Jimmy Everest Center for Cancer and Blood Disorders in Children

William H. Meyer, M.D.
Ben Johnson Professor and Chief
Sheila M. Crow, M.A.
Heather C. Huszti, Ph.D.
Christa H. Johnson, Ph.D.
René Y. McNall, M.D.
Ruprecht Nitschke, M.D. (Emeritus)
Joan B. Parkhurst, M.D.
Charles L Sexauer, M.D.

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 medical director of the Oklahoma Center for Bleeding Disorders. This comprehensive hemophilia center was established in 1978 and is the only center in Oklahoma. We see patients from a four-state area.

Our patients participated in the early Alphanate prospective studies for surgical safety and efficacy. We continue to use the product extensively for Von Willebrand Disease and selected Factor VIII Deficiency patients. This includes treatment of joint bleeds and routine procedures in addition to open-heart surgery and recalcitrant Factor VIII inhibitors.

Von Willebrand Disease affects 1-3% of the population, regardless of sex, nationality or ethnic background. For an affected individual, each offspring has a 50% chance of inheriting the disorder. 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. Thus DDAVP is inadequate for the treatment of significant bleeds, surgery, fractures or multiple trauma. It has numerous contraindications including head trauma and patients with hypertension, 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 two separate methods. 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 receives only a single viral-inactivation process. Cryoprecipitate is not treated by any viral-inactivation method and donor-screening tests cannot detect infectious persons in the 'window' period. There is no recombinant Von Willebrand factor concentrate available in the U.S. and there are efficacy problems with the European product. My patients were devastated by the prior contamination of their factor products with HIV and hepatitis. The current families

02P-0435 C8

HEMATOLOGY-ONCOLOGY SECTION • P.O. Box 26307 • Oklahoma City, Oklahoma 73126 • (405) 271-4412 • FAX: (405) 271-3265
Academic Office • (405) 271-5311 • FAX: (405) 271-3756

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 supply of factor concentrates has been somewhat unpredictable over the years due to local manufacturing issues (closure for routine maintenance, inspection and corrections for recent implementation of Good Manufacturing Standards) as well as international issues (competition for sole-supplier product, corporate priorities, transportation issues after terrorist attacks). Since a manufacturing suite can only produce a single dose size at a time, there are periods where a specific dose may be unavailable. Particularly with products manufactured overseas, U.S. treatment needs do not receive the highest priority. While it is inconvenient for adults to combine small doses, it is wasteful to use only part of an adult sized-vial to treat an infant – and administration of the entire vial could cause medical complications.

I am gravely concerned that without the (very long) awaited FDA indication, the manufacture of Alphanate may cease. For proper medical care, we must have a stable supply of safe Von Willebrand Factor concentrate in a full range of available doses. 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 patients or their management, please do not hesitate to contact me at 405-271-3661.

Sincerely,

C. L. Sexauer – MD

Charles L. Sexauer, M.D.
Medical Director
Oklahoma Center for Bleeding Disorders