EXECUTIVE SUMMARY FOR THE PATIENT ENGAGEMENT ADVISORY COMMITTEE MEETING

Patient-Centered Informed Consent

Executive Summary

October 30, 2024

PEAC Executive Summary – Patient-Centered Informed Consent

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Disclaimer: This Executive Summary is for discussion purposes only and does not represent draft or final guidance. It is not intended to propose or implement policy changes regarding regulation of informed consent for medical products. In addition, the references cited herein are for informational purposes only and should not be construed as endorsements.

Introduction

Clinical research relies on individuals who volunteer to participate in clinical studies. These individuals are making an essential contribution to scientific knowledge relating to medical products, and it is important that their decision to participate in the study is informed and voluntary. It is the research community's ethical obligation to make sure all clinical study participants are enrolled in a clinical study only once they understand key aspects of the proposed study. This includes pertinent information about the investigational medical product, benefits and risks, and other commitments such as visits, procedures and cost related to participation in the proposed study.

Once a potential participant has been informed of these clinical study elements through the informed consent process, they may decide to volunteer. At which point the site investigators are responsible for ensuring the potential participant, or their legally authorized representative, signs an informed consent form.

A large and growing body of literature suggests that informed consent documents and processes have been inadequate, often failing to fully inform potential participants in a clear and comprehensible way about the research in which they may be participating. In many cases the informed consent process consists of presenting potential participants with a long, complex document that does not effectively highlight the information that they would say is most important to them in making an informed decision.[1]

FDA regulations specify requirements for informed consent in research that falls under its oversight. Protecting the rights, safety and welfare of people who participate in clinical studies is a critical aspect of the mission of the U.S. Food and Drug Administration (FDA). FDA oversees clinical studies to ensure they are designed, conducted, analyzed and reported according to federal law and good clinical practice (GCP) regulations.[2]

[1] https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2779247

[2] https://www.fda.gov/science-research/science-and-research-special-topics/clinical-trials-and-human-subject-protection

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The agency has recently issued multiple guidance documents[3] related to informed consent and proposed changes to our regulations.[4] If our regulations are finalized as proposed, this would enhance the informed consent process for people considering participating in clinical studies to help them decide whether they should participate in the trial. For example, the proposed rule would revise the requirements regarding the content, organization, and presentation of information in the informed consent form and require that key information most likely to help a potential participant understand the study be presented first before other information about the study. To that end, the agency is conducting this Patient Engagement Advisory Committee (PEAC) to solicit input from patients, caregivers and other interested parties on how to improve informed consent documents and processes to make them more patient-centered.

Basics of Informed Consent

Protection of potential participants in clinical studies are part of FDA's existing regulations. FDA's regulations in 21 CFR parts 50 and 56 are intended to protect the rights, safety, and welfare of human subjects[5] participating in FDA-regulated clinical investigations. In particular, 21 CFR part 50 specifies requirements for informed consent, and includes the following:

> "[With certain narrow exceptions] no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative....[The informed consent must include] a description of any reasonably foreseeable risks or discomforts to the subject."

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[3] See FDA Guidance "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
See FDA guidance "Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors." Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent
See FDA draft guidance "Key Information and Facilitating Understanding in Informed Consent Guidance for Sponsors, Investigators, and Institutional Review Boards." Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/key-information-and-facilitating-understanding-informed-consent-guidance-sponsors-investigators-and. When final, this guidance will represent FDA's policy.

[4] On September 28, 2022, FDA issued proposed rules to harmonize certain provisions of 21 CFR parts 50 and 56 with the 2018 revised Common Rule to the extent practicable and consistent with other statutory provisions (see 87 FR 58733 at https://www.federalregister.gov/documents/2022/09/28/2022-21088/protection-of-human-subjectsand-institutional-review-boards, and 87 FR 58752 at https://www.federalregister.gov/documents/2022/09/28/2022-21089/institutional-review-boards-cooperativeresearch). The comment period for the proposed rules officially closed on December 28, 2022. These proposed changes to FDA regulations are not currently in effect.

[5] FDA acknowledges that its regulations use the term "subject" or "human subject," to refer to these individuals, but patients may be familiar with a different term. Therefore, in this document, the term "participant" is used instead.

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"Informed consent" has been defined as "the process by which a volunteer confirms his or her willingness to participate in the research after having been informed of all aspects of the trial that are relevant to the volunteer's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form."[6] (A participant's legally authorized representative may provide consent on their behalf.)

"Patient-centered informed consent," refines that definition to incorporate ensuring that the experiences, perspectives, needs, and priorities are meaningfully incorporated into decisions including the agreement to participate in a clinical study.[7]

FDA expects the informed consent process to go beyond obtaining a signature on an informed consent form. Obtaining documentation of a participant's informed consent is only part of the consent process. Informed consent involves providing a prospective participant, or their legally authorized representative (LAR), with adequate information to allow for an informed decision about participation in a trial prior to enrollment. In accordance with our current regulations, an informed consent process must include the following, among other requirements[8]:

- pertinent information about the investigational medical product,
- the reasonably foreseeable risks and discomforts to the participant, including risks of the medical product and also any benefits to the participant or to others which may reasonably be expected from the research,
- appropriate alternative procedures or courses of treatment, if any, and
- what visits, procedures, tasks and other commitments are anticipated in order to participate in the clinical study.
- Where applicable, the informed consent must include information on any additional costs to the subject that may result from participation in the research.
  In addition, the potential clinical study participant must be given sufficient opportunity to consider whether or not to participate in the clinical study under circumstances that minimize the possibility of coercion or undue influence.

In summary, an informed consent process is intended to provide the information necessary for an individual to make a fully informed decision about their participation. This includes deciding to accept potential risks associated with a clinical study in exchange for the potential for any anticipated benefits to the participants and/or the importance of the knowledge to be gained.

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[6] https://www.niaid.nih.gov/research/dmid-protocols-informed-consent
[7] Definition adapted from https://www.sciencedirect.com/science/article/pii/S0022354923000515#bib0014 and https://www.fda.gov/drugs/development-approval-process-drugs/patient-focused-drug-development-glossary
[8] See 21 CFR part 50

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The Need for Updated Regulation

There is general consensus among those who study informed consent that existing documents and processes often inadequately provide information in such a way as to ensure potential participants have the full understanding they need to make truly informed decisions about research participation—especially with regard to key information, such as why a clinical study is being done, what will be required of them, what the key risks and benefits are, and that participation is voluntary. At the same time, there is growing interest in integrating patient-centered perspectives into all aspects of clinical studies, including informed consent.[9,10]

These trends have motivated an effort to amplify and where necessary update policy aimed to improve informed consent and make it more patient-centered. In particular, there is strong interest in improving the informed consent process by moving the research community toward the following best practices[11]:

- Enlisting simple, clear language
- Taking into account the health literacy challenges faced by much of the population
- Making an effort to assess whether the consent-giver truly understands what they have signed
- Relying less on purely textual documents by making use of graphics, videos, digital tools, and more interactive and conversational formats.

A combination of these informed consent practices can improve comprehension and better address patient concerns and interests and have been the focus of recent FDA guidance documents.[12,13]

[9] https://www.ncbi.nlm.nih.gov/books/NBK580262/
[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4504054/
[11] https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Informed_Consent_Recs.pdf https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Informed_Consent_Discussion_Tool.pdf https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Informed_Consent_Sample_Informed_Consent_Model.pdf
[12] https://www.sciencedirect.com/science/article/pii/S1551714416300854
[13] See also FDA draft guidance "Key Information and Facilitating Understanding in Informed Consent Guidance for Sponsors, Investigators, and Institutional Review Boards." Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/key-information-and-facilitating-understanding-informed-consent-guidance-sponsors-investigators-and. When final, this guidance will represent FDA's policy.

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More recently, FDA published a proposed rule[14] that, if finalized as proposed would enhance the informed consent process for people considering participating in clinical studies to help them decide whether they should participate in the study. It would revise the current requirements regarding the content, organization and presentation of information in the informed consent form, and require that key information most likely to help a potential participant understand the study be presented first, before other information about the study. These changes are intended to facilitate important discussions between a prospective clinical study participant and their health care provider or other trusted advisor about whether a specific clinical study is an appropriate option. We also hope these proposed changes, if finalized will invite broader participation in clinical research, advancing our efforts to ensure that clinical studies reflect the diversity of patient populations and that these patient populations feel engaged by the clinical research community.

Special Considerations for Medical Device Studies

Most issues relevant to patient-centered informed consent apply to all clinical studies, whether they focus on medical devices, drugs, biologics, or combination products. But clinical studies of some medical devices may require special attention in the development or administration of informed consent documents and processes. Some devices may entail unique risks, protocols or burdens, or require more extensive explanation to ensure adequate comprehension. Some examples:

- Implants[15] usually require surgical procedures that may be associated with a range of significant risks, including removal in the event of a failure. In addition, a participant needs to be aware of follow-up commitments, including inpatient hospital stays, or recurrent outpatient visits, as well as post-surgical recovery expectations The impacts of having an implant may play out over years, and additional risks may appear over time.[16]

[14] On September 28, 2022, FDA published a proposed rule to amend its regulations to modernize, simplify, and enhance oversight of FDA-regulated human subject research (87 FR 58733), available at: https://www.federalregister.gov/documents/2022/09/28/2022-21088/protection-of-human-subjects-and-institutional-review-boards. The comment period for the proposed rule officially closed on December 28, 2022. These proposed changes to FDA regulations are not currently in effect.

[15] An implant is defined in 21 CFR 860.3(d) as “a device that is placed into a surgically or naturally formed cavity of the human body.” The regulation further specifies that “[a] device is regarded as an implant for the purpose of this part only if it is intended to remain implanted continuously for a period of 30 days or more, unless the Commissioner determines otherwise in order to protect human health.”

[16] E.g.: https://www.fda.gov/medical-devices/breast-implants/risks-and-complications-breast-implants https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10676178/ https://www.sciencedirect.com/science/article/pii/S2949705123000063

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- Diagnostic tests typically have unique risks of false negatives and false positives[17], and each may be associated with very different potential impacts on a patient.[18]
- Devices that use software or other digital capabilities are subject to privacy and cybersecurity risks that typically go beyond those associated with drugs or devices without this functionality.[19]

Patient and Community Input

FDA seeks to create opportunities for patients and the community to inform the development of improved informed consent approaches, that better assist people considering participating in a clinical study in making fully informed decisions about whether or not to participate in research. The convening of this Patient Engagement Advisory Committee (PEAC) is one such key opportunity.

Among the topics discussed at this PEAC meeting, FDA hopes patients and other interested parties will consider the following from their perspective:

- Information that would ideally be presented as key information in informed consent documents and conveyed during verbal discussions.
- Aspects of how information identified as key information is presented to help potential participants make an informed decision about participating. Aspects might include, for example, the order in which information is presented, its accessibility to a wide range of patients, and the extent to which the information includes health equity and cultural considerations.

[17] Diagnostic tests are intended to detect a specific target (substance, virus, biomarker, etc.) in a sample taken from the human body, such as blood or saliva. A false negative result means that the test says the target is not found even though the target is actually present in the sample. A false negative result may lead to delayed diagnosis or inappropriate treatment, which may cause people harm including serious illness and death. False negative results on an infectious disease test can also lead to further spread of the disease, as actions to limit exposure might not be taken if an individual believes they do not have the infection. A false positive result means that the test says the target is found even though the target is not actually present in the sample. A false positive result may lead to a delay in both the correct diagnosis and appropriate treatment for the actual cause of a person's condition, which could be another life-threatening disease or condition than what the initial test was looking for. False positive results on an infectious disease test could also lead to further spread of the disease, as actions to limit exposure might not be taken if an individual believes they are already infected. Adapted from: https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/counterfeit-home-otc-covid-19-diagnostic-tests

[18] E.g.: https://www.sciencedirect.com/science/article/abs/pii/S027227120700131X?via%3Dihub

[19] E.g. https://www.tandfonline.com/doi/full/10.1080/17434440.2018.1483235#d1e141

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- Effective approaches for providing information to potential clinical study participants with particular attention to process and content that would meet the needs of various populations. Populations include those with diverse racial, ethnic, socioeconomic, gender and sexual orientations; underserved populations; various age groups, including children and the elderly; and individuals with physical or cognitive differences.
- Ways in which technology could be leveraged in the development of informed consent documents and processes for collecting informed consent for participation in clinical studies.
- Aspects of implementing electronic or digital consent materials and processes that should be considered.

The PEAC will provide an opportunity for patients, patients' family members, caregivers, and a range of medical product interested parties to share experiences with informed consent in clinical studies, and describe their needs, interests, and concerns with regard to improving informed consent documents and processes. FDA anticipates that the input and discussions may be impactful for the agency's future guidance. The discussion is intended to also build on the insights generated by the Clinical Trials Transformation Initiative (CTTI's) Informed Consent Project Expert Meeting, held in 2015.[20]

Interested parties other than patients, family members and caregivers that are likely to participate in the PEAC include different FDA Offices, other U.S. agencies, industry key opinion leaders, and academic clinical study sponsors.

The PEAC input is also intended to inform FDA's ongoing work with sponsors, investigators, and Institutional Review Boards (IRBs) in developing strategies for more effectively integrating informed consent best practices into reality .

FDA also encourages interested parties to consider developing innovative ways, including enlisting appropriate available technologies, to provide key information that may help prospective participants better understand the possible risks and benefits and make a fully informed decision regarding whether to participate in a clinical study. FDA anticipates that receiving direct input from prospective participants and the caregivers who assist them may help to ensure the key information and overall informed consent content and process is patient-centered.

Strategies for Improving Informed Consent

[20] https://ctti-clinicaltrials.org/ctti-informed-consent-project-expert-meeting/

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Research into informed consent has identified a range of shortcomings and also points to strategies to consider for improving informed consent documents and processes. As part of the PEAC meeting, aspects for consideration of the informed consent documents and processes include, but are not limited to, the following:

Length: One published study found the median length of informed consent documents is 27 pages.[21] Many studies suggest that clinical study participants are more likely to understand a clinical study and the implications of participation if they are presented with a shorter, simpler document.

Key information: The revised Common Rule[22] requires consent information to "begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research."[23] The need to succinctly highlight information that is most important and helpful to participants in coming to an informed decision, and placing that information up front in the informed consent material, is a consistent theme in the literature.[24]

There are different ways that key information might be presented. One clinical study found that providing clinical study participants with a bulleted fact sheet improved their comprehension of the research information.[25] The CTTI has found that information is best provided in three "tiers": One for the key information required by regulation, one for other information that may be relevant to participants, and a third for an introduction to or summary of the clinical study.[26]

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[21] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3208469/

[22] The revised Common Rule refers to the final rule (82 FR 7149, January 19, 2017) codified in 45 CFR part 46, subpart A. The revised Common Rule is intended to better protect human subjects involved in research, while facilitating research and reducing burden, delay, and ambiguity for the regulated community. Prior to the most recent revisions to the Common Rule, FDA's regulations were largely consistent with the requirements in the Common Rule, with a few exceptions generally arising from differences in FDA's mission or statutory authority. Section 3023 of the Cures Act directs the Secretary of HHS to harmonize differences between HHS's and FDA's human subject protection regulations to the extent practicable and consistent with other statutory provisions. FDA has issued a notice of proposed rulemaking (see 87 FR 58733 at https://www.federalregister.gov/documents/2022/09/28/2022-21088/protection-of-human-subjectsand-institutional-review-boards, and 87 FR 58752 at https://www.federalregister.gov/documents/2022/09/28/2022-21089/institutional-review-boards-cooperativeresearch) proposing to amend 21 CFR parts 50 and 56 in accordance with the harmonization requirement in the Cures Act.

[23] 45 CFR 46.116(a)(5)(i)

[24] https://www.thehastingscenter.org/irb_article/barriers-to-change-in-the-informed-consent-process-a-systematic-literature-review/

[25] https://pubmed.ncbi.nlm.nih.gov/25475879/

[26] https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Informed_Consent_Recs.pdf

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The information that is typically considered key to informed consent documents and processes can vary from clinical study to clinical study and between different participants. Consulting with prospective participants may be helpful in gaining additional perspectives. The following types of information would typically be among those considered key in most clinical studies, and in many cases are recommended elements[27]:

- A statement that consent for research is being sought and that participation is voluntary.
- A statement that a decision not to participate in the clinical study, or to discontinue participation, will involve no penalty or loss of benefits.
- A clear description of the purpose of the clinical study and relevant details of the protocol.
- A description of any randomization[28] and placebo[29] components.
- An explanation of why a person might want or not want to participate.
- The expected duration of the prospective subject's participation.
- A high-level description of the major procedures involved.
- A description of common or serious risks and discomforts.
- A list of any reasonably expected benefits.
- A description of any alternative procedures or courses of treatment that might be appropriate.
- Any medical treatments and compensation available in the case of injury.

For a sample key information section developed for a hypothetical clinical study, see FDA draft guidance, sample included as an Appendix in the guidance "Key Information and Facilitating Understanding in Informed Consent Guidance for Sponsors, Investigators, and Institutional Review Boards."

https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Informed_Consent_Discussion_Tool.pdf
https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Informed_Consent_Sample_Informed_Consent_Model.pdf

[27] See FDA draft guidance "Key Information and Facilitating Understanding in Informed Consent Guidance for Sponsors, Investigators, and Institutional Review Boards." Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/key-information-and-facilitating-understanding-informed-consent-guidance-sponsors-investigators-and. When final, this guidance will represent FDA's policy.

[28] Randomization is the process in which researchers evenly assign study participants into a group receiving the experimental treatment being studied, and others into a group receiving standard or no treatment. Participants are assigned to a group based on chance, not choice. You have the same chance to be placed in any of the test groups. Source: https://www.fda.gov/patients/clinical-trials-what-patients-need-know/glossary-terms

[29] A placebo is an inactive substance or other intervention that looks the same as, and is given the same way as, an active drug or treatment being tested. The effects of the active drug or other intervention are compared to the effects of the placebo. Source: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/placebo

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Language, complexity and health equity: Not only do clinical study participants frequently lack understanding of some elements of key information, such as risks and randomization, studies have consistently shown that some clinical study participants may not realize they are even involved in a clinical study—despite having signed the informed consent document.[30] These gaps in comprehension reflect the fact that conventional informed consent documents utilize language that is often too complex for many participants and includes too many unfamiliar terms and concepts without clearly explaining them.

Research has suggested that one out of seven people in the U.S. have health-literacy skills below a fourth-grade reading level.[31] Moreover, people from populations underrepresented in research often have lower literacy levels.[32] To improve comprehension and health equity, information would ideally be presented in plain, clear, simple language, with careful explanations of scientific and medical terms. Participants with limited English proficiency would ideally be given information in their primary language. Less essential details about the clinical study can be placed further back in the document. Illustrations can also be an important aid to comprehension, especially for those at lower literacy levels.

Interaction: Studies have shown that potential participants achieve better comprehension if in addition to receiving a document they also engage in a dialogue with someone from the research team—preferably someone who is a skilled, trained communicator[33]. Providing potential participants with a chance to ask questions, along with providing them with a list of questions they may want to ask, has also been shown to help. Further, providing a "formative evaluation"--essentially a comprehension quiz—at the end of any presentation of information may aid in its comprehension, but it would be important for it not to serve as a barrier to participation.[34]

Electronic informed Consent (eIC): Studies have shown that eIC presentations promote greater participant engagement than paper documents, along with improved retention of information.[35] Electronic presentations can include graphics, animation, video, and interactive elements, all of which can improve comprehension, and can be designed for laptop computers, tablets, and phones.[36]

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[30] E.g.: https://sigmapubs.onlinelibrary.wiley.com/doi/10.1111/jnu.12097
[31] https://eric.ed.gov/?id=ed493284
[32] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3703948/
[33] https://pubmed.ncbi.nlm.nih.gov/15467062/
[34] https://pubmed.ncbi.nlm.nih.gov/31948345/
[35] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10504628
[36] See FDA guidance "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

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Researchers have noted that care should be taken in the design of eIC presentations, given that many people have developed the habit of quickly paging through the consent information that is ubiquitous with software, online services, and apps. In addition, people tend to scan only a portion of the information on a screen, ignoring the rest. One review suggested the strategiesto improve engagement with eICs[37]:

- Use interactive features to improve participant engagement and comprehension
- Tailor e-consent to the needs of the participant group
- Ensure adequate data security and management procedures
- Consider the practicalities of e-consent

Health equity may be advanced through eIC which is able to accommodate different ways potential participants may process information to increase comprehension. For example, blocks of text can be replaced with easier-to-comprehend graphic elements and inclusion of interactivity using eIC can also be beneficial. In addition, videos have been shown to increase comprehension and enrollment among patients who have historically been underrepresented in clinical studies.[38]

Privacy and security: Informed consent documents should clearly indicate how confidentiality of collected information will be maintained and how personal information may be shared, including with the FDA.

As a general practice, the more sensitive the information that will be collected, the more it should be clearly identified in the consent document or presentation. Both the revised Common Rule and FDA's proposed regulations, if finalized as currently proposed, require, among other elements of informed consent, that the informed consent process and document include specifying whether individual research results will be disclosed to potential clinical study participants.[39] In addition, FDA is proposing that consent include a description of how information or biospecimens[40] may be used for future research.

Limitations: Researchers have pointed out that while studies of informed consent processes have identified certain broad strategies that seem to improve engagement and comprehension among potential clinical study participants, they have not singled out any particular approach to

[37] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7487205/
[38] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5891825/
[39] https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116
[40] A biospecimen is a sample of material, such as urine, blood, tissue, cells, DNA, RNA, or protein, from humans, animals, or plants. Biospecimens may be used for a laboratory test or stored in a biorepository to be used for research. Source: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/biospecimen

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informed consent that works better than others for all participants in all clinical studies.[41] In addition, it has been observed that participants often form their opinions about participation largely based on information sources other than the consent materials they are given—for example, through word of mouth, online media, or social networks[42]. As a result, clinical study sponsors are encouraged to tailor their approaches to informed consent documents and processes based on the individuals participating and the particulars of the clinical study, as well as to experiment with different informed consent formats and strategies. The need to take different patients' different situations into account makes patient engagement in informed consent content and process design all the more important.

FDA's Actions

FDA has been active in encouraging best practices in informed consent document and processes, and has issued draft and final guidance and proposed updated our regulations, as appropriate. Actions over the last decade include the following:

- In 2016, FDA published final guidance on electronic informed consent processes—"eIC"—to supplement or replace paper-based informed consent processes, encouraging the inclusion of diagrams, images, graphics, videos, and narration, as well as methods to help assess how well the potential participant understood the information presented to them.[43]
- In 2022, FDA published a proposed rule that, if finalized, would require that key information be presented at the beginning of the consent documents and processes to help potential participants understand the key aspects of the clinical study. The regulation would also facilitate important discussions between a prospective clinical study participant and their health care provider or other trusted advisor about whether a specific clinical study is an appropriate option.[44]
- In 2023, FDA published updated final guidance on informed consent that reemphasized the value of pictures, diagrams, or other visual aids to improve understanding. It also

[41] E.g.: https://www.thehastingscenter.org/irb_article/barriers-to-change-in-the-informed-consent-process-a-systematic-literature-review/

[42] E.g.: https://www.centerwatch.com/articles/26825-trials-see-spike-in-social-media-patient-advocacy-and-website-recruitment-approaches

[43] See FDA guidance "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

[44] On September 28, 2022, FDA published a proposed rule to amend its regulations to modernize, simplify, and enhance oversight of FDA-regulated human subject research (87 FR 58733), available at https://www.federalregister.gov/documents/2022/09/28/2022-21088/protection-of-human-subjects-and-institutional-review-boards. The comment period for the proposed rule officially closed on December 28, 2022. These proposed changes to FDA regulations are not currently in effect.

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suggested that consent forms that are long, complex, legalistic, and have a high grade-level readability[45] may overwhelm prospective subjects.[46]

- In March 2024, FDA published a draft guidance describing how the key information provisions of the 2022 proposed rule, if finalized as currently proposed, might be implemented.[47]

This PEAC meeting will be helpful in guiding the agency in its efforts to modernize, promote, support and enhance patient-centered informed consent.

Future Opportunities

Various interested parties have expressed interest in promoting efforts to advance the best practices of obtaining patient-centered informed consent. FDA encourages continued progress in improving informed consent documents and processes. Among the opportunities that have been suggested by interested parties:

- Better leveraging input from and engagement with patients and caregivers related to reasonable-patient-centered informed consent decisions.[48]
- Developing communities of practice focused on patient-centered informed consent[49]
- Obtaining patient input on key aspects of clinical study plans, including patient-centered informed consent considerations, earlier in the medical-device product development cycle. [50]
- Applying a scientific approach to understanding patient preferences related to informed consent decisions. This approach involves studying how patients weigh benefits and risks in their decision making about whether to participate in a clinical study, including applying preference methodology to understanding their decisions. Applying a more

[45] Reading level describes the level of reading skills of the reader. Keeping reading levels as low as possible supports effective communication. Source: DuBay, William. "The principles of readability." *Impact Information* (2004).
[46] See FDA guidance “Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors.” Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent
[47] See FDA draft guidance “Key Information and Facilitating Understanding in Informed Consent Guidance for Sponsors, Investigators, and Institutional Review Boards.” Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/key-information-and-facilitating-understanding-informed-consent-guidance-sponsors-investigators-and. When final, this guidance will represent FDA’s policy.
[48] E.g.: https://jamanetwork.com/journals/jama/fullarticle/2516469
[49] E.g.: https://karger.com/mpp/article/23/Suppl.%201/60/202610
[50] E.g.: https://www.centerwatch.com/articles/25356-seeking-patient-input-early-helps-ensure-minority-participation-in-trials

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rigorous scientific approach has been touted as potentially reducing risks in clinical trial design by making clinical study enrollment and participation more predictable.[51]

Concluding Summary

Ethical research requires that potential participants in a clinical study are provided high-quality informed consent documents and processes that leave them with a full and clear understanding of the study and how it might impact them, including risks, benefits, commitments, burdens, and other aspects of participation.

Increasing clinical study participation by a wide variety of patients requires continued work and innovative approaches. FDA is committed to encouraging and, where appropriate, supporting and partnering in such work. One key step of this work is gathering input from patients, patient family members and caregivers, and from all the many interested parties in clinical research. FDA envisions that doing so will help ensure that new informed consent documents and processes meet the needs of a wide range of clinical research participants, as well of all those who will be involved in developing, soliciting, or overseeing informed consent.

Informed consent is a cornerstone of clinical research. Addressing its current shortcomings is a vital undertaking deserving of attention from all interested parties.

[51] E.g.: https://acrpnet.org/2024/04/12/an-approach-to-a-benefit-risk-framework

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