



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
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Memorandum

Date: January 23, 2004  
From: Mark Weinstein, Ph.D. *MW*  
Associate Deputy Director, OBRR/CBER  
Subject: Establishing a Docket regarding the Factor VIII Inhibitor  
Workshop of November 21, 2003  
To: Docket Number 2004N-0033

The Food and Drug Administration, Center for Biologics Evaluation and Research, in co-sponsorship with the International Association for Biologicals (IABs), held a workshop entitled "Factor VIII Inhibitors" on November 21, 2003 at Lister Hill Auditorium, Bethesda, Maryland. The purpose of the event was to address regulatory and scientific concerns about inhibitors to factor VIII induced by Antihemophilic Factor (factor VIII) products. These inhibitors arise in a significant minority of patients with hemophilia and make replacement therapy problematic.

The workshop covered a broad range of topics including the potential need for a new reference standard and methodology for inhibitor assays, variations in clinical trial design, and the benefits and risks of harmonizing standards with other regulatory entities. Other issues discussed included epidemiological aspects of inhibitor formation, and a proposal for an international prospective clinical study on inhibitor formation. Regulatory, medical, scientific, and manufacturing authorities, including those from Canada and the European Union participated at the conference. Slide presentations and the transcript of this meeting are available on this docket, and at <http://www.fda.gov/cber/summaries.htm>, and <http://www.fda.gov/cber/minutes/workshop-min.htm>. The Federal Register notice of the meeting is at "Factor VIII Inhibitors; Public Workshop; October 20, 2003, 68 FR 59942".

While the workshop provided much valuable information, too little time was available at the end for full audience participation. We have established this docket to continue collecting information about factor VIII inhibitors, and comments on the workshop presentations. The docket responses will be used to inform us about the need and feasibility of establishing new inhibitor assay standards and methodologies, stakeholders' opinions about current upper and lower limits of acceptable inhibitor formation in clinical trials, and the use of plasma-derived versus recombinant factor VIII controls in pharmacokinetic trials, among other issues. The information may also be useful in the drafting of guidance on clinical trials to evaluate potential inhibitor formation from factor VIII products.

The docket will be open for at least a year to serve as a continuing source of information about factor VIII inhibitors. Submitters to this docket are encouraged to comment not only on the workshop, but on the responses of other submitters, and to provide new information on factor VIII inhibitors, or proposals for new studies.

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