

CON: No drugs currently marketed or proposed for marketing have been tested in a fashion adequate to fulfill such criteria. It is not certain that appropriate testing could be practically carried out. Many investigators, as well as drug firms, feel such criteria are unreasonable.

Drugs in other classes are considered useful even if they produce only minor or temporary improvement. Nor is it clear that anorectics are *not* useful as adjunctive therapy for obesity over the long-term; the data are simply not available.

3. Approve anorectics based on short-term trials, but simultaneously require long-term studies.

PRO: More data might be obtained on the course of obesity treated with and without drugs. The FDA would maintain more control over the drugs than if unqualified approval were given.

CON: The type of data to be obtained has not been established. Even if long-term administration of drugs were to be tested, it is debatable whether anorectic drugs should be given chronically. Even if long-term trials revealed no difference between drug-treated and placebo-treated groups, the fact remains that more subjects lose more weight over the short term on active drugs. A collaborative study of the magnitude and thoroughness necessary for meaningful results would represent investment of research effort on the scale of the UGDP study. Neither FDA nor, probably, the research community appears able or willing to design and carry out a definitive, unequivocal trial of the necessary scope. The methodology and results of any single study would be disputed, and it appears somewhat unlikely that a satisfactory study is possible.

B. With respect to amphetamines, including oral methamphetamine

The second major area in which alternative courses of action should be distinguished is with regards to the amphetamines (assuming that other anorectics are considered effective.) These three alternatives are considered mutually exclusive.

1. Label amphetamines to exclude use in obesity.

PRO: This would eliminate the major indication for amphetamines, and so would decrease the amount distributed and susceptible to misuse. Manufacturing quotas would be lowered accordingly, thus restricting the amounts produced. The action would eliminate a controversial indication. It would be tacitly approved by many laymen and physicians, probably the majority. Effective alternative drugs are available.

Elimination of the use of amphetamines in obesity would be a dramatic action against abusable drugs which the public would easily understand and approve. Both laymen and some experts have advocated that amphetamines not be prescribed or labeled for obesity. This is because of the abuse of the drugs, and the belief that widespread use increases the opportunity for abuse and, furthermore, may "inoculate" susceptible subjects in weight-reduction programs who might otherwise not have been exposed to the drugs. It is almost certain that pressure to eliminate the use of amphetamines in treating obesity will continue. Alternative agents are available. Abuse of the amphetamines has been far more extensive in the United States than abuse of alternative agents. If amphetamines are labeled only for use in patients refractory to other anorectics this would be an indication for which the drugs in a strict sense have not been tested.

CON: The action would be contrary to the explicit recommendations of FDA consultants and the majority of academic figures who have been heard from. It would restrict *medical* use because of *non-medical* abuse, and data are skimpy with respect to any relationship between the two. Alternative drugs appear to possess abuse potential, too. Decreasing the supply of legally manufactured amphetamines would increase the price of amphetamines on the street, and illicit labs would increase in response to the demand. As noted in the PRO section of recommendation B.1, it would be more appropriate to use the Controlled Substances Act to reduce the drug abuse problem associated with the widespread use of these drugs in the treatment of obesity.

2. Label the amphetamines for restricted use in obesity, e.g., for patients refractory to other drug therapy.

PRO: This is consistent with the recommendations of the consultants. It would take account of the now well-documented action of amphetamines in producing weight loss. The selection of a restricted group of patients would work further to restrict use of the drugs; although not explicitly recommended by consultants, it would be in line with their discussions. The action would