World Federation of Hemophilia Product Selection Statement

The selection of safe, effective medicinal products is the responsibility of national regulatory and health agencies. In the case of clotting factor concentrates, whether plasma-derived or recombinant, these decisions can be complex and require careful consideration of important questions regarding both patient safety and clinical efficacy.

The WFH has developed guidelines to aid regulatory authorities in the selection process, where a pre-established national framework for the review and selection of treatment products is absent. Adherence to a strict review process is especially important when considering products that are new or are less well known within the global community.

A government or regulatory authority can ensure the safety and efficacy of a blood product by determining the source of the plasma, the viral inactivation processes used in manufacturing, and the results of clinical trials related to the product in question. For recombinant or plasma-derived products, sponsors must provide complete information about 1) studies demonstrating the efficacy of inactivation and removal steps to clear pathogens; 2) evidence confirming clinical efficacy in the treatment of bleeding; and 3) pre- and post-marketing studies showing no increased incidence of inhibitors.

To properly assess a product, national regulatory agencies must have information on the starting material, the manufacturing process and the final product. This information should include:

The quality of plasma raw material, including:
- Regulatory status of the plasma supplier
- Donor epidemiology
- Donor acceptance criteria
- Detailed description of testing performed on the blood/plasma
- Quality assurance measures
- Post donation information system, including inventory hold (inventory hold is not always required although it is used by many manufacturers.)
- Plasma pool size
- Testing of the plasma pool and/or units comprising the pool

The manufacturing process, including:
- Manufacturing steps and related in-process controls
- Pathogen inactivation and/or removal steps
- Process consistency
- Batch release specification

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The final product, including:

- Potency of the product and shelf life
- Product history
- Clinical studies demonstrating the product’s efficacy
- Pre-marketing clinical data on inhibitors
- Post-marketing authorization studies and pharmacovigilance information on: Incidence of inhibitors; incidence of infusional toxicities; and the incidence of adverse events

Other ways to ensure product safety and efficacy are to request a copy of the Marketing Authorization from a reference country or to request Batch Release testing by a qualified regulatory agency in another country (possibly the country of manufacture). It can also be useful to have information on where else in the world the product is currently on the market.

Because by their nature biological products like clotting factor concentrate carry the risk of transfusion-transmitted infection and the risk of development of inhibitors, the WFH advises that patient organization concerns about the safety and efficacy of products be expressed to the relevant authorities including asking them to share (when possible) the information they have obtained from the manufacturer in answer to the key questions outlined above. A more detailed explanation of these concepts can be found in the WFH publication *Guide for the Assessment of Clotting Factor Concentrates (2008)*.

The WFH is not a regulatory agency and cannot make recommendations relating to the safety or efficacy of specific blood products. The regulatory authority in a particular country must make these judgments based on domestic legislation, national health policies, and clinical best practices.

Endorsed by the WFH Blood Products Safety, Supply and Availability Committee, approved by the WFH Executive, February 2012.