The University of Oklahoma
Health Sciences Center
DEPARTMENT OF MEDICINE
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Philip C. Comp, M.D., Ph.D.
Director,
Thrombosis and Coagulation Laboratory

April 3, 2003

Dockets Management Branch
Food and Drug Administration
Room 1-23
12420 Parklawn Dr
Rockville, MD 20857

Re: Docket #02P-0435 (Citizen Petition)

Dear Sirs,

I am the adult hematologist for the Oklahoma Center for Bleeding Disorders. This comprehensive hemophilia center was established in 1978 and is the only center in Oklahoma. This multi-disciplinary program sees and coordinates care for patients within a four-state area.

We have used Alphanate extensively over a decade for persons with Von Willebrand Disease and selected individuals with Factor VIII Deficiency.

Von Willebrand Disease is undoubtedly the most common inherited bleeding disorder. It affects 1-3% of population – crossing all lines of gender, ethnicity and socio-economic status. The majority of these patients are mild and may respond to a synthetic product, DDAVP. However, this product may not be used more than twice within a week due to its mechanism of action. DDAVP is inadequate for the treatment of significant bleeds, surgery, fractures or multiple trauma. It has numerous contra-indications including head trauma and most notably for me - patients with hypertension, congestive heart disease, seizure disorders or who are currently pregnant. In these situations, Von Willebrand Factor must be given.

Alphanate is a plasma-derived blood product that is virally inactivated by solvent-detergent and heat treatments. It is manufactured in the U.S. Humate-P is currently the sole product with the FDA indication for Von Willebrand Disease. It is manufactured overseas and treated with pasteurization. Cryoprecipitate is not treated by any viral-inactivation method and current donor-screening tests cannot detect

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Oklahoma Center for Bleeding Disorders • CHO 3308 • P.O. Box 26307 • Oklahoma City, Oklahoma 73126
(405) 271-3661 • FAX: (405) 271-3756

infectious persons in the 'window' period. There is no recombinant Von Willebrand factor concentrate available (or pending) in the U.S. and there are efficacy problems with the European product. My patient population was devastated by the prior contamination of factor products with HIV and hepatitis. Today's 'medical consumers' are extremely sensitive to issues of viral safety and control of inherent risk with the use of a blood product, especially with the recent concerns of West Nile Virus and Creutzfeldt-Jakob (Mad Cow) Disease.

The vast majority of my patients are deeply concerned about lifetime caps on medical benefits and out-of-pocket expenses. Unit-to-unit, Alphanate is much less expensive than Humate-P.

Many patients are able to have local treatment and procedures under our guidance. Based on specific dosing instructions for units of Ristocetin Cofactor, the local institution obtains the necessary factor product. Because Alphanate does not have current FDA indication for Von Willebrand Disease, vials are not labeled with Ristocetin Cofactor contents. Although this information is available from the manufacturer, the hospital supplier may be unaware. Unless someone calls for the assay of each available vial size, the institution has a choice of ordering Humate-P (at a much higher cost to the patient) or using a flat conversion formula for Alphanate dosing. This may result in under-dosing (rare) or dramatic over-dosing with Alphanate, which may be catastrophic in adults with age-related risks for excessive clotting.

I am deeply disturbed that the FDA has continued to delay the Von Willebrand Disease-indication for Alphanate. Patient safety is jeopardized by the lack of Ristocetin Cofactor labeling on this product that is a standard treatment for Von Willebrand Disease. Two competing products in the marketplace should reduce the price as well as improve the general supply and available dose range. In the strongest terms, I urge you to give Von Willebrand Disease approval for Alphanate.

Thank you for considering this matter. If you have questions about these adults or the management of inherited bleeding disorders, please do not hesitate to contact me at 405-271-3661.

Sincerely,

Philip C. Comp

Philip C. Comp, M.D., Ph.D.
Professor of Medicine