Key Steps to Commercialisation Readiness in Europe

The steps to commercialisation readiness are complex, multi-faceted and often left too late in the launch strategy of a pharmaceutical product. This can be particularly problematic in Europe where the diversity of national legislation can make supply chain logistics very challenging. Among the issues faced, particularly for companies outside the EU are defining the product's logistics, identifying stakeholders who will be involved in the supply chain in Europe, and ensuring that all these individuals are ready to assume their roles soon after the product's approval (Marketing Authorisation) with the relevant Licences and Quality Technical agreements in place.

Depending on the complexity of the storage and transportation conditions of the product, and the number of stakeholders envisaged for the supply chain, experience shows that preparing all these steps can take up to two years for quality assurance, commercial and supply chain departments. And, while the European Union has harmonised wholesale distribution regulations and introduced good manufacturing and good distribution practices in the pharmaceutical legislation (Directive 2001/83/EC[1] and Directive 2003/94/EC[2] and Guidelines 2013/C 343/01,[3] respectively), which have helped patients to access medicines faster, there are still different post-approval requirements in each EU Member State, and also in the United Kingdom and Switzerland.

Among these differences, the importation, distribution and release of medicines in the EU, UK and Switzerland are still country-specific requiring national authorisations to permit these activities. Moreover, in our experience, getting the necessary licences to ensure an efficient supply chain in all targeted territories requires significant preparation.

Adopting a Systematic Approach

Before starting the commercialisation journey, it's important to map out a strategy for the short-, medium-, and long-term that considers the countries where the product should be launched and when. Knowing this will prevent early missteps that will require costly and complex changes (for example, identifying the EU site of importation and the establishment of the EU supply chain with appropriate low market licences).

From experience, it is advisable to start coordinating commercialisation steps before late-stage development of a product is completed – ideally when there is enough data to give companies greater confidence of a successful marketing authorisation approval by regulators.

One of the first considerations should be to ensure the product can be supplied to the patient once it has been authorised, since a common source of frustration is challenges with the supply chain. In addition, the European Medicines Agency (EMA), through its Medicines Shortages Steering Committee, and some EU agencies, have placed an emphasis on addressing supply chain vulnerabilities and measures to avoid shortages of medicines.[4]

Companies entering the European market can also struggle with decisions about where to set up their EU headquarters or marketing authorisation holder (MAH) and how best to weigh financial and strategic considerations. Key to those decision is being able to have all the necessary stakeholders and/or partners in place to support the marketed product, including pharmacovigilance, regulatory and medical information professionals, is quality management and compliance. Quality management and compliance teams can support the identification of compliant supply chains and risk assess supply chain challenges.

To determine the right approach, it's important to consider local regulations together with economic considerations as well as the company's objectives. The following questions deserve a comprehensive analysis: Which countries is the company targeting for commercialisation? Where is the product likely to be manufactured and how will that impact the supply chain as well as import licences? Has the company identified a local partner or does it plan to apply for an appropriate licence authorising it to manufacture or import, distribute/commercialise the product?

Companies with their sights set on Europe also need to consider whether and how they will manage commercialisation in Switzerland and in the United Kingdom, since these territories represent important marketplaces, though neither are part of the EU or European Economic Area (EEA).

Need for a 'Commercialisation Licence'

Obtaining a Marketing Authorisation (MA) for a medicinal product is of course a critical prerequisite before placing a product on the market, but the MAH must also ensure that batch testing and release of the product is managed properly by authorised sites. Depending on where the bulk/finished product has been partially or fully manufactured in the EU/EEA or in a third country, the importation and QP batch certification can be complex and the MAH must ensure that all importation/batch certification sites hold a Manufacturing & Importation Authorisation (MIA).[5]

The MAH must also identify and select distributors who will supply the product to the different targeted EU markets, and ultimately to retail pharmacies and hospitals. These distributors must hold a Wholesale Distribution Authorisation (WDA) defined in the EU Regulation.[6]

Some EU countries, *e.g.*, France or Germany, also require a national WDA on top of the European WDA granted to Distributors for the commercialisation of medicinal products. These national WDAs are also delivered by national competent authorities that certify that the WDA holder meets GDP requirements.[7] WDAs are directly placed under the supervision of a Responsible Person ("RP") who is named on the license, and who is the Authorities' single point of contact for most if not all matters related to the commercialisation of the product.

Understanding Country-specifics

One of the most complex countries in Europe from a commercialisation perspective is France, which expects very rigorous oversight of product distribution and lifecycle management. On the other hand, France has put in place attractive early access programmes that offer the hope of faster revenues compared to other EU

markets which experience has shown to have less attractive legislative frameworks in this regard or have lengthy price & reimbursement procedures (which can also be the case in France).[8]

Companies seeking to market their products in France must have an "Exploitant" Authorisation,[9] which is defined under the French Public Health Codex as the organisation responsible for drugs "exploitation", *i.e.* commercialisation under the responsibility of a Responsible Person (also known as the "Pharmacien Responsable"). The Exploitant can be a separate entity from the MAH, which can be based anywhere in the EU. "Exploitation" refers to any activity that applies to the commercialisation of medicinal products in France (including quality management and compliance with pharmaceutical legislation, pharmacovigilance activities, market batch release, etc.).

While the definition of the Exploitant is not included in the European regulations, it is highly advisable that a company seeking to market a medicinal product in France hold an Exploitant status locally or partner with a consultancy in France to manage the Exploitant requirements, since many exploitation activities require native French speakers with deep knowledge of the French regulation and specific local requirements.

Being outside of the EU, the United Kingdom also brings additional commercialisation complexities. A national WDA is also mandatory for any company that supplies medicinal products to the UK market. WDAs issued by the national competent authority, the MHRA. In addition, a role of Responsible Person (import) (RPi) unique to the UK, has been introduced. The RPi is responsible for confirming QP certification and oversight of products imported into Great Britain from countries on an Approved Country for Import list (initially, this refers to countries in the EEA).

Just as in France, Germany, and the UK, in Switzerland, there is also a need for a national WDA.[11] In addition, companies looking to commercialise their products in Switzerland must have a local entity to apply for marketing authorisation, given that EU approvals are not recognised by Swissmedic, the national competent authority.[12] This is because Swissmedic requires a Responsible Person based in Switzerland who can quickly access the site in case there are any issues with a product that need to be resolved quickly.

To obtain a WDA from Swissmedic, the request must be carried out by a company legally established in Switzerland and for which a Responsible Person also based in the country has been nominated to supervise QA activities and maintain the Quality Management System. The RP is also in charge of releasing batches for the Swiss market and is the 'QA voice' in contact with Swissmedic and the concerned Cantonal Inspectorate.

Indeed, given that Switzerland is a federation of states, there are also Cantonal considerations in Switzerland, with some regulations being federal, and others Cantonal, which our experience shows adds further complexities for companies seeking to set up a local presence and commercialise their pharmaceutical products in the country. Cantonal inspectors conduct regular inspections, on behalf of Swissmedic, and the MAH must ensure all their procedures and an effective quality management system are in operation under the close supervision of the Responsible Person named on the WDA.[13]

Preparing for Commercialisation Complexities

Understanding the complexity of supplying medicines within European markets, establishing local/regional entities and the associated licences required does create commercialisation challenges for non-EU companies. However, early planning and a well-executed commercialisation strategy enable companies to better navigate these important markets and expand the reach of their products.

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Frederic Pailloux

Frederic Pailloux, Pharm.D., M.Sc., is Senior Director, Head Swiss Operations & QA/Responsible Person, at PLX Healthcare Services (Switzerland) GmbH. Frederic defines and implements strategies for efficient commercialisation readiness of medicines in the EU and Switzerland. As QA and GDP specialist, he also supports companies by helping them build their Quality Management System, and acts as a local contract QA/RP for Switzerland.