Clinical Database

A clinical database (which contains all of the information on the CRFs) is not necessary for BE submissions to the OGD. Also, it is rare that such a database would be required by the FDA for a single dose BE or BA study (in volunteers) to support an NDA submission. However, some companies require all CRF data to be entered into a database so that these data can be included in the overall safety database for the NDA. It should be apparent that inclusion of such a database will increase the cost of the study. Companies should carefully review proposals from CROs to determine if such a database has been included.

Bioanalytical

Any bioanalytical method used for a human BA/BE study should conform to current FDA guidance [2] on analytical validation and should be conducted according to the FDA cGLPs.

Bioanalytical Method/Technology Requirements

Ideally, a CRO should have a validated analytical method in place before dosing the clinical trial. On occasion, a pharmaceutical company may need to contract the method development and validation to a CRO. Because the method ruggedness is dependent on the development and validation processes, these processes should be closely evaluated before committing a BA or BE study to any CRO.

Project Timelines and Turnaround Time

Project timelines are highly method specific. Sample analysis timing and throughput should be discussed, understood, and agreed upon before project agreement. Most CROs have standard turnaround times that will apply unless they are otherwise negotiated. It is also important to negotiate the timeline for the final written analytical report; otherwise, standard CRO timelines will be assumed. These standard timelines may be acceptable; however, it is important to get all timelines committed in writing.

Analytical Report and Data Format

If a client-specific bioanalytical report format, template, or file is to be used to record data, the format, template, or file, along with any instructions, must be provided to the laboratory before or with the shipment of samples. Sponsors should be aware that implementation of client-specific formats may result in additional charges.

Assay of Samples from Placebo-Treated Subjects

Generally, samples from placebo-treated subjects are not an issue with BE studies. However, some BA studies may include placebo treatments so that safety can be more appropriately evaluated. For these studies, it is essential to communicate with the CRO regarding the handling and analysis of these samples. All CROs will charge for each sample that is assayed; some CROs will assay all samples, whether or not they were generated in a placebo treated subject. If the firm does not require placebo-treated samples to be analyzed (because they generally will not provide any meaningful pharmacokinetic data), it is important to provide the randomization schedule to the laboratory before analysis.