April 2, 2001

To: Dr. D. T. Dunn
MRC Clinical Trials Unit
222 Euston Road
London, UK, NW1 2DA

Dear Dr. Dunn:

In a 1992 Lancet paper entitled “Risk of human immunodeficiency virus type 1 transmission through breastfeeding” (Dunn DT et al. Risk of Human Immunodeficiency Virus Type 1 transmission through breastfeeding. Lancet. 1992 Sep 5; 340: 585-8) you performed a meta-analysis of 6 studies comparing the risk of children of HIV-positive mothers becoming HIV-positive themselves based on whether their mothers breastfed or formula fed. You estimated an “additional risk of transmission through breastfeeding of 14%” based on, according to a footnote in Table II (p. 586), a “Weighted average of study-specific differences”.

I attempted to recalculate this figure, weighting the percentage difference in each of the trials by the total number of women in the trial, and obtained a difference of 18%. Since the number of women in the breastfeeding arms was generally much lower than in the formula arm, I thought that perhaps you had weighted by the number of breastfeeding women. I performed this calculation and obtained a difference of 16%.

**Question 1:** Please explain exactly how you weighted the study-specific differences.

My first attempt to calculate the excess risk of breast-feeding was to simply add up all the columns in your table II to calculate percentages based on the meta-total (e.g. count of all HIV+ children with breastfeeding mothers in all trials divided by the count of all breastfeeding mothers to calculate the fraction of breastfeeding mothers who transmitted). Doing this I obtained a difference of only 11% (27%-16%).

**Question 2:** Please explain why you chose to use a weighted average, and not simply calculate percentages based on the total data in Table II?

Furthermore, unpublished Australian data from Ziegler et al provided the highest excess risk. Eliminating this data (which, being unpublished, has not been subject to thorough peer review) reduced the difference even further to only 9% (25%-16%).

**Question 3:** Do you know if the Ziegler data from Australia has ever been published?

I appreciate a response to my three questions at your earliest convenience.

Regards,

David R. Crowe, President
Alberta Reappraising AIDS Society