

The above shows a trend which suggests that the rate of weight loss declines as the drug is used. This trend is also evident in the data for the other subgroups. This possible lessening of effectiveness, whether it be weight loss or appetite depression, appears to be an additional factor for consideration in evaluating the evidence submitted to date and the claims proposed for this product.

Finally, there appear to be several miscellaneous items which have a bearing on the validity of the data submitted and appear worthy of consideration.

It was noted in Table A that the study number series changed from the 2000's to the 3000's. It may be worth while to learn whether those in one series are considerably older studies, perhaps not as well controlled, or blind, and perhaps using a range of dosage and protocols more apt to be classified as phase I or phase II studies.

There are two additional Tables submitted, F and G. Table F contains information which confirms the several biases mentioned earlier. This table shows the number of subjects in each drug treatment group falling into specific classes of percent overweight.

It will be noted that the placebo group had 5 subjects who were the least overweight, while the 60 mg/day group had only one subject, despite a numerically larger overall sample size. The placebo had only 5 subjects who were in the greatest overweight class, while the 60 mg/day group had 13 subjects. This constitutes a disproportion in the other direction. Please note this shift in the bar graphs in Fig. X. This disproportion in the distribution of patients in the placebo and 60 mg groups with respect to percent overweight was tested statistically and found to be significant, $p < 2.05$. The 60 mg group is represented by relatively more studies and more subjects and appears to be the pivotal drug group for comparison purposes.

This table also shows the spottiness in the number of patients studied on the other dosages and the poor basis for trying to make comparisons with placebo.

The other interesting phenomenon revealed by this table is the correlation between the amount of weight lost and the percent overweight. This relationship is quite apparent in the placebo and 60 mg groups. Weight loss is greatest in the groups that were most overweight. This relationship is also shown in Figure X at the bottom. Even the placebo trend lines have an upward bias. Again this places the placebo at a disadvantage because it contained proportionately fewer of these subjects.

Table G shows the results of applying two different tests of statistical significance to the pooled data. The data are the same as these in Tables C, D, E and F with all the gaps, non-comparabilities and biases mentioned before. These tests require certain conditions or assumptions before they can be applied to data. Among these is the assumption that the groups to be tested are actually comparable in a clinical and experimental sense and are free from any bias which may distort study balance, group averages or the variability of individual results around group averages. These conditions are far from met here: we cannot assume that theoretical and practical deficiencies have somehow balanced out or that their effects are minimal.

The tests show strong statistical significance in favor of the drug groups as one would suspect. They reflect the data as presented and calculated; they do not tell how much, actually or on a relative basis, the drug groups are superior. Some suggestion of drug efficacy is evident in these data, but the statistical evidence is not very meaningful under the uncertain circumstances and biases surrounding the data.

Finally, the data as presented to us in these tables may not be completely correct or complete. The Colmore Study (2005), supposedly one of the better clinical efforts, shows data only for placebo. Data for 12 subjects on the 60 mg/day dosage and 12 subjects on the 120 mg/day dosage are not shown.

Some of the entries for representing a 2, 4 or 6 week interval from baseline, actually were taken from data obtained a week prior to or after these indicated intervals.

The table does not show all weight data obtained in these studies. As Mrs. Pogue's initial report indicated, some weight measurements were taken at variable intervals, others at odd weekly intervals, and some at periods beyond those reported in these tables.