strual cycle, including occasional inter-menstrual bleeding and spotting and sometimes with the period being missed entirely, may occur. Thus, the approved labeling certainly indicates that some of the "earliest possible" signs of pregnancy may be false ones which do not justify discontinuance of the medication. Accordingly, a warning to the physician to discontinue the drug at the "earliest possible" signs of the condition the drug is meant to prevent is not consistent with the approved labeling.

Under these circumstances, we see no justification for any attempt to predicate a criminal prosecution in the factual situation above described.

Your letter states that "contraindication for psychic depression in the approved labeling is directed to patients with a history of psychic depression and not just to those with presently observable psychic depression." However, the language used in the labeling approved by the Food and Drug Administration is not that clear or unambiguous. The labeling stated under "contraindications" that "patients with a history of psychic depression should be carefully observed, and the drug is discontinued if depression recurs to a marked degree." The advertisement stated that the drug was contraindicated in "severe depression."

Thus, the labeling does not say the drug should not be used in patients with a history of psychic depression or even that it must be discontinued if that condition should appear. Its use is contraindicated only if the condition reappears to a marked degree. The advertising statement contraindicating the drug in the event of severe depression, therefore, does not significantly differ from that of the labeling. Its terseness is not a vice, indeed, a "brief summary" not a verbatim quote of the labeling is all that the Act requires.

It will be observed that it is also arguable that the flat contraindication of the advertisement may be considered to be more restrictive than the permissive and rather ambiguous wording of the labeling.

While the labeling of the drug might well have included under the heading "side effects" a warning about the blood clotting possibilities of the drug, the fact is that it did not. The Food and Drug Administration approved labeling which treated it in another fashion, and many courts and juries would consider it manifestly unfair for the Government to attempt to impose criminal sanctions for the failure of the subject to set this condition out as a side effect without having first been advised of the necessity so to do.

Additionally, the agency's position is considerably weakened by the fact that in the labeling the coupling of the reference to blood clotting with the favorable comment of the Ad Hoc Advisory Committee has the effect of minimizing the potential threat to the patient. This circumstance would also tend to diminish the seriousness of the failure to list the condition as a "side effect."

Much of the same objection applies to the contention relative to the failure to set forth as a side effect a statement found in the labeling under a different heading relative to the effect of estrogens on calcium and phosphorus. In addition to the questionable fairness of a prosecution in these circumstances, the labeling statement does not refer to a definite knowledge that the drug has a deleterious effect on calcium and phosphorus metabolism but only to a general medical learning that estrogens are known to have such an influence. The complaint, therefore, seems to relate to a failure to list as a side effect of the drug a matter of medical learning which is applicable to estrogens. Thus, the information does not seem to relate to a side effect of the drug advertised, and for that reason a prosecution based upon this omission is not sound.

Nor do we believe that the failure of the advertisement to include the specific details relative to the length of experience with the drug forms a basis for criminal action. Such information was not required as a part of the statement in the labeling concerning side effects, and the advertisement did, by inference at least, inform the physician that "prolonged observations" had not taken place.

That portion of the advertisement which speaks of the low incidence of side effects does not appear to constitute a violation of the statute. In our view, the advertisement does not falsely represent the incidence of side effects which attends the use of the drug. Although we think it is at least debatable whether the advertisement claims a superiority over other products in connection with the incidence of side effects, such statements are within the area of allowable promotion of the drug. The statute is, in our opinion, oriented toward requiring truthfulness in the area pertaining to safety and effectiveness. We do not read the legislative history as indicating that the statute is designed to prevent the usual effort to convince consumers that the advertiser's product is superior to other almost identical products so long as the factual statements are true.