Foreword

This volume is a collection of the papers presented at the week long Conference on Adaptive Designs held at Mt. Holyoke College in the summer of 1992. Professors Steve Durham, Nancy Flournoy, Gordon Simons, and Michael Woodroofe should be congratulated on organizing such a successful conference. It was deemed advantageous to publish these excellent papers in a single volume rather than have them published separately in a variety of statistical journals. All the papers have been critically reviewed.

The scientific community widely regards the randomized clinical trial with a 50-50 treatment allocation rule as the "gold standard" for generating scientific evidence to evaluate two competing regimens. However, there has been an ongoing ethical concern with regard to the implementation of such trials. The principal ethical issue is that about half of the patients on a randomized clinical trial receive an inferior treatment. This has motivated statistical scientists to develop new methods for planning clinical trials. The two main directions of this research have been to: (i) develop early stopping rules so that a trial can be terminated early with the possibility of reducing the overall number of patients on a randomized clinical trial; and (ii) develop methods which make use of the accruing outcome data that allow changing the treatment allocation rule during the course of the trial. In a broad sense, (i) is a special case of (ii).

The area of research in (ii) is referred to as "adaptive clinical trials" and is one of the main topics of this volume. The principal idea is, during the course of the study, to allocate proportionally fewer patients to treatments which appears to be accruing less favorable endpoint information. The desirability of utilizing an adaptive allocation scheme is especially appealing in studies where the major response variable has a clear cut definition of success and/or failure and can be observed without long follow-up time. For example, in a recent trial to evaluate the drug AZT in reducing the risk of maternal-infant HIV transmission, a 50-50 randomization scheme was utilized to allocate 239 pregnant women to the AZT group and 238 mothers to the placebo group from April 1991 through December 1993. The endpoint for the study is either the newborn being HIV positive or negative. Although it may take more than 24 weeks after the birth to safely claim that an infant is HIV negative, a positive HIV infant can be accurately identified within