LITERATURE SEARCH RESULTS

FOR THE SYSTEMATIC REVIEW OF IMMUNOTOXICITY ASSOCIATED WITH EXPOSURE TO PERFLUOROOCTANOIC ACID (PFOA) OR PERFLUOROOCTANE SULFONATE (PFOS)

May 2016
(updated for results of literature search from May 18, 2016)

Office of Health Assessment and Translation
Division of the National Toxicology Program
National Institute of Environmental Health Sciences
National Institutes of Health
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
LITERATURE SEARCH RESULTS

Literature Search

Search terms were developed to identify all relevant published evidence on immunotoxicity or immune-related health effects potentially associated with exposure to PFOA or PFOS by (1) reviewing Medical Subject Headings for relevant and appropriate immune terms, (2) extracting key immune health effects and immunotoxicity terminology from reviews and a sample of relevant primary data studies, (3) use of the chemical-specific search terms for PFOA from a draft systematic review of developmental PFOA exposure and fetal growth1, and adaptation of the chemical-specific PFOA search strategy to generate search terms for PFOS. A combination of relevant subject headings and keywords were subsequently identified. A test set of relevant studies was used to ensure the search terms retrieve 100% of the test set. The following 9 electronic databases were searched using a search strategy tailored for each database (specific search terms used for the PubMed search presented in Appendix 1; the search strategy for other databases are available in the protocol [http://ntp.niehs.nih.gov/go/749926]). No language restrictions or publication year limits were imposed, and the databases were searched on October 28, 2014 and October 22, 2015, with a final updated search on May 18, 2016.

Databases Searched

- Cochrane Library
- EMBASE
- PubChem
- PubMed
- Scopus
- Toxline
- Web of Science

Searching Other Resources

The reference lists of all included studies, relevant reviews, finalized or recent draft federal hazard assessments2,3,4,5,6, commentaries, and other non-research articles were manually searched for


additional relevant publications. NTP published a Request for Information about ongoing studies or upcoming publications on immune-related health effects of PFOA or PFOS in the Federal Register [80 FR 48886 (August 14, 2015)]. Studies identified by the public in response to the 2015 request for information or after posting of the protocol and initial list of included studies were also included.

**Literature Search Results**
The electronic database searches retrieved 3197 individual references, and 20 additional references were identified by technical advisors or from reviewing reference lists in published reviews and included studies. From the total references retrieved, 2788 were excluded during the title and abstract screening and 241 were excluded during the full text review. The screening results are outlined in a study selection diagram with reasons for exclusion documented at the full text review stage (*Figure 1*). The 148 included studies are listed below in the section for “list of included studies”; there are 33 human studies, 93* animal studies, and 27* in vitro/mechanistic studies.

*Figure 1. Study Selection Diagram*

![Study Selection Diagram](image)

* Five publications contained data relevant to both experimental animal studies and *in-vitro* studies

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REFERENCES INCLUDED AFTER FULL-TEXT REVIEW

List of Included Studies

*studies identified in the updated literature search May 2016

Studies in humans


Literature Search Results for Systematic Review of Immunotoxicity Associated with Exposure to PFOA or PFOS


Studies in non-human animals


Literature Search Results for Systematic Review of Immunotoxicity Associated with Exposure to PFOA or PFOS


Kannan K, Yun SH, Rudd RJ, Behr M. 2010. High concentrations of persistent organic pollutants including PCBs, DDT, PBDEs and PFOS in little brown bats with white-nose syndrome in New York, USA. *Chemosphere* 80(6): 613-618.


Qazi MR, Nelson BD, Depierre JW, Abedi-Valugerdi M. 2010. 28-Day dietary exposure of mice to a low total dose (7 mg/kg) of perfluorooctanesulfonate (PFOS) alters neither the cellular compositions of the thymus and spleen nor humoral immune responses: does the route of administration play a pivotal role in PFOS-induced immunotoxicity? *Toxicology* 267(1-3): 132-139.

Qazi MR, Nelson BD, Depierre JW, Abedi-Valugerdi M. 2012. High-dose dietary exposure of mice to perfluorooctanoate or perfluorooctane sulfonate exerts toxic effects on myeloid and B-lymphoid cells in the bone marrow and these effects are partially dependent on reduced food consumption. *Food Chem Toxicol* 50(9): 2955-2963.


Thomford PJ. 2001. 4-Week capsule toxicity study with ammonium perfluorooctanoate (APFO) in Cynomolgus monkeys. Sponsor: APME Ad-Hoc APFO toxicology working group. 159.

Thomford PJ. 2002. 4-week capsule toxicity study with perfluorooctane sulfonic acid potassium salt (PFOS; T-6295) in Cynomolgus monkeys. Sponsor: 3M. 235.


Zheng L, Dong GH, Jia JH, He QC. 2009. Immunotoxic changes associated with a 7-day oral exposure to perfluorooctanesulfonate (PFOS) in adult male C57BL/6 mice. *Arch Toxicol* 83(7): 679-689.

Zheng L, Dong GH, Zhang YH, Liang ZF, Jin YH, He QC. 2011. Type 1 and Type 2 cytokines imbalance in adult male C57BL/6 mice following a 7-day oral exposure to perfluorooctanesulfonate (PFOS). *J Immunotoxicol* 8(1): 30-38.


**In vitro experimental studies**


Literature Search Results for Systematic Review of Immunotoxicity Associated with Exposure to PFOA or PFOS


**APPENDIX**

**Appendix 1. Literature Search Strategy**

The strategy for this search is broad for the consideration of immune-related endpoints and comprehensive for PFOA or PFOS as an exposure or treatment in order to ensure inclusion of relevant papers. The search terms for PubMed are provided below. The specific search strategies for other databases are available in the protocol ([http://ntp.niehs.nih.gov/go/749926](http://ntp.niehs.nih.gov/go/749926)).

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