One Route, Many Languages: Managing Translation Complexities in the EMA Centralised Procedure

The Centralised Procedure of the European Medicines Agency (EMA) gives pharmaceutical companies a single point of access to the EU member states for new drugs and biologics. Approval via the Centralised Procedure effectively provides a consensus position between the 28 member states on a new medicine's quality, safety and efficacy. However, companies using the procedure must also convey the risks, benefits and other particulars of their medicine in terms understandable to regulators, doctors, patients and the general public in each member state.

To achieve this, detailed product information needs to be translated into multiple languages, in keeping with any local nuances or preferences of the various member states. This requires not just linguistic expertise but the ability to go "beyond" translation and to manage a complex, rigorous and extremely time-sensitive procedure that weighs heavily on Marketing Authorisation Holders (MAH).

Going Central

Centralised approval in the EU is a gateway to the world's second largest pharmaceutical market. Only the US market is bigger, despite the growing challenge from fast-emerging economies such as China.

Almost all new and innovative medicines are assessed for entry to the EU market through the Centralised Procedure. Marketing authorisations are valid in every EU member state plus three European Economic Area (EEA) countries: Iceland, Norway and Liechtenstein.

This consolidated approval process contrasts sharply with the varying national conditions for pricing, health technology assessment and reimbursement of medicines in the EU. Given the increasing difficulty of negotiating these additional market-access hurdles, it is all the more imperative that regulatory approval through the Centralised Procedure runs as smoothly as possible.

Translating Product Information

In general, all data, information and communications addressing the quality, safety and efficacy of medicines in Marketing Authorisation Applications (MAAs) filed through the Centralised Procedure must be presented in English. The Product Information (PI) annexes, including the Summary of Product Characteristics (SmPC) and the Labeling and the Patient Information Leaflet (PIL), must also be in English.

This PI will then need to be translated into the official languages of all the other member states, and subsequently signed off by the relevant authority in each of those countries. That can involve translations into 24 of the official EU languages as well as the relevant EEA languages (Norwegian, Icelandic and German for Liechtenstein). Translations of the PI must not only provide identical content in each of the required languages, but be sensitive to local nuances around, for example, medical terminology, cultural norms, readability or educational levels.

The Centralised Procedure has a strict time frame for translating and revising the PI, within which "at risk" translation, implementation of review changes, management of linguistic review cycles and other administrative functions need to be carried out. This is where a language solutions provider makes all the difference, particularly one that can demonstrate the high level of expertise required to ensure compliance with EMA-approved templates, and the capacity to manage all EMA languages in highly complex, multilingual project workflows.

How The Procedure Works

In most cases, translation assignments for pharmaceutical companies run along familiar lines. "The process of translate, edit and proofread [TEP], with relevant desktop-publishing and quality-assurance steps, is typical of many transactional translation projects", explains RWS Life Sciences' Head of European Sales, Ben Rainforth.

"The EMA's Centralised Procedure, on the other hand, is something quite different. It involves a demanding multiple-step process, with complex workflows, various stakeholders and very tight deadlines at every stage", Rainforth adds.

In particular, once the EMA's Committee for Medicinal Products for Human Use (CHMP) has adopted an opinion recommending that a product should be approved for use across the EU, companies have only five days to: finalise the English version of the PI, translate their PI documents into all of the relevant member-state languages and return these translations to the EMA, which will forward them for linguistic review to the member states.

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Translating At Risk

Given the challenges involved in meeting this five-day deadline, the language solutions provider, in collaboration with the pharmaceutical client, has to translate the draft PI documents "at risk." This means the provider starts the translation, editing and formatting process at or before day 180 of the Centralised Procedure. By that point, the CHMP will have decided whether to request an oral explanation from the applicant and/or produce a list of outstanding issues, giving a strong indication of whether the MAA is likely to proceed as planned, and what may need to be amended.

"The pharmaceutical company receives a Preliminary Assessment Report [PAR] from the CHMP approximately 30 days prior to the opinion date", Rainforth notes. "The PAR provides guidance to the pharmaceutical company as to the likelihood of the product gaining a positive opinion at day 210. At this stage, we would be given the go-ahead from the pharmaceutical company to begin the translations at risk."

Day 210 also triggers the five-day period within which all draft translations of the PI should be submitted to the EMA. Having made an early start with the translations "at risk", the language solutions provider can promptly adjust its translations to include any final modifications made by the CHMP in the English draft of the PI annexes.

"If the CHMP provides a positive opinion, we already have the 24 language versions in our hands", Rainforth comments. "The CHMP might implement minor changes to the English. If they do, within that five-day period we simply update the existing translations to match the new English."

Linguistic Review

The next step is a detailed linguistic review of the PI translations by individual member state reviewers between days 215 and 229 of the Centralised Procedure. By the end of that period, member-state comments are sent to the MAH, which then has until day 235 to coordinate with the language solutions provider on implementing any necessary amendments and to send the tracked and final texts to the EMA.

This is where local nuances come to the fore. They might

involve terminology that has a particular emphasis in one member-state language versus another. “And the member-state reviewers will ensure that the text is in line with their national medicines regulatory body’s approved wording”, adds Hannah Walmsley, Senior Project Manager at RWS Life Sciences. Once all of the files are returned, though, “we have the member-state comments reviewed by our linguists, and then also by the client affiliate reviewers”, Walmsley continues.

RWS Life Sciences also makes sure that the files are in the correct format, according to standards the EMA has laid down in its Quality Review of Documents (QRD) templates. “A pharmaceutical company we have recently begun working with used to check QRD compliance themselves”, Rainforth says. “This process was administratively burdensome to their people, who were being taken away from their core functions.”

During these steps, RWS Life Sciences may be dealing with a pharmaceutical company headquartered in the UK but with offices in Germany, Italy, Spain, France or other member states. “We are in constant communication with the pharmaceutical company's affiliates and distributors and the member state reviewers", Rainforth comments. “We take all of the administrative work from the pharmaceutical company and we drive this process.”

Liaising With Stakeholders

The client affiliates “are reviewing the member state comments and confirming whether or not they agree with them”, Walmsley notes. Ideally, the affiliates will accept the member state’s amendments. Wherever there is disagreement, though, RWS Life Sciences will liaise between all of the stakeholders until an agreed final version is confirmed. The final versions of the PI annexes in all 25 languages (including English) are then submitted to the EMA by day 235.

After that, the PI annexes in all of the languages are forwarded to the European Commission, which signs off the product for market entry. RWS Life Sciences then finalises each of the 25 approved PI annexes – the 24 foreign-language files plus the English version – by adding the Appendix V approval dates and details of national reporting systems for adverse drug reactions. RWS Life Sciences provides this service, as well as earlier administrative tasks such as creating bookmarked PDF versions of the final Word files in all languages and ensuring that they are tested for accurate functionality. The final approved PI annexes, complete with Appendix V details, are submitted to the EMA by day 237 of the Centralised Procedure.

Procedure Management

All of these activities are facilitated by RWS Life Sciences’ Waypoint Regulatory Plus translation-management platform, a secure and customised portal through which documents are transferred to the affiliates for review, and archived after finalisation. This platform “is very easy and intuitive to use”, Walmsley observes. “There’s an integrated version history. If you get some feedback at the end of the procedure, you can easily go back and identify the author who introduced the text, or restore a previous version. It gives affiliate reviewers easy access to documents or relevant reference materials, and they can provide comment for relevant files. This is an extremely valuable tool that allows us to manage procedures effectively on a day-to-day basis.”

In dealing with the demands and complexities of the Centralised Procedure, RWS Life Sciences not only leverages years of linguistic and regulatory expertise, but also extends its remit substantially into the realm of procedure management, involving multiple activities, timelines and relationships, and reducing substantially the administrative burden on clients. “We offer a procedure management service”, Walmsley says. “This goes beyond management of a standard translation project. It involves managing an entire procedure that’s complex, with many stakeholders involved, in addition to the provision of translation and review services across all EMA languages. We handle the whole process.”