To complete the review of our studies in which we are indirectly involved, I will mention that we have participated in the monitoring of the prospective study of oral contraceptive users being conducted under support from the National Institute of Child Health and Development at the Kaiser Permanente Foundation in Walnut Creek, Calif.

In addition, we have participated in the review of two planned retrospective studies relating to the possible effects of oral contraceptives on carcinoma of the breast submitted to and approved by the National Institute of Child Health and Development. Funding for these studies has not yet been approved.

This investment in research, in our judgment, is necessary to better define the hazards of the oral contraceptive.

The questions of safety must be answered in so far as is possible for science to find the answers. And we at the Food and Drug Administration must continuously review our previous decisions in light of new scientific knowledge.

We have plans underway to develop other studies. These include the effect of oral contraceptive drugs in prediabetic and diabetic patients; cytogenetic studies in spontaneous and induced abortions; development of other techniques to assess the effects of oral contraceptives on endocrine function during adolescence; and the metabolism of the hormonal contraceptives and possible interaction with other drugs.

In order to get these studies under way, it will require an increase in our current research budget from approximately $700,000 in fiscal year 1970, to over $3 million.

I would like to turn to another subject which will require very substantial funding if we are to do an effective job. This is the need for a comprehensive drug surveillance system.

Because of the limited nature of premarketing clinical trials, we cannot expect to observe all of the adverse reactions that may occur. We are dealing with comparatively small numbers of patients who are screened carefully and regularly. The difficulty of detecting adverse reactions is great. Our statisticians tell us that an adverse reaction expected to occur at a rate of 1 in every 1,000 will not be observed at all in 37 percent of studies using 1,000 subjects. In other words, to be 90 percent certain of observing such a high rate of adverse reaction, a study would need to include 10,000 or more subjects.

Therefore, it is essential that all approved drugs be kept under close surveillance through an effective adverse reaction reporting system. At present this system in the United States depends for the most part on voluntary submission of adverse reactions by physicians and hospitals and, of course, the required reports from the drug manufacturers. It is unfortunate, but true, that we receive reports on only a small percentage of the total number of adverse reactions that occur. This limited access to the medical record makes it extremely difficult to evaluate cause and effect. We must move in the direction of significantly improving our surveillance system. I would estimate it would take at least a third of our present budget to establish such a comprehensive reporting system.