the contention that meprobamate enhances the safety of the primary ingredient, dextroamphetamine (21 CFR 3.86(a)(1)).

2. Trodella, G. P., "Comparative Efficacy of Bamadex Tablets, Bamadex Minus Meprobamate, and Placebo in the Control of Obesity and Measurement of Side Effects," unpublished study, 1971. The results of this study with respect to side effects were very similar to those in the Parsons' study. The investigator reported three side effects in the Bamadex group, one in the dextroamphetamine group, and two in the placebo group. Since Lederle's own statistical analysis concluded that the differences in the incidence of side effects for the three groups were not statistically significant, the results of this study do not support Lederle's contention that meprobamate significantly decreases the adverse reactions associated with dextroamphetamine, as required by 21 CFR 3.86(a)(1).

This study shares the same defect as the Parsons' study previously described in that the investigator failed to explain the methods of observation and recording of results with respect to side effects, 21 CFR 314.111(a)(5)(ii)(*a*)(*3*). No details are given as to whether subjects were questioned as to whether they experienced side effects, or whether only the investigator's observations were counted.

With respect to weight loss (both overall clinical response and average weight loss), Lederle admitted that at the end of the second 21-day period, Bamadex was inferior (both overall clinically and in average weight loss) to the placebo, and at the end of the first 21-day period Bamadex was only equal to a placebo in average weight loss.

3. Bowlan, W. L., "Comparative Efficacy of Bamadex Tablets, Bamadex Minus Meprobamate and Placebo in the Control of Obesity and Measurement of Side Effects," unpublished study, 1971. In this study the incidence of side effects was low for all three groups (one on Bamadex, two on dextroamphetamine, and four on placebo). Statistical analysis failed to demonstrate any statistically significant differences between the active medication with respect to side effects. Consequently, this study fails to support Lederle's contention that meprobamate decreases the side effects associated with dextroamphetamine and therefore, fails to provide evidence that meprobamate enhances the safety of the principal active component of Bamadex as required by 21 CFR 3.86(a)(1).

Lederle did not attempt to perform any statistical analysis on the anorectic data (21 CFR 314.111(a)(5)(ii)(*a*)(*5*)).

No details are given as to whether the subjects were questioned as to whether they experienced side effects or whether only the investigator's observations were counted. Therefore, this study fails to explain the methods of observations and recording of result as is required by 21 CFR 314.111(a)(5)(ii)(*a*)(*3*).

The three tablet studies, whether taken individually or together, failed to show a significant decrease in side effects for Bamadex patients when compared to patients who used dextroamphetamine alone. In fact, the combined results for the tablet studies show more side effects for Bamadex patients (14) than for the dextroamphetamine patients (4).

C. *Combined statistical analyses.*—Lederle submitted a combined statistical analysis of the side effects and mean weight loss for the Bamadex, dextroamphetamine, and placebo groups in the six studies reviewed above and a combined statistical analysis of the three sequel studies alone. Since these analyses are dependent upon the data obtained from the individual studies, and since the individual studies have been shown to be not adequate, and well-controlled within the meaning of 21 CFR 314.111(a)(5)(ii), any analysis of such data can only yield results that have no scientific validity.

The tabulation for the sequel studies shows discrepancies between the number of side effects recorded by Lederle and the number disclosed by examination of the individual case reports. In the Schein study, Lederle noted only one side effect for the Bamadex group while the case reports reveal that patient No. 222 experienced depression. In the Miller study, Lederle noted only three side effects for the Bamadex group, whereas both Lederle's initial analysis and the case reports show four side effects. Any statistical analysis which is based upon inaccurate reporting of data cannot provide substantial evidence to support drug effectiveness (21 CFR 314.111(a)(5)(ii)(*a*)(*2*)(*iii*)).

Lederle has failed to show that it was justified in pooling the results of the three sequel studies. Thus no details were provided as to whether or not the groups in each study were comparable with respect to concurrent drug use and whether each investigator observed and recorded his data in the same manner. The scanty information that was provided shows that theer were differences in