

the CRO clinical personnel are often more familiar with the CRO format that will result in fewer questions back to the client.

Clinical Study Population

Many, if not most, BA/BE studies are conducted in healthy volunteers. In the past, apparently to reduce variability and liability, most sponsors chose to perform most BA/BE studies in healthy, young, male volunteers. However, the most recent FDA guidance for BA/BE studies [6] states as follows:

Unless otherwise indicated by a specific guidance, subjects recruited for in vivo BE studies be 18 years of age or older and capable of giving informed consent. This guidance recommends that in vivo BE studies be conducted in individuals representative of the general population, taking into account age, sex, and race. We recommend that if the drug product is intended for use in both sexes, the sponsor attempt to include similar proportions of males and females in the study. If the drug product is to be used predominantly in the elderly, we also recommend that the sponsor attempt to include as many subjects of 60 years of age or older as possible.

The FDA guidance provides leeway for the clinical study population. However, the RFP needs to specifically address the expected composition of the volunteer population. To expedite recruitment, it is best to use males and females without specifying a specific ratio of males to females. The study population is also defined by the drug product; for example, an oral contraceptive BE study would be conducted only in females, while that for a hormone replacement product should be conducted in postmenopausal females. Given the difficulties in recruiting some of these special populations, it is important that the sponsor define (upfront) the maximum number of dosing groups that may be allowed.

Inclusion/Exclusion Criteria

The protocol inclusion/exclusion criteria such as acceptable ranges for age and weight, race restrictions, and whether smokers will be allowed to participate can affect the clinic's ability to recruit and can have a significant effect on the cost of the clinical trial. The FDA BA/BE guidance [6] continues as follows:

If the drug product is to be used predominantly in the elderly, we also recommend that the sponsor attempt to include as many subjects of 60 years of age or older as possible. We recommend that the total number of subjects in the study provide adequate power for BE demonstration, but it is not expected that there will be sufficient power to draw conclusions for each subgroup. Statistical analysis of subgroups is not recommended. We recommend that restrictions on admission into the study generally be based solely on safety considerations. In some instances, it may be useful to admit patients into BE studies for whom a drug product is intended. In this situation, we recommend that sponsors and/or applicants attempt to enter patients whose disease process is stable for the duration of the BE study. In accordance with § 320.31, for some products that will be submitted in ANDAs, an IND may be required for BE studies to ensure patient safety.

Because a BA/BE study for any given drug product may or may not require special inclusion criteria, it is best that any expectations be documented in the RFP. These criteria will affect recruitment and the study cost; when comparing proposals