

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

November 10, 2015

To: File for Cerium Oxide (CAS # 1306-38-3)
From: Michael Depa, Air Quality Division, Toxics Unit
Subject: Screening Levels

The Initial Threshold Screening Level (ITSL) for cerium oxide is $0.9 \mu\text{g}/\text{m}^3$ with annual averaging time. The ITSL was based on an Environmental Protection Agency (EPA, 2009) Reference Concentration (RfC) pursuant to Rule 232(1)(a). EPA (2009) based their RfC on a subchronic rat inhalation study (BRL, 1994) that showed increased incidence of alveolar epithelial hyperplasia in the lungs of male and female rats. Dose levels were 0, 5, 50.5, or $505.7 \text{ mg}/\text{m}^3$ for 6 hours/day, 5 days/week for 13 weeks. The results revealed statistically significant increases in absolute and differential neutrophil counts in the blood, treatment-related increases in the absolute and relative weight of the lungs in both males and females dosed at 50.5 and $507.5 \text{ mg}/\text{m}^3$ and in the relative spleen weight of male rats at $507.5 \text{ mg}/\text{m}^3$, discoloration or pale areas and uncollapsed parenchyma in the lungs of male and female rats at $\geq 50 \text{ mg}/\text{m}^3$ and pale foci in female rats at $5 \text{ mg}/\text{m}^3$, and dose-related alveolar epithelial and lymphoid hyperplasia and pigment accumulation in the lungs, lymph nodes, and larynx of males and females at $\geq 5 \text{ mg}/\text{m}^3$. The dose of $5 \text{ mg}/\text{m}^3$ was identified as a lowest-observed-adverse-effect-level (LOAEL).

EPA (2009) used their Benchmark Dose Software to calculate a benchmark concentration (BMC) and the lower 95 percentile on the concentration (BMCL). EPA adjusted the exposure concentration to continuous exposure (i.e., $\text{BMCL}_{\text{ADJ}} = 1.6 \text{ mg}/\text{m}^3$) and derived the Human Equivalent Concentration ($\text{BMCL}_{\text{HEC}} = 0.86 \text{ mg}/\text{m}^3$) using their software for calculating a regional deposited dose ratio as a dosimetric adjustment factor. A total uncertainty factor (UF) of 1000 was applied to the point of departure (POD) of $0.86 \text{ mg}/\text{m}^3$:

3 for extrapolation from animals to humans (UFA: animal to human),
10 for consideration of interindividual variability (UFH: human variability),
10 for extrapolation from a subchronic study (UFS), and
3 for database deficiencies (UFD).

It should be noted that a factor of 3 was used to account for deficiencies in the cerium oxide database (UFD). Regarding the database uncertainty factor, EPA (2009) stated:

The database includes multiple case reports of inhalation exposure to workers and a single 13-week subchronic inhalation study in rats. The effect from the subchronic rat inhalation study that was used for the derivation for the RfC (i.e., alveolar epithelial hyperplasia in the

lungs) may be an early indicator of the more overt toxicity that is found in humans (i.e., interstitial lung disease) exposed to cerium oxide in the workplace. The database does not include an exposure and recovery study that could demonstrate the persistence or, conversely, the adaptive nature of the alveolar or lymphoid hyperplasia that was observed.

Previously, the averaging time (AT) assigned to cerium oxide was 24 hours, as per the default methodology (Rule 232(2)(b))(see attached memo from Gary Butterfield dated September 30, 2009). The current file review concludes that the AT may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b). Therefore, the AT is set to annual.

References

BRL. 1994. (Bio-Research Laboratories). Final report for a 90-day inhalation neurotoxicity and toxicity study by exposure to a dry powder aerosol of ceric oxide in the albino rat with cover letter dated 013095. Produced by Bio-Research Laboratories, Montreal, Canada for Rhone-Poulenc Inc. Submitted under TSCA Section 8E; EPA Doc. No. 89-950000107; NTIS No. OTS0556254. [An external peer review was conducted by EPA in August 2006 to evaluate the accuracy of experimental procedures, results, and interpretation and discussion of the findings presented. A report of this peer review is available through the EPA's IRIS Hotline, at (202) 566-1676 (phone), (202) 566-1749 (fax), or hotline.iris@epa.gov (e-mail address) and on the IRIS website (www.epa.gov/iris).]

EPA. 2009. Integrated Risk Information System (IRIS) U.S. Environmental Protection Agency. Chemical Assessment Summary. National Center for Environmental Assessment. Cerium oxide and cerium compounds; CASRN 1306-38-3
http://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/1018_summary.pdf

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

September 30, 2009

To: Cerium oxide file (CAS # 1306-38-3)

From: Gary Butterfield

Subject: Screening level for Cerium oxide

The EPA has just released (9-29-09) a new RfC for cerium oxide of $0.9 \mu\text{g}/\text{m}^3$. EPA did not have an RfC for this chemical previously. The old ITSL ($0.1 \mu\text{g}/\text{m}^3$ set by AQD in 2005) for this chemical was based on the same study used by EPA 2009. See the IRIS printout for details on how the RfC was derived.