man. Each panel reviewed not only the various distinct chemical entities but also all formulations and dosage forms of all suppliers and all claims made for each of them. They used the data furnished by the manufacturers or suppliers, the findings reported in the literature, the original new drug application and their collective experience to determine whether the claims were supported by substantial evidence of efficacy and to place each into one of the categories provided in the guidelines.

The simplest categories and earliest decisions were for drugs and claims determined to be either "effective" or "ineffective," but between these black and white categories there were shades of gray termed "probably effective" or "possibly effective" depending on the amount and nature of the supporting data available. Still others, which might strictly speaking be effective, but which the panels considered undesirable or which they could not support for good clinical reasons were called "effective but . . ." —and the reasons for this classification were spelled out. For drugs in fixed combinations still another category was required when one component was effective with respect to a given claim, but the other or others either were not effective for that claim or added an unnecessary risk of toxicity; the term "ineffective as a fixed dose combination" was then applied.

Obviously, these determinations, though simple for a majority of useful agents and for most of the claims made for each of them, unveiled many defects in the current labeling. For some the panels suggested specific changes or even rewrote or prepared prototype "package inserts" to expedite the revisions that would eventually be required to make the claims acceptable. In others, suggestions were offered about the type of data still required to make the claims acceptable. The ultimate responsibility for acceptance or modification of the recommendations of the Drug Efficacy Study rests with the present commissioner of the FDA, Dr. Herbert L. Ley, Jr., to whom the last report was delivered on April 15. However, since the various panels and the Policy Advisory Committee already included a major segment of the expertise of the country, and since the FDA could hardly expect its own limited staff to add more than legal, regulatory and practical administrative features to expedite the problems of compliance, very few changes of substance are likely to be made by that agency.

The reports of the Drug Efficacy Study are sent to the interested manufacturers for their comments and objections before orders for compliance are officially promulgated. Manufacturers may ask for and usually would be granted additional time to provide or accumulate additional data. Hearings may be held to air objections, and although the manufacturer also has recourse to the courts for final adjudication if he considers the decisions improper, it should be possible to settle most of the details amicably without prolonged legal procedures. However, because of the tremendous financial stakes, there are certain to be some legal battles ahead. (3) If those who oppose the panels' conclusions can provide "substantial evidence" for their views with data acceptable to the FDA and expert advisers, some of the decisions can be altered.

Elsewhere in this issue appears one of the summary reports prepared by the chairmen of two of the five panels that dealt with anti-infective agents. The report, which was approved by the members of all five panels and the Policy Advisory Committee, concerns only two of the many types of combinations of anti-infective drugs, and its essence has been well publicized. The *Journal* prints the report in fuller detail, however, so that physicians may examine the reasons for the recommendations made, and may understand how the panels applied themselves to consider both general principles (as in the section of the report dealing with oral penicillinsulfonamide preparations) and specific therapeutic claims (section on combination of penicillin and streptomycin for parenteral use). Such examination and understanding of the panels' difficult task is crucial, for the decisions may have a tremendous impact on the practices of the drug industry and the medical profession.

The entire Drug Efficacy Study should greatly affect research workers and clinical investigators as they evaluate the efficacy and safety of new drugs. Its influence on patient care may be even greater. Many physicians obviously have found fixed drug combinations convenient and, on the basis of their own clinical impressions, believe them to be useful and effective. They may have felt encouraged in their faith by the facts that these drugs were available with the implied sanction of the FDA, and that they were marketed by some reputable firms. At the same time, however, those who used the fixed combinations either ignored or were unaware of repeated contrary admonitions of experts in the field. Now, in the best interests of their patients, physicians should be willing to re-examine the bases of their prescribing practices in the light of the sobering judgment submitted by the Drug Efficacy Study.