

an unencumbered warning, which have been received and considered in conjunction with the proposed revision of § 1.3 published in the FEDERAL REGISTER of September 16, 1974 (39 FR 33229), are addressed in the final regulation published elsewhere in this issue of the FEDERAL REGISTER.

The proposed warning does, however, contain a statement acknowledging the controversy that exists over the interpretation of the UGDP study and states that, in spite of this, the UGDP findings provide adequate scientific basis for a warning. The purpose of this statement is to emphasize clearly the basis for the warning. Comments on specific wording in the proposed warning are invited by this notice. The Commissioner advises, however, that he does not intend to reopen consideration of the principle of an unencumbered warning which is embodied in the final regulation relating to § 1.3.

The Commissioner concludes that, from the standpoint of patient safety, it is prudent to apply the possible increased risk of cardiovascular mortality for tolbutamide and phenformin to other sulfonylurea and biguanide drugs in view of the similarities in chemical structure and mode of action for members within each of these two categories. This position was endorsed by the Endocrinology and Metabolism Advisory Committee of the FDA at its meeting on June 28, 1971, but additional comment at this time would also be appropriate.