be readily established using analytical similarity studies and clinical pharmacology studies.
- A product that needs a trial in patients is likely a borderline biosimilar product, the Agency asserts.

A clear understanding of the mind-set of the FDA can be had from how it responded to the criticism as well as a lawsuit to defend approving a low–molecular weight heparin (LMWH) product without any clinical studies. The FDA says that this scientific approach is reflected in five criteria, which involve (a) the physical and chemical characteristics of enoxaparin, (b) the nature of the heparin material and the chemical process used to break up heparin chains into smaller pieces, (c) the nature and arrangement of components that constitute enoxaparin, (d) certain laboratory measurements of the product's anticoagulant activity, and (e) certain aspects of the drug's effect in humans. These five criteria ensure that a generic enoxaparin drug product will have the same effects as the brand name drug product when injected into a patient. Although the EMA guideline requires clinical studies to demonstrate comparable effectiveness to a similar LMWH, the FDA notes that its approach (i.e., the five criteria) is more sensitive to differences between two enoxaparin products than the clinical studies recommended in the EMA guideline are (http://www.fda.gov/Drugs/DrugSafety/Postmarketdrugsafetyinformationforpatientsandproviders/ucm220037.htm).

The most significant advice that I can offer to biosimilar sponsors is *not* to offer to do any phase 3–type studies unless specifically asked for by the FDA, in the review of data at the Type 3 meeting level. When the FDA tells you the design and scope of the study needs a review—you would know then that your application is weak.

If it takes a clinical study in patients to establish effectiveness, then it is not a good biosimilar product; clinical testing does not replace analytical similarity, the clinical pharmacology, and, where applicable, nonclinical evaluation.

10.4 Meeting the FDA

From the initial advisory meeting (which is free) to Type 4 meetings, the FDA has opened its doors for continued consultation with biosimilar developers; the sponsor must take advantage of these meetings regardless of how confident it feels about its product. There is no hearsay reliance on approvals given to others. Because of the stiff fee you will pay under BsUFA as shown in Table 10.1 for 2016, it pays to make use of these meetings. Know that if you fail to pay on a timely basis, you will have an automatic full clinical hold.

Notice the fee structure wherein a separate category of without clinical studies is provided, which simply asserts the mind-set of the FDA that