**[P-T-118] U.S. INHIBITOR PILOT PROJECT: STUDY DESIGN AND METHODS VALIDATION**

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**Introduction:** The Universal Data Collection (UDC) Program of the Division of Blood Disorders at the Centers for Disease Control and Prevention (CDC) has initiated a pilot project at 9 U.S. Hemophilia Treatment Centers to perform post market surveillance for inhibitors. Goals are to prospectively collect risk factor and product exposure data, to provide centralized inhibitor monitoring, and to correlate inhibitor formation with genotype.
**Methods:** Patients provide infusion logs with data on product brand, dose, and reason infused. A blood specimen is collected at baseline, annually, at product switch, or for clinical indication. Plasma and cells for DNA are shipped on cold packs to CDC, where inhibitor testing is done by the Nijmegen modification of the Bethesda assay, using commercially prepared buffered normal pooled plasma (BNPP) and deficient plasma from a hemophilic donor. A positive control with a known inhibitor titer is run with each assay. Specimens are screened for inhibitor at 3 parts patient plasma to 1 part BNPP. Positive specimens are retested in dilutions. Results are reported in Nijmegen-Bethesda units (NBU). The intron 22 inversion of the FVIII gene is detected using a modified version of long-range PCR. Utilizing the ABI 3730 Automated DNA sequencer, FVIII and FIX genes are sequenced in both directions, including both the 5' and 3' untranslated regions.
**Results:** In the first year, 438 patients (80% hemophilia A) were enrolled. Comparison of 50 cold pack specimens to frozen specimens shipped on dry ice showed a correlation coefficient of 0.998. 406 inhibitor tests have been performed. The effects of infused FVIII or FIX and heat treatment of specimens are being investigated. More than 200 gene analyses have been done.
**Conclusions:** Centralized monitoring of inhibitors is feasible and promotes quality control. Concurrent mutation analysis will add to the data on risk factors. International coordination of such data collection will produce a powerful tool for surveillance.
Soucie JM, Miller CH, Creary M, Hooper WC, Abshire TC, Brettler DB, Bockenstedt P, DiPaola J, Massey G, Neff A, Shapiro A, Tarantino M, Wicklund BM, DiMichele D, U.D.C. Working Group. U.S. INHIBITOR PILOT PROJECT: STUDY DESIGN AND METHODS VALIDATION. *J Thromb Haemost 2007*; **5** Supplement 2: P-T-118

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