

ORDER DISMISSING AN AMENDED COMPLAINT AND REINSTATING AN
ORDER IN REGARD TO THE ALLEGED VIOLATION OF THE FEDERAL TRADE
COMMISSION ACT

*Docket 7176. Amended Complaint, November 15, 1965—Decision,
June 17, 1969*

Order dismissing an amended complaint issued November 15, 1965, 68
F.T.C. 1221, and reinstating the suspended order of November 7, 1958,

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55 F.T.C. 705, which prohibited a New York City distributor of drugs from deceptively advertising its weight-reducing preparation, "Hungrex * * * with P.P.A."

Mr. Richard Whittington Whitlock for the Commission.

Mr. Solomon H. Friend of *Bass & Friend*, New York, N.Y., for respondents.

CERTIFICATION OF RECORD BY JOHN B. POINDEXTER, HEARING
EXAMINER

MARCH 16, 1967

PRELIMINARY STATEMENT

This matter arises out of an amended complaint issued by the Federal Trade Commission on November 15, 1965 [68 F.T.C. 1221], in amendment of, and in substitution for, its original complaint issued on June 27, 1958, in Docket No. 7176, wherein Alleghany Pharmacal Corp., a corporation, and Harry Evans, and Vincent J. Lynch, individually and as officers of said corporation, were charged with falsely advertising a so-called "reducing" preparation called "HUNGREX * * * with P.P.A.," in violation of the Federal Trade Commission Act.

The original complaint alleged, among other things, that, typical of respondents' advertisements, were the following:

A Very Powerful
Yet Safe Reducing Drug
Now Released for Public Use!

* * * * *

Imagine the thrill of overweight men and women who lost up to 5 lbs. the very first week * * * 10 pounds in 2 weeks * * * up to 20 lbs. the very first month * * *.

The complaint further alleged that, through the use of said advertisements, respondents represented that:

1. The preparation is safe to use by all obese persons;
2. Obese persons can expect the preparation to cause a weight loss of five (5) pounds in one week, ten (10) pounds in two weeks, and twenty (20) pounds in one month.

Whereas, in truth and in fact, it was alleged, said advertisements were false and misleading in that (1) the preparation is not safe to use by all obese persons having heart disease, high blood pressure, diabetes, or thyroid disease; and (2) no specific

predetermined weight reduction can be achieved by using respondents' preparation for a prescribed period of time. Thus, it is seen that the thrust of the original complaint was directed toward respondents' advertisements with respect to (1) the *safety* of the drug, and (2) claims of *predetermined* weight reduction during a prescribed period of time. The *effectiveness* of the drug preparation as an appetite depressant and weight-reducing agent was not questioned.

The complaint further alleged that the dissemination by respondents of said false advertisements constituted an unfair and deceptive act and practice within the intent and meaning of the Federal Trade Commission Act.

Thereafter, under date of September 3, 1958, the corporate respondent and the individual respondents entered into a written agreement with complaint counsel for a consent order to be entered in the proceeding in accordance with the form of order contained in the agreement, which purported to dispose of all the issues in the proceeding as provided by Section 3.25 of the Rules of Practice of the Commission then in effect. The agreement was approved by the Bureau of Litigation.

On September 25, 1958, the then hearing examiner, Everett F. Haycraft, accepted the agreement and issued an initial decision which contained an order to cease and desist in the form which had been agreed to by the parties, and set out below. Thereafter, on November 7, 1958 [55 F.T.C. 705], the Commission adopted as its own the initial decision of the hearing examiner, which required respondents, in connection with the offering for sale, sale or distribution of the preparation HUNGREX * * * with P.P.A., or any other preparation of substantially similar composition or possessing substantially similar properties, whether sold under the same name or any other name, to forthwith cease and desist from, directly or indirectly:

1. Disseminating or causing to be disseminated any advertisement by means of the United States mails or by any means in commerce, as "commerce" is defined in the Federal Trade Commission Act, which advertisement represents, directly or indirectly:

- (a) That said preparation is safe to use by all obese persons;
- (b) That any predetermined weight reduction can be achieved by the taking or use of said preparation for a prescribed period of time.

2. Disseminating or causing the dissemination of any advertisement by any means for the purpose of inducing or which is likely to induce, directly or indirectly, the purchase in commerce, as "commerce" is defined

in the Federal Trade Commission Act, of said preparation, which advertisement contains any of the representations prohibited in paragraph 1 hereof.

Pursuant to said consent order to cease and desist, respondents revised their advertisements for HUNGREX . . . with P.P.A. by removing therefrom those aspects of the advertisements which were prohibited by said consent order to cease and desist, to wit, all representations that HUNGREX * * * with P.P.A. was safe to use by all obese persons or that any predetermined weight reduction could be achieved by the taking or use of said preparation for a prescribed period of time. Thereafter, respondents filed with the Commission the required reports indicating the manner in which respondents had complied with such consent cease and desist order. By letter dated August 10, 1959, the Acting General Counsel of the Commission advised respondents that, upon the basis of the information contained in said reports, respondents were in compliance with the order (RX 18). Since that time, respondents have continued to sell and advertise said drug preparation HUNGREX * * * with P.P.A., which present advertisements represent, directly or indirectly, that HUNGREX * * * with P.P.A. is an effective appetite depressant and weight-reducing agent, and is adequate and effective in the treatment, control, and management of obesity, in reliance on the provisions of said consent cease and desist order issued by the Commission on November 7, 1958.

On June 10, 1965, the Commission issued an order to show cause why the proceeding in Docket No. 7176 should not be reopened upon the basis of a decision by the United States District Court for the District of New Jersey entitled *The United States of America v. 60 28-Capsule Bottles, More or Less and 47 7-Capsule Bottles, more or less, of an article of drug labeled in part: "UNITROL * * **", 211 F. Supp. 207 (1962), *aff'd*, 325 F. 2d 513 (1963), wherein it was held, among other things, that P.P.A. has no significant pharmacological value as a weight-reducing agent. In its order to show cause, the Commission stated that the above decision in the *UNITROL* case caused it (the Commission) to believe that, in truth and in fact, the said drug preparation HUNGREX * * * with P.P.A. has no significant pharmacological value as an appetite depressant or weight-reducing agent, and is not adequate or effective in the treatment, control or management of obesity, and, accordingly, that respondents' advertisements are thus misleading in material respects, and constitute "false advertisements" as that term is defined in the Federal Trade Commission Act.

On July 12, 1965, respondents filed their answer denying the factual allegations contained in the order to show cause and opposed the reopening.

By order issued November 15, 1965, the Commission reopened the proceeding and simultaneously issued the instant amended complaint, charging respondents with misrepresenting, not only the effectiveness of their preparation HUNGREX * * * with P.P.A. as an appetite depressant or weight-reducing agent, but also the safety of the preparation. Harry Evans and Vincent J. Lynch, joined as respondents in the original complaint, were again named in the amended complaint, along with Chester Carity, individually and as an officer of corporate respondent. The order reopening the proceeding did not disturb the consent cease and desist order which had been issued on November 7, 1958, and left the vacation, amendment or modification of that order, if any, to the final disposition of this matter.

The order reopening the proceeding further provided that the matter should be assigned to a hearing examiner for hearings to be conducted in accordance with Subparts C, D, E, and F of the Rules of Practice; that, after conclusion of hearings, the hearing examiner should certify the record, together with a report of his findings, conclusions and recommendations with respect thereto, to the Commission for final disposition. The order further provided that the hearing examiner's report should be served upon the parties in the same manner as an initial decision, and the parties should have the same rights of appeal therefrom, in accordance with the provisions of Section 3.22 of the Rules of Practice.

Pursuant to said reopening order, the matter was assigned to the undersigned hearing examiner for hearing on the charges set forth in the amended complaint. These hearings have been held. Proposed findings of fact, conclusions of law, and recommendations were filed by respective counsel on January 30, 1967. These have been considered. All proposed findings and conclusions not specifically found or concluded herein are rejected.

Upon the basis of the entire record, the hearing examiner reports the following findings of fact, conclusions of law, and recommendations to the Commission for its final disposition.

FINDINGS OF FACT

1. Respondent Alleghany Pharmacal Corp. is a corporation organized and doing business under the laws of the State of

New York, with its office and principal place of business located at 16 West 61st Street, New York, New York (Amended Complaint; Answer).

2. Respondents Harry Evans and Vincent J. Lynch resigned as officers of the corporate respondent on March 4, 1958, prior to the issuance of the original complaint herein on June 27, 1958. Since their resignations, the said Evans and Lynch have had no connection with the corporate respondent (Affidavits attached to Agreement Containing Consent Order to Cease and Desist, dated September 3, 1958; Answer to Amended Complaint; Tr. 632-33).

3. The individual respondent Chester Carity is the president of the corporate respondent and sole stockholder thereof (Tr. 634). His activities, functions and duties as president of corporate respondent were and are performed in his capacity as an officer of said corporation and not in his individual capacity, including his supervision of advertising on behalf of corporate respondent, which is prepared by an advertising agency (Tr. 635, 641). His address is the same as that of the corporate respondent (Amended Complaint; Answer).

4. The corporate respondent is now, and for some time past has been, engaged in the advertising, sale, and distribution of a so-called weight-reducing preparation in tablet form designated on the label on the outside of the container package as "HUNGREX * * * with P.P.A.," each tablet containing "Phenylpropanolamine Hydrochloride, 25 mgm." as the active ingredient, with the following directions for use and cautionary warning printed on the outside of the package container:

Adults: 1 tablet 1/2 hour before each meal. To be swallowed with water or juices. Do not take more than 3 tablets in any 24 hour period.

* * * * *

CAUTION: Should not be used by persons with heart or thyroid disease, high blood pressure or diabetes except on medical advice (CX 10).

5. Typical of corporate respondent's present advertising of HUNGREX * * * with P.P.A. is CX 9 which, it was stipulated, is substantially identical to the proposed advertising copy which corporate respondent submitted to the Commission on April 9, 1959 in connection with one of its reports of compliance with the consent cease and desist order previously issued by the Commission on November 7, 1958 (Tr. 444), and approved by letter dated August 10, 1959 (RX 18). A copy of this advertisement (CX 9)

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appeared on page 28 of the May 26, 1965 issue of the Westfield Suburban News, Westfield, New Jersey, as follows:

CX-9

May 26, 1965

WESTFIELD SUBURBAN NEWS PAGE 28

ORDER TODAY ***

LOSE WEIGHT BY FRIDAY

Just take a tiny
Hungrex table before
meals * * and banish those
hated extra pounds as
you banish hunger! Why?
Because Hungrex is
the most powerful
reducing aid ever
released for public use
without prescription!
Suppresses hunger pangs
so effectively, it actually
limits the ability of
your body to produce
knowing hunger
sensations! Result? You
don't feel hungry * * * down
goes your calorie intake
and down goes your
weight.

Lose Weight
The First Day!
Thousands now lose
weight who never thought
they could * * report
remarkable weight losses
of 7 * * 20 * * even
41 pounds in a short
while. So if you're tired
of half-way measures
and want really effective
help in reducing
send for Hungrex
today. Hungrex will simply
amaze you! You'll be
slimmer next week or your
money back. No
prescription needed.

Copr. 1959 Alleghany Pharmacal Corporation

Ask for HUNGREX

with P. P. A.

The Most Powerful Reducing Aid
Ever Released for Public Use!

BARON'S DRUG STORE

243 E. Broad St.

Westfield, N.J. * *

6. The amended complaint alleges that, through the use of said advertisements, respondents have represented, and are now representing:

1. That the preparation is safe to use by all obese persons;
 2. That the preparation is an effective appetite depressant and weight-reducing agent;
 3. That the preparation is adequate and effective in the treatment, control and management of obesity;
- whereas, in truth and in fact:

1. The preparation is not safe to use by all obese persons having heart disease, high blood pressure, diabetes, or thyroid disease;

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2. The preparation has no significant pharmacological value as an appetite depressant or weight-reducing agent;

3. The preparation is not adequate or effective in the treatment, control or management of obesity.

Therefore, the amended complaint alleges, the advertising is misleading in material respects and constitutes "false advertising" as that term is defined in the Federal Trade Commission Act. The dissemination by respondents of said false advertising constitutes unfair and deceptive acts and practices in commerce, in violation of Sections 5 and 12 of the Federal Trade Commission Act.

7. To establish the allegations of the amended complaint that HUNGREX * * * with P.P.A. has no significant pharmacological value as an appetite depressant or weight-reducing agent, and is not adequate or effective in the treatment, control or management of obesity, complaint counsel relies primarily on the written report of a so-called "study" entitled "Comparative Effectiveness of Phenylpropanolamine and Dextro Amphetamine on Weight Reduction," bearing the names of Joseph F. Fazekas, M.D., Washington, D.C.; Wilfred R. Ehrmantraut, M.D., Silver Spring, Maryland; Kenneth D. Campbell, M.D., Washington, D.C.; and Marie C. Negron, B.S., Laurel, Maryland, as authors. The written report of the "study" appeared in the June 27, 1959 issue of the Journal, published by the American Medical Association, at pages 1018 through 1021 thereof. During hearings, it was sometimes referred to as the "Fazekas" report, and is the basis upon which complaint counsel relies to show that HUNGREX * * * with P.P.A. is not an effective appetite depressant or weight-reducing agent. A copy of the Fazekas report was received in evidence at the hearings as CX 3.

8. In the presentation of his case-in-chief, complaint counsel called two witnesses, Kenneth D. Campbell, M.D., of College Park, Maryland, a coauthor of the Fazekas report (CX 3), and Frederick William Wolff, M.D., a clinical pharmacologist, of Takoma Park, Maryland. On direct examination, Dr. Campbell testified in corroboration of the Fazekas report (CX 3), and Dr. Wolff testified, among other things, that he had studied the report and agreed with the conclusions reached by the authors and considered its statistical design to be adequate. As a rebuttal witness, complaint counsel offered the testimony of Arthur Grollman, M.D., of Dallas, Texas.

9. Six witnesses testified on behalf of respondents: Edward

Settel, M.D., of New York, New York; Frederick B. Bohensky, M.D. of Brooklyn, New York; Raymond Healy, M.D., of Miami, Florida; Theodore Feinblatt, M.D., of Brooklyn, New York; E. L. Ladenheim, of New York, New York, a professor of mathematics and statistical analyst; and Harold Silverman, of West Orange, New Jersey, a research scientist. Doctors Settel and Healy testified concerning the efficacy of P.P.A. as an appetite depressant on their own patients; Doctors Feinblatt and Bohensky testified concerning studies they had made of the effects of P.P.A. on humans and dogs; Professor Ladenheim testified concerning the statistical study he had made of the Fazekas report (CX 3); and Mr. Silverman testified in general support of an article prepared by him and which was published in the American Journal of Pharmacy, dated February 1963, Volume 135, pages 45 to 54. The article is entitled "Phenylpropanolamine—Misused? Or Simply Abused?." A copy of this article was received in evidence as RX 7.

10. Dr. Kenneth Campbell, coauthor of the Fazekas report (CX 3), was the principal witness offered by complaint counsel. On both direct and cross-examination, Dr. Campbell testified concerning the arrangements for, and the details in connection with the Fazekas study (CX 3).¹ In view of the reliance by complaint counsel upon the study to establish the allegations of the amended complaint, the testimony of Dr. Campbell will be discussed in detail.

11. Dr. Campbell graduated from Boston University School of Medicine in 1940 with an M.D. degree, and since 1948, has been engaged in the part-time practice of general medicine. He is employed by the United States Food and Drug Administration, and is Medical Liaison Officer between that administration and the United States Post Office Department (Tr. 75). On direct examination, Dr. Campbell testified that the drug phenylpropanolamine hydrochloride, sometimes called "P.P.A.," was

¹ This hearing examiner rejects the "history" of the Fazekas study and its "protocol" as stated by complaint counsel on page 5 of his proposed findings. There, counsel says: "The history of this study, and its protocol, were noted in detail by the District Court in the Unitrol case, as follows," and counsel then purports to quote from the decision of that Court relating to the procedure used in the Fazekas study. The record made in the Unitrol case is not in evidence in the present proceeding, although complaint counsel offered the entire transcript of testimony taken in the Unitrol case in evidence in the present proceeding. Instead, the hearing examiner bases his findings of fact in the present proceeding upon the oral testimony of witnesses and documentary evidence received during hearings in this proceeding. Of course, the hearing examiner takes official notice of the decisions of the District Court and Court of Appeals referred to in the Preliminary Statement on page 993 hereof.

placed on the market 25 to 30 years ago under the trade name of "Propadrine" by Merck, Sharp & Dohme, a pharmaceutical house. He further testified that the Post Office Department decided that a study should be made of the effect of phenylpropanolamine hydrochloride in curbing appetite, as compared to a positive control, dextro amphetamine, known to be an appetite depressant, and with a placebo, a tablet or capsule composed of inert ingredients (Tr. 78-79).

12. Dr. Campbell identified CX 3 as being a copy of the Fazekas study, and stated that it was in the nature of a "quadruple blind" study, meaning that neither the investigators, patients, nor personnel connected with the study had knowledge of the contents of any of the capsules (Tr. 81). On direct examination, Dr. Campbell further testified concerning the study: Approximately 81 mentally deficient (idiopathic²) patients at an institution in Laurel, Maryland, called The Children's Center, which gives custodial care to the mentally deficient, were selected for the test. The patients are kept in cottages on the premises, supervised by attendants. About one hour before the patients were to go into the dining hall, a bell was rung and each patient proceeded to the room where he received the medication prescribed for that particular patient (Tr. 93). The 81 mentally deficient patients were divided into four units or divisions of approximately 20 patients each. The patients in the first unit were given phenylpropanolamine hydrochloride at a dosage level of 25 milligrams three times each day, as shown in Table 1 of CX 3. The patients in the second unit were given phenylpropanolamine at a dosage of 50 milligrams three times each day, as shown in Table 2 of CX 3. The patients in the third unit were given dextro amphetamine at a dosage level of 5 milligrams three times each day, as shown in Table 3 of CX 3. The patients in the fourth unit were given the placebo three times each day, as shown in Table 4 of CX 3 (Tr. 80; CX 3). There was no restriction on the caloric intake of any of the patients during the course of the six-week study. The object of the study was to determine if phenylpropanolamine depressed the appetite center in the central nervous system in such a manner that the anorexigenic or appetite-depressant effect was experienced by the patient, which then, in turn, would be reflected by loss of weight (Tr. 81-2). Dr. Wilfred R. Ehrmantraut, coauthor of the so-called "Fazekas" study, CX 3, was the doctor in charge

² By "idiopathic," it is meant that the cause of their mental deficiency was not known.

at The Children's Center in Laurel, and selected the patients included in the study (Tr. 82).

13. Dr. Campbell pointed out that in Table 1, under patient No. 6, in CX 3, there is a typographical error in the figures in the last column under the heading "Total Weight Change, Lb." of "+3.0." This figure should be "-1.0." This would change the "Mean values" at the end from "-0.9" to "-1.0." The difference in "Mean values" of one tenth of a pound is not enough to be of significance, in Dr. Campbell's opinion (Tr. 84-6). Dr. Campbell further testified that the three authors of the study decided to use mentally deficient patients because they wanted to obviate or prevent psychological factors that creep into a study when the person knows that it is intended to reduce weight or depress appetite, "so this was an ideal group for our purposes. They were not cognizant of why they were getting the medicine, so their responses were not tainted or tinged in any way by their knowledge of the drug or for what its purpose was, or the purpose of the study" (Tr. 87-8). Dr. Campbell further testified that, in Table 1, on page 1019 of CX 3, seventeen patients are listed, who purportedly were given 25 milligrams of phenylpropanolamine three times each day. One of these patients, No. 13, is listed as an idiot; the other 18 patients were imbeciles, morons, and mentally retarded persons (Tr. 89). Dr. Campbell testified that the "Mean weight loss" of these 19 patients should be "-1.0" for the six-week period (Tr. 91-2); that the "Mean weight loss" of the 18 patients in Table 2 of CX 3, who purportedly were given 50 milligrams of phenylpropanolamine three times each day, was "-0.8 lbs."; that the "Mean weight loss" of the 21 patients in Table 3 of CX 3, who purportedly were given 5 milligrams of dextro amphetamine three times each day, was "-4.6 lbs."; and that the "Mean weight change" of the 21 patients listed in Table 4 of CX 3, who purportedly were given the placebo three times each day, was a gain of "+0.3 lbs." (Tr. 91-2).

14. Dr. Campbell explained that the asterisk in the tables in CX 3 indicates that, at the two-week periods, the weight changes, if any, were not recorded because the patient was not available for weighing (Tr. 93-4). However, Dr. Campbell further testified that the nonrecording of these weights in the four tables does not have any significant effect upon the conclusions drawn from the study because they are equally distributed throughout the four groups of patients, and they cancel each other out (Tr.

96). Dr. Campbell further testified that he went out to the Center once or twice a week to see if there were enough of the capsules on hand and if the patients were receiving them; he made unannounced visits to the various cottages to watch and see that the patients took the capsules, and conferred with Dr. Ehrmantraut concerning the progress of the study (Tr. 98). In concluding his direct examination, Dr. Campbell testified that, in a "double blind" study, such as the Fazekas study, neither the physician nor the patient knows what drug is used until the study is completed, and the code label removed and the identity of the drug disclosed; and that, as a result of the study, Dr. Campbell and Doctors Fazekas and Ehrmantraut concluded that phenylpropanolamine in a dosage of 25 milligrams three times per day has no significant value as a depressant of the appetite.

15. On cross-examination, Dr. Campbell testified as follows: In either June, July or August, 1958, Dr. Campbell called Dr. Fazekas on the telephone, and asked him if he (Fazekas) would be interested in undertaking an evaluation of phenylpropanolamine hydrochloride as an appetite-depressant agent, and Dr. Fazekas stated that he would be willing to undertake such a study (Tr. 133-34); and that he (Campbell) may have told Dr. Fazekas that he needed such a study in order to support his position in a case wherein the Government was trying to prove that P.P.A. was not effective as an appetite depressant (Tr. 135). The Fazekas study actually began around October 16, 1958 (Tr. 132).

16. Dr. Campbell further testified on cross-examination that, at the time he participated in the Fazekas study (CX 3), he was not "fully aware" of the position of the Food and Drug Administration as to the usefulness of P.P.A. as an appetite depressant, but he thought "their position was that it was suspect" (Tr. 173-74), and that he was not aware of the two letters from the Food and Drug Administration, dated July 5, 1957 (RX 4), and October 23, 1957 (RX 5), approving the following wording on labels for the use of phenylpropanolamine hydrochloride:

PPA is useful as an appetite suppressant in the dietary management [control] of obesity (Tr. 175).

17. Dr. Campbell further testified on cross-examination: Effective (anorexigenic) appetite-depressant drugs are prescribed by physicians in conjunction with a weight-reducing diet. "These drugs are so potent that they are restricted to the prescription

legend." These drugs are used because they enable the patient to be satisfied with a fewer number of calories, and impart a feeling of well being to the patient, which is necessary when you limit his caloric intake (Tr. 181-82). Dr. Campbell admitted that one or two of the patients included in the study were epileptics, and some had marked brain damage due to cerebral palsy, could not feed themselves and required help to partake of food (Tr. 186). Nevertheless, Dr. Campbell testified that these brain injuries, which existed in these particular patients, were not important in an evaluation of the study (CX 3) because they did not affect the patients' "appetite control centers" of the brain, and, for this reason, were unimportant in the evaluation of the study (Tr. 187).

18. After testifying that these pre-existing brain injuries had no effect upon the action of appetite depressing drugs because the brain injuries did not affect or damage the patients' appetite control centers, and admitting that he was assuming that appetite depressing drugs work on the appetite control centers of the brain, Dr. Campbell was asked if he agreed or disagreed with a statement by Dr. Walter J. Modell in his book *Drugs of Choice*, 1962, page 308 (CX 6 for identification), where, in effect, Dr. Modell stated that the effectiveness of appetite depressing drugs is not due to any action on the appetite control centers, but is due to action upon a higher center, situated in an area different from the appetite control center, and whether, in referring to "appetite depressing drugs," Dr. Modell included phenylpropanolamine hydrochloride. Dr. Campbell stated he could not answer the question without also referring to another page of the book. At that point, counsel began arguing between themselves and the hearing examiner called for order in the hearing room, whereupon Dr. Campbell announced that he was leaving and didn't "have to take it either." Dr. Campbell began picking up his books and papers (Tr. 188-194). After a recess, and after Dr. Campbell had been requested to answer counsel's questions "Yes" or "No," unless he could not so answer without an explanation when he should so state, the hearing was resumed and Dr. Campbell finally answered, "yes, with an explanation," to the question previously asked by counsel. The question was whether Dr. Modell, in referring to "appetite depressing drugs" in the excerpt from his book referred to by counsel and which was read by Dr. Campbell, included "Phenylpropanolamine Hydrochloride" (Tr. 195-96).

19. Dr. Campbell further testified on cross-examination: Restriction of caloric intake is the basic requirement in the reduction of weight, but, in the Fazekas study, no dietary restriction was placed upon the 81³ patients; in fact, a minimum of 3000 calories was placed before each patient at each meal, which was well above the energy requirements for the patient, and he naturally would, in most cases, gain weight (Tr. 197). In answer to a question by counsel for respondents, Dr. Campbell stated that patient No. 14, shown in Table 1 of CX 3 to have gained 11 1/2 pounds during the test, was a compulsive eater who had a heart disease with fluid retention (Tr. 213). The patients were so mentally deficient that they responded to the "very pleasant tinkle" of a bell at mealtime; however, Dr. Campbell did not think that placing the 3000 calories of food in front of the patients, after their having been conditioned over a period of time to the tinkle of the bell, did not have any more effect on the will power of the mentally deficient patients than the effect on soldiers by blowing a whistle or bugle "during World War Two when they would let us know that chow was ready" (Tr. 197-201). After some equivocation, Dr. Campbell stated that the soldier or normal person responding to a bell at mealtime is not responding by way of a conditioned reflex in the same manner that the mentally deficient patient responded to the bell, and finally agreed that the soldier was exercising some judgment as to what he would eat and how much, whereas, the mentally deficient patients in the study were not in a position to make rational judgments (Tr. 201-204). Dr. Campbell further testified that "in most clinical studies with these drugs, they have been used in connection with a low calorie diet," and each person serves as his own control, that is, for a stated number of weeks, unknown to the patient, he is given a placebo. This is one of the recognized ways to eliminate psychological influences. This is called a "double blind cross-over" study (Tr. 206-207).

20. In spite of the statement in the right-hand column at the top of page 1019 of CX 3, that begins

The 81 patients selected for the study were divided into four approximately equal groups, and each subject of each group was given one of the four preparations under investigation three times a day, one hour before meals, for a period of six weeks,

³ Although the report (CX 3) states, and Dr. Campbell testified, that 81 mentally deficient patients were used in the study (Tr. 80), divided into four approximately equal units, the report also notes that one patient in Table 2 and one patient in Table 3 were dropped from the study after the first two weeks, leaving only 79 patients in the study.

Dr. Campbell admitted that a number of patients in each of the four units or tables of the study were allowed to go home on week-ends or at other times, at which times such patients were away from the cottage grounds and Dr. Campbell did not know whether such patients received the medication, as the report states (Tr. 220-223). According to Table 1, patients Nos. 8, 9, and 10 were not present for weighing at either the end of the four-week period or the six-week period, which was the end of the study; "They were home with their parents or their brothers or sisters or family" (Tr. 222). Therefore, Dr. Campbell testified, he did not know whether the patients did or did not receive the medication when they were off the premises on week-ends or at other times (Tr. 221-23). Under Table 2, three patients were not available for weighing at the end of either the four-week period or six-week period, and, while away from the premises, may not have received the medication; in Table 3, four patients were not weighed at the end of either the four-week period or six-week period; and in Table 4, five patients were not weighed at the end of either the four-week period or six-week period. Dr. Campbell stated that, similar to the patients in Table 1, while these patients were absent from the premises or at home or elsewhere, he was not able to say that these absent patients received the medication (Tr. 224-28; CX 3).

21. Counsel for respondents questioned Dr. Campbell concerning the second sentence of the paragraph in the upper right-hand column on page 1019 of the Fazekas report, CX 3, wherein it is stated,

The drugs were administered by cottage supervisors (not aware of the identity of the drugs) who made certain of their ingestion by the subjects and were responsible for recording the weekly weights of all cottage residents participating in the investigation,

and inquired who wrote the sentence. Dr. Campbell answered that Dr. Fazekas actually wrote it, but that he (Campbell) had read three rough drafts of it (Tr. 229) and, at that time was aware from his examination of the cottage records during the course of the study that some of the patients had been allowed to go home on week-ends and at other times, but he did not notify the Food and Drug Administration or the Post Office Department about this (Tr. 223). Consequently, at such times when the patients were away from the premises, the cottage supervisors could not give them the medication, and Dr. Campbell could not be certain that the patients had taken the medication (Tr. 230-

33). Accordingly, it is found that, contrary to the statements in the report (CX 3), the drugs were not administered by cottage supervisors to each of the subjects "three times a day * * * for a period of six weeks," as stated in the said report (Tr. 229).

22. Dr. Campbell further testified on cross-examination that he did not have a court case in mind when he and his coauthors designed the Fazekas study (Tr. 236), and does not know, where an asterisk appears in the report (CX 3), whether the patient was actually getting the drug, but was just not available for weighing, or whether the patient was not getting the medication (Tr. 237). Dr. Campbell further testified on cross-examination that, according to Table 1 of CX 3, fourteen out of the nineteen patients who took 25 milligrams of P.P.A. three times a day lost anywhere from one to ten pounds in weight (Tr. 238-39); according to Table 3, seventeen of the twenty-one patients taking dextro amphetamine, the prescription drug, lost from one to ten pounds (Tr. 240); and, according to Table 4, thirteen of the twenty-one patients taking the placebo gained weight (Tr. 241). Dr. Campbell further testified that he had not read and had never seen the article by Doctors Fazekas, Ehrmantraut, and Kleh reporting a "Study of Effectiveness of Certain Anorexigenic Agents," referred to in footnote No. 2 at the bottom of page 1021 of CX 3 (Tr. 250); nor had he read the article by Dr. Harris reporting a study entitled "Clinically Useful Appetite Depressants," also referred to in footnote No. 2 (Tr. 250-51).

23. On cross-examination, Dr. Campbell also testified that dextro amphetamine, sometimes called "Dexedrine," is generally used as an adjunct to a low calorie diet (Tr. 253). Counsel then asked Dr. Campbell if it were not true that, in addition to the test substances that were given to these patients, some of the patients were given other drugs to retard epileptic seizures, and he answered:

A. Yes, but no drug was given that would interfere with this study.

Q. That is what we would like to find out. What drugs were given, Doctor, to these others.

A. Dilantin (Tr. 256).

* * * * *

Q. And isn't it true, sir, that some of these patients were also on phenobarbital?

A. Where are you getting that information from? Have I got it?

Q. I am not giving you any information. I am asking you a question (Tr. 256-57).

* * * * *

THE WITNESS: They were given tranquilizers, anticonvulsants, insulin, and what did you say, phenobarbital?

Q. Yes.

A. Yes, it could be (Tr. 257).

Dr. Campbell admitted that, at the time the 79 patients involved in the Fazekas study (CX 3) were being given the test drugs listed in Tables 1, 2, 3, and 4, twenty-eight of these patients were also being given one or more additional drugs, such as phenobarbital, meprobamate, anticonvulsants, "Miltown," etc., as follows: Of the 19 patients listed in Table 1 of CX 3 who were supposed to be receiving 25 milligrams of phenylpropanolamine hydrochloride three times each day, patients Nos. 5 and 6 were also receiving a tranquilizer Miltown, and phenobarbital; patient No. 12 was also receiving Miltown and phenobarbital, plus an anticonvulsant; patient No. 16 was also receiving insulin; patient No. 17 was also receiving insulin and a combination of meprobamate-phenobarbital (Tr. 263). In Table 2 of CX 3, of the 18 patients supposed to be receiving 50 milligrams of P.P.A. three times each day, patients Nos. 1, 3, and 8 were also receiving a meprobamate-phenobarbital combination; patients Nos. 12, 13, and 14 were also receiving anticonvulsants; and patient No. 15 was also receiving a combination of meprobamate-phenobarbital, and anticonvulsants (Tr. 264). Of the 21 patients listed in Table 3 of CX 3 who were supposed to be receiving 5 milligrams of dextro amphetamine three times each day, patients Nos. 1, 2, 5, 6, and 14 were also receiving the meprobamate-phenobarbital combination; patients Nos. 15, 16, 17, 19, and 20 were also receiving anticonvulsants (Tr. 264). Of the 21 patients listed in Table 4 of CX 3 who were supposed to be receiving the placebo three times each day, patients Nos. 1 and 5 were also receiving a combination of meprobamate-phenobarbital; patient No. 15 was also receiving a combination of meprobamate-phenobarbital, plus anticonvulsants; patient No. 17 was also receiving a combination of meprobamate-phenobarbital; patient No. 18 was also receiving anticonvulsants; and patient No. 21 was also receiving a combination of meprobamate and phenobarbital (Tr. 264).

24. Dr. Campbell further testified on cross-examination that dextro amphetamine acts to reduce appetite by working upon the central nervous system; that phenobarbital may neutralize the excitant or stimulative effects of dextro amphetamine; and that, ordinarily, the drugs phenobarbital and dextro ampheta-

mine are not combined when dextro amphetamine is being used along with a low calorie diet for weight-reducing purposes (Tr. 257-58). Dr. Campbell testified that an I.Q. of 70 is the beginning line of a mental defective, and the intelligence quotient level does not have any effect upon or relationship to the action of the drug on the central nervous system (Tr. 281). Dr. Campbell was asked on cross-examination if it were not true that the therapeutic effectiveness of a recognized pharmacologically potent anorexigenic agent may in mentally deficient subjects be neutralized by cortical or subcortical influences. Dr. Campbell answered, "I wasn't aware of that, and I don't believe it * * * . I don't believe it is true" (Tr. 282). Counsel for respondents then exhibited to Dr. Campbell page 1020 of the written report of the study of which he was coauthor, CX 3, where, in the last sentence of the paragraph immediately preceding the section in the right-hand column headed "Comment," is the statement:

Thus, the therapeutic effectiveness of a recognized pharmacologically potent anorexigenic agent may, even in mentally deficient subjects, be neutralized, possibly by cortical or subcortical influences.

Counsel then asked Dr. Campbell which statement is true: The statement in CX 3 or the statement made by Dr. Campbell in his testimony. Dr. Campbell then said that counsel for respondents had used the word "will" in his question; counsel stated that he (counsel) had used "may" (Tr. 282-83). The hearing examiner then asked the reporter to read the question as counsel for respondents had asked it two times, successively, and as the reporter had reported it stenographically. The reporter read aloud the question which counsel had asked Dr. Campbell two times on cross-examination, and the word "may" was asked in the question both times by counsel for respondents (Tr. 284).

25. After repeated questioning, Dr. Campbell finally acknowledged that, in the quotation from CX 3 above set out, the authors of CX 3 were attempting to explain why it was that so many of the patients under Table 3 who were taking dextro amphetamine, the potent prescription appetite depressant, actually gained weight, whereas, a normal person would be expected to lose weight. In other words, the authors of CX 3 explained the unusual phenomenon of some of these mentally deficient patients actually gaining weight while taking dextro amphetamine, instead of losing weight, as would normally be the case, by saying that these mentally deficient patients had multiple variables which

influenced weight reduction, and that is why they gained instead of losing weight (Tr. 284-87).

26. Counsel for respondents then asked Dr. Campbell if it isn't true that the results of the study (CX 3) in which he participated do not preclude the possibility that P.P.A. would be effective in a receptive or susceptible population of normal intelligence when properly motivated to lose weight, and, after several unresponsive and unrelated answers, Dr. Campbell finally replied, "No, we did not" (Tr. 288). Dr. Campbell continued looking at papers and thumbing through papers in front of him, and counsel repeated the question by asking Dr. Campbell if it was his testimony that the study (CX 3) in which he participated

does not leave open the possibility that PPA may be effective in a susceptible and normal population which is motivated to lose weight? (Tr. 289), and Dr. Campbell replied: "PPA has no value as an appetite depressant" (Tr. 289). Counsel again asked the question a third time, if his study (CX 3) left open the possibility

that the drug may be effective on a receptive and susceptible population that is sufficiently motivated and that is mentally alert, and not mentally deficient (Tr. 289),

and Dr. Campbell answered: "In my opinion, it doesn't" (Tr. 289). Counsel then asked Dr. Campbell if his report (CX 3) said anything about "leaving it open," and Dr. Campbell replied: "Yes, I have to find out if we said anything in here" (Tr. 289). Dr. Campbell was given time to re-read the report (CX 3), especially the statement in the left-hand column near the bottom of page 1021, as follows:

* * * In view of the generally recognized effectiveness of psychological forces alone on appetite control, these results do not preclude the possibility of weight loss in a receptive or susceptible population when phenylpropanolamine, or even a placebo, is administered along with sufficient psychological motivation provided by a physician (Tr. 290),

and Dr. Campbell finally answered, "Yes," that he had made such statement in the report (CX 3; Tr. 291).

27. In testifying on direct examination that P.P.A. was not an effective appetite depressant but was one of the "do-nothing" drugs, Dr. Campbell testified on cross-examination that, in so testifying, he relied 50 percent on his study (CX 3) and 50 percent on the concurrence of informed medical thinking, such as "the up-to-date issues of Goodman and Gilman and other texts that you have available there" (Tr. 293-94).

28. Counsel then proceeded to cross-examine Dr. Campbell with reference to whether he agreed or disagreed with certain statements in specified medical texts concerning the use of P.P.A. as an appetite depressant. Dr. Campbell was asked whether he agreed or disagreed with the following statements on pages 1892-1893 of The Dispensatory of the United States of America, 25th Edition (CX 5), concerning phenylpropanolamine hydrochloride:

Phenylpropanolamine is slightly less active than amphetamine in its effects on the circulation and apparently has little if any psychic stimulative action * * *. The advantages claimed for it are that it can be taken by mouth without producing the nervous symptoms characteristic of amphetamine, and with no other unpleasant symptoms * * *. Hirsh (*J. Med.*, 1939, 20, 84) reported that it is useful to kill the appetite in the treatment of obesity, as it does not produce nervous disturbances * * *.

Dose.—The recommended oral dose is 25 to 50 mg. administered at 3- to 4-hour intervals as indicated.

Dr. Campbell agreed that phenylpropanolamine hydrochloride is used successfully in solution or tablet form for allergic and asthmatic conditions, but he did not agree with the statement that it is effective as an appetite depressant (Tr. 300-302).

29. Counsel for respondents then asked Dr. Campbell whether he agreed or disagreed with the statement in the textbook entitled Pharmacology and Therapeutics by Dr. Arthur Grollman, published in 1960 (RX 8), wherein, on page 291, it is stated:

*Phenylpropanolamine hydrochloride (propadrine), * * *.*

In action it resembles ephedrine closely. Like the latter it constricts the capillaries and shrinks the mucous membranes when applied locally. Its action is somewhat more prolonged than that of ephedrine. It is used in asthma and hay fever, to alleviate nasal congestion and to depress appetite in obesity.

Counsel then referred to two later editions of the same textbook by Dr. Grollman, page 306 of the Fifth Edition, published in 1962 (RX 9), and page 326 of the Sixth Edition, published in 1965 (RX 10), wherein the same statements with respect to P.P.A. as those contained in the 1960 edition (RX 8), quoted above, are repeated, and asked Dr. Campbell if he agreed or disagreed with the statements, and Dr. Campbell replied that he disagreed with the portion of each statement to the effect that P.P.A. depresses the appetite (Tr. 303-306).

30. Counsel for respondents then asked Dr. Campbell if he agreed or disagreed with the statement in a book entitled The

Merck Index, Seventh Edition, 1960 (RX 11), wherein, on page 805, is stated the following:

Phenylpropanolamine Hydrochloride * * *

Med. Use: Sympathomimetic agent employed in bronchial asthma and hay fever, as anorexant for control of obesity, antihypotensive agent during spinal anesthesia. Used topically as nasal decongestant. Dose: * * * 25 to 50 mg.

Dr. Campbell testified that he disagreed with the statement that P.P.A. is effective in the depression of appetite (Tr. 306-308).

31. Counsel for respondents then referred to a book entitled The Amphetamines by Professor Chauncey D. Leake, professor of pharmacology at The Ohio State University, Columbus, Ohio, copyright 1958, date of publication not given (RX 12), where, on pages 12 and 13, there is a chart or table with the heading "Table of the Amphetamines and Relatives," which lists the names of various amphetamines, their respective chemical names, their chief sympathomimetic action, and the ordinary dosage for each drug. Among the drugs listed on page 13 is phenylpropanolamine hydrochloride (Propadrine), and under the heading "Chief Sympathomimetic Action," it is stated "appetite depressant," and, under the heading "Ordinary Dosage" is listed 25 to 50 mgm orally." Dr. Campbell was asked whether he agreed or disagreed with the statement that P.P.A. is an effective appetite depressant, and he replied:

I disagree with the statement as relates its efficacy of phenylpropanolamine as an appetite depressant (Tr. 309-310).

32. Counsel for respondents then referred to the Eighth Edition of a book entitled A Manual of Pharmacology And Its Applications To Therapeutics and Toxicology by Torald Sollmann, M.D., professor emeritus of pharmacology and materia medica, School of Medicine, Western Reserve University, Cleveland, Ohio, published in 1957 (RX 13). Counsel asked Dr. Campbell whether he agreed or disagreed with several quotations which counsel read from pages 509 and 510 of the book referring to the use of amphetamines for the control of obesity, including the following from the first paragraph at the top of page 510 thereof:

* * * The d-isomer ("Dexedrine") is effective as well as the usual racemic form. Phenylpropylamine ("Propadrine") is less effective, but also less excitant (Tainter, 1944).

Dr. Campbell testified that he disagreed with that portion of the statement "relating to its efficacy in the treatment of obesity" (Tr. 311-13).

33. Counsel for respondents then questioned Dr. Campbell concerning the contents of a book entitled Pharmacology in Medicine by Victor A. Drill, Ph.D., M.D., lecturer in pharmacology, Northwestern University Medical School, Second Edition, 1958 (RX 14), and asked Dr. Campbell whether he agreed or disagreed with the following statements contained therein on pages 400-401:

Phenylpropanolamine Hydrochloride is similar in action to ephedrine but is somewhat more pressor and slightly less stimulant. Propadrine is used principally as a topical nasal decongestant when given orally in doses of 25 milligrams. Although it is stated that this drug does not produce central stimulation to any great degree, it is active enough to be used for controlling the appetite. This action is the same as will be described below for amphetamine (Tr. 315).

Dr. Campbell replied that he disagreed with that portion of the statement to the effect that phenylpropanolamine hydrochloride is effective in the treatment of obesity (Tr. 314-16).

34. Counsel for respondents then referred to a book entitled Clinical Pharmacology by D. R. Laurence, M.D., M.R.C.P., Reader in Pharmacology and Therapeutics in the Department of Pharmacology, University College, and the Medical Unit, University College Hospital Medical School, London, England, published in 1963 (RX 15), and asked Dr. Campbell whether he agreed or disagreed with the following statement on page 285 thereof, under the heading "Remarks":

* * * like ephedrine but sometimes used to reduce appetite (50 mg. daily).

Dr. Campbell replied that he disagreed with the statement that the drug was effective "to reduce appetite" (Tr. 316-17).

35. Counsel for respondents then referred to a book entitled Remington's Practice of Pharmacy by Martin and Cook, Twelfth Edition, 1916 (RX 16), and asked Dr. Campbell, among other things, whether he agreed or disagreed with the following statement contained on page 844 thereof with respect to the drug phenylpropanolamine hydrochloride:

White powder, freely soluble in alcohol and water, forming a neutral aqueous solution. Uses: similar to ephedrine, in hay fever, bronchial asthma, obesity, and locally to shrink mucous membranes. Its action is more prolonged than that of ephedrine. Dose: locally, 1 to 3 per cent aqueous solution; orally, 25-50 mg. 3 times a day (Tr. 323).

Dr. Campbell replied that he disagreed with the reference "to its use in obesity" (Tr. 319-325). In reply to a further question by counsel, Dr. Campbell testified that he was not familiar with an article on obesity control by Dr. A. D. Jonas of New York, published in The American Practitioner and Digest of Treatment, Volume 1, September 1950, page 933, wherein Dr. Jonas states that:

Patients selected for the study were not considered if they were mentally retarded, pre-psychotic and psychotic individuals (Tr. 332-33).

The quotation from this publication was not offered nor received in evidence at the hearing.

36. Continuing his cross-examination of Dr. Campbell, counsel for respondents asked the doctor whether, because a book on drugs does not recite on a particular page that the drug is not useful as an appetite depressant, he would thereby conclude that the drug is not useful as an appetite depressant, to which Dr. Campbell replied, in effect, that, when current knowledge comes to the attention of authors of books on Pharmacology and other medical tests, the authors revise the books periodically "to catch up with new indications for use or delete indications for use that have not been found valid" (Tr. 335-36). Counsel then referred to the Eighth Edition of A Manual of Pharmacology And Its Applications To Therapeutics and Toxicology by Dr. Torald Sollmann, page 507, a textbook previously referred to in paragraph numbered 32 above, wherein a reference was made to P.P.A., but nothing was said about its being useful as an appetite depressant. Counsel then asked Dr. Campbell whether, assuming the date of the book to be 1965, and that page 507 of the book refers to P.P.A. but on that page does not make any reference to P.P.A.'s being an appetite depressant in the dietary management of obesity, he (Campbell) would conclude that the drug was not useful for that purpose simply because there was no reference on that page to its usefulness, if any, as an appetite depressant. In answer to the question Dr. Campbell replied that he would conclude that any reference to P.P.A. as an appetite depressant had been deleted from the book for the reason that, in his opinion, the latest information

had filtered finally into the text, and it was now known to the Medical Community at Large that phenylpropanolamine hydrochloride was not effective as an appetite depressant (Tr. 336-37).

Counsel for respondents then referred to a reproduced copy

of page 507 of Dr. Sollmann's book, which was marked for identification and received in evidence as RX 17. (Reproduced copies of pages 509 and 510 from said book were previously received in evidence as RX 13.)

37. The second witness offered by complaint counsel was Frederick William Wolff, M.D., a clinical pharmacologist, and, at the time of the hearing, director of research at the Washington Hospital Center, Washington, D.C., and professor of medicine at George Washington University School of Medicine, and director of the section of experimental Therapeutics, Department of Medicine at that school (Tr. 350-51). At complaint counsel's request, Dr. Wolff had previously examined a copy of the Fazekas report (CX 3), and stated at the hearing that he approves the statistical design thereof and agrees with the conclusions reached by the authors (Tr. 351). Dr. Wolff testified, among other things, that: He is familiar with the drug phenylpropanolamine hydrochloride; that it has been in use for more than 20 years (Tr. 351); and that it "was first used for obesity for a number of years, but to the best of my knowledge, it is now generally used as a nasal decongestant" (Tr. 354). In the course of his practice, Dr. Wolff stated that he has occasion to consult with obese patients, but he seldom prescribes drugs; if he has to prescribe a drug for a patient, it is dextro amphetamine. He does not prescribe phenylpropanolamine hydrochloride (Tr. 355). He generally does not prescribe any drug because:

(1) the evidence is suggestive that they are effective only for a very limited period of time and (2) I know that all appetite depressants have considerable side effects and can also lead to barbituration and even addiction. And it is my view that they are dangerous drugs, so I try not to prescribe them. If I have to prescribe them I prescribe dexedrine for a short period of not more than four weeks. Beyond six weeks, in all of these drugs, appetite depressants, they appear to lose their effect after four to six weeks (Tr. 356).

Replying to a question of complaint counsel as to whether the failure by the authors of the study to record the weights of three patients at the end of the four and six weeks periods (where the asterisks are shown in Table 1 of CX 3) would invalidate the study, Dr. Wolff replied that he thought "the figures that are missing probably do not really change the total result very much" (Tr. 358), because the weight loss during the "first two weeks is probably the most important one. As time goes on, all weight depressants begin to lose their effectiveness"

(Tr. 359). Dr. Wolff testified that his comments with regard to the missing weight figures in Table 1 also applied to Tables 2, 3, and 4, because, "in this particular study, at least, the majority of the data is tabulated. At least, you are sure that the patients have taken the pill. In this, of course, you never know in out-patients to be sure" (Tr. 359). He stated that it is "exceedingly important" that the patient take the pill during the study (Tr. 359).

38. Dr. Wolff was of the opinion that the choice of the 81 mentally deficient institutionalized patients was valid for the study, and the absence of any dietary restrictions during the six-week study period was also valid because the patients involved in this study (CX 3) were mentally deficient and, therefore, the usual patient-doctor relationship did not exist. In most clinical drug studies of appetite depressants, two things are used: a pill and a measure of diet restrictions. These mentally deficient patients did not have any personal physician nor any personal discipline. Therefore, "Whatever you think the result means, it must be due to the pills" (Tr. 360-61). Dr. Wolff testified that he did not consider phenylpropanolamine hydrochloride, given in dosages of 25 milligrams three times each day, to be adequate or effective in the treatment, control or management of obesity. Also, he did not consider phenylpropanolamine hydrochloride to be safe for use on an over-the-counter basis by obese persons, because:

All drugs have a multitude of effects, not all of which are desired. Among the undesirable effects there are effects on the cardiovascular system; they may increase the heart rate; they may raise the blood pressure; they may cause nervousness; they may be dangerous in cases that are mentally imbalanced or that may have a prior disease, or that may have high blood pressure or angina pectoris. In my own experience, with all of these agents, the most dangerous effect is the one of habituation or addiction (Tr. 362-63).

Dr. Wolff testified that phenylpropanolamine hydrochloride is currently being used by the medical profession as a nasal decongestant (Tr. 363).

39. On cross-examination, Dr. Wolff agreed that all of the nasal decongestant preparations are sold over-the-counter without prescription, and the food and drug laws presently require that the label contain a statement that the preparation should not be used by persons with thyroid, cardiovascular, or high blood pressure conditions (Tr. 364). Dr. Wolff testified that, in his opinion, for a weight loss to be "significant," it must be a

minimum of 5 lbs. over a period of one week among a group of 26 persons (Tr. 365). Individuals vary, so he considers a group of 26 persons, and he means "normal people" on a reducing diet, who are attempting to stick to a proper diet with proper instructions (Tr. 366). According to Table 3 in CX 3, twenty-one mentally deficient patients with no diet restrictions and who were supposed to be taking dextro amphetamine, a prescription drug, lost an average of minus 2.2 lbs., a total of about 34 ounces or about 1 1/2 ounces per patient over the first two-week period, whereas, Dr. Wolff considered a weight loss, to be significant, must be at least 5 lbs. per week among a group of 26 normal people (Tr. 365-66). According to Table 1 of CX 3, the 19 mentally deficient patients taking phenylpropanolamine lost an average of minus 0.9 lbs. during the first two-week period, but Dr. Wolff testified that he did not make a statistical evaluation of the two tables to compare the comparative effectiveness of P.P.A. and dextro amphetamine (Tr. 368).

40. Dr. Wolff further testified that he would be suspicious of any study which reported that pills were given patients when, in fact, they were not really given (Tr. 374). In his opinion, a written report of a clinical study should report what was actually done and that, if, in fact, certain drugs were not administered to patients by hospital attendants, a written report of that study should not recite that those certain drugs had been administered to such patients by hospital attendants (Tr. 375-76). Dr. Wolff also testified that he had had no personal experience with phenylpropanolamine, but that it is chemically related to the amphetamine family (Tr. 376). Dr. Wolff testified that, although he had read papers on studies which reported that phenylpropanolamine is an effective appetite depressant on persons of normal intelligence, he was not satisfied with the conclusions (Tr. 376-77). Dr. Wolff testified that the Fazekas study (CX 3) is not a "cross-over" study, where the patients are both on a placebo for a period and are then placed on the drug (Tr. 380).

41. Counsel for respondents questioned Dr. Wolff concerning statements in textbooks to the effect that phenylpropanolamine hydrochloride is used as an appetite depressant, including the statements in Dr. Grollman's book *Pharmacology and Therapeutics*, Fifth Edition, 1962 (RX 9), where, on page 306, he describes the action of P.P.A. and says:

It is used in asthma and hay fever, to alleviate nasal congestion and to depress appetite in obesity.

Dr. Wolff observed that, in so stating, Dr. Grollman does not thereby recommend that it is used to depress the appetite; he merely says that P.P.A. is used "to depress the appetite in obesity"; he does not evaluate the drug (Tr. 398). According to Dr. Wolff, the fact that a medical textbook states that a certain drug is used for certain purposes does not mean that the drug works successfully for those purposes; "things get in textbooks that are completely misleading sometimes" (Tr. 399). Also, Dr. Wolff stated that he does not respect the judgment of other well regarded physicians in all situations, necessarily, because " * * * I have never found two doctors who could agree about everything, except what he should contribute to his favorite charity" (Tr. 394). Dr. Wolff further testified that it is bad practice for a physician to select a drug from a list contained in a book, and one of the worst is entitled a "Physician's Desk Reference To Pharmaceutical Specialties and Biologicals," which had been previously offered in evidence as CX 4 but rejected by the hearing examiner (Tr. 400). Dr. Wolff gave as his opinion that a really effective and active drug should not be sold "over-the-counter," because, if it does work, it has powerful side effects (Tr. 408-409); and that most drugs should be sold by prescription only (Tr. 411). He further testified that a tolerance, a refractoriness, develops in all persons given appetite-depressant drugs after a few weeks (Tr. 376).

42. The testimony of respondents' witnesses will now be discussed. The first witness for respondents was Edward Settel, M.D., of New York, New York, a specialist in internal medicine (Tr. 476). Dr. Settel has been practicing medicine in New York City and Brooklyn, New York, since 1938, is on the staff of several hospitals in Brooklyn, is a member of various medical societies, and has contributed articles to medical journals (Tr. 476-78). Dr. Settel has done at least 50 to 60 research studies in drug evaluation, of which 90 percent have been published in recognized medical journals. A statement of Dr. Settel's educational background and a list of published articles and his affiliations were received in evidence as RX 19. At the request of counsel for respondents, Dr. Settel conducted a study of P.P.A. as an appetite depressant (Tr. 481). The study was what Dr. Settel characterized as a "double-blind" study with a "cross over" of the drug, plus a placebo, for a period of six weeks, of 30 persons living in a middle-class urban community, who were at least 10 percent or more overweight according to the statistical

tables of the Metropolitan Life Insurance Company. In the opinion of Dr. Settel, these middle-class people most often go to a doctor seeking help to lose weight (Tr. 482). The report of his test was received in evidence as RX 20. In his test, neither the subjects nor the physician knew which tablet, "A" or "B," was the drug P.P.A. and which was the placebo (Tr. 482). In the cross over, the patients who had been taking tablet A for three weeks were switched without their knowledge, and without the knowledge of Dr. Settel, to tablet B, and the patients on tablet B were switched to tablet A, and the patients were placed on a "measured 900 calorie diet as the base line" (Tr. 483). In this manner, each patient served as his own control for the purpose of determining which tablet was more effective (Tr. 483). The patients were selected at random. At the conclusion of the study, Dr. Settel concluded that tablet A was a more effective anorexiant agent than tablet B. Subsequently, Dr. Settel learned that tablet A was the active drug P.P.A. (Tr. 483-84). Dr. Settel concluded from his study that P.P.A. was a relatively safe drug, and, while there was a total of some 1260 patient days of treatment, there was only one complaint from one patient who experienced a dryness of the mouth for a couple of days (Tr. 503).

43. Dr. Settel testified that he had examined the Fazekas report (CX 3), and did not consider it to be scientifically sound for several reasons: First, the patients in that study were mental defectives, including imbeciles and morons, with primary mental lesions (meaning that the cause of their mental deficiency was unknown), and he would not test a drug which works on the cortical and subcortical area of the brain on people who have primary mental lesions (Tr. 504); second, although the Fazekas study (CX 3) reports that it was a double blind study, it was actually a single blind study, meaning that Dr. Fazekas and his associates knew which drug was the placebo and which was dextro amphetamine, because persons associated with the study would naturally become aware of the patients who were receiving dextro amphetamine since its powerful effects would be readily observable by its action on the patients (Tr. 504); third, while the study (CX 3) reports that it was conducted on obese patients, Dr. Settel questioned whether some of the patients were really obese, according to the age, weight, and height of the patients which are shown in the tables in CX 3 (Tr. 505-506); fourth, Dr. Settel considered the Fazekas report (CX 3) to be unsound because Dr. Fazekas, according to the statements in the report,

used different standards in comparing the effectiveness of P.P.A. and dextro amphetamine. When referring to the purported effectiveness of dextro amphetamine, Dr. Fazekas used the words "statistically significant," but, when referring to the purported results from P.P.A., he did not use the words "statistically significant," but used only the word "significant" (Tr. 506-507). In the opinion of Dr. Settel, the same technique should be used in evaluating both drugs. Fifth, Dr. Settel called attention to the statement on page 1020 of CX 3 where Dr. Fazekas admits that "the therapeutic effectiveness of a recognized drug to control appetite in mentally deficient subjects can be neutralized by cortical and subcortical influence" (Tr. 507). Dr. Settel then explained that an anorexiant drug is supposed to improve appetite control, and appetite control is a summation of a pattern of cortical, or brain, influences, motivation, will power, and desire to lose weight. In mentally deficient people, subcortical influences are present in such a confused and low degree that it is impossible to evaluate a drug or a series of drugs on such a patient, because they do not represent the same cortical and subcortical influences that "you have in the normal cross-section of the population" (Tr. 507-508). In his study, Dr. Fazekas states that dextro amphetamine in those patients may be neutralized because of their mental condition. In answer to a question by the hearing examiner, Dr. Settel defined cortical and subcortical as follows:

These are the influences of the higher level of the brain, the gray matter, the part of the brain involved in reasoning, cogitation, emotion. The subcortical influences are those in the lower level of the brain that have to do with subconscious or unconscious influences, and these, of course, also are bound up tightly with appetite, appetite control, hunger, loss of hunger, mood, euphoria, and other basic physiological processes such as respiration, heartbeat, and so forth (Tr. 508).

44. Dr. Settel further testified that P.P.A. was not intended for idiots, imbeciles, and morons. It was intended to be used by the normal population with normal desires to lose weight. If the drug is to be tested for its efficacy, it should not be tested in an area where it is not used nor intended to be used, that is, among the mentally deficient, "which can distort the actual effect of the drug" (Tr. 509). According to Dr. Settel, the use of mentally deficient persons in the Fazekas test (CX 3) could distort the comparative effectiveness of P.P.A. and dextro amphetamine, and render the study completely insupportable from a scientific standpoint (Tr. 510). Furthermore, Dr. Settel pointed out that

the patients involved in the Fazekas study were not selected at random, because the written report (CX 3) shows that the patients in Table 3, who were given dextro amphetamine, had an approximately 30 percent higher average I.Q. than those in Table 1 who were taking P.P.A. Therefore, other things being equal, it was to be expected that those patients receiving dextro amphetamine would show a greater weight loss (Tr. 510).

45. When the attention of Dr. Settel was directed to the right-hand column near the top of page 1019 of the Fazekas report (CX 3), where it is stated, among other things, that "the drugs were administered by cottage supervisors," and he was asked what effect, if any, it would have on the validity of the report, if, on some occasions, some of the patients went home on weekend passes and did not receive the drug from the cottage supervisors while at home, Dr. Settel replied that, if this were true, the entire report would be vitiated (Tr. 512). Dr. Settel stated that this was so, for the reason that it is important that the patient receive the drug, and the very fact of the patient's being at home in a different atmosphere, with relatives and friends feeling sorry for the patient, would affect the validity of the study (Tr. 512). Dr. Settel stated that he did not use dextro amphetamine in his study of P.P.A., because he was not evaluating the relative efficacy of the two drugs, but only wanted to know whether P.P.A. had any measurable and significant anorexiant effect (Tr. 518). On cross-examination by complaint counsel, Dr. Settel emphasized that the use of dextro amphetamine on the mentally deficient patients would produce reactions on such patients sufficient to show to the cottage personnel which patients were being given the drug (Tr. 521, 522). Dr. Settel stated that, if the patients in the Fazekas study (CX 3) suffered cerebral damage, from birth, injury, or palsy (as testified by Dr. Campbell), this would affect the demonstrable result of the use of P.P.A. and dextro amphetamine on such patients (Tr. 550). Dr. Settel further stated that his use of a 900 calorie diet on the patients in his study did not distort the conclusion he reached that P.P.A. was an effective anorexiant drug, because the use of the 900 calorie diet created a constant set of conditions for all 30 patients (Tr. 551).

46. Frederick B. Bohensky, M.D., of Brooklyn, New York, another witness for respondents, testified that, in his practice, he has treated several thousand patients for obesity since 1943 (Tr. 642, 645). Dr. Bohensky is familiar with the drug phenyl-

propanolamine hydrochloride, has used it in his practice, and has found it effective on patients as an anorexigenic agent (Tr. 646). Near the end of November 1959, Dr. Bohensky undertook an evaluation of P.P.A. as an appetite-depressing agent on healthy dogs. Dr. Bohensky selected dogs to use in his study, because he believed that a dog would be an "unbiased subject" and "would act closely and almost identically with its responses to the human being" (Tr. 647); and, in so doing, he would eliminate all psychological factors (Tr. 651); also, because the Food and Drug Administration, Department of Pharmacology, had, itself, utilized dogs to test the efficacy of amphetamine preparations (Tr. 651). In making this study, Dr. Bohensky used the following procedure: Dr. Bohensky obtained 20 healthy dogs from an animal hospital, and for a period of three weeks the dogs were given an adequate diet of food and fluid, according to their weight. The dogs were exercised and weighed daily by the same attendant at the animal hospital, and their weight was tabulated at each weighing (Tr. 648). After Dr. Bohensky had established what he considered to be a good nutritional status, each dog was given one quarter of a milligram of phenylpropylpropanolamine per pound of body weight, which would be equivalent to 75 milligrams for a human being weighing 300 pounds. Dr. Bohensky said that P.P.A. in a dosage of a quarter of a milligram per pound of body weight per dog was an effective appetite depressant, and that the results from his study could be translated to human beings (Tr. 651). Upon the basis of his test and his personal experience with the use of phenylpropylpropanolamine hydrochloride, Dr. Bohensky was of the opinion that P.P.A. is an effective anorexigenic and weight-reducing agent, and is effective in dosages of 75 milligrams per day, taken 25 milligrams before each meal, by human beings (Tr. 652).

47. Dr. Bohensky was of the opinion that the choice of subjects in the Fazekas study (CX 3) was unfortunate, for the reason that P.P.A. acts on the central nervous system and should not have been tested upon mentally deficient patients whose central nervous systems were impaired (Tr. 657). Dr. Bohensky did not agree with the stated conclusions of Dr. Fazekas that P.P.A. was not an effective anorexiant for several reasons: In the Fazekas report (CX 3), the subjects were not used as controls against themselves, in that each of the four units of patients were given different preparations and none of the patients were given all of the drugs; the patients in Tables 1 and 2 of CX 3

were given phenylpropanolamine hydrochloride; the patients in Table 3 were given dextro amphetamine; and the patients in Table 4 were given the placebo. Dr. Fazekas tested each drug on different individuals, and did not utilize the same people by giving one unit of patients dextro amphetamine for a stated period of time, then switching these same patients over to phenylpropanolamine for the same period of time, and later switching the same patients to the placebo for a like period of time. If Dr. Fazekas had followed such a procedure, said Dr. Bohensky, in spite of the unfortunate choice of subjects, Dr. Fazekas could have compared P.P.A. with dextro amphetamine and P.P.A. with a placebo on the same patients (Tr. 658, 659), and his failure to do so in this regard invalidates the study. Dr. Bohensky was of the opinion that a weight loss of 4.6 lbs. for the 21 patients in the Fazekas study (CX 3) taking dextro amphetamine is not a gratifying result, and, in his opinion, would have been more with normal patients (Tr. 659). Dr. Bohensky further stated that, if some of the patients in the Fazekas study were allowed to go home, contrary to the statement in the report that the drugs were administered by "cottage supervisors," the report would be inaccurate (Tr. 660).

48. Dr. Bohensky further testified that the mentally deficient patients in the Fazekas study reacted differently from normal patients, in that some of them even gained weight while taking dextro amphetamine, whereas, a normal patient would have lost weight (Tr. 673). If the mentally deficient patients in the Fazekas study were being given other drugs, such as barbiturates and "Dilantin," in addition to P.P.A. and dextro amphetamine, their reactions to dextro amphetamine and P.P.A. may have been contra-acted and unnoticed (Tr. 675). In conclusion, Dr. Bohensky stated that the fact that two dogs in his study died of starvation does not detract from his conclusions as to the usefulness and safety of P.P.A. in human beings as an appetite depressant, because normal human beings, for whom P.P.A. is intended, can stop taking it when they have attained the desired weight reduction (Tr. 684-85).

49. Raymond W. Healy, M.D., a practicing physician from Miami, Florida, was the next medical witness for respondents (Tr. 688). Dr. Healy graduated from St. Louis University School of Medicine in 1951, interned for one year at Jackson Memorial Hospital in Miami, and since that time has been practicing in Miami where he has treated from 5000 to 6000 patients for

obesity conditions (Tr. 690). Dr. Healy is a general practitioner in internal medicine and is primarily interested in obesity (Tr. 698-99). At the request of The Odrinex Company, he conducted a clinical study of the comparative effectiveness of P.P.A. and dextro amphetamine on 30 normal patients over an eight-week period (Tr. 690-93, 699). The patients were weighed each week. Dr. Healy testified that, in his clinical study, he had been giving his patients dextro amphetamine to reduce their appetities, while on a low calorie diet, along with vitamins, if necessary. In this study, Dr. Healy selected every third to fifth patient who came to his office to be treated for obesity, and gave that patient P.P.A. instead of dextro amphetamine. He continued giving each third or fifth patient P.P.A. in order to get a general sampling among all of his patients. Of the 30 patients on whom Dr. Healy made the study of P.P.A., 22 were persons who were already patients of Dr. Healy, and 8 were new patients. The patients visited Dr. Healy's office at the same approximate time each week, at which time the patients were weighed and their blood pressure and pulse taken; these were recorded (Tr. 691, 693). The P.P.A. was placed in envelopes and given to each patient with directions for their use during that week. Dr. Healy assumed that the patients took the pills, because he did not believe that the patients came to his office, paid his regular fees, and did not take the pills (Tr. 693-94). From his study, Dr. Healy concluded that P.P.A. was safe to use and effective in reducing the appetite in about 80 percent of his patients involved in the test (Tr. 698).

50. Dr. Healy testified that, in order to lose weight, the patient must be motivated and must eat less food, consume fewer calories; a study of the effectiveness of a appetite-depressing pill given by attendants at an institution to mentally deficient subjects, whose diet is not restricted but are allowed to eat as much food as is placed before them, some of whom were allowed to go home on week-ends, would be worthless (Tr. 694-95). He stated that "a person will lose weight if they eat less food than they burn up. If you start with somebody who wants to lose weight, they know they have to eat less. If they are given pills to take the edge off the appetite, they will stick to the diet and they will lose" (Tr. 695); the function of the pill is to help the patient resist food and make it easier to stick to his diet; if you put a lot of food in front of him, he can't stick to it (Tr. 696-97). Dr. Healy further testified that " * * * You can't run a test by putting a lot of food in front of people, especially mental de-

fectives that have no reason to not eat, and expect to kill the appetite" (Tr. 697).

51. The fourth medical witness for respondents was Theodore Feinblatt, M.D., of Brooklyn, New York, who has practiced in internal medicine since 1948, is a member of several medical societies, and author of articles published in medical journals. A written statement of his educational and medical background was received in evidence as RX 26. Dr. Feinblatt testified that he had conducted more than 50 clinical investigative studies, including a study of P.P.A. which he and his father, Henry M. Feinblatt, also a physician, made in 1957 (Tr. 780-81). His father, Dr. Henry Feinblatt, was a diplomate of the Board of Internal Medicine and a fellow of the American College of Physicians (Tr. 781). The study referred to was entitled "Safety and Anorexiant Action of Timed Disintegration Capsules 75 mg. for the Treatment of Obesity," and a copy thereof was received in evidence as RX 27. Although the study was conducted on 30 of their obese patients to determine the safety of the time-disintegrating factor of the preparation, the way the P.P.A. was released after it was taken by the patient (Tr. 793-94), they found, as a result of their study, that the treatment with the time-disintegrating capsule of phenylpropanolamine in a 75 milligram dose was effective as an anorexiant agent for the treatment of obesity, and that there were no toxic effects from it, such as insomnia, nervousness, or other objectionable side effects, or failure of the time-disintegrating factor in the capsule (Tr. 797-98, 807). Dr. Feinblatt further testified, on cross-examination, that he uses phenylpropanolamine hydrochloride today in his practice in the treatment of patients with obesity (Tr. 800, 809). Dr. Feinblatt testified that, if he were going to make a study of the efficacy of P.P.A. as an appetite depressant, he would use normal subjects, not mentally deficient subjects (Tr. 814). Dr. Feinblatt testified that the use of P.P.A. or any other drug as an appetite depressant depends on the stimulation of the higher centers of the brain and the patient's desire and cooperation to lose weight and, therefore, the use of mentally deficient subjects in the Fazekas study is "not too valid" as a test of the efficacy of P.P.A. as an appetite depressant (Tr. 816).

52. E. L. Ladenheim, of New York, New York, a professor of mathematics at the Polytechnic Institute of Brooklyn, New York, testified concerning a statistical analysis he had made of the Fazekas report (CX 3) and the conclusions that can properly be

drawn therefrom (Tr. 557-594). Professor Ladenheim received an A.B. degree in electrical engineering from City College of New York in 1940, graduated from the United States Naval Academy Postgraduate School in Annapolis, Maryland, in 1941, and received a Master's degree in electrical engineering from Brooklyn Polytechnic Institute in 1948. Professor Ladenheim has been associated with that institution since 1948, and has been a professor of mathematics there since 1952, teaching all undergraduate courses in mathematics and both graduate and undergraduate courses in probability and statistics (Tr. 557-58). A written statement of Professor Ladenheim's education and professional background, together with a list of his written articles and papers, was received in evidence as RX 21. In addition to his duties as a professor at Brooklyn Polytechnic Institute, he is currently engaged in doing statistical data analysis and evaluation in connection with the inertial navigational systems being supplied to the Apollo missile tracking ships for the Department of Defense, and teaches a course in graduate statistics to engineers employed at the Sperry Gyroscope Company (Tr. 559-560).

53. Professor Ladenheim testified that he had made an objective study of the Fazekas report (CX 3) at the request of counsel for respondents, and, from this study, he concluded that the conclusions in the report, itself, are erroneous and misleading (Tr. 564-565), because a double standard was used in evaluating the results and conclusions of the study with respect to the relative efficacy of phenylpropanolamine hydrochloride and dextro amphetamine. In evaluating the efficacy of P.P.A. in reducing the weights of the patients in the Fazekas study (CX 3), Dr. Fazekas used the word "significant," whereas, in referring to the efficacy of dextro amphetamine, he used the words "statistically significant" (CX 3, pp. 1020, 1021; Tr. 565-66). He testified that: In statistics, the words "significant" and "statistically significant" have entirely separate and unrelated meanings; the authors of the Fazekas report (CX 3) avoided the use of the words "statistically significant" in referring to the efficacy of P.P.A. as demonstrated from the data in Table 1; in other words, the authors of the Fazekas report (CX 3) cannot truthfully say that the results of the use of P.P.A. on the subjects in Table 1 "fail to demonstrate a statistically significant reduction in weight" of the patients in Table 1; and, "in the statistical sense, 'statistical significance' is a term used in connection with accepting or re-

jecting a given hypothesis at a given level of acceptance" (Tr. 566). Professor Ladenheim gave it as his opinion that the authors of CX 3 came to a conclusion and then worded the results in such a fashion as to substantiate this conclusion, because nowhere in the report (CX 3) is there any statement of the method or analysis used to reach the stated conclusion; it is just arbitrarily stated (Tr. 576). Professor Ladenheim stated that the statistical problem involved in the Fazekas report (CX 3) is almost identical to the standard problem that appears in the standard text that Professor Ladenheim uses, *Elements of Mathematical Statistics*, by Paul Hoel, professor of mathematics at the University of California in Los Angeles (Tr. 567-68).

54. Professor Ladenheim testified that he used what he called the "T" statistic method in his statistical analysis of the Fazekas report (CX 3; Tr. 569), which takes into account not only the mean, but the variants of the mean (Tr. 570). In the "T" statistic method, prior to the use of the "T" statistic, you first establish various hypotheses and test against these. For example, in order to test a statistical hypothesis by this method, you set up a statement or hypothesis that there is or is not a significant difference in the mean between two samples that are being tested. In this case, Professor Ladenheim first set up the hypothesis that there is no difference in the mean between P.P.A. and the placebo (Tr. 570), that there is no difference in the mean or weight change in the two dosages of P.P.A. in Tables 1 and 2, in other words, P.P.A. was tested against itself (Tr. 570), and that there is or is not a difference in P.P.A. and dextro amphetamine (Tr. 570-571).

55. Professor Ladenheim also tested the P.P.A. data in Table 1 in four different ways: First, by taking all the data; by taking the data without the two extreme points of an 11 1/2 lb. gain and a 10 lb. loss in patients Nos. 14 and 17, respectively; by taking the data without one of the extreme points; and then by taking the data without the other extreme point (Tr. 572). By the first method, he found that the results rejected the hypothesis that P.P.A. had no value with 84 percent confidence, meaning that the probability of making a mistake in rejecting that hypothesis is only 16 percent (Tr. 571). With both extreme points omitted (patients Nos. 14 and 17), he found that the hypothesis was rejected at the 96 percent confidence level (Tr. 572), and he rejected the hypothesis with one and then the other of the extreme points omitted at significant confidence levels (Tr. 574).

From these figures, Professor Ladenheim concluded that the results of the use of P.P.A. shown in Table 1 were "statistically significant," and that the authors of CX 3 studiously avoided use of the words "statistically significant" when referring to the weight loss from using P.P.A. shown in Table 1, because the authors could not, with all honesty, state that the results in Table 1 had no statistical significance (Tr. 574).

56. Professor Ladenheim applied a similar test to the results in Table 3 and found that they show statistical significance; he also applied the test to the results in Table 4 and found that the use of the placebo did not show statistical significance (Tr. 575). Furthermore, he concluded that there was an 88 percent to 92 percent difference between Tables 1 and 2 using P.P.A. and Table 4 using the placebo, and could not explain how Dr. Fazekas could have concluded that P.P.A. was equivalent to the placebo, or was not significant when compared to dextro amphetamine (Tr. 576).

57. Professor Ladenheim also ran a "T" statistic test on the results shown in Tables 1, 2, 3, and 4 of the Fazekas report (CX 3) for the first two weeks of that test (Tr. 577). (It will be noted that the weights of all patients in each of the four units were recorded in each of the tables for the first two weeks of the Fazekas study. Dr. Wolff, one of the witnesses offered by complaint counsel, testified that he considered the first two weeks of the Fazekas study the most important, because, as time goes on, "all weight depressants begin to lose their effectiveness" [Tr. 359], and also for the first two weeks, "you have all the figures" [Tr. 372].) In his statistical test of the data contained in Table 1 covering the first two weeks of that test where the 19 patients were taking 25 milligrams of P.P.A. three times a day, he found that the data rejected the hypothesis at a 93 percent confidence level, as compared to a 99 percent confidence level for the dextro amphetamine in Table 3, as compared to no rejection with the placebo (Tr. 577-78). From his statistical analysis, Professor Ladenheim concluded that the 25 milligrams of P.P.A. were more powerful as a weight-reducing agent than the placebo, but not as powerful as the dextro amphetamine (Tr. 578, 580).

58. Harold Silverman, a pharmaceutical chemist and pharmacologist, of West Orange, New Jersey, also testified for respondents (Tr. 716). He testified that he received a B.S. degree in 1951, an M.S. degree in 1952, and a Doctor of Science degree in 1956, all from the Philadelphia College of Science. Dr. Silverman

testified that he had formerly served as associate professor of pharmacy at Long Island University and professor of pharmacy at Brooklyn College of Pharmacy (Tr. 717), and was the author of several articles in the field of Pharmacy and Pharmacology, which were listed in a written statement of his educational background and received in evidence as RX 25. The testimony of this witness related to an article written by him entitled "Phenylpropanolamine—Misused? Or Simply Abused?," which was published in Volume 135, pp. 45-54, of the February 1963 issue of the American Journal of Pharmacy, Philadelphia, Pennsylvania, a copy of which was received in evidence as RX 7. Dr. Silverman testified that he prepared his article out of scientific interest occasioned from reading the copy of the Fazekas report (CX 3) which appeared in the June 27, 1959 issue of the Journal of the American Medical Association. Dr. Silverman testified that he believed that the Fazekas report (CX 3) maligned P.P.A., and out of sympathy for the drug P.P.A., he wrote the article in order to answer the Fazekas report (CX 3) and "* * * to put things into their proper perspective" (Tr. 724-25). Before writing the article, Dr. Silverman first reviewed medical textbooks and journals containing writings and articles dealing with anorexiant, including P.P.A., and interviewed scientists, pharmacologists, and physicians who were familiar with anorexiant, in order to obtain their views as to the effectiveness of P.P.A. as an appetite depressant (Tr. 723, 725). Dr. Silverman stated that he had reviewed the data contained in the Fazekas report (CX 3) and questioned the method and outline of the study, itself (Tr. 727). Dr. Silverman questioned the validity of the use of mentally deficient patients in the Fazekas study, and stated that, in the body of the report (CX 3), Dr. Fazekas, himself, indicated that he (Fazekas) had a reservation that mentally deficient patients should be used in a study of this type (Tr. 729). He stated that he interpreted the data in the Fazekas report (CX 3) to show that P.P.A. is effective, but that Dr. Fazekas phrased his conclusions in ambiguous language so as to indicate that the weight loss from the use of P.P.A. was not significant, whereas, the weight loss from the use of dextro amphetamine was statistically significant (Tr. 727-28).

59. Dr. Silverman also criticized the Fazekas study in its comparison of P.P.A. with dextro amphetamine. A more proper procedure would have been to compare P.P.A. with a placebo, using the double blind cross-over technique (Tr. 729). The use

of dextro amphetamine prevented the Fazekas study from being double blind, because the stimulating effect of the use of dextro amphetamine on the patient would be plainly evident to the attendants at the institution (Tr. 730).

60. As a rebuttal witness, complaint counsel offered the testimony of Arthur Grollman, M.D., an eminent physician, author, and, since 1944, a professor at Southwestern Medical School of the University of Texas, located in Dallas, Texas. Complaint counsel, in answer to a question by this hearing examiner as to what the nature of the testimony by Dr. Grollman would be, stated that Dr. Grollman would controvert the testimony given by respondents' witnesses, and is qualified in the design, study, and protocols of clinical studies to determine the efficacy of drugs (Tr. 839). Counsel further stated that " * * * I believe that Prof. Grollman is eminently qualified, among the half dozen men in the country most qualified to present our side of the statistical aspect of the Fazekas study, which is, of course, the key to this case" (Tr. 840). At the time of the hearing, Dr. Grollman was chairman of the Department of Experimental Medicine at that institution (Tr. 902-903). Dr. Grollman is the author of a textbook designed for physicians and students entitled Pharmacology and Therapeutics, excerpts from several editions thereof having been received in evidence herein as RX 8, 9, and 10 (Tr. 909-910). Dr. Grollman testified that he became familiar with phenylpropanolamine hydrochloride shortly before it appeared on the market for general use about 30 years ago (Tr. 911).

61. Dr. Grollman testified, among other things, that, at complaint counsel's request, he had re-examined a copy of the Fazekas report (CX 3), and accepts the language in the conclusions of the authors of that report to the effect that P.P.A. is not effective in its reducing action (Tr. 913); that he considers mentally deficient patients as valid subjects to test the drug P.P.A.; and that he does not believe that 25 milligrams of P.P.A. taken three times per day is an effective appetite depressant and weight-reducing agent, unless combined with caloric restriction (Tr. 957). Finally, he was asked if phenylpropanolamine hydrochloride, given in dosages of 25 milligrams three times daily, is adequate and effective in the treatment, control, and management of obesity, and Dr. Grollman replied:

Not unless combined with caloric restriction. It might be helpful then, but certainly as a method of treatment alone I would say definitely no (Tr. 957).

In answer to a further question by complaint counsel, Dr. Grollman testified:

I don't think the doctor-personal relation can make you lose weight no matter how favorable you felt towards him. It might affect the way you carried out his orders, but it wouldn't affect your weight (Tr. 947).

62. On cross-examination, Dr. Grollman was asked by respondents' counsel how he was able to reconcile his testimony on direct examination with the statements in various editions of his textbook entitled Pharmacology and Therapeutics, such as on page 326 of the Sixth Edition (RX 10), wherein he states, among other things, that P.P.A. "is used in asthma and hay fever, to alleviate nasal congestion and to depress appetite in obesity." Dr. Grollman explained this by saying that he was merely stating the facts, that it is used by physicians for these purposes, that is, "in asthma and hay fever, to alleviate nasal congestion and to depress appetite in obesity," without indicating that it was good, bad, or indifferent (Tr. 958-962); that his recital of the use of P.P.A. was in the order of its more frequent use, that is, in his opinion, physicians use P.P.A. to depress appetite in the treatment of obesity less frequently than they use it for the treatment of asthma, hay fever, and nasal congestion (Tr. 963).

63. As a matter of fact, Dr. Grollman does not use any of the prescription drugs in the treatment of obesity because, in his opinion, they do more harm than good. This includes dextro amphetamine (Tr. 964-965), because, in some patients, these drugs cause nervousness, insomnia, etc. (Tr. 965-67). Dr. Grollman puts the amphetamine preparations and P.P.A. in the same category as anorexic agents. He defined an anorexic agent as one which causes a person to lose his appetite (Tr. 967). In reply to a question, Dr. Grollman further testified that, if he were designing a study for the purpose of testing the effectiveness of P.P.A. as an appetite depressant, he would test it on the type of people he was interested in testing, "the average patient, the average citizen, who is too fat" (Tr. 981-982).

64. Dr. Grollman further testified that he had not recently made a statistical evaluation of the Fazekas study (CX 3), using what he calls the "P value" method (Tr. 988), and accepted the statements and conclusions contained in the report as being correct (Tr. 988, 991). Dr. Grollman stated that a mathematical, statistical evaluation of data is not always necessary (Tr. 991); that "* * * statistics don't prove it, but merely give you some reference * * * . Likelihood either of error or your conclusion

being correct" (Tr. 987-88); "I took his word for what he quotes there. I didn't recalculate it" (Tr. 988); "* * * one often doesn't even need that. One can just judge from data to draw a conclusion" (Tr. 990). In reply to a further question as to whether it is first necessary to put "data through a statistical mill" before drawing a conclusion, Dr. Grollman stated that this is not always necessary; that, frequently, statistics have a tendency to mislead; that the statistics pretend to give data which common sense and observation would suffice to "show you was the case" (Tr. 991). Dr. Grollman further testified that: It is important that the patients receive the medication, because that is the basic part of the experiment (Tr. 995), and at the same time with respect to meals, because their effect is dependent upon the time of their administration (Tr. 994). He further testified that if, in the clinical study of a drug, it happened often in the course of that study that the patient did not actually receive the drug he was supposed to receive, a written report of the study should indicate any deviation from the claimed conditions of the procedure; otherwise, it would affect the conclusions to be drawn by the reader of the study (Tr. 996).

65. Dr. Grollman further testified that: The total weight change referred to in the extreme right-hand column of the tables in CX 3 purports to show the difference between the weight of the patient at the commencement of the study and his weight at the end of the study, the sixth week; and, from reading the report, he did not assume that some of the patients were not available for weighing at the end of the sixth week, or that some went home and came back a few days later and were weighed (Tr. 997). Dr. Grollman was then asked to examine Table 1 in CX 3, especially the next-to-last column under the heading "Weight Change" at the end of the sixth week and the asterisks for patients Nos. 8, 9, and 10 which indicate that, at the end of the sixth week, the weights for these three patients were not recorded (Tr. 997), and Dr. Grollman replied:

That certainly is an incongruity. He would have to weigh them at the end of six weeks if he is going to say what change occurs over that period (Tr. 998).

66. Although the report purports to give the total weight change in each patient from the beginning to the end of the study under each of the four tables, the report does not say why the weights were not recorded for the patients where the asterisks appear (Tr. 999). Dr. Grollman agreed that, if any of the

patients went home, there would be no certainty that the patient received the medication, and, according to Dr. Grollman, "* * * that would be a poor experiment if you left it to a patient, particularly an idiotic patient" to take the medication; "You would want to insure * * * that they took the drug which you are testing" (Tr. 1000). Dr. Grollman was referred to the right-hand column near the top of page 1019 of CX 3 where the report states, among other things, that "The drugs were administered by cottage supervisors (not aware of the identity of the drugs) who made certain of their ingestion by the subjects," and asked the question if, in fact, the subjects were not available to receive the drugs and had been allowed to go home on weekend passes, the quoted statement would be "Misleading and incorrect," and Dr. Grollman answered that this would "certainly detract from the faith that you put in the integrity of the author" (Tr. 1002).

67. Aside from the general observations by several medical witnesses that appetite-depressing drugs should not be sold without prescription, over-the-counter,⁴ or that appetite-depressing drugs should not even be used in weight-reducing programs because of their harmful side effects, such as nervousness, insomnia, etc., there was no evidence offered at the hearings to substantiate the allegation in the amended complaint that corporate respondent represents that P.P.A. is safe to use by all obese persons. An order of the Commission in this proceeding, issued November 7, 1958, adopting the initial decision of the hearing examiner, which ordered corporate respondent, its officers, and Harry Evans and Vincent J. Lynch, individuals, and respondent's agents and employees to cease and desist from representing that P.P.A. is "safe to use by all obese persons," is still in effect and outstanding. In the order of the Commission issued November 15, 1966, reopening this proceeding, that cease and desist order was not vacated, but was left in effect pending final disposition of this reopened proceeding. Pursuant to the above order of the Commission issued November 7, 1958, in which corporate respondent was ordered to cease and desist from representing that P.P.A. "is safe to use by all obese persons," corporate respondent revised its advertising by removing therefrom those aspects of the advertisements which were prohibited by the consent cease and desist order adopted by the Commission on November 7, 1958, to wit, all representations

⁴ The propriety of the sale of appetite-depressing drugs without a physician's prescription is not in issue in this proceeding.

that HUNGREX * * * with P.P.A. is "safe to use by all obese persons" or that any predetermined weight reduction could be achieved by the taking or use of the preparation for a prescribed period of time. The label on the HUNGREX * * * with P.P.A. package now bears the following, among other, wording: "CAUTION: Should not be used by persons with heart or thyroid disease, high blood pressure or diabetes except on medical advice" (Finding 4 herein; CX 10).

68. Thereafter, corporate respondent filed with the Commission the required reports showing the manner in which it had complied with such consent cease and desist order adopted by the Commission on November 7, 1958. Among such reports filed with the Commission to show how corporate respondent had complied with such cease and desist order was an advertisement for HUNGREX * * * with P.P.A., which, it was stipulated at the hearing, was substantially identical with corporate respondent's present advertising (Tr. 444; CX 9). After the receipt by the Commission of the copy of this advertisement, along with the other reports showing corporate respondent's manner of compliance with the original cease and desist order, the Acting General Counsel of the Commission, by letter dated August 10, 1959, advised corporate respondent that it was in compliance with the cease and desist order (RX 18). So, it is seen that corporate respondent's present advertising (CX 9) is substantially identical to the advertising copy which respondent submitted to the Commission in April 1959 (Tr. 444).

69. A typical example or statement of respondent's advertising, which is alleged to be false and misleading, is purported to be set out and quoted in Paragraph Five of the amended complaint. The first line of this "typical" advertisement, as alleged in Paragraph Five of the amended complaint, reads as follows: "SAFE REDUCING DRUG * * *" This allegation in the amended complaint is not supported by the evidence. The only evidence offered by complaint counsel concerning corporate respondent's advertising representations was the label on the package containing respondent's preparation HUNGREX * * * with P.P.A. (CX 10), set out in Finding 4 herein, and the copy of respondent's advertisement (CX 9) set out in Finding 5 herein. Nowhere in either advertisement (CX 9, 10) does the statement "SAFE REDUCING DRUG" appear. All statements and representations by respondent as to the safety of the drug were eliminated in compliance with the original cease and desist order,

and respondent's present advertising omits any reference to the safety of the drug.

70. Also, the main body of the quotation in Paragraph Five of the amended complaint studiously omits material parts of the advertisements which refer to the efficacy of the drug to reduce appetite and thus help reduce calorie intake. The order reopening this proceeding and also the amended complaint rely on the Fazekas study (CX 3) to establish the allegations that P.P.A. is not an effective appetite depressant and weight-reducing agent, and is not adequate and effective in the treatment, control, and management of obesity. The undisputed testimony is that P.P.A. and all other anorexiant drugs are used by normal persons as appetite depressants, along with a reduction in the intake of food, a so-called diet program. The drug assists the patient in reducing his intake of food, making it easier for him to resist the desire for the usual amount of food he is accustomed to consuming. The amended complaint does not allege that respondent's advertising represents that HUNGREX * * * with P.P.A. is an effective appetite depressant and weight-reducing agent in and of itself, without a concomitant reduction of food intake by the person taking the drug. The evidence found herein establishes the premise that, if a normal person has a desire to lose weight, then P.P.A., taken in dosages of 25 milligrams, three times a day, along with a reduction in food intake by the patient, will be an effective appetite depressant in the treatment of obesity.

71. Since complaint counsel must carry the burden of proof and relies wholly on the Fazekas report (CX 3) to establish the allegations of the amended complaint that

1. HUNGREX * * * with P.P.A. is not safe to use by all obese persons having heart disease, high blood pressure, diabetes, or thyroid disease;
2. The preparation has no significant pharmacological value as an appetite depressant or weight-reducing agent;
3. The preparation is not adequate or effective in the treatment, control or management of obesity,

the hearing examiner has made detailed findings of the testimony of Dr. Campbell, one of the coauthors of the Fazekas study. These are set out in Findings 10-36 herein. His testimony, especially on cross-examination, raises serious questions as to the reliability of the so-called study. The stated purpose of the Fazekas study was to test the comparative effectiveness of P.P.A.

as an appetite depressant with dextro amphetamine on mentally deficient patients. The report of the study (CX 3) makes numerous affirmative statements of fact with respect to the procedures used and followed in the study. For example, the report (CX 3) states that each patient was given the stated medication three times each day by supervisory attendants who made sure of their ingestion by the patients. However, cross-examination of Dr. Campbell revealed that many of these statements were not true. Many of the patients were allowed to go home on week-ends and at other times. While the patients were at home, the supervisors at the institution could not have made sure that the patients ingested the medication three times a day, as the report states. Cross-examination of Dr. Campbell revealed other inaccuracies and misstatements in the report, which are set forth in the findings and will not be repeated here. The errors, misstatements, inaccuracies, and omissions in the Fazekas report (CX 3), as found herein, especially Findings 10-36, take from the study a considerable degree of credibility which might otherwise be given to it.

72. Several reputable physicians who testified for respondents questioned the objectivity of the Fazekas test. Some were of the opinion that mentally deficient patients were not valid subjects for the test; that reasonably accurate results cannot be obtained from testing the effects of P.P.A. on such patients, because the drug does not work the same on mentally deficient patients as on normal persons. Also, many of the patients in the Fazekas study were receiving other potent drugs in addition to P.P.A., as shown in Finding 23 herein. One drug may offset the effects of the other.

73. Several of the physicians who testified for respondents made clinical tests of P.P.A. and found it to be effective as an appetite depressant in the treatment, control or management of obesity, without any harmful effects. P.P.A. was found safe to use. One physician, who testified at the hearing, stated that he uses P.P.A. in his practice in the treatment of obesity in some of his patients. Dr. Grollman acknowledged that P.P.A. is used by some physicians as an appetite depressant in the treatment of obesity. Numerous recognized medical texts state that P.P.A. is used to depress the appetite in the treatment of obesity. Considering all of the evidence of record, it is found that the allegations of the complaint have not been established by a preponderance of the evidence.

Final Order

74. With respect to the request for dismissal of the amended complaint against the individuals Harry Evans and Vincent J. Lynch, and Chester Carity, individually and as an officer of corporate respondent there is nothing in the record to indicate that these individual respondents might in the future violate Sections 5 or 12 of the Act in their individual capacities. To justify naming an officer as an individual, there must be something in the record suggesting that he would be likely to engage in the practices in the future as an individual; *The Lovable Company, et al*, Docket No. 8620 (1965). For these reasons, the individual respondents should be dismissed from the proceeding.

CONCLUSION

It is concluded that the amended complaint herein should be dismissed.

RECOMMENDATIONS

The hearing examiner respectfully recommends:

1. That the amended complaint [68 F.T.C. 1221] herein be dismissed.
2. That the order to cease and desist heretofore issued by the Commission on November 7, 1958 [55 F.T.C. 705], in this proceeding be continued in effect against the corporate respondent, but that said order be rescinded or amended so as to no longer apply to the respondents Harry Evans and Vincent J. Lynch in their individual capacities.
3. That no order should be issued against the respondent Chester Carity, named in the amended complaint, either as an officer of corporate respondent or in his individual capacity.

FINAL ORDER

The Commission having issued an order to cease and desist in this matter November 7, 1958; and

The Commission on November 15, 1965, having reopened this matter and having issued an amended complaint, having assigned the matter to a hearing examiner for the taking of evidence and certification of findings and recommendations to the Commission on a newly proposed cease and desist order, and having directed that the existing order to cease and desist remain in effect pending disposition of the amended complaint; and

Complaint

75 F.T.C.

The hearing examiner having filed his Certification of Record with the Commission on March 16, 1967, and

The Commission having determined, without expressing any opinion as to the accuracy of the findings and conclusions in the Certification of Record, that it would not be in the public interest to pursue this matter further:

It is ordered, That the amended complaint issued on November 15, 1965, be dismissed as to all respondents without prejudice to the right of the Commission to take such further action in the future as may appear to be appropriate.

It is further ordered, That the order to cease and desist issued by the Commission November 7, 1958 remain in effect as to all respondents named therein.
