In reviewing the place of anorectic agents in the treatment of obesity, we decided to review the entire therapeutic class. Here are the drugs involved, by generic name (Slide). The list begins with the various amphetamines and Preludin, goes through marketed congeners of the amphetamines of which many practitioners are unaware—Plegine, Didrex, Ionamin, Tenuate, and Pre-Sate—, includes three non-marketed compounds, some of which may be different from the amphetamines,—and ends with a drug at one time marketed over-the-counter for weight control, phenylpropanolamine.

We have looked at the class as a whole for several reasons. One reason might be called intellectual and administrative consistency, that is, that comparable drugs be evaluated in a similar way. But the most important reason involves abuse of these drugs. The abuse potential of the amphetamine and phenmetrazine has been relatively well defined, particularly by events here, in Sweden and Japan. The abuse potential of the lesser known compounds is much more poorly defined. But we believe it should be considered carefully across the board, lest an action decreasing the availability of certain drugs merely lead to the abuse of others, in the way that restrictions on the amphetamines in Sweden appeared to lead to abuse of phenmetrazine and methylphenidate (Slide 2). Here are the prescriptions written for antiobesity agents. The profound drop in amphetamine prescribing represents the impact of the placing of these drugs in Schedule II of the Comprehensive Drug Abuse Act, with its requirements that prescriptions be non-refillable and that separate records be kept. We are watching the prescribing rates for amphetamine cogeners, which are here combined. Will some of them merely replace the amphetamines in the legitimate treatment of the obese—or will their use become characterized by the excesses associated with the abuse of amphetamines?

There appear to us to be a number of options for action in respect to anorectic drugs. They involve removal of drugs, relabeling drugs, rescheduling them, recommending quotas, and requesting further tests. In more detail, the options are as follows:

1. It is conceivable that the amphetamines or other anorectics might be removed totally from the market. The practitioner would then be obligated to use alternative drugs or diet alone in treating the obese. In this respect we see little place for the use of parenteral amphetamines, and at this moment have some doubt about the oral amphetamines when suitable alternatives appear available.

2. The amphetamines and other anorectics might be relabeled in a consistent fashion indicating use only in certain patients, for example those refractory to other regimens or otherwise characterized, or only under certain conditions, for example, only after a brief trial in which the patient is observed to lose weight. The amount of weight loss to be expected and a reasonable duration of therapy might also be indicated.

3. The congeners of amphetamines might be placed in Schedule III or Schedule II of the Drug Abuse Act. Schedule III serves chiefly to alert prescribers to abuse potential; drugs in Schedule II are under fairly severe restrictions referred to previously.

4. Quotas might be imposed on the production of anorectic drugs to decrease their availability for abuse and diversion. At present quotas may only be set for drugs in Schedule II.

5. Further testing, both for clinical efficacy and for potential to induce dependence, might be required for some or all anoretic agents. In respect to abuse potential, drugs might be scheduled in Schedule III or II pending results of studies. A prominent problem here is the uncertain predictive value of even the most promising tests, the self-administration studies in primates.

As you all know, data on which to base a rational choice among these options or against them vary also in quality and quantity for different drugs. For some of the most important questions they may be almost lacking.

In particular, there are unanswered questions as to clinical efficacy and as to abuse potential, and we have concentrated our efforts on these questions. In respect to efficacy, the most important is that of how the pharmacologic effect of anorectic drugs is translated into clinical terms. Weight loss is the chief desideratum. But how much, expressed in what terms, at what rate, for how long? And in what percentage of obese subjects, and what are the characteristics of those who lose? For how long should the drugs be tried before the drug is considered a failure? Given answers to some of those questions, can the different drugs be distinguished one from another, or ranked in terms of efficiency? Are