Plasma Protein Therapeutics Association

11 December 2006
Reference: DGEN 06014

Towards an Improved EU Variation System

PPTA comments on the consultation paper of the European Commission dated 20 October 2006

KEY ITEM 1: Harmonisation and national authorisations

- PPTA supports inclusion of purely national authorisations within the scope of the revised variations legislative framework – leading to harmonisation of standards across the Member States.
- PPTA supports change in co-decision legal basis to include national variations as soon as possible.
- PPTA asks for a short transition phase to the new system (< 2 years).

KEY ITEM 2: ICH Q8 / Q9 / Q10

- PPTA welcomes introduction of a less prescriptive approach in defining changes, which require variations.
- The practical implementation of a design space concept requires further outlining
- Introduction or change of design space would be subject to a MAA or type II variation.
- Changes within the ranges of an approved design space should not require any regulatory filing
- PPTA suggests regulatory contracts as part of MAAs and type II variations, e.g. pre-approved protocols where data in compliance with the concept of the pre-approved protocol can be submitted as variation IB or notification later.
- A science-based risk management approach should be allowed in full responsibility of MAH obviating the need for all inclusive change category lists. Rather risk management criteria and examples should be predefined.

Boulevard Brand Whitlock, 114/5 · 1200 Brussels BELGIUM · tel : +32.2.705.58.11 · fax : +32.2.705.58.20
VAT: BE453 837 462 · e-mail: pptaeu@pptaglobal.be · www.pptaglobal.org
PPTA Offices in Brussels · Washington · Annapolis · Tokyo

KEY ITEM 3: "Do and Tell" Procedure

- PPTA welcomes the introduction of the Annual Report concept for minor changes (type IA) besides immediate notifications for administrative changes.
- The timing should be defined by the MAH, e.g. based on the EU birthday.
- The option for bundling annual reports for several products is appreciated, for maximum efficiency this should be possible simultaneously for all affected Member States
- A combination with PSUR submissions should be possible.
- The list of proposed type IA changes in Annex 8.1 is appreciated as exemplary.
- An approach with an all-inclusive list will limit flexibility of the system.

KEY ITEM 4: Single Evaluation of Common Changes

- PPTA appreciates the introduction of bulk variations for a change affecting several products.
- The work sharing in variation assessment should not be optional but mandatory for the member states where the MAH requests it. It should include type IB and II variations.
- PPTA also welcomes the proposal of introducing the work sharing between national competent authorities where the change is common to several medicinal products. The PMF concept has shown that a single evaluation of certain quality aspects that are common to several medicinal products is feasible and can significantly reduce workload both for competent authorities and companies.
- PPTA asks to allow also for shared assessment for changes affecting just one product licensed in more than one member state. This could include a combination of changes (umbrella variation) and line extensions.
- The MAH would define the coordinator member state (if not EMEA) and the CMS.

KEY ITEM 5: Type IB procedure by default

- PPTA understands that lists of type II variations as well as type IA changes would be established and that changes not listed would be handled as type IB by default.
- The introduction of a "Tell, Wait 30 Days and Do" variation by default is appreciated by the majority of PPTA member companies, but members also support the EFPIA proposal.
- Again, the science-based risk management approach should be allowed for classifying the changes.
- A list of examples, that would fit the type IB category, could be provided to help implementation.

OTHER ITEMS

Variation conditions for biologicals:

- The reclassification examples in Annex 8.2 are appreciated. The list of exemplary type I A and I B variations should be extended further (see also PPTA proposal).
- In general, a science based risk management is favored over a rigid tick box list approach.

PMF

- PPTA welcomes the establishment of a variation system for PMF.
- An implementation guideline would be helpful.
- As with variations for biologicals in general, the classification for changes to the PMF should not necessarily be subject to type II variations. A lot of these changes are straight forward and do not require extensive review.
- PPTA suggests elimination of the second step procedure as the product license impact could be included in the first step assessment (expansion of the successful shared assessment concept).

CMD

- The role of the CMD in view of arbitration procedures should be legally reflected.

Monographs and Certificates of Suitability

- PPTA appreciates inclusion of administrative changes in annual reports.

Fixed deadlines for formal update of licenses following regulatory approval

- PPTA supports a clear timeline to allow for timely, synchronised implementation of changes.