

# WHAT IS DISCUSSED BE

## Interaction between the European Medicines Agency

BY ILKA VON HOEGEN

**PLASMA PROTEIN THERAPIES** are marketed globally, but their approval and the subsequent monitoring of the therapies throughout their life cycles is done by National Competent Authorities, with often different approaches and philosophies towards licensure of medicinal products. It is inevitable that the divergent national approaches result in redundancies and are cumbersome for both, manufacturers as well as regulators.

Regulators recognize the problems and in recent years have commenced to work towards more similarity in their regulatory approaches. In 2003 the European Commission's European Medicines Agency (EMA) and the U. S. Food and Drug Administration (FDA) signed confidentiality arrangements as part of a framework for collaboration between the two agencies. After agreeing on the implementation plan and an extension of the agreement in 2005 the arrangements were extended indefinitely in 2010. Additionally, in 2008, both agencies agreed on an action plan on transatlantic administrative simplification that would benefit both the industry and the regulators by leveraging resources.

The scope of the exchanges between EMA and FDA is on centrally authorized products in the EU (unlike the US, European regulation of therapies includes that of the individual member states as well as the EU). While FDA cannot share personal data or trade secrets, it can share non-public information, such as commercial confidential, investigative, and pre-decisional information. The agencies also share preliminary thinking on guidance development, policies, internal analyses and enforcement actions.


The agencies exchange assessment reports, share pharmacovigilance and inspection information. They also perform joint manufacturing facility inspections. Regular interaction takes place in topic specific groups, the so-called clusters, for example for pediatrics, orphans,



BLITZ, YURAI23 / ISTOCK, PHOTO OBJECTS.NET, BONOTOM STUDIO

# HIND CLOSED DOORS?

(EMA) and the US Food and Drug Administration (FDA)

An American flag on a stand is positioned in front of a white door with a gold handle. The flag is the central focus of the left side of the page. The background is a light-colored wall with a white door and a patterned rug on the floor.

pharmacoeconomics, or pharmacovigilance. Recently a blood cluster has been established which will focus on plasma protein therapies. As in the other clusters, experts from both agencies address policy issues, guidance, product development and potential product safety signal. It is the ambitious aim of the exercise to establish streamline approaches to global product development starting with scientific assessments and potential agreement on the design of clinical studies and other particulars.

Are these developments a step into the right direction? Do pharmaceutical manufacturers have a choice? Probably not, the exchange is under way and both agencies have agreed not to disclose what they share.

Information is flowing back and forth throughout the entire life cycle of a product, from the first development phase, when a manufacturer seeks scientific advice through to product approval and product surveillance. FDA and EMA are sharing listings of ongoing EMA marketing authorization application and FDA applications (NDAs/BLAs) during the product evaluation phase giving both agencies the opportunity to follow product development and approval, even if the product is not intended for the market under their jurisdiction.

If a manufacturer intends to market the product in both markets, he needs to avoid inconsistency in the information provided to either side. With different regulatory schemes and reporting requirements, maintaining consistency is not as easy as it might seem.

Manufacturers have the option to seek Parallel Scientific Advice to ensure that both agencies have agreed the development plan for a candidate product, which should in the end facilitate the approval of the product in the US and the EU. The manufacturer submits the necessary documentation with a view to serve the needs of both agencies and waits for a positive opinion. But what if there is no agreement? Then the manufacturer has several options, depending of the nature of the discrepancies. He could approach both agencies individually with a submission tailored to the FDA's or EMA's needs. He could focus only on one market, either EU or US. But then the agencies exchange information that are not

**In the current situation providing consistent information is a difficult task, since it is well accepted that the overall philosophy of FDA and EMA are frequently divergent.**

disclosed and leave the manufacturer in a situation of greatest uncertainty and risk to lose the investment.

Increased communications and forums for regulatory Policymakers make information related to negative events more easily and quickly transmitted. This often results in making a local event into a global event.

In the current situation providing consistent information is a difficult task, since it is well accepted that the overall philosophy of FDA and EMA are frequently divergent. While EMA has established a catalogue of detailed guidance documents for manufacturers to follow, the FDA has a more flexible approach, making decisions on a case-by-case basis until it gains sufficient experience to develop formal guidance. The EMA Roadmap 2015 foresees to simplify the very complex EU system and the current proposal resembles the FDA approach, thus giving hope for transatlantic administration simplification in the future.

Within the agreements between the agencies there are elements that are designed to precisely address the need to develop common understandings, for example the exchange on guidance development or a practical example, the joint facility manufacturing inspections.

Product surveillance is another area of cooperation. Regulatory participants exchange findings on new safety signals and discuss interpretation of the data with a view on potential label/SmPC changes. It has to be noted that there are a number of differences between FDA's Risk Evaluation and Mitigation Strategies (REMs) and EMA's Risk Management Plan (RMP) mainly in relation to risk communication, where EMA relies mostly on SPCs while the FDA has Communication plans in place to directly inform patients and health care professionals. Again, a manufacturer providing product to both markets has to accommodate the different expectations of both agencies with a view on the mutual exchange between them.

The globalization of pharmaceutical regulation and distribution is part of today's reality. Manufacturers of pharmaceutical products have to respond to the challenges arising from cooperation between regulatory authorities albeit with different approaches and philosophies. ☞

*ILKA VON HOEGEN is PPTA Europe's Senior Director, Quality & Safety*

Save the Date

# PPTA'S 20<sup>TH</sup> ANNIVERSARY EVENT

Wednesday, June 20, 2012  
6:30 PM

The Pavillion  
at the Ronald Reagan Building  
Washington, DC

Silent Auction  
and Dinner

Special Recognitions  
and Reminiscing

SAVING AND IMPROVING LIVES  
20 Years  
PPTA  
Plasma Protein Therapeutics Association