



Hemophilia Federation of America

Advocacy For Persons With Clotting Disorders

December 18, 2003

Jay Lozier MD Ph.D
Chairman of the Organizing Committee
Workshop on Factor VIII Inhibitors
FDA/CBER/OBRR
1401 Rockville Pike HFM-340
Rockville, MD 20852

Dear Dr. Lozier,

May we compliment you on your Inhibitor Workshop (11/21/03) and your work in enhancing the lives of the men with hemophilia in our community. Development of specific factor inhibitors associated with transfusion of blood, plasma, cryoprecipitate and specific factor concentrates has been a known complication since treatment became available. Your timely workshop was in response to the heightening concern that inhibitor development may increase with newer factor products and that this will become a major medical issue for our younger generation of men/boys with hemophilia who have been virally “free.”

Complications associated with inhibitor development in the past 25 years have been overshadowed by the devastation caused by blood-borne infections. It is for this very reason that we are now preparing a letter of concern about a statement made during the Inhibitor Workshop meeting. This statement was made with regard to factor made by recombinant method rather than that which is plasma-derived. It relates to the proposed FDA guidelines to support licensure of new factor concentrates. These guidelines will also address the development of inhibitors with the use of newer products and different factor VIII molecules.

One suggested requirement for licensure made by the FDA spokesperson was that all new products need to be tested in comparison to plasma-derived products as a “gold standard” for the pharmacokinetic studies. However, a pharmacokinetic evaluation will not be able to be used to determine the risk of inhibitor development after multiple treatments. In addition, a comment from the audience pointed out that use of a plasma-derived product may be of concern to both subjects as well as investigators with respect to infectious

complications as a safety issue. The response was that the FDA does not consider that a difference in safety exists between recombinant and plasma derived products.

While it is a patient's choice to agree to a clinical study, investigators participating in the study are sending a message that they believe plasma-derived products are equally safe from infectious agents. Such a study would be in contrast to the current general clinical practice of many hemophilia treaters and in conflict with the recommendations made by MASAC.

In the context of this issue, as regarding product safety addressed this past year with the Department of Health and Human Services, we are very concerned that, again, the disregard for the potential safety of our patients' products may result in a shift in policy in the future. We would ask for reconsideration of the recommendation that plasma derived products be used as the standard for pharmacokinetic studies. Since all manufacturers presently have a recombinant product that has already been compared to a plasma derived product, we would ask that a recombinant product now be used as the "gold standard."

Thank you for your consideration of our points. We look forward to your reply.

Sincerely,

Jan Hamilton

Jan Hamilton
Executive Director
For
HFA Medical Advisory Professional Board
Jamie Siegel, MD and Christopher Walsh, MD Co-chairs

Cc: Jay Epstein
Mark Weinstein