One: The finding of excess mortality in the tolbutamide group was due to the data obtained from just a few clinics. These are objections we do not find valid.

Two: The studies of Keen et al. and of Paasikivi contradict the UGDP.

Three: The baseline differences among the treatment groups account for the finding of the adverse effects from tolbutamide. On this point I might remark that none of the criticis, to my knowledge, has given serious consideration to the multiple logistic method that was used by the UGDP to take the effect of baseline risk factors into account. Until they do this they have not carried out an adequate review of the UGDP analysis.

The CHAIRMAN. And your group did do that?

Dr. WHITE. Yes, we did.

Four: The findings on the effect of tolbutamide are flawed by the failure to adapt dosage to individual need.

Five: The evidence was not adequate to justify the discontinuation of the oral drugs.

In our analysis of the UGDP data we have used the same multiple logistic model as was employed by the UGDP investigators, but have taken additional variables into account to allow for the time each subject was under study and for differences between clinics. We confirm the principal finding from the simpler study of failure rates; namely, that the cardiovascular death rate was higher in patients receiving tolbutamide than in those receiving placebo. This difference remains after adjustment for the effect of baseline variables and cardiovascular risk factors.

We have also made an analysis in which the extent of adherence to assigned treatment was taken into account. The highest death rate was found in the tolbutamide group who adhered 100 percent to their treatment and who did not modify the dose.

In an analysis of the data from the Bedford trial we found no difference in death rate between the placebo and the tolbutamide group. As indicated above, we do not interpret this failure to find a difference as a contradiction of the more thorough UGDP study.

The conclusion of the committee is that it remains with the proponents of the oral agents to conduct scientifically adequate studies to justify the continued use of such agents.

The CHAIRMAN. Well, put in different words, are you saying that it is the judgment of the Biometric Society that it was a statistically valid sample, and a scientifically conducted study, and that the results of the study—are the conclusions valid? Is that what you are saying?

Dr. WHITE. Yes. We support the principal findings of the UGDP study. We do make some minor criticisms in the report, but we do, in general, support the main finding.

The CHAIRMAN. And the main finding is what?

Dr. WHITE. That there is an excess mortality in the group receiving tolbutamide as compared with the group on the placebo.

The CHAIRMAN. Well, did you find any evidence at all that the oral hypoglycemic drugs retarded or prevented vascular complications of diabetes?

Dr. WHITE. That aspect of the study is one that we did not undertake. We considered that our main responsibility was to look into