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PERSPECTIVES

Enhancing Informed Consent Forms for Medical Devices: International Regulatory Guidance and Ethical Recommendations

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Abstract: Many developers of medical devices face a new reality with the increasing demand for clinical evidence that is generated by clinical investigations. This affects biotechnology companies, start-ups and academic research centres. The participants' informed consent form (ICF), which includes the participant information sheet (PIS), is among the critical documents that are part of the clinical investigation. While many countries around the world follow the principles of good clinical practice (GCP), there are country-specific variations of the ICF requirements. In addition, many of the country guidelines are focused on medicinal products rather than medical devices. Clinical investigations involving medical devices have their unique challenges and need additional guidance to help developers improve the ICF and PIS content. This review provides information on the latest regulatory recommendations from Europe, USA and Asia regarding the content of the ICF and offers practical advice from professionals experienced in preparing ICFs. It also includes some ethical considerations that must be taken into account.

Keywords: informed consent, medical devices, GCP

Introduction

In 2000, the USA Food and Drug Administration (FDA) conducted an inspection of the French manufacturer of breast implants, Poly Implant Prothèse (PIP). Among many other issues, they discovered that the company had used commercial silicon instead of medicinal silicon without notifying the authorities. The replacement caused increased rupture and leakage of the breast implants. As a result, the manufacturer lost its licence to sell their product in the USA and was under review in many other regions around the world. Similar issues were observed with another manufacturer – the Dutch company Rofil. In 2011 further investigations showed that the usage of unapproved silicon increases the risk of breast cancer in women with breast implants.[1]

These unfortunate developments triggered international review of the safety and efficacy assessment of all medical devices. Many devices that were exempt from clinical investigations were required to generate clinical data to support the safety and efficacy of the device. One of the biggest challenges that medical device manufacturers face is the lack of clear guidance and recommendations for clinical research with medical devices. The existing regulatory documents are general and designed based on drug manufacturing. While there is knowledge that is transferable to medical devices, this is not always appropriate. The implementation of the drug development ICF content and structure directly into medical device studies created additional complexity, including unnecessary information and ambiguity while overlooking important information about the devices. For example, often the list of adverse events in the informed consents is based on literature research of similar medical devices and not actual reported safety data from the device, however this is not clearly stated in the document provided to the patients.

The purpose of the recommendations in this review is to create a framework, which will help medical device manufacturers design master templates for their ICFs that then can be used globally. The regulatory requirements are changing fast in different regions of the world so the aim of this review is to provide structure. However, when developing local versions of the ICF, the latest regulatory requirements of the country or regions should be taken into consideration.

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Unlike the traditional drug clinical trials, medical device investigations often include vulnerable patients who require surgical or other intervention. This review touches on ethical issues when including vulnerable patients and provides guidance on considering the participant population when designing the ICF.

The regions in the scope of this review are the USA, United Kingdom, European Union, Malaysia and Taiwan. The regulators in North America and Europe are well known to set the international standards for conducting clinical research. Often other regions accept medical devices approved by the USA and European regulators and align their regulatory requirements to allow speedy access of new medical devices to their markets. Taiwan and Malaysia were selected as representative of Asian countries, however there was not much information on informed consent for medical device studies. This review could be used as a benchmark for companies planning to conduct clinical investigations on a global scale.

Methodology

The current review includes regulations and guidelines for the described regions as of Dec 2024. The selected regions have guidelines on developing informed consent documents, which is not common in many parts of the world. These regulations and guidelines were used to create an overview of the different regions. As a result, a table with the core ICF requirements was developed which covers all main recommendations of the regions – see Table 1. This is the first review in medical devices, which offers framework on an international level and combines regulatory and practical advice.

In addition, 3 long term members of the Welsh Research Ethics Committees (REC) in the UK (one of them an author) have provided feedback and recommendations on the content of the review. As members of REC, they are involved in monthly review of 3–4 clinical trials applications.

A member of the clinical research team at Southampton University NHS Foundation Trust in the UK was also involved in the final review and feedback, which provided the perspective of the hospital involved in clinical research. The clinical research teams are routinely involved in developing and reviewing ICFs for academic and commercial clinical trials.

The authors of this article are also routinely involved in preparation of ICFs for different clinical trials and indications. Many advice in this review are based on practical experience and feedback from Ethics Committees in the UK.

The Medical Device Perspective of the Latest United States Food and Drug Administration (FDA) Recommendations for the Content of ICFs

Over the years, ICFs have grown lengthier and more complex. This was partially due to changing regulatory requirements, but also to attempts from drug developers to cover all possible risks associated with new treatments. The result of this tendency is that ICFs have become so complicated that potential participants struggle to understand the objectives of

Table 1 Comparison Table on the Core Regulatory Requirements in the Different Regions

Informed Consent Information According to Regulatory Requirements	USA	EU	UK	Taiwan	Malaysia
Recommendation on layout and format	Yes	Yes	Yes	No	No
Information on risk, benefits and discomforts	Yes	Yes	Yes	Yes	Yes
Patient involvement recommendations	Yes	Yes	Yes	No	No
Transparency wording requirements	No	Yes	Yes	No	No
Information that could make the medical device culturally unacceptable	No	No	No	No	Yes
Personal information about the patient listed on the consent form	No	No	No	Yes	No
Information on prohibition and restrictions	Yes	Yes	Yes	Yes	Yes
Witness present at the consent process	Yes	No	No	Yes	No

the research. Developers of medical devices have followed the same trend when it comes to ICFs. The reasons for this could vary from using consultants working in drug development who are used to the lengthy and complex style to trying to mimic the drug studies as best practice. The US FDA is one of the many agencies that has pushed against this trend towards complexity. In its guidance from March 2024[2], it recommends creating a shorter and clearer ICF that will allow participants to more readily assess whether or not they want to take part in research. While the core requirements for the ICF remain, there are some additional aspects that medical device developers can consider when designing and developing their ICFs.

Size and Format of the ICF

In its guidance, the FDA recommends that the ICF should be short and that the information be presented in an easily accessible way for participants. It also encourages the usage of new technologies in the consent process. This is particularly important for medical device developers because often the devices could be better explained in a short video or pictorial. For example, an animation could be a highly successful approach in explaining a medical device to children in paediatric studies.

In terms of format, the US regulator explains that ICFs could use bubbles, rounded boxes creating a discrete unit of information, bullet points or two columns. However, it is important to consider the patient population and whether these methods will be appropriate. For example, text-to-speech software used by visually impaired people is not able to read tables and may have issues with bubbles or similarly formatted text. If the participants are expected to have some level of visual impairment, it is important that they are provided with an ICF in an appropriate format. In such cases, they can benefit from an audio recording or a bigger font on the written document. Participants with dementia may also benefit from simplified ICFs and repeated information.[2,3]

Developers are encouraged to reach out to patient groups and patient communities to discuss the best approach to consent.[4] They can also perform more in-depth analysis as part of their patient diversity plans and consider the level of knowledge of different participant groups.

Key Information

The FDA mentions that it is important for the key information to be included at the beginning of the consent, although it acknowledges that this information could vary between different clinical trials.[2] For example, if the medical device is implantable, it is important to include information on whether the device is available on the market, the location of the implantation, hospitalisation requirements and duration, and any risks from the procedure. Often the ICF contains a lot of information about the standard of care procedures and requirements, which will confuse patients and regulators as it is not clear what is part of the study. This is why medical device developers must remember that the ICF should contain information about the study and any standard of care should be mentioned briefly. The investigator explaining the study to the participant should discuss all available treatment options as part of the consent process.[5]

One of the biggest challenges in clinical investigations is avoiding technical language. Often it is nearly impossible to explain a complex procedure such as a heart implant without using terminology. A potentially helpful approach for the developers is to think about how they would explain the procedure to a child and try to use visual materials such as photos or graphs to help improve understanding. Educational videos that will help the physicians to explain the procedure to participants could be very successful in improving understanding of the clinical trial and also help physicians to explain complex procedures.[2,5]

The recommendation to provide sufficient details is another big challenge for developers. Many tend to allow themselves to be carried away with details, which inevitably makes the ICF more complex and confusing to participants. Remembering that the participants will not necessarily have a degree in science could help developers to stay focused on the content. However, despite there being a large amount of literature recommending what information should or should not be provided in an ICF, it is important to recognise that patients are not a homogeneous group, and the appropriate amount or detail of information preferred by a patient may differ on a case-by-case basis. It is therefore important that investigators are knowledgeable about the study and on hand to answer any questions from patients seeking further information.[2,5]

In terms of providing the patient with trial and device information, it may be preferable to provide the PIS document first, separate to the ICF, in order to avoid accidental signing of the ICF without first confirming understanding by experienced researchers at the point of face-to-face consent. It is good practice for researchers obtaining consent to check the participants' comprehension by asking them some simple questions at the end of their discussion of the clinical investigation, and prior to patients signing the ICF. This will allow them to identify parts that are not clear to ensure that patients are fully informed and to improve the PIS and ICF by revising them.

If the clinical investigation is collecting data to train artificial intelligence (AI) algorithms, it is important that this is clearly explained in the PIS. Any use of AI to collect data as part of a medical device should be explained in appropriate non-technical language.

The ICF must specify if any data will be shared with third parties, for example, for data analysis, vendors supporting travel and accommodation, etc.[2] Including this information is critical to making participants aware of whether their data will be transferred to different regions with different data protection laws.

Risks, Benefits and Discomforts

Another big challenge for developers is assessing the risks of the device. It is standard practice to include in the ICF all possible risks, including disease-related risks. Often there is no separation between the disease-related and medical device-related risks, which makes it difficult for participants to obtain a realistic picture of these risks. Separating disease-related and device-related risks could have a significant benefit for the clarity of the ICF.

In its guidance, the FDA mentions that participants must be made aware of the risks to others.[5] For example, if the medical device is an implantable device that emits radiation, the ICF should contain information on whether there is a risk to others living or working with the participants or those who have frequent contact with them (for example, healthcare providers).

It is important to mention that the FDA recommends that when providing alternative treatments, participants must be informed of the risks and benefits of these treatments.[5] For example, if the medical device is robotic surgery, the ICF should contain information on the risks and benefits of the open surgery option.

While placebo-controlled clinical investigations are not very common in medical devices, such studies do take place. In such cases, participants must be made aware of the risks of having sham procedures and how these risks will be mitigated. Developers also need to explain to participants how they will maintain the blinding of the study – for example, participants may be asked to wear eye masks during the procedure or listen to music on headphones so that they do not see and hear what the physicians are doing during the procedure.

Explaining benefits is another challenge for developers, as the majority have a tendency to downplay the benefits, even though they already have clinical evidence for these benefits. This is often the case with medical devices that have been on the market for a while but are studied for new indications. The reason for this could be that developers are extra cautious or feel that they should do it since this is a research project.

In terms of risks and discomforts, the FDA has provided recommendations to include those that are related to the actual procedure or are additional to the standard of care.[2,5] This is another area that is misunderstood by developers, who tend to include all possible risks and discomforts in a similar fashion as for drug studies. Often these risks are based purely on literature research and have never been observed with the medical device.

If the clinical investigation is collecting data to train AI algorithms, it is important for participants to be made aware of all potential risks – for example, the fact that the data cannot be removed from the model and that any personal data collected could be unexpectedly produced by the model. This information needs to be presented in a balanced manner without any technical language to help participants understand the risks. A similar approach should be used for other studies collecting data for AI models. Participants need to be made aware that the company intends to use the data for such purposes in the future. Clarity and transparency are the keys to proper informed consent.

Patient Involvement

In the patient involvement guidelines, the FDA discusses how patients' willingness and unwillingness to accept certain risks associated with the medical device could be useful information in helping the agency in the overall review of the

device risk and benefit assessment.[4] Demographic information could be very beneficial in analysing the patient population and their views on the risks. Such analysis could also be very helpful for FDA assessments. The information could be captured by participant surveys or documented as part of their visit attendance in the form of an unstructured interview. In some cases, the information could be gathered at the point of consent, depending on the device type. It is important to remember that treatment preferences may vary among physicians as well, which could affect the participants' decisions.

The FDA guidelines clarify that collecting participants' feedback on the medical device is relevant not only to devices used directly by participants but also to devices affecting the quality of life or unmet needs of the participants.[4]

The Medical Device Perspective of the Latest United Kingdom and European Union Recommendations for the Content of ICFs

Writing a good ICF that includes a patient information sheet remains an ongoing challenge, despite the updated United Kingdom (UK) Health Research Authority (HRA) guidelines.[6]

One of the very first steps in designing a high-quality ICF is to understand the study protocol design and its targeted population. In principle, companies like to include all the necessary elements, without making it overwhelming and/or overpowering for the participants while providing a clear concept of the study. An ICF should serve its purpose as much as possible rather than be a tick-box exercise to satisfy the regulatory authorities. Therefore, it remains a constant challenge to find the right balance, and it may require some experience before the developers feel comfortable and confident in preparing, especially in the area of clinical investigations, where the level of technical information could be higher and more complex.

Although medical device developers might prepare a master ICF, it is important for reviewers to adapt the whole document for its actual purpose, by adapting and transcribing more complex information for participants with average clinical and technical understanding while considering the country-specific recommendations. This section discusses the regulatory expectations in the UK and European Union (EU). Below are some elements that should be considered.

Language

It is important to simplify the use of technical and medical terminology as much as possible and to avoid jargon.[6] The developer of the ICF should use lay language explanations so the key information is easily understood and visualised where appropriate. Although it is typically necessary for the ICF to include some technical and medical terminology, it is important to be selective on the technical content by considering how detailed and lengthy the information should be for a potential average participant to understand the main points of clinical design and purpose. Where possible, technical jargon should be replaced with a heavily descriptive format, ideally making it an "Easy Read" explanation to the level of younger adults. The reviewer should consider if it is appropriate to use electronic media since there is still a population with low technology literacy and limited internet access. Therefore, it is important to have alternative formats without ignoring the preference of the whole patient population, as some may enjoy using electronic media. EU recommendations by the European Medicines Agency (EMA) are that participants have face-to-face discussions with the physicians conducting the study as part of the consent process; however, they also accept online face-to-face real-time discussions.[6] When opting for online consent processes, researchers should consider having paper back-up in case of difficulty accessing Wi-Fi for patients at home or staff in hospitals, as this cannot always be relied upon.

Use of Diagrams, Pictures, Short Videos, Tables and Suitable Animated Illustrations

It is very helpful to incorporate relevant and easy-to-comprehend visual tools to enhance participants' comprehension of the study design, especially for new medical devices and processes with which participants may not be familiar. This can also help to minimise overly worded ICF content. Applying such tools contributes to visualising protocol design processes with less effort and greater efficiency while at the same time providing more concise and purpose-made information content.[6]

Layout/Format

It is always recommended that ICF document design starts with a Lay Summary at the beginning that introduces the participant to the key points about the research – such as study title, sponsor, specified participants' involvement, place and time of the study, the main question and why the research is needed – using plain language, shorter sentences (up to 20 words) and shorter paragraphs (up to 3 sentences).[6]

ICF information can often be lengthy and could discourage individuals from carefully reading through it. Therefore, avoiding many details on topics that participants might not be as interested in is good to consider. For example, there is no need for a lengthy explanation of the standard of care procedures for patients who have chronic disease and have extensive experience with the standard of care requirements. It is important to check this balance with patient groups and charities, such as the UK Patient and Public Involvement and Engagement (PPIE) group.[7] Layering the study information would also assist readers to feel more engaged and better visualise the processes. Proofreading also helps a lot in removing words that are overly technical or unintentional repetitions and can assist in composing the document content in a clearer and more concise way, offering the reader a better understanding of the study complexity.

Depending on the clinical investigation type, there are different ICF expectations:[6]

1. ICF for adults with capacity to consent.
2. ICF for minors (under 18 years of age, of different age groups) or people without capacity to consent. There will be different versions for the appropriate age groups. Vulnerable people without capacity or with fluctuating capacity also need to have ICFs written at an appropriate level.
3. ICF for the research team. This is in cases where information is collected from the researchers.
4. ICF for pregnant partners. This is when information is collected from a pregnant partner, including information about the foetus(es)/baby/babies.
5. ICF for a parent/guardian/legal representative.

Adolescents and people without capacity or with fluctuating capacity require a child-level approach with the use of simple and less wordy information, plenty of appropriate simple illustrations and, where possible, a short video, while trying to use friendly language. The complex legal type of wording that is used in some adult ICFs will not be appropriate in such cases.

Although these are recommended points for any standard ICF, it is always good to emphasise and recap key points in well-formatted documents, such as by maintaining well-spaced pages, using shorter paragraphs and avoiding chunky headings. In addition, good practice is to use recommended font types (Arial, Calibri, Verdana Helvetica) of sufficient size (12 points at least), emphasise the most important details in bold and, where appropriate, use bullet points and numbered lists.[6]

It is recommended that translated versions of the patient information sheet are reviewed by native speakers who can make sure the wording and the translation are adequate. EU countries prefer professional translators with the appropriate certificates of translation.[6]

Patient Involvement

Involving public contributors such as patient groups and charities in the review process and design helps not only patients but also regulatory agencies, which will have more reassurance that the opinions of potential participants have been considered. Ethics committees tend to appreciate and recommend patients' involvement in ICF preparation. Taking extra time and effort to tackle these recommendations will help to minimise the chance of requests for additional information during the regulatory review process. Therefore, purely in the interests of time, it is important to follow up on four recommended principles for using public involvement: 1. involving the right people, 2. involving enough reviewers, 3. describing how it helps, and 4. not overdoing by involving too many participants or participants who are not relevant.[6]

Occasionally, reviewers outside the UK can also be considered, especially in a multistate study and where the sponsor is internationally based. Considering public involvement recommendations (approximately 2–3 people) is pivotal in the review process to reach a well-balanced document that will be fit for purpose for the average research participant.[7]

Potential Risks and Inconveniences

Potential risks and benefits are one of the important sections of the ICF, allowing participants to receive details in a clear and lay-friendly way. Participants should feel comfortable with the clear and balanced presentation of the risks and benefits. It is also recommended to mention what other existing alternative treatments and procedures for the targeted indication are available so that participants can be aware of all the options.[6]

Potential Benefits

This section should also clarify any financial interests and benefits, and describe what and how exactly they apply to a study – for example, if travel expenses are covered, if patients are paid a stipend, etc. Some participants can be under the impression that research participation automatically offers certain financial support and covers some parts of participation (for example, travel costs). Often in studies that mimic the standard of care and where research risk is minimal, participants may not be automatically entitled to any financial support unless there is any incident resulting from direct research procedures, in which case the study insurance would apply. This is why the contact information for questions, injury reporting and emergency situations should always be added in, including the compensation, where applicable. In some EU countries, Ethics Committees may have concerns about coercion and could request that independent physicians be involved in clinical investigations involving surgical interventions. Since the surgeons are the ones who consent the patients for the study, all efforts should be made to avoid any possible influence. For example, consenting clinicians should ensure that patients are made fully aware of their right to participate or to decline participation and that not taking part will not prevent them from receiving standard of care treatment. Patients should be given a balanced view of potential benefits and risks of participation, and sufficient time (at least 24 hours) to come to a decision, with the opportunity to discuss this with friends and family. Particular caution should be taken with vulnerable patients, such as prisoners and elderly people, who may be more easily influenced to participate. Those obtaining consent from vulnerable populations should consider also obtaining consent from a legal representative if the patient lacks capacity to have sufficient understanding to make a decision themselves.[6]

Transparency

Transparency has gradually been receiving more attention and has become an area of great focus in the ethical part of research. Currently, there are expectations that every study will be registered in the public domain. The public domain will contain information about timelines, results, safety profiles, the history of previously performed studies and relevant research information, sharing collected research data and tissue (including for future studies). Although there are cases where companies may request temporary deferral due to patient concerns, the tendency is for all clinical investigations to be published on a public database, and this should be disclosed to all potential patients in the ICF.[6]

The transparency requirements in the UK include the use of HRA-recommended wording that covers the General Data Protection Regulation (GDPR) and other common patient confidentiality elements.[6] Using the recommended transparency wording helps medical device developers, during the approval processes, to avoid being asked to revise these ICF sections. While the GDPR is currently the same in the UK and EU, the overall approach to consent is different, and unlike the EU, the UK regulatory authorities do not consider written consent as the only provision for collecting data. This means that data collection in the UK could be under the public interest clause rather than purely participant consent signature. Furthermore, EU countries require much more detailed information about data protection and processing, including information on European data protection officers and specific details on where the participant information will be handled.

It is also important to keep in mind that a study's informed consent is an ongoing process, as additional information can become available that potentially affects patients' health and clinical procedures. New information should therefore always be acknowledged and provided to participants in a timely manner. The need for participants to consent on an

updated document could vary depending on the study. For example, if the study is testing a single-use blood test and new information becomes available at a later stage, it may not be necessary to re-consent the participant but only to inform them in writing and confirm that they are still interested in continuing their participation. It is the study site's responsibility to ensure that they have robust processes in place to implement the entire consent process. This includes clear documentation of consent discussions in the medical records and correct site file maintenance of initial and updated consent forms.[6]

The Medical Device Perspective of the Latest Taiwan and Malaysia Recommendations for the Content of ICFs

While the format and information expected to be included in the ICFs for Malaysia and Taiwan do not deviate from the GCP recommendations, there are some country-specific requirements that need to be considered.

Malaysia Country-Specific ICF Requirements

The patient information sheet in Malaysia needs to contain information if there is any kind of randomisation in the clinical investigation, and the process must be explained to the participants.[8] While placebo clinical trials are relatively rare, sometimes there are studies comparing investigational medical devices with standard of care practices. In such cases, the number of patients allocated to the different treatment groups must be defined.

The ICF must also contain information on all invasive procedures involved in the study.[8] This is not limited to surgery only, but should include data collection, biopsies and other diagnostic procedures that could be classified as invasive.

Another important piece of information required is the risk to the embryo, foetus and breast-fed infants if participants who are pregnant or could become pregnant are considered for the study. Depending on the type of device, if the developers need information about the baby, this should be clarified in the ICF.

The regulators in Malaysia expect that if there are no benefits from the clinical investigation, this should be clearly stated in the ICF.[8] This could be relevant for studies collecting user experience information via surveys and interviews, as although patients may welcome the opportunity to express their views on their experiences, there may not be a direct benefit for them in terms of the healthcare they receive. The ICF should also outline the compensation and/or any alternative treatments in case of injury. For example, this could be information that the study has insurance covering such costs.

The ICF in Malaysia should also include any information about the medical device that could make it culturally unacceptable.[8] For example, the Muslim population must be made aware if products not accepted by their religion are used in the development of the medical devices.

It is recommended that any participants who are not able to consent for themselves (for example, children under 16 years of age) are provided with adequate information for their understanding of the clinical trial.[8] If they are capable of signing and dating an assent form, they should be encouraged to do so.

Taiwan Country-Specific ICF Requirements

Taiwanese authorities have some very specific requirements regarding ICF content.[9] For example, the ICF should contain a list of all sub-investigators involved in the study, and details about the patient: name, age, sex, contact details and relevant medical history that makes them eligible for the study.[10]

The ICF should also contain information on whether the medical device is approved for use in Taiwan or whether it is used off-label for the specific indication.[10] In order to support better transparency, the ICF must include the main eligibility criteria. This is also done to help patients have better understanding of whether they are eligible for the clinical investigation and to make sure they discuss any potential issues with the researchers. However, including all eligibility criteria with a great deal of terminology and technical terms will not be appropriate, and these should be adapted to the level that the participant can understand.

Another important section includes any prohibitions, restrictions and compliance requirements for the study.[10] These could be, for example, any dietary or fasting requirements prior to the procedure.

The ICF should also include information on any possible reasons for discontinuing the clinical trial; for example, significant delay in recruitment could be a reason for early termination.[10]

The expectations for participants who cannot read are that the researchers will provide an impartial witness not related to the clinical investigation team who will read the information to the participants and provide support.[10] In such cases, the participant or their legal representative is still expected to sign the ICF or use a finger print.

The authorities do not allow legal representatives to represent participants in non-therapeutic clinical trials, unless the study meets specific requirements.

Ethical Considerations for Medical Device Informed Consent

As with any clinical trial, there are numerous ethical issues to consider when obtaining informed consent for clinical investigations. For informed consent to be considered ethical, participants must be given sufficient information about the research study and device, be capable of understanding relevant trial information and be able to make a voluntary decision to participate as per GCP expectations. These requirements are typically addressed in the PIS and ICF documents. However, due to the nature of the patient population in clinical investigations, involving patients requiring medical intervention, many participants may lack capacity to consent due to their health, or may not have the opportunity to consent due to situational factors such as emergencies and time pressure.[11] Therefore, it is important for researchers to implement clear frameworks for medical device trials to obtain a representative sample and ensure the wellbeing of patients.

What to Disclose?

When developing an ICF, researchers must consider the information being given to the patient to ensure they are sufficiently informed to make a decision to participate. Most importantly, the potential risks of the procedure must be disclosed and be ethically justified by the potential benefits. According to the "interest principle" the interests of the participants are of utmost importance in research, and therefore consent alone is insufficient if the risks imposed on the participants do not align with their interests.[12] As with any experimental product, there is often limited safety and efficacy data at the time of consent, which has seen patients consent to high-risk medical device procedures without pre-existing knowledge of the outcomes.[13] Furthermore, the increasing use of AI in medical devices, which may not have a risk of causing direct harm to a participant, means researchers are faced with ensuring that patients understand potential "performance-related" risks, such as incorrect information outputs and data breaches.[14]

Consequently, the development of an informative ICF that clearly and thoroughly sets out the risks, benefits and purpose of the trial is essential for ensuring that participants have the opportunity to act according to their best interests, and ethical consent is obtained. Updated EU guidelines released in 2014 clarify what is regarded as a clinical benefit for a medical device and should be used by researchers where appropriate when disclosing this to participants.[15] The guidelines also highlight that although not all clinical benefits and risks of a medical device can be predicted, information should be drawn from similar medical devices already on the market or from retrospective data of patients receiving the device for other purposes.

Participants should also be made aware of other trial procedures aside from the medical device itself, such as imaging (MRI, CT, X Ray), which carry their own risks. They should also receive information on certain requirements for medical devices such as access to Wi-Fi or a smartphone. It is important to clarify this as not all patients will have access, so this may impact their ability to participate. Furthermore, the ICF should include details of patients' right to withdraw and the consequences of this. Although withdrawing will not affect their right to receive alternative treatment, they may have to undergo further procedures to remove a device, and should be informed of this if so.

Promoting Capacity to Consent

Since medical device studies are investigating medical interventions in patient populations rather than healthy controls, individuals approached to participate in clinical trials may have limited or fluctuating capacity to consent due to the health problem for which they are receiving the intervention, or a comorbid condition. For example, patient populations for neural device studies may have impaired cognition, which can limit their ability to understand research procedures sufficiently to consent.[16] In such situations, clinicians must perform an appropriate assessment of capacity to consent as

part of the Mental Capacity Act (2005) or other country-specific regulations regarding patients who do not have capacity to consent.

A recent Trial Working Conduct Group[11] highlighted the importance of having a clear assessment process for determining capacity to consent, which is laid out in trial protocols and uses standardised testing tools, such as the MacArthur Competence Assessment Tool for Clinical Research.[17] In cases where the patient is deemed to lack capacity to make an informed decision, consent can be sought from a legal representative acting in the patient's best interest, such as a friend or family member, although this comes with its own considerations, discussed later in this article.

Alternatively, patients may have capacity to consent but have limited ability to communicate their decision, for example, stroke patients who have communication difficulties such as aphasia or apraxia,[18] or where there is a language barrier between patient and clinician[19] that means confirming understanding of trial procedures or completing an ICF is difficult or impossible. This potentially poses a risk of consent-based recruitment bias, whereby the study sample is not representative of the true patient population due to exclusionary consent pathways.[20]

In order to address capacity and communicative barriers in consent to medical device studies, many researchers have suggested alternative communication tools for ICFs to create an adaptable consent pathway tailored to individual patient needs. For example, many trials are now using electronic informed consent (eConsent), which uses digitalised multi-media trial information in place of, or in addition to, ICF, and can be made available in different languages.[21] This can be particularly useful for medical device studies, where patients who probably have limited medical knowledge can view demonstrations of trial procedures to ensure their understanding.

Such eConsent methods are associated with an improved understanding of medical procedures, risks and benefits,[22] and can be used to enhance decisional capacity of prospective trial participants.[23] Importantly, the Trial Working Conduct Group highlight that trial information should be adaptable to differing communication abilities across all trials, not only those that anticipate a need for them, as communication difficulties that limit consent accessibility can be present in any population.[11] When developing guidelines for these alternatives, the group also emphasises the importance of co-producing with individuals with communication difficulties to ensure their perspectives are considered, and adaptations can be tailored to each participant's communication needs.

Furthermore, it is especially important to ensure that all patients are given equal opportunity to consent, regardless of conditions such as cognitive impairment or intellectual disabilities, which often see patients excluded from trials due to the additional time and resources required to provide trial information and complete ICFs.[24] Omitting patients with limited capacity may lead to unrepresentative samples, biased results and limited evidence-based healthcare, thus furthering existing health disparities within these populations. The National Institute for Health and Care Research (NIHR) INCLUDE Impaired Capacity to Consent Framework[25] should be used to help researchers design trials that are more inclusive and ensure resources are directed towards facilitating capacity in those who are impaired.

Situational Factors Requiring Proxy Consent

Time may also be an important consideration during the informed consent process for clinical trials of medical devices, as these devices are often being trialled in emergency procedures where there is insufficient time to obtain consent from the patient and the treatment is considered life-saving. In these situations, consent may be sought from a legal representative, such as a family member or friend, or a parent if the patient is under the legal consent age. Such representatives should act according to the patient's best interests or any prior wishes the patient may have expressed regarding participating in research. However, in some cases, there is no opportunity to obtain consent from the patient or representative, and clinicians must make decisions to implement a medical device without the patient's prior consent, known as deferred consent.

When obtaining consent from a legal representative or guardian, this first requires appropriate identification of an individual to act on behalf of the patient, and their ability to clearly consider the investigational device and to determine the preferences of the patient. Concerningly, legal representatives or guardians incorrectly predict patient wishes in around a third of cases[26] and this can a have significant impact on patient physical and mental wellbeing if the patient subsequently expresses their wish to remove the medical device once they regain decision-making capacity,[27] particularly due to the invasive nature of many of these devices.

Although proxy consent comes with issues, it is undoubtedly necessary in some cases where life-saving care is required. Legal representatives or guardians must therefore receive adequate information about the experimental medical device through clear ICFs, including an explanation as to why it is not possible to seek direct consent from the patient, as it is unlikely they will have pre-existing understanding of the device or have discussed preferences with the patient beforehand. Previously, little guidance has been given on how a representative should come to a decision. However, decision aids have recently been developed that could help researchers to support legal representatives or guardians by informing them of their role as decision maker and encouraging consideration of the patient's values.[28]

Furthermore, the UK HRA has published the CONNECT guidance[29] for research in emergency settings, which sets out circumstances in which patients can be enrolled on clinical trials without their prior consent. Researchers should consult this guidance during pre-trial design and during discussions with legal representatives or guardians and should understand the emergency circumstances that allow for intrusive research to be performed without prior consent from a patient or their representative. In some countries, such as the UK, there are independent expert organisations (Confidentiality Advisory Group (CAG)) that could provide advice in such cases. It is important for researchers to treat consent as an ongoing process, so in situations of deferred consent, patients should always be approached for consent when they regain decision-making capacity and be given access to an ICF.

Discussion

Developing a good-quality ICF is critical to making sure that participants understand the purpose of the research. On the other hand, having a poor-quality ICF could put potential participants off the idea of taking part in research, either because they cannot understand the research or because they misunderstood the value or risks. However, the quality of the ICF is just one part of the problem.

As this is an up-and-coming area of research, it is important for medical device developers to consider that not everyone involved in clinical research has the knowledge and experience to consent participants and document it in the correct way. There are many physicians, such as surgeons, who may not have had exposure to clinical research but are now researchers in clinical trials. These physicians will have GCP training, but this does not mean that they are familiar with the expectations of consenting participants for clinical research. For example, many may not be familiar with the fact that, unless it is an emergency, participants should be allowed at least 24 hours to consider their participation and that this recommendation is in place to minimise the risk of coercion by forcing the patient to decide on the day of the procedure. This time period also allows patients sufficient time to process and consider the information presented to them, discuss with others and make a fully informed decision regarding their participation.

Developers must make sure that all team members involved in obtaining informed consent are aware of common issues, such as signing the wrong ICF version in error, missing signatures, not clearly indicating corrections, wrong dates, etc. The researcher consenting the participant needs to carefully check the consent document and make sure it is completed correctly. The developers need to make sure that the researchers have the final approved version of the ICF. Reconsenting on updated ICFs is another significant issue since it could easily be missed by investigators. They may not be aware that there is a new version for the participants to sign or that the patients do not attend the hospital frequently enough for the researchers to see them in person to sign the consent in a timely manner. Developers must discuss these potential complications very early in the study and consider alternative arrangements, such as electronic informed consent, video discussion, etc., to combat this issue. While including participants and their families in the ICF review is very valuable, it is important for developers to involve the correct patient population in the review. Often patients with general medical conditions are contacted for feedback on research involving patients with rare diseases, and while their views are important, they may not necessarily represent the views of the targeted population.

While involving different ethnic groups could be challenging in terms of translation of ICFs, the developers should consider all available options that could support language versions of the ICF, such as using AI tools for language translations, and electronic consent forms.

Since more and more medical device studies are entering global clinical research, it is pivotal to address these key ethical points in light of improving and further developing the management of research while seeing it as a new chapter within the framework of clinical research ethics. Improving the informed consent process in clinical trials of medical

devices is crucial for ensuring ethical standards and protecting patient autonomy. The correct content and amount of information has the ability to enhance patient decision-making capacity, whereas a large amount of overly complex medical terminology may discourage a patient from making an informed decision according to their own best interests. Therefore, it is important to tailor the information as much as possible to the individual patient in accordance with the principles of "patient-centred care".[30]

The unique challenges posed by medical device trials, such as patients' varying capacities to consent and the urgency of certain medical interventions, require careful consideration by researchers who are developing ICFs, particularly those who have not previously worked in clinical research. This includes addressing potential risks, providing alternative communication tools, and using available guidelines and frameworks. Additionally, when proxy consent is required, clear guidance and decision aids should be provided to legal representatives to help them act in the best interest of the patient. Ultimately, by treating consent as an ongoing process and continually refining consent procedures, researchers can uphold the highest ethical standards while advancing medical device innovations.

The ICF needs to be clear, concise and fit for purpose. It is a document that must change and improve with time and not simply a template in the company's procedures. Involving clinicians and patients early in the development of the ICF is a critical step in creating a good-quality document that will be useful for future participants. Another step in the ICF development is to consider all country-specific guidelines for the country where the document will be used to make sure that the final ICF meets all the regulatory expectations. The proposed checklist below is designed to help as a guide to improving ICFs in medical devices (Table 2).

Table 2 Proposed Checklist

No.	Recommendations	Yes	No	Not Applicable
1	Include a simple, one-page summary of the study's purpose, procedures, risks, and benefits.			
2	Add pictures, graphs, or videos to assist participants in understanding the research.			
3	Ensure the ICF is accessible for participants with impairments, disabilities or language barriers.			
4	Emphasize that participation is voluntary.			
5	Explain that participants can withdraw from the study at any point without consequences, and implications of this for the medical device.			
6	Provide detailed information about standard care procedures as part of the study.			
7	Clearly explain if data is used to train AI algorithms and any related risks or future data uses.			
8	Mention if data will be shared with third parties, such as for data analysis, vendors supporting travel and accommodation, etc.			
9	Clearly outline both disease-related and device-related risks in separate sections.			
10	Provide information about the risks and benefits of alternative treatments or procedures.			
11	Written in the primary languages of the target participants and uses simple, non-technical language.			
12	Include detailed explanations of care procedures, especially for participants with chronic diseases.			
13	Provide contact details for inquiries, injury reporting and emergencies.			
14	Outline any study-related prohibitions, restrictions, and compliance requirements.			

(*Continued*)

Table 2 (Continued).

No.	Recommendations	Yes	No	Not Applicable
15	Include information on any possible reasons for discontinuing the clinical trial.			
16	Emphasize that participation is voluntar.			
17	Explain that participants can withdraw from the study at any point without consequences.			
18	Include a plain language description of risks to an embryo, fetus, or nursing infant, if the participant is or could become pregnant.			
19	Clearly state any compensation offered and explain what medical care will be provided in case of injury.			
20	Ensure the ICF addresses the needs of vulnerable populations, including minors, the elderly, and those with impaired decision-making abilities.			

Conclusion

In conclusion, developing a high-quality ICF is an essential component of ethical clinical research, particularly in the rapidly evolving field of medical device trials. A well-crafted ICF ensures that potential participants fully understand the research purpose, risks and benefits, ultimately empowering them to make informed decisions. Addressing the challenges unique to medical device research – such as the involvement of inexperienced clinical investigators, the urgency of certain interventions, and the need for clear, patient-centred communication – is critical for maintaining ethical standards.

By incorporating early feedback from both clinicians and patients, tailoring content to patient-specific needs, and adhering to local regulatory requirements, researchers can significantly enhance the effectiveness of ICFs. Employing innovative solutions such as electronic informed consent and clear guidance for proxy consent further strengthens the process.

Ultimately, the ICF should be a dynamic document that evolves alongside regulatory and ethical standards and trial amendments, acting as a facilitator of patient autonomy and ethical clinical practice. By prioritising these measures, developers and researchers can uphold the integrity of clinical trials, foster trust with participants, and drive meaningful advancements in medical device innovation.

An international collaboration between regulatory agencies, Ethics Committees, manufacturers, researchers and patients can help to improve the consent forms for patients participating in medical device investigations. There is a need of special guidelines for documents development in medical devices studies.

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