lated with objective observations of the patients during sleep. A significant correlation had also been demonstrated for the results obtained with two types of subjects: medical students and psychiatric patients. . ." Each subject served as his own control. According to the authors, ". . . fenfluramine disturbs sleep and therefore a CNS stimulating action appears evident.

"It seems that, because of their lack of sleep, the subjects felt dull and dizzy during the mornings following the fenfluramine test nights. . ."

". . . It is then questionable whether daytime drowsiness is a manifestation of a truly sedative effect of fenfluramine, or rather a symptom of fatigue following primary excitation. No facilitation of normal sleep has ever been reported, although a few cases of insomnia were."

In this connection, an article by Oswald, I. Brit. Med. Jour. 1968 Vol. 1, pages 796–799 states: "One may take the example of diethylpropion reported by Seaton et al. (1961) from Edinburgh to be an effective appetite reducer with 'no evidence of undue central nervous stimulation or insomnia . . . no important side effects'. Time, however, showed that diethylproprion like dexamphetamine and phenmetrazine was a pep pill causing elevation of mood and of the pace of thinking. . ."

The Edinburgh group has since reported on the effective new slimming drug, fenfluramine, again reporting 'no evidence of stimulation of the central nervous system.' Oswald found that diethylproprion caused 1) frequent awakenings; 2) suppression of paradoxical (RAM) sleep. Fenfluramine caused neither but caused frequent shifts into and increased time in stage 1 sleep, at the expense of stages 3 and 4.

J. Evaluation

The present submission contains 3 controlled studies; the sponsors summaries of these studies appear on pages 236 to 269. The summaries contain a blank for the protocol number as Item 2; however, this number has been left off, and so far I have not been able to find protocols in IND 1703 for Fisch (Study 2), Rosenberg, Anderson, or Hollingsworth. On only two sets of case report forms, those for Owen and Stern, are heights given, therefore it is impossible to determine the degree of obesity present. The results are expressed as average weight change per week. This is an inadequate method of expressing results; a far better and more revealing method is to tabulate the actual number of pounds the patient is considered to be overweight and the actual number of pounds of weight loss. According to the sponsor's summaries their conclusions are as follows:

Owen No. 2002—the doses employed in this study are not anorexigenic.

Fisch No. 2009:

Ponderex 40 mg t.i.d	−0.54
Ponderex 20 mg t.i.d	−1.00
Placebo	−0.43

Rosenberg No. 2016:

[In pounds per week]

	1st period	2d period	Both periods
Fenfluramine, 40 mg, t.i.d	−0.75	−0.51	−0.61
Fenfluramine 20 mg, t.i.d	−1.12	−.01	−.72
Placebo	−.47	+.08	−.20

"The number of patients in the study was small and therefore no definitive statement may be made regarding the results. Weight loss from fenfluramine was greater than placebo but the magnitude of difference was not great."

	Pounds per week
Anderson No. 2020:	
Fenfluramine	1.4
Placebo	0.34
Hollingsworth No. 2025:	
Ponderex	1.70
Placebo	1.46
Roginsky No. 2050–B:	
Ponderex 40 mg b.i.d	0.54
Ponderex 30 mg b.i.d	0.92
Ponderex 20 mg b.i.d	0.68
Placebo	0.29