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1. INTRODUCTION

In a report that was published as a supplement to the November 1970 issue of *Diabetes*, The University Group Diabetes Program (UGDP) concluded that in patients with adult-onset diabetes, "talbutamide and diet may be less effective [in prolonging life] than diet alone . . . at least insofar as cardiovascular mortality is concerned." (*1, 2*) Of the subjects treated with tolbutamide, 12.7% died from cardiovascular causes, as compared with 6.2% or fewer in the other treatment groups. As a result of these findings, the Food and Drug Administration (FDA) recommended that tolbutamide should be used only in patients who had adult-onset, stable diabetes that could not be controlled by diet alone, and who, for some good reason, could not be treated with insulin.

The findings of the UGDP and the action of the FDA had a dramatic impact. Tolbutamide had been in general use in the treatment of diabetes since about 1956 and was thought to be a safe and effective drug. The UGDP report was carefully scrutinized by many, and, though defended by some, was severely and exhaustively criticized by others. A group of the critics started legal action to enjoin the FDA from issuing a labeling order that would discourage the use of tolbutamide.

In 1971 the UGDP reported that treatment with phenformin hydrochloride also resulted in an excess cardiovascular death rate and indeed, an excess overall death rate. (*3*) These findings have not been widely discussed, and their impact on the treatment of diabetes is unclear.

The UGDP study is the largest controlled clinical trial of oral hypoglycemic agents to date. Other studies of these agents are in progress, with preliminary results, however, that appear to differ from those of the UGDP. The National Institutes of Health (NIH), which has funded the UGDP, felt the need of a review of evidence available in all the trials. Accordingly, on June 9, 1972, the director of the NIH at that time, Robert Q. Marston, MD, wrote as follows to the chairman of the group presenting this report:

References at end of article.