expected to be on chronic medications for a period of many years. It is important in planning these long term studies to allow the clinician to change the medication if it is in the best interests of the patient. This can result in an altered dose or even a change in the medication. The UGDP protocol did allow the clinician this freedom. A protocol which does not allow this flexibility may not be in the best interests of the patients under study. In addition to modified or changed medications, patients may, on occasion, not take their medication at all. In the Biometrics Report, these problems were examined in considerable detail. It is our conclusion that the greatest statistically significant difference between tolbutamide and placebo occurs in the group who have taken their prescribed medication in exactly the manner specified in the protocol for the entire period of follow-up.

To conclude, I wish to state that the interpretation of the data is difficult due to the small number of deaths relative to the total number of patients. In our endeavors we have analyzed the data in many other ways which have not been put into our final report. Our conclusion is that the weight of evidence points to tolbutamide as being responsible for excess cardiovascular mortality.