 2016 to evaluate the readability of ICFs.

The investigators collected data from the ICFs, using variables related to structure, readability, and comprehension.

The investigators found that the mean grade-reading levels of the ICFs ranged from 10th grade to college level (Table 2), higher than the recommended 6th to 8th grade level, when measured by major readability evaluation tools (the SMOG readability grade level formula, the Flesch-Kincaid Index Grade Level Readability Formula, the Flesch Reading Ease test, and the Dale-Chall readability formula).

Overall, the ICFs and informed consent (IC) processes, as described in the IDE application, lacked components that enhanced participants' comprehension, such as short sentences (e.g., no more than 8 to 10 to words) and the use of pictures, tables, and diagrams.

CDRH investigators believe that information about ICFs' readability, comprehension, and structure will help support current and future efforts to improve the IC process. The intent of the article is to demonstrate that improvements are needed in the IC process and to encourage clinical trial stakeholders to consider implementing those approaches that optimize patient comprehension in the development of their IC processes.

1. Introduction

Legally effective informed consent has been a long-standing requirement for FDA-regulated clinical studies 21 CFR § 50.20. However, informed consent forms (ICFs) are often thought to be too long, too complex, and too difficult for participants to understand because they are not written in a way that enhances a study participant's comprehension or addresses the participant's informational needs enabling

Abbreviation: AGRID, Anesthesiology, General Hospital, Respiratory, Infection Control, and Dental Devices; ANOVA, The Analysis of Variance Test; AWL, Coxhead Academic Word List; CDRH or Center, Center for Devices and Radiological Health; CT, Chemistry and Toxicology; CV, Cardiovascular Devices; FDA or Agency, Food and Drug Administration; IC, Informed Consent; ICF, Informed Consent Form; ICP, The Informed Consent Process; IDE, Investigational Device Exemptions; IH, Immunology and Hematology Devices; MD, Microbiology Devices; MGPD, Molecular Genetics and Pathology Devices; NPM, Neurological and Physical Medicine Devices; OENT, Ophthalmic and Ear, Nose and Throat Devices; ORP, Orthopedic Devices; RGU, Reproductive, Gastro-Renal, and Urological Devices; RH, Radiological Health Devices; SMOG, A Simple Measure of Gobbledygook, a readability formula developed by G. Harry McLaughlin; SU, Surgical Devices

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them to make an informed decision about study participation [2]. To further examine this issue, we surveyed all ICFs from investigational device exemptions[2] (IDE) applications over a two-year period. This survey evaluated the ICFs' basic structure and characteristics, such as the total number of pages, words, and words per sentence. Additionally, data were collected on the ICFs to assess readability, comprehension, and other characteristics that may affect patient understanding [1]. In order to assess whether readability and comprehension among ICFs might vary according to the novelty or complexity of the study and device, data on the ICFs' readability was further analyzed based on the type of study for which the ICF was written. In addition, data was analyzed by medical device type[3] to gain insight, as to whether there may be differences in any particular sector of the industry. The null hypotheses for both study type and medical device type are that no difference exists among the ICFs in these categories. We believe that the results of this type of analysis can help target future approaches to improving ICF readability.

2. Background

2.1. FDA requirements for the informed consent (IC) process

In accordance with 21 CFR parts 50 and 56, clinical investigations of FDA-regulated medical products are required to follow FDA regulations governing the protection of human subjects. In particular, 21 CFR part 50 requires that the language be understandable to the participant or their legally authorized representative, as well as outlines the elements to be provided to each participant in seeking informed consent. Such elements include the following: Descriptions of the study; any foreseeable risks or discomforts to the participant; and the benefits of participating in the study. Alternative treatment options available to the participant should also be presented, as well as statements describing the voluntary nature of the participant's participation, and, among other items, the extent, if any, to which confidentiality of the participant's records will be maintained.

While FDA's regulatory requirements for informed consent are prescriptive to protect the public health, they do not; however, preclude the use of alternative formats or modalities during the IC process. That is, FDA regulations do not require that the IC process only include a standard written document to read and sign. FDA considers alternative approaches to enhance patient comprehension of the ICF and IC process. For example, FDA welcomes the use of electronic systems and processes that may employ multiple types of electronic media to obtain informed consent. FDA issued guidance in December 2016 entitled, "Use of Electronic Informed Consent – Questions and Answers; Guidance for Institutional Review Boards, Investigators, and Sponsors"[4] to provide further information on the use of electronic systems.

One of the required elements of an IDE application is an informed consent document; as such, FDA reviews all informed consent documents of an IDE application to ensure that regulatory requirements are met. Assessment of presence or absence of required elements is straight-forward. However, ascertaining whether an ICF is written in a manner that would enhance a potential participant's understanding is less so. The analysis presented in this article aims to explore this issue by systematically assessing readability and comprehension of ICF's from FDA IDEs.

2.2. Informed consents can be lengthy, complex, and difficult to understand

Current thinking in the human subject research community strongly suggests that past and current processes of obtaining informed consent are not working. ICFs are difficult to understand [3] because they are not "easy-to-read." [4] One unfortunate result of complex and lengthy ICFs is that research participants have variable and often limited understanding of the information being presented to them. Joffre et al. (2001) noted that among a cohort of patients, who participated in cancer trials, 70% did not understand that the experimental treatment was unproven and 74% did not recognize that the treatment was not standard [5]. When looking at parents' comprehension of ICFs for their children's participation in a leukemia clinical trial, Chappuy et al. (2009) found that although 81% of parents felt that the information provided with the request for consent was appropriate, half could not explain the aim of the clinical trial nor its potential benefits to their child – only one-third of the parents were aware that alternative treatments existed [6]. With regards to the amount of information included in the informed consent, studies show that patients value transparency in the IC process; although, they prefer less information than is typically provided in a standard written ICF [2,7,8].

2.3. Current trends in informed consent readability and comprehension

In March 2015, the Clinical Trials Transformation Initiative sponsored an expert meeting on informed consent[5] [9]. Experts agreed that any efforts to restructure the informed consent process should focus on several key themes including, developing shorter and simpler ICFs and an evaluation of the ICFs using plain language and reading level assessments[6].

Revisions to the Federal Policy for the Protection of Human Subjects[7] include new provisions to provide prospective participants with key information they might want to know when making informed decisions about whether to participate in clinical studies and to enhance their understanding of that information[8].

Past research[9] has already identified certain approaches to obtaining informed consent, which participants appear to favor and associate with improved readability and comprehension. These include using oral recitation or video, as well as incorporating visual aids in the informed consent form, such as charts, larger font, diagrams, and more white space. We sought to learn about these approaches and aspects to determine whether any were incorporated into CDRH's IDE program informed consents.

One approach was the use of verbal/oral script as an alternative approach to a written ICF [10]. The value of the oral component of the

[2] An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data. An approved IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device without complying with other requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) that would apply to devices in commercial distribution. See http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowToMarketYourDevice/InvestigationalDeviceExemptionIDE/

[3] The device types are based on the former CDRH Divisions within which the device was previously reviewed. CDRH's organizational structure has changed since this data was collected.

[4] See Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers – Guidance for Institutional Review Boards, Investigators, and Sponsors available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-informed-consent-clinical-investigations-questions-and-answers.

[5] See Clinical Trials Transformation Initiative (CTTI) available at: https://www.ctti-clinicaltrials.org/files/ic-meetingsummary_2015-03-10_final.pdf.

[6] Id.

[7] Federal Policy for the Protection of Human Subjects, 82 FR 7149, available at: https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf.

[8] The revised Common Rule became effective on January 21, 2019. See 83 FR 28497, available at: https://www.gpo.gov/fdsys/pkg/FR-2018-06-19/pdf/2018-13187.pdf. FDA intends to undertake notice and comment rulemaking to harmonize, to the extent applicable, FDA regulations with the revised Common Rule, per Section 3023 of the 21st Century Cures Act (Pub. L. 114-255).

[9] Id.

IC process in higher risk trials was observed in a Danish cardiac stent study [11], where participants were enrolled while experiencing cardiac events. In accordance with Danish informed consent requirements, participants were informed about the study both orally and in writing. When surveyed after the study on the IC process, a majority of participants, including those who consented, but were unable to complete the study, felt satisfied with the IC process, even if the physicians had a very short time to obtain consent. Furthermore, only 28% of trial participants and 7% of non-participants read the one-page information sheet before making a final decision. For this reason, the authors concluded that physicians and research ethics committees should focus on improving the oral component of the informed consent process.

In addition to oral informed consent, current trends also demonstrate that the use of electronic or video-based approaches during the IC process can enhance comprehension. For example, when participants used an iPad as part of the IC process, comprehension, enjoyment, and overall satisfaction, were slightly higher compared to paper-based informed consent [12–14]. Sonne et al. (2013) conducted a pilot study testing the use of video clips for simulated research studies, where all participants read both a paper version and the video iPad version of the same mock consent and were randomized according to which format they reviewed first. Almost all participants reported that the videos improved their comprehension and 79% preferred the video format compared with 13%, who preferred the paper format [15].

A systematic review of 42 trials on interventions to improve research participants' understanding in informed consent [16] found that of the 12 trials evaluating multimedia interventions, 5 showed significant improvements in comprehension. In addition, 6 of the 15 trials evaluating enhanced consent forms (e.g., extended discussion time, additional written information, and use of simple teaching aids) showed statistically significant improvement in understanding. However, the authors of this article found that these 6 trials were of limited quality based on the author's quality criteria which included: Whether a trial was randomized; whether the trial evaluated real or simulated IC processes; the number of participants in the trial; and whether the trial was published in a peer reviewed journal. Furthermore, 3 of the 5 trials that evaluated extended (oral) discussion showed statistically significant improvement in understanding. All the test/feedback trials showed statistically significant improvements in comprehension, but may have mistaken rote memorization for improved understanding. Overall, satisfaction and willingness to enroll were never significantly diminished by an intervention. The authors concluded that having a study team member or a neutral educator spend more time talking one-on-one to study participants appeared to be the most effective available way of improving research participants' understanding; however, further research is needed to confirm this [16].

3. Materials and methods

3.1. Search strategy and selection criteria

Informed consents for approved IDEs submitted to CDRH for fiscal years 2015 and 2016, which ran from October 1, 2014 to September 30, 2016, were included in our survey. IDEs that were either approved or approved with conditions were included in the cohort. Informed consents from IDEs that were withdrawn or not approved, and screening informed consents were excluded. For uniformity and consistency in the results, the most current version of the informed consent was evaluated.

3.2. Data abstraction

The IDE file number was entered into CDRH's internal tracking system; the appropriate IDE file was accessed through FDA's Image 2000 software[10]; the identity and status (approved or approved with conditions) was confirmed; and the type of IDE study (Pivotal/Early Feasibility/Traditional Feasibility) was recorded[11]. IDEs that did not fall into one of these three main categories were grouped together under the category – other study types. Furthermore, the latest amendment of the informed consent was identified. The informed consent was extracted as a portable document format (PDF) file and saved as a Microsoft (MS) Word file. The Word file was then reviewed to make sure there were no errors in the lettering and characters when the file was converted from PDF to Word.

We began by analyzing the content, structure and language used in the ICFs. Data on the following variables were collected: the number of pages per ICF; the average number of words per sentence; the total number of words; the total number of tables and the total number of figures. A more detailed review was completed on each section of the ICF to evaluate the number of words per section. The sections included the introduction to the study, the study procedure, the benefit of participating in the study, the possible risk the participants may encounter, the alternative treatment options the participant may have, the voluntary nature of participation, and the confidentiality of participants' information (including sections titled – "How will my personal data be used?").

The availability of electronic informed consent was also documented as either "yes" or "no." FDA defines electronic informed consent as "… [the use of] electronic systems and processes that may employ multiple electronic media (e.g., text, graphics, audio, video, podcasts, and interactive websites, biological recognition devices, and card readers) to convey information related to the study and to obtain and document informed consent."[12] The protocol and informed consent were also reviewed to determine whether any addenda and/or appendices were included.

3.3. Readability predictions and evaluation

In evaluating the readability of the ICFs, we used the SMOG readability grade level formula, the Flesch-Kincaid Index Grade Level Readability Formula, the Flesch Reading Ease test and the Dale-Chall readability formula. For the Flesch-Kincaid Index Grade Level Readability Formula, we employed both the algorithm embedded in MS Word 2010 using the spelling and grammar check function and an internal assessment tool. Both MS Word 2010 and the internal assessment tool were used because the MS Word 2010 tool seemed to use a formula that depended on paragraphing and bulleted lists. The formula from the internal assessment tool did not depend on paragraphing and accounted for text presented in list form. The tool was also used to run the Dale-Chall and SMOG formulas automatically, not manually as is usually the case.

The Flesch Reading Ease test describes the ease of reading and has been widely used in evaluating medical text. Its formula incorporates sentence length and syllable count and produces a score from 0 to 100, with a higher score corresponding to greater ease of reading. Specifically, scores of 30 and below would correspond to college and college graduate-reading level. The Flesch-Kincaid, SMOG, and Dale-

[10] The Image 2000 Document Management System is the central repository for document-management activities for Premarket - Postmarket data. See CDRH CeSub at https://www.fda.gov/downloads/ForIndustry/FDAeSubmitter/UCM108191.pdf.

[11] See Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies Guidance for Industry and Food and Drug Administration Staff available at: https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm279103

[12] See Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers – Guidance for Institutional Review Boards, Investigators, and Sponsors supra note 7

Chall formulas all assess readability in terms of academic grade level where the higher levels (e.g., 11th and above) correspond to graduate level text.

An additional measure of both language and readability was the number of academic words. The value of measuring academic words is based on the assumption, although unproven, that the more academic words a text has, the less comprehensible it would be to persons who do not have a college education; hence, the readability of lay persons would decrease. The academic word count was based on the Coxhead Academic Word List (AWL)[13].

We collected data on the format and content of the ICFs, which were analyzed for readability using the variables described above. We collected descriptive statistics including mean, standard deviation, median, 25% quantile (Q1), 75% quantile (Q3), maximum (Max), and minimum (Min), which assessed all data, as well as data by study type and medical device type. The medical device type are represented with the following labels: Anesthesiology, General Hospital, Respiratory, Infection Control, and Dental Devices (AGRID); Cardiovascular Devices (CV); Chemistry and Toxicology Devices (CT); Immunology and Hematology Devices (IH); Microbiology Devices (MD); Molecular Genetics and Pathology Devices (MGPD); Neurological and Physical Medicine Devices (NPM); Orthopedic Devices (ORP); Ophthalmic and Ear, Nose, and Throat Devices (OENT); Reproductive, Gastro-Renal, and Urological Devices (RGU); Radiological Health Devices (RH); and Surgical Devices (SU)[14]. All statistical analyses were performed using SAS version 9.4.

4. Results

For fiscal years 2015 and 2016, CDRH received a total of 399 applications for IDEs with one ICF per application. Among the 399 ICFs, the largest proportion were pivotal studies (174/399, 43.6%), followed by traditional feasibility studies (128/399, 32.1%), early feasibility studies (76/399, 19%), and other study types (21/399, 5.3%). The category of "other study types" refers to a minority of IDE's with alternative study designs and were grouped together for the purpose of this analysis. CV devices had the largest number of studies including, the highest number of pivotal studies. NPM devices had the highest number of traditional feasibility and early feasibility studies. (Table 1).

The structure and content of the ICFs differed broadly across many variables. The mean and median values are listed in Table 2. For example, the mean number of pages was 13, but ranged from a minimum of 2 pages to a maximum of 37 pages. Even larger variations could be seen when we analyzed other variables related to ICF structure and content including, the total number of words, (minimum: 790; maximum: 17,115; mean: 4882.9) words per sentence, and the total number of words in distinct sections.

The variables used to determine readability included the MS Word Flesch-Kincaid Index Grade Level Readability Formula and Flesch Reading Ease test, the internal assessment tool Flesch-Kincaid Index Grade Level Readability Formula, the SMOG Grade Level, and the Dale-Chall Grade Level formulas. There was less variability in these results such that across all measures (quantitative measures are shown in Table 2), the mean grade level was at least equivalent to the 10th grade-reading level or higher. We also determined the number of unique

Table 1
Fiscal years 2015 and 2016 investigational device exemption study types and FDA medical device type.

Medical device type	Early feasibility	Traditional feasibility	Pivotal	Other study types	Total (%)
AGRID	2	5	8	0	15 (3.8%)
CV	23	16	51	12	102 (25.6%)
CT	4	21	8	2	35 (8.8%)
IH	0	0	1	0	1 (0.3%)
MD	0	0	0	1	1 (0.3%)
MGPD	1	10	10	2	23 (5.6%)
NPM	21	32	17	0	70 (17.5%)
ORP	2	2	19	1	24 (6.0%)
OENT	4	5	15	2	26 (6.5%)
RGU	11	21	23	1	56 (14%)
RH	1	3	2	0	6 (1.5%)
SU	7	13	20	0	40 (10%)
Total (%)	76 (19%)	128 (32.1%)	174 (43.6%)	21 (5.3%)	399

academic words for each ICF using the internal assessment tool. The number of unique academic words is based on the Coxhead AWL[15] and is a measure of the 570 semantic fields (i.e., sets of words grouped together because they share the same meaning). These fields were selected because they appear with great frequency in a broad range of academic textbooks[15].

A statistical analysis was performed to evaluate whether any differences in readability existed between the medical device type or study type. Table 3 shows the ICFs' readability scores by medical device type using the different readability assessment tools. Table 4 shows the ICFs' readability scores by the study type.

When using the Dale-Chall Readability Formula, which categorizes readability by different ranges of grade levels, about half of ICFs were written at the 13-15th grade level (e.g., graduate level) followed by the more advanced 16th and above grade level. A relatively small proportion were written at the 11-12th grade level. This trend was seen when IDEs were categorized either by study type or device type. See Table 5 and Table 6.

Tables 7 and 8 represent each ICF's structure and format by medical device type and by study type.

4.1. Statistical analysis

We used the Pearson's Chi-Square Test [17] to determine whether there was a statistically significant difference in the Dale-Chall reading grade level between medical device type and found no differences (See Table 5, p-value = .14). When the reading grade level was measured using the Flesch-Kincaid Index Grade Readability Formula (using both the MS Word and the internal assessment tool), the Flesch Reading Ease test and the SMOG tool using the one-way Analysis of Variance (ANOVA) [18] method, we found that there was a significant difference in reading-grade level between medical device type, as *p*-values for all the readability formulas were less than 0.005. However, the absolute difference of the measurements was not large when compared to the corresponding standard deviation, as the statistical significance may have been due to the sample size. When looking at unique academic words, we found no difference between medical device type from the one-way ANOVA analysis ($p = .08$).

We performed similar analyses to determine whether there were any differences in readability between study types and found that a significant difference was observed when measured by the Flesch Kincaid Index Reading test, SMOG level, and Flesch Reading Ease test (*p*-values of 0.01, 0.01, and 0.004, respectively).

[13] The Academic Word List (AWL) was developed by Averil Coxhead at the School of Linguistics and Applied Language Studies at the Victoria University of Wellington, New Zealand. Available at http://www.uefap.com/vocab/select/awl.htm

[14] Most medical devices can be classified by finding the matching description of the device in Title 21 of the Code of Federal Regulations (CFR), Parts 862-892. As such, the medical device types are reviewed by each division within CDRH as classified in the CFR. https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHOffices/UCM331223.pdf

[15] Id.

Table 2
Overall summary statistics for selected features of ICFs.

Selected feature	Mean (standard deviation)	Median (Q1, Q3)
SMOG grade level[a]	14.1 (1.2)	14.1 (13.4,14.9)
Flesch-kincaid index grade level readability formula–internal assessment tool[a].	12.4 (1.6)	12.4 (11.3, 13.3)
Number of unique academic words	204.2 (132.1)	156.0 (122, 257)
Number of pages	13.0 (5.0)	12.0 (9.0, 16.0)
Average number of words per sentence	20.0 (3.3)	19.7 (17.9, 21.7)
Total number of words	4882.9 (2165.7)	4521.0 (3456.0, 5859.0)
Flesch-Kincaid index grade level readability formula[a]	10.5 (1.3)	10.5 (9.7, 11.3)
Flesch reading ease test[b]	51.9 (6.3)	51.6 (47.6, 56.0)
Total number of tables	0.5 (1.2)	0 (0, 1)
Total number of figures	0.2 (0.8)	0 (0, 0)
Number of words per section		
Introduction	520.9 (344.4)	455.0 (319, 653)
Study procedure	1246.1 (955.2)	1002 (575.0, 1613.0)
Benefit	80.9 (73.5)	66.0 (43.0, 97.0)
Risk	845.9 (682.6)	653.0 (365.0, 1150)
Study alternative	75.2 (56.4)	63 (40, 95)
Voluntary	135.1 (87.3)	124.0 (70, 180)
Confidentiality	435.4 (295.5)	369.0 (200.0, 600.0)

[a] The SMOG Grade level and Flesch-Kincaid Index Grade Level Readability Formula correspond to U.S. academic grade level or the number of years of education necessary to understand the written material therefore higher scores (e.g., 11th grade and above) are considered graduate-reading level.

[b] For the Flesch Reading Ease test scores the equivalent grade levels are 0–49 (college or college graduate); 50–59 (10th to 11th grade); 60–69 (8th to 9th grade); 70–79 (7th grade); 80–89 (6th grade); and 90–100 (5th grade).

Table 3
Readability by medical device type.

		AGRID (N = 15)	CV (N = 102)	CT (N = 35)	IH (N = 1)	MD (N = 1)	MGPD (N = 23)	NPM (N = 70)	ORP (N = 24)	OENT (N = 26)	RGD (N = 56)	RH (N = 6)	SU (N = 40
SMOG grade level	Mean	14.4	14.5	13.5	15.3	14.0	14.2	13.9	14.6	14.0	14.1	14.2	13.4
	Std Dev	0.8	1.1	1.1	–	.	1.2	1.1	1.6	1.2	0.9	0.7	1.4
Flesch-Kincaid index grade readability formula –internal assessment tool	Mean	11.3	12.7	11.8	14.3	12.5	13.0	12.0	12.9	12.3	12.4	12.7	11.8
	Std Dev	1.0	1.4	1.7	-	.	1.6	1.4	1.9	1.5	1.7	1.0	1.6
Number of unique academic words	Mean	248.7	212.4	218.7	84.0	192.0	222.0	220.6	187.5	175.8	167.2	330.8	179.2
	Std Dev	102.5	135.2	112.1	–	.	120.1	188.7	105.1	93.4	82.4	152.3	110.6
Flesch reading ease test	Mean	48.6	50.8	57	53.0	50.7	52.1	52.3	50.2	50.1	50.8	52.0	54.9
	Std Dev	5.2	5.9	6.1	.	.	8.5	5.1	6.2	6.1	5.7	5.2	7.2
Flesch Kincaid Grade Level readability formula	Mean	11.3	10.7	9.5	10.1	10.8	10.7	10.3	10.8	10.8	10.6	10.4	9.9
	Std Dev	1.0	1.2	1.4	–	.	1.9	0.9	1.2	1.3	1.1	0.9	1.5

Table 4
Readability by study type.

		Early feasibility (N = 76)	Traditional feasibility (N = 128)	Other study types (N = 21)	Pivotal (N = 174)
SMOG grade level	Mean	14.3	13.8	14.0	14.2
	Std Dev	1.1	1.1	1.2	1.3
Flesch-Kincaid index grade readability formula – internal assessment tool	Mean	12.5	12.1	12.2	12.6
	Std Dev	1.3	1.6	1.4	1.6
Academic word	Mean	218.4	187.6	186.8	212.2
Number of unique academic words	Std Dev	184.6	108.0	108.8	122.7
Flesch reading ease test	Mean	50.0	53.1	53.7	51.6
	Std Dev	5.4	6.9	6.4	6.1
Flesch Kincaid grade readability formula	Mean	10.7	10.2	10.1	10.6
	Std Dev	1.0	1.4	1.2	1.3

Using the ANOVA method, we sought to determine whether there were any significant differences between readability formulas, i.e., the Flesch-Kincaid Index Grade Readability Formula using both MS Word and the internal assessment tool, and the Flesch Kincaid Index Reading test. We found that a difference exists between the two methods (p-value less than 0.0001). However, using the 2-way ANOVA method, there is no statistical evidence to conclude that the different algorithms performed heterogeneously across medical device type or study types, respectively, with p-values (of the interaction terms of the respective factor by method) 0.90 and 0.76, respectively.

5. Discussion

Past research has shown the ICF and the IC process are too complexed and as a result study participants may not completely understand the benefits, risks and requirements associated with the study. This article demonstrates an additional perspective whereby even when informed consents, such as the 399 IDEs surveyed from CDRH, meet regulatory requirements, they were not written in a way that promoted participants' comprehension.

For example, for simplifying the structure and content of the ICF,

Table 5
Dale-Chall reading grade level by medical device type.

Dale-Chall grade level[a]				
FDA medical device type	11–12	13–15	16 and above	Total
AGRID	0	8	7	15
CV	3	44	55	102
CT	3	25	7	35
IH	0	0	1	1
MD	0	0	1	1
MGPD	0	10	13	23
NPM	4	38	28	70
ORP	1	11	12	24
OENT	1	15	10	26
RGU	1	25	29	56
RH	0	2	4	6
SU	8	19	13	40
Total	21	197	181	399

[a] The Dale-Chall Grade levels correspond to U.S. academic grade level with the scale beginning at 4th grade and ending at college level reading; grades 13 and above. In the sample there were no scores below the 11th – 12th grade level.

Table 6
Dale-Chall reading grade level by study type.

Dale-Chall grade level				
Study type	11–12	13–15	16 and above	Total
Early feasibility	2	28	46	76
Traditional feasibility	5	77	46	128
Other study types	2	10	9	21
Pivotal	12	83	79	174
Total	21	197	181	399

Table 8
Informed consent structure and format by study type.

		Early feasibility (N = 76)	Traditional feasibility (N = 128)	Other study types (N = 21)	Pivotal (N = 174)
Number of pages	Mean	13.2	12.8	12.2	13.2
	Std Dev	5.0	5.3	3.4	5.1
Average number of words per sentence	Mean	20.0	19.7	20.5	20.1
	Std Dev	2.8	3.3	3.8	3.3
Total number of words	Mean	4911.1	4808.5	4566.0	4963.7
	Std Dev	1970.2	2069.0	1430.3	2388.6
Total number of tables	Mean	0.3	0.6	0.8	0.5
	Std Dev	0.6	1.0	1.5	1.5
Total number of figures	Mean	0.5	0.1	0.3	0.3
	Std Dev	1.1	0.4	0.6	0.8
Number of words per section					
Introduction	Mean	530.7	523.2	532.5	513.6
	Std Dev	411.4	378.4	215.4	298.1
Study procedure	Mean	1213.3	1329.2	1082.7	1219.2
	Std Dev	782.2	922.8	860.8	1055.3
Benefit	Mean	98.4	67.1	76.8	83.8
	Std Dev	131.3	45.5	40.3	54.1
Risk	Mean	1072.7	833.8	717.5	771.2
	Std Dev	836.0	671.7	561.2	609.2
Study alternative	Mean	86.3	69.4	71.4	75.1
	Std Dev	72.2	48.8	52.1	54.0
Voluntary	Mean	127.3	127.0	158.9	141.7
	Std Dev	75.6	94.1	108.0	83.7
Confidentiality	Mean	403.4	429.4	575.5	437.0
	Std Dev	219.2	330.9	339.9	288.9

Table 7
Informed consent structure and format by medical device type.

		AGRID (*N* = 15)	CV (*N* = 102)	CT (*N* = 35)	IH (N = 1)	MD (N = 1)	MGPD (*N* = 23)	NPM (N = 70)	ORP (N = 24)	OENT (N = 26)	RGD (N = 56)	RH (N = 6)	SU (N = 40)
Number of pages	Mean	12.1	12.4	15.9	6.0	14	18.5	12.5	12.9	11.7	11.1	17.7	13.5
	Std Dev	7.8	3.6	6.1	.	.	7.4	4.5	3.6	4.0	4.4	5.6	4.3
Average Number of words per sentence	Mean	20.5	20.2	19.1	17.4	24.4	21.5	19.3	21.4	20.2	20.0	18.8	19.6
	Std Dev	1.8	3.5	3.8	.	.	3.4	2.9	4.3	3.2	2.6	1.5	2.9
Total number of words	Mean	4036.6	4631.3	6130.9	1934.0	7138.0	7719.5	4918.5	4715.3	4483.8	3975.2	5615.8	4595.1
	Std Dev	1977.7	1472.8	2939.3		.	4007.2	1862.0	1430.3	1774.0	1633.0	1404.4	1570.9
Total number of tables	Mean	0.5	0.4	0.7	0.0	1.0	1.7	0.4	0.3	0.4	0.3	1.0	0.6
	Std Dev	1.0	0.9	1.1	–	.	3.5	0.8	0.5	0.8	0.5	0.6	0.9
Total number of figures	Mean	0.3	0.4	0.5	0.0	0.0	0.0	0.1	0.2	0.1	0.2	0.2	0.3
	Std Dev	0.8	1.0	1.2	–	.	0.2	0.6	0.6	0.4	0.5	0.4	0.6
Number of words per section													
Introduction	Mean	411.9	511.5	643.6	335.0	974.0	577.9	466.6	602.9	557.5	492.5	368.0	524.1
	Std Dev	253.8	262.5	465.2	.	.	385.7	282.2	225.5	487.5	317.0	218.4	472.8
Study Procedure	Mean	1109.3	1051.1	1976.9	130.0	1982.0	1980.0	1388.4	912.3	991.3	1031.9	1156.0	1173.6
	Std Dev	1007.1	673.4	1518.7	.	.	1293.5	919.3	625.9	668.2	709.8	595.9	938.3
Benefit	Mean	62.6	109.3	49.0	42.0	55.0	63.1	74.0	94.5	87.0	74.9	65.5	65.5
	Std Dev	34.9	120.4	34.6	.	.	53.6	42.9	50.5	48.5	46.1	23.4	32.8
Risk	Mean	501.1	783.9	673.0	182.0	1123.0	1486.4	1020.4	869.0	923.5	616.1	1967.3	709.4
	Std Dev	472.3	523.8	368.8	.	.	1242.0	755.1	498.0	761.6	533.8	1033.1	475.0
Study Alternative	Mean	51.2	80.1	60.9	34.0	102.0	72.1	73.8	105.2	86.8	72.3	74.2	67.3
	Std Dev	49.5	63.4	35.7	.	.	81.6	47.8	78.9	50.5	51.8	33.0	42.1
Voluntary	Mean	134.7	152.5	133.9	53.0	72.0	78.7	111.9	155.6	143.1	134.0	242.5	136.9
	Std Dev	79.6	88.1	85.4	.	.	41.5	75.7	90.3	92.4	89.1	221.4	136.9
Confidentiality	Mean	436.2	437.2	469.1	145.0	892.0	618.9	439.8	521.1	394.2	383.3	347.5	345.5
	Std Dev	312.6	283.5	362.1	.	.	365.4	277.6	325.8	214.4	248.5	165.7	302.9

the Agency for Healthcare Research and Quality's Informed Consent and Authorization Toolkit for Minimal Risk Research suggests including the use of plain language, simple sentence structure, short sentences, (e.g., no more than 8 to10 to words) as well as the use of pictures, tables, and diagrams[16]. In our data set, the average sentence length was double that recommendation and each informed consent had on average less than one table, diagram, or figure.

Overall, the ICFs were written at a higher-than-recommended grade level[5]. Furthermore, our statistical analysis showed that there were significant differences in readability among the informed consents written for a specific clinical study design or medical device type. In addition, we found that a single ICF, in the sample from the IH medical device type, had the highest readability score of all 399 ICFs. This ICF was not included in the statistical analysis because it is the single representative sample, but data from the sample was included in the descriptive statistics.

Current research also shows that patients prefer the use of alternative approaches for obtaining consent, such as oral presentations, interactive and video-assisted consent formats, and electronic participant information sheet with basic information as part of the informed consent process versus solely the written approach of getting consent. We were unable to assess whether any of these approaches were used, as none of the IDEs reviewed explicitly confirmed or denied their use in the IC process. As discussed previously, FDA regulations do not preclude the use of any of these approaches; however, study participants must be presented with a written or electronic form, which must be signed.

This survey is limited by the well documented drawbacks associated with readability formulas, which requires that caution be taken with their use. For example, grade level scores tend not to be precise and are thought to ignore certain factors that affect comprehension including, the role of the reader. In addition, when looking at the different formulas, the grade levels scores provided by each formula can be different for the same text[17]. To address some of these limitations, we opted to use different readability formulas: The MS word Flesch-Kincaid Readability Formula and the internal assessment tool, which also included the Flesch-Kincaid Readability Formula plus the SMOG and Dale-Chall formulas[18] to determine readability and gives a value for each method. We did find that grade-reading levels were high across all readability formulas. In some testing, not described here, we also observed that results from the MS word Flesch-Kincaid Readability Formula sometimes depended on the arrangement of text, but results from the internal assessment tool Flesch-Kincaid Readability Formula did not.

Another limitation is human error, as the data was collected by six different CDRH investigators. This was mitigated by each investigator following detailed instructions for data collection and data entry protocol, as well as reoccurring review of the data entry spreadsheets to ensure that the data was entered correctly and that there were no missing values. Finally, although the investigators are members of CDRH staff, none were involved with the regulatory review and approval of the IDEs included in the survey. Therefore, there was little to no risk of investigator bias.

6. Conclusions

There are several factors to consider when improving the informed consent process. Some basic factors that should be considered include assessments of the potential participants' literacy [19], language, and the presence of significant vison or hearing impairments. Additionally, other less obvious factors such as age, cognitive status, bias, and caregiver literacy should not be overlooked[19].

Once a thorough assessment of these factors has been completed, the development of the informed consent process should include an assessment of which processes and approaches to informed consent, such as those discussed in this article, could be used to help to optimize patient comprehension. It is also important to ensure that the potential participants understand the study, the associated potential risks and benefits to participating in the study and alternative treatment options, as well as any other information that could affect a participant's decision to participate. Our survey has shown that while the informed consent forms evaluated in this survey met FDA's regulatory requirements[20], their readability and comprehension levels were found to be high and may have impeded participant understanding, thereby needing improvement.

FDA will continue to work collaboratively with industry to improve informed consent forms and the process overall in hopes of enhancing the readability of ICFs and participant comprehension which could lead to increased participant enrollment and retention, thereby making the medical device clinical trial enterprise less burdensome for all.

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