have 80% of subjects with HIV-1 RNA below the lower limit of detection at 48 weeks. If a drug company would like to plan a new study with power $(100-\beta)$ of 90% and a type I error rate (α) of 5%, what sample size would be needed to establish the equivalence of a new drug candidate if the clinically acceptable difference is 10%? To calculate the sample size, we can translate the request into the sample size formula as $p=0.8$, $d=0.1$, and the value of the quantity $(z_{1-(\alpha/2)}+z_{1-\beta})^2$ is obtained from Table 10.2 corresponding to $\alpha=0.05$ and $\beta=0.1$ (ie, 10.5). Plugging these values into the our sample size formula, we see that:

$$n=\frac{2(0.8)(0.2)(10.5)}{(0.1)^2}=336.$$

Here, 336 subjects would be needed for each treatment group or the total size of the trial should be 672 subjects.

b. Example 8: Sample Size Calculation for Equivalence of Two Proportions

Consider a drug candidate for the treatment of HIV in naive subjects that is expected to have 85% of subjects with HIV-1 RNA below the lower limit of detection at 48 weeks. If a drug company would like to plan a new study with power $(100-\beta)$ of 90% and a type I error rate (α) of 1%, what sample size would be needed to establish the equivalence of a new drug candidate if the clinically acceptable difference is 12%? To calculate the sample size, we can translate the request into the sample size formula as $p=0.85$, $d=0.12$, and the value of the quantity $(z_{1-(\alpha/2)}+z_{1-\beta})^2$ is obtained from Table 10.2 corresponding to $\alpha=0.01$ and $\beta=0.1$ (ie, 14.9). Plugging these values into the our sample size formula, we see that:

$$n=\frac{2(0.85)(0.15)(14.9)}{(0.12)^2}=263.85$$

Here, 264 subjects would be needed for each treatment group or the total size of the trial should be 528 subjects.

XIV. OTHER HELPFUL CONSIDERATIONS

Sample size calculations should refer to the number of subjects required for the primary analysis. If the number of subjects in the primary analysis will deviate from the number of subjects randomized, then the sample size will need to be adjusted accordingly. For instance, certain studies are allowed to make use of a modified intent-to-treat population (mITT) defined as all subjects randomized who receive at least one dose of study drug and have at least one postbaseline measurement. The sample size calculation for such studies should calculate the number of subjects needed for the mITT population, not the number of subjects to be randomized. If it is expected that roughly 10% of the subjects randomized will fail to meet the criterion for inclusion in the mITT population, the numbers from the sample size calculation would need to be adjusted accordingly to yield the appropriate number of subjects to be randomized. In the case of the pain study discussed earlier, if the sample size calculation indicates a total of 264 subjects in the mITT population are necessary to detect the 0.8 unit difference at 90% power, then we would need to randomize at least 294 subjects in order to obtain the 264 subjects necessary for our primary analysis.

As a reminder, the sample size calculations presented in this chapter represent simple formulas which can be applied when certain assumptions are met. There are a number of considerations common in clinical trials which could necessitate the use of more sophisticated statistical methods. These include, but are not limited to, having unknown or unequal variances, inclusion of interim analyses, use of