

G. Effectiveness

The analysis supplied by the sponsor consists, as is often the case, of pooled data. Efficacy is expressed in terms of rate of weight loss per week. I do not believe this is a valid analysis, since dropouts are usually not considered in arriving at averages. In addition, the actual number of pounds lost by the patient is more important than the rate of weight loss. When efficacy is expressed in terms of pounds per week lost, there is an implication that the rate of weight change is constant, but there is abundant evidence to indicate that this is far from the case. The weight loss according to the figures compiled by the sponsor are as follows:

Investigator:	Rate of weight loss pounds per week
Owen	+0.02
Fisch:	
60 mg per day	-1.00
120 mg per day	-0.54
Rosenberg:	
60 mg per day I	-1.12
60 mg per day II	-0.01
120 mg per day I	-0.75
120 mg per day II	-0.51
Anderson	-1.4
Hollingsworth	-1.7
Roginsky:	
40 mg per day	-0.54
60 mg per day	-0.92
80 mg per day	-0.68
Bacon:	
20 mg per day	} same as placebo
40 mg per day	
60 mg per day	
Stern 80 mg per day	-0.34

Judging from the number of weeks on fenfluramine and the weight loss as expressed in pounds per week, it would appear that the absolute weight loss was very small, and in the case of Dr. Owen, Dr. Hollingsworth and Dr. Bacon the results were about the same as with placebo. In connection with Dr. Rosenberg's study they make the statement on page 245 of Vol. 3.1 that the number of patients in the study was small and therefore no definite statement may be made regarding the results; but there were 34 patients involved in a crossover design, therefore I do not believe that their statement is valid. An attempt to evaluate the data submitted is hampered by the fact that I cannot find protocols for Drs. Rosenberg, Fisch, Anderson and Hollingsworth.

H. Laboratory studies

"Of the total number of laboratory examinations done in 319 patients there were 63 abnormal values. A majority of abnormalities were minor alterations in hematological parameters or changes in the urinalysis. No incidence of agranulocytosis or pancytopenia were noted and many of the changes reverted to normal later in the investigation. Whether these changes in laboratory values were drug related was not always clear but when in doubt they were considered probably drug related. The mechanism of reproduction is unclear.

"There were no major changes in the blood chemistry values. Hepatic and renal function appeared to be unaffected by fenfluramine even after long periods of administration."

I. Adverse reactions

Much emphasis has been laid on the fact that fenfluramine is supposedly a central nervous system depressant rather than stimulant in spite of its close relationship to amphetamine. A paper entitled "Fenfluramine. Study of its Central Action Through its Effect on Sleep" was presented at the 4th Annual Meeting of the Canadian Society of Chemotherapy by Gagnon, M-A, et al. (Vol. 3.1, p. 175). The study was undertaken to determine whether or not fenfluramine produces insomnia like amphetamine does. The subjects consisted of 66 chronic patients, 19 women and 47 men, in a psychiatric hospital. In a double-blind study two doses of fenfluramine 40 mg and 80 mg were compared with placebo. Medications were given at 8:15 p.m.; a questionnaire was given to the patients the following morning. This questionnaire had previously been used for the assessment of hypnotic agents. "... the results of the questionnaire had been corre-