

Actions from Peer Review of the Draft NTP Monograph on the Systematic Review of Long-Term Neurological Effects Following Acute Exposure to the Organophosphorus Nerve Agent Sarin

February 4, 2019

The National Toxicology Program (NTP) convened a Peer Review Panel (“the Panel”) via webcast on February 4, 2019, to peer review the *Draft NTP Monograph on the Systematic Review of Long-Term Neurological Effects Following Acute Exposure to the Organophosphorus Nerve Agent Sarin*. Meeting information, including the draft monograph, is currently archived under NTP’s [“Past Events.”](#)¹ A meeting report will be prepared and posted to the NTP website when completed.

The [Panel](#)² peer reviewed the draft monograph and provided its opinion on NTP’s preliminary level of evidence conclusions and hazard identification conclusions on long-term neurological effects following acute sarin exposure. NTP will consider the Panel’s peer-review comments in finalizing the monograph. When completed, the monograph will be published on the [NTP website](#).³

Preliminary Level of Evidence Conclusions

Cholinesterase Levels: Animal Studies

- The Panel voted to accept (5 yes, 2 no, 0 abstentions) the level of evidence conclusion as written: the scientific evidence from experimental animal studies for a decrease in cholinesterase levels during the initial time period (>24 hours to 7 days) after acute sarin exposure supports a ***moderate level of evidence***.
- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion as written: the scientific evidence from experimental animal studies for a decrease in cholinesterase levels during the intermediate time period (8 days to 1 year) after acute sarin exposure supports a ***moderate level of evidence***.
- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion as written: the lack of scientific evidence from experimental animal studies for changes in cholinesterase levels during the extended time period (>1 year) after acute sarin exposure supports an ***inadequate level of evidence***.

Cholinesterase Levels: Human Studies

- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion as written: the scientific evidence from human studies for a decrease in cholinesterase levels during the initial time period (>24 hours to 7 days) after acute sarin exposure supports a ***high level of evidence***.
- The Panel recommended unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion with the following marked changes: the scientific evidence from human studies for changes in cholinesterase levels during the intermediate time period (8 days to 1 year) after acute sarin exposure supports a ***moderate low level of evidence***.
- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion as written: the lack of scientific evidence from human studies for changes in

¹ <https://ntp.niehs.nih.gov/go/meeting>

² https://ntp.niehs.nih.gov/ntp/about_ntp/monopeerrvw/2019/february/rosterdmp20190204_508.pdf

³ <https://ntp.niehs.nih.gov/go/sarin>

cholinesterase levels during the extended time period (>1 year) after acute sarin exposure supports an ***inadequate level of evidence***.

Visual and Ocular Effects: Animal Studies

- The Panel voted to accept (5 yes, 2 no, 0 abstentions) the level of evidence conclusion as written: the lack of scientific evidence from experimental animal studies for visual and ocular effects during the initial time period (>24 hours to 7 days) after acute sarin exposure supports an ***inadequate level of evidence***.
- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion as written: the lack of scientific evidence from experimental animal studies for visual and ocular effects during the intermediate time period (8 days to 1 year) after acute sarin exposure supports an ***inadequate level of evidence***.
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Learning, Memory, and Intelligence: Animal Studies

- The Panel recommended unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion with the following marked change: the scientific evidence from experimental animal studies for effects on learning, memory, and intelligence during the initial time period (>24 hours to 7 days) after acute sarin exposure supports a ***moderate low level of evidence***.
- The Panel recommended unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion with the following marked change: the scientific evidence from experimental animal studies for effects on learning, memory, and intelligence during the intermediate time period (8 days to 1 year) after acute sarin exposure supports a ***moderate low level of evidence***.
- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion as written: the scientific evidence from experimental animal studies for effects on learning, memory, and intelligence during the extended time period (>1 year) after acute sarin exposure supports a ***low level of evidence***.

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memory, and intelligence during the initial time period (>24 hours to 7 days) after acute sarin exposure supports an ***inadequate level of evidence***.

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Nervous System Morphological and Histological Changes: Animal Studies

- The Panel voted to accept (5 yes, 2 no, 0 abstentions) the level of evidence conclusion as written: the scientific evidence from experimental animal studies for nervous system morphological and histological changes during the initial time period (>24 hours to 7 days) after acute sarin exposure supports a ***moderate level of evidence***.
- The Panel voted to accept (5 yes, 2 no, 0 abstentions) the level of evidence conclusion as written: the scientific evidence from experimental animal studies for nervous system morphological and histological changes during the intermediate time period (8 days to 1 year) after acute sarin exposure supports a ***moderate level of evidence***.
- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the level of evidence conclusion as written: the lack of scientific evidence from experimental animal studies for nervous system morphological and histological changes during the extended time period (>1 year) after acute sarin exposure supports an ***inadequate level of evidence***.

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Other Outcomes That Did not Reach Hazard Conclusions

- The Panel concurred with the statement that the evidence from both the human and animal studies of sleep disruption, anxiety and fear, avoidance and depression, activity/strength, other neurological symptoms, electroencephalogram, and other sensory effects after acute sarin exposure supports ***inadequate or low levels of evidence*** due to fewer studies, inconsistency in findings, heterogeneity of data, and study limitations.

Preliminary Hazard Identification Conclusions

- The Panel voted to accept unanimously (7 yes, 0 no, 0 abstentions) the hazard identification conclusion as written: for the initial time period (>24 hours to 7 days) following acute sarin exposure, sarin is ***known to be a neurological hazard to humans*** based on suppression of cholinesterase which indicates nervous system disruption via acetylcholine build up.
- The Panel voted to accept (6 yes, 1 no, 0 abstentions) the hazard identification conclusion with the following marked change: for the intermediate time period (8 days to 1 year) following acute sarin exposure, sarin is ***suspected to be a neurological hazard to humans*** based on multiple effects including suppression of cholinesterase, visual and ocular effects, ~~effects on learning and memory~~, and morphological and histological changes in nervous system tissues.
- The Panel voted to accept (6 yes, 1 no, 0 abstentions) the hazard identification conclusion as written: for the extended time period (>1 year) following acute sarin exposure, sarin is ***suspected to be a neurological hazard to humans*** based on multiple effects including effects on learning and memory, and morphological and histological changes in nervous system tissues.