



March 1, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket number 2005D-0030, Draft Guidance for Industry on Clinical Lactation Studies--Study Design, Data Analysis, and Recommendations for Labeling.

Gentlemen:

I find the aforementioned document to be generally well thought-out and thorough with one exception: the age of the infant is not adequately taken into consideration. In my research and clinical practice, I have found that the infant age is one of the most important factors in determining the advisability of maternal drug use during breastfeeding. In our analysis of the published literature, we found that at least 63% of reported cases of adverse reactions were in neonates and 78% were 2 months or under; only 4% of adverse reactions occurred in infants over 6 months of age.¹ Several factors could contribute to this finding: 1) more newborn infants are breastfed than older infants; 2) infants over 6 months (and many between 1 and 6 months) receive only part of their daily nutrition from breastmilk, thereby reducing the daily dosage of any drugs in milk; 3) drug metabolism and excretion in neonates, and particularly preterm infants, is not well developed, potentially leading to drug accumulation; 4) plasma protein binding may be less in neonates; 5) the blood-brain barrier is more permeable in newborn infants.^{2,3}

Because of factors 2-5 above, study results in neonates are not directly transferable to older infants and vice versa. What is often reported and recommended in current package inserts are isolated case reports of adverse events in newborns apparently caused by drug excretion into breastmilk. These findings are then translated into broad recommendations against breastfeeding while taking the drug in question. This sort of recommendation does a great disservice to mothers who are breastfeeding older infants and their infants. In the breastfeeding community, these admonitions are widely perceived, rightly or wrongly, to be aimed at diminishing drug manufacturer liability rather than in helping health professionals and their patients to make informed decisions.

With these thoughts in mind, I have the following recommendations on the draft document:

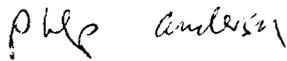
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1. The Mother-Infant Pair Design section beginning at line 207 should specifically recommend that the age of infants studied and their extent of breastfeeding be reported. The results should be broken down by age group and state whether or not preterm infants were studied.
2. The Precautions/Nursing Mothers section should explicitly state on lines 688 and 689 that the infant age and preterm birth status should be mentioned and recommendations should be reported separately by age group (e.g., preterm, neonate, older infants). Any differences in applicability of the recommendations between exclusively and partially breastfed infants should also be mentioned.

I hope these comments are given consideration in the formulation of the final document.

Sincerely,



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References:

1. Anderson PO, Pochop SL, Manoguerra AS. Adverse drug reactions in breastfed infants: less than imagined. Clin Pediatr. 2003;42:325-40.
2. Anderson PO. Medication use while breast feeding a neonate. Neonatal Pharmacol Q. 1993;2:3-14.
3. McNamara PJ, Abbassi M. Neonatal exposure to drugs in breast milk. Pharm Res. 2004;21:555-66.