On September 28, 1961, exactly six months after the onset of drug therapy, the following eye changes were noted:

There was bilateral hazyness deep to the cornea which made visualization of the fundus very difficult. Although not able to definitely localize this lesion it was the impression of the examiners that this change was in the anterior lenticular capsule.

At the examination on October 5, 1961, the dermatitis was severe and the animal completely blind. The eyes were similar bilaterally and the impression of the examiners was anterior lens cataractoid changes.

At the examination of October 12, 1961, no additional eye changes were noted, but the dermatitis continued to be widespread and severe.

In the rat study, at 40 mg/kg/day, twelve out of twelve males and six out of seven females have opacity in one or both eyes. In a similar group where vitamins and cholesterol are added to the drug diet, there are nine out of twelve males and eight out of twelve females with eye opacities.

In each case, the eye changes in the rats were preceded by hair loss and severe changes in the skin.

W. M. K.

[Inter-Department Memo, Oct. 19, 1961]

To: Mr. F. N. Getman.
From: F. Jos. Murray.
Subject: MER/29.

John Nestor of the FDA called at 8:40 a.m. today to advise they had given consideration to the letter we proposed to send to physicians on MER/29 side effects. Nestor raised the following points:

1) The FDA does not have sufficient pertinent facts to enable them to make a decision on the letter. It is their fear that side effects may be more extensive and more severe than stated in the letter, and it might, therefore, be misleading and lead the physician to a false sense of security.

2) The FDA wants all facts available to us on the cases of eye changes, including the actual case records. They also request a written copy of the letter we propose to send.

3) The FDA wants a statement from us to the effect that we have supplied all toxicity data in animals and man, including that available to us from outside sources. (The implications here are obvious and on pressing Nestor he offered as an example a comment that a Dr. Wong of Howard University visited us in April to describe results in chickens indicating interference with ovulation. Dr. Wong states we ignored the results, and Nestor declared this could be grounds for suspension of the NDA.)

4) Nestor stated he had discussed MER/29 with several experts and there is concern that there are numerous other serious side effects involved. These include: baldness, lenthyosis, impotence, interference with ovulation, induction of abortion, interference with adrenal function, and reticulocytosis together with hepolytic anemia as found by Page.

Dr. Nestor stated he had discussed the problem last night with Dr. Siegel and it is their feeling they have enough evidence to suspend the NDA. He also stated that their statistician has advised them that our claims for significant lowering of cholesterol levels are not true.

I told Nestor we would want to see him as quickly as possible but that we would have difficulty pulling together material to answer all these charges before next week. He agreed and indicated he would make himself available any day of the week. We are aiming at a conference on Thursday, October 26.

[Inter-Department Memo, Oct. 24, 1961]

To: Mr. W. R. Marschalk.
From: Frank N. Getman.
Subject: FDA action on MER/29.

Sherry Silliman and Fred Lamb have both advised me that a New Drug Application may not be suspended or revoked without a hearing—such hearings are not public. Apparently, however, the fact that a hearing is being called does become publicized.