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Language Barriers in Global Trials

Effective native language communication is an essential component in the success of international clinical trials, and as the number of trials conducted in newly emerging regions—including countries in Latin America, Central and Eastern Europe (CEE), and Asia—continues to increase, so does the challenge of overcoming language barriers. According to U.S. government publications,¹ 8.9% of clinical trials registered with U.S. health authorities are conducted in emerging countries of Asia, 7.4% in Latin America, 7.1% in Central and Eastern Europe (CEE), and 1.6% in Africa. These numbers are growing exponentially.

The challenge is multifaceted, because the translation of clinical trial documents requires a high level of precision and accuracy compared to other types of documents. Language equivalents must be carefully chosen, and any cultural factors must be taken into account. Documents must be back translated in order to ensure that the original meaning has not been misconstrued, and translators must determine the closest language equivalents in cases where exact translations do not exist. This requires not only high proficiency in both the source and target languages, but also demands an understanding of the culture, a background in the field of clinical research, and familiarity with local regulatory procedures.

Depending on country-specific requirements, certain regulatory documents must be translated into the official language of the host country. In some countries, such as China, all regulatory documents must be translated. In addition, patient materials such as informed consent forms must be provided in the patient's native language. However, the issue of language is complicated by the fact that not all patients are proficient in their country's official language. Urbanization trends in many emerging countries have resulted in diverse patient populations with considerable linguistic and cultural differences from place to place, or even within single cities.

Limited education among some patient populations in emerging countries poses an additional challenge. Thus, an assessment of patient demographics at a particular site must be performed to help ensure that the translated documents are effective and prevent delays in regulatory approval, particularly for such documents as informed consent forms. Linguistic validation and cultural adaptation are necessary as part of the translation process of any patient-related materials, despite the additional time and cost.

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Dealing with Language

Among emerging regions dominant in clinical research, patient populations are commonly quite diverse. A look at the numerous emerging countries with exponential growth in clinical research clearly demonstrates the complexity of the situation (see Figure 1). Often there are multiple translation requirements; in most cases, documents submitted to regulatory authorities must be translated into the host country's official language, and institutional review boards and ethics committees have specific translation requirements for patient-related materials. To further complicate the situation, in some countries, there is more than one official language.

In several Asian countries, English is an official language, but many patients do not have adequate proficiency in it. Some of these countries

have multiple official languages, such as in Singapore, where Malay, Mandarin Chinese, Tamil, and English are all official languages.² In India, not only are there many different national languages, but there are several official languages; more than a dozen are recognized by the government and many more at the state level (Hindi, native to one-fourth of India's population, is one of at least ten dominant Indian languages).³ In addition to numerous dominant languages, there are hundreds of regional Indian dialects. Because India is such a multilingual country, commonly patients must be given a verbal explanation in their own language prior to signing written informed consent forms.⁴

Meanwhile, for European Union member countries in CEE, there can also be multiple translation requirements. In Ukraine, regulatory documents must be provided in both of the country's official languages, Ukrainian and Russian.⁵

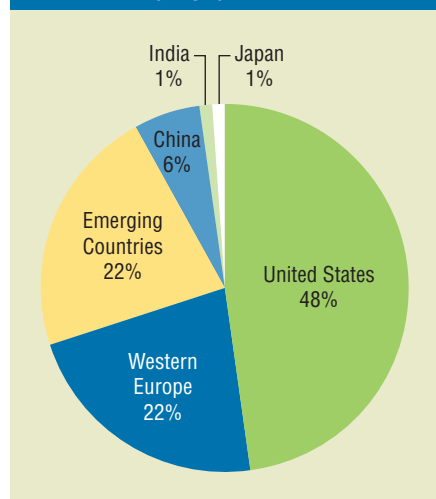
Even in countries where there is only one official language, such as China (Mandarin Chinese), Russia (Russian), Turkey (Turkish), Mexico (Spanish), or Brazil (Portuguese), great care must be taken to identify linguistic differences among patient populations and in culturally adapting patient documents. Often there are minority languages other than the official language, or regional dialects that must be considered. For example, in China, several dominant languages other than Mandarin Chinese are spoken by a relatively large portion of the population, including Taiwanese, Cantonese, and Shanghaiese.⁶ In Russia, many ethnic minorities speak Russian as a second language, and there are several regional dialects that have subtle differences in meaning or word use.⁷ In Turkey, although most people speak Turkish (the official language), regional dialects and other languages spoken by ethnic minorities must also be taken into account by translators.^{8,9}

Indigenous populations in many Latin American countries have significantly influenced how the Spanish language is spoken in their particular region (i.e., Mexico, Bolivia, Colombia, Ecuador, and Peru).¹⁰ Moreover, there are considerable differences among spoken regional dialects of Spanish even within the same country (e.g., in Mexico).¹⁰ Borrowed words from dominant indigenous languages and regional differences must therefore be taken into consideration when translating patient materials. In Brazil, despite the fact that there are no regional dialects of Portuguese, there are several dominant ethnic populations whose first language differs from the country's official language.¹¹

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In many emerging countries, levels of education and proficiency in the country's official language play a major role among certain patient population. Some patients may need to have documents verbally explained to them in their own dialect or native language. Moreover, despite improving literacy rates, in many emerging countries, large patient populations have high rates of illiteracy. For example, in many Latin American countries, women and indigenous populations have reportedly lower reading comprehension and higher illiteracy rates than the national averages.¹² India's literacy rate is estimated at 61% of the total adult population;¹³ however, there is a great amount of variability throughout different regions and among different socioeconomic levels. In addition, illiteracy is significantly higher among women.¹⁴

Figure 1 Clinical Trials Around the World



Lack of healthcare education and poor reading skills make these populations particularly vulnerable. Beyond the issue of translation, therefore, further measures must be taken to help ensure adequate comprehension among illiterate patient populations in emerging countries. Thus, the language component must be carefully addressed in order to ensure adequate patient understanding throughout clinical trial participation.

Translation

One of the most common translation issues is related to the fact that some languages differ significantly from languages in which the majority of clinical trial documents are originally prepared (e.g., English or Western European languages). As a result, certain words or phrases cannot be easily translated, since equivalents (or the concepts themselves) do not exist in every language. Moreover, vast differences in culture and everyday practices result in differences in language use, and pose considerable challenges in providing meaningful translations. The translation process therefore involves identifying words or phrases that do not translate well and determining which equivalent best relays the intended meaning. Idiomatic phrases are especially problematic, as they often differ drastically between cultures. The translation of any patient-related documents needs special consideration to ensure that the culture of the country or region is taken into account.

Translating from one language into another unrelated language is especially difficult since often there are vast grammatical and structural differences. Moreover, back translation—an important step in the translation of clinical trial documents that ensures that the original meaning remains intact—works best between languages that are closely related. In cases where languages differ significantly, further

comparison is required and translators must come up with the most acceptable functional equivalents. For example, Mandarin Chinese has several unique elements that make translation from other languages, such as English, more challenging. For one thing, the written language uses characters rather than letters. Moreover, there are two character types, Traditional Mandarin characters (common in Taiwan and Hong Kong) and Simplified Mandarin characters (primarily used in mainland China). In addition, sentence structure differs significantly, and often Chinese phrases

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or words have multiple (even opposite) meanings. Some words are represented by the same characters despite differences in grammatical form. For example, in Mandarin Chinese the words for “assess,” “assessing,” and “assessment” all use the same character. Thus, the construction of a sentence in Mandarin Chinese may differ considerably from the original English.

The Russian language presents its own challenges, especially when translating from English into Russian. Although the Cyrillic alphabet is not entirely unrelated to the Latin alphabet, Russian differs from English in several aspects, including grammar and word order, and has one of the most complicated punctuation systems.¹⁵ A comparison of the Turkish language (90,000 words), and English (600,000 words) reveals the reason that Turkish translations are commonly significantly shorter than their English equivalents—evidence that English words may not have exact Turkish equivalents.¹⁶

For Spanish and Portuguese in Latin America, this is less of an issue; not only are these languages more closely

related to English, but their written form is the same as that from which they are derived (i.e., Castilian Spanish and European Portuguese, respectively). However, translators must take into account differences in the way these languages are spoken in Latin American countries versus Europe; overlooking differences in meaning, language use, or distinct cultural aspects will result in inaccuracies. For example, many words from indigenous languages in Latin America have replaced Spanish words; in Mexico, some Nahuatl words have permanently

been adopted into Mexican Spanish, such as *jicara* (gourd/small cup) and *aguacate* (avocado/ pear/idiot). There also are regional differences within each country that must be taken into account.

Translating Informed Consent

One of the most important patient documents is the informed consent form. Accurate translation and cultural adaptation are crucial to ensuring that informed consent is obtained ethically. Translated informed consent forms must be properly validated for content. Even a single word can change the entire meaning of a phrase, something which can be especially catastrophic in clinical research. Ethics committees commonly delay the initiation of a trial as a result of a poorly translated informed consent form.

According to the Declaration of Helsinki,¹⁷ informed consent forms must follow a given set of accepted guidelines in order to help ensure that patient rights are protected. Thus, translating these documents presents additional challenges to an already complex pro-

cess. In some emerging countries where clinical research is less established, it may be difficult to relay crucial concepts to patients, such as those related to potential risks or to placebos, since these terms do not exist in all languages. Several studies, particularly in African countries, have encountered this problem.¹⁸

One of the major challenges in translating informed consent is to successfully relay the text in layperson's terms. Inexperienced translators who are not familiar with these requirements tend to use more academic terminology that is not as easily understood by individuals who are not in the medical profession. In many emerging countries, not only is language a major barrier (especially where there are multiple regional dialects or several dominant languages), but many patients may have limited education as a result of their economic situation. In these cases, the informed consent form must undergo more rigorous scrutiny. When necessary, clinical investigators who are fluent in the languages or dialects of the region must relay the information verbally. In some countries, such as India or many Latin American countries, poor education and regional linguistic differences can create considerable barriers to informed consent if not properly addressed.

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Even when informed consent forms are carefully translated and culturally adapted, this does not ensure that all participants will understand the information. The text must also be checked for reading level and length. Pretesting translated informed consent forms

with individuals from the study prior to submitting documents to regulatory authorities and ethics committees provides helpful insight into potentially problematic phrases or words, and helps to ensure that the documents will be well understood by study participants. However, additional research is needed in many emerging countries to better determine methods to increase comprehension, especially for participants with inadequate or marginal reading abilities.

Linguistic Validation and Cultural Adaptation

Over the course of a study, in addition to informed consent forms, several types of patient documents must be translated. Some of these, such as patient questionnaires and patient reported outcomes (PROs), are especially susceptible to cultural differences. As a result, patient responses often must be reassessed for inaccuracies due to cultural differences. These documents must therefore undergo a complex process of linguistic validation and cultural adaptation, which often takes several weeks to complete. The more the target language differs from the source language (most commonly English), the more challenging the translation.

Since language is greatly influenced by culture, frequently words or phrases must be changed in order to more accurately convey a message. For example, one study aimed at defining symptom scales for patients in China reported that because Mandarin Chinese does not use superlatives, "the worst" had to be translated as "extremely bad" to represent severity on a scale. Several other issues related to differences between English and Chinese languages were reported.¹⁹

Although it is not always simple to adapt patient questionnaires for more than one language, studies commonly undergo this rigorous process in order to achieve an instrument that can be

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compared cross-culturally. Often, this process requires pretesting the material on study participants to ensure that it is culturally sensitive. In one study aimed at adapting PROs from English into 14 different languages, numerous cultural and linguistic issues became apparent during translation. For example, in translating a single item—"Under each heading, please tap the ONE box that best describes your health TODAY. Please tap on the scale to indicate how your health is TODAY"—translators encountered the following issues: A Hungarian interviewer reported that the word "press" had to be substituted for "tap" since patients were not able to provide answers by "tapping." The Eastern European translators reported that "section" or "groups" had to be substituted for "heading," since there was no correct literal translation. In Latin American Spanish, the emphasis of "tap ONE box," meaning only one, became lost in translation due to the requirement for an article in Spanish (i.e., "una" or "la").²⁰ These studies further emphasize the importance of accuracy and cultural content in translating patient-related materials.

Conclusions and Recommendations

Overcoming linguistic and cultural barriers is one of the biggest challenges in outsourcing clinical trials to emerging regions. As the number of global trials continues to increase, there is a greater need to adequately address

these issues. Translation of clinical trial documents requires a high level of accuracy and demands an understanding of cultural elements. Quality and cultural context are especially important in the preparation of patient-related materials, where not only the accuracy of the text being translated, but how a message is conveyed, is of critical importance.

The translation of informed consent forms is complicated by the fact that many patient populations in emerg-

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ing regions do not speak the official language of their country. In addition to different languages, regional dialects and cultural differences must be considered. Moreover, in some emerging countries, many patients may have limited reading abilities; in such cases, informed consent documents must undergo higher scrutiny, and pretesting may be useful in order to better ensure patient understanding.

Over the course of a study, in addition to informed consent forms, other culturally sensitive documents, such as patient questionnaires and PROs, must be translated. These documents must undergo a complex process of linguistic validation and cultural adaptation in order to create effective instruments in the target language. Despite the time and cost of these methods, studies have shown the importance of this process in ensuring adequate patient understanding. Translating from one language into another unrelated language is especially difficult, since often there are vast grammatical and structural differences, and determining functional equivalents is not always a simple process. Despite the translation challenges, linguistic and cultural barriers can largely be overcome if properly addressed.

The impact of language barriers on timely initiation and completion of a trial, as well as on the accuracy of patient data and the protection of patient rights, must not be underestimated. It is the sponsor's responsibility to provide clear original documents and to work closely with clinical investigators to ensure that good clinical practice guidelines are followed and regulatory documents—including patient materials—are accurately and appropriately translated. Success in

global trials is therefore directly related to effective communication between sponsors, investigators, and patients. In particular, patient recruitment, the informed consent process, PROs, and patient compliance are all greatly dependent on adequately overcoming language barriers and understanding cultural differences.

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Karen I. Politis Virk, MS, is director of biotech and pharmaceutical research at Language Connections in Boston, Mass. Prior to joining Language Connections, she worked in research and development at several pharmaceutical and biotech companies as a research associate in molecular biology, including MicroGeneSys, Wyeth Ayerst, TransKaryotic Therapies, and Cubist Pharmaceuticals. Her experience includes the development of products for human clinical trials, particularly the human AIDS vaccine. She can be reached at karen@languageconnections.com.