Data submitted in general fail to demonstrate that the sedative constituents of anorectic combinations contribute to the total effect claimed for the drug (with the possible exception of Eskatrol), so that continued marketing would not be consistent with the FDA combination policy. Elimination of combinations would permit substantial decrease in manufacturing quotas. It would also eliminate certain drugs, (e.g., Dexamyl) which appear to possess qualities attractive to special subpopulations of addicts. The sedative or tranquilizer components produce adverse effects of their own. Phenothiazines, e.g., as in Eskatrol, have never been clearly shown to produce anti-anxiety effects as single entities, let alone in combination. The trials carried out with Eskatrol exhibit technical deficiencies.

CON: Small studies of one combination contrast with other studies in suggesting that prochlorperazine (in Eskatrol) reduces the adverse effects associated with d-amphetamine. (However, prochlorperazine, a phenothiazine, may produce serious adverse effects of its own under certain conditions). The manufacturers of Eskatrol especially have expressed the importance of this product to the firm and may be assumed ready to contest an adverse decision.

3. Require labeling describing the reservations many experts have with regard to use of anorectic drugs. A draft wording is attached (Tab D).

PRO: This is a strong recommendation of FDA consultants. Omitting such labeling appears somewhat inconsistent with principles of full disclosure. Requiring it will prevent unjustified promotional claims from being made. These labeling statement may mollify the critics of anorectic drugs.

CON: The reservation are serious enough to raise questions as to the wisdom of using these drugs at all: for some people they may raise questions as to FDA's wisdom in permitting the drugs to be marketed. Certain practitioners, e.g., bariatricians, will disagree with the statements.

4. Require fenfluramine labeling to include reference to the possibility of unusual adverse effects. (See Tab J for draft wording.)

PRO: It would slightly offset the promotional advantage given fenfluramine by the proposed less restrictive scheduling. This balance is particularly desirable, since with fenfluramine an advantage (Schedule IV) which is basically unimportant for the majority of patients may lead physicians to ignore aspects of fenfluramine's pharamcologic profile which may for many patients be less desirable e.g., potential for producing diarrhea, sedation, or mild post-treatment depression.

CON: This action appears not to have adverse implications.

5. Require anorectic drug labeling for consumer.

PRO: Information would be provided to the patient so that he may participate in a controversial decision. He will be more fully informed on the benefits and risks of anorectic drugs. This would be consistent with the general movement toward more complete informing of the consumer.

CON: Guidelines for determining drugs requiring consumer-oriented labeling have not been established Anorectic drugs do not appear to be more hazardous than many other drug classes which do not have consumer-oriented labeling.

F. Certain ancillary or implementing actions

The fifth area in which alternative courses of action may be distinguished consists of ancillary or implementing actions. (These are all recommended.)

1. Publish an article on anorectics in the *Drug Bulletin* (see draft, Tab A).

PRO: This is desirable no matter what we do, since physicians will learn of our actions sonner or later. The *FDA Drug Bulletin* has been established for such purposes.

CON: Publication may retard our action. We are under pressure to act as soon as possible.

2. Publish a *Statement of Policy and Interpretation* in the *Federal Register* with respect to anorectics. (See draft preamble to SPI, Tab B).

PRO: This will establish explicitly and officially our policy towards these drugs. Even as a proposal it would establish many points for the record.

CON: This would commit us to a firm policy, whereas we may wish to revise policy after assessing the impact of our initial actions.

3. Publish a *Statement of Policy and Interpretation* for amphetamines.

PRO: This would be an appropriate follow-up to the August 8, 1970, SPI on amphetamine, which led to the current amphetamine submissions. It would enables us to make desirable distinctions between amphetamines and other anorectics.

CON: This should not be allowed to prevent speedy action on individual amphetamine NDA's.