The Bulletin also stated that the sulfonylurea agents are indicated in the treatment of adult-onset, nonketotic diabetes mellitus which cannot be adequately controlled by diet and reduction of excess weight alone and when, in the judgment of the physician, insulin treatment is not feasible.

From the time the results of the UGDP study were first reported, the study was subjected to intense criticism by both clinicians and statisticians (ref. 6 through 12). The basic scientific criticisms of the study were as follows:

1. Patient selection was inappropriate in that many patients had such mild diabetes that neither oral drugs nor insulin was indicated.

2. Total mortality in the tolbutamide group was not significantly different from that in the placebo group.

3. Excess cardiovascular mortality occurred in only a few clinics.

4. Randomization was not successful; therefore, the tolbutamide group was not comparable to the other groups at the outset of the study with respect to baseline cardiovascular risk factors.

5. With the exception of the variable insulin group, patients were maintained on a fixed drug dosage, contrary to the principles of good medical practice.

6. The use of tolbutamide and phenformin in the study was terminated prematurely, i.e., before definitive results were obtained.

7. The results of the study are contradicted by the studies of Keen (ref. 13 through 15) and of Paasikivi (ref. 16).

These criticisms were in turn analyzed by representatives of the UGDP (ref. 17) and by a statistician who had served as a consultant to the UGDP (ref. 18) and were rejected as a basis for invalidating the conclusions of the UGDP study. By this time, however, a widespread