NATIONAL HEMOPHILIA FOUNDATION
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MASAC Document #228

MASAC STATEMENT REGARDING USE OF VARIOUS CLOTTING FACTOR ASSAYS TO MONITOR FACTOR REPLACEMENT THERAPY

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on April 13, 2014, and adopted by the NHF Board of Directors on June 5, 2014.

There is wide variability of factor activity level results depending upon the assay selected to perform the task (i.e. one stage assays vs. chromogenic assays). In certain scenarios, a chromogenic assay may be preferable to a one-stage assay, or it may be a useful adjunct for diagnosis. Currently, chromogenic assays are limited in availability in the U.S. for routine clinical use. Awareness of the strengths and weaknesses and increasing the availability of both assays will aid in the assay choice in a given clinical situation. (1)

We are entering an era in which therapeutic products to treat hemophilia A and B are produced by genetic modification and post-translational changes of the factor molecule. These new molecules are, in some cases, magnifying limitations with the assays currently available for monitoring replacement therapy. It has been widely recognized that there is marked variability between factor VIII and factor IX one-stage assays performed in different laboratories, owing to the numerous combinations of aPTT reagents, instruments, calibration standards, and factor-deficient plasmas available. In addition, the variability among the aPTT-based assays is greater when attempting to measure factor levels near the lower limits of the assay range. Moreover, in some test conditions the aPTT may not be sensitive enough to screen for mild factor VIII and factor IX deficiencies, and reliance on the one-stage aPTT assay alone may not allow accurate characterization of some forms of mild hemophilia.

These problems are either minimized or not seen when chromogenic assays are performed. Chromogenic assays have become widely utilized in Europe, and the European Pharmacopoeia requires that potency of all factor products be assigned using a chromogenic assay. In the U.S., however, there are not enough FDA-approved chromogenic assays, and such assays may be more costly than the one-stage assays.

Therefore MASAC recommends the following:

1. Laboratories routinely performing factor assays on patients with hemophilia should strongly consider the addition of factor VIII and factor IX chromogenic assays when these assays are approved by the FDA.

2. Laboratories routinely performing factor assays should participate in regular proficiency testing as well as in field surveys being done by manufacturers of newer clotting factor concentrates.

3. Manufacturers of chromogenic factor assays are encouraged to bring their products to the U.S. market for clinical availability.

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4. FDA should expedite approval of chromogenic assays for factor activity levels, including factor IX, to ensure that the newer modified factor products are being monitored appropriately. This will ensure that these products are being used safely and appropriately in individuals with hemophilia and other bleeding disorders to prevent the potential consequences of over- or under-dosing.

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