Robert H. McMaster; Frank Getman; E. R. Beckwith; and Dr. E. F. Van Maanen.

During the morning, only three of the above individuals participated actively in the discussion and were present during the bulk of the morning visit. These were Dr. F. Joseph Murray, Dr. Robert H. McMaster and Dr. Carl Bunde.

The morning discussion was spent primarily in discussing clinical problems relating to the work on humans, primarily between Dr. Nestor and these three gentlemen.

Dr. Nestor pointed out that he was primarily interested in getting details of reports concerning adverse effects of MER 29 since February 23, 1962. During this phsae of the investigation, it was agreed that the firm had already furnished a list up to March 9, but without individual case histories. The representatives of the firm assured Dr. Nestor that these case histories would be forwarded to him.

During the morning, we had a general discussion concerning the incidence and prevalence of cataracts in both the general population and in people who are treated with MER 29.

At this time, Dr. McMaster informed us of two additional cases of cataracts which had been reported to the company since March 9th. One of these was a six year old boy at the Mayo Clinic.

We agreed to meet with Dr. Van Maanen after lunch to discuss some animal toxicity studies on MER 29.

After lunch, we met with Dr. Van Maanen, Dr. F. Joseph Murray and Dr. William King in Dr. King's office. Dr. King asked us what information we desired to see, and Dr. Goldenthal advised him that we desired to see some of the raw worksheet data on the chronic studies on rats, dogs and monkeys administered MER 29. First, a general discussion was had in regard to the general occurrence of cataracts in these three species who had received MER 29 chronically.

Dr. King stated that in their recent dog studies, all of the dogs receiving 40 milligrams per kilogram body weight of MER 29 developed cataracts after six and a half months of treatment. They had conducted similar studies in dogs in which the dogs had received supplemental vitamin administration, and after approximately 7 months of MER 29 administration, the compound was stopped, and the animals were given 2 gm of cholesterol per animal daily. Two of the five dogs in the study died earlier in the study. They showed all the signs typical of adrenal insufficiency. The three surviving dogs were not sacrificed and were kept on a normal control diet plus cholesterol supplement. Dr. King reported that the cataracts in these dogs appeared to be regressing.

At this point, Dr. King was asked if they saved all tissues and slides from the autopsies on all of the animals receiving MER 29. Dr. King replied in the affirmative.

At this point, Dr Nestor asked if they had any way of detecting MER 29 in the tissues. Dr. Van Maanen replied that they had no method for detecting MER 29 in the tissues.

Dr. Nestor then asked if the eyes of the monkeys had been examined, and if they had been preserved. Dr. King checked and then replied that the eyes had not been studied and had not been preserved.

As a result of this line of questioning, we then asked to see the raw data on the monkey studies. Dr. King then got a bound notebook and showed us a monkey study on MER 29. However, the notebook produced contained a monkey study which was not included in their New Drug Application. None of the monkey identification numbers matched the numbers in the New Drug Application. During this time, Dr. Murray had sent from his office a copy of their animal data on MER 29 which was part of the NDA. On the autopsy sheet of the monkeys in the New Drug Application, it was stated that the data on the monkeys was contained in Notebook 848 R. We then asked Dr. King if we could see this notebook. Dr. King ordered this notebook produced. A reference to these monkeys labeled M25, M34, and M51 were found on page 16 of this notebook. On this page, it was stated that the monkeys were started on the drug, MER 29 on 4/7/58 at a dose of 10 milligrams per kilo body weight twice a day. From the autopsy sheets in the NDA, these three animals were autopsied in February, 1959. Dr. King was asked how this represented sixteen months of administration as represented in the NDA. At first, he was unable to explain this and later Dr. Van Maanen stated that this was a second phase of this study and that the animals had received a higher dose of MER 29 for six months prior to this.