INTERNATIONAL MOLYBDENUM ASSOCIATION
THE VOICE OF THE MOLYBDENUM INDUSTRY

9 September 2016

TO: Washington State Department of Ecology

AT: Kara Steward

FR: International Molybdenum Association

RE: Molybdenum and compounds – Request to consider removal from the CPSR CHCC list

The International Molybdenum Association (IMOA), based in the UK, with worldwide membership including several US molybdenum producers and processors, is aware from a recent ListServ communication that Washington State Department of Ecology (ECY) is embarking upon a review of its 2009 Children's Safe Products Reporting Rule. This submission is a request to remove molybdenum and compounds from the current CHCC list, for the reasons given in this document. A chemical should only be placed on the CHCC list if there is "credible scientific evidence" of specific adverse effects such as harm to the normal development of a fetus or child, reproductive harm, or damage to immune or nervous systems.

Background:

In November 2015 IMOA representatives, Sandra Carey and Jay Murray, met with Carol Kraege and Joshua Grice of ECY to put forward the principal scientific reasons why molybdenum & compounds should not continue to be included in the high priority list of chemicals of high concern to children. At that meeting ECY shared with us their 2009 'include in list' rationale, summarized below:

Toxicity: *Reprotext database B ranking for reproductive toxicity*

Exposure: *Found in Danish EPA reports about presence in a Child Product*

Potential for Population Exposure: Chemical found in the NHANES biomonitoring studies

Rationale for removal from CHCC list:

Reprotext is a subscription-based database, hence not one that is freely or publicly available, hindering transparency of information and peer review. For molybdenum, the most recent entries and assessment for reproductive toxicity is 1972, which now, over 40 years later, is on a basis that would not even be considered worthy for 'initial screening' status. ECY indicated that whilst it was

'somewhere to start' back in 2009, they were now less inclined to retain this reference source as a criterion in their upcoming review of the CHCC list, particularly given the absence of transparency.

- Importantly, significant new data is available since 2011, in the form of two OECD protocol-compliant GLP studies, conducted in the USA, that have been published and should be included in any assessment of the toxicology of molybdenum and its compounds. Both studies are summarised in the table below, are peer-reviewed publications, and are available on-line on an Open Access basis (i.e. free to download from the links in the table). The 90-day oral repeated dose toxicity study OECD TG 408, was extended to include additional reproductive toxicity parameters from OECD TG 416:

Study type	Key findings	Reference
90-day oral repeated dose toxicity study, acc. OECD TG 408, under GLP. The test item disodium molybdate dihydrate was administered via feed to male and female rats at doses equivalent to 5, 17 and 60 mg/kg$_{bw}$/day of molybdenum. The study includes **additional parameters from OECD TG 416** on reproductive toxicity (vaginal cytology, oestrous cycle, sperm parameters (count, motility and morphology, testicular spermatid counts), and also includes a 60 day recovery phase.	Reduced bodyweight gains were observed only in the 60 mg Mo/kg bw/day dose group. The effect was more pronounced in males, which was partly due to a slightly reduced food intake and partly due to reduced food conversion efficiency. During the recovery phase food consumption in the 60 mg/kg bw/day males and females returned to a value comparable to the control animals. Light microscopic evaluation of control and 60 mg Mo/kg bw/day animals showed test item-related findings in the kidneys (slight diffuse hyperplasia of the proximal tubules) of two 60 mg Mo/kg bw/day females. No such findings were reported for the animals after the 60-day recovery phase. The **NOAEL for general toxicity was 17 mg Mo/kg bw/day** based on the effects on body weights and kidneys seen at 60 mg Mo/kg bw/day. **The NOAEL for effects on reproductive organs, sperm and oestrous cycle is 60 mg Mo/kg bw/day**. There were no test substance related changes in the male or female reproductive tissues (testes, epididymis, prostate, seminal vesicles, ovaries, uterus or vagina). There were no test substance-related effects on vaginal cytology and oestrous cycles during weeks 7-9 of the dosing phase (i.e., the period during which vaginal cytology and oestrous cycles were evaluated). No test-item related changes in organ weight of testes or secondary sex organs and no effect on spermatid or sperm counts,	F. Jay Murray, Frank M. Sullivan, Asheesh K. Tiwary, Sandra Carey, 90-Day subchronic toxicity study of sodium molybdate dihydrate in rats, Regulatory Toxicology and Pharmacology, Volume 70, Issue 3, December 2014, Pages 579-588, ISSN 0273-2300, http://dx.doi.org/10.1016/j.yrtph.2013.09.003 or http://www.sciencedirect.com/science/article/pii/S0273230013001487

	motility or morphology were observed. All other recorded microscopic findings were considered incidental and unrelated to administration of disodium molybdate dihydrate. They occurred at similar incidences in the control and test substance treated groups or they were sporadic with no relationship to dose.	
Prenatal developmental toxicity study, acc to OECD TG 414, under GLP. The test item disodium molybdate dihydrate was administered via feed to pregnant female rats during gestational days 6 through 20, in four dose groups (ca. 3, 10, 20 and 40 mg Mo/kg bw/day).	There were no treatment or dose-related effects on maternal body weights, weight changes, feed consumption in grams/day or grams/kg, body weight/day, or on maternal clinical observations, pregnancy indices, or maternal organ weights at any dose. There were also no biological or statistical differences among groups for the numbers of ovarian corpora lutea/female, for uterine implantation sites, or for uterine implantation losses per female at any dose. Statistically significantly increased copper levels in kidneys and livers were observed at 40 mg Mo/kg bw/day, but not at 20 mg Mo/kg bw/day. Therefore, the **NOAEL for maternal toxicity is 40 mg Mo/kg bw/day**, and the NOEL for maternal toxicity is 20 mg Mo/kg bw/day. There were no biological or statistical differences among groups for the numbers of foetuses, foetal sex ratios, foetal body weights, foetal external, visceral or skeletal malformations or variations per female at any dose. The incidences of the few foetal malformations and the more common foetal variations observed in the study were comparable to the historical control database of the laboratory on this rat strain and supplier. The foetal effects in this study also did not exhibit any treatment- or dose- related pattern of increased incidences and/or severities. **The NOAEL for developmental toxicity is therefore 40 mg Mo/kg bw/day**.	F. Jay Murray, Rochelle W. Tyl, Frank M. Sullivan, Asheesh K. Tiwary, Sandra Carey, Developmental toxicity study of sodium molybdate dihydrate administered in the diet to Sprague Dawley rats, Reproductive Toxicology, Volume 49, November 2014, Pages 202-208, ISSN 0890-6238. http://dx.doi.org/10.1016/j.reprotox.2014.09.001 or http://www.sciencedirect.com/science/article/pii/S089062381400238X

- The above summary is an extract from the OECD-agreed effects dataset (phys-chem, human health and environment sections) on highly soluble molybdenum salts that is accredited by the OECD for its Mutual Acceptance of Data (MAD) status, and publicly available since early 2014. Such status is an endorsement of the scientific quality of the dataset after independent review by scientists from OECD member countries that participate in the Cooperative Chemicals Assessment Program (CoCAM). In the case of the molybdate effects dataset, it was reviewed by CoCAM scientists from the USA, as well as from Australia,

Canada, Japan, The Netherlands and the United Kingdom. MAD status means the dataset is the starting point to be taken into consideration whenever OECD member countries draft or review regulations about this substance. The USA is an OECD member country, hence its relevance to the Washington State legislation in question.

For your ease of reference, the highly soluble molybdenum salts dataset summary, called a SIAP (SIDS Initial Assessment Profile), is attached to this submission. It is also published under the auspices of United Nations on the OECD website on this webpage: http://webnet.oecd.org/HPV/UI/SIDS_Details.aspx?id=5c88d62f-4401-4cad-b521-521a4bd710f3

The SIAP concludes: *"For the molybdenum salts category substances adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme. No health hazards have been identified for acute toxicity, irritation, sensitisation, mutagenicity, reproductive toxicity and carcinogenicity. A health hazard for repeated dose toxicity cannot be ruled out for the three category substances based on effects observed at the highest tested dose of 60 mg Mo/kg bw/day in a 90-day oral toxicity study conducted with the test substance sodium molybdate dihydrate. Taking into account the low degree of severity of the observed effects, it is concluded that the category substances have a low repeated dose toxicity hazard. "*

- Recent and publicly available information about molybdenum & compounds, in the context of their hazard and risk assessment for compliance with the chemicals management EU REACH Regulation (EC No. 1907/2006) can be found on the website of the European Chemicals Agency: http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances . You will doubtless therefore be interested to access the entries on molybdenum, soluble and less soluble molybdenum compounds. A read-across approach is used where the most soluble molybdenum compound (sodium molybdate dihydrate) is tested to generate molybdate effects data on the toxicology endpoints, and then the data is read-across, where appropriate, to the progressively less soluble molybdenum substances. The molybdate effects dataset submitted by the International Molybdenum Association for EU REACH is the same one that received OECD Mutual Acceptance of Data status. There is no reproductive hazard conclusion, and neither is there any EU-wide harmonised reproductive hazard classification under Annex VI of the EU Classification, Labelling and Packaging Directive (which enshrines GHS into EU legislation).

- The negligible risk of health effects to be caused by molybdenum has also been reflected in the World Health Organisation Guidelines for Drinking Water Quality, which since 2011 no longer establishes a formal guideline value for molybdenum in drinking water. Only for guidance purposes is a health-based value of 0.07 mg Mo/L indicated. The rationale for not deriving a formal guidance value is indicated as: '(Molybdenum) occurs in drinking water at

concentrations well below those of health concern'. (Reference: pages 177 & 394 of The World Health Organization Guidelines for Drinking-Water Quality, Fourth Edition, 2011. ISBN 978 92 4 154815 1). The US Environmental Protection Agency has not established a drinking water standard for molybdenum and for guidance purposes published a Lifetime Health Advisory value of 0.04 mg Mo/L.

- The rationale given by Washington State refers to a publication by Meeker et al. (2008) that "reported an inverse association between background levels of molybdenum exposure in men and sperm quality and concentration". It is an exercise in statistical tests of many possible associations. The same paper, however, finds no association between Pb in blood of men and semen quality, when Pb is a known reproductive toxicant. The statistical methodology used by Meeker et al. has been critiqued by other scientists, who question the existence of any robust basis for the reported suggestive findings, and that the latter have been over-stated by the authors. See Sorahan, T. and Sullivan, F.M.: (2009): Molybdenum Exposure and Semen Quality: How Robust Is the Evidence of an Effect? - Environ. Health Perspectives 117(9), Issue 9 (open access: http://ehp.niehs.nih.gov/0900922/). IMOA requested Dr. Meeker to share his raw data for review, or to make the original samples available for analysis with a better Limit of Detection (since 70% of the samples in his study were below the LoD), but both requests were declined.

- With regard to exposure in terms of presence in a children's product, the rationale given by Washington State is the statement that "Molybdenum was found in a pencil case and school bags in testing of children's school supplies by the Danish EPA".
  Having reviewed the full report by the Danish EPA[1], it is important to be aware that:
  - (i) Molybdenum was not at all identified by the Danish EPA as a substance of concern in children's school supplies. The focus of the survey was on other organic chemicals and some metals for which toxicity concerns have clearly been established, like DEHP, DINP, lead, nickel and cadmium.
  - (ii) molybdenum only features at all in the report because samples underwent a multi-element-screening analysis using X-Ray-Fluorescence analysis, which covers almost the complete periodic table of elements.
  - (iii) 28 samples were analyzed for molybdenum, and molybdenum was below the detection limit in 24 of those samples. The detection limits are in the range of 0.1-3.5 µg/g. In three samples (one from a pencil case and two from the same school bag), molybdenum was quantifiable above detection limit (DL), but was very close to the DL at 3.2, 2.2 and 4.5 µg/g, i.e. below 0.0005 %. In only one sample from a school bag (not further described), molybdenum was detected at a concentration clearly above the detection limit, at 36.8 µg/g or 0.00368 % - a still miniscule amount.

[1] Available for download at: http://www.mst.dk/service/publikationer/publikationsarkiv/2007/aug/survey-as-well-as-health-assessment-of-chemical-substances-in-school-bags,-toy-bags,-pencil-cases-and-erasers/

- Molybdenum is an *essential trace element for humans* and mammals and plants. Molybdenum-containing enzymes catalyse redox reactions and are found in many plants and animal organisms. In animals and humans, sulphite oxidase, xanthine oxidoreductase, aldehyde oxidase and mitochondrial amidoxime reducing components require molybdenum linked with a pterin (molybdopterin) as the cofactor. Certain intake levels of molybdenum are therefore essential and indispensable for humans to ensure a normal physiological function. Molybdenum does and *should* feature in the US NHANES biomonitoring data for this reason. The European Food Safety Authority has concluded that "Molybdenum is efficiently and rapidly absorbed at a wide range of intakes, and the body is able to maintain homeostasis through the regulation of excretion via the urine. … Storage of molybdenum in mammals is low, and most tissue molybdenum is thought to be associated with molybdoenzymes." [2] As an essential element, and given that homeostasis prevents accumulation in the body, molybdenum is a frequent constituent of over-the-counter essential vitamin and mineral supplements.

- The Food and Nutrition Board (FNB) at the US Institute of Medicine has established Estimated Average Requirements (EAR) for molybdenum ranging from 13 µg Mo/day for children 1-3 years of age to 34 µg Mo/day for adults. These are minimum intake levels understood to be required to maintain a normal physiological function. For comparison, Upper Intake Levels (UL) have also been established by the FNB in 2001, indicating that a molybdenum intake of 0.6 mg/day (600 µg/day) is considered safe for example for Children 4-8 years of age. For more details see http://www.nap.edu/catalog/10026/dietary-reference-intakes-for-vitamin-a-vitamin-k-arsenic-boron-chromium-copper-iodine-iron-manganese-molybdenum-nickel-silicon-vanadium-and-zinc

- Most recently, in September 2015, the US Dept. of Health and Human Services, Food and Drug Administration (FDA) derived Permitted Daily Exposure (PDE) values for molybdenum, that it considers to be protective of human health for all patient populations[3]:

MOLYBDENUM

Summary of PDE for Molybdenum

Molybdenum (Mo)			
	Oral	Parenteral	Inhalation
PDE (µg/day)	3400	1700	11

[2] Scientific Opinion on Dietary Reference Values for molybdenum. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA), European Food Safety Authority (EFSA), Parma, Italy. EFSA Journal 2013;11(8):3333

[3] Q3D Elemental Impurities, Guidance for Industry, US Dept. of Health and Human Services, Food and Drug Administration, September 2015: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm371025.pdf

This FDA document uses the Murray et al (2014) 90-day repeat dose toxicity study (page 2 of this document) as a key study.

- On the point that molybdenum is not at the lower end of Washington State's reporting frequency, it would be incorrect to automatically correlate that with an adverse exposure risk. In fact a high percentage of occurrence is reported as 'Contaminant – no function'. The explanation is that molybdenum can be found in metals for retail applications because metals are fully recyclable and so a molybdenum-containing metal can be a component of the recycled feedstock for producing 'new' steels and alloys. Bound in a steel/alloy matrix at macroscopic level it is not bio-available to any significant extent and does not constitute an adverse exposure risk.

- Through recent dialogue with the EPA Office of Water (Dr. Joyce Donohue) in Washington D.C., we are aware that the EPA Molybdenum Health Advisory has been updated in draft form, to take into account an assessment of the most recent robust scientific evidence such as the afore-mentioned studies in the OECD MAD dataset. Although the revised Mo Health Advisory is not yet publicly available, Dr. Donohue indicated she would be amenable to providing yourselves with a copy. We would encourage you to contact Dr. Donohue (Email: Donohue.Joyce@epa.gov) to request this document as an authoritative EPA regulatory assessment.

- It is also notable that in the recently published paper 'A Toxicological Framework for the Prioritization of Children's Safe Product Act Data', (April 2016), authored by well-respected scientists such as Professor Elaine Faustmann (University of Washington), molybdenum & compounds scored a zero for reproductive toxicity, and likewise a zero when priority ranking substances for inclusion in the CHCC.

- As expressed in this submission document, IMOA considers the scientific rationale and selection criteria to continue to include molybdenum & compounds in the list of chemicals of concern to be insufficient and now outdated some 7 years after its inception in 2009.

- A point worthy of mention is that without any approach from IMOA, the State of Maine in 2012 did not include molybdenum in any of their 3 tiers of priority lists when implementing similar legislation[4]. They initially sourced the list from Washington State but then performed their own assessments.

- Aware, however, of the evident trend for other US States (e.g. Vermont and Oregon) to adopt similar legislation that imports wholesale the existing Washington State CHCC list, we

[4] http://www.maine.gov/dep/safechem/

consider it is especially incumbent upon Washington State to ensure it rules in accordance with the available robust science, otherwise substances are inappropriately and prejudicially stigmatized. Whilst doubtless an unintentional consequence, it is nevertheless a serious and far-reaching one given the domino effect. The extract below from document OAR-333-016, December 2015 of Oregon Health Authority substantiates this point:

> Ms. Carey's written comments are attached to this report as "Exhibit 8".
>
> **Agency response:**
> The agency thanks Ms. Carey for her comments.
>
> The agency will not be removing molybdenum & compounds from its current draft list as requested. As specified in statute, the initial List of High Priority Chemicals of Concern for Children's Health shall include on the list "chemicals that are listed on the Washington State Department of Ecology's Reporting List of Chemicals of High Concern to Children on the effective date of this 2015 Act." With the inclusion of an Emergency Clause provision in the statute, the Act was effective
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> on July 27, 2015. As of July 27, 2015, molybdenum & compounds were included on the Washington State Department of Ecology's Reporting List of Chemicals of High Concern to Children, therefore requiring molybdenum & compounds to be included on Oregon's initial List of High Priority Chemicals of Concern for Children's Health

When IMOA visited Vermont Dept. of Health (VDoH) in July 2015, it was the same response as Oregon in terms of why molybdenum & compounds was included on their initial list of chemicals of concern, i.e. their legislation required a cut/paste of the Washington State list. Making matters worse, VDoH also indicated it would be approximately 2 years before they put a de-listing request system into place, effectively stymying any recourse to further action and catalysing inappropriate stigmatization of the substances.

Likewise, the communication multiplier effect of the information now being available through the Interstate Chemical Clearing House serves to further intensify stigmatization. It is therefore absolutely critically important that a substance should only be on the CHCC list when robust scientific studies and weight of evidence warrant it.

In conclusion, based on the credible scientific evidence, we respectfully request Washington State Dept. of Ecology to remove molybdenum and compounds from its current CHCC list. IMOA is available and at your disposal to further discuss any aspect of this communication.

Yours faithfully

Sandra Carey
IMOA HSE Executive

Kindly respond to:

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SIDS INITIAL ASSESSMENT PROFILE

Category Name	Highly soluble molybdenum salts
Chemical Name(s) and CAS No(s).	Sodium molybdate: CAS 10102-40-6 for sodium molybdate dihydrate CAS 7631-95-0 for sodium molybdate (anhydrous) Ammonium dimolybdate: CAS 27546-07-2 Ammonium heptamolybdate: CAS 12054-85-2 for ammonium heptamolybdate tetrahydrate CAS 12027-67-7 for ammonium heptamolybdate (anhydrous)
Structural Formula(s)	$Na_2MoO_4 \cdot 2\ H_2O$ Na_2MoO_4 $(NH_4)_2Mo_2O_7$ $(NH_4)_6Mo_7O_{24} \cdot 4\ H_2O$ $(NH_4)_6Mo_7O_{24}$

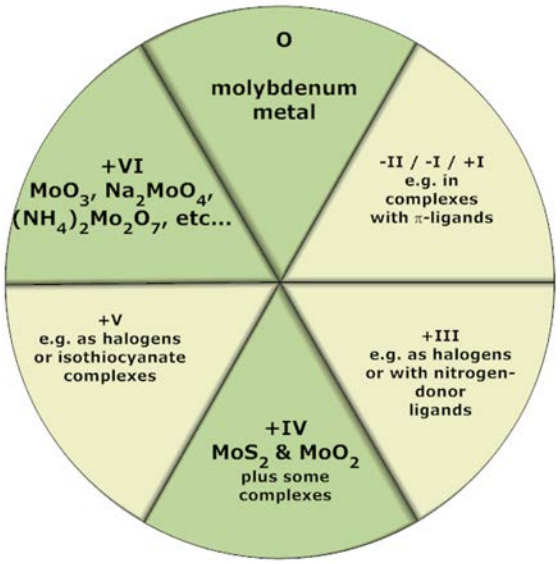
SUMMARY CONCLUSIONS OF THE SIAR

Rationale for molybdenum salts category

The substances included in this category are the higher volume molybdate salts available on the market.

The category is based on a common moiety of concern, the molybdate anion $[MoO_4]^{2-}$. All category members are potential contributors of this moiety. The counter ions of the molybdate salts (i.e. sodium and ammonium), due to their ubiquitous presence in biota and/or their essential role in human physiology, are not addressed further as they are not considered to contribute to any toxicity of the molybdate salts.

The chemistry of molybdenum is complex, allowing a wide range of valences as summarised in the graph below:



Several of these are only stable in isolated complexated form, and only three forms are industrially produced: molybdenum metal (valency 0), MoS_2 and MoO_2 (+IV) and various molybdates as well as MoO_3 (+VI). However, it has been demonstrated that upon dissolution in aquatic media, molybdenum substances of the valency states 0, +IV and +VI transform into the hexavalent molybdate anion.

Environment:

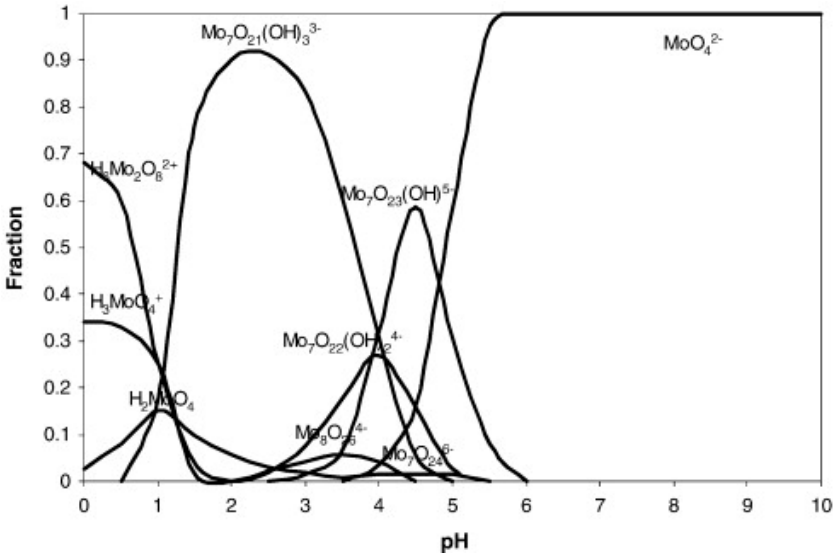
The speciation of molybdenum in aqueous media as a function of pH and molybdenum concentration has been thoroughly investigated and reported upon in open literature. Under environmentally relevant conditions, molybdenum compounds transform rapidly to the molybdate anion, $[MoO_4]^{2-}$, as underpinned by the UV-spectra of aqueous solutions of molybdenum compounds that demonstrate that molybdate is the only dissolved molybdenum species present. Also, under physiological conditions (pH > 6.5), the sole molybdenum species present is the molybdate anion. The derivation of environmental fate data such as adsorption/desorption coefficients and bioconcentration/bioaccumulation factors are based on measured concentrations of dissolved and total molybdenum in water/solids/biological tissues, and reflect the physicochemical and biological properties of the molybdate anion.

Environmental effects testing is conducted using sodium molybdate dihydrate as the model compound given that it is the most soluble, and the results, where appropriate, form the basis of read-across to the endpoints for less soluble substances.

Human Health:

The category includes the three molybdate substances sodium molybdate, ammonium dimolybdate and ammonium heptamolybdate. They are characterised by high water solubility (>> 100 mg/L) and under physiological circumstances will dissociate into the molybdate anion ($[MoO_4]^{2-}$. This is also the species by which molybdenum as an essential trace element is taken up into the body from nutritional sources.

The species in solutions of sodium molybdate at dilute concentrations (i.e. below ca. 10 mg/L) and neutral pH is the molybdate ion, $[MoO_4]^{2-}$; as the pH is lowered, the $[MoO_4]^{2-}$ ion becomes increasingly protonated, yielding $[HMoO_4]^-$ and finally $[H_2MoO_4]$ species. At higher concentrations, the protonated molybdate species are in equilibrium with the heptamolybdate anionic species. The distribution of molybdenum species in aquatic media as a function of pH is shown in the graph below at an exemplary total molybdenum concentration of 21.2 mmol/L. In conclusion, at physiologically relevant concentrations and pH, the only molybdenum species present is the molybdate $[MoO_4]^{2-}$ anion:



The human health hazard assessment addresses a large variety of effects and different exposure patterns (acute/long-term, local/systemic...). In general, for toxic effects requiring systemic uptake of the chemical, grouping is applied for all substances in the category, based on the molybdate anion $[MoO_4]^{2-}$ as the common and only physiologically relevant ion upon dissolution. Molybdate is the form in which molybdenum is taken up into organisms and is present in blood. In most cases the key toxicological studies considered in such chapters on systemic effects have been conducted with the soluble substances sodium molybdate and/or ammonium dimolybdate.

Analogous substance justification

Since the toxicological effects of substances within the category are associated with the release of molybdate anions, in some cases (*repeated dose inhalation toxicity and carcinogenicity*) data on the analogous substance molybdenum trioxide (CAS 1313-27-5) are included, but limited to the assessment of systemic toxicological effects. In this context, it is important to note that molybdenum trioxide is moderately soluble and reacts with water under acidification to molybdate anions as follows:

$$MoO_3 + H_2O \rightarrow [MoO_4]^{2-} + 2\ H^+$$

Based on the above considerations, molybdenum trioxide upon systemic uptake into the body will be present in dissolved form as molybdate anions, and therefore toxicity/toxicokinetic data can be read across from molybdenum trioxide to the category substance for systemic toxicity. Note: for local effects, the strong acidification during the dissolution/dissociation reaction with water is considered to impart the unique irritation potential of molybdenum trioxide, which is not observed with the molybdates encompassed in the category.

Annex 1 of this document is a table identifying the category members and the compounds used for read across for each endpoint.

Physical-chemical Properties

Sodium molybdate is typically marketed as the dihydrate, which is a colourless to white, odourless crystalline powder, with a relative density of 2.59 (measured at 23.3 °C). Upon heating of the hydrated form, water of crystallization is lost and the anhydrous form is formed. The melting point for anhydrous sodium molybdate is reported at 687 °C. The water solubility at 20°C is 654.2 g/L (measured) for sodium molybdate dihydrate, corresponding to 259 g Mo/L.

Ammonium dimolybdate is a white-to-greyish, and odourless powder, with a relative density of 2.97 (measured at 20 °C). Ammonium dimolybdate decomposes from ca. 150 °C (evolution of ammonia). Formation of ammonium octamolybdate takes place from ca. 225 °C, with subsequent calcination to MoO_3 at higher temperatures. Distinct melting or boiling points are not available. The water solubility of ammonium dimolybdate at 20 °C is 228.4 g/L (measured), corresponding to 129 g Mo/L.

Ammonium heptamolybdate is typically marketed as the tetrahydrate, which is a colourless or slightly greenish

or yellowish, odourless, crystalline powder with a relative density of 2.86 (measured at 20 °C). A decomposition temperature of ammonium heptamolybdate of 90 °C is reported in literature. This likely refers to the evolution of water of crystallisation when heating the tetrahydrate form. At higher temperatures, evolution of ammonia is expected. Distinct melting or boiling points are not available. The water solubility of ammonium heptamolybdate tetrahydrate at 20 °C is 206.5 g/L (measured), corresponding to 112 g Mo/L.

Remark: Vapour pressure, Kow and pKa are considered relevant parameters for the fate and effects assessment of organic chemicals only. They are not applicable to metals/inorganics and thus not mentioned above.

Essentiality

Molybdenum is an essential trace element for humans and mammals. Molybdenum-containing enzymes catalyse redox reactions and are found in many plants and animal organisms. In animals and humans, sulphite oxidase, xanthine oxidoreductase, aldehyde oxidase and mitochondrial amidoxime reducing component require molybdenum linked with a pterin (molybdopterin) as the cofactor. In plants, molybdenum is essential to growth as a component of the enzymes nitrate reductase and nitrogenase.

Human Health

Toxicokinetics

The distinction between the highly bioaccessible category substances and other poorly accessible molybdenum substances has been verified in *in vitro* bioaccessibility studies with six different molybdenum substances. Sodium molybdate (representative for the three highly water-soluble category substances) is characterised by high bioaccessibility (60 - 100%), whereas other moderately to poorly soluble molybdenum substances (such as molybdenum metal, molybdenum dioxide and molybdenum disulfide) have shown a low bioaccessibility (less than 1 - 6%). Separate investigations, however, document that upon dissolution, substances with different initial oxidation state of the molybdenum atom(s) all transform to the molybdate anions.

Dermal absorption: in vitro (human skin), the dermal absorption of sodium molybdate has been shown to be low to negligible (ca. 0.2% of the applied dose).

Absorption following ingestion or inhalation: published animal data on the toxicokinetics of molybdenum substances suffer from several shortcomings and are not considered relevant for human health hazard characterisation. However, recently conducted repeated dose animal toxicity studies included blood kinetics, from which a valuable comparison of absorption following inhalation and oral exposures to molybdate substances can be derived. When comparing blood monitoring data from 28d and 90d oral studies with those from a 2yr inhalation study, it is reasonable to assume that molybdate blood levels in rats following inhalation of 100 mg/m^3 molybdenum trioxide (ca. 67 mg Mo/m^3) are similar to those resulting from dietary exposure to 17 - 20 mg Mo/kg bw/d (in the form of sodium molybdate in the diet). These blood values show that molybdenum trioxide administered by inhalation in the NTP study (as 100 mg MoO_3/m^3) was readily absorbed, yielding a systemic molybdate dose comparable to approx. 20 mg Mo/kg bw/d.

Relevant human data on inhalation absorption are not available for any molybdenum-derived substance.

Oral absorption (human data): metabolic ward studies with male human volunteers involving a combination of dietary molybdenum levels (22, 72, 121, 467 and 1,490 µg Mo/d) and dual stable isotope tracer methodology (^{97}Mo/^{100}Mo or ^{95}Mo/^{96}Mo administered either orally or i.v.) yielded the following conclusions:

- the oral absorption of molybdates is in the range of approx. 85% - 93%;

- dietary constituents may play a role in uptake efficiency: whereas oral absorption in fasted subjects is close to 100%, the co-administration in matrices such as solid food or black tea can reduce absorption to as much as 50% and 10%, respectively.

Distribution: Upon uptake, the highly soluble molybdate anions are widely distributed in the body. The highest molybdenum concentrations are found in kidneys, liver and bone. However, there is no apparent accumulation of molybdenum in animal or human tissues.

Metabolism: The highly bioavailable molybdate substances in the category are not subject to metabolism.

Excretion: The elimination of molybdates in humans from plasma is rapid and predominantly via renal excretion (>80%) with less via faeces (<10%); increasing dietary molybdate intake results in elevated absorption but with a concomitant rise in urinary excretion, whereas the fraction of tissue deposition decreased, indicating that the uptake of molybdates is not regulated at the level of absorption, but instead renal elimination

appears to be the most relevant pathway for regulating systemic levels of molybdates.

Metal-metal interactions: using stable Mo/Cu isotopes (^{97}Mo, ^{100}Mo and ^{65}Cu), the influence of molybdate intake on the metabolism of copper was investigated in human depletion/repletion studies: neither did the variation of molybdate dietary intakes (22-1490 µg/d) nor an extended depletion/repletion period have any statistically significant effect on serum or urinary copper levels, and copper absorption and retention was also largely unaltered. Overall, very low or high dietary molybdate intakes up to 1490 µg/d did not influence copper metabolism or copper status when receiving a stable intake of 1.63 mg/ Cu/d for a period of 120 days.

Acute toxicity

Table: available key study data for acute toxicity

Route of administration / endpoint / test guideline	**Test substance**	**Endpoint value**
Inhalation (OECD TG 403)		
LC_{50}, rat(m/f)	Sodium molybdate (anhydrous) Na_2MoO_4	> 1930 mg/m³
LC_{50}, rat(m/f)	Ammonium dimolybdate $(NH_4)_2Mo_2O_7$	> 2080 mg/m³
Dermal (OECD TG 402)		
LD_{50}, dermal, rat (m/f)	Sodium molybdate (anhydrous) Na_2MoO_4	> 2000 mg/kg bw
LD_{50}, dermal, rat, (m/f)	Ammonium dimolybdate $(NH_4)_2Mo_2O_7$	> 2000 mg/kg bw
Oral (OECD TG 401)		
LD_{50}, oral, rat (m/f)	Sodium molybdate (anhydrous) Na_2MoO_4	4233 mg/kg bw
LD_{50}, oral, rat (m/f)	Ammonium dimolybdate $(NH_4)_2Mo_2O_7$	3883 mg/kg bw

In the dermal studies with sodium and ammonium molybdate, there were no signs of systemic reaction to treatment, no indication of dermal irritation and no macroscopic abnormalities upon necropsy. In the acute oral studies with sodium and ammonium dimolybdate, there were no bodyweight changes or macroscopic abnormalities; clinical observations in most animals included pilo-erection, hunched posture, abnormal gait, lethargy and decreased respiratory rate, ptosis and diarrhoea. In the acute inhalation toxicity studies with these two substances, only minor bodyweight losses were observed, but there were neither clinical observations indicative of a response specific to the test material nor any macroscopic or microscopic findings of toxicological relevance.

In conclusion, sodium molybdate and ammonium dimolybdate show low acute toxicity, when taken up via the oral, dermal or inhalation route. Based on the category justification ammonium heptamolybdate is expected to also be of low acute toxicity.

Skin, eye and respiratory irritation

Table: available key study data for skin and eye irritation

Test substance	**Study type**	**Result**
Sodium molybdate (anhydrous) Na_2MoO_4	Skin irritation, *in vivo* (OECD TG 404)	Not irritating
	Eye irritation, *in vivo* (OECD TG 405)	Not irritating
Ammonium dimolybdate $(NH_4)_2Mo_2O_7$	Skin irritation, *in vivo* (OECD TG 404)	Not irritating
	Eye irritation, *in vivo* (OECD TG 405)	Not irritating

Reliable *in vivo* skin and eye irritation studies are available for sodium molybdate and ammonium dimolybdate. These studies demonstrate that these substances are not irritating to skin or eyes. In the absence of endpoint-specific test systems for respiratory irritation, reference is made to acute inhalation toxicity studies

with the category members sodium molybdate and ammonium dimolybdate: no clinical observations were made during exposure or during the subsequent the observation period that would represent test-substance-related signs of respiratory irritation. No macroscopic or microscopic findings indicating irritation were made in the respiratory tract following terminal necropsy. The third substance in the category, ammonium heptamolybdate, is not assumed to be irritating or corrosive to skin, eyes or the respiratory tract either, based on chemical similarity and similar water solubility as ammonium dimolybdate. A saturated solution of ammonium heptamolybdate in water has a pH of 5.8, so that no irritating effects are expected due to extreme acidity or alkalinity values, either.

Skin Sensitisation

Table: available key study data for skin sensitisation

Test substance	**Study type**	**Result**
Sodium molybdate (anhydrous) Na_2MoO_4	Skin sensitisation studies in guinea pigs (maximisation test) (OECD TG 406)	Not sensitizing
Ammonium dimolybdate $(NH_4)_2Mo_2O_7$	Skin sensitisation studies in guinea pigs (maximisation test) (OECD TG 406)	Not sensitizing

Guinea pig maximisation tests with sodium molybdate and ammonium dimolybdate do not indicate a sensitising potential of these substances. It is unlikely that the very similar ammonium heptamolybdate would exhibit sensitising properties. In patch tests on humans with 1% ammonium heptamolybdate in water a very low positive response rate is reported (3 out of 787 patients in 7 years). In conclusion, the substances in the molybdenum salts category do not show a potential for skin sensitisation.

Repeated-dose Toxicity

Table: available key study data for repeated dose toxicity

Test substance	**Study type / details**	**Key results**
Sodium molybdate (dihydrate) $Na_2MoO_4 \cdot 2\ H_2O$	In a 90-day **oral** repeated dose toxicity study, OECD TG 408 with additional parameters from OECD TG 416,which also included a 60 day recovery phase, disodium molybdate was administered to male and female rats at doses of 5, 17 or 60 mg/kg bw/day of Mo (administered as sodium molybdate dihydrate via feed).	Reduced bodyweight gains were observed only in the 60 mg Mo/kg bw/day dose group. The effect was more pronounced in males, which was partly due to a slightly reduced food intake and partly due to reduced food conversion efficiency. During the recovery phase food consumption in the 60 mg/kg bw/day males and females returned to a value comparable to the control animals. Light microscopic evaluation of control and 60 mg Mo/kg bw/day animals showed test item-related findings in the kidneys (slight diffuse hyperplasia of the proximal tubules) of two 60 mg Mo/kg bw/day females. No such findings were reported for the animals after the 60-day recovery phase. Compared to controls, serum copper levels, and liver and kidney copper concentrations, were significantly increased in both males and females in the group given the highest dose of 60 mg Mo/kg bw/day. Without any toxicological or histopathological correlate, these increases are not considered adverse. The **NOAEL was 17 mg Mo/kg bw/day** based on the effects on body weights and kidneys seen at 60 mg Mo/kg bw/day.
Molybdenum trioxide MoO_3	A 13-week **inhalation** toxicity study with molybdenum trioxide in rats	Finding (rats): At all exposure concentrations, no treatment-related effects on mortality, clinical signs, final mean body weights, organ weights,

	and mice (NTP) was in compliance with FDA GLP Regulations, 21 CFR, Part 58. The results are well-documented; historical control data are also included. 10 male + 10 female rats or mice per group were exposed in chambers to 0, 1, 3, 10, 30, 100 mg MoO_3/m^3 for 6.5 hours per day, 5 days per week for 13 weeks. The test substance is characterised as follows: MoO3, purity: ca. 99%, particle size: MMAD (µm) ± GSD in the range from 1.33 ± 1.93 to 1.60 ± 1.83. The NTP also conducted 2-year inhalation studies in rats and mice at 0, 10, 30 and 100 mg MoO_3/m^3. In addition to local effects in the lung, a comprehensive set of systemic end points was studied including body weight changes, reproductive parameters, and full histological evaluation of a wide range of tissues including the reproductive organs.	haematology or clinical chemistry parameters, sperm counts or motility and liver copper concentrations were observed at all concentrations. No treatment-related gross or microscopic lesions were observed. **Thus, the concentration of 100 mg MoO_3/m^3 (corresponding to 66.7 mg Mo/m^3) represents a true NOAEC** in this 13-week inhalation study on rats, since no adverse effects were seen up to and including the highest concentration tested. Findings (mice): There were no adverse treatment-related effects on mortality, clinical signs, final mean body weights, organ weights, haematology or clinical chemistry parameters, and epididymal weights, sperm counts, or motility were observed at any concentrations. Also, no treatment-related gross or microscopic lesions were observed. However, there were significant increases in liver copper concentrations in female mice exposed to 30 mg/m^3 and 100 mg/m^3, as well as in male mice exposed to 100 mg/m^3 compared to those of the control groups; without any toxicological or histopathological correlate, these increases are not considered adverse. Thus, the 13-week inhalation study on mice yields a **NOAEC of 100 mg MoO_3/m^3 (corresponding to 66.7 mg Mo/m^3), and a NOEC of 10 mg MoO_3/m^3 (corresponding to 6.7 mg Mo/m^3).** **In the two year studies in rats and mice,** regarding systemic effects, despite the longer exposure duration, no adverse systemic effects were observed in the 2 year studies in rats and mice and both the 13-week and 2-year inhalation studies resulted in identical NOAECs for systemic toxicity of 100 mg MoO_3/m^3.

Human data has been evaluated and is considered to be of insufficient relevance and/or reliability to derive definitive conclusions on the repeated dose toxicity of molybdenum substances.

The sub-chronic inhalation toxicity study with MoO_3 is applicable to molybdates in so far as the general systemic toxicological effects and parameters can be read across to molybdate salts (see justification for category and analogous substance).

In the 90-day oral toxicity study with sodium molybdate dihydrate effects were observed at the highest dose of 60 mg Mo/kg bw/day (with the NOAEL at the next lower dose at 17 mg Mo/kg bw/day). Therefore, a health hazard for repeated dose toxicity cannot be ruled out for the three category substances. Taking the low degree of severity of the observed effects into account, it is concluded that the category substances have a low repeated dose toxicity hazard.

Genetic Toxicity

In a bacterial reverse mutation assay/Ames test with multiple strains of *Salmonella typhimurium* (OECD TG 471) sodium molybdate dihydrate was negative both with and without metabolic activation. An *in vitro* test on induction of micronuclei in cultured human peripherial blood lymphocites (OECD TG 487) sodium molybdate dihydrate was negative with and without metabolic activation. In an *in vitro* test for mutations at the thymidine kinase (tk) locus of mouse lymphoma cells (OECD TG 476), sodium molybdate dihydrate was negative with and without metabolic activation. Based on these results and further supporting data, molybdate salts are considered to be non-genotoxic *in vitro*.

Reliable *in vivo* genotoxicity studies are not available.

Carcinogenicity

Two year NTP toxicology and carcinogenicity studies describe molybdenum trioxide (analogous substance) administration to rats and mice via inhalation at doses up to 100 mg MoO_3/m^3 (ca. 67 mg Mo/m^3). It is applicable to molybdates in so far as the general systemic toxicological effects and parameters can be read across to molybdate salts (see rationale for category and use of data from analogous substance). Both in rats and mice (male and female), there was no evidence of systemic carcinogenicity in the NTP study. The local effects in the respiratory tract observed following inhalation of MoO_3 are considered to be specific to MoO_3 and are not to be read across to the category substances.

Based on these results, the molybdenum substances discussed in this SIAP are considered to have no carcinogenic potential.

Toxicity to reproductive organs and fertility and on developmental toxicity

Table: available key study data for toxicity to reproductive organs and fertility of molybdenum substances

Test substance	**Study type / details**	**Key results**
Sodium molybdate (dihydrate) $Na_2MoO_4 \cdot 2\ H_2O$	In a 90-day repeated dose toxicity study (OECD TG 408) disodium molybdate was administered to male and female rats at doses of 5, 17 or 60 mg/kg bw/day of Mo (molybdenum in disodium molybdate dihydrate) via feed. **In addition to the standard examination parameters, the following examinations were conducted to assess any adverse effects on sexual function and fertility: vaginal cytology, oestrous cycle, sperm parameters (count, motility and morphology, testicular spermatid counts), in accordance with OECD TG 416.**	**The NOAEL for effects on reproductive organs, sperm and oestrous cycle is 60 mg Mo/kg bw/day.** There were no test substance related changes in the male or female reproductive tissues (testes, epididymis, prostate, seminal vesicles, ovaries, uterus or vagina). There were no test substance-related effects on vaginal cytology and oestrous cycles during weeks 7 - 9 of the dosing phase (i.e., the period during which vaginal cytology and oestrous cycles were evaluated). No test-item related changes in organ weight of testes or secondary sex organs and no effect on spermatid or sperm counts, motility or morphology were observed. All other recorded microscopic findings were considered incidental and unrelated to administration of disodium molybdate dihydrate. They occurred at similar incidences in the control and test substance treated groups or they were sporadic with no relationship to dose.
Sodium molybdate (dihydrate) Na_2MoO_4 . 2 H2O	A guideline compliant **prenatal developmental toxicity study** (according to OECD TG 414, under GLP) in rats with the test item sodium molybdate is available. Exposure was during gestational days 6 through 20 via the diet, in four dose groups (ca. 3, 10, 20 and 40 mg Mo/kg bw/day) and a control group (plain diet).	There were no treatment or dose-related effects on maternal body weights, weight changes, feed consumption in grams/day or grams/kg, body weight/day, or on maternal clinical observations, pregnancy indices, or maternal organ weights at any dose. There were also no biological or statistical differences among groups for the numbers of ovarian corpora lutea/female, for uterine implantation sites, or for uterine implantation losses per female at any dose. Statistically significantly increased copper levels in kidneys and livers were observed at 40 mg Mo/kg bw/day, but not at 20 mg Mo/kg bw/day. **Therefore, the NOAEL for maternal toxicity is 40 mg Mo/kg bw/day, and the NOEL for maternal toxicity is 20 mg Mo/kg bw/day.** There were no biological or statistical differences among groups for the numbers of foetuses, foetal

		sex ratios, foetal body weights, foetal external, visceral or skeletal malformations or variations per female at any dose. The incidences of the few foetal malformations and the more common foetal variations observed in the study were comparable to the historical control database of the laboratory on this rat strain and supplier. The foetal effects in this study also did not exhibit any treatment- or dose- related pattern of increased incidences and/or severities. **The NOAEL for developmental toxicity is therefore 40 mg Mo/kg bw/day.**

Effects on fertility: A 90-day repeated dose toxicity study (OECD TG 408) with disodium molybdate (dihydrate) is available which was modified to additionally assess any adverse effects on sexual function and fertility. At the highest tested dose (60 mg Mo/kg bw/day, administered as ca. 151 mg $Na_2MoO_4 \cdot 2\ H_2O$ via feed) there were no test substance-related effects on vaginal cytology and oestrous cycles. No test-item related changes in organ weight of testes or secondary sex organs and no effect on spermatid or sperm counts, motility or morphology were observed.

Developmental toxicity: A guideline compliant prenatal developmental toxicity study (according to OECD TG 414, under GLP) in rats with the test item sodium molybdate (dihydrate) is available. At the highest tested dose (40 mg Mo/kgbw/day, administered as ca. 100 mg $Na_2MoO_4 \cdot 2\ H_2O$ via feed) no dose-related adverse effects on development of the offspring were observed.

Conclusion

For the *molybdenum salts category substances* adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

No health hazards have been identified for acute toxicity, irritation, sensitisation, mutagenicity, reproductive toxicity and carcinogenicity. A health hazard for repeated dose toxicity cannot be ruled out for the three category substances based on effects observed at the highest tested dose of 60 mg Mo/kg bw/day in a 90-day oral toxicity study conducted with the test substance sodium molybdate dihydrate. Taking into account the low degree of severity of the observed effects, it is concluded that the category substances have a low repeated dose toxicity hazard.

Environment

Physicochemical processes like hydrolysis, photo-oxidation and (bio-)degradation are not relevant for chemical inorganic substances such as elemental molybdenum and molybdenum salts that only occur in the environment as molybdate.

Transport and distribution of naturally-occurring elements such as molybdenum over the different environmental compartments is predominantly determined by their solubility and binding affinities to organic matter and other solid particles that occur in soil and sediment (e.g., clay particles, precipitated hydroxides). All of the molybdenum compounds of this category are highly soluble. Therefore, when entering in the aquatic environment as the soluble molybdate, precipitation as an insoluble inorganic is unlikely to occur. Typical K_d values for molybdenum to suspended solids, sediment and soil are 2793, 1778 and 871 L/kg, respectively. No McKay Level III modelling was conducted as this type of modelling is not relevant for the inorganic substances of this category.

Reported whole-body bioaccumulation factors for fish vary more than 2 orders of magnitude (i.e., 0.05 – 71.6) but, as theoretically predicted for essential elements, there is a distinct close relationship between exposure concentration and BAF, i.e., decreasing BAFs with increasing Mo-levels in the water column, showing homeostatic control of Mo by these organisms. Similar findings are observed for aquatic invertebrate species. The homeostatic control of Mo in fish (*O.mykiss*) is observed to continue to function up to and within the milligram range of exposure. Bioaccumulation factors in the terrestrial compartment are situated around 0.2 - 4 for plants and 0.4 - 3.4 for invertebrates (dry weight basis).

There are no indications or evidence that biomagnification occurs in aquatic or terrestrial food chains.

Aquatic toxicity of molybdate (expressed as mg Mo/L) (test substance: sodium molybdate dihydrate unless indicated otherwise)

The following acute toxicity test results have been determined for aquatic species. Values are based on measured levels unless specified otherwise:

Species	**Endpoint**	**Value (mg Mo/L)**	**Type[a]**	**Guideline**
Pimephales promelas	96h-LC_{50}	609.1	s-s	OECD TG 203
Oncorhynchus mykiss	96h-LC_{50}	7600[b] 800-1320[b] 781-1339[c]	s-s s s	OECD TG 203
Daphnia magna	48h-LC_{50}	130.9[b] 2729.4 2847.5 1680.4-1776.6	s s s s-s	OECD TG 202 EPA/600/4-90/027F ASTM 1980 OECD TG 202, EPA OPP 72-2
Ceriodaphnia dubia	48h-LC_{50}	1005.5-1024.6	s-s	OECD TG 202, EPA OPP 72-2
Girardia dorotocephala	96h-LC_{50}	1226	s-s	ASTM 2002
Pseudokircheriella subcapitata	72h-E_rC_{50} (growth rate)	362.9, >419.9, 1094.5, 1568.9[d] 289.2 – 390.9[e] geomean: 331.1[f]	s s	OECD TG 201

[a]: f-t: flow-through ; s-s: semi-static / static renewal ; s: static
[b]: nominal
[c]: recalculated LC_{50}, logistic fit
[d]: UGhent strain ; [e]: CIMM strain (most sensitive strain tested)
f: geometric mean of 4 values for the CIMM strain

The following aquatic chronic toxicity test results have been determined for the freshwater environment. Values are based on measured exposure levels unless mentioned otherwise.

Species	**Endpoint**	**Value (mg Mo/L)**	**Type[a]**	**Guideline**
Fish				
Oncorhynchus mykiss	78d-$EC_{10,biomass}$ 32d-$NOEC_{mortality}$ 32d-$NOEC_{mortality}$ 12m-$NOEC_{mortality,growth}$	43.2 200[b] 750[b] >17	f-t f-t s-s f-t	OECD TG 210 EPS 1/RM/28 EPS 1/RM/28 No guideline specified
Oncochynchus kisutch	20wk-$NOEC_{develop}$	≥ 19.5	f-t	No guideline specified
Pimephales promelas	34d-$EC_{10,biomass}$ 32d-$EC_{10,biomass}$	39.9 90.9	f-t n.s.	OECD TG 210 ASTM E1241-98
Invertebrates				
Daphnia magna	21d-$EC_{10,reproduction}$	62.8 105.6 108	s-s s-s s-s	OECD TG 211 OECD No 211 ASTM, 1997
Ceriodaphnia dubia	7d-$EC_{10,reproduction}$	50.8-78.2	s-s	EPA-821-R-02-013
Chironomus riparius	14d-$EC_{10,growth\ rate}$	121.4	s-s	OECD TG 218
Brachyonus calyciflorus	48h-$EC_{10,reproduction}$	193.6	s	conform to APHA 8420, 1998
Gastropods				
Lymnaea stagnalis	28d-$EC_{10,growth\ rate}$	221.8	s-s	No guideline specified
Amphibians				
Xenopus laevis	4d-$EC_{10,development}$	115.9	s-s	conform to APHA

				8420, 1998
Algae and higher plants				
Pseudokirchneriella subcapitata	72h-$E_rC_{10,growth\ rate}$	156[b] 283.8[d] 62.5–366.2[d] 61.2–88.7[e] geomean: 74.3[cf]	s s s s	OECD TG 201
Lemna minor	7d-$EC_{10,growth\ rate}$	241.5	s	OECD TG 221

[a]: f-t: flow-through ; s-s: semi-static / static renewal ; s: static ; n.s.: not specified
[b]: based on nominal value
[c]: geometric mean of 4 values that were obtained with the most sensitive strain
[d]: UGhent strain ; [e]: CIMM strain (most sensitive strain tested)
f: geometric mean of 4 values for the CIMM strain

The following aquatic chronic toxicity test results have been determined for the marine environment. Values are based on measured exposure levels:

Species	**Endpoint**	**Value (mg Mo/L)**	**Type[a]**	**Guideline**
Fish				
Cyprinodon variegatus	28d-$EC_{10,biomass}$	84.1	f-t	ASTM E1241
Invertebrates				
Acartia tonsa	20d-$EC_{10,F1\ development}$	7.96	s-s	ASTM STP667
Americamysis bahia	28d-$EC_{10,growth/development}$	>116	f-t	ASTM E1191-97, EPA OPPTS 850.1350
Molluscs				
Crassostrea gigas	48h-$EC_{10,development}$	1,174	s	ASTM 724-98
Mytilus edulis	48h-$EC_{10,development}$	4.4[b]	s	No guideline specified
Algae and higher plants				
Dunaliella tertiolecta	72h-$EC_{10,growth\ rate}$	881	s	ISO 10253
Phaeodactylum tricornutum	72h-$EC_{10,growth\ rate}$	169.9	s	ISO 10253
Ceramium tenuicorne	72h-$EC_{10,growth\ rate-length}$	274	s	ISO 10253
Echinoderms				
Strongylocentrotus purpuratus	48h-$EC_{10,development}$	325.8	s	ASTM E1563-95, EPA/600/R-95/136
Dendraster excentricus	48h-$EC_{10,development}$	233.6	s	ASTM E1563-95, EPA/600/R-95/136

[a]: f-t: flow-through ; s-s: semi-static ; s: static
[b]: effect levels based on nominal levels ; no guidance specified ; test substance was ammonium heptamolybdate

Terrestrial toxicity of molybdate (expressed as mg Mo/kg dw) (test substance: sodium molybdate dihydrate)

Terrestrial chronic toxicity test results have been conducted on 10 different soil types. Ranges of EC_{10}-values – based on measured Mo-levels - were determined for the following organisms (test name/OECD TG No.):

Species	**Endpoint**	**Value (mg Mo/kg dw)**	**Guideline**
Plants			
Brassica napus	21d-EC_{10}	5–2,847	ISO 11269-2
Trifolium pratense	21d-EC_{10}	5–1,505	ISO 11269-2
Lolium perenne	21d-EC_{10}	15–3,479	ISO 11269-2

Lycopersicon esculentum	21d-EC_{10}	9–1,578	ISO 11269-2
Hordeum vulgare	4d-EC_{10}	28–436	ISO 11269-1
Soil invertebrates			
Enchytraeus crypticus	28d-EC_{10}	67.2–>2,817	OECD TG 220
Eisenia andrei	56d-EC_{10}	8.88–455	OECD TG 222
Folsomia candida	28d-EC_{10}	39–1,865	ISO 11267
Micro-organisms			
Substrate-induced nitrification	28d-ÈC_{10}	35 – >10,001	ISO 14238
Substrate-induced respiration	24h-EC_{10}	10 – >10,003	OECD TG 217
Plant residue mineralisation	28d-EC_{10}	164 – >10,003	No guideline specified

Bioavailability models have been developed for the terrestrial environment. These models describe the relationship between specific soil parameters on one hand (soil pH, organic matter content), and the no-effect concentration for a specific organism and end parameter on the other hand. Toxicity of molybdate to soil organisms generally decreases (i.e. increasing EC_{50} values) with decreasing pH and increasing clay content, organic matter content and iron oxide content. The range of each parameter in the tested soils more or less defines the range of applicability for these relationships.

All the ecotoxicological information that is presented here has been published in peer-reviewed journals.

Conclusion

For the *highly soluble molybdenum salts category* adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Molybdate released from the substances in this category has a low bioaccumulation potential, and is regulated in aquatic organisms up to the mg/L range. *Highly soluble molybdenum salts category* substances do not present a hazard for the environment based on their low hazard profile.

Exposure

Production: Global production levels of category substances totalled approximately 30,000 tonnes in 2011. EU tonnage bands indicate the smallest tonnage band within the category as 100 – 1,000 tonnes for ammonium heptamolybdate, and the largest for both ammonium dimolybdate and sodium molybdate as 1,000 – 10,000 tonnes. Main production countries include: Chile, China, Germany, United States of America. Main uses for the category substances range from corrosion inhibition, to flame retardant/smoke suppressant, to micronutrient input into mineral supplements and fertilizers.

Environment: Molybdenum is a naturally occurring element that can be found at background levels in water, sediment and soil. The main input of (anthropogenic) molybdenum in the environment as a result of industrial activities will occur via the aquatic compartments (effluent, mine tailings) where it will be present in the form of molybdate. A part of this dissolved fraction will bind to the sediment layer (K_d of 1778 L/kg, see Environment section). Anthropogenic input to the terrestrial compartment will occur through the application of sewage sludge to land, or via stack emissions (local point source).

Environmental monitoring: Background levels of molybdenum in water, sediment and soil are reported in the EU FOREGS Geochemical Atlas (Forum of European Geological Surveys). Typical background concentration levels in Europe are 0.28 µg Mo/L for surface water, 0.58 mg Mo/kg dw for sediment, and 0.59 mg Mo/kg dw for topsoil. Extensive datasets with ambient Mo-levels in water were received from different EU-countries (Belgium, Finland, Germany, The Netherlands, Sweden, United Kingdom), and country-specific reasonable worst-case (RWC) ambient levels were situated between 0.62 and 5.1 µg Mo/L (typical EU-value: 2.30 µg Mo/L). The RWC ambient level represents the 90^{th} percentiles of ambient waters that are not directly affected by point source contamination (diffuse sources only). For the terrestrial compartment there is a large (n >5000) data set on ambient Mo-levels in European arable and grassland soils, resulting in ambient reasonable worst-case values of 0.86 mg Mo/kg dw and 1.04 mg Mo/kg dw, respectively. Using the limited information on ambient molybdenum concentrations in sediment (data for Finland, Germany, Spain, Sweden, United Kingdom), a reasonable worst-case ambient concentration of 3.77 mg Mo/kg dw was determined.

Human Exposure: Trace levels of molybdenum (present as soluble molybdate) are found in a wide variety of foods, and human exposure to molybdenum may occur via the diet, drinking water and occupational exposure from mining operations and industrial uses.

Occupational Exposure: Workers can be exposed to dusts of molybdenum substances during their manufacture and use. Primary routes of exposure at the workplace are via inhalation and dermal contact. Direct oral exposure (ingestion) is considered to be negligible; however, indirect oral exposure in connection with the inhalational exposures may give a contribution to the internal systemic dose. Inhaled material that is deposited in the mouth and upper airways can be subject to mucociliary clearance and then swallowed.

The category substances are not of particular concern regarding local effects on the skin, and absorption through skin is negligible. As a matter of general industrial hygiene, to protect against general dusts and also against heat in some workplaces, protective clothing and gloves are worn where necessary.

Inhalation exposure is possible where dry powder forms of molybdenum metal or molybdate salts are handled, e.g. raw material handling, substance transfer between reaction vessels, and packaging/bagging operations. With regard to molybdenum metal, abrasive techniques such as polishing or grinding, and hot processes like forging, cutting and welding can lead to the formation of metal dusts or fumes. At such workplaces, direct exposure of the worker is reduced by risk management measures, such as automation or enclosure of the process or installation of exhaust ventilation systems. If such measures are not applicable – or where necessary, in addition to those measures - personal respiratory protective equipment is used.

Consumer Exposure: Opportunities are few for consumer exposure to category substances. Sodium molybdate and ammonium dimolybdate are added in trace amounts (as molybdate) to mineral supplements. Sodium molybdate is also used as a micronutrient in fertilizers, a water treatment chemical and in coolants/anti-freeze.

Annex I: Overview of toxicological data (reliable study results) for substances in the molybdate salts category and use of analogous substance data

	molybdate salts category			analogous substance
	sodium molybdate	**ammonium dimolybdate**	**ammonium heptamolybdate**	**molybdenum trioxide**
Acute toxicity, oral	OECD TG 401: LD_{50} = 4233 mg/kg bw (anhydrous sodium molybdate)	OECD TG 401: LD_{50} = 3883 mg/kg bw	Estimated [(1)]: LD_{50} = ca. 3400 mg/kg bw (anhydrous ammonium heptamolybdate)	*)
Acute toxicity, dermal	OECD TG 402: LD_{50} > 2000 mg/kg bw (anhydrous sodium molybdate)	OECD TG 402: LD_{50} > 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw (anhydrous ammonium heptamolybdate) (read-across within category)	*)
Acute toxicity, inhalation	OECD TG 403: LC_{50} > 1930 mg/m³ (anhydrous sodium molybdate)	OECD TG 403: LC_{50} > 2080 mg/m³	Estimated [(1)]: LC_{50} > ca. 1500 mg/m³ (anhydrous ammonium heptamolybdate)	*)
Skin irritation	OECD TG 404: not irritating	OECD TG 404: not irritating	not irritating (read-across within category)	*)
Eye irritation	OECD TG 405: not irritating	OECD TG 405: not irritating	not irritating (read-across within category)	*)
Respiratory irritation	OECD TG 403: not irritating	OECD TG 403: not irritating	not irritating (read-across within category)	*)
Skin Sensitisation	OECD TG 406: not sensitising	OECD TG 406: not sensitising	not sensitising (read-across within category)	no data
Mutagenicity/Genetic toxicity	OECD TG 471,476,487: not mutagenic / not clastogenic	not mutagenic / not clastogenic (read-across within category)	not mutagenic / not clastogenic (read-across within category)	no data
Repeated dose toxicity, oral	90-day study (OECD TG 408): NOAEL, systemic = 17 mg Mo/kg bw/day LOAEL, systemic = 60 mg Mo/kg bw/day	NOAEL, systemic = 17 mg Mo/kg bw/day LOAEL, systemic = 60 mg Mo/kg bw/day (read-across within category)	NOAEL, systemic = 17 mg Mo/kg bw/day LOAEL, systemic = 60 mg Mo/kg bw/day (read-across within category)	no data
Repeated dose toxicity, inhalation	$NOAEC_{rats/mice}$ (systemic effects) = 66.7 mg Mo/m³ $NOEC_{mice}$ = 6.7 mg Mo/m³) (read-across for systemic effects from analogous substance)	$NOAEC_{rats/mice}$ (systemic effects) = 66.7 mg Mo/m³ $NOEC_{mice}$ = 6.7 mg Mo/m³) (read-across for systemic effects from analogous substance)	$NOAEC_{rats/mice}$ (systemic effects) = 66.7 mg Mo/m³ $NOEC_{mice}$ = 6.7 mg Mo/m³) (read-across for systemic effects from analogous substance)	90-day and 2-year studies in rats and mice (similar to OECD TG 413+453): $NOAEC_{rats/mice}$ (systemic effects) = 66.7 mg Mo/m³ (highest test concentration) $NOEC_{mice}$ = 6.7 mg Mo/m³)

Reproductive toxicity: effects on fertility	90-day study (OECD TG 408) with additional parameters addressing fertility: $NOAEL_{fertility}$ = 60 mg Mo/kg bw/day (highest dose)	$NOAEL_{fertility}$ = 60 mg Mo/kg bw/day (read-across within category)	$NOAEL_{fertility}$ = 60 mg Mo/kg bw/day (read-across within category)	no data
Reproductive toxicity: developmental toxicity	Developmental toxicity study (OECD TG 414): $NOAEL_{development}$ = 40 mg Mo/kg bw/day (highest dose) $NOAEL_{maternal}$ = 40 mg Mo/kg bw/day (highest dose) $NOEL_{maternal}$ = 20 mg Mo/kg bw/day	$NOAEL_{development}$ = 40 mg Mo/kg bw/day $NOAEL_{maternal}$ = 40 mg Mo/kg bw/day $NOEL_{maternal}$ = 20 mg Mo/kg bw/day (read-across within category)	$NOAEL_{development}$ = 40 mg Mo/kg bw/day $NOAEL_{maternal}$ = 40 mg Mo/kg bw/day $NOEL_{maternal}$ = 20 mg Mo/kg bw/day (read-across within category)	no data
Carcinogenicity	NOAEL (systemic carcinogenicity) = 66.7 mg Mo/m³ (read-across for systemic effects from analogous substance)	NOAEL (systemic carcinogenicity) = 66.7 mg Mo/m³ (read-across for systemic effects from analogous substance)	NOAEL (systemic carcinogenicity) = 66.7 mg Mo/m³ (read-across for systemic effects from analogous substance)	2-year inhalation studies in rats and mice (similar to OECD TG 453): NOAEL (systemic carcinogenicity) = 66.7 mg Mo/m³ (highest test concentration)

*) Since data from the category substances are available, the existing supportive data for MoO_3 as an analogous substance is not presented. Data from the analogous substance MoO_3 is only used where no data for category substances is available: for repeated dose toxicity (absence of systemic effects following inhalation of MoO_3) and for carcinogenicity (absence systemic carcinogenicity following inhalation of MoO_3).

[1)] The LD_{50} and LC_{50} for anhydrous ammonium heptamolybdate have been estimated based on the experimentally determined LD_{50}/LC_{50} anhydrous sodium molybdate as the worst case surrogate. The re-calculation is based on the stoichiometric content of Mo in each compound.