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CROSS-DIMENSIONAL ALLIANCES

Working Together: A European Perspective



A GLANCE AT PPTA CORRESPONDANCE OR PROMOTIONAL MATERIALS **reveals the focus of this Association and the medicinal products produced by its members:** **biological lifesaving therapies either recombinant or fractionated from a** **very unique starting material—human plasma. In essence, what PPTA represents is not** **"Big Pharma," but a very specific niche sector serving patients with rare diseases.** **To further highlight their uniqueness these plasma protein therapies are exempted** **from biological products regulations from the European Medicines Agency (EMA) and** **World Health Organisation (WHO) biosimilars guidelines.**

On the other hand, plasma protein therapies also fall under the scope of broader pharmaceutical legislation applicable to all medicinal products with respect to marketing authorization and changes to these, which are regulated in the European Union (EU) Variations regulation. How can such a small sector influence these overarching provisions in the overall rumble of "Big Pharma" influence?

One has to look at the issue from a different angle. Market authorization of a medicinal product and maintenance throughout its life cycle are subject to the same procedures for all medicinal products. It is obvious that manufacturers have common interests: efficient procedures of market access and maintenance at affordable costs. The revision of the EU Variations Regulations in 2008 to establish a simpler, clearer and more flexible legal framework, while guaranteeing the same level of public and animal health protection was of particular interest to the manufacturers of biological medicinal products, i.e. recombinant and plasma-derived, because this product class has never enjoyed the pragmatic approach applied to classical pharmaceuticals. Any variation to a Marketing Authorization automatically triggered a Type II variation and it appears questionable, whether such an expensive and time consuming procedure is always justified, particularly for minor changes without any impact on the quality, safety or efficacy of the final product.


As per the initiative of PPTA since 2004, a number of Associations representing biological manufacturers such as EuropaBio, International Plasma Fractionation Association (IPFA), European Vaccine Manufacturers (EVM) and others formed an alliance

to promote their objective for a simpler, clearer and more flexible legal framework to reduce the regulatory hurdles for biological products where appropriate. Due to the EU Commission's precautionary attitude towards biological medicinal products these hopes were not fulfilled: At a specific meeting on biological products between the associations, EU Commission and EMA in the course of the public consultation period for the new Variations regulation it was regulators remained firm in their belief that the level of experience with biological products is not sufficient to permit a relaxation of regulatory surveillance of these products. But would there at least be a reduction in the fees payable for variations procedures?

In times with budget restrictions in all areas of the public sector an institution that is dependent on the support from national authorities and independent experts such as the EMA is faced with particular challenges to keep their performance and expertise according to the state-of-the-art. At the EMA workshop "Outcome of the Evaluation of the EMA, the Future Sustainability of the System" EMA representatives informed attending pharmaceutical manufacturers that the balance between fees and the level of service is no longer provided. Bottom line, prices are going up, but by 400%? Such a significant increase was experienced by one PPTA member company when they filed a group of variations to the Plasma Master File (PMF). Instead of the expected invoice of 57,200 Euros the company was asked to pay 237,900 Euros, because EMA charged each variation in the group separately, which was previously not the case. This change in procedure was not

announced and thus took manufacturers completely by surprise. PPTA immediately contacted the other associations and together a very strong complaint was submitted to the EU Commission and other relevant institutions and committees. Subsequently, PPTA and EuropaBio met EU Commission and EMA representatives for more in depth discussions.

In October 2010, the EMA published amendments to the Management Board implementing rules on the Agency's fees in relation to extensions of marketing authorization, Type II variations, annual fees, variations to the PMF and Vaccines Antigen Master File (VAMF). For PMF and VAMF the introduction of a maximum fee of 57,000 Euros for a group of variations (containing at least one Type II variation) is a great achievement, which will facilitate the filing of Type II variations to a PMF between annual updates. Since the VAMF is not a procedure that is used by vaccine manufacturers, PPTA was the only group that benefited from this particular amendment. Some other outcomes of the revision are also notable, such as the grouping and work sharing procedures, where now the fee for the third variation is reduced from 57,200 Euros to 19,100 Euros.

This example shows how a constructive bundling of forces between the different representations of pharmaceutical manufacturers enables small sectors such as the one represented by PPTA to be heard and to influence regulatory decision making processes. 

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