HEMOPHILIA AND THROMBOSIS CENTER ANGELO BIANCHI BONOMI
World Health Organization
Collaborating Center for Inherited Coagulation Disorders

MAILING ADDRESS
A. BIANCHI BONOMI
HEMOPHILIA AND THROMBOSIS CENTER
VIA PACE, 9 – 20122 MILANO
TEL. 02/55035421 – 02/50320713
TELEFAX 02/50320723
e-mail piermannuccio.mannucci@unimi.it
pmmannucci@libero.it

U.S. Food and Drug Administration
To Whom It May Concern:

Milano, March 31th, 2003

Recommendation For The Approval Of Antihemophilic Factor (Human), ALPHANATE® For The Treatment Of Patients With Von Willebrand Disease (VWD)

I understand that, in the USA, Alphanate® is still under consideration for licensing in VWD patients. I would like to draw to your attention the following areas where, in my considered opinion, the development of this product represents an important advance in the treatment of this disease.

Firstly, ALPHANATE® is a "high purity" factor concentrate made by a process that incorporates two specific and complementary virus inactivation steps (solvent-detergent treatment and terminal dry heat-treatment). The use of such "dual virus inactivated products" is recommended (CPMP/BWP/269/95 reference) as they may offer a greater margin of safety compared to older products made by processes including only one specific virus inactivation step. As an additional benefit, the higher purity of Alphanate® allows a smaller injection volume which is more comfortable for patients.

Secondly, ALPHANATE® has been licensed for VWD in a number of European countries and has been used successfully for a number of years.

Thirdly, ALPHANATE® is the only factor concentrate therapy for VWD patients for which clinical efficacy and safety has been investigated by means of a large, prospective clinical study (reference Mannucci et al Blood 2000). This allows dosing recommendations for Alphanate® to be made on the basis of sound pharmacokinetic principles. Other available factor concentrate therapies are supported only by retrospective analyses of clinical use.

Finally, as a physician routinely treating patients with VWD, I strongly support the licensing of alternative products such as ALPHANATE® as this provides greater therapeutic choice and an assurance of continued product supply to this patient group.

Sincerely yours,

P.M. Mannucci
Professor and Chairman of Medicine
University of Milan

C12