identical to those reported for rats in another study on MER/29—at a different dosage level and for a different duration.

In a second rat study, according to the New Drug Application, 20 rats per dosage group received MER/29 for three months. The NDA states that "In the rats receiving 40/mg/kg/day of MER/29, 8 out of 20 had grossly visible opacity of the cornea . . . there was also an associated conjunctivitis." The firm held that this was not a drug induced phenomenon since it was also observed in control rats. When we checked their laboratory records, however, we found that actually 60 rats per dosage level had been administered MER/29. At the time of our review of the New Drug Application, we had no knowledge of these further studies.

These additional data, which were withheld by the William S. Merrell Company, established conclusively that MER/29 was capable of inducing cataract formation. After the three month sacrifice, there were approximately 40 rats per dosage level still receiving MER/29. On March 28, 1960, approximately four months after the start of the experiment, and *before the New Drug Application was approved*, the eyes of the remaining rats were examined. The firm's notebooks state that the eyes of many of the rats receiving MER/29 "did not react to light or motion, therefore giving the appearance of being blind." At the highest dose level, 25 out of the 36 rats showed this blinding effect. Only 1 of the 38 control rats showed this effect. None of this data was submitted for inclusion in the New Drug Application. This omission is extremely serious since knowledge that MER/29 was causing cataracts in rats certainly would have caused the FDA to delay, and probably to withhold, permission to market the drug. As it developed, cataracts were one of the most disturbing features of toxicity which occurred in patients after the drug was released.

As early as November 1960, the William S. Merrell Company had been notified by another pharmaceutical firm, Merck, Sharp and Dohme, that MER/29 had shown extremely serious adverse effects in their experiments with rats and dogs; the drug had produced cataracts and other eye changes. Moreover, Merrell representatives had actually visited Merck, Sharp and Dohme during January 1961, to examine the affected animals. No mention of these findings to the Food and Drug Administration was made by the William S. Merrell Company until January 2, 1962, when FDA and the William S. Merrell Company had received reports that this drug caused cataracts in human beings.

The original brochure contained a caution that MER/29 should not be administered during pregnancy. On September 23, 1960, approximately five months after the New Drug Application became effective. Dr. Talbot sent a letter to the William S. Merrell Company. In this letter, Dr. Talbot made mention of adverse effects of MER/29 in pregnant rats. He stated his concern over the administration of MER/29 to premenopausal women who would know whether they were in the first trimester of a pregnancy. On October 23, 1961, Dr. Nestor requested the William S. Merrell Company to submit all data concerning adverse and toxic reactions resulting from MER/29 therapy in both animals and humans. On October 26, 1961, the William S. Merrell Company submitted results of fertility and sterility studies on MER/29 in rats to Dr. Nestor. Part of this study was conducted by the William S. Merrell Company and another part was conducted by Endocrine Labs., Madison, Wisconsin. These studies showed that at certain dosage levels MER/29 caused a marked reduction in the rate of conception. In addition, the percentage of the litters surviving was also affected. These effects were observed when the female received MER/29 prior to and during cohabitation with male rats. These experiments were all completed in March of 1960 and a final report was prepared in October of 1960. However, these results were not submitted to FDA until one year later, and only at the urgent request of Dr. Nestor. The William S. Merrell Company did not submit these data even though Dr. Talbot questioned them about this matter in his letter of September 23, 1960. These data should have been submitted much earlier. If we had had this information in the file, we would certainly have inserted at least a caution in the brochure against the use of MER/29 in women of childbearing age. Dr. Talbot was even considering this caution without having these adverse data at his disposal.

In this statement I have described my part in the MER/29 investigation and outlined the major aspects of those investigations insofar as my involvement was concerned. I feel that it can be concluded, from the evidence available, that the William S. Merrell Company withheld some important information and mis-