From: a-dreger@northwestern.edu
Subject: follow-up questions
Date: September 3, 2010 9:43:55 AM GMT-04:00
To: robert.nelson@fda.hhs.gov
Cc: efeder@american.edu, director@aiclegal.org, Diane.Murphy@nih.hhs.gov

Dear Dr. Nelson,

Yesterday afternoon, the OHRP provided us your memo regarding prenatal dexamethasone (attached). We sincerely appreciate your work on this matter and have the following questions and requests for you, the responses to which will facilitate the understanding of your findings among professional ethicists and patient advocates.

1. You indicate that Dr. New "received an IND exemption from FDA in 1996 under 21 CFR 312.2(b) for the administration of dexamethasone during pregnancy for the purpose of preventing virilization in females with congenital adrenal hyperplasia." Please provide us a copy of the documentation of that exemption. (A PDF scan is fine.)

2. Please also explain whether this exemption had any specific beginning and ending date, if it is not clear from the copy.

3. Please provide us information (preferably original documentation) about why this exemption was given and what evidence and ethical considerations were taken into account when the exemption was given. We are interested, for example, in why the FDA considered first-trimester treatment with a Class C drug to be acceptable as an experimental treatment aimed at a non-lethal condition when at least 7 out of 8 of the fetuses exposed would not even have the targeted non-lethal condition. (We are trying to understand the limits of what the FDA will provide an exemption for, or at least the limits as they existed in 1996. Perhaps if those limits have changed, you can educate us about where to learn more about the historical shift.)

4. Dr. New directly advertises her clinical services regarding prenatal dx for CAH to prospective patients by saying that "the treatment has been found safe for mother and child." (Quote from http://www.newchf.org/testing.php) Is the reason the FDA allows her to declare this off-label use of a pregnancy class C drug "safe for mother and child" in advertisements for her own clinic that she does not work for the maker of the drug?

5. Is the FDA presently concerned about doctors advertising off-label uses directly to prospective patients (including pregnant women) as safe and/or effective?

6. Could we (in general) reasonably expect the FDA to be disproportionately alert where DTC advertising of off-label first-trimester treatments specifically designed to

change fetus's bodies for non-lethal conditions is concerned?

7. In producing your findings, were you privy to the most recent consensus regarding this off-label use from the American Academy of Pediatrics, the Lawson Wilson Pediatric Endocrine Society, the European Society for Paediatric Endocrinology, the European Society for Endocrinology, and the Society for Pediatric Urology? (If you were, it would seem you were aware of what their literature review showed, and what they concluded, somewhat differently from you. If you were not, we would be happy to share it with you.)

8. In producing your findings, did you ascertain what percentage of untreated affected females will have a urogenital sinus that results in problems requiring surgical correction? Relatedly, are you aware that the most recent consensus of the 5 medical societies mentioned in question 7 acknowledges that "The condition being treated, while fraught with emotional complexities, *is directed toward a cosmetic outcome* rather than aiming to preserve life or intellectual capacity"? (Emphasis added.)

9. In producing your findings, were you aware of any evidence that ambiguous genitalia represent a threat to the health (physical or mental) of those who have them? If so, what is that evidence?

My colleagues and I would appreciate a prompt written reply so that we can better understand your findings as we share them with others. Please feel free to answer in a series of responses if you have the answers to some of these items now, and will have the answers to the others later. Thank you.

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