NATIONAL HEMOPHILIA FOUNDATION
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MASAC Document #209

MASAC STATEMENT ON BIOSIMILARS

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on May 6, 2012, and adopted by the NHF Board of Directors on June 22, 2012.

Treatment for hemophilia A and B involves the administration of clotting factor concentrates that are safe and effective, but unfortunately they are expensive life-long therapies, especially for patients with severe disease who must receive treatment on a regular basis. One proposal to reduce the cost of this therapy is to develop biosimilars, which are biologic products patterned after the original concentrates. Under recently published FDA Guidance documents on biosimilars, they may not be required to undergo the same rigorous clinical trial testing as the original clotting factor concentrates. Clinical data requirements will be determined by the FDA on a case-by-case basis.

Despite being fundamentally similar to the original products, biosimilars are not identical. The complexity of large-molecule biological therapies and the intricacies of the manufacturing process make it impossible to exactly replicate a biological product. Unfortunately, even minute changes in the protein molecule could have dramatic consequences for the patient.

The most significant adverse event facing people with hemophilia today is the risk of developing an inhibitory antibody. The potential for each of the new biosimilars to induce formation of inhibitory antibodies is unknown. However, since each biological molecule is modified in a different way, each bears the potential to produce inhibitors.

Thus, clinical trials are essential to the approval process to ensure that biosimilars are safe and effective and meet an appropriate standard of immunogenicity. Since non-human trials are not necessarily indicative of human reaction, human clinical trials should not be bypassed. Clinical studies should not arbitrarily be deemed unnecessary, because information derived from these studies is essential to making an educated decision about the safety and efficacy of a particular product. Decisions on study design should be carefully made on a case-by-case basis, taking into account the significant risk of developing inhibitory antibodies.

MASAC believes that it is necessary to proceed with caution when accepting new products or therapies, and an approval pathway that shortcuts the vetting process poses a significant risk to patients. We are mindful of the need to create a new regulatory pathway for biosimilars, but this pathway should not result in shortcutting safety standards. The FDA must provide assurance that the safety and efficacy of biosimilars have not been compromised. Until a framework guaranteeing their safety and quality is established, we urge that follow-on plasma

protein or recombinant therapies, including therapies for patients with hemophilia, be excluded from any abbreviated regulatory pathway. If these therapies are included in the abbreviated pathway, rigorous clinical trials must be required.

MASAC urges harmonization in clinical trials requirements between FDA—CBER (Center for Biologics Evaluation and Research) and FDA—CDER (Center for Drug Evaluation and Research) when drugs seeking approval in CDER are destined for use in the bleeding disorders community. (Until now, all factor products have been approved by CBER.) MASAC further urges the FDA to require additional post-marketing surveillance to monitor for any potential risk whenever biosimilars are approved by either center.

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