effectiveness as defined by Feldman(21). The largest amount a patient in this study could receive during the flexible dosage period was 300 mgs./day, the upper limit of Feldman's range. That 150 mgs./day was not optimal is clearly demonstrated by the increments in mean dosage of mepazine shown in Figure 1. Although the mean daily dose of mepazine given to patients during the flexible dosage period was 190 mgs., in the final weeks of the study, approximately a third of these patients were receiving the maximum amount allowed by the study protocol (300 mgs.) and side effects were minimal. In the light of current knowledge, it may be assumed that the unit dose of mepazine used in this study should have been approximately that of chlorpromazine.

The interpretation of the finding that the 4 remaining phenothiazines did not differ significantly is not an obvious one. Statistical logic does not permit the conclusion that these compounds are identical in action. Interpretation must be guided by the experimental conditions which produced the results. The purpose of random assignment of patients to treatment, the double blind procedure and statistical adjustment for initial differences was to prevent one treatment group from having an advantage over any other except in terms of the treatment being evaluated. The flexible dosage schedule was chosen to allow each drug to be evaluated at approximately optimal dosage. The choice of criteria of clinical effectiveness was intended to encompass a large portion of the domain of psychopathology. The reliability of the MSRPP was investigated and considered satisfactory. However, some may feel that such measures are either too insensitive to capture the subtle nuances of drug differences or have missed important areas of behavioral change. Within the limitations of this design, the findings are consistent and are considered reliable.

The high dropout rate (168 patients, 26%) in this study raised two questions. First, was there any evidence of selective dropout related to treatment group? In terms of total number of dropouts in each treatment group from all causes, there were no significant differences between the groups. However, a disproportionate number of patients on trifluprómazine were out of the hospital (26 of a total of 85) prior to the end of the treatment period. It is difficult to evaluate this as a biasing factor, in that 16 of these patients left against medical advice or without permission, which may not necessarily relate to the results of treatment. A disproportionate number of patients on phenobarbital and mepazine (16 of a total of 23) were dropped because of lack of improvement or worsening of their condition. This situation was consistent with the clinical findings and did not constitute a source of obscuring bias. Second, were these patients different in any way from those completing the study? Patients who left the hospital prior to the end of the study for whatever reason were in general not as ill initially as those remaining until the end of the study. Patients leaving without medical approval, the greatest number of whom were in the trifluprómazine group, had lower morbidity scores, were less depressed and withdrawn and showed less disturbance in thinking before treatment than did those who remained in treatment for the entire period.

When this study was conceived, the controlled evaluation of side reactions and abnormal laboratory results during therapy with phenothiazine drugs was considered potentially more important than therapeutic differences between the drugs. In some respects this prediction was true, though not in the manner thought. The most outstanding finding was the comparative paucity of severe abnormalities, accounting for only a 3% loss in the total sample. Next in interest was the lack of difference in prevalence of abnormal symptoms, signs, and laboratory tests between the phenothiazines and, surprisingly, phenobarbital. In the case of phenobarbital, these abnormalities included such adverse behavioral effects as depression or agitation, autonomic effects such as blurred vision or dry mucous membranes, such presumed central nervous effects as akathisia, as well as eosinophilia, leucocytosis, leucopenia and abnormal hepatic tests. In many instances, these abnormalities probably represented manifestations of schizophrenia or spontaneous fluctuations completely unrelated to drug