

[Draft of Proposed Letter]

MARCH 24, 1961.

DR. FRANK J. TALBOT,
Food and Drug Administration, New Drug Branch,
Bureau of Medicine, Temporary Building "S"
Washington, D.C.

DEAR DR. TALBOT: Reference is made to our New Drug Application, 12-066, for MER/29 (triparanol). Our attention has been called to several reports concerning thinning or texture change of hair, and while it is difficult to access the importance of these reports (particularly since there have also been reports of increased hair growth), we feel some mention should be made in our literature. Accordingly, we propose to modify the last sentence under "side effects" in our existing brochure. This sentence now reads: "Isolated reports have been received of nausea, vomiting, temporary vaginal bleeding, and dermatitis." We would like to change this to: "... temporary vaginal bleeding, dermatitis, and thinning of the hair."

If you have no objection to the proposed change, we shall plan to make it at the time of our next printing.

Sincerely yours,

F. JOS. MURRAY.

[Inter-Department Memo, Mar. 28, 1961.]

From: Robert T. Stormont.
To: Mr. Smith Richardson, Jr.
Subject: MER-29—Complaints of Hair Changes.

According to Woodward's memo, the reported incidence of hair thinning in only 54 cases out of a total of approximately 300,000 cases who have received MER-29. This would mean that less than two people out of every 10,000 receiving MER-29 report some loss of hair. I wouldn't be at all surprised if two or more adult people out of 10,000 *not* receiving any MER-29 at all reported some definite hair loss during a few months period of observation. Furthermore, I wonder if there are any data on the incidence of hair-thinning associated with nicotinic acid therapy. Of course, it is quite probable that there are *unreported* cases of hair-thinning associated with MER-29 therapy, but I find it rather difficult to be convinced, on the basis of these data alone, that MER-29 is definitely responsible.

The observations of Dr. McHardy are also somewhat puzzling. In addition to two cases of hair-thinning he reports six cases of definite hair growth. Apparently, there have also been at least two other cases of hair growth associated with MER-29 therapy. I don't know what this means, but I find it difficult to believe that MER-29 is perhaps the long awaited cure for baldness.

We know that people observed spontaneous thinning of the hair or changes in its color or texture long before MER-29 was available. Furthermore, we know that a smaller percentage of people have experienced a spontaneous regrowth of hair. I don't wish to imply that there is no expectation for such phenomena. Systonic diseases accompanied by fever, thyroid therapy and certain hormonal imbalance states, undoubtedly, can result in alopecia or hair-thinning. Have all such known causative factors been ruled out in the MER-29 cases? I presume that they have in view of McMasters statement "that there can be no doubt of the association of MER-29 therapy with these changes."

I will now put on my other hat and argue on the other side. Hair loss doesn't occur spontaneously without any cause whatsoever. If we rule out known probable causes and are left just with MER-29, is there any other reason to believe that MER-29 could be responsible. The answer is probably affirmative in that MER-29 probably does have some endocrine effect. This is inferred from its chemical structure and the reports of vaginal bleeding associated with its use. Therefore, it is both possible and likely that those scattered reports of hair changes could be attributable to MER-29.

In summary, I would say that the weight of the evidence seems to indicate that MER-29 may produce some hair changes in a very small proportion of cases. However, I do not believe it is fair to say that this is proven beyond any doubt. Nevertheless, I am inclined to go along with the recommendations of the Merrell group as I am sure that at least one or more of the physicians who have observed this effect on the hair of several of their patients during MER-29 therapy will publish their findings in the near future. I don't particularly like McMasters sug-