that the telbuvidine-treated subjects received telbuvidine plus a placebo resembling the active-control pill, and the active-control arm subjects received active-control pills plus a placebo resembling the telbuvidine pill. This type of trial design is called "double dummy." The desired effect of using the "double-dummy" technique was allocation concealment.

e. Correcting for the Placebo Effect—Aliskirin for Hypertension

This is from a clinical trial on *aliskirin* for hypertension. The information is from the *Medical Review* for NDA 21985, available from March 2015 on the FDA's website.

The primary endpoint in this clinical trial is *diastolic blood pressure* (DBP). The data included a figure (Fig. 7.1) (Fig. 12 in the *Medical Review*) and a table (Table 7.1) (Table 13 in the *Medical Review*). According to the FDA's *Medical Review*, the reductions in blood pressure were typically seen after 2 weeks of therapy, and maximal reductions in blood pressure occurred at 4 weeks of therapy. This time-course is evident in the figure (Fig. 7.1). Data from the placebo arm are in the top line (open diamonds). Data with the highest dose of the study drug (aliskiren) are the lowest line (open squares). The two intermediate lines are from the intermediate doses of study drug (150 and 300 mg).

The placebo effect is evident from the reductions in blood pressure occurring in the placebo arm of the various clinical trials, that were included in the NDA submission.

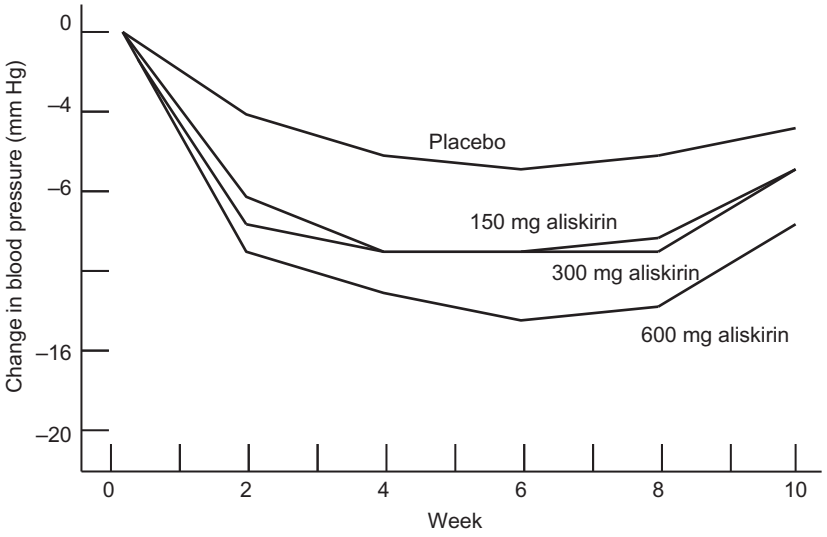

FIGURE 7.1 Sponsor's change from baseline in DBP.

TABLE 7.1 Reviewer's Placebo-Subtracted Changes from Baseline in Seated Trough Cuff DBP in the Five Pivotol Studies

Study	Median Group *n*	Placebo	Placebo-Subtracted DBP Change		
			150	300	600
2308	169 subjects	−4.9	−5.4	−6.2	−7.6