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LIFE SCIENCES

A Checklist for eCOA Solution Deployment.

Best practices and considerations.

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Origin and Modern Vista

In 2002, there was only a small number of eCOA providers. Each one had their own bespoke solution. Interactive Voice Response System (IVRS) was still a useable method for patient diaries, though there were significant limitations (numbers of items, time taken for patient input, voice talent, etc.). Using modified handheld devices (Palm Pilots, HP PDAs, etc.) meant that the amount of programming needed to migrate a paper instrument on to a digital platform was not insignificant. Not only did it take human resources programming the devices, it was very time consuming and meant taking into account language translation and shipping of the devices to sites; if there were an international component to the study then Customs and border crossings had to be accounted for in the scheduling of the study. The vast majority of studies performed electronically at this time was post-marketing. The risk profile for error for a primary endpoint using electronic was too great.

However, it was the perfect proving ground for electronic patient self-reported data capture. There was an increasing amount of evidence that evolving from paper would lead to more accurate data. Indeed, there was evidence that the data would be cleaner and less subject to abuse (Stone et al). Equivalence was a major concern and the lack of directive increased anxiety in the COA and Sponsor community. Some guidance was offered in the form of ISPOR Guidance. In 2013, this guidance was formulated into a Notifying Body Guidance.

That was a catalyst in that now there was a roadmap of how measures should be handled that also defined guardrails for minor, moderate, and major equivalence for electronic migration.

Reaching Maturity

Over the next several years, more and more Sponsors adopted an electronic modality for self-reported clinical outcome assessments (COA), but it wasn't until the past decade that there were rumblings of new eCOA providers entering the market.

In the mid-2010s, most focus was on Patient Recruitment (PR) and patient-facing data capture. This was in line with the FDA new directive of "putting the patient first and center." So many tech companies realizing they could harness the power of social media to reach a particular patient population meant an explosion in the eClinical world. Bespoke Patient Recruitment companies (non-CRO/Sponsor in-house) saw a massive increase in demand. Pursuing often the same patient cohort, they competed with ever-deeper penetration of social media data and a more targeted approach. Indeed, at this time many CROs acquired some of these bespoke PR companies while others created their own in-house PR division. Natural progression meant that CROs were offering more and more aspects of the study process. Standalone eClinical companies that focused on one aspect of the electronic revolution (EDC, IRT, etc.) began to increase their offerings also.

These single offering eClinical companies now had a full suite of "e" products all interlinked

(eConsent, eTMF, RTMS) and the eClinical Suite was born. No longer were CROs consigned to just Study Operational outsourcing limits; now they could offer their own services. No more White Label offerings; now they had in-house capabilities. Moreover, eClinical providers were no longer a single service supplier. They could now offer almost every portion of a study, from Site Activation and PR to eConsent, IRT, and EDC. So why not eCOA?

Today's Landscape

As more and more eClinical companies broadened their offerings to encompass more aspects of a complete study it would only be natural to include in their arsenal an eCOA solution.

Unfortunately, such a solution is significantly more complex than virtually all other "e" offerings. Moreover, direct patient data (self-reported) is more guarded by Study teams than any aspect of the study process.

Many eClinical companies appreciated the complexity of the undertaking and either acquired an eCOA solution or went about creating one. Others treated it more akin to an EDC solution, i.e., data in, data out. There was also misleading nomenclature used, as "surveys" hinted at a simple form-like questionnaire that could be readily rendered. The reality is significantly different. The rules and regulations do not allow for variance in most cases for items used in a measure. The slightest possibility of introducing a bias into a migrated instrument makes the process of building a solution far more complex than a simple survey form rendered on a computer screen.

How the International Perspective Has Changed Everything

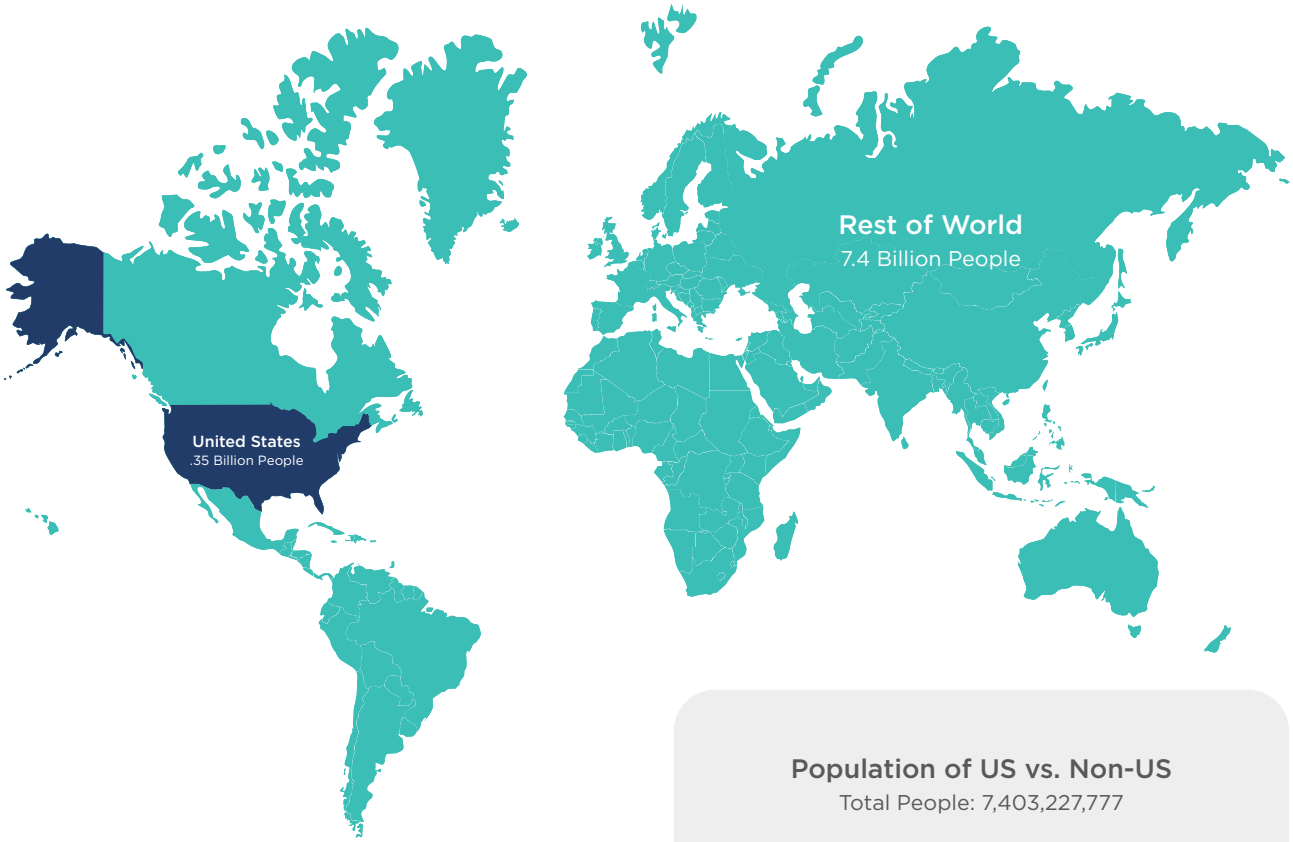
The drivers to include a diverse population in any study have made for a more global perspective.

What was previously a mostly US and Western Europe model is not the case anymore. The clinical study world became larger. More than seven billion inhabitants live in non-English speaking territories, which is a significant challenge to Study Teams and for eCOA providers. Clinician-facing material is often supplied in English as a norm, but any patient-facing material must be presented in the mother tongue. The rendering also must be true to the original source material; therein lies the challenge.

Where Are the Patients From?

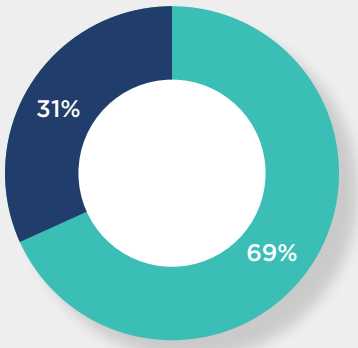
Geography

The country contributing the most clinical trial partipants was the United States. Compated to the population of the entire world (7.4 Billion), the US (0.35 Billion) makes up a little more than 4% of the world population.



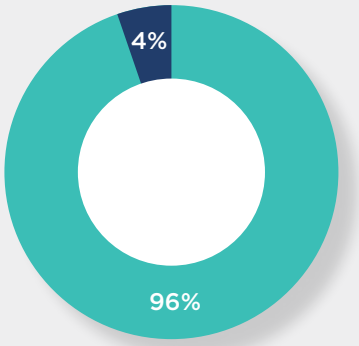
Total Participants by US vs. Non-US

Total Participants: 131,749



Population of US vs. Non-US

Total People: 7,403,227,777



Global Participation in Clinical Trials Report - www.FDA.gov

How Does Global Participation Change by Year?

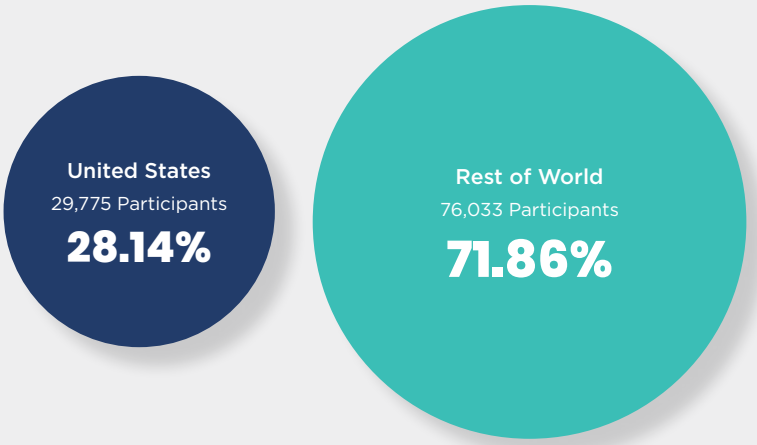
The FDA is approving more NDAs than ever before that include an overseas component.

The Number of Studies, Patients, and Geographies Is Increasing

Participation in clinical trials varies by year. In calendar year 2015, there were 105, 808 participants in pivital clinical trials. In calendar year 2016, there were 25,941 participants in pivital clinical trials.

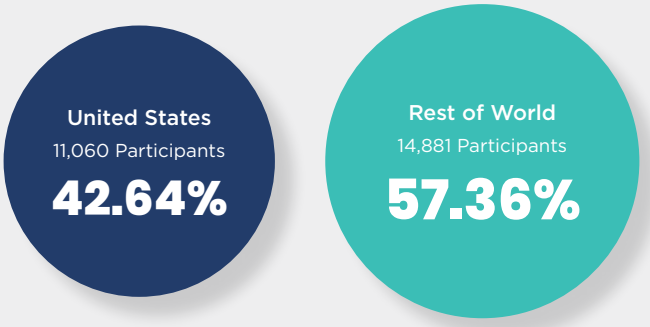
Calendar Year 2015

Total Participation: 105,808



Calendar Year 2016

Total Participation: 25,941



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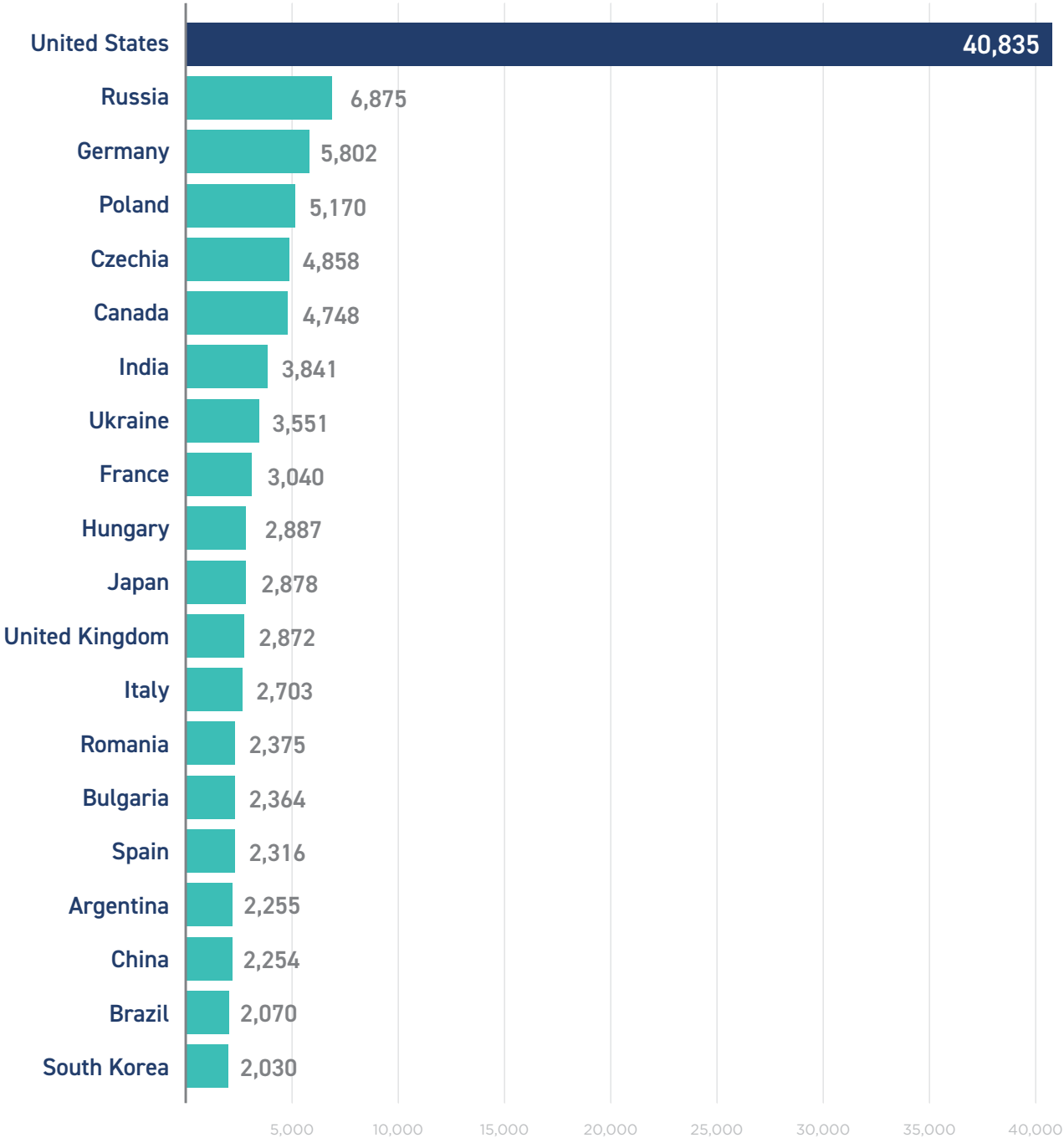
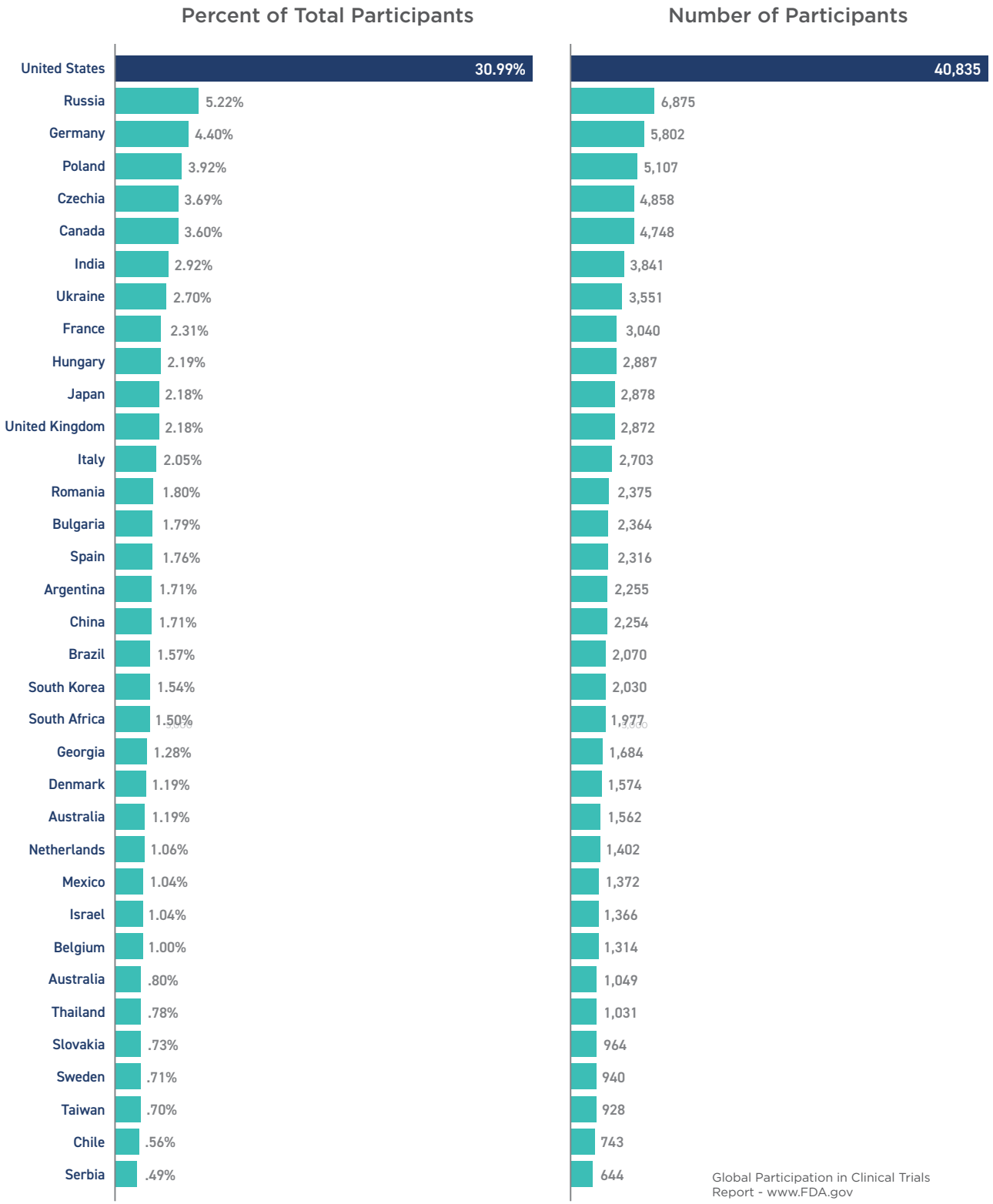
Country Breakdown

Top 20 countries by number of clinical trial participants in 2015–2016



Trial Participants by Country

The top ten countries enrolling clinical trial participants are the United States (40,835), Russia (6,875), Germany (5,802), Poland (5,170), Czechia (4,858), Canada (4,748), India (3,841), Ukraine (3,551), France (3,040), and Hungary (2,887).



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Linguistically Validating Instruments

Translation of a validated instrument/measure entails a very complex methodology outlined in the ISPOR guidelines.

A process that 10 years ago could only be performed by a small number of Language Service Providers (LSPs) has proliferated and concretized, becoming the de-facto process to use. However, this complex process (Fig. 1) is not easily replicated and should not be demeaned nor commoditized. This process requires significantly different resources and scientific understanding than all other translation processes. The risk for error is real and the consequences are great.

Linguistic Validation Process

Figure 1.

Translation Is Only Half the Battle

Translated instrument strings need to be migrated to the target device (Fig. 2). In a bring-your-own-device (BYOD) model, translated strings are included in the application.

That app is downloaded by the patient and with the necessary registration, and that patient has the ability to complete their assessment following the frequency parameters prescribed. If the instrument is rendered in English, it is a straightforward endeavor. However, when it comes to any language other than English, it is a very different proposition. Internationalization (L10N) or Globalization (G10N) is the industry in-word for "localizing" a language into another. Taking into account the cultural differences, on paper, said differences are well defined. However, for validated instruments the challenges are more obvious, as are the errors.

eCOA Integration Process

Figure 2.

Localization / Globalization

- Most vendors claim they are internationalized but some may not have this capability
- Dynamic text is a way of dealing with changes in strings but it still pulls up some issues—example below;
  - Example: How many pills of {MedicationName} have you taken in total for your osteoarthritis pain {{RelativeDay}}, {{DiaryDate}}?
  - It's an issue in terms of incorrect translations because other languages do not function the same grammatically as English (Spanish and German for example)
  - One may approve one population or possibility of text insertion for screens, but if another party is chosen in the trial and it is not reviewed by the original LSP, there is no way to confirm it will look right on the actual device
  - There can be surprises in terms of turnaround times and word count—maybe a translatable file has 1,200 words but when you populate all the dynamic text it turns into 15,000 words, the time for which was not allotted, and time and cost are impacted negatively
  - Delivery and First Patient In (FPI) dates are missed. This is singularly the most detrimental scenario in the migration/translation process
- Right-to-left (RTL) languages (Hebrew, Arabic) are major problems for some eCOA vendors, as are double-byte (expandable) characters (Chinese, Japanese and Korean etc.)
- All platforms should be built for automatic text expansion

Libraries

- A complex issue. Pulling measures from past studies and re-using those assets opens up significant issues for version control and quality.
- Different platforms for COA vs. UI vs. training, as an example, leading to needing different version control on all different material types.
- No standardized policies on managing how re-use files are used across sponsors and how to handle escalations of errors on old studies.

Screenshot Review

- eCOA vendors need to avoid populating screens and releasing them to the LSP. This increases the number of review rounds and delays the end product.
- Where possible use technology and automation to reduce the human element of review. Reducing rounds of review protects the FPI date.
- Companies need to focus on product review. Using screenshot capture and submitting said screenshots for the review process leads to inaccurate review and increases the risk for error.
- Platforms must have a streamlined capability to re-upload versions between rounds. Again, this reduces the rounds of review and protects the integrity of the instrument. ***Manual edits should be avoided if possible***
- Automated integration should be employed. Making changes in real time and avoiding a simulated environment is best practice. This again reduces the risk profile and reduces review rounds.

Your Checklist

Checklist for Selecting and Deploying an eCOA Solution	
Ensure your LSP is employing suitable, qualified, and experienced resources for the translation process	☐
Ensure there is scientific support offering governance over the SOPs and resources utilized throughout the entire process	☐
Ensure your eCOA partner is employing best of breed L10N practices	☐
Ensure they support RTL languages	☐
Ensure they support expanding screen languages	☐
Outline clearly re-using/previously deployed Instruments *Version control must be transparent and comprehensive* *Different platforms for COA vs. UI vs. training all require robust version control oversight*	☐
Automate the screenshot review process as much as possible	☐
Leverage technology to reduce the number of reviews	☐
Leverage technology to automate as many manual processes as possible, reducing the risk for error	☐
Reduce the error risk and review round by being able to make changes in real time	☐
Have the ability to re-upload versions between review rounds	☐

Want to learn more about COA and eCOA solutions?

Contact us or email us at COASolutions@transperfect.com