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Molybdenum toxicology & ecotoxicology

IMO A list of best available science: recent guideline-compliant and GLP studies, technical dossiers, reviews & assessment reports

The entry into force in 2006 of the EU REACH Regulation about hazard identification and risk assessment of chemical substances was the principal driver for IMO A and its Molybdenum Consortium¹ to extensively gather and review information about the toxicology and ecotoxicology of molybdenum compounds. Much of the earlier literature reporting experimental studies of molybdenum toxicity was found to be contradictory and incomplete (e.g. failing to unambiguously characterise test substances, conditions, procedures and analyses). To overcome such deficiencies and uncertainties, and to provide well founded, reliable and objective data for the community, over the circa last two decades IMO A has initiated and continues to support new studies that are conducted according to contemporary & internationally recognised guidelines (e.g. OECD), and subsequently also publishes such studies in peer-reviewed scientific journals.

This document provides references and links to pertinent recent research on the toxicology and ecotoxicology of molybdenum compounds. It includes OECD protocol-compliant studies, subsequently peer-review published, and recent reviews, monographs and assessment reports from the scientific and regulatory community, e.g. by US ATSDR, OECD, IARC, Health Canada, "Patty's Toxicology", "Ullmann's Encyclopedia". (The vastly outdated 1992 US IRIS database for molybdenum is intentionally absent).

Technical dossiers, reviews and assessment reports:

- The EU REACH Molybdenum Consortium has updated the registration dossiers for several molybdenum compounds in 2021, and non-confidential data from these dossiers is publicly available via the website of the European Chemicals Agency:
<https://echa.europa.eu/information-on-chemicals/registered-substances>
- US ATSDR, 2020. Toxicological Profile for Molybdenum. Agency for Toxic Substances and Disease Registry (ATSDR). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Open Access: <https://www.atsdr.cdc.gov/toxprofiles/tp212.pdf>
- Ullmann's Encyclopedia of Industrial Chemistry (7th Ed., 2020) contains a recently updated comprehensive review on molybdenum compounds, their chemistry and uses.
https://onlinelibrary.wiley.com/doi/10.1002/14356007.a16_655.pub2
- In 2020, Health Canada conducted screening assessments and concluded that MoS₂ and

¹ IMO A (www.imoa.info) was founded in 1989 as a non-profit trade association with scientific purposes. It represents 85% of western world production facilities and all western world molybdenum conversion facilities. IMO A works to raise awareness about the unique properties of molybdenum; its beneficial effects on materials performance; its bio-essentiality for humans, plants and animals; its safety in use and its contribution to sustainable development. Amongst IMO A's core activities is an extensive program lead by the Association's Health, Safety and Environmental (HSE) Committee to develop robust scientific data concerning the impact of molybdenum ("moly" or "Mo") on human health and the environment. IMO A established a consortium ("MoCon") in 2007, still fully operational today, to comply with the extensive hazard and risk data requirements of the European Union's REACH Regulation No. 1907/2006 (<https://www.molybdenumconsortium.org/>).

MoO₃ are identified as being of low concern using the ecological risk classification of inorganic substances and three human health science approaches. Open Access: <https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/screening-assessment-substances-low-concern.html>

- 2013 OECD SIDS on “Highly Soluble Molybdenum Salts” with Mutual Acceptance of Data (MAD) status. Open Access: http://webnet.oecd.org/HPV/UI/SIDS_Details.aspx?id=5c88d62f-4401-4cad-b521-521a4bd710f3
A key point about an OECD SIDS dataset, such as this molybdate effects dataset, is that it acts as the starting point for OECD-member regulatory reviews, as its content has been reviewed and quality-endorsed by a panel of multiple OECD-member state member scientists. Specifically Japan was a review panel member, together with Australia, Canada, Netherlands, UK and USA.
- Patty’s Toxicology, 2023. Molybdenum Chapter. Klipsch K., Aveyard L., Carey S., Hubbard S., Levy L., Mitchell P. Purchase from: <https://doi.org/10.1002/0471125474.tox161>

Toxicology / human health – peer-reviewed publications:

- Burzlaff, A., Beevers, C., Pearce, H., Lloyd, M., Klipsch, K., 2017. New studies on the *in vitro* genotoxicity of sodium molybdate and their impact on the overall assessment of the genotoxicity of molybdenum substances. *Regulatory Toxicology and Pharmacology* 86, 279–291. Open Access: <https://doi.org/10.1016/j.yrtph.2017.03.018>
- Following up on three *in vitro* studies described in Burzlaff et al. (2017, see above), in 2020 IMO A commissioned an *in vivo* micronucleus assay of sodium molybdate by oral gavage in rats (OECD TG 474). The study result was negative. The study report can be provided upon request. A publication in a peer-reviewed journal is planned.
- Murray, F.J., Sullivan, F.M., Tiwary, A.K., Carey, S., 2014. 90-Day subchronic toxicity study of sodium molybdate dihydrate in rats. *Regulatory Toxicology and Pharmacology* 70, 579–588. Open access: <https://doi.org/10.1016/j.yrtph.2013.09.003>
- Murray, F.J., Tyl, R.W., Sullivan, F.M., Tiwary, A.K., Carey, S., 2014. Developmental toxicity study of sodium molybdate dihydrate administered in the diet to Sprague Dawley rats. *Reproductive Toxicology* 49, 202–208. Open Access: <https://doi.org/10.1016/j.reprotox.2014.09.001>
(Note: this publication describes an OECD TG 414 compliant prenatal developmental toxicity study of molybdenum (as sodium molybdate via diet) at up to 40 mg Mo/kg bw/day. No adverse effects were observed at any dose level on the dams, or on embryofetal survival, fetal bodyweight, or development, with no increase in malformations or variations. This study was recently extended to a top dose of 120 mg Mo/kg bw/day, the maximum tolerated dose in pregnant female rats, resulting in an unbounded NOAEL for developmental abnormalities and irreversible foetal effects of > 120 mg Mo/kg bw/day (> 300 mg sodium molybdate dihydrate /kg bw/day). See bullet point below for the 2023 peer-reviewed publication.
- Aveyard L., Murray F.J., Hubbard S.A., Hoberman A.M., Carey S., 2023. OECD 414 Supplementary Prenatal Developmental Toxicity Study of Sodium Molybdate Dihydrate in the Rat, and Benchmark Dose Evaluation. *Reproductive Toxicology*, Vol. 120, September 2023, 108443. Open Access: [https://authors.elsevier.com/sd/article/S0890-6238\(23\)00117-X](https://authors.elsevier.com/sd/article/S0890-6238(23)00117-X)
- Murray F.J., Aveyard L., Hubbard S.A., Hoberman A.M., Carey S., 2023. Sodium Molybdate Dihydrate does not exhibit Prenatal Developmental Toxicity or Reproductive Toxicity in Sprague-Dawley Rats maintained on a Marginal Copper Diet. *Reproductive Toxicology*, Vol

120, September 2023, 108442. Open Access: [https://authors.elsevier.com/sd/article/S0890-6238\(23\)00116-8](https://authors.elsevier.com/sd/article/S0890-6238(23)00116-8)

- Murray, F.J., Sullivan, F.M., Hubbard, S.A., Hoberman, A.M., Carey, S., 2019. A two-generation reproductive toxicity study of sodium molybdate dihydrate administered in drinking water or diet to Sprague-Dawley rats. *Reproductive Toxicology* 84, 75–92. Open Access: <https://doi.org/10.1016/j.reprotox.2018.11.004>
- International Agency for Research on Cancer (IARC), 2018. Welding, molybdenum trioxide, and indium tin oxide, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Open Access: <https://publications.iarc.fr/569>. Molybdenum trioxide (CAS 1313-27-5) is ranked by IARC as “Possibly carcinogenic to humans (Group 2B)”. In the EU since 2009, based on UN GHS, it has the broadly similar EU harmonized hazard classification of Carcinogen Category 2 (H351: Suspected of causing cancer).
- Molybdenum, Essentiality & Human Health: https://www.imoa.info/molybdenum-media-centre/molybdenum_videos.php

Ecotoxicity – peer-reviewed publications:

- K.A.C. De Schampelaere, W. Stubblefield, P. Rodriguez, K. Vleminckx, C.R. Janssen (2010): The chronic toxicity of molybdate to freshwater organisms. I. Generating reliable effects data. *Science of The Total Environment*, Volume 408, Issue 22, Pages 5362-5371. <https://doi.org/10.1016/j.scitotenv.2010.07.041>.
- D.G. Heijerick, L. Regoli, W. Stubblefield (2012): The chronic toxicity of molybdate to marine organisms. I. Generating reliable effects data. *Science of The Total Environment*, Volume 430, Pages 260-269. <https://doi.org/10.1016/j.scitotenv.2012.03.045>
- D.G. Heijerick, L. Regoli, S. Carey (2012): The toxicity of molybdate to freshwater and marine organisms. II. Effects assessment of molybdate in the aquatic environment under REACH, *Science of The Total Environment*, Volumes 435–436, Pages 179-187. <https://doi.org/10.1016/j.scitotenv.2012.05.075>
- D.G. Heijerick, S. Carey (2017): The toxicity of molybdate to freshwater and marine organisms. III. Generating additional chronic toxicity data for the refinement of safe environmental exposure concentrations in the US and Europe. *Science of The Total Environment*, Volume 609, Pages 420-428. <https://doi.org/10.1016/j.scitotenv.2017.07.070>

Note: In order not to breach copyright rules IMO A cannot supply copies of these publications but several of them are free/open-access and can be obtained directly on-line using the links and references above (or purchased in electronic format).

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