DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
Atlanta GA 30333
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James Bilstad, M.D.
FDA/CDER/ODE-II/HFN-800
5600 Fishers Lane
Room 13B28
Rockville, Maryland 20857

Dear Dr. Bilstad:

Dr. Cordero and I thank you for the opportunity to attend your March 9, 1988 meeting to discuss concerns about human malformations caused by isotretinoin. We look forward to participating in the April 26, 1988 meeting with FDA's Dermatology Advisory Committee to discuss the issue further. For your information, I have enclosed a copy of the final draft of the MMWR article on isotretinoin-caused malformations in New Jersey. It is not much changed from the draft you saw earlier, but does include some revisions suggested by your colleagues at the March 9 meeting.

As I noted at the March 9 meeting, I am very concerned that there are babies being born with malformations caused by isotretinoin and believe that strong action is required to prevent further occurrences. At the meeting, I also mentioned that I am concerned that any action taken to help prevent the occurrence of defects caused by isotretinoin needs to be coordinated with similar actions to prevent the occurrence of defects due to exposure to etretinate. A further area of concern is the possibility that there will be other applications to the FDA for approval for similar drugs. Parallel action will be needed to prevent defects caused by other, as yet unapproved, retinoids.

We presume that the marketing approval of isotretinoin and etretinate involved assumptions that the drug users would follow the recommendations to avoid exposures during pregnancy, and, in the event of failure, that the birth of affected children would be avoided by induced abortion. We now know that this prevention regimen is not 100 percent effective. I would be appreciative if you could share with me the approach that was taken by the FDA and its advisory committees in making the decisions to approve these drugs. Specifically, I would like to know what procedures were followed to arrive at an accounting of the benefits and risks of the use of these drugs. It is clear to me that a new accounting is needed at this time, and any guidance that might be derived from past discussions on isotretinoin or etretinate would be helpful.

As a related matter, I would appreciate learning from you about the composition of the Dermatology Advisory Committee - specifically, I would like to know who are the members, what are their areas of professional competence, and what are their professional affiliations. I am interested to know if the committee will be composed largely of dermatologists, specialists who will quickly appreciate the benefits of these drugs, but who might not so readily apprehend the magnitude of the risks. If the Dermatology Advisory Committee is largely composed of dermatology specialists, it might be useful to supplement the Committee with a few ad hoc members who are familiar with obstetric and pediatric issues. Another possibility might be to hold a joint meeting of the Dermatology and Fertility and Maternity Drug Committees to help assess the situation.

A final area of concern to me is the recent publicity that has been received by Retin-A. It appears that it will be in very great demand by the American public. Although the drug is a potent animal teratogen, it is my understanding that it is unlikely to cause human problems because the drug is used topically and the absorbed dosages are thought to be very low. Is my understanding correct? Is there a need for more studies on human absorption following topical application, particularly when the skin is compromised by disease or injury?

Again, thank you for the opportunity to participate in the deliberations on this important issue. I look forward to hearing from you.

Sincerely yours,

J. David Erickson, D.D.S., Ph.D.
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Enclosure

cc:
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