a warning be issued whenever there is sufficient evidence from controlled or uncontrolled studies to believe that a drug may be hazardous or carry a risk and that such warning is necessary for safe and effective use of the drug by physicians and patients. The Federal Food, Drug, and Cosmetic Act provides no standard for the amount or character of scientific evidence required for the issuance of a warning. The decision to require a warning is a matter of judgment which must be made in light of both the available scientific evidence and the opinion of experts who interpret that evidence. The Commissioner believes that the UGDP study is a validly conducted trial and accepts the opinion of the Biometric Society committee and other experts that the increased cardiovascular mortality found in this trial to be associated with these drugs cannot reasonably be attributed to scientific shortcomings in the study. Under those circumstances, a clear warning is necessary even though a residual uncertainty over the correctness of the study may be present. Warnings may properly be required on the basis of evidence that falls short of conclusive proof.

In conformity with Food and Drug Administration policy that warnings must be presented in unambiguous terms without disclaimers or qualifications that would undermine or destroy their usefulness, there is no mention in the proposed warning of other studies involving the oral hypoglycemic drugs. The mention of studies in which increased cardiovascular mortality was not found would serve only to encumber the warning and would therefore not be consistent with revised § 1.3. Comments concerning the principle of