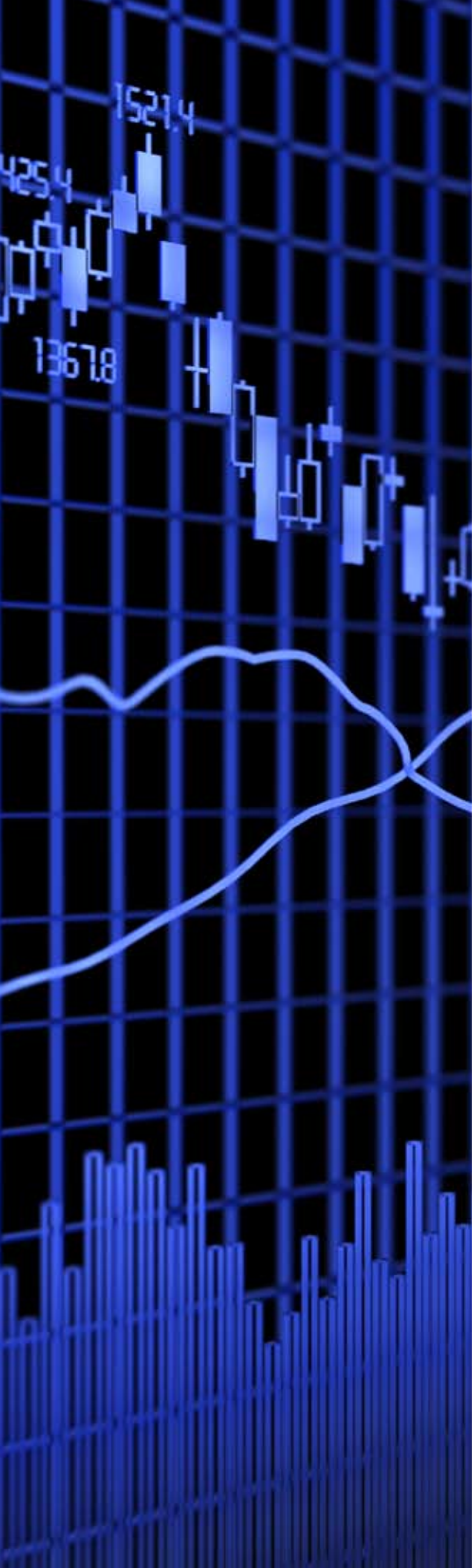


TransPerfect Life Sciences

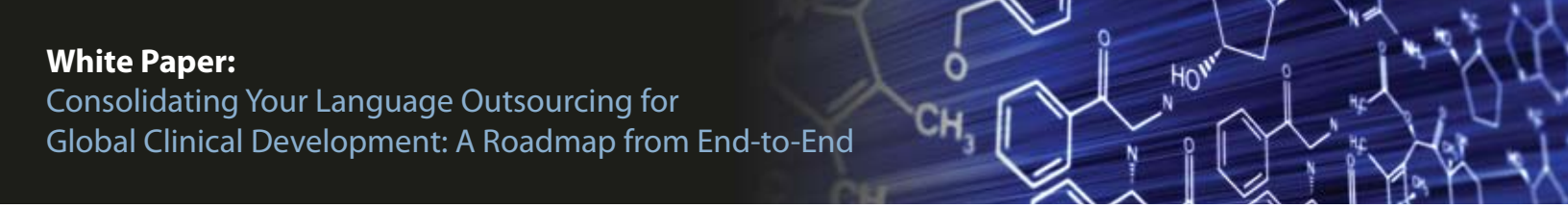
Consolidating Your Language Outsourcing for Global Clinical Development: A Roadmap from End-to-End

White Paper

TRANSPERFECT

White Paper:

Consolidating Your Language Outsourcing for Global Clinical Development: A Roadmap from End-to-End



The role of the language service provider (LSP) in clinical development is changing. Traditionally, translation has been handled reactively—sponsors and CROs only turned to their individual LSPs when an immediate need arose. While this method evolved out of necessity, its shortcomings are clear: high prices, excessive delays, and poor quality and consistency—all of which can lead to increased patient risk. Today, however, the world's best LSPs are better positioned than ever to serve clinical development clients with end-to-end, multidimensional language solutions.

As more and more clinical trials are being conducted internationally, and the clinical development world becomes increasingly globally dispersed, it also becomes more competitive. Those companies who take a measured and consolidated approach to global communications will earn an edge in a number of areas, including consistency, speed, cost, risk management, and regulatory review.

Despite these benefits, many organizations have found it difficult to make the transition to a consolidated model. Companies involved in clinical research are often, both knowingly and unknowingly, using dozens or even hundreds of LSPs or linguists for their clinical trials. How is this possible? With strategic partnerships ruling today's clinical research environment, the lack of central decision-making is the primary contributing factor: sponsors partner with CROs, CROs partner with in-country representatives and agencies, and in-country agencies partner with subcontracting linguists, and so forth. This occurs for a number of reasons:

- Global trials are often decentralized and different offices or locations have existing relationships with local providers
- There is a perceived convenience in pushing the translation procurement responsibility downstream to a CRO or an in-country partner
- Many incorrectly assume that there is a quality benefit achieved by completing translations in-country

Though the above reasons for the status quo are common and most companies can point to one or more as justification of their current arrangement, the benefits of consolidation are simply too broad to ignore. In the following pages, we'll show you a panoramic snapshot of what a consolidated end-to-end solution would look like across a general clinical development timeline. Whether you're looking to supplement your existing global initiatives or would like to fully transition to a consolidated approach, this paper will provide you with a clear roadmap to determine the ideal solution for your organization.

WHY CONSOLIDATE?

Improved Quality and Consistency Through Centralized Translation Memory

Every single LSP you work with, whether directly or indirectly, should maintain an evolving Translation Memory (TM) and style/term glossary. (If you have any LSPs that aren't offering these, they should be the first to go.) Your TM and glossary are living documents that capture your translated language and reflect your stylistic, linguistic, and branding preferences, storing all of this vital information so it can be leveraged in future translation projects. During the translation process, documents are analyzed against your TM for segments of text that match exactly to previously approved translations (100% match), as well as segments that represent a near-match (fuzzy-match terms). With a properly built and used TM, these segments do not require new translation, and with an easy proofreading process, they are incorporated into your final translation.

In a decentralized vendor environment, each LSP holds a different TM (or sometimes no TM at all), which means your organization gets only a small fraction of the potential cost or consistency benefits with each translation. When multiple providers are involved, divergence in the translated terminology is unavoidable, and without a centralized TM, it's likely that over time identical source content will be translated differently from one provider to the next. However, by consolidating to a single partner or a small, trusted group, you can guarantee that all work leverages your organization's unified TM and glossary, and you can immediately reap the quality and consistency benefits associated with a managed, core database of terminology.

Cost Savings

By cutting down the number of LSPs you use, the quantity of work you send to each provider in turn increases. You are therefore in a much stronger negotiating position to seek volume-based discounts and partner-inclusive preferred pricing.

The heightened budgetary oversight in a centralized approach has a direct positive impact on costs regardless of where you are in the clinical development process. As a sponsor, you might get a bill from your CRO with a single line-item charge for translation. Likewise, CROs often get similarly general bills from in-country partners that include translation costs. In both cases, sponsors and CROs are deprived of vital oversight abilities. There is no way to know the exact details of the charges, such as per-word rates, TM usage, possible service mark-ups, or even which LSP is being used.

By consolidating, you can negotiate a global pricing contract that extends to all of your partners. Additionally, by drawing on your core TM, there will be greater amounts of matching text not requiring new translation. You are now actively (through global contract negotiation) and passively (by monitoring itemized translation spend and TM statistics) reducing costs.

Expedited Timelines

Time savings are particularly critical given the value imperative of time-to-market in clinical research. With the cost of developing a single biopharmaceutical product averaging over $1.2 billion USD[1], expedited timelines allow you to get your product to market as quickly as possible, and thereby increase ROI.

When you utilize a centralized TM, the ratio of matching text leveraged against existing translations is far greater, meaning fewer words will require time-consuming and costly human translation. Furthermore, when your terminology is dependably consistent with past documents, the amount of time spent on reviews and revisions is significantly reduced.

General project turnaround times are a point of negotiation – albeit to a much lesser extent than costs – with LSPs. High-volume clients can demand faster turnaround times with decreased rush premium charges. While it's important to remember that demanding too much in the way of speed can compromise quality, sometimes a matter of a single day can be critical.

HOW AN END-TO-END LSP ALLIANCE FITS WITHIN THE CLINICAL TRIAL WORKFLOW

While every clinical development program is different, we'll use a general framework to illustrate the full potential of a consolidated LSP approach.

Pre-Clinical and Phase I Development

Traditional document translations are the most common need in pre-clinical development and phase I trials—you may look to your LSP to handle documents such as research papers, patents, and pre-clinical study reports. It's important to realize that each of these documents, though pertaining to the same trial, requires distinct subject-matter expertise. Your LSP should assign patents to a linguistic team with legal expertise, while pre-clinical study reports should go to a team more versed in the appropriate scientific terminology. In many ways, the needs you encounter here are the most straightforward that you will come across, but they cannot be taken lightly by assigning them to linguistic teams based on target language alone.

By avoiding the trap of transactional procurement (i.e. sending seemingly basic translations out to any vendor that promises to work quickly and cheaply) at this early stage, you lay a foundation that will pay long-term dividends as you move through clinical development. Specifically, you start the process of building your active TM and glossary with trial-specific terms that will be needed to maximize terminology matching and stylistic consistency throughout the development lifecycle for each therapy.

Phase II and Phase III

As you move deeper into clinical development with phase II and phase III trials, the role of your LSP becomes more complex. No longer are your needs limited to document translation—now you are presented with a host of new requirements that go far beyond the written word. In fact, phase II and III trials are the stages which represent the widest range of language needs.

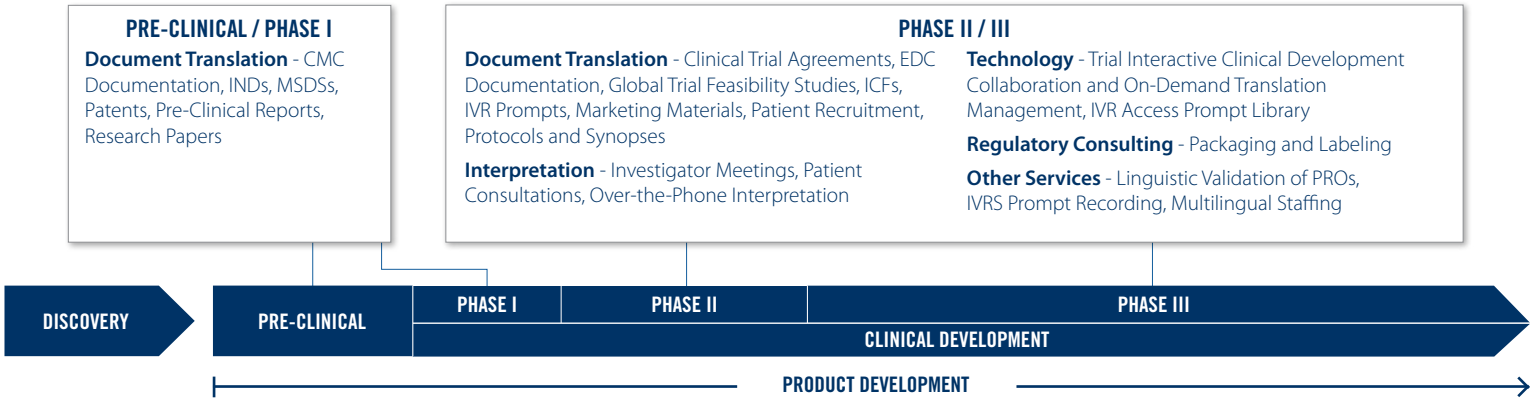
Patient-Facing Elements
The biggest change with respect to language is that you are now handling patient-facing information. In conducting a global trial, you will rely on your LSP to ensure that you present accurate information at investigative sites around the world.

Starting with patient recruitment strategies and leading all the way up to staffing native-speaking personnel at investigative sites, study subjects are keenly aware of whether a company is or isn't truly invested in developing therapies for their particular disease indication. Your LSP will make sure that vital documents like informed consent forms (ICFs) are translated appropriately and don't appear to be choppy, word-for-word adaptations from an English source. This high level of accuracy is vital both for maintaining credibility with patients and for meeting the rigorous requirements of each country's ethics committees.

Interpreters may become necessary at investigative sites, whether to conduct patient interviews or simply to assist investigative site personnel with a multilingual population. On an even larger scale, you may need international contract staffing services to provide investigative sites with local site personnel. Also, in instances where face-to-face interpretation or a local staff member is unavailable or impractical, your LSP can provide over-the-phone interpretation (OPI) services. While OPI is not an equivalent substitute for a face-to-face interpreter or native-speaking investigative site personnel, it is a valuable and cost-saving tool to have at your disposal, particularly given the fact that the best OPI providers offer connection times of less than 30 seconds.

Patient-Reported Outcomes
One of the most tricky and delicate areas of language services is linguistic validation for patient-reported outcome (PRO) measures. With PROs becoming almost a mandate in global clinical trials due to FDA and other regulatory Guidance Documents[2], ensuring that your PRO measures are conceptually equivalent and culturally appropriate is vital to trial success. Promising therapies have failed to make it to market because – due to the lack of linguistic validation of trial PRO measures for target languages – a statistical benefit to patients could not be adequately demonstrated. As the acceptance of your data hinges on your ability to show that the instruments are equivalent across all study populations, every available precaution must be taken to ensure that the linguists and project managers working in this area have the requisite experience to handle PROs properly. This means that linguistic validation must be considered an entirely different process, or even a separate practice area, from standard document translation, and that a documented and proven methodology specific to PROs must be in place.

Investigator-Facing Elements
While many translated documents are for patient use, your LSP will also be tasked with translating investigator-facing materials such as study protocols and protocol synopses, investigator brochures, and clinical trial agreements; for each they will draw on your translation memory for existing terminology and then add newly translated text into the TM to be used in the future.



Should you so choose, you may have a review team checking and editing your TM as well to make sure that any new stylistic choices you've made as a company are properly incorporated by your LSP.

Interpretation on the investigator side is common as well, as you will likely have multi-country investigator meetings; or perhaps you will present your data at therapeutic medical symposia that require standard consecutive or conference-style simultaneous interpretation. While it may seem logical to enlist an event planning service for these meetings, those services often outsource the interpretation component to an LSP with a hefty markup. A true end-to-end LSP partnership means that the same client services team handling your document translations is also the one you can trust with your conference interpretation and multilingual company initiatives.

Interactive Voice Response Systems (IVRS)
IVRS is another area where your LSP partner will play a central role. For multilingual trials, IVR prompts will need to be translated into all study languages; however, the source-language IVR strings often don't lend themselves to word-for-word translations. While many LSPs can make a case for their ability to translate IVR prompt scripts, an end-to-end partner can take your source-language scripts and complete translation, voice recording, and testing, and then deliver system-ready prompts with little to no involvement required on your end. Much like TM, part of the value of a long-term LSP relationship is the ability to leverage past work; if your LSP offers an organization and storage solution for translated prompts, you're ensured of never having to record the same prompt twice. Since organizations often utilize prompts across multiple trials, having access to all translated text and voice prompts in a logical and organized fashion represents an immediate return on investment for your LSP relationship.

Regulatory Review and Phase IV

Much like in pre-clinical and phase I development, the variety of language needs required during these stages is relatively narrow. Compilations of documents into eCTDs and MAAs/NDAs may need to be translated. Additionally, you may need global labeling solutions (PIM), translation with XML output, or translation of specialized materials such as batch records and manufacturing documentation. For all of these types of documents, you will benefit from drawing upon the existing TM to make sure that the terminology once again remains consistent with all documents completed to date.

While your LSP has a role in packaging and labeling translation, in some cases it might not be entirely clear how to request translations in these areas given the sometimes differing requirements from one international market to the next.

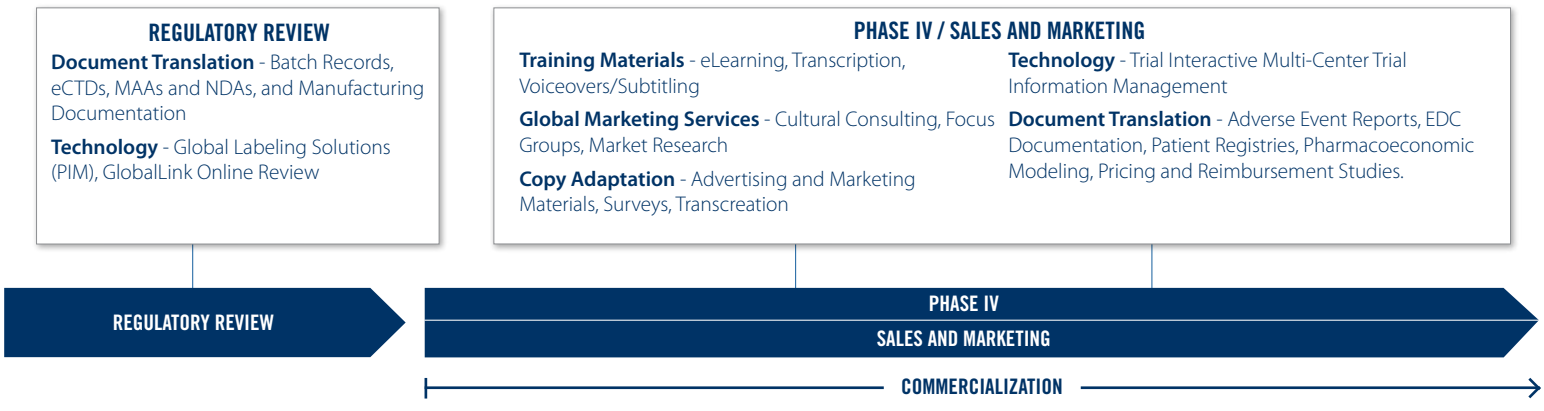
A good LSP can offer regulatory consulting services that take this knowledge burden off your employees and guarantee that your work is done exactly the way it needs to be done the first time.

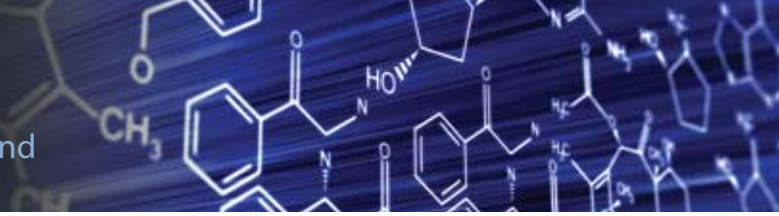
Commercialization

Whether your sales and marketing strategy is based in-house or with an agency, an enormous amount of thought and work goes into creating a campaign that's "just right." However, when the time comes to expand your advertising initiatives to international markets, simply translating the material from one language to another is not a winning game plan. The fact is, for a number of social, political, cultural, and linguistic reasons, concepts don't perfectly translate from country to country. With an ultimate goal of producing a final global campaign that reads as if it was originally conceived and written in the native language of the target country, your LSP should understand that making a mistake can have potentially catastrophic – and often well-publicized – results, but executing an intelligent global campaign can bring rich rewards.

Given the fact that a "word-for-word" translation is not an option in this case, you should work with your LSP to determine the ideal solution for your campaign, which may include agency-style services such as in-country market research, focus group assembly, copy adaptation, and cultural consulting. Along those same lines, if you are using a healthcare marketing agency for your source-language campaigns, you can maximize the success of your global initiatives and further ensure consistency of your branding across every language by requiring your marketing agency to utilize your LSP for all of your international campaigns.

Borrowing from the legal world, the DuPont model for service procurement is a valuable standard to reference. This model states that a corporation's vendors, when third-party outsourcing is required, must utilize subcontractors named on a list that the corporation has vetted and approved. Since the only way to guarantee the standard of service from a third level of vendors – LSPs in this case – is to screen the vendors yourself, you should require your agency to work from an approved list of vendors. As a valued client, you have leverage with your healthcare marketing agencies, and the end result is that you enjoy the benefits of maximum quality with your preferred LSPs. Furthermore, this model actually makes the agencies' jobs easier, as they are not burdened with vendor selection and rate negotiation, and they can proceed freely knowing that they are working with a partner already approved by their client.





DEFINING AN END-TO-END PROVIDER, AND HOW TO CHOOSE AN LSP

With such a strong case for LSP consolidation and a clear picture of how an end-to-end partner fits into the clinical development lifecycle, the final item to explore is how you would go about selecting and forming the ideal LSP partnership.

Quality System Certifications

While there are many factors that will contribute to your decision-making process, the number-one factor you must consider is quality. Size, speed, and pricing are important considerations as well, but all are of little value to clinical development if not combined with a quality end-product.

First and foremost, a quality-focused LSP will be certified to industry-recognized standards. The two most applicable standards for quality control in the language services industry are ISO 9001 and EN 15038:2006. The former has been around for quite some time and is likely familiar to most in the clinical world. While ISO 9001 is a non-industry specific standard, its stipulations for process management, continuous improvement, and customer satisfaction are nonetheless extremely valuable to an industry whose pursuit of quality is ongoing.

The shortcoming of ISO 9001 specific to LSPs is that its primary areas of focus – process and service – do not specifically address quality for translation. Accordingly, with the goal of authoring a global standard specifically addressing translation quality, the European Committee for Standardization has published EN 15038:2006. This relatively new standard considers project management, technical and human translation resources, and the actual translation and review process. Though born in Europe, EN 15038:2006 is a globally applicable standard.

There is a newly minted American counterpart, ASTM F 2575-06, but it functions more as a guide than as a true standard. While both directives address similar translation-specific subjects, there is no official process for becoming certified to the ASTM provisions. LSPs can claim compliance, but without a third-party certification those claims are not verifiable.

Maintaining quality system certifications is both expensive and time-consuming, so you can be sure that companies that have spent the time and money certifying to ISO 9001:2000 or EN 15038:2006 truly value quality as a corporate objective, while those that have certified to both standards represent the absolute highest achievable level of certified quality.

Linguist Screening and Subject-Specific Expertise

Even in the presence of the most stringent quality systems, every language has innate limitations when it comes to translation. Accurately conveying a specific message from one language to another requires a process that goes far beyond straight literal translation. A major limitation in the LSP industry is that there is no central, unified body responsible for certifying linguists' abilities and subject-specific expertise. For clinical development, it is critical that you devote part of your vendor qualification process to exploring exactly how linguists are identified, screened, and evaluated both initially and on an ongoing basis.

A provider with true end-to-end capabilities should have verifiable standards, including linguists' native-speaking language backgrounds, years of experience, and documented expertise in specific areas pertaining to clinical development. And don't assume that in-house linguists are always best; it's generally preferable that linguists have recently spent time in their target countries so as to keep up with the linguistic and cultural changes that will naturally occur over time. LSPs should also be able to show how they handle translation requests with different technical requirements—clinical study reports versus ICFs, for example.

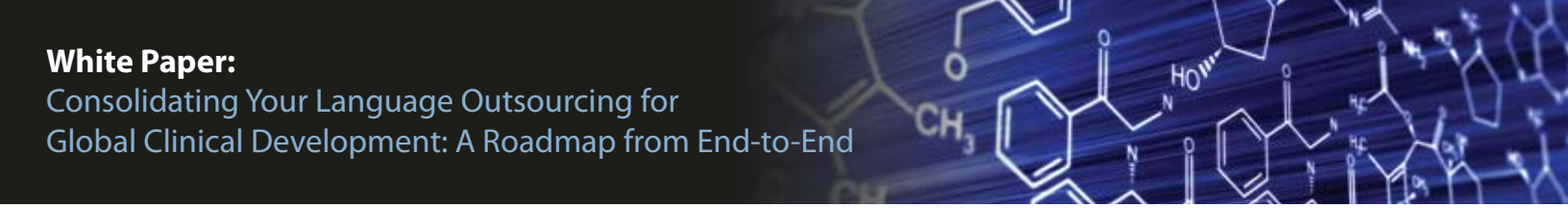
Beyond Traditional Translation Memory Tools

The human role in translation remains the backbone of the language services industry, as we're still many years away from having reliable machine translation technology. It's important to distinguish, however, between machine translation and computer-assisted translation (CAT) tools. Given the rudimentary nature of the existing technology, machine translation should never be considered a viable option in the context of clinical development (for proof of this, simply use an online free translation tool to translate a paragraph into any language, and then have that same tool translate back into English and compare the output to the original paragraph). Computer-assisted technology, however, (which includes translation memory tools) is an absolutely indispensable ally.

It's easy to think of TM as a black and white concept, as the long-held advice has always been to ask one of a couple simple yes/no questions of potential LSPs: "Will you be using TM tools?" or "Do you have a TM glossary for us?" If the answer was "yes" to either, then the instinct was to assume that you'd covered your bases for ensuring the highest level of consistency and accuracy as well as maximizing your cost and time savings.

These questions and conclusions ignore a fundamental flaw in the system—your TM is only as useful and accurate as the translations used to create it, and even the most capable translators in the world may not be privy to your specific stylistic preferences or corporate terminology choices. Consider this: A linguist your LSP has used for multiple projects in the past is found to have made an error so egregious that you decide to ban that individual from all future projects with your company. Though you may think you've prevented problems going forward, all previous translations that linguist has completed are already committed to your TM. Unless you have the ability to review or change your TM, undetected errors that linguist made long ago might find their way into future translations without your knowledge, introducing an unacceptable element of risk.

To prevent this type of problem, demand access to your TM as well as your glossary. A simple mantra that you should follow is: "*The more access, the better.*" Simply put, you will get the most out of your LSP relationship, and in return your LSP can provide you the best level of service, if you assume an active role and have the tools to maximize your involvement in the relationship. The two components of TM and glossary access that you should consider are, first, the ability to easily review, edit, and update your TM and glossary, and second, the way in which these changes are made.



Traditionally, TMs and glossaries have been built, maintained, and updated at the desktop level by each LSP. If you want to review or make edits, you have to request the file from each LSP, make edits, and send them back to the vendor, hoping your changes are implemented properly. New technology allows your TM to reside on a server, making it accessible from anywhere, at any time. You can designate access privileges to anyone, including multiple LSPs and your reviewers, and the end result is lightning-fast accessibility and maximized consistency across your documents, whether using one or multiple LSPs.

Language solutions have come a long way from the days of basic desktop TMs that captured "gold" and "fuzzy" match text strings—there are now robust technology solutions available that give you unprecedented access, control, and ownership over your TM, with incredible quality benefits, as well as time and cost savings relative to the translation process itself and the support activities that surround it. In a high-volume translation environment, using advanced TM technologies that can provide real-time updates to TM and glossaries is essential to ensuring that branded content is consistent across all languages at all times.

Emerging Workflow Technologies

When large clinical trials can involve 50 translation requests a day or more, technologies that can help streamline document submission and delivery, as well as centrally track project status and costs, are key to a successful centralization plan. In many cases, new technologies like online web portals and virtual data rooms have replaced email as the preferred medium of file transfer and collaboration between client, LSP, and reviewer due to the simplicity they offer and the confidentiality they guarantee. It's important to look for LSPs that have life sciences-dedicated technology that provides a secure, user-friendly interface and important features such as project upload and download, quote request capabilities, document storage, cost tracking, and metrics. All of these features will be extremely helpful in centrally tracking translation requests and budgeting for language services.

In many cases, these tools can be used outside of the vendor/client relationship. Virtual data rooms, popular for translated document exchange and review, can also be used for worldwide trial collaboration. When translated documents are posted, they are instantly accessible to users around the world. In global trials, open communication and transparency between internationally dispersed stakeholders is vital, and therefore the ability to instantly share translated materials between sponsor, CRO, and investigative sites is a significant advancement.

Vertical and Horizontal Scalability

The final element to look for in an end-to-end provider is vertical and horizontal scalability. Imagine the most involved, biggest, ugliest possible need in the world of language services—and then double it. You must make absolutely sure that your chosen partner or partners have the vertical capabilities and resource pool to handle your company's biggest needs both now and ten years from now. Since you will now be looking to one or several vendors to handle a quantity of work that was once dispersed among dozens or hundreds of outlets, planning for this contingency guarantees that your vendor will always deliver.

Horizontally, you must consider all the different departments involved in the clinical development lifecycle, and whether or not your LSP has specific solutions to meet the needs of each. Beyond clinical documentation alone, there may be specialized needs such as legal contracts and agreements, or media services such as training materials, eLearning, subtitling, and voiceovers. Websites may need translation for global audiences, and the technical acumen required of an LSP to accomplish this successfully is significant.

If at any point you encounter a project with a volume your LSP can't handle or in a subject area your LSP doesn't serve, you've essentially forfeited the consolidation benefits you've worked so hard to secure. Careful partner selection will help you to avoid this pitfall entirely.

CONCLUSION

Consolidation of language solutions in the clinical development world should be viewed as an absolute necessity that happens to impart some key benefits. In this paper we've explored the case for consolidation, viewed a brief profile of how an end-to-end solution might look within the context of a model clinical development program, and laid out various data points to consider when selecting a comprehensive LSP. By factoring this guidance into your vendor qualification process, you can guarantee several key benefits for your global clinical development. Not only will you realize an immediate improvement in the quality and consistency of your translated work, but a close LSP alliance streamlines collaboration and organization, saves money and time, and most importantly, instills among all stakeholders the confidence that your most important and sensitive materials are handled by a partner you trust.

[1] Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2008 (Washington, DC: PhRMA, March 2008).

[2] *Guidance for Industry, Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims*. (2006). Retrieved April 27, 2009, from U.S. Department of Health and Human Services, Food and Drug Administration. Web site: http://www.fda.gov/cder/guidance/5460dft.pdf