physicians of these drugs. Let me emphasize that this view does not require that we conclude the study provides absolute proof of hazard. The UGDP study is an adequate and well-controlled study -- by far the most extensive and bast examination of the long term effects of oral hypoglycemic agents yet undertaken -- and the finding of an increased cardiovascular mortality in tolbutamide and in phenformin-treated patients cannot be attributed to any shortcomings of study design or execution. This finding, despite any residual uncertainty that may remain, requires a clear warning to physicians. Prudence dictates that a warning be issued whenever there is sufficient evidence to believe that a drug may be hazardous or carry a risk and that such warning is necessary to assure the safe and effective use of the drug by physicians.

Enough time has now passed for interested persons to have studied the Biometric Society report and the recent detailed UGDP report on phenformin. The Agency has, therefore, published for comment a regulation proposing new labeling for the oral hypoglycemic labeling. Interested persons may comment on the proposal by September 5, 1975, and a public hearing will be held on August 20, 1975. Final labeling regulations will not be published until after all comments and materials have been considered.

The proposed labeling contains two sections of particular importance: a Boxed Warning stating that there may be an increased risk of cardiovascular death associated with the use of oral hypoglycemic drugs and a new indications section that limits use of these drug to patients