2. We have grouped below certain questions and suggested analyses into three general areas; which could be worked on separately or simultaneously. More specifically, we would suggest additional work along the following lines:

a. Efficacy:

(1) Introduce time as a factor to answer some of the following questions:

(a) Does weight loss per week yield the same conclusions as looking at final weight?

(b) Is there treatment x time interaction? Sex x time, etc?

(c) Is it true that the patients lose weight at a decreasing rate over time? Is the trend linear?

(d) Make tables of lengths of time in study for the treatments and try to describe the patients which continue longest by age, sex, race, initial weight, etc.

(e) Estimate the missing observations.

(f) Do the random fluctuations differ in magnitude over time, and is there a trend?

(2) Ascertain a description of the population which would best to benefited with amphetamine treatment.

(3) Obtain a description of the population which will use or now uses the drug to demonstrate that the applicant has considered a comparable population.

(4) Describe the evidence of importance of accompanying diet.

(5) What conclusions can be made about appetite suppression and can a protocol be made to consider it?

(6) Make conclusions about diet, exercise, and combinations from the existing data.

(7) Detailed comparison of continuous and interrupted therapies and effect of washout at beginning and/or end.

(8) Approach and describe investigators to find who has a better success and/or safety by characteristics.

(9) Analyze with treatment, age, severity, sex, and baseline, and time in the model.

(10) What can be concluded with a followup.

(11) Can it be tested if the double-blind were broken, and what would be the effect if it were?

(12) Is amphetamine weight loss anthropometrically equivalent to diet weight loss?

b. Safety:

(1) Analyze the safety data, like blood pressure, and pulse by the analysis of variance.

(2) Give a summary and describe the dropouts by length of study, age, side reactions, etc. by treatment.

(3) Define and describe the effect of chronicity.

c. Statistical:

(1) Calculate the power of the test or the probability of rejection the hypothesis of equal treatment effects for selecter alternative hypotheses from the data submitted.

(2) Make tables or graphs of the power to help determine the sample sizes and study length to detect specific differences with specified probabilities.

(3) Design protocols which will allow adequate study of drug, diet, exercise, and combination drugs.

(4) Further consideration of comparability of treatment groups by age, variance, etc. for both baseline and post.

(5) Pool studies.

(6) Compare the physicians' ideal weights with those of the Metropolitan Life Tables.

3. Please let us know if this proposal is satisfactory.