IX. *Labeling evaluation*

A. Identity disclosure.—Adequate.

B. Clinical uses.—It is questionable that the indication for the medical management of obesity has been supported by the study.

C. Adverse effects should include a discussion of Cagnon's observation on the stages of sleep.

D. "Reproduction studies in 5 animal studies have been carried out (see Reproduction and Teratology). However, since studies of the safety of Ponderex in human pregnancy have not been performed, its use in women who are pregnant or who may become pregnant or in lactating mothers is not recommended at this time."

E. Technical requirements.—Adequately met, according to Chemist Review of February 24, 1969.

X. *Consultations*

See statistician's report of 4/25/69, Vol. 3.1, IND 1703, which was received April 6, 1964, had not been reviewed by a Medical Officer between March 10, 1965 and the date it was re-assigned to me, 3/17/69. It comprises 10 large volumes.

XI. *Conclusions*

I recommend that a non-approvable letter be sent to the sponsor for the following reasons:

Although sponsor claims that efficacy has been demonstrated, he relies on the rate of weight loss per week rather than giving actual amounts of weight loss. An analysis of the 8 controlled studies yields the following approximate average cumulative weight changes following fenfluramine or placebo:

Investigator and dose in (milligrams per day)	Duration in weeks	Weight change in pounds
Owen: 40	2	Ineffective
Fisch:		
60	4	−4.8
120	4	−2.6
Placebo	4	−.3
Rosenberg:		
60	6–8	−3.6
120	6–8	−4.7
Placebo	6–8	−1.7
Andersen[1]	3	
Hollingsworth:		
A. 120	8	−18.8
Placebo	8	−2.9
B. Placebo	8	−12.8
120	8	−7.6
Roginsky:		
40	12	−11.2
60	12	−14.1
80	12	−7.0
Placebo	12	−4.4
Bacon:		
A. 20–60	4	−4.8
B. Placebo	4	−2.7
Placebo	4	+.7
20–60	4	−2.2
Stern:		
80	8	−3.0
Placebo	8	−.5

[1] Case report forms inadequate as regards dates.

Where as the sponsor claims that Owen's dosage was too small, we note that Roginsky using the same dosage achieved a weight loss better than most of the other investigators. On the other hand, Hollingsworth found a greater weight loss with placebo than did most of the other investigators with fenfluramine.

On page 245 sponsor states that the number of patients in Dr. Rosenberg's study was small and therefore no definite statement may be made regarding the results; however, there were 34 patients in a cross-over study, which is more than the number of patients in the studies done by Owen, Andersen or Bacon and almost the same as the number in Dr. Hollingsworth's study. In Dr. Hollingsworth's study, sponsor states on page 249 that the average weight loss on fenfluramine was −1.7 lbs/wk as compared to −1.46 lbs/wk on placebo. On page 256 sponsor states that Dr. Bacon's study shows ". . . fenfluramine equal to placebo in effectiveness. However, subjects lost more weight in the first period of the study regardless of drug used. Therefore, design of study not good to detect weight loss effect. Also, study periods too short . . .". The study period was 4 weeks—equal to Dr. Fisch's and more than Dr. Owen's or Dr. Anderson's.

The case reports forms submitted for Dr. Hollingsworth and Dr. Rosenberg are partially illegible.

The case reports forms for Dr. Anderson are inadequate in that actual dates are not given above the weights; only elapsed time. The dates that are recorded elsewhere on the Case Report Forms are ambiguous.