Accepted Manuscript

Title: Best Practices for Developmental Toxicity Assessment
for Classification and Labeling

Authors: George Daston, Aldert Piersma, Leonello Attias,
Manon Beekhuijzen, Connie Chen, Jennifer Foreman, Nina
Hallmark, Isabelle Leconte

Please cite this article as: Daston George, Piersma Aldert, Attias Leonello,
Beekhuijzen Manon, Chen Connie, Foreman Jennifer, Hallmark Nina, Leconte
Isabelle.Best Practices for Developmental Toxicity Assessment for Classification and
Labeling.*Reproductive Toxicology* https://doi.org/10.1016/j.reprotox.2018.05.001

Best Practices for Developmental Toxicity Assessment for Classification and Labeling

George Daston1*, Aldert Piersma2, Leonello Attias3, Manon Beekhuijzen4, Connie Chen5, Jennifer Foreman6, Nina Hallmark7, Isabelle Leconte8

1- Procter & Gamble, Cincinnati, OH USA
2- RIVM, Bilthoven, Netherlands, and IRAS, University of Utrecht, Netherlands
3- Istituto Superiore di Sanità, Rome, Italy
4- Charles River, 's-Hertogenbosch, The Netherlands
5- HESI, Washington, DC USA
6- ExxonMobil Biomedical Sciences, Inc., Annandale, NJ USA
7- Bayer SAS, Sophia Antipolis, France
8- Charles River laboratories France Safety Assessment SAS

*- corresponding author

Highlights

- Classification and labeling of chemicals as hazards is occurring at an increasing pace in Europe as laws regulating chemicals are implemented. It is important to use best practices in order to appropriately interpret developmental toxicity data. Recommendations are made concerning data quality, improved study designs, the proper interpretation of maternal toxicity data, interpretation of mechanistic data, and defining the limits of chemical classes are presented.

Abstract

Many chemicals are going through a hazard-based classification and labeling process in Europe. Because of the significant public health implications, the best science must be applied in assessing developmental toxicity data. The European Teratology Society and Health and Environmental Sciences Institute co-organized a workshop to consider best practices, including data quality and consistency, interpretation of developmental effects in the presence of maternal toxicity, human relevance of animal data, and limits of chemical classes. Recommendations included larger historical control databases, more pharmacokinetic studies in pregnant animals for dose setting and study interpretation, generation of mechanistic data to resolve questions about whether maternal toxicity is causative of developmental toxicity, and more rigorous specifications for what constitutes a chemical class. It is our hope that these recommendations will form the basis for subsequent