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Translation of Informed Consent in Clinical Trials

Informed consent is a key legal and ethical step to all clinical trial proceedings, and the translation of related documents must be held to an extremely high standard.

Every day, new breakthroughs are made in modern medicine, and clinical trials are a vital component of the process that brings those developments to the public. Given that clinical trial participants often sample completely new drugs and medicines, ensuring their informed consent to participate in research is ethically and legally integral to clinical trial proceedings.

As with practices in many industries in our rapidly globalizing world, clinical trials are beginning to be outsourced. Studies designed in the United States could be conducted in India, and drugs developed in Germany could be administered in Mexico. Because of these international connections, and the medical and legal jargon that is often necessary for explaining procedures or the effects of a particular medicine, the danger of misunderstandings increases exponentially.

Participants in clinical trials must be accurately informed of the precise details of the study in a way that they can understand, as miscommunications about the effects of a drug could have disastrous and even life-threatening effects. Thus, the translation of informed consent documents must be held to an extremely high standard. Informed consent document translation can face a number of challenges resulting from a lack of linguistic or even cultural equivalents for key concepts, and the fact that some participants may not be proficient in a country's official language must also be taken into account.

Background

Biopharmaceutical clinical trials have historically been predominantly carried out in countries in North America and Western Europe, but a shift is rapidly occurring as a growing number of clinical trials are being carried out in "emerging" nations and regions, such as China, India, Eastern Europe, and Latin America.[1] The U.S. still holds the lion's share of active trial sites worldwide, with more than eight times the amount seen in Germany, the next highest contender.[1] Further, although 66% of all trial sites are still located in the top five traditional countries (U.S., Canada, Britain, Germany, and Australia), countries in emerging regions are starting to pick up the pace of clinical trial development.[1]

The establishment of international guidelines for clinical research may play a role in the expanding globalization of clinical trials, the rise of contract research organizations in emerging regions, and, as with other outsourced industries, the ability to recruit a large number of participants at a lower cost.

As of 2011, 8.9% of clinical trials registered with the U.S. government were in Asia, 7.4% in Latin America, 7.1% in Central and Eastern Europe, and 1.6% in Africa.[2] These numbers continue to grow as nations and regions increase their trial capacity. In fact, the trial capacity of several Eastern European, Latin American, and Asian countries is rapidly approaching that of the more traditional regions from a minimal starting point just a few years ago, indicating that the global shift in location of clinical trials will only become more pronounced as time goes on.[1]

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The Urgency of Informed Consent

Patients must be well informed about the potential risks and benefits of any major medical decision, especially the decision to enroll as a subject in a clinical trial. Although such studies are strictly regulated to ensure that drugs are generally safe by the time they reach human test subjects, experimental new drugs could have adverse effects on patients who are taking other medication(s) or who have preexisting conditions. Failing to properly inform prospective subjects of the potential risks of participating in a clinical trial could result in patient illness, extreme discomfort, or even death.

Thus, patients need to be aware of the potential risks of a trial. As a key legal and ethical step to all clinical trial proceedings, informed consent is tightly governed by both U.S. and international standards, including the Council for International Organizations of Medical Sciences' International Ethical Guidelines for Biomedical Research Involving Human Subjects and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use's Guideline for Good Clinical Practice.[3]

The World Medical Association's 1964 Declaration of Helsinki, while not a legally binding document, is the most internationally recognized standard for human research ethics, and is reflected in the legislation of clinical trial regulations in nations around the globe. In its original wording, the Declaration of Helsinki states that:

> [E]ach potential subject must be adequately informed of the aims, methods, . . . the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time . . . . After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely given informed consent, preferably in writing.[4]

FDA Expectations

The U.S. Food and Drug Administration (FDA) requirements for informed consent share many of the same tenets of the Declaration of Helsinki. True informed consent must ensure that prospective subjects are accurately and impartially informed of the potential risks and benefits of a trial, and that the subjects maintain their rights and do not waive the investigating body from liability. Consent must be given freely, without misleading influence or coercion. Information may be provided in written or oral form, although consent itself is required in written form.

In addition to these standard criteria for informed consent, the FDA inserts the stipulation that "The information that is given to the subject or the representative shall be in language understandable to the subject or the representative,"[5] and that the "informed consent document properly translates complex scientific concepts into simple concepts that the typical subject can read and comprehend."[6]

The Complexities of Comprehension

Full comprehension depends on presenting to patients complete, accurate information about the study in which they will participate, as well as complex scientific information in a way that they will be able to understand. The prospective subject will be less likely to carefully read an information sheet that is too long, or one filled with complicated legal or scientific jargon.[7]

A number of studies have demonstrated that many clinical trial information sheets are difficult for the average person to understand.[8] Thus, although technically they have been provided with all the relevant information, trial participants often do not have a full comprehension of the potential effects of the study.

Readability can be improved by using mechanisms such as outlining, bulleting, numbering, illustrations, and diagrams, and by replacing scientific terms with more commonly understood terms wherever possible.[7] For instance, an informational document intended for doctors or other healthcare professionals implementing a clinical trial may say something like "Ancillary treatments, such as antipyretics, may be required and should be provided to

patients by the study team."[9] However, a layperson who is not in the healthcare or pharmaceutical fields is unlikely to know exactly what that means, so the same information on an informed consent document should read more like "If you develop a fever, the study team will provide you with feverreducing medication as needed."

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In general, language should be simplified as much as possible to ensure maximum patient understanding during the document translation. Indeed, readability is a major concern in informed consent documents even in their original language. With the rapid global expansion of clinical research, informed consent documents need to be available in the language best understood by the individual participant. Thus, these documents must be properly translated to ensure that the patient understands the procedure, potential risks, and other necessary information.

Standards and Methods for Translation

The International Organization for Standardization (ISO) published ISO 2384, an international standard for document translation, in 1977, to ensure the integrity of the structure and information presented in translations. For U.S.-administered studies, the FDA requires that consent documents must be provided to prospective non–English-speaking trial subjects, and to prospective subjects with limited English proficiency, in the language with which they are most comfortable.

Consent documents submitted for review in another country must be translated into that country's official language, and additional translation requirements are imposed by institutional review boards. However, this can still be complicated, because many countries have more than one official language (e.g., India, which has more than a dozen). Many others have a number of widely spoken minority languages that are not nationally recognized, as in China, where the only official language is Mandarin, but a large percentage of the population speaks vastly different regional dialects.[2]

In the event that "a non–English-speaking subject is unexpectedly encountered, investigators will not have a written translation of the consent document and must rely on oral translation,"[5] or sight translation, during which a translator reads the consent document and simultaneously translates its contents aloud. As sight translation is generally done *ad hoc*, when the translator has no previous knowledge of the subject matter or time to prepare, this is not a preferred method of conveying medical information to prospective trial subjects. In cases when oral translation and sight translation is necessary, the FDA warns that "investigators should carefully consider the ethical/legal ramifications of enrolling subjects when [such] a language barrier exists."[6]

There are several other methods by which a consent document can be translated. Machine translation is one of the fastest and cheapest translation methods, but tends to translate things word-for-word, rather than contextually and in complete thoughts that are grammatically and culturally correct. Although many advances have been made in machine translation that can convey a general sense of the translated material, it still does not consistently produce accurate results, and is not ideal for documents with complex and important information, such as consent forms.[10]

Best Practices in Translation

Professionals in the translation field generally agree that for the most accurate, grammatically correct, and culturally coherent results, a multistep process of translation and localization must be employed.[8] Rather than simple text conversion, as with machine translation, content must also be adapted to make the message of a document accessible and effective for target audiences.

Although many advances have been made in machine translation that can convey a general sense of the translated material, it still does not consistently produce accurate results, and is not ideal for documents with complex and important information, such as consent forms.

It is best to use a translator whose mother tongue is the target language. When dealing with specialized legal or scientific texts, such as consent documents, a translator with a background in the sciences or a scientific or medical consultant should be used. The document should also go through "back translation," in which the text is translated back into the source language by a different translator to ensure the integrity of the content. The document should also be reviewed by various editors and proofreaders to maximize

the accuracy and cultural coherency of the text.[8]

Also, translating legal or medical documents such as informed consent forms must maintain the clarity of the original and not use complex terminology that the average person will not be able to understand.[2] As mentioned above, to accurately transfer both the accuracy and readability of medical and legal information into other languages, the translator or interpreter needs to be familiar with legal and medical terminology in both the source and the target language, or else use a medical consultant.

More difficulties can arise when the source and target language and culture are extremely different; key terms in an informed consent document may not have parallels in the target language and will need to be further explained or culturally adapted to make sense. For instance, some cultures have no concept of or word for "placebo," or for certain side effects or other potential hazards.[2,7]

Cultural Cautions

In addition to challenges in accurately conveying information for informed consent across different languages and cultures, cultural differences themselves often provide obstacles to informed consent or the implementation of clinical trials. For instance, in Burkina Faso, there is a cultural stigma against drawing blood, so it would be difficult to carry out a trial there if blood samples were required.[3] Also, although the Declaration of Helsinki and legislation in most countries mandate obtaining consent in writing, even signing a document can have negative connotations for some individuals in Middle Eastern cultures, who believe that verbal agreement should be sufficient.[3]

In contrast to the patient-centric approach of patient/doctor cooperation and the emphasis on informed patient decision-making often taken for granted in the U.S., doctors in Japan and India are held in extremely high esteem and are widely undisputed as absolute healthcare experts. Offering their patients full disclosure about the unknown or potentially negative effects of an experimental treatment or a new drug in a clinical trial could be seen as appearing ignorant, or compromising their reputation as the medical authority. Moreover, because of the level of trust that tends to be placed in healthcare professionals in these countries, prospective subjects may be more unlikely to question their doctors or demand full information about the trial proceedings.[3]

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As a final example of cultural complications, in Mali, any potential study must first be presented to the elder leaders of the community in which the study would be carried out. They must assess and approve it before a representative is allowed to approach potential subjects about participating in the study.[3]

Conclusion

Multilingual translation is not only essential to the health, legal, and ethical concerns surrounding informed consent in clinical trials, but is a complex and multifaceted process that builds a cultural and linguistic bridge between healthcare professionals and their patients.

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