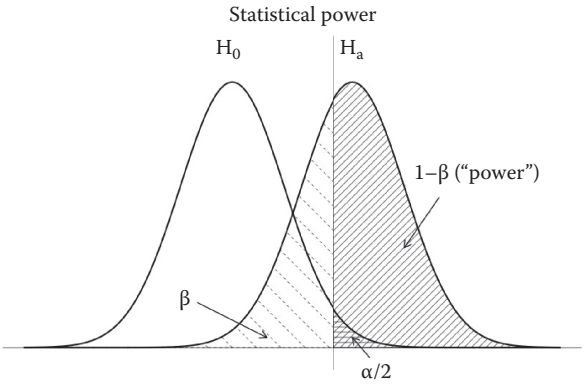

Figure 9.12 Statistical power of test.

9.8.5 Equivalence interval

This is an interval established based on the variability of the reference product, such as $1.5*\sigma_R$; the σ value is derived from an independent set of reference lots. The 90% CI for the difference of means of the test and reference product (separate lots tested side by side) should reside within the equivalence interval.

9.8.6 Quality range

This is a range established based on the standard deviation of the reference product, $X*\sigma_R$ side by side; the majority of values of the test product are expected to fall within this range; this will likely be 90% of values, and the X value will be 3, but the developer will have to justify this range.

9.8.7 One sample

Each lot contributes one value for each attribute being assessed. This condition, in essence, ignores any lot-to-lot variability of both the reference product and the proposed biosimilar product; the difference between means; and the inflation/deflation in variability between the reference product and the proposed biosimilar product. However, this is allowed by intention. Some researchers have criticized it mainly because of their lack of understanding of GMP considerations. In Tier 1 and Tier 2 testing, the standard deviation of the reference product is obtained from one lot contributing one value and not multiple samples from the same lot because if the lot is released, it is expected to have statistical compliance with within-lot variability; a similar assumption is made for the test product. This fine point is missed by commentators who are not fully familiar with GMP manufacturing aspects, and several suggestions have been made including testing multiple samples from each lot; using the lower of the 95% confidence limit of standard