

Appendix C

## APPENDIX C

Excerpt from the March 25, 2004 Joint Dermatologic and Ophthalmic  
Drug and Non-Prescription Drug Advisory Committee Meeting,  
Gaithersburg, Maryland.

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

JOINT SESSION WITH THE  
NONPRESCRIPTION AND DERMATOLOGIC DRUGS  
ADVISORY COMMITTEE

VOLUME II

Thursday, March 24, 2004

8:00 a.m.

Hilton Washington DC North  
620 Perry Parkway  
Gaithersburg, Maryland

A F T E R N O O N P R O C E E D I N G S

[1:00 p.m.]

Open Public Hearing

DR. WOOD: We are going to do the public comment period. All the people who have requested time in the public comment period have got a number, and I will call you up by number.

You have 10 minutes to present and we will strictly enforce the 10-minute rule. At the end of the 10 minutes, the microphone will go dead and only your lips will be moving.

Let's get started with No. 1.

MR. ROTH: I am Jerry Roth. I am president and owner of Hill Dermaceuticals. I was present at the last Advisory Committee meeting on pediatric corticosteroids for pediatrics. I recognize some of the panel members from the last one, so I hope I don't bore you here because I am presenting this information.

I remember Dr. Chesney said you are supposed to say if anybody paid your way here. I paid my own way, so as I said before, I am one of

the dinosaurs left in this industry.

First of all, in presenting this data, it is not our intention in any way, shape, or form to want our product Derma-Smoothe/FS to be nonprescription. It is a prescription and we intend it to stay that way, but we felt that this is giving you a little bit of data that you have not maybe heard earlier today.

[Slide.]

First of all, Derma-Smoothe/FS contains 0.01 percent fluocinolone acetonide in a peanut oil base. It is considered a low to medium potency corticosteroid, and I wanted to present HPA axis suppression studies that were done in patients 2 to 12 years of age.

You have heard a lot today about vehicles and I think that this will give you once again a little bit additional evidence.

[Slide.]

This is a multi-center, open-label safety study. What you haven't heard yet is this was done in patients with greater than 50 percent body

involvement.

The dosage, it was also brought up that everything was once a day. The dosage on this was twice daily for a period of 4 weeks. The criteria was evaluation with the cosyntropin stimulation test.

Derma-Smothe/FS was one of the first drugs that was studied for safety and efficacy, the Rules, as have been mentioned, have changed since that time, and you will see that Day 1, prior to the first treatment, and at the end of treatment we had a pre-stimulation cortisol level and then immediate followed by stimulation, and then the post-stimulation cortisol level was at 60 minutes.

At that time, the protocol or the Agency only request cosyntropin tests. It wasn't differentiated between 60 minutes and 30 minutes at that time.

[Slide.]

The population that I want you to recognize is that 18 of the patients had greater than 75 percent body involvement, and 16 had 50 to

75 body involvement. We calculated the amount of drug by what was returned, and the average drug use per day was about 9.5 plus or minus 4.7 mL/day. Now, this is important because there is something, vehicles and drug exposure.

[Slide.]

Just to remind those who aren't physicians, regarding body surface area, when you are talking about this much, 50 to 75, or 75, you are talking about the chest, front and back, legs, front and back, arms, a substantial area. Once again, I believe this is the only drug that had been tested with that level besides hydrocortisone of that amount of body surface.

[Slide.]

Before the treatment, prior to treatment, now we did averages because this is a public hearing, each of the data individually is on file with the Agency, and this was approved, so each individual case report form is on file.

Anyway, the average pre-stimulation was 11.63. At 60 minutes, it was 26.82, the doubling

which you should see.

[Slide.]

After 4 weeks of treatment, there was very little change, 11.26, and after post-stimulation, it was 25.06. Of the 34 patients, there was not one that experience any adrenal suppression.

[Slide.]

The exposure we feel is very important. Derma-Smoothe/FS is a 4-ounce container. Within this container, there is 12 mg of fluocinolone. You will see that the average patient, the 4 ounces, 118 mL, lasted 12 days. The patient was exposed to not more than 1 mg of fluocinolone per day. On the basis, which is the generally accepted percent of absorption of 1 to 2 percent, that is an infinitesimal amount that is absorbed.

What is important is this is an oil vehicle, the spreadability is great. This particular cream is 60 grams, and there are 60 mg of corticosteroid in this cream. To cover a vast majority of the body, it would require a lot more cream to do this than of this oil, so you may use

quite a bit more of the cream. I think that was brought out earlier.

So, therefore, vehicles are important and possibly does have substantial amount regarding safety data.

[Slide.]

In conclusion, after 4 weeks of daily application of Derma-Smoothe/FS , involving 50 to 90 percent of the body surface area, there was no change in the morning baseline value of the cortisol, nor did it affect the cortisol stimulation of ACTH.

You might wonder, well, if there is so little amount of steroid does it work, with this small amount on the body, after 4 weeks, 60 percent of the patients showed excellent or 75 to 100 percent improvement.

Would you like to ask me any questions especially on the amount of surface? I think, just to follow up, Dr. Wilkin has said that the tests are becoming a bit more sophisticated. We are ready to commence down to 3 months with this

product in greater than 30 percent of the body area, and we will be following, I think there was a question if you have any adrenal suppression, will you be following those patients. In that protocol, we will be. We don't expect any, but we will test until we have data.

Second of all, once again, there was also a statement that companies often just do this because they are required. That is some of the case, but in any cases it is not, and in this case, it is not. It was our request to do these.

Yes, sir.

DR. WOOD: Dr. Nelson has a question for you.

DR. NELSON: I was told it had better be a good one, hopefully, it is. You had mentioned in passing that it is generally accepted that 1 to 2 percent of corticosteroids are absorbed topically. I was just wondering what is the data and how generally accepted is that?

MR. ROTH: That is in the Textbook of Corticosteroids, I believe it is by Dr. Howard

Mayback. That is a generally accepted textbook.

DR. NELSON: For all corticosteroids?

MR. ROTH: I believe, yes, on topically applied, yes. That is why the amount that you are exposed to is quite substantial.

DR. WHITMORE: I don't know that that applies to all corticosteroids. I think hydrocortisone versus the others--

DR. WOOD: Let's hold all of our questions to all of the speakers at the end, otherwise, we will take forever to do this. Let's go through all the speakers and then we will take questions for them at the end.

MR. ROTH: I can quote out of the textbook if you would like.

DR. WOOD: Teresa has handed me a late-breaking statement that I need to read.

Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decisionmaking. To ensure such transparency at the open public hearing session of the Advisory Committee meeting, the FDA