

amphetamines more effective in more people than newer congeners—or could they be replaced by these congeners?

The FDA has in the form of new drug applications and notices of investigations an unparalleled repository of data, supplied by manufacturing firms, including in most cases the individual patient data sheets from patients in clinical trials. These exist both for the newest submissions and for those pertaining to most of the older drugs. (Slide).

These are the numbers of applications on file with FDA for anorectics. They constitute over 1100 volumes of material. We believe they contain data which if analyzed will clarify the answers to a number of the questions just referred to. Conventional hand-retrieval and scholarly review of this mass of material is beyond our resources of both staff and time. We thus chose to screen material relevant to efficacy, and submit controlled, double-blind studies to analysis by computer rather than by medical officers. Characteristics of each subject, as well as each study, and follow-up data at each visit were coded and key punched on standard data cards. The cards are then interrogated in different programs, and data tabulated or analyzed in various ways. Here are some of the background facts and findings obtained so far. (Slide) There are now 206 studies available for analysis on anorectic agents. Of these about 143 are parallel studies. The great majority of the studies deal with dextroamphetamine, methamphetamine, diethylpropion, phentermine, phenmetrazine, chlorphentermine, fenfluramine, clortermine, and mazindole. The duration of the studies ranges from 3 weeks to 6 months, although few, if any studies retain a significant number of subjects for longer than 16 weeks.

I had hoped to present a comprehensive overview of all studies. Although those working on the computer end of the project have achieved a great deal, programs are still not fully debugged, so that we are running behind, and I am most regretfully unable to talk on the basis of knowledge of 206 thoroughly analyzed studies. What we do have is satisfying but not startling. In those infrequent studies with relatively low drop-out rates in which obese subjects were treated for eight or twelve weeks with drugs such as dextroamphetamine, phenmetrazine, diethylpropion, fenfluramine and chlorphentermine or with placebo, those treated with active medication do show a weight loss of almost a pound a week more than those on placebo, or about 1 to 2 pounds per week total weight loss. Preliminary analyses in terms of percent of initial weight lost, or percent of excess weight lost appear to confirm the differences. The role of the investigator is important, but even investigators who achieved maximal weight loss on placebo induced even more with active drug. Comparisons between drugs are generally only possible indirectly and so are imperfect at present; but the weight loss induced through the use of different drugs appears to be of the same order of magnitude—no one drug has appeared superior. We now believe that the project will be finally completed by August 1, instead of July 1, as originally projected.

In respect to the question of relative abuse potential of amphetamine congeners, the data remain meager, as you know. Similar toxicologic and pharmacologic profiles suggest that the drugs differ chiefly in potency. Monkey self-administration data and human "liking" scores are present only for a few drugs and are of uncertain value. Are amphetamine congeners relatively little abused for intrinsic reasons—or merely because of the easy availability of the cheaper prototype compound? Confronted with incomplete data, do we attempt to predict abuse potential—or do we wait until there is a full-blown epidemic of abuse of a given drug?

This is one of the questions we ask your comments and advice on in discussion today and tomorrow.

Ultimately, we must all weigh the potential benefits of these drugs against the risks of the drugs. Here we hope that in giving your opinion, you will consider risk in its largest sense—not simply the innate clinical toxicity of the anorectics, but the risk to the public health of potential abuse. We do want to hear what these drugs mean in medical practice. But we also must think in the somewhat less familiar terms of drug abuse. Here is a problem from which we cannot divorce our thinking in favor of medical considerations. It is here that the information gaps are greatest, and where we need the broadest, best informed, and most open discussion of the questions on which reasonable and consistent national regulatory policy and medical attitudes towards anorectics must be based.

The questions which must be asked regarding the balance between the benefits to be gained by the use of appetite suppressants in weight reduction and the