



National Toxicology Program

U.S. Department of Health and Human Services

**LITERATURE SEARCH RESULTS FOR THE
SYSTEMATIC REVIEW OF LONG-TERM
NEUROLOGICAL EFFECTS FOLLOWING ACUTE
EXPOSURE TO THE ORGANOPHOSPHORUS
NERVE AGENT SARIN**

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Office of Health Assessment and Translation
Division of the National Toxicology Program
National Institute of Environmental Health Sciences

LITERATURE SEARCH RESULTS

Literature Search

Search terms were developed to identify all relevant published evidence that addresses the research question on long-term neurological health effects potentially associated with acute, sublethal exposure to sarin in humans and animals by (1) using the search term “sarin” and related synonyms “GB” or sarin’s IUPAC ID “(RS)-propan-2-yl methylphosphonofluoridate”, (2) without restriction by health outcome or key words to identify long-term neurological effects. A test set of relevant studies was used to ensure that the search terms retrieved 100% of the test set. The following eight electronic databases were searched using a search strategy tailored for each database by an informationist on the evaluation team (specific search terms used for the PubMed search are presented in [Appendix 1](#)); the search strategy for other databases are available in the protocol. No language restrictions or publication year limits were imposed and the databases were searched in April 2016, with a final updated search on January 19, 2017.

Databases Searched

- Cochrane Library
- DITIC
- EMBASE
- NIOSHTIC
- PubMed
- Scopus
- Toxline
- Web of Science

Searching Other Resources

The reference lists of all included studies, relevant reviews or reports, commentaries or letters on specific studies, and other non-research articles were manually searched for additional relevant publications.

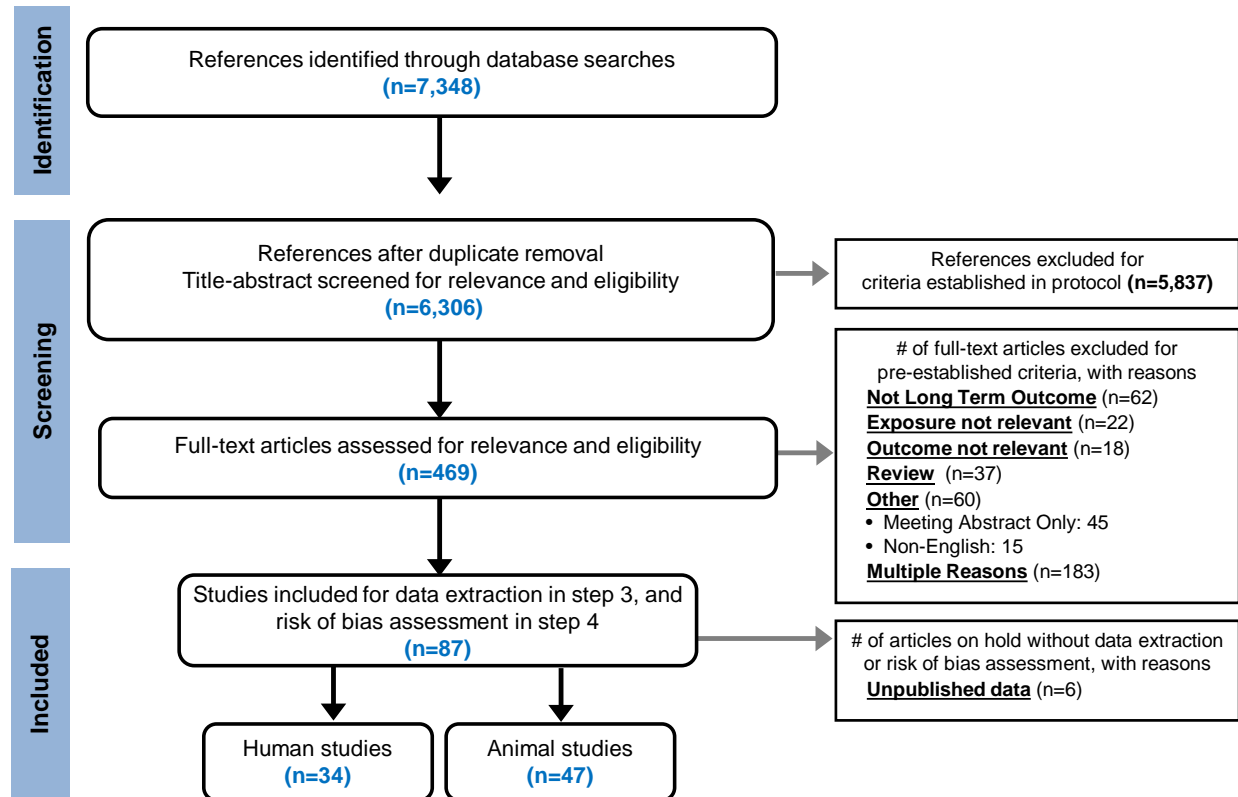
Given that incidents of human exposure to sarin includes terrorist attacks and military personnel, the search was conducted to identify the anticipated range of evidence for human studies; original papers may include non-peer-reviewed studies, for example, reports from US military observational studies, as well as uncontrolled studies, case series, or case reports. In all instances, the paper must: (1) document exposure to sarin; (2) confirm both acute symptoms, *i.e.*, cholinergic crisis; and (3) assess and report some long-term neurological health effects from the exposure.

Literature Search Results

The electronic database searches retrieved 6,306 references. Ninety-three percent of the total references retrieved (5,837) were excluded during the title and abstract screening and 381 references were excluded during the full text review for not satisfying the PECO criteria. The screening results are outlined in the study selection diagram with reasons for exclusion documented at the full text review stage ([Figure 1](#)). After full text review, 87 studies were considered relevant, which included 34 human studies and 47 animal studies. However, 2 of the human publications and 4 of the animal publications included data published in another study, so there were 32 human datasets within the 34 human studies and 43 animal datasets within the 47 animal studies. When multiple publications presented the same

data, a single study was selected for extraction (e.g., the first or most complete reporting) and all of the studies were included in the HAWC project database for this sarin evaluation (<https://hawcproject.org/assessment/302/>) and were reviewed to answer risk-of-bias questions regarding the datasets that were extracted. In addition, 6 studies were identified that included unpublished data. The unpublished data were reviewed, but determined not to have any data that would change the hazard conclusions because the data were either subsequently published, were not published by authors who had published several other studies on the topics, the data did not add any useful evidence to the sections, or the data only added to the heterogeneity of the data; therefore, it was not extracted or included in the assessment. The list of included references are provided below.

Figure 1. Study Selection Diagram



REFERENCES INCLUDED AFTER FULL-TEXT REVIEW

List of Included Studies

Studies in Humans

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APPENDICES

Appendix 1. Literature Search Strategy

The search terms and databases searched are provided below.

Database	Search Terms
Cochrane Library	(sarin or zarin or "o Isopropylmethyl Phosphonofluoridate" or "ortho Isopropylmethyl Phosphonofluoridate" or "ortho-Isopropylmethyl Phosphonofluoridate" or "Isopropyl methylphosphonofluoridate" or "Isopropyl Methylfluorophosphonate" or "(RS)-propan-2-yl methylphosphonofluoridate" or (GB and organophos*) or (GB and nerve)):ti,ab,kw
Embase	'sarin':ab,ti OR 'sarin'/exp OR 'o isopropylmethyl phosphonofluoridate':ab,ti OR 'ortho isopropylmethyl phosphonofluoridate':ab,ti OR 'ortho-isopropylmethyl phosphonofluoridate':ab,ti OR 'isopropyl methylphosphonofluoridate'/exp OR 'isopropyl methylphosphonofluoridate':ab,ti OR 'isopropyl methylfluorophosphonate':ab,ti OR '(rs)-propan-2-yl methylphosphonofluoridate':ab,ti OR (gb:ab,ti AND organophos*:ab,ti) OR (gb:ab,ti AND nerve:ab,ti)
NIOSHTIC-2 Publications	Sarin[title] OR sarin[abstract] OR zarin[title] OR zarin[abstract]
NIOSHTIC-2 Publications	GB[abstract] AND nerve[abstract]
NIOSHTIC-2 Publications	GB[title] AND nerve[title]
NIOSHTIC-2 Publications	GB[abstract] AND organophos*[abstract]
NIOSHTIC-2 Publications	GB[title] AND organophos*[title]
PubMed/MEDLINE	(sarin[tiab] OR sarin[mesh] OR zarin[tiab] OR "o Isopropylmethyl Phosphonofluoridate"[tiab] OR "ortho Isopropylmethyl Phosphonofluoridate"[tiab] OR "ortho-Isopropylmethyl Phosphonofluoridate"[tiab] OR "Isopropyl methylphosphonofluoridate"[tiab] OR "Isopropyl Methylfluorophosphonate"[tiab] OR "(RS)-propan-2-yl methylphosphonofluoridate"[tiab] OR (GB[tiab] AND organophos*[tiab]) OR (GB[tiab] AND nerve[tiab]))
Scopus	Title-Abs-Key((sarin OR zarin OR {o Isopropylmethyl Phosphonofluoridate} OR {ortho Isopropylmethyl Phosphonofluoridate} OR {ortho-Isopropylmethyl Phosphonofluoridate} OR {Isopropyl methylphosphonofluoridate} OR {Isopropyl Methylfluorophosphonate} OR {(RS)-propan-2-yl methylphosphonofluoridate} OR (GB AND organophos*) OR (GB AND nerve)))
TOXLINE	Title: sarin[ti] OR sarin[mh] OR zarin[ti] OR "o Isopropylmethyl Phosphonofluoridate"[ti] OR "ortho Isopropylmethyl Phosphonofluoridate"[ti] OR "ortho-Isopropylmethyl

Database	Search Terms
	Phosphonofluoridate"[ti] OR "Isopropyl methylphosphonofluoridate"[ti] OR "Isopropyl Methylfluorophosphonate"[ti] OR "(RS)-propan-2-yl methylphosphonofluoridate"[ti] OR (GB[ti] AND organophos*[ti]) OR (GB[ti] AND nerve[ti])
Toxline	Abstract: sarin[ab] OR sarin[mh] OR zarin[ab] OR "o Isopropylmethyl Phosphonofluoridate"[ab] OR "ortho Isopropylmethyl Phosphonofluoridate"[ab] OR "ortho-Isopropylmethyl Phosphonofluoridate"[ab] OR "Isopropyl methylphosphonofluoridate"[ab] OR "Isopropyl Methylfluorophosphonate"[ab] OR "(RS)-propan-2-yl methylphosphonofluoridate"[ab] OR (GB[ab] AND organophos*[ab]) OR (GB[ab] AND nerve[ab])
Web of Science	TS=(sarin OR zarin OR "o Isopropylmethyl Phosphonofluoridate" OR "ortho Isopropylmethyl Phosphonofluoridate" OR "ortho-Isopropylmethyl Phosphonofluoridate" OR "Isopropyl methylphosphonofluoridate" OR "Isopropyl Methylfluorophosphonate" OR "(RS)-propan-2-yl methylphosphonofluoridate" OR (GB AND organophos*) OR (GB AND nerve))