NAME OF PROJECT: Establishment of a standard for Factor VIII Inhibitors

Subcommittee: Factor VIII, Factor IX and Rare Coagulation Disorders

- Person responsible (Chair / Principal Investigator): Dr. Koen Mertens (The Netherlands)

- Members:
  - Dr. Sanj Raut (UK)
  - Dr. Martin Lee (USA)
  - Dr. Gary Gilbert (USA)
  - Dr. Alok Srivastava (India)
  - Dr. Carel M. Eckmann (The Netherlands)

- Aim / Mandate of the project:
The initial aim of this project was to establish the 1st International Standard for Factor VIII Inhibitors. This project has been approved at the 2003 SSC Meeting, and was subsequently endorsed by WHO and EMEA. The initial study, which included 22 laboratories and 5 candidate materials, has been performed by Dr. Raut from NIBSC. In 2006 he presented an interim analysis at the SSC meeting in Oslo and at the WHO-ECBS meeting in Geneva. None of the candidate materials was considered suitable for establishment as the 1st International Standard for FVIII Inhibitors. This was due to a variety of reasons, in particular to the overall poor quality of the data reported. In 2007, a ‘post-hoc’ statistical analysis on the raw data has been performed in order to assess the validity of the individual inhibitor estimates. This revealed that most participants performed inhibitor assays in a format that does not allow any statistical evaluation. As proposed at SSC meetings in 2008 and 2010, the only option to proceed would be a new, more controlled collaborative study. The aim of the present project is to provide (1) recommendations for the assessment of statistically valid inhibitor titres, and (2) a reference reagent (not necessarily a standard) to facilitate inhibitor testing. These tools will be essential for the successful establishment of an International Standard for FVIII Inhibitors in the future.

- Methodology (in very brief, not more than 1 paragraph):
For this study several new materials have been produced, including new recombinant antibodies which are cloned from the immune repertoire from inhibitor patients. We will investigate whether these monoclonals are suitable for “like versus like” testing of polyclonal patient samples. At NIBSC studies have been performed on a new assay format as an alternative to the regular Bethesda/Nijmegen assay. These recent developments may provide a starting point for bringing this project to some completion.

- Year of starting: original project started in 2003, and the current feasibility study in 2012

- Year of completion (expected): 2015