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July 29, 1983

EIS Officer

Accutane (Isotretinoin) Teratogenicity

The Record (Teratology File)

On July 25, 1983, I spoke with Dr. John Pepper of Roche Laboratories (212 695-1400) concerning case reports of teratogenicity from Accutane (isotretinoin), a retinoid related to both retinoic acid and retinol (Vitamin A). Roche has received 4 case reports of children born with malformations whose mothers took Accutane in first trimester. Information is incomplete on the case histories but the following is all that we know so far:

(1) infant with atretic ear canal, deformed ears, systolic murmur

(2) infant with hydrocephalus

(3) infant with microcephaly, rudimentary ear with atretic canal, and other defects; died before 1 month of age

(4) infant with hydrocephalus probably secondary to aqueductal stenosis

On the basis of these cases, Roche mailed a letter to all U.S. physicians and pharmacists emphasizing that Accutane is contraindicated in pregnancy (see attached letter). The types of defects seen in these case reports are similar to those noted in animal studies and mentioned in a letter from Roche in November 19 or (see attached). These include spina bifida, missing or reduced tail and caudal vertebrae, reduced femurs, fused sternebrae, cleft palate, eye defects, hydrocephalus and exencephaly.

On July 25, 1983, Godfrey Oakley of BDB called Dr. John Burns at Roche Labs (201 235-2811) to disucss Accutane teratogenicity. Dr. Burns reportedly said that Roche would recommend that any woman exposed to Accutane during pregnancy have an elective abortion, that Roche was considering the drug to have nearly 100% teratogenicity and that he felt that the relationship between Accutane and the malformations in the case reports was causal. Roche has had no reports of normal outcomes in exposed women, althought they certainly could have occurred. Dr. Pepper earlier had informed me that although the information sent us in November, 1982 said that no fetal abnormalities were reported in the Accutane clinical trials, in fact there were no outcomes to evaluate. Of the 4 pregnancies occuring during the trials, 2 women elected to abort their fetuses, one child was dead at 26 weeks gestation secondary to a prolapsed cord, and one child was delivered at term and was normal. Retrospectively, it was determined that this latter mother was noncompliant and never took the drug during her pregnancy.

On July 26, 1983, I discussed these cases with Dr. Franz Rosa. He had information on an additional case. This mother used isotretinoin topically only during first trimester and delivered a child with cleft palate. Dr. Rosa will forward to us the case reports on the Roche cases as soon as he has the information.

July 27, 1983. Dr. Rosa has the information on the 4 case reports from Roche and will send them to Birth Defects Branch. He would like to receive copies of any reports that we develop about pregnancy exposures to Accutane and their outcomes.

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cc: Dr. Godfrey P. Oakley, Jr.
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