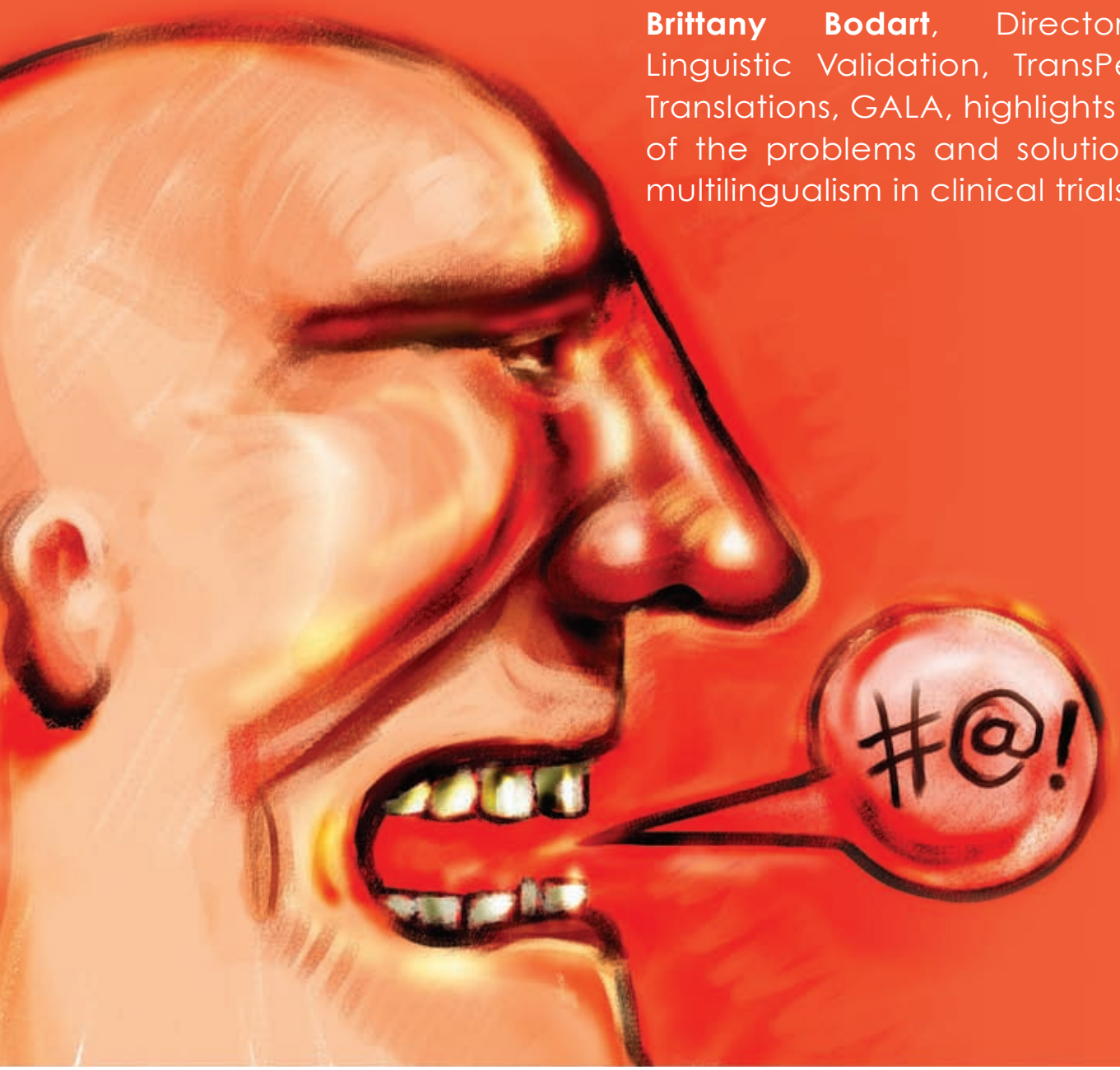
INTERNATIONAL PROS
ECLIPSING THE TOWER OF BABEL

Brittany Bodart, Director of Linguistic Validation, TransPerfect Translations, GALA, highlights some of the problems and solutions for multilingualism in clinical trials.



For those in clinical research, PROs (patient-reported outcomes) are familiar and critical tools for gathering valuable insight into symptoms, side effects, and safety in the clinical testing of pharmaceutical products. Compiling this information is a necessary step in moving a product from the lab to hospitals and pharmacies.

However, when a clinical study goes international and includes PRO endpoints that span multiple countries, companies can face a Tower of Babel that needs to be deciphered before the study can be completed. As in any domestic clinical research project, pharmaceutical research conducted internationally faces the inherent hurdles of evaluating patients' qualitative responses and transforming them into quantitatively valid data. Most companies now use eDiaries or IVR Systems to produce more uniform, quantitative responses, whilst also eliminating the error-prone transcription stage.

But when the study is conducted in multiple countries, the PROs must first be translated and then submitted to linguistic validation. When executed successfully, linguistic validation provides assurance that the translated PRO questionnaires, when presented in aggregate, will approximate the same meaning across diverse linguistic and cultural groups. Administering such a process can be tricky. Costs are high for multiple language translations, and companies must fill a workflow gap between linguistic validation of the PROs and the programming of its content onto the PDAs or IVRs.

Nevertheless, by deploying a sophisticated linguistic validation methodology, pharmaceutical companies can have more confidence in their PRO materials, and in the reliability and validity of the data collected. Additionally, companies should embrace alternative patient reporting techniques and strongly consider taking a more holistic approach to their translation efforts, incorporating time and cost-saving language management tools.

Accurate Data

Linguistic validation is a methodology that allows researchers to better manage the complexities of international studies by preparing cognitively equivalent translated instruments (questionnaires); that is, documents that approximate the same meaning and thus elicit "apples to apples" responses across diverse linguistic and cultural groups. This allows for pooling of data and comparing of results across countries. The process of linguistic validation is not defined simply by the translation of a language version but rather the formation of a commonly agreed-upon version built up through several steps.

Researchers should be familiar with every aspect of linguistic validation so they can take a holistic approach in identifying and addressing contingencies that may arise. Additionally, companies can count on better outcomes, faster completion of the clinical trial process, and a higher degree of accuracy when they view linguistic validation as one aspect of the entire clinical trial process.

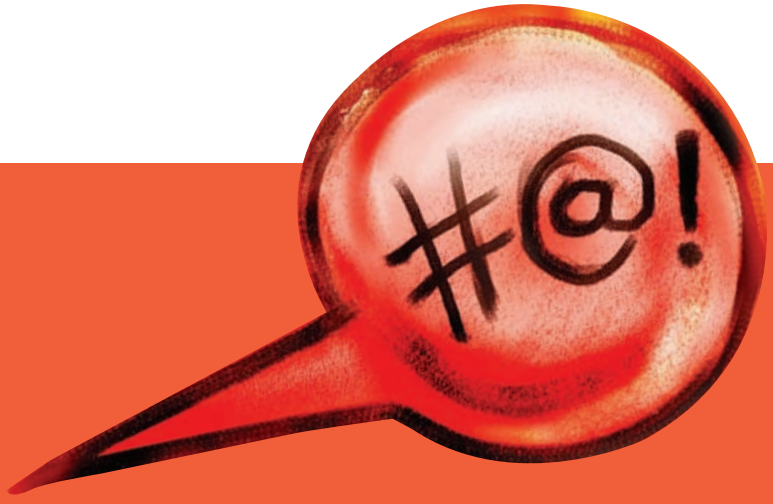
An effective PRO linguistic validation begins with a preparatory step in which the instrument is assessed in collaboration with its original developer. This step is necessary in order to thoroughly define the concepts underlying each item in the questionnaire.

> TIME AND COST-SAVING TRANSLATION MANAGEMENT TOOLS COUPLED WITH A SOLID LINGUISTIC VALIDATION PROCESS AND PATIENT RECORDING TECHNIQUES WILL NOT ONLY IMPROVE THE QUALITY OF PATIENT REPORTING, BUT ALSO ENSURE MORE EFFICIENT AND COST EFFECTIVE LONG-TERM TRANSLATION MANAGEMENT

The next step involves either single or dual-forward translation, editing and proofreading. During this process, two teams of linguists produce separate translations of the instrument: the translator renders the text into the target language, the editor reviews and refines the document to ensure that the text reads as if it were originally written in the target language, and the proofreader checks the translation against the original to verify that the source is accurately reflected.

All of the documents are then reviewed by an independent linguist, typically located in-country, with a superior level of experience and expertize in understanding the particular target patient population. This individual will resolve any discrepancies, thereby creating a single final version of the forward translation.

Next, another native speaker performs a precise back-translation, providing a snapshot into how the message is being conveyed to the target audience. After all discrepancies have been reconciled, and all linguistic decisions have been reported on in detail, the translation is considered ready for pilot testing with a sample group of individuals within the target population. Typically, during this cognitive interviewing stage, five to ten representatives of the target population of varying educational backgrounds, gender, and ages are selected for interview. These interviews are intended to assess the level of comprehensibility in the translated instrument, measure the cognitive equivalence of the translated items, test alternative translations, and highlight any items — by way of oral interview — that, for linguistic or cultural reasons, are problematic or difficult to convey in the target language.



After evaluation of the translated document's cognitive equivalence to the original instrument, any complementary suggestions from the cognitive interviewing stage are evaluated for incorporation into the translation. At this time, another independent linguist will verify the integrity of the final version of the translation. Once the linguistic validation process is complete, the project manager presents a final report that details and explains all edits, and summarizes the cognitive interview results.

Professionals who develop linguistic validation methodologies for clinical trials are very familiar with the processes required and can guide a company through the complexities. The Globalization and Localization Association (GALA), a not-for-profit association of more than 300 language services and technology companies, is one place companies can look for advice. The GALA website, www.gala-global.org, is filled with information on language services and includes a database of providers. In fact, GALA's Language Technology and Services Directory shows that half (153) of the members provide services to the medical and pharmaceutical sectors.

More Linguistic Considerations

One aspect of the linguistic validation process that requires careful planning and consideration is cognitive interviewing. In the majority of cases, this stage of the process represents the first time the instrument is seen by outside individuals who have little or no medical background. The patients' answers to the questions are not statistically relevant during this phase, but the patients' reactions to the questions will help to determine how the instrument is presented during the actual trial phase; how it is presented can have an impact on the validity of the data, and therefore the outcome of the study.

The linguistic validation planning phase also needs to consider how the PRO will be administered. Computer or web administration, PDAs and IVR Systems have advantages over the traditional pen-paper methods due to their time-stamp capabilities and the elimination of the error-prone stages. However, transitioning a traditional written PRO into one of these formats involves additional levels of complexity. The FDA Draft Guidance of 2006 includes a recommendation for additional validation to support the development of a PRO instrument when the mode of administration is changed, ie when a pen/paper instrument is modified to be delivered via a PDA.

As the linguistic validation process is intended to reflect the same level of rigour and consideration taken in developing the source instrument, there is an inherent need to address the mode of delivery in the linguistic validation process, particularly during the pilot testing stage. Flexibility in the methodology of administering this pilot testing is vital in order to achieve the end goal of equivalency to the original instrument. While time and cost are the two main constraints of the linguistic validation process, this level of diligence in evaluating the comprehensibility of the PRO in its intended mode of administration is invaluable in ensuring that the validity of the PRO is not diminished during the transition to a non-paper format. While linguistic accuracy is an important consideration, knowing how the intended concept will be conveyed and understood is critical to the success of each PRO campaign.

Holistic Approach

While no part of the clinical trial process is simple, linguistic validation tends to be viewed as one of the most difficult. It is no surprise then that many pharmaceutical companies source the translation and management of linguistic validation to third-party providers who can execute translation and delivery while adhering to ISPOR (International Society For Pharmacoeconomics and Outcomes Research) and government guidelines. The days of ad hoc translation of single documents generated during the drug development process are behind us. Through a comprehensive approach to language services, companies are not only able to ensure that they are following regulatory guidelines to the letter, but also increase efficiency in the trial process and reduce costs.

For example, while all translations during the linguistic validation stage must be done from scratch and not delineate from the concept definitions as characterized by the developer, other parts of the clinical trial process benefit from translation memory (TM) technology, which can reduce costs and increase efficiencies. TM tools allow translators to leverage pre-existing translations that are mapped to source language. Any time that a source language, phrase, or sentence appears in the TM database, the linguist is given the option of accepting prior translations of that same content segment. This process greatly increases the consistency of translated material, speeds up delivery of final files, and helps reduce costs, as charges for proofreading repeat text are much lower than those for translating new text. The more translation processes are centralized, the greater the size of the translation memory. With each subsequent translation project, the amount of repeat text increases significantly. This is one of the reasons why it is advisable to think holistically about any translation requirements as they relate to all phases of drug development. From internal R&D documentation and patent applications, to clinical trials material and even healthcare marketing efforts, the centralization of translation efforts and use of translation memory can significantly reduce translation costs.

Time and cost-saving translation management tools coupled with a solid linguistic validation process and patient recording techniques will not only improve the quality of patient reporting, but also ensure more efficient and cost effective long-term translation management. **Pharma**

Further Information

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