Noble study, there were patients receiving anti-inflammatory agents with analgesic properties, antihistamines with sedative properties, and major tranquilizers, any of which could interfere with central nervous system side effects. Similarly, patients in the Bamadex group also used thyroid and diuretic drugs which could also influence weight reduction.

This study also fails to explain the methods of observation and/or recording of results as required by 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. Thus, as before, there is no way to determine the accuracy or quality of the data relating to adverse reactions, and hence there is no way to scientifically assess the result. Although the investigator reported only one side effect for the Bamadex group, a check of the patient reports showed that an additional patient, No. 222, experienced depression and had to be switched to other medications. This indicates that the investigator had not accurately observed and/or recorded the results (21 CFR 314.111(a)(5)(ii)(*a*)(*3*)). There were 6 patients in the dextroamphetamine group who experienced side effects.

Even if these deficiencies are ignored, Lederle's own statistical analyst admits that there was no statistically significant difference found in the side effects reported for the three groups. This study, therefore, fails to provide evidence that meprobamate contributes to the claimed effects within the meaning of and as required by 21 CFR 3.86(a)(1).

With respect to the claimed anorectic effect, this study shares the identical defects as the just-reviewed Noble study, i.e., the author failed to assure group comparability with respect to the use of concomitant medication (21 CFR 314.111(a)(5)(ii)(*a*)(*2*)(*iii*)) and failed to explain the methods of observation and recording of results (21 CFR 314.111(a)(5)(ii)(*a*)(*3*)).

The investigator initially defined a "satisfactory" response as a loss of at least 9 pounds for the 9-week period. Under this definition, he found no statistically significant difference between the three groups, i.e., the placebo group did as well as the Bamadex group. Accordingly, a second, less stringent, standard was adopted which defined "satisfactory" response to be a loss of at least 6 pounds for the first and last 3-week periods. Using this criterion, the results of the Bamadex and dextroamphetamine groups were found to be satistically significant when compared to the placebo group, and the differences between the Bamadex and dextroamphetamine groups were not statistically significant. Lederle's statistical analysis of the mean weight losses claimed statistically significant differences for the Bamadex and dextroamphetamine groups over the placebo group for the end of both active treatment periods (1 to 3 and 7 to 9 weeks) and overall (weeks 1 to 9). However, since the study was not adequate and well-controlled, as discussed above, these reported results are not reliable or scientifically evaluable.

3. Miller, Jerome, "A Comparison of Bamadex Sequels, Dextroamphetamine, and Placebo on Weight Loss and Side Effects in 90 Patients", unpublished study, 1971. This study also followed the basic protocol used in the Noble and Schein studies with only one exception: To assure more reliable weight-loss data, followup weighings were done in circumstances similar to the original weighings with respect to time of day, scales, and clothing.

As with the previous studies, this study failed to assure group comparability with respect to the concurrent use of other drugs which could have interferred with the central nervous system side effects and the claimed anorectic effects (21 CFR 314.111(a)(5)(ii)(*a*)(*2*)(*iii*)). Although the author did explain that he conducted the weighings at the same time of day and under similar conditions with regard to scales and clothing, he failed to explain whether or not, and if so how, he took into account such variables as caloric intake and menstrual cycles (21 CFR 314.111(a)(5)(ii)(*a*)(*3*)).

For the third consecutive time, Lederle's statistical analysis showed that there was no statistically significant difference between the three groups with respect to the incidence of side effects. Therefore, this study, too, fails to provide evidence that meprobamate contributes to the claimed effects within the meaning of and as required by 21 CFR 3.86(a)(1).

With respect to anorectic effects, the investigator's own clinical evaluation showed that the number of Bamadex-treated patients with an overall satisfactory clinical (weight loss) response was strikingly similar to the number for the placebo group and smaller than the dextroamphetamine group (Bamadex Sequels, 12; dextroamphetamine, 20; placebo, 10). Since the placebo and Bamadex groups were nearly identical with respect to this variable, if anything, the