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Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research
Department of Health and Human Services
Food and Drug Administration
Rockwille, Maryland 20867 re: DocketNo. 00P-1330/CP1

Dear Dr. Woodcock,

After waiting six months I was finally happy to hear a response to my citizen's petition of May 30. I know how difficult it must be for you to sign on to a response that you have personally not researched. This response raises questions on how to handle a petition that is critical of the performance of the Dermatology section.

I fear that the analysis you have sent me is seriously flawed. It should be sent to be re-reviewed by persons not intimately connected with the Dermatology management. I am told that this may fit under the title of a "quality assurance analysis". Below I give a technical response to your report.

I. Your report claims that the DHT reduction actually fell from 53.95% at 0.2 mg to 57.56% at at 1.0 mg. To report such numbers with four significant figures is unscientific. It claims that you had sufficient experimental accuracy to distinguish a difference of .015% in the measurements. Not with only 100 patients per point!
The statistical accuracy in the FDA material I received from the FDA could not even accurately measure the magnitude of the 3.6% difference that is claimed.

Of course the whole argument misses the point. There is no evidence that a further 3.6% drop in the DHT should make any appreciable change in hair growth but my argument is that increasing the dose by a factor of five is a large increase to be considered if one is to take the drug for a lifetime and is concerned about deleterious side effects. (Actually the data show that .05 mg would suffice, a reduction of 20. (I am certain that the FDA does not subscribe to the view that side effects over long periods is unrelated to drug dose.)

2) As to subject questionaires on efficacy: The data I obtained from the FDA showed that actual counting of hairs with a camera did not agree with qualitative questionaires.

3) You claim that the "FDA does not require that dose ranging studies demonstrate statistical difference between dosages". Where does such a requirement appear in FDA rules and if it does could you inform me where to find it? If that statement were published it would be an embarassment to the FDA. I am sure that it cannot be your opinion.

4) It is claimed that a positive slope was determined in the data. Yet you state that the data points were at .01 mg 0.2 mg and 1.0 mg. One cannot possibly include the .01 mg point in estimation of a slope since there

00P-1330 LET 1

is zero effect at .01, indistinguishable from the placebo dose. One can only use points above about .02 mg to examine the slope vs dosage. You state that the study showed that the .01 mg dose was ineffective. Of course, just like the .00 (placebo) dose. You approved a 100 times larger dose than the .01 mg.

The SUDDEN change occurs somewhere around .02 to .05 the drop being huge, dropping down to 60%. Thus the .01 data are irrelevant to the analysis.

5) I firmly agree with the view that efficacy data must take precedence over chemical or physical measurements. But only if they are measured over the same dosage range. This was not done in the data on which your decisions were made. Further, if it were true that 1.0 mg was better than 0.2 mg, the FDA should have asked for data on 5.0 mg. That is the "Proscar" dosage. Those pills have been available for many years and, in fact, the hair growth was first observed in persons taking the 5.0 mg finasteride dosage for BPH!

Conclusions

The statistical arguments you have given and those supplied to me earlier by the director of the Dematology branch reveal an unfamiliarity with statistics and a lack of recognition of systematic errors that demeans your office. It reveals an unfamiliarity with the conditions under which efficacy can be chosen over quantitative measurements.

Please reply to this letter soon for I hope it would indicate that you would make a timely internal review of its basis. I really do not want to appeal your conclusions to the office of Steven Unger and I am confident that your internal analysis will be of great value.

We have good video-conferencing here if you would like to have some of your people have a discussion with me.

Very truly yours,

Sherman Frankel
Professor of Physics

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