

## Perfluorooctane sulfonate (PFOS) and Its Salts and Transformation and Degradation Precursors

Perfluorooctane sulfonate (PFOS) and its salts are perfluorinated organic compounds with surfactant properties. Common salts of PFOS include the ammonium, diethanolamine, potassium, and lithium forms. PFOS can be released from several fluorochemicals, such as perfluorooctane sulfonamide (PFOSA), N-ethyl perfluorooctane sulfonamidoethanol (N-EtFOSE), and N-ethylperfluorooctane sulfonamide (N-EtFOSA) by transformation or degradation processes.

PFOS and its salts and precursors are used in the manufacture of a wide array of industrial and household products, including fire fighting foams, and coatings for fabrics, leather, food packaging and paper products. PFOS has not been produced in the U.S. since 2000; however, there is continued production and use of chemicals that can be transformed or degraded to release PFOS.

PFOS is resistant to thermal, chemical and biological degradation and is persistent in the environment. It is readily absorbed into biota and has a tendency to accumulate with repeated exposure. It is present in fish and other foods. Human biomonitoring studies indicate widespread exposure of the population to PFOS. For example, PFOS was detected in all 1562 serum samples analyzed from participants in the 1999-2000 National Health and Nutrition Examination Survey (NHANES) (Calafat *et al.*, 2007). PFOS crosses the placenta, accumulates in amniotic fluid (Midasch *et al.*, 2007), and has been detected in umbilical cord blood (Apelberg *et al.*, 2007).

PFOS and its salts and transformation and degradation precursors passed the animal data screen, underwent a preliminary toxicological evaluation, and are being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

### Epidemiological data

- Retrospective occupational cohort studies
  - Mortality study of workers at a perfluorooctanesulphonyl fluoride-based fluorochemicals production facility in Decatur, Alabama: Alexander *et al.* (2003); EFSA (2008, p. 77)
    - *Increased risk of death from bladder cancer seen in exposed workers (based on three cases)*
  - Bladder cancer incidence in workers at a perfluorooctanesulphonyl fluoride-based fluorochemicals production facility in Decatur, Alabama: Alexander and Olson (2007); EFSA (2008, p. 77)

- *No increased risk of bladder cancer associated with PFOS exposure*

### **Animal carcinogenicity data**

- Long-term feeding studies
  - 104-week studies in male and female Crl:CD (SD) IGS BR rats: (reviewed by OECD, 2002, pp. 34-37).
    - *Increase in hepatocellular adenoma in males (by pairwise comparison and trend)*
    - *Increases in hepatocellular adenoma and carcinoma combined in females (by pairwise comparison and trend), and increases in thyroid follicular cell adenoma and carcinoma combined, and mammary fibroadenoma/adenoma and carcinoma combined in females (by pairwise comparisons)*
  - 52-week exposure and additional observation until death in male Crl:CD (SD) IGS BR rats
    - *Increase in thyroid follicular cell adenomas (by pairwise comparison)*

### **Other relevant data**

- Genotoxicity
  - Review: EFSA, (2008, p. 73)
    - *Mutagenicity in *Salmonella typhimurium*, *Saccharomyces cerevisiae* and *E. coli* (negative)*
    - *Chromosome aberrations in human peripheral blood lymphocytes (negative)*
    - *In vivo mouse bone marrow micronucleus assay (negative)*
    - *Unscheduled DNA synthesis in rat liver primary cultures (negative)*
- Immune system effects
  - 10-day dietary exposure in C57BL/6 male mice: Qazi *et al.* (2009a, 2009b)
    - *Thymus and spleen atrophy, decreased CD45+CD8+ thymocyte and splenic B lymphocyte counts, increased production of TNF-alpha and IL-6 by peritoneal macrophages treated with LPS in vitro*
  - Seven-day gavage exposure in male C57BL/6 mice: Zheng *et al.* (2009)

- *Decreased lymphocyte counts, decreased plaque forming cell response, decreased natural killer (NK) cell activity, and decreased lymphocyte proliferation response*
  - Gestation exposure on days 1-17 in B6C3F<sub>1</sub> mice: Keil *et al.* (2008)
    - *Decreased NK function and IgM antibody production*
  - 28-day gavage exposure in male and female B6C3F<sub>1</sub> mice: Peden-Adams *et al.* (2008)
    - *Reduced NK activity in males*
    - *Altered T cell subpopulations, reduced sheep red blood cells, PFC response and TNP-LPS IgM titer in males and females*
- Neuroendocrine system effects
  - Two-week intraperitoneal exposure study in female Sprague-Dawley rats: Austin *et al.* (2003)
    - *Altered estrous cycle (irregular/persistent)*
    - *Increase in serum corticosterone*
    - *Decrease in serum leptin*
    - *Increased norepinephrine concentration in hypothalamus*
- Structure activity considerations
  - Similar in structure to perfluorooctanoic acid (PFOA, C8), another eight carbon perfluorinated compound that increased testicular Leydig cell, pancreatic acinar cell and hepatocellular tumor incidence in rats.

## References<sup>1</sup>

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<sup>1</sup> Excerpts or the complete publication (presenting epidemiology or toxicology information) have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.

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