



February 7, 2007

OUR STN: BL 125251/0

Octapharma Pharmazeutika Produktionsges. m.b.H
Attention: Barbara Rangetiner, Ph.D.
Oberlaaer Strasse 235
A-1100 Vienna, Austria

Dear Dr. Rangetiner:

This letter is in regard to your biologics license application (BLA) submitted under section 351 of the Public Health Service Act.

We have completed an initial review of your application dated December 12, 2006 for von Willebrand Factor Concentrate (Human) to determine its acceptability for filing. Under 21 CFR 601.2(a), we have filed your application today. The review goal date is October 14, 2007. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

While conducting our filing review, we identified the following potential review issues

1. Please submit data from non-clinical toxicology studies following single and multiple dosing with (von Willebrand Factor Concentrate (Human)). These studies should demonstrate safety of von Willebrand Factor Concentrate (Human) at multiples of the maximum expected clinical dose (e.g. 10-fold or higher). One single and one multiple dose study will be sufficient to support licensure.
2. Please provide safety data on polysorbate 80 (0.1%) added to the end product diluent to support exposure at multiples of maximum intended clinical exposure (e.g. 10-fold or higher).
3. We consider the study for pharmacokinetic comparison between WILATE and Humate-P, the U.S. licensed product, in von Willebrand disease patients (Study WIL-12) as the pivotal controlled trial in this BLA and the data from the uncontrolled trials in von Willebrand disease as supportive. Although at the present time, this BLA is fileable, licensure for each indication (treatment of spontaneous and trauma-induced bleeding episodes, ~~prevention of bleeding episodes~~) will be based on the adequacy and quality of the data supporting each claimed indication.
4. Please present your approach to fulfill the requirements for the submission of pediatric data under the Pediatric Research Equity Act. You would need to address use of your product in pediatric subpopulations by age. If waiver or deferral is to be requested for certain subpopulations, please provide your rationale.
5. To facilitate the clinical review, please provide electronic versions in Microsoft Word for Table of Clinical Investigators in Section 1.3.4 of Module 1, Sections 2.5 and 2.7 of Module 2, as well as the following parts of clinical study reports on von Willebrand disease in Module 5:

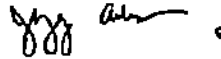
- WIL-12 pp 1-125
- TMAE-105 pp 1-77
- TMAE-109 pp 1-63
- TMAE-104 pp 1-67
- TMAE-106 (protocol) pp 1-53

6. Please provide Section 5.3.5.3.1 of Module 5 in adobe acrobat format.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

Should you need additional information or have any questions concerning administrative or procedural matters please contact the Regulatory Project Manager, Franklin T. Stephenson, at (301) 827-6165

Sincerely yours.



Alan E. Williams, Ph.D.
Director
Division of Blood Applications
Office of Blood Research and Review
Center for Biologics Evaluation and Research