Data Collection Worksheet

Please Note: The Data Collection Worksheet (DCW) is a tool to aid integration of a PhenX protocol into a study. The PhenX DCW is not designed to be a data collection instrument. Investigators will need to decide the best way to collect data for the PhenX protocol in their study. Variables captured in the DCW, along with variable names and unique PhenX variable identifiers, are included in the PhenX Data Dictionary (DD) files.

Individual Pharmacokinetic Study Using One-stage Clotting Factor Assay - Extended Half-life Factor VIII Products

Sample Collection

The PhenX Hemophilia Inhibitors Working Group (WG) recommends that investigators follow the sample collection procedures outlined in Lippi et al. (2012) to ensure quality specimens for coagulation testing. These recommendations include basic criteria for venipuncture (e.g., proper patient identification, use of correct techniques, appropriate devices and needles) as well as additional guidance for critical parameters which can affect the outcome of clot-based tests. These critical parameters include prevention of prolonged venous stasis, collection of nonhemolyzed samples, order of blood draw, and appropriate filling and mixing of collection tubes.

Additionally, the WG highlights that blood should be collected by direct venipuncture into 3.2% sodium citrate tubes and filled within 11% of fill line. A second tube should be collected. A discard tube should be drawn if using a winged butterfly collection system.

Sample Processing

The WG recommends that investigators follow the sample collection procedures outlined in Adcock Funk et al. (2012). The procedures include that:

- unprocessed or processed sodium citrate samples remain capped and at room temperature until testing,
- samples should not be refrigerated or stored on ice or in an ice bath,
- samples should be transported vertically, and
- processed samples should not be agitated during transportation to avoid remixing of components.

Additionally, samples can be transported and stored as:

- unprocessed sodium citrate whole blood samples,
- whole blood samples centrifuged and maintained in sodium citrate tubes, or
- plasma processed by centrifugation and aliquoted into a second tube.

Ideally, whole blood samples should be processed to platelet poor plasma (PPP) within 1 hour of collection and assayed within 4 hours of collection.

If centrifuging samples, the centrifuge should be validated so that post-centrifuged samples contain less than 10,000 platelets/microliter. Centrifuged samples should be frozen immediately and can be stored at -20° C for 2 weeks. Samples should be transferred to ≤ -70° C for longer storage, including shipment.

Extended Half-life Factor VIII Products: One-stage Clotting Factor Assay

There are a number of different assays and instruments that are available to perform the one-stage clotting factor assay. However, the WG notes the activity of Factor VIII extended half-life products measured by the one-stage clotting factor assay can vary according to the reagents and instrumentation. Some one-stage assays are not suitable to monitor specific extended half-life products (see "General References"). Therefore, Investigators should select an assay that aligns with the one used to determine the potency of the extended half-life product.

Once an assay is chosen for a particular study, the WG recommends that no changes in the protocol be made over the course of the study. Because results can vary with the instrumentation and reagents, the WG recommends that the investigator record the make and manufacturer of equipment, the repeatability and coefficients of variation for the assay, and the reagents used.

Extended Half-life Factor VIII Products: Individual Pharmacokinetic Study

Prior to pharmacokinetic evaluations, participants should undergo a treatment-free washout period lasting longer than five half-lives. Samples should be taken before infusion (baseline), 10-15 minutes after infusion, and then up to eight other time points that cover 2.5 half-lives of the extended half-life Factor VIII products. The Hemophilia Inhibitors WG notes that the timepoints necessary for the pharmacokinetic study to cover 2.5 half-lives will depend on the specific extended half-life Factor VIII product being used and can be identified in relevant pre-licensure studies. Investigators should report which timepoints were used.

Extended Half-life Factor VIII Products: Interpretation of Individual Pharmacokinetic Study Results

The half-life of extended half-life Factor VIII products is highly variable and the level at which an inhibitor is suggested has not been established.