

Groupe, Cathy [Cathy.Groupe@fda.hhs.gov]

March 15, 2007

Anesthetic and Life Support Drugs Advisory Committee
Food and Drug Administration; Department of Health and Human Services

RE: Request for Formal Oral Presentation
Public Advisory Committee Meeting – March 29, 2007

Dear Sirs:

Although I am unable to attend the meeting, as a board-certified pediatric anesthesiologist I have specific areas of concerns regarding the Committee's deliberation of the neurodegenerative findings in juvenile animals exposed to anesthetic drugs and guidance for future clinical studies.

The relevant animal studies and implications have been nicely summarize by the FDA in the recent Mellon publication.[1]

I am particularly concerned that the Committee and the Agency have too narrow a focus concerning the pediatric patient at risk. Although the animal data have used very young animals as a model to study these potential harmful effects, I do not believe we know the specific age range at which to consider children to be beyond the risks of potential neurodegenerative or neurotoxic effects. It is clear that in pediatric patients – including those past the neonatal stage - certain volatile anesthetics can produce acute neurophysiological and/or behavioral changes. In response to the occurrence of epileptiform activity with sevoflurane, changes in the product labeling were made.[2] We frequently see emergence responses that are clearly signs of CNS agitation and delirium.[3] Sadly, as a pediatric anesthesiologist, I have no long term data to say that there is no harm in these events.

I would encourage the Advisory Committee to request additional studies of anesthetic agents in *all* pediatric patients. Our young patients – with years of development and maturation ahead of them – need additional studies to determine the safest approach to anesthesia care. Anesthesia clinicians would benefit from the insight of future studies looking at the long-term impact of volatile anesthetics and other agents used frequently in the provision of anesthesia care.

Thank you for consideration of these comments. If I can provide more details to the Committee, please contact me.

William T. Denman, MD, FRCA
Medical Director
Vice President, Medical Affairs
tyco Healthcare

1. Mellon RD, Simone AF, Rappaport BA. Use of anesthetic agents in neonates and young children. *Anesth Analg* 2007;104:509-20.
2. Vakkuri A, Yli-Hankala A, Sarkela M, et al. Sevoflurane mask induction of anaesthesia is associated with epileptiform EEG in children. *Acta Anaesthesiol Scand* 2001;45:805-11.
3. Meyer RR, Munster P, Werner C, Brambrink AM. Isoflurane is associated with a similar incidence of emergence agitation/delirium as sevoflurane in young children--a randomized controlled study. *Paediatr Anaesth* 2007;17:56-60.