Homework #4

Due on 11/25/2019 at 8:30am

1. (a) As we know, we are able to examine whether testing treatment is significantly better than control in a non-inferiority trial without inflating the family-wide type I error rate. So should we always take advantage of this “free lunch” and always use the non-inferiority design (as opposed to superiority design)? Please justify your answer.

(b) After a non-inferiority clinical trial, a new therapy may be accepted as effective, even if its treatment effect is slightly smaller than the current standard. It is therefore possible that, after a series of trials where the new therapy is slightly worse than the preceding drugs, an ineffective or harmful therapy might be incorrectly declared efficacious; this is known as 'bio-creep'. What would you recommend the investigator to avoid bio-creep when designing a non-inferiority trial?

(c) In FDA’s guideline for non-inferiority trials, the majority of discussion was to quantify the treatment effect of active control. Why this is so important? Please discuss what consequence we have to take if the treatment effect of active control compared to placebo (i.e., M1) is not properly specified (i.e., discuss the cases that the assumed value for M1 is too large or too small).