the drug on patients that determined whether the product would be considered safe and effective. Congress therefore included in the 1938 Act a provision under Section 201(n) which provided that differences of opinion with respect to the effectiveness of a drug could be handled by stating both sides of the issue in labeling.

Since 1938, enormous progress has been made in the methodology for evaluating both the safety and the effectiveness of a therapeutic agent. Congress therefore concluded in 1962 that unsubstantiated expert opinion could no longer suffice to establish the effectiveness of drugs, and that in the future controlled clinical studies would be required. The concept of using the package insert to debate the proper medical use of a drug was thus replaced by a requirement that the drug be proved safe and effective by the most rigorous scientific standards available.

Congress has delegated to the Food and Drug Administration the legal duty of determining whether substantial evidence exists to prove the safety and effectiveness of drugs. While these determinations often involve close questions, they are questions that are required by law to be resolved definitively, and they cannot be avoided. Because of the importance of the issues involved, we often consult outside experts, advisory committees, and professional organizations. In the vast majority of instances, including this one, the decisions on safety, effectiveness, and labeling comport with the weight of medical and scientific opinion.

It must be recognized that there is probably no statement in any package insert for any drug on which at least one, and perhaps more, individuals could not be found to raise questions that they believe important and significant, backed up by at least some kind of literature reference or opinion. The Food and Drug Administration is required, however, to determine the conditions of use under which the drug has been proved safe and effective by substantial evidence. This requires the Food and Drug Administration to act as an independent arbiter on medical issues, and means that inevitably its decisions will not meet with unanimous scientific agreement.

Unless this is done, the welter of conflicting and confusing statements that would be found in package inserts would overwhelm the practicing physician and create chaos for the public. It is not the function of the package insert to present all sides of an issue. This is properly done in textbooks and journal articles, and in scientific discussion. The function of the package insert is to set out, in relatively concise terms, a summary of the conditions for use, based upon the best scientific evidence presented to the Food and Drug Administration about the drug. Except perhaps in rare instances where there is substantial evidence on both sides of an issue, therefore, it is inappropriate to utilize the package insert to present all aspects of the evidence relating to safety and effectiveness, or otherwise to debate medical questions.

We do believe in testing the validity of our determinations through the normal process of scientific debate and peer review, as well as through the statutory appeal processes. Where we are shown to be in error, we have not been slow to correct that error.

It would be the rare situation where there is substantial evidence that both proves and disproves the safety or effectiveness of a drug, and thus justifies equal consideration in labeling. Certainly, that is not the situation involved here. In virtually all cases, including this one, analysis of the available data and information leads to a reasonably reliable determination one way or the other. It is therefore our opinion that there is no basis for requiring or permitting the labeling of oral hypogycemic agents to present a variety of view-pointn on the safety and effectiveness of these drugs, since to do so would abdicate the legal responsibility of the Food and Drug Administration and result in highly confusing and misleading labeling.

II. THE MEDICAL ISSUES

Your petition questions the scientific reliability of the UGDP Study on a number of grounds, the argues that it is not adequate support for concluding that, in the treatment of diabetes, diet alone should first be used, and then insulin, and then the oral hypoglycemic agents. We have carefully reconsidered this matter in the light of the arguments contained in your petition. Our position on the validity of the UGDP Study, on the weight that should be given to that and other studies, and on the labeling that will be required as a result of the available scientific evidence relating to safety and effectiveness of diabetic treatment methods, is set out in full below.