forms so that the analysis is based on unreliable data. FDA's interpretation and statistical analysis of the patient report forms shows there was no statistically significant reduction in side effects with Bamadex. It should be emphasized, however, that FDA does not rely on its analysis for its action but rather on the failure of Lederle's data to meet the statutory and regulatory criteria for adequate and well-controlled studies (section 505(d) of the act (21 U.S.C. 355(d)) and (21 CFR 314.111(a)(5)(ii))).

Finally, even if all these discrepancies are ignored, Lederle's statistical analysis based on Lederle's interpretation of the patient report forms fails, with equal conclusiveness, to demonstrate any significant reduction in side effects for Bamadex. This judgment holds true whether the three sequel studies are judged individually or collectively, whether the three tablet studies are judged individually or collectively, and whether all six studies are combined. It is obvious that the unanalyzed list of side effects, by itself, is of no evidentiary value. Since this data is incorporated into Lederle's combined statistical analysis, its significance stands or falls with the evaluation of that report.

With respect to the interpretation of the patient report forms, Lederle contends that FDA incorrectly characterized the incidence of side effects. This is simply not the case. Lederle's carelessness in tabulating its own data is clearly evidenced by two instances: (1) Lederle's table, which summarizes the combined number of side effects (and upon which Lederle bases its overall statistical analysis), does not even square with its own earlier reported findings for each individual study; Lederle lists three side effects in its summary table for the Bamadex group in the Miller study, and Dr. Miller's summary lists four side effects; and (2) in the Parson tablet study, no side effect was recorded by Lederle for patient No. 632 despite the investigator's comment, "Didn't find medication very helpful. Too much of a tranquilizer—a hindrance in his work. Didn't alter appetite. Also seemed to cause impotence (no previous trouble)."

There were many similar instances throughout the studies where the investigator's comment regarding adverse reactions went unnoticed by Lederle. The issue of correctness of interpretation of patient report forms need never be reached since Lederle's own analysis fails to demonstrate any statistically significant reduction of side effects for Bamadex compared to dextroamphetamine.

Lederle also contends that since meprobamate has been found effective for the relief of anxiety and tension and in the treatment of diseases in which anxiety and tension are manifest, and since dextroamphetamine has been found effective in the management of weight reduction, that Bamadex Sequels, which contains both of these ingredients, must be recognized as effective for its claimed effect: the management of obesity with minimal overstimulation of the central nervous system.

This reasoning is fallacious because (1) that meprobamate is effective for anxiety and tension or in the treatment of diseases accompanied by anxiety and tension is irrelevant to the issue of its effectiveness, or lack thereof, for its claimed effect in Bamadex since there is no proof that central nervous system side effects are related to the conditions of anxiety and tension; and (2) Lederle's argument is, as a matter of law, insufficient since although each of the components of a drug may be safe and effective, it does not necessarily follow that a combination of the same ingredients will be effective. (See 21 CFR 310.3(h); *United States* v. *An article of drug* * * * *Ferestrol*, 294 F. Supp. 1307 (N.D. Ga., 1968), aff'd 415 F. 2d 390 (C.A. 5, 1969); *United States* v. *41 Cases* * * *, 420 F. 2d 1126 (C.A. 5, 1970); *United States* v. * * * *Nerac Alcohol Acne Gel*, CCH F.D. Cosm. L. Rep. ¶40,836 (N.D. Ill., 1971); *United States* v. *An article of drug* * * * *Patrol C. Medicated*, 362 F. Supp. 424 (S.D. Cal., 1973); *United States* v. *An article of drug* * * * *"Mykocert"*, 345 F. Supp. 571 (N.D. Ill., 1972); *United States* v. * * * *"Asper Sleep"*, CCH F.D. Cosm. L. Rep. ¶40,832 (N.D. Ill., 1971). The reasoning behind these cases is particularly cogent where, as here, one of the ingredients, meprobamate, is recommended by the labeling for the combination for a use different from that for which it has been found effective. In such a case, there can be no basis for a claim that the effectiveness of meprobamate is established for its role in the combination. Thus, the clinical evidence must be the determinant of whether meprobamate contributes to the effect of Bamadex or makes the principal ingredient safer. However, as shown above, the clinical evidence submitted by Lederle not only fails to demonstrate that meprobamate makes a contribution to the claimed effect, but suggests that it reduces the effectiveness of the principal ingredient, dextroamphetamine.

Lederle next argues that Bamadex Sequels must be found safe because the product was approved on the basis of safety in 1960, and there has been no clini-