



NATIONAL HEALTH COUNCIL

April 30, 2024

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Key Information and Facilitating Understanding in Informed Consent; Draft Guidance for Sponsors, Investigators, and Institutional Review Boards (FDA-2022-D-2997)

Dear Sir/Madam,

The National Health Council (NHC) appreciates the opportunity to provide comments to the Food and Drug Administration (FDA) in response to the Key Information and Facilitating Understanding in Informed Consent; Draft Guidance for Sponsors, Investigators, and Institutional Review Boards (draft guidance).

Created by and for patient organizations over 100 years ago, the NHC brings diverse organizations together to forge consensus and drive patient-centered health policy. We promote increased access to affordable, high-value, equitable, and sustainable health care. Made up of more than 170 national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient organizations. Other members include health-related associations and nonprofit organizations including the provider, research, and family caregiver communities; and businesses and organizations representing biopharmaceuticals, devices, diagnostics, generics, and payers.

General Comments

The NHC applauds the FDA's efforts to enhance the clarity, accessibility, consistency, and an informed consent process that meets the needs of participants. These efforts align with our commitment to ensuring that health policies and practices are patient-centered and reflective of the needs of those they aim to serve. The draft guidance represents a positive step forward in ensuring that participants are fully informed and actively engaged in the decision-making process regarding their participation in clinical research.

Key Points of Support

Conciseness and Focus of Key Information

The NHC supports the FDA's emphasis on beginning the informed consent document with concise, focused presentations of key information. This approach respects the participant's need for clear and accessible information, which is crucial in aiding their decision-making processes. Feedback from patients consistently underscores the need for clear and concise information that respects their cognitive load and emotional context, especially when making critical health decisions. Simplifying the initial sections of consent forms to highlight the most critical elements can prevent information overload and ensure that participants are

not overwhelmed by complex details at the outset. This method not only prioritizes the participant's comprehension but also aligns with best practices in health communication that suggests a focused approach can significantly enhance understanding and retention of important information.

Research in the field of medical ethics and health literacy consistently shows shorter, more targeted consent forms improve participant understanding without compromising the quality of the informed consent process. Studies have found that when consent forms prioritize key information at the beginning, participants are better able to recall specific details about the study, such as the purpose, risks, and benefits, as well as their rights as participants. This improved recall is critical as it ensures that participants are truly informed when they decide to consent to a study.^{i,ii,iii,iv}

Furthermore, the NHC believes that starting with key information aids in building trust between researchers and participants. When participants understand what is expected of them and what they can expect from the study, it sets a foundation of transparency. This transparency is essential not only for ethical reasons but also for practical ones – it can lead to higher participation rates and lower dropout rates in clinical trials.

The NHC appreciates the inclusion of summaries or bullet points that can help participants quickly grasp the essence of the study without delving into the more technical aspects immediately. These summaries can act as signposts throughout the consent document, guiding the participant through more detailed information in a structured, digestible, and understandable way.

Use of Plain Language and Understandable Format

The NHC fully endorses the draft guidance's emphasis on the use of plain language and the organization of information to facilitate understanding in informed consent documents. Clarity in communication is not just about convenience; it is a fundamental aspect of ethical medical practice and research. By ensuring that information is presented in a way that is easily comprehensible, we uphold the principle of respect for autonomy, enabling participants to make informed decisions based on a clear understanding of their involvement in the research.

The importance of using plain language in health communications is well-documented in literature. Studies have shown that complex medical jargon and dense information formatting can significantly hinder a participant's ability to comprehend essential details about clinical trials, such as the nature of the research, potential risks, expected benefits, and their rights as participants.^{v,vi} Employing plain language is about clarity and effectiveness; it aims to communicate information in a way that is accessible and understandable without oversimplifying or reducing the content's accuracy. This is particularly critical for populations with varying levels of health literacy, where failing to adjust the complexity of language can result in misunderstandings and potentially uninformed consent.^{vii,viii,ix}

Moreover, the organization of consent documents plays a crucial role in how information is perceived and understood. Structuring these documents so that they logically flow from general information to specific details, and separating distinct sections with clear headings, can assist participants in navigating the text more effectively. This structured approach helps individuals identify and understand key elements of the research without being overwhelmed by the volume of information presented.

To enhance the effectiveness of informed consent, the NHC recommends that the FDA encourage researchers to incorporate design elements that increase readability. This includes the use of bullet points for listing risks and benefits, tables for comparing treatment options, and diagrams to explain complex procedures or study timelines. Additionally, integrating feedback from participant focus groups on the layout and presentation of consent forms can provide valuable insights into user experiences and preferences, ensuring that the documents meet the needs of diverse populations.

Incorporation of Participant Perspectives

The NHC strongly supports the draft guidance's emphasis on incorporating the perspectives of participants into the development of informed consent materials and recommends the structured inclusion of patient voices in every phase of consent material development from initial drafting through to final approval. This ensures all materials are vetted for patient-centeredness and accessibility. Recognizing and valuing participant insights not only aligns with ethical research practices but also enhances the relevance and effectiveness of the consent process. By actively involving participants, especially from diverse backgrounds, researchers can ensure that the materials reflect the actual concerns and needs of those involved in the studies, thereby fostering trust in the clinical trial process and enhancing participant retention.

Incorporating participant perspectives involves more than just asking for feedback; it requires a deep engagement strategy that considers the cultural, educational, and socio-economic contexts of potential research participants. Studies have shown that when participants feel their views are genuinely considered in the planning and execution of clinical trials, there is a marked increase in trust and cooperation, leading to higher enrollment rates and greater compliance with study protocols.^{x,xii} This approach not only improves the quality of the research data but also reinforces the moral integrity of the research process.

Furthermore, the draft guidance's recommendation to consult with patient organizations in the development of consent materials is a vital step toward true patient-centered research. These groups can provide invaluable insights into the language and concerns that resonate most with patients, helping to tailor the consent process to be more understandable and relevant. For instance, insights from these groups can lead to the identification of common misconceptions or anxieties about clinical research, which can then be directly addressed in the consent materials. Patient organizations are uniquely situated to understand a breadth of perspectives within a patient community, such as those whose condition has high levels of heterogeneity.

To implement this effectively, the NHC recommends the FDA explicitly include in the guidance the recommendation that researchers establish ongoing partnerships with patient organizations and involve them early in the consent design process. This collaboration should extend beyond initial consultations to include reviews of draft materials and even co-development of content in some cases. Additionally, leveraging technology to facilitate broader community engagement through virtual town hall meetings or online surveys can further expand the reach and depth of participant input. However, engagement with patient organizations should be done in conjunction with direct engagement with participants, not as a substitute.

We recognize and appreciate the FDA's ongoing efforts to diversify clinical trial participation. It is crucial that this draft guidance aligns with and supports these broader initiatives, creating a cohesive framework that enhances inclusivity and equity in clinical research. Coordinating these efforts will maximize their impact, promoting an integrated approach to patient diversity and engagement.

Recommendations for Enhancement

While the NHC commends the FDA's efforts in revising the informed consent process to enhance clarity and accessibility, we also recognize opportunities for further enhancement to ensure the draft guidance fully realizes its potential in fostering a truly patient-centered approach. In the spirit of constructive feedback, the NHC proposes several key recommendations that aim to refine the draft guidance. These suggestions are designed to expand the scope of the draft guidance, address potential gaps, and promote a deeper integration of patient-centric practices in clinical research settings. By considering these enhancements, we can collaboratively work toward a consent process that not only meets regulatory requirements but also excels in engaging participants in meaningful ways.

Addressing Diverse Populations

The NHC strongly recommends that the FDA's draft guidance further emphasize strategies for addressing the needs of diverse populations in the informed consent process. This enhancement is crucial to ensure that informed consent materials are not only comprehensively understandable but also culturally competent, reflecting the diverse societal fabric that constitutes clinical trial participants.^{xiii}

To address this, the draft guidance should include detailed guidelines on developing informed consent materials that are sensitive to the cultural, linguistic, and educational backgrounds of potential participants. This involves more than just translating documents into different languages. It requires an understanding of cultural nuances, health literacy levels, and accessibility needs that may influence how information is perceived and understood. For instance, people from certain cultural backgrounds might have specific concerns or misconceptions about clinical research that need to be addressed directly in the consent materials to ensure clarity and trust.

The FDA should encourage researchers to collaborate with cultural competency experts and community leaders from diverse groups to co-develop these materials. This partnership can help ensure that the language, tone, and content of consent forms are appropriate and resonate with the target demographic. Additionally, the guidance could suggest methods for testing these materials with focus groups from the intended participant pool to gauge their effectiveness and make necessary adjustments before they are finalized.

Moreover, the guidance could recommend the use of visual aids and other alternative communication tools to bridge language and literacy gaps. Infographics, videos, and interactive digital content can play a significant role in making complex information more accessible and engaging for people with varying levels of health literacy.

To support these efforts, the NHC suggests that the FDA facilitate access to resources and training for researchers on how to effectively engage with and create materials for diverse populations. This could include workshops, webinars, and online resources that provide insights into cultural competence in research settings.

By expanding the draft guidance to include specific strategies for engaging diverse populations, the FDA will enhance the inclusivity and effectiveness of the informed consent process. This not only aligns with ethical research practices but also ensures that all participants, regardless of their background, have a clear and thorough understanding of their involvement in clinical research. This approach fosters a more equitable research environment where all participants can make informed decisions based on consent materials that reflect their needs and contexts.

Expansion on Innovative Presentation Methods, Including Development of Examples

The NHC recommends that the FDA's draft guidance on informed consent further elaborate on the use of innovative presentation methods. While the draft guidance commendably encourages diverse formats and technologies, providing more detailed examples and outlining best practices would greatly aid sponsors, investigators, and Institutional Review Boards (IRBs) in effectively implementing these recommendations. This expansion is crucial because the effectiveness of informed consent documents can be significantly enhanced through the thoughtful integration of digital tools and multimedia resources, which can cater to varying literacy levels and learning preferences among participants.

Interactive digital consent forms, for instance, offer an excellent opportunity for improving participant understanding. These forms can utilize embedded explanatory videos, pop-up glossaries for medical terms, and interactive Q&A sections that participants can engage with at their own pace. Such features make the consent process more engaging and can help ensure that participants fully understand the study requirements, procedures, and their rights. Additionally, real-time feedback mechanisms can be integrated, allowing participants to ask questions and receive clarifications seamlessly as they go through the consent materials.

Moreover, incorporating visual aids like diagrams, timelines, and infographics can help simplify complex research protocols into understandable segments, enhancing the likelihood that diverse populations, including those with various literacy levels and English proficiency, fully grasp the materials. Visual aids are not just supplementary but can be central to the comprehension process for many people. They provide a quick overview of the study's structure and timelines, which can otherwise be daunting in text-only formats. For instance, flowcharts can effectively illustrate the sequence of study procedures, and infographics can summarize the potential risks and benefits in a more digestible manner.

While best practices in this area also include the development of mobile-friendly consent applications that participants can access conveniently on their smartphones or tablets, it is essential to consider the specific demographics of the patient population recruited for the trial. These applications could provide push notifications to remind participants of key study dates and any follow-up actions they need to take, further integrating the consent process into the daily lives of participants. However, for those who may not be proficient with technology, alternative or supplementary methods should be provided to ensure that all participants can engage with the consent process equally. This tailored approach ensures that the use of technology enhances accessibility without creating barriers for those less familiar with digital tools.

To assist in the adoption of these methods, the NHC recommends that the FDA provide a toolkit or portal where researchers can access templates, software recommendations, and

case studies of successful implementations. Such resources would not only foster uniformity and compliance across different studies but also encourage innovation within the boundaries of regulatory expectations and ethical considerations.

By expanding the draft guidance to include detailed instructions and examples on innovative presentation methods, the FDA can help ensure that informed consent materials are not only informative but also accessible and engaging for all participants, regardless of their background or familiarity with clinical research procedures.

Clarification on the Role of IRBs and Ethics Committees

The NHC suggests that the FDA's draft guidance could benefit greatly from further clarification on the roles that IRBs and ethics committees play in supporting the implementation of enhanced informed consent practices. This clarification is essential as these bodies are pivotal in overseeing the ethical dimensions of clinical research, ensuring that studies adhere to the highest standards of participant protection and consent integrity.

IRBs and ethics committees have the authority and responsibility to review how informed consent documents are prepared and presented. Their role ensures that the consent process is not only compliant with regulatory requirements but also is reflective of ethical standards that prioritize participant understanding and voluntary participation. However, there is often variability in how these bodies interpret and enforce guidelines related to informed consent. By providing more detailed recommendations, the FDA can help standardize these interpretations and practices across different institutions and studies.

For instance, the draft guidance could include specific examples of best practices for IRB reviews of informed consent materials. These examples could illustrate how IRBs might evaluate the readability and comprehensibility of consent forms, assess the adequacy of information on the risks and benefits, and review the methods proposed for presenting complex information. Additionally, the guidance could suggest metrics or benchmarks that IRBs could use to measure the effectiveness of consent processes, such as participant comprehension tests or feedback surveys.

Moreover, the guidance could discuss the potential for IRBs and ethics committees to play a more proactive role in the continuous improvement of informed consent practices. This may include requiring periodic updates to consent materials based on new insights from ongoing research or changes in regulatory standards. It could also involve encouraging IRBs to facilitate training sessions for researchers on best practices in informed consent formulation and presentation.

To support these enhancements, the NHC recommends the development of a comprehensive training module for IRB members and ethics committees that covers the nuances of evaluating informed consent materials. This training could be made available through webinars, workshops, or as part of the certification process for IRB members, ensuring that they are well-equipped to make informed decisions that enhance participant understanding and engagement.

Expanding the draft guidance to include detailed roles and responsibilities of IRBs and ethics committees will not only enhance the consistency and quality of reviews but also reinforce the importance of ethical oversight in adapting informed consent processes to

better serve participants' needs. This approach will ultimately contribute to more ethically sound and participant-centered clinical research practices.

Greater Emphasis on Regular Feedback

The NHC recommends that the draft guidance emphasize the importance of regular feedback mechanisms in the informed consent process. Regular feedback is crucial for adapting and refining consent materials to reflect participants' evolving needs and understanding as clinical research progresses. This ongoing dialogue can identify areas where misunderstandings persist and provide insights into how documents can be improved to meet the highest standards of clarity and comprehensiveness. Moreover, as stakeholders gain a better understanding of the risks involved in the trial, such as the side effect profiles of the product, it may become necessary to update and re-obtain consent from the participants. This ensures that all parties are fully informed of any new risks or information that may affect their continued participation in the trial.

To effectively implement continuous feedback, the draft guidance should encourage sponsors and researchers to establish routine check-ins with participants at various stages of the clinical trial. These check-ins could be structured as brief interviews or surveys that probe participants' understanding of the consent they provided and their continued willingness to participate in the trial. This practice not only reaffirms the voluntary nature of participation but also respects participants' autonomy by keeping them informed and involved throughout the research process.

Moreover, the FDA could recommend the use of digital tools that facilitate real-time feedback. For example, electronic consent forms (eConsent) platforms can be designed to allow participants to ask questions and express concerns at any point during the study. These platforms can collect data on common areas of confusion or concern, which can then be analyzed to improve future consent processes. By leveraging technology, researchers can maintain an open channel of communication with participants, enhancing the responsiveness and participant-centered nature of trials.

Additionally, the guidance could suggest that IRBs play a role in reviewing feedback collection and response strategies as part of the initial protocol approval and during periodic reviews. This approach would ensure that feedback mechanisms adhere to ethical standards and genuinely serve the interests of participants. IRBs could require researchers to demonstrate how participant feedback has been used to modify and improve consent materials. This review should particularly focus on instances when significant changes are made, ensuring that these adjustments are meaningful and effectively address participants' concerns raised during the feedback process.

Finally, to support these recommendations, the NHC suggests creating a repository of best practices and case studies that illustrate successful implementations of continuous feedback in informed consent processes. This resource could serve as a reference point for researchers and IRBs alike, promoting a culture of continuous improvement and participant engagement across clinical research.

By emphasizing the importance of continuous feedback in the draft guidance, the FDA can help ensure that informed consent is not just a one-time formality but a dynamic, ongoing process that adapts to the needs and experiences of participants. This approach not only

enhances ethical standards but also fosters trust and transparency, ultimately improving participant satisfaction and the overall quality of clinical research.

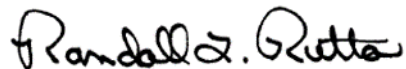
Education about the Clinical Trial Process

To demystify the clinical trial process for participants, the NHC further recommends the development of educational materials that elucidate the roles and interactions between drug companies, Contract Research Organizations (CROs), and IRBs. This educational initiative should aim to clarify the responsibilities and safeguards in place throughout the trial process, enhancing transparency and trust. Such resources would help patients understand not just the 'what' and the 'how' of clinical trials, but also the 'who' and the 'why' behind the operations, further empowering them to make informed decisions about their participation. Educational materials should be accessible in format and language and widely disseminated to reach diverse patient populations, ensuring comprehensive understanding across all groups.

Conclusion

The NHC appreciates the opportunity to provide comments to the FDA in response to draft guidance and supports the agency's initiative to improve the informed consent process. We look forward to continuing our collaboration with the FDA and other stakeholders to advance patient-centered health policy and practice. Please do not hesitate to contact Eric Gascho, Senior Vice President of Policy and Government Affairs, if you or your staff would like to discuss these comments in greater detail. He is reachable via e-mail at egascho@nhcouncil.org.

Sincerely,



Randall L. Rutta
Chief Executive Officer

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