APPENDIX A. ATSDR MINIMAL RISK LEVEL WORKSHEETS

MRLs are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified route and duration of exposure. MRLs are based on noncancer health effects only; cancer effects are not considered. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the NOAEL/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (≥365 days) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive substance-induced endpoint considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

APPENDIX A

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Human Health Sciences, expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published MRLs. For additional information regarding MRLs, please contact the Division of Toxicology and Human Health Sciences, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop S102-1, Atlanta, Georgia 30329-4027.

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Molybdenum
CAS Numbers: 7439-98-7
Date: May 2020
Profile Status: Final
Route: Inhalation
Duration: Acute

MRL Summary: There are insufficient data for derivation of an acute-duration inhalation MRL for molybdenum due to the limited number of endpoints examined in the only available animal studies.

Rationale for Not Deriving an MRL: The database on the acute inhalation toxicity of molybdenum is limited to several 4-hour studies in rats exposed to ammonium dimolybdate (Jackson et al. 1991a), molybdenum trioxide (Jackson et al. 1991b, 1991d; Leuschner 2010), or sodium molybdate (Jackson et al. 1991c) and a 14-day study in rats and mice exposed to molybdenum trioxide (NTP 1997). No effects on lethality or the respiratory tract (most only examined the lungs) were observed at concentrations of 1,200 mg molybdenum/m^3 and higher (Jackson et al. 1991a, 1991b, 1991c, 1991d; Leuschner 2010); several of the studies reported decreases in body weight on days 2–3 post-exposure (Jackson et al. 1991b, 1991c, 1991d). The NTP (1997) study evaluated the effect of molybdenum trioxide on the nasal cavity and on body weight in rats and mice exposed 6 hours/day, 5 days/week for 14 days. No adverse effects were observed in the nasal cavity. However, weight loss was observed at the highest concentration tested (200 mg molybdenum/m^3); decreases in body weight gain were observed in male rats exposed to 67 mg molybdenum/m^3 and in female rats and mice exposed to 200 mg/m^3. Given the limited number of endpoints examined, the decrease in body weight gain was not considered a suitable basis for an acute-duration inhalation MRL because the database is inadequate for identifying the critical target of molybdenum toxicity following acute-duration inhalation exposure.

Agency Contacts (Chemical Managers): G. Daniel Todd

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Molybdenum
CAS Numbers: 7439-98-7
Date: May 2020
Profile Status: Final
Route: Inhalation
Duration: Intermediate

MRL Summary: There are insufficient data for derivation of an intermediate-duration inhalation MRL for molybdenum due to the lack of studies identifying a critical target of toxicity.

Rationale for Not Deriving an MRL: Information on the intermediate-duration toxicity of molybdenum is limited to 90-day studies of molybdenum trioxide in rats and mice conducted by NTP (1997) that examined a wide range of potential targets, including reproductive endpoints. No toxicologically significant alterations were observed at concentrations of molybdenum trioxide as high as 67 mg/m^3. Consistent with ATSDR's practice of not using free-standing NOAELs as a POD, an intermediate-duration inhalation MRL was not derived.

Agency Contacts (Chemical Managers): G. Daniel Todd

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Molybdenum trioxide
CAS Numbers: 1313-27-5
Date: May 2020
Profile Status: Final
Route: Inhalation
Duration: Chronic
MRL 0.002 mg molybdenum/m^3
Critical Effect: Respiratory effect, squamous metaplasia of the epiglottis in female rats
Reference: NTP 1997
Point of Departure: $BMCL_{10}$ of 1.60 mg molybdenum/m^3 ($BMCL_{HEC}$ of 0.071 mg Mo/m^3)
Uncertainty Factor: 30
LSE Graph Key: 11
Species: Rat

MRL Summary: A chronic-duration inhalation MRL of 0.002 mg molybdenum/m^3 was derived for molybdenum trioxide based on an increased incidence of squamous metaplasia of the epiglottis in female rats exposed to 6.7 mg molybdenum/m^3 as molybdenum trioxide 6 hours/day, 5 days/week for 2 years (NTP 1997). The MRL is based on a $BMCL_{10}$ of 1.60 mg molybdenum/m^3 (human equivalent concentration [HEC] of 0.071 mg molybdenum/m^3) and a total uncertainty factor of 30 (3 for extrapolation from animals to humans with dosimetric adjustments and 10 for human variability).

Selection of the Critical Effect: There are limited data on the toxicity of inhaled molybdenum in humans. A study of workers at a molybdenite roasting facility exposed to molybdenum trioxide and other oxides found no alterations in lung function but did find increases in serum uric acid levels (Walravens et al. 1979); the TWA molybdenum concentration was 9.46 mg molybdenum/m^3. Another study of workers exposed to ultrafine molybdenum trioxide dust reported respiratory symptoms (dyspnea and cough), radiographic abnormalities, and impaired lung function (Ott et al. 2004); the study did not provide monitoring data. Confidence in these cohort studies was considered very low (see Appendix C for additional information).

Data on the chronic toxicity of molybdenum in laboratory animals is limited to 2-year studies in rats and mice exposed to molybdenum trioxide (NTP 1997). In these studies, NTP (1997) examined a wide range of potential targets of toxicity. Adverse effects were limited to the respiratory tract, specifically the nasal respiratory and olfactory epithelium, epiglottis, and lungs. The respiratory tract was considered the critical target of molybdenum trioxide toxicity.

Selection of the Principal Study: The NTP (1997) study was selected as the principal study.

Summary of the Principal Study:

NTP. 1997. Toxicology and carcinogenicity studies of molybdenum trioxide (CAS No. 1313-27-5) in F344/N rats and B6C3F1 mice (inhalation studies). National Toxicology Program, Research Triangle Park, NC. NT PTR 462.

Groups of male and female F344/N rats and B6C3F1 mice (50/sex/species/group) were exposed to target concentrations of 0, 10, 30, or 100 mg/m^3 molybdenum trioxide (0, 6.7, 20, and 67 mg molybdenum/m^3) 6 hours/day, 5 days/week for 106 (rats) or 105 (mice) weeks; actual concentrations were within 15% of the target level. The average mass median aerodynamic diameter particle sizes (and geometric standard deviation, σ_g) were 1.5 (1.8), 1.6 (1.8), and 1.7 (1.8) μm for the 6.7, 20, and 67 mg/m^3 concentrations,

respectively. The following parameters were used to assess toxicity: twice daily cage-side observations, body weights (weekly for 12 weeks, at 15 weeks, monthly thereafter, and at termination), and histopathological examination of major tissues and organs. In addition, bone density and femoral curvature studies were conducted in 10 animals/sex/species/group.

No significant alterations in survival rates or body weight gain and no toxicologically significant alterations in bone density or curvature were found. Non-neoplastic lesions were only observed in the nose, larynx, and lungs; a summary of the type of lesions and incidences is presented in Table A-1. The severity of the respiratory lesions was concentration related. Significant increases in the incidence of alveolar/bronchiolar carcinoma and/or adenoma were observed in mice: carcinoma in male mice at ≥6.7 mg/m^3, adenoma or carcinoma (combined) in male mice at 6.7 and 20 mg/m^3, adenoma in female mice at ≥20 and 67 mg/m^3, and adenoma or carcinoma (combined) in female mice at 67 mg/m^3. In rats, the incidence of alveolar/bronchiolar adenoma or carcinoma (combined) was increased in males; however, the incidences (0/50, 1/49, 1/49, 4/60) were within the range of historical controls and NTP considered this to be equivocal evidence of carcinogenic activity.

Table A-1. Incidence of Non-Neoplastic Respiratory Tract Lesions in Rats and Mice Exposed to Molybdenum Trioxide for 2 Years

	Concentration (mg molybdenum/m^3)			
	0	6.7	20	67
Male rats				
Hyaline degeneration of nasal respiratory epithelium	2/50	7/49	48/49[a]	49/50[a]
Squamous metaplasia of epiglottis	0/49	11/48[a]	16/49[a]	39/49[a]
Chronic lung inflammation in alveolus	2/50	3/50	25/50[a]	47/50[a]
Female rats				
Hyaline degeneration of nasal respiratory epithelium	1/48	13/49[a]	50/50[a]	50/50[a]
Hyaline degeneration of nasal olfactory epithelium	39/48	47/49[b]	50/50[a]	50/50[a]
Squamous metaplasia of epiglottis	0/49	18/49[a]	29/49[a]	49/50[a]
Chronic lung inflammation	14/50	13/50	43/50[a]	49/50[a]
Male mice				
Nasal suppurative inflammation	2/50	6/50	10/49[b]	8/50[b]
Nasal olfactory epithelium atrophy	3/50	5/50	3/49	10/50[b]
Hyaline degeneration of nasal respiratory epithelium	11/50	13/50	11/49	41/50[a]
Squamous metaplasia of epiglottis	0/50	26/49[a]	37/48[a]	49/50[a]
Laryngeal hyperplasia	1/50	3/49	6/48	41/50
Histiocyte infiltration in the lungs	2/50	16/50[a]	9/49[b]	9/50[b]
Alveolar epithelial metaplasia	0/50	32/50[a]	36/49[a]	49/50[a]
Female mice				
Hyaline degeneration of nasal respiratory epithelium	26/49	23/50	28/49	48/49[a]
Hyaline degeneration of nasal olfactory epithelium	22/49	14/50	14/49	36/49[a]

Table A-1. Incidence of Non-Neoplastic Respiratory Tract Lesions in Rats and Mice Exposed to Molybdenum Trioxide for 2 Years

	Concentration (mg molybdenum/m^3)			
	0	6.7	20	67
Squamous metaplasia of epiglottis	1/49	36/50[a]	43/49[a]	49/50[a]
Laryngeal hyperplasia	1/49	1/50	7/49	35/50
Alveolar epithelial metaplasia	2/50	26/50[a]	39/49[a]	46/49[b]

[a]Significantly different from controls; p≤0.01.
[b]Significantly different from controls; p≤0.05.

Source: NTP 1997

Selection of the Point of Departure for the MRL: The MRL was based on a $BMCL_{10}$ of 1.60 mg molybdenum/m^3 for squamous metaplasia of the epiglottis in female rats.

Benchmark dose (BMD) modeling was conducted for the respiratory tract lesions with statistically significant increases in incidence at ≥6.7 mg/m^3 (squamous metaplasia of the epiglottis in male and female rats and mice, hyaline degeneration of the nasal respiratory and olfactory epithelium in female rats, histiocyte infiltration in the lungs in male mice, and alveolar epithelial metaplasia in male and female mice). The incidence data (Table A-1) provided adequate fit for four endpoints (squamous metaplasia in male rats, female rats, and female mice and hyaline degeneration of the nasal respiratory epithelium in female rats). The results of the BMD modeling are presented in the Benchmark Dose Modeling subsection and are summarized in Table A-2.

Table A-2. Summary of Benchmark Dose Modeling

Endpoint	Selected model	BMC_{10} (mg Mo/m^3)	$BMCL_{10}$ (mg Mo/m^3)
Squamous metaplasia of the epiglottis in male rats	Multistage, 2-degree (Table A-4 and Figure A-1)	4.36	3.53
Hyaline degeneration of the respiratory epithelium in female rats	Log-logistic (Table A-5 and Figure A-2)	5.87	4.82
Squamous metaplasia of the epiglottis in female rats	Weibull (Table A-6 and Figure A-3)	1.97	1.60
Squamous metaplasia of the epiglottis in male mice	Gamma (Table A-7 and Figure A-4)	1.30	1.06

BMC = benchmark concentration; BMCL = 95% lower confidence limit on the benchmark concentration

A summary of the potential POD values is presented in Table A-3. Because there are dosimetric differences in regional respiratory tract deposition of aerosols between animal species, a comparison was made between the human equivalent concentration PODs (POD_{HEC}). The lowest POD_{HEC}, $BMCL_{HEC}$ of 0.071 mg molybdenum/m^3 for squamous metaplasia of the epiglottis in female rats, was selected as the POD for the MRL.

Table A-3. Summary of PODs and HECs

Endpoint	PODs (mg Mo/m^3)	RDDR values[a]	HECs[b] (mg Mo/m^3)
Squamous metaplasia of the epiglottis in male rats	3.53 (BMCL)	0.459	0.28
Hyaline degeneration of the respiratory epithelium in female rats	4.82 (BMCL)	0.248	0.21
Hyaline degeneration of the olfactory epithelium in female rats	6.7 (LOAEL)	0.248	0.30
Squamous metaplasia of the epiglottis in female rats	1.60 (BMCL)	0.248	0.071
Squamous metaplasia of the epiglottis in male mice	1.06 (BMCL)	0.441	0.08
Histiocyte infiltration in the lungs of male mice	6.7 (LOAEL)	1.046	1.3
Alveolar epithelial metaplasia in male mice	6.7 (LOAEL)	1.046	1.3
Squamous metaplasia of the epiglottis in female mice	6.7 (LOAEL)	0.367	0.44
Alveolar epithelial metaplasia in female mice	6.7 (LOAEL)	3.067	3.7

[a]RDDR values specific for each region of the respiratory tract (extrathoracic, tracheobronchial, and pulmonary) were calculated using EPA's RDDR calculator with reference body weights of 0.40, 0.25, 0.040, and 0.035 kg for male rats, female rats, male mice, and female mice, respectively, and reported particle sizes and particle size distributions.
[b]HEC calculated by multiplying the duration-adjusted POD (POD x 6 hours/24 hours x 5 days/7days) by the RDDR value.

BMCL = 95% lower confidence limit on the benchmark concentration; HEC = human equivalent concentration; LOAEL = lowest observed adverse effect level; POD = point of departure; RDDR = regional deposited dose ratio for the specific region of the respiratory tract

Adjustment for Intermittent Exposure: The PODs were adjusted for intermittent exposure (6 hours/day, 5 days/week).

Calculation of Human Equivalent Concentration: HECs were calculated for each potential POD by multiplying the duration-adjusted POD by the regional deposited dose ratio (RDDR) for the specific region of the respiratory tract. The RDDR is a factor used to adjust particulate exposure concentration in animals to a predicted concentration in humans that would be associated with the same dose delivered to a specific region of the respiratory tract or to the blood (EPA 1994). The RDDRs were calculated using EPA's RDDR calculator with reference body weights of 0.40, 0.25, 0.040, and 0.035 kg for the male rats, female rats, male mice, and female mice, respectively, the reported particle sizes, and particle size distributions. The particles were assumed to be monodispersed given that the σ_g was 1.8.

Uncertainty Factor: The $BMCL_{HEC}$ is divided by a total uncertainty factor (UF) of 30.

- 3 for extrapolation from animals to humans with dosimetric adjustments
- 10 for human variability

$$BMCL_{HEC} \div UFs = MRL$$
$$0.071 \text{ mg molybdenum/m}^3 \div 30 = 0.002 \text{ mg molybdenum/m}^3$$

Other Additional Studies or Pertinent Information that Lend Support to this MRL: This MRL is specific to molybdenum trioxide; there are insufficient data to evaluate the health effects associated with inhalation exposure to other molybdenum compounds.

Benchmark Dose Modeling: The incidence data (Table A-1) for respiratory tract lesions, which had significant increases in incidence at ≥6.7 mg/m^3 (squamous metaplasia of the epiglottis in male and

female rats and mice, hyaline degeneration of the nasal respiratory and olfactory epithelium in female rats, histiocyte infiltration in the lungs in male mice, and alveolar epithelial metaplasia in male and female mice), were fit to all available dichotomous models in EPA's Benchmark Dose Software (BMDS, version 3.1) using the extra risk option. Adequate model fit was judged by three criteria: goodness-of-fit statistics (p-value >0.1), visual inspection of the dose-response curve, and scaled residual at the data point (except the control) closest to the predefined benchmark response (BMR). Among all of the models providing adequate fit to the data, the lowest BMCL was selected as the POD when the difference between the BMCLs estimated from these models was >3-fold; otherwise, the BMCL from the model with the lowest Akaike's Information Criterion (AIC) was chosen. For all lesion types, a BMR of 10% was used. Since the incidence of hyaline degeneration in the olfactory epithelium of female rats was essentially the same response level across groups, the data were not modeled since they provide limited information on the dose-response relationship. The incidence data for histiocyte infiltration in the lungs in male mice, alveolar epithelial metaplasia in male mice, squamous metaplasia in female mice, and alveolar epithelial metaplasia in female mice did not fit any of the available dichotomous models. The model predictions for the other endpoints are presented in Tables A-4, A-5, A-6, and A-7 and the fits of the selected models are presented in Figures A-1, A-2, A-3, and A-4.

Table A-4. Model Predictions for Squamous Metaplasia of the Epiglottis in Male Rats Exposed to Molybdenum Trioxide (NTP 1997)

Model	DF	χ^2	χ^2 Goodness-of-fit p-value[a]	Scaled residuals[b]: Dose below BMC	Scaled residuals[b]: Dose above BMC	Scaled residuals[b]: Overall largest	AIC	BMC_{10} (mg/m^3)	$BMCL_{10}$ (mg/m^3)
Gamma[c]	2	3.07	0.22	0.00	1.55	1.55	169.98	4.36	3.53
Logistic	2	9.45	0.01	1.50	0.93	-2.47	181.70	ND	ND
LogLogistic[d]	2	3.56	0.17	0.00	0.98	-1.42	170.75	3.80	2.23
LogProbit[d]	2	3.74	0.15	-0.00	0.93	-1.51	170.95	ND	ND
Multistage (1-degree)[e]	3	3.07	0.38	0.00	1.55	1.55	167.98	4.36	3.53
Multistage (2-degree)[e,f]	***3***	***3.07***	***0.38***	***0.00***	***1.55***	***1.55***	***167.98***	***4.36***	***3.53***
Multistage (3-degree)[e]	3	3.07	0.38	0.00	1.55	1.55	167.98	4.36	3.53
Probit	2	9.17	0.01	1.60	0.90	-2.37	181.01	ND	ND
Weibull[c]	2	3.07	0.22	0.00	1.55	1.55	169.98	4.36	3.53

[a]Values <0.1 fail to meet conventional goodness-of-fit criteria.
[b]Scaled residuals at doses immediately below and above the BMC; also the largest residual at any dose.
[c]Power restricted to ≥1.
[d]Slope restricted to ≥1.
[e]Betas restricted to ≥0.
[f]Selected model. BMCLs for models providing adequate fit were sufficiently close (differed by <3-fold). Therefore, the model with the lowest AIC was selected.

AIC = Akaike Information Criterion; BMC = maximum likelihood estimate of the exposure concentration associated with the selected benchmark response; BMCL = 95% lower confidence limit on the BMC (subscripts denote benchmark response: i.e., $_{10}$ = exposure concentration associated with 10% extra risk); DF = degrees of freedom; ND = not determined, goodness-of-fit criteria, p<0.10

Figure A-1. Fit of 2-Degree Multistage Model to Data on Incidence of Squamous Metaplasia of the Epiglottis in Male Rats Exposed to Molybdenum Trioxide

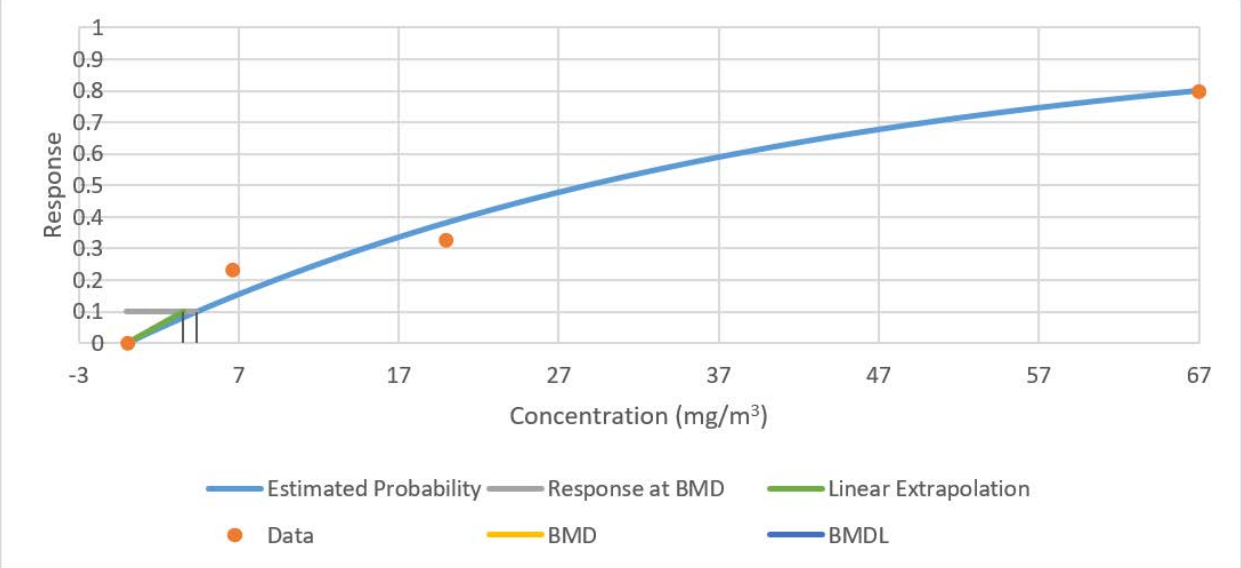


Table A-5. Model Predictions for Hyaline Degeneration of the Nasal Respiratory Epithelium in Female Rats Exposed to Molybdenum Trioxide (NTP 1997)

Model	DF	χ^2	χ^2 Goodness-of-fit p-value[a]	Scaled residuals[b] Dose below BMC	Dose above BMC	Overall largest	AIC	BMC_{10} (mg/m³)	$BMCL_{10}$ (mg/m³)
Gamma[c]	2	4.41	0.11	0.14	-1.03	1.82	77.98	3.69	2.85
Logistic	3	5.04	0.17	-1.20	-0.37	1.86	77.15	3.78	2.95
LogLogistic[d,e]	***2***	***0.02***	***0.99***	***0.00***	***-0.00***	***0.13***	***70.45***	***5.87***	***4.82***
LogProbit[d]	1	0.00	0.99	-0.00	-0.00	-0.00	72.42	5.92	4.73
Multistage (1-degree)[f]	2	18.41	0.00	0.28	-3.28	-3.28	95.80	ND	ND
Multistage (2-degree)[f]	2	2.81	0.24	0.20	-1.21	-1.21	74.57	3.40	2.54
Multistage (3-degree)[f]	2	0.02	0.99	0.01	-0.05	0.15	70.46	4.77	2.39
Probit	2	0.48	0.79	0.49	-0.28	0.49	71.03	4.09	3.12

[a]Values <0.1 fail to meet conventional goodness-of-fit criteria.
[b]Scaled residuals at doses immediately below and above the BMC; also the largest residual at any dose.
[c]Power restricted to ≥1.
[d]Slope restricted to ≥1.
[e]Selected model. BMCLs for models providing adequate fit were sufficiently close (differed by <3-fold). Therefore, the model with the lowest AIC was selected.
[f]Betas restricted to ≥0.

AIC = Akaike Information Criterion; BMC = maximum likelihood estimate of the exposure concentration associated with the selected benchmark response; BMCL = 95% lower confidence limit on the BMC (subscripts denote benchmark response: i.e., $_{10}$ = exposure concentration associated with 10% extra risk); DF = degrees of freedom; ND = not determined, goodness-of-fit criteria, p<0.10

Figure A-2. Fit of Log-logistic Model to Data on Incidence of Hyaline Degeneration of the Nasal Respiratory Epithelium in Female Rats Exposed to Molybdenum Trioxide

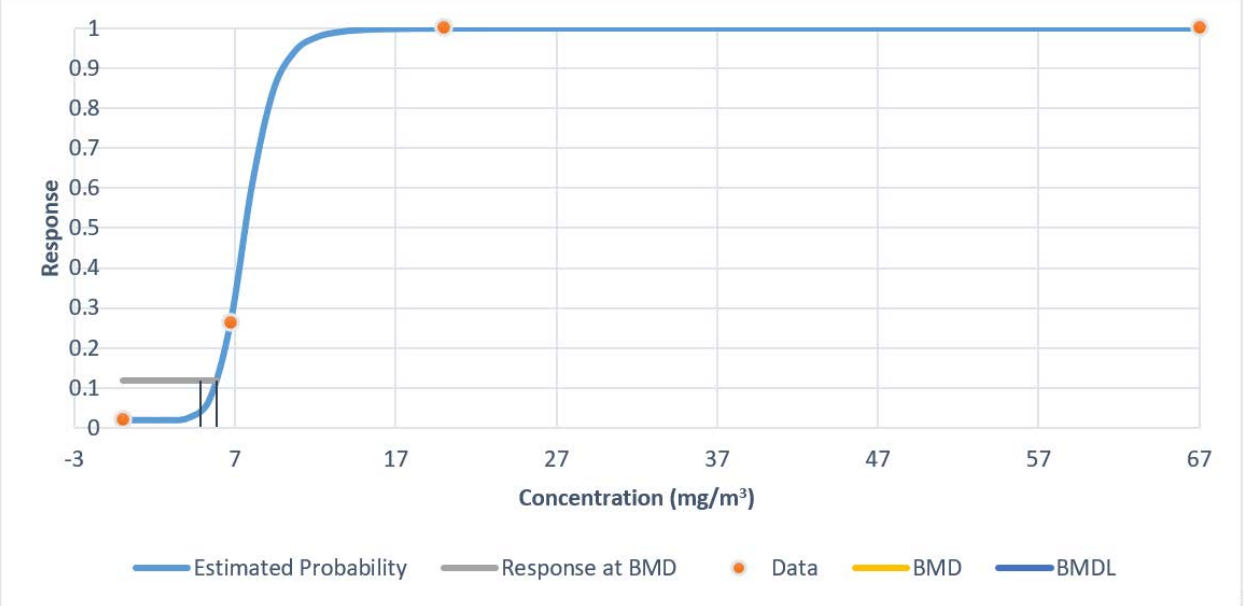


Table A-6. Model Predictions for Squamous Metaplasia of the Epiglottis in Female Rats Exposed to Molybdenum Trioxide (NTP 1997)

Model	DF	χ^2	χ^2 Goodness-of-fit p-value[a]	Scaled residuals[b] Dose below BMC	Scaled residuals[b] Dose above BMC	Scaled residuals[b] Overall largest	AIC	BMC_{10} (mg/m^3)	$BMCL_{10}$ (mg/m^3)
Gamma[c]	2	2.05	0.36	0.00	1.00	1.00	146.51	1.97	1.60
Logistic	2	15.55	0.00	-2.67	2.17	-2.67	163.85	ND	ND
LogLogistic[d]	1	5.02	0.03	-0.00	0.82	-1.58	152.04	ND	ND
LogProbit[e]	2	4.16	0.12	-0.00	0.79	-1.51	148.92	2.76	1.41
Multistage (1-degree)[e]	3	2.05	0.56	-0.00	1.00	1.00	144.51	1.97	1.60
Multistage (2-degree)[e]	1	2.05	0.15	-0.00	1.04	1.04	148.50	1.99	1.60
Multistage (3-degree)[e]	1	1.98	0.16	-0.00	1.11	1.11	148.42	2.02	1.61
Probit	2	17.51	0.00	-2.85	2.00	-2.13	166.05	ND	ND
Weibull[f]	***3***	***2.05***	***0.56***	***-0.00***	***1.00***	***1.00***	***144.51***	***1.97***	***1.60***

[a]Values <0.1 fail to meet conventional goodness-of-fit criteria.
[b]Scaled residuals at doses immediately below and above the BMC; also the largest residual at any dose.
[c]Power restricted to ≥1.
[d]Slope restricted to ≥1.
[e]Betas restricted to ≥0.
[f]Selected model. BMCLs for models providing adequate fit were sufficiently close (differed by <3-fold). Therefore, the model with the lowest AIC was selected.

AIC = Akaike Information Criterion; BMC = maximum likelihood estimate of the exposure concentration associated with the selected benchmark response; BMCL = 95% lower confidence limit on the BMC (subscripts denote benchmark response: i.e., $_{10}$ = exposure concentration associated with 10% extra risk); DF = degrees of freedom; ND = not determined, goodness-of-fit criteria, p<0.10

Figure A-3. Fit of Weibull Model to Data on Incidence of Squamous Metaplasia of the Epiglottis in Female Rats Exposed to Molybdenum Trioxide

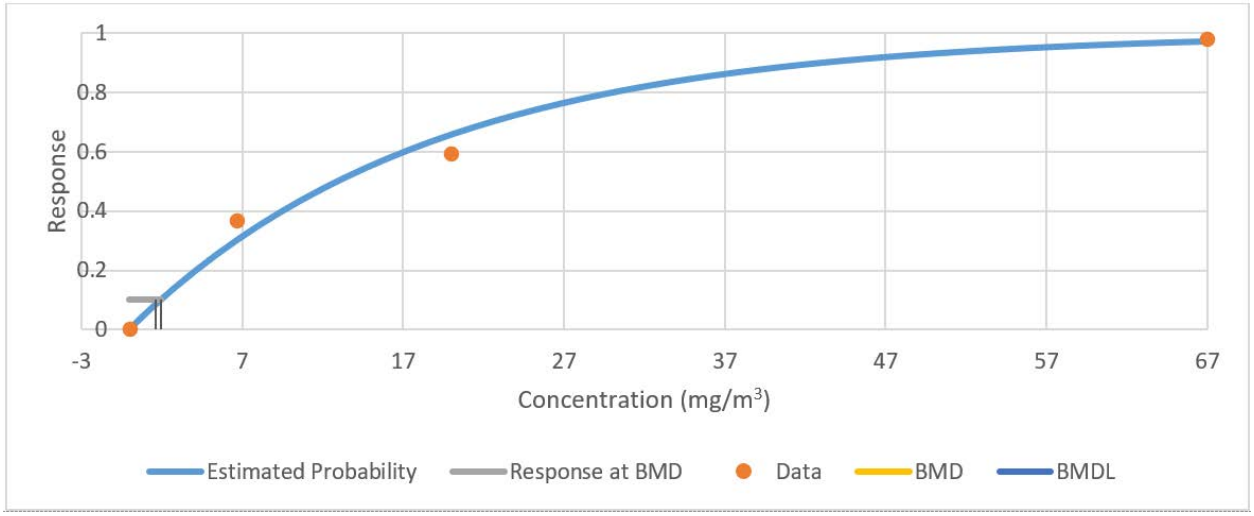


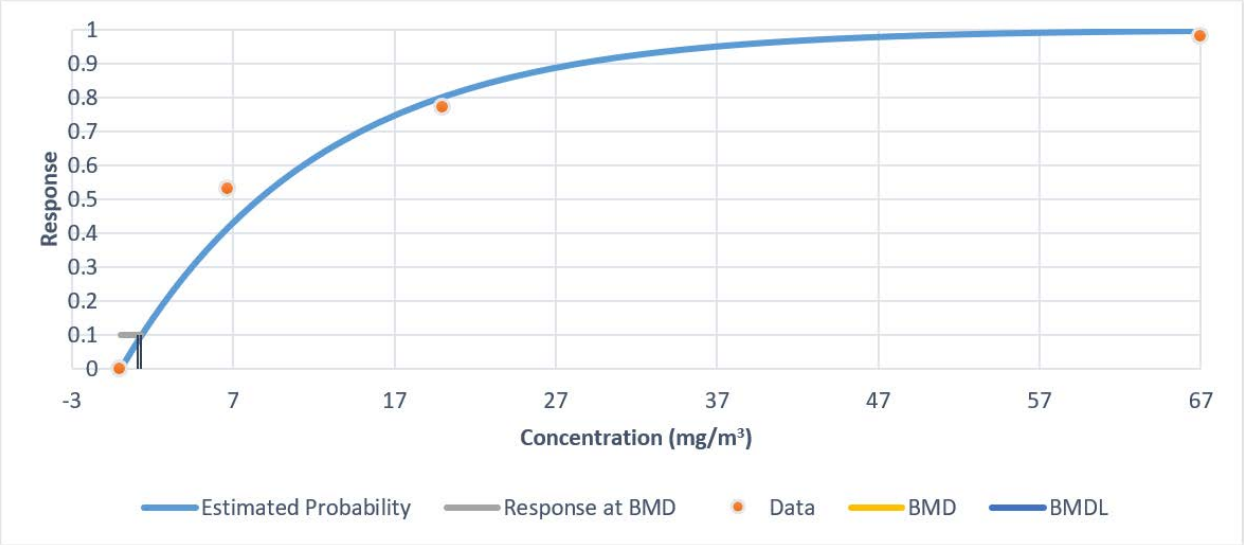
Table A-7. Model Predictions for Squamous Metaplasia of the Epiglottis in Male Mice Exposed to Molybdenum Trioxide (NTP 1997)

Model	DF	χ^2	χ^2 Goodness of fit p-value[a]	Scaled residuals[b] Dose below BMC	Dose above BMC	Overall largest	AIC	BMC_{10} (mg/m^3)	$BMCL_{10}$ (mg/m^3)
Gamma[c,d]	***3***	***5.55***	***0.14***	***-0.00***	***1.60***	***-1.65***	***135.46***	***1.30***	***1.06***
Logistic	2	61.77	0.00	-3.19	2.80	-6.62	164.85	ND-1	ND-1
LogLogistic[e]	1	1.42	0.23	-0.00	0.34	-0.85	134.73	ND-2	ND-2
LogProbit[d]	1	0.88	0.35	-0.00	0.31	-0.70	136.12	ND-2	ND-2
Multistage (1-degree)[f]	2	5.55	0.06	-0.00	1.60	-1.65	137.46	ND-1	ND-1
Multistage (2-degree)[f]	3	5.55	0.14	-0.00	1.60	-1.65	135.46	1.30	1.06
Multistage (3-degree)[f]	3	5.55	0.14	-0.00	1.60	-1.65	135.46	1.30	1.06
Probit	2	90.03	0.00	-3.63	2.65	-8.24	171.89	ND-1	ND-1
Weibull[c]	3	5.55	0.14	-0.00	1.60	-1.65	135.46	1.30	1.06

[a]Values <0.1 fail to meet conventional goodness-of-fit criteria.
[b]Scaled residuals at doses immediately below and above the BMC; also the largest residual at any dose.
[c]Power restricted to ≥1.
[d]Selected model. BMCLs for models providing adequate fit were sufficiently close (differed by <3-fold). Therefore, the model with the lowest AIC was selected.
[e]Slope restricted to ≥1.
[f]Betas restricted to ≥0.

AIC = Akaike Information Criterion; BMC = maximum likelihood estimate of the exposure concentration associated with the selected benchmark response; BMCL = 95% lower confidence limit on the BMC (subscripts denote benchmark response: i.e., $_{10}$ = exposure concentration associated with 10% extra risk); DF = degrees of freedom; ND-1 = not determined, goodness-of-fit criteria, p<0.10; ND-2 = not determined, BMCL was 10 times lower than lowest non-zero dose

Figure A-4. Fit of Gamma Model to Data on Incidence of Squamous Metaplasia of the Epiglottis in Male Mice Exposed to Molybdenum Trioxide



Agency Contacts (Chemical Managers): G. Daniel Todd

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Molybdenum
CAS Numbers: 7439-98-7
Date: May 2020
Profile Status: Final
Route: Oral
Duration: Acute

MRL Summary: There are insufficient data for derivation of an acute-duration oral MRL for molybdenum due inadequate information on the molybdenum and copper intake in the acute-duration studies reporting adverse reproductive effects and the conflicting results between the acute-duration studies and high-quality, intermediate-duration studies.

Rationale for Not Deriving an MRL: A small number of studies have evaluated the acute toxicity of molybdenum. One human study (Deosthale and Gopalan 1974) examining a limited number of potential endpoints did not find alterations in urinary uric acid levels in subjects exposed to doses as high as 0.022 mg molybdenum/kg/day for 10 days. In rabbits, exposure to 1.2 mg molybdenum/kg/day as ammonium heptamolybdate in the diet for 14 days resulted in a 60% increase in serum triglyceride levels (Bersenyi et al. 2008); no histological alterations were observed in the liver or kidneys. The toxicological significance of this finding is not known and has not been reported in a study of male rabbits exposed to 0.58 mg molybdenum/kg/day as ammonium heptamolybdate (Bersenyi et al. 2008) or rats exposed to 60 mg molybdenum/kg/day as sodium molybdate for 90 days (Murray et al. 2014a).

Reproductive effects have been observed in male and female mice and rabbits. In female mice, an increased rate of abnormal MII oocytes was observed at 11 mg molybdenum/kg/day (Zhang et al. 2013). A second acute-exposure study in rabbits exposed to 1.2 mg molybdenum/kg/day as ammonium heptamolybdate for 14 days (Bersenyi et al. 2008) and an intermediate-duration oral study in rats exposed to 60 mg molybdenum/kg/day as sodium molybdate for 90 days (Murray et al. 2014a) did not find histological alterations in the ovaries. In males, a significant decrease in sperm concentration and motility and an increase in sperm abnormalities were observed at 25 mg molybdenum/kg/day in mice (Zhai et al. 2013). A rabbit study reported a reduction in mature spermatocytes in rabbits exposed to 0.58 mg molybdenum/kg/day, but did not report the incidence or statistical significance (Bersenyi et al. 2008). Intermediate-duration studies in rats did not find significant alterations in sperm parameters in rats exposed to 60 mg molybdenum/kg/day as sodium molybdate for 90 days (Murray et al. 2014a) or in rats exposed to 40 mg molybdenum/kg/day as sodium molybdate in a 2-generation study (Murray et al. 2019). Interpretation of the Zhang et al. (2013) and Zhai et al. (2013) studies is limited by the lack of information on the copper content of the “commercial standard pellet” diet used in these studies and the lack of information on molybdenum doses. ATSDR estimated doses using the reported molybdenum concentration in the drinking water and reference values for water consumption and body weight (Zhang et al. 2013) or the midpoint of the reported body weights and an estimated water consumption based on this body weight (Zhai et al. 2013).

The acute-duration oral database was not considered suitable for derivation of an MRL due to the limited information on the molybdenum and copper intake and the conflicting results between the findings of the Zhang et al. (2013) and Zhai et al. (2013) studies with the intermediate-duration Murray et al. (2014a, 2019) studies.

Agency Contacts (Chemical Managers): G. Daniel Todd

APPENDIX A

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:**	Molybdenum
CAS Numbers:	7439-98-7
Date:	May 2020
Profile Status:	Final
Route:	Oral
Duration:	Intermediate
MRL	0.06 mg molybdenum/kg/day
Critical Effect:	Renal effect, proximal tubule hyperplasia
Reference:	Murray et al. 2014a
Point of Departure:	NOAEL of 17 mg molybdenum/kg/day
Uncertainty Factor:	100
Modifying Factor:	3
LSE Graph Key:	14
Species:	Rat

MRL Summary: An intermediate-duration oral MRL of 0.06 mg molybdenum/kg/day was derived for molybdenum based on an increased incidence of renal proximal tubule hyperplasia in rats exposed to sodium molybdate in the diet for 90 days (Murray et al. 2014a). The MRL is based on a NOAEL of 17 mg molybdenum/kg/day, a total uncertainty factor of 100 (10 for extrapolation from animals to humans, and 10 for human variability), and a modifying factor of 3 (to address concern that reproductive/developmental alterations may be sensitive outcomes in populations with marginal copper intakes). The MRL is calculated based on the assumption of healthy dietary levels of molybdenum and copper and represents the level of exposure above and beyond the normal diet.

Selection of the Critical Effect: Several adverse effects have been reported in intermediate-duration oral studies in laboratory animals. Observed effects include kidney damage (Bompart et al. 1990; Murray et al. 2014a, 2019), decreased body weight gain (Bompart et al. 1990; Lyubimov et al. 2004; Mills et al. 1958; Murray et al. 2014a; Van Reen and Williams 1956; Williams and Van Reen 1956), hematological effects (Arrington and Davis 1953; Lyubimov et al. 2004), reproductive effects (Fungwe et al. 1990; Jeter and Davis 1954; Lyubimov et al. 2004; Murray et al. 2014a; Pandey and Singh 2002; Wang et al. 2016), and developmental effects (Pandey and Singh 2002).

The toxicity of molybdenum can be influenced by several factors including animal species; previous dietary history; relative amounts of dietary molybdenum, copper, and sulfur; and the form of molybdenum. Copper nutritional status is particularly important in evaluating the relevance of animal toxicity studies for establishing an MRL. Marked differences in the distribution of molybdenum and copper and the toxicity of molybdenum have been observed in rats exposed to high doses of molybdenum and maintained on a copper-deficient diet compared to those maintained on a copper-adequate diet (Brinkman and Miller 1961; Johnson et al. 1969; Nederbragt 1980, 1982; Sasmal et al. 1968). Since the average copper intake of the U.S. population exceeds the dietary requirements (NAS 2001), studies in which animals were fed inadequate levels of copper were not considered relevant for MRL derivation and were excluded from further consideration. Similarly, studies in which the molybdenum was administered as ammonium tetrathiomolybdate were also excluded since administration of tetrathiomolybdate compounds can result in shifts in the copper levels in rats fed copper-adequate diets (increases in serum and kidney copper levels and decreases in liver copper levels) (Mills et al. 1981a), and copper supplementation of rats exposed to ammonium tetrathiomolybdate resulted in a reversal of adverse effects (Lyubimov et al. 2004). A summary of the NOAEL and LOAEL values for studies with adequate copper in the diet is presented in Table A-8.

Table A-8. Summary of Health Effects Following Intermediate-Duration Oral Exposure to Molybdenum

Species, duration (route)	NOAEL	LOAEL	Effect	Reference (compound)
Body weight				
Rat 147–158 days (diet)		40	22% decrease in maternal body weight gain on GDs 0–7; <10% decrease over entire study	Murray et al. 2019 (sodium molybdate)
Rat 90 days (diet)	17	60	Decrease in body weight gain in males; terminal weights 15.2% less than controls	Murray et al. 2014a (sodium molybdate)
Rat 5 weeks (diet)		74	36% decrease in body weight gain	Mills et al. 1958 (sodium molybdate)
Rat 8 weeks (gavage)	40	80	Decrease in body weight gain; terminal body weight was 26% lower than in controls	Bompart et al. 1990 (ammonium heptamolybdate)
Rat 6 weeks (diet)	85			Williams and Van Reen 1956 (sodium molybdate)
Rat 6 weeks (diet)		90	22% decrease in body weight gain	Williams and Van Reen 1956 (sodium molybdate)
Rat 4–5 weeks (diet)		110	46–48% decrease in body weight gain	Van Reen and Williams 1956 (sodium molybdate)
Rat 147–158 days (drinking water)	40			Murray et al. 2019 (sodium molybdate)
Hematological effects				
Rabbit 30–84 days (diet)	25	54	Anemia	Arrington and Davis 1953 (sodium molybdate)
Rabbit ≥8 weeks (diet)	7			Jeter and Davis 1954 (sodium molybdate)
Rat 90 days (diet)	60			Murray et al. 2014a (sodium molybdate)
Rat 6 weeks (diet)	70			Gray and Daniel 1954 (sodium molybdate)
Kidney effects				
Rat 90 days (diet)	17	60	Slight diffuse hyperplasia in proximal tubules	Murray et al. 2014a (sodium molybdate)
Rat 8 weeks (gavage)	40	80	Diuresis and creatinuria and decreases in creatinine clearance	Bompart et al. 1990 (ammonium heptamolybdate)
Rat 147–158 days (diet)	40			Murray et al. 2019 (sodium molybdate)
Rats 147–158 days (drinking water)	40			Murray et al. 2019 (sodium molybdate)

Table A-8. Summary of Health Effects Following Intermediate-Duration Oral Exposure to Molybdenum

Species, duration (route)	NOAEL	LOAEL	Effect	Reference (compound)
Reproductive effects				
Rat 8 weeks (drinking water)	0.76	1.5	Prolonged estrus phase; no effect on female fertility	Fungwe et al. 1990 (sodium molybdate)
Rat 60 days (gavage)	3.4[a]	10[a]	Decreases in sperm count and motility; increases in sperm abnormalities	Pandey and Singh 2002 (sodium molybdate)
Rat 60 days (gavage)		10[a]	Decreases in male fertility	Pandey and Singh 2002 (sodium molybdate)
Mouse 100 days (drinking water)		100	Decreased sperm density and motility	Wang et al. 2016 (unspecified molybdenum compound)
Rat 90 days (diet)	60		No treatment-related alterations in sperm parameters; no alterations in vaginal cytology, estrus cycle, or histology of male or female reproductive tissues	Murray et al. 2014a (sodium molybdate)
Rat ≥8 weeks (diet)	7		No effect on fertility	Jeter and Davis 1954 (sodium molybdate)
Rat 2 generations (diet)	40		No effects on sperm parameters, estrous cycling, or fertility	Murray et al. 2019 (sodium molybdate)
Rat 2 generations (drinking water)	40		No effects on sperm parameters, estrous cycling, or fertility	Murray et al. 2019 (sodium molybdate)
Developmental effects[b]				
Rat (males only) 60 days (gavage)		10[a]	Increased post-implantation losses, increased resorptions, decreased number of live fetuses, and decreases in fetal weight and crown-rump length	Pandey and Singh 2002 (sodium molybdate)
Rat ≥8 weeks (diet)	7			Jeter and Davis 1954 (sodium molybdate)
Rat GDs 6–20 (diet)	37.5			Murray et al. 2014b (sodium molybdate)
Rat 2 generations (diet)	40			Murray et al. 2019 (sodium molybdate)
Rat 2 generations (drinking water)	40			Murray et al. 2019 (sodium molybdate)

[a]Adjusted for intermittent exposure (5 days/week).
[b]The copper content of the basal diet (6 g/kg diet) in the Fungwe et al. (1990) study is below the recommended level of 8 g/kg required for pregnancy and lactation. Thus, the observed developmental effects are not included in this table.

GD = gestation day; LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level

The Fungwe et al. (1990) study identified the lowest LOAEL value: prolonged estrus phase without an effect on fertility in rats exposed to 1.5 mg molybdenum/kg/day as sodium molybdate in drinking water for 8 weeks (Fungwe et al. 1990). However, this finding was not selected as the critical effect because other high-quality studies have not reported estrus cycle alterations in a 90-day (Murray et al. 2014a) study or 2-generation study (Murray et al. 2019). Additionally, confidence in this study is decreased by the limited information on doses. The study reported molybdenum drinking water concentrations but did not calculate doses. ATSDR estimated doses using reference values for body weight and drinking water consumption. As presented in Table A-9, a comparison with the molybdenum liver concentrations in this study with levels reported in the Murray et al. (2014a, 2019) studies suggested that these estimated doses may have underestimated the actual doses. In the Fungwe et al. (1989) study, the average liver molybdenum level was 10.76 µg/g in the 15 mg/kg/day group; in the Murray et al. (2014a, 2014b) studies, the liver molybdenum level was 4.10–4.92 µg/g in the 17 mg/kg/day groups.

Table A-9. Comparison of Molybdenum Liver Concentrations in Female Rats

Study	Dose Liver molybdenum concentration				
Murray et al. 2019[a] (water exposure, unless noted)	0 mg/kg/day	5 mg/kg/day	17 mg/kg/day	40 mg/kg/day	40 mg/kg/day (dietary exposure)
	2.96 µg/g	3.18 µg/g	4.10 µg/g	6.48 µg/g	7.23 µg/g
Murray et al. 2014a[b] (dietary exposure)	0 mg/kg/day	5 mg/kg/day	17 mg/kg/day	60 mg/kg/day	
	2.46 µg/g	3.51 µg/g	4.92 µg/g	13.0 µg/g	
Fungwe et al. 1989[c] (water exposure)	0 mg/kg/day	0.76 mg/kg/day	1.5 mg/kg/day	7.6 mg/kg/day	15 mg/kg/day
	2.63 µg/g	5.01 µg/g	5.03 µg/g	7.77 µg/g	10.76 µg/g

[a]Parental generation.
[b]Liver concentrations reported in Murray et al. (2019).
[c]Liver concentrations from a study by Fungwe et al. (1990) utilizing the same water concentrations as Fungwe et al. (1989).

The next highest LOAEL is 14 mg molybdenum/kg for decreases in sperm count and motility, increased sperm abnormalities, decreased male fertility, increased post-implantation losses, decreased number of live fetuses, and decreased fetal weight in a study of male rats receiving gavage doses of sodium molybdate 5 days/week during a 60-day period (Pandey and Singh 2002). The reliability of this LOAEL is uncertain due to the lack of information on the copper content of the diet and because decreases in fertility and alterations in sperm parameters have not been observed in other high-quality studies involving exposure to 40 mg molybdenum/kg/day via the diet or drinking water in a 2-generation study (Murray et al. 2019) or 60 mg molybdenum/kg/day via the diet in a 90-day study (Murray et al. 2014a). Additionally, no developmental effects were observed in single-generation (Murray et al. 2014b) or 2-generation (Murray et al. 2019) studies in rats exposed to 37.5–40 mg/kg/day.

As with the reproductive and developmental effects, only one study reported hematological effects. Anemia was reported in rabbits exposed to 54 mg molybdenum/kg/day as sodium molybdate in the diet for 30–84 days (Arrington and Davis 1953). This is considered a low-quality study because the molybdenum was sprayed on the food pellets but there was no measurement of actual dietary

concentrations, only 2–5 animals per group were tested, and no information was provided on which hematological parameters were altered. Additionally, the diet may not have provided adequate copper levels since copper supplementation was administered to the 54 mg/kg/day group to prevent deaths in the 3/5 animals that exhibited "severe toxic symptoms" characteristic of copper deficiency.

If the reproductive, developmental, and hematological effects are excluded because they were reported in lesser-quality studies and were not confirmed in higher-quality studies, then the lowest LOAEL is 60 mg/kg/day for body weight and renal effects (Murray et al. 2014a). A 15% decrease in body weight gain was observed in male rats; no significant alterations were observed in females. Although a decrease in food consumption was also observed at this dose level, decreases in food efficiency observed at this dose suggest that the decrease in body weight was not solely related to the decreased food intake. The renal effects consisted of slight diffuse hyperplasia in the renal proximal tubules of 2/10 female rats. The investigators (Murray et al. 2014a) noted that this effect is an uncommon background finding in rats of this age and considered it to be treatment related; they also suggested that the effect may be due to the high levels of copper in the kidneys. Kidney effects (degeneration followed by regeneration) have been observed in rats exposed to high levels of copper in the diet (Haywood 1985). A second molybdenum study (Bompart et al. 1990) reported diuresis, creatinuria, decreases in creatinine clearance, and increases in daily excretion of immunoreactive kallikrein in rats administered 80 mg molybdenum/kg/day via gavage for 8 weeks. These alterations are suggestive of decreased glomerular function and distal tubule damage; the absence of changes in the brush border enzymes alanine aminopeptidase and γ-glutamyl transpeptidase suggests no damage to the proximal tubule functional capacity. The study did not include histopathological examination of the kidneys. Although the incidence of proximal tubular hyperplasia was not statistically significant in the high-dose females in the Murray et al. (2014a) study, support for identifying this as the critical effect comes from the Bompart et al. (1990) study, which found evidence of impaired renal function in rats exposed to a slightly higher dose.

Several studies have reported decreases in body weight gain; the lowest LOAEL for this effect was 40 mg molybdenum/kg/day as sodium molybdate in the diet in a 2-generation study (Murray et al. 2019). This study reported a 22% decrease in body weight gain on GDs 0–7 in the parental-generation females. The difference in body weight gain over the length of the study was <10% lower than the controls. This was not observed in the F1 generation and was not observed in P or F1 generation rats similarly exposed to 40 mg molybdenum/kg/day as sodium molybdate in the drinking water (Murray et al. 2019). Decreases in body weight have also been observed at higher molybdenum doses (Bompart et al. 1990; Mills et al. 1958; Murray et al. 2014a; Van Reem and Williams 1956). The decrease in body weight gain observed in the Murray et al. (2019) study was not selected as the basis of the MRL because it was not replicated in the F1 generation or in rats exposed via drinking water (Murray et al. 2019).

Selection of the Principal Study: The Murray et al. (2014a) study was selected as the principal study because it identified the lowest LOAEL for renal effects.

Summary of the Principal Study:

Murray FJ, Sullivan FM, Tiwary AK, et al. 2014a. 90-Day subchronic toxicity study of sodium molybdate dihydrate in rats. Regul Toxicol Pharmacol 79:579-588.

Groups of 10 male and 10 female Sprague-Dawley rats were exposed to 0, 5, 17, or 60 mg molybdenum/kg/day (actual concentrations were 0, 4.5, 15.1, and 54.8 mg/kg/day, respectively, in males and 0, 5.4, 19.0, and 65.2 mg/kg/day, respectively, in females and the average overall intakes were 0, 5.0, 17.1, and 60.0 mg/kg/day, respectively) as sodium molybdate dihydrate in the diet for 91 and 92 days; additional groups of rats (10/sex/group) were similarly exposed to 0 or 60 mg/kg/day for 91–92 days and then continued on the basal diet for 60 days. The basal diet contained 906.5 µg/kg molybdenum and

14.23 mg/kg copper; the investigators estimated that the control group received 0.08 mg molybdenum/kg/day. The following parameters were used to assess toxicity: cage-side observations, weekly clinical examinations, ophthalmic examination, weekly body weight measurements, measurement of hematological (hemoglobin, hematocrit, erythrocyte, platelet, mean corpuscular hemoglobin concentration, mean corpuscular volume, red cell distribution width, total and differential leukocyte, reticulocyte, and prothrombin time) and serum chemistry (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, blood urea nitrogen, creatinine, glucose, cholesterol, triglycerides, total protein, albumin, uric acid, total bilirubin, sodium, potassium, chloride, calcium, and inorganic phosphorus) parameters, organ weights (adrenal glands, brain, epididymides, heart, kidneys, liver, ovaries, pituitary gland, prostate gland and seminal vesicles, spleen, testes, thymus, thyroid/ parathyroid glands, and uterus with cervix), and histopathology examination of major tissues and organs in control and 60 mg/kg/day groups (primary and recovery groups) and the adrenal glands from males and kidneys from females in the 5 and 17 mg/kg/day groups. Additionally, sperm counts and sperm mobility and vaginal cytology and estrus cycles were evaluated.

Significant decreases in body weight gain were observed at 60 mg/kg/day in males starting at week 1 and in females starting at week 6. Terminal body weights were 15.2 and 5.6% less than controls, with only the males being significantly different from controls. At the end of the recovery period, the 60 mg/kg/day males weighed significantly less (9.5%) than controls. Decreases in food consumption were observed on numerous occasions in the males exposed to 60 mg/kg/day; a decrease in food conversion efficiency was also observed in this group. No significant or treatment-related alterations in hematological or serum chemistry parameters were observed. Significant decreases in absolute brain, liver, heart, spleen, and pituitary weights were observed in males exposed to 60 mg/kg/day; however, there were no significant alterations in relative organ weights. Treatment-related histopathological alterations were limited to a slight diffuse hyperplasia in the renal proximal tubules in 2/10 females in the 60 mg/kg/day group; the investigators considered it to be treatment-related because it is an uncommon finding at this age. No significant alterations in vaginal cytology or estrus cycles were observed. Similarly, no significant alterations in spermatid or sperm counts or sperm morphology were observed in males. A slight decrease in sperm motility was observed at 60 mg/kg/day; however, this was likely attributable to the control group having a value that approached the upper limit among historical controls and was not considered treatment related. No alterations in reproductive organ weights or histological alterations were observed.

Selection of the Point of Departure for the MRL: The NOAEL of 17 mg molybdenum/kg/day was selected as the POD for the MRL. BMD modeling was not considered because a response was only observed at the highest dose tested. A dataset exhibiting a response only at the highest dose level would likely provide limited information regarding the shape of a dose-response curve.

Calculations: The investigators estimated doses using body weight and food consumption data.

Intermittent Exposure: Not applicable.

Uncertainty Factor and Modifying Factor: The NOAEL is divided by a total uncertainty factor (UF) of 100 and a modifying factor (MF) of 3

- 10 UF for extrapolation from animals to humans
- 10 UF for human variability
- 3 MF for concern that reproductive and/or developmental effects may be a more sensitive endpoint than kidney effects in populations with marginal copper intakes. The copper content of the Murray et al. (2014b, 2019) reproductive/developmental studies used a commercial diet with a fairly high copper content. In contrast, the Fungwe et al. (1990) study, which reported

reproductive effects, utilized a diet that was slightly higher than the dietary requirement. The differences in the copper contents of the diet may explain differences between the study results.

MRL = NOAEL ÷ (UFs x MF)
0.06 mg molybdenum/kg/day = 17 mg molybdenum/kg/day ÷ ((10 x 10) x 3)

Other Additional Studies or Pertinent Information that Lend Support to this MRL: Selection of the POD is supported by the Bompart et al. (1990) study, which found decreases in kidney function in rats administered sodium molybdate.

The MRL is calculated based on the assumption of healthy dietary levels of molybdenum and copper and represents the level of exposure above and beyond the normal diet.

Agency Contacts (Chemical Managers): G. Daniel Todd

MINIMAL RISK LEVEL (MRL) WORKSHEET

***Chemical Name*:** Molybdenum
CAS Numbers: 7439-98-7
Date: May 2020
Profile Status: Final
Route: Oral
Duration: Chronic

MRL Summary: There are insufficient data for derivation of a chronic-duration oral MRL for molybdenum. The only available experimental study was considered a low-quality study that was not considered a suitable basis for an MRL.

Rationale for Not Deriving an MRL: Data on the chronic toxicity of molybdenum come from several population-based studies; most of these studies looked for associations between background exposure to molybdenum and adverse health outcomes. No laboratory animal studies were identified.

Koval'skiy et al. (1961) found increases in blood uric acid and symptoms of gout in residents living in Armenia with high levels of molybdenum in the soil and food; the investigators estimated that the residents were exposed to 10–15 mg/day (0.14–0.21 mg/kg/day). A series of small studies of residents living in areas of Colorado with high levels of molybdenum in the drinking water did not find significant increases in uric acid levels; one study estimated that molybdenum intake was 500 μg/day (0.007 mg/kg/day) (EPA 1979). Other studies have found significant associations between serum or urinary molybdenum levels and the severity of complications from diabetes (Rodriguez Flores et al. 2011), high blood pressure (Yorita Christensen 2013), semen quality (Meeker et al. 2008), testosterone levels (Meeker et al. 2010), and psychomotor index in infants (molybdenum levels were measured in the mothers) (Vazques-Salas et al. 2014). However, none of these studies established causality, and the molybdenum levels accounted for only a small percentage of the variance.

Although the Koval'sky et al. (1961) study provided an estimated dose, the study was not considered suitable for derivation of a chronic-duration oral MRL for molybdenum. The study has a number of deficiencies that limit the interpretation of the results: (1) the control group consisted of 5 individuals compared to 52 subjects in the exposed group; (2) no information was provided on the controls to assess whether they were matched to the exposed group; (3) it does not appear that the study controlled for potential confounders, such as diet and alcohol, which can increase uric acid levels; and (4) NAS (2001) noted that there were potential analytical problems with the measurement of serum and urine copper levels.

Agency Contacts (Chemical Managers): G. Daniel Todd

APPENDIX B. LITERATURE SEARCH FRAMEWORK FOR MOLYBDENUM

The objective of the toxicological profile is to evaluate the potential for human exposure and the potential health hazards associated with inhalation, oral, or dermal/ocular exposure to molybdenum.

B.1 LITERATURE SEARCH AND SCREEN

A literature search and screen was conducted to identify studies examining health effects, toxicokinetics, mechanisms of action, susceptible populations, biomarkers, chemical interactions, physical and chemical properties, production, use, environmental fate, environmental releases, and environmental and biological monitoring data for molybdenum. ATSDR primarily focused on peer-reviewed articles without publication date or language restrictions. Non-peer-reviewed studies that were considered relevant to the assessment of the health effects of molybdenum have undergone peer review by at least three ATSDR-selected experts who have been screened for conflict of interest. The inclusion criteria used to identify relevant studies examining the health effects of molybdenum are presented in Table B-1.

Table B-1. Inclusion Criteria for the Literature Search and Screen

- Health Effects
  - Species
    - Human
    - Laboratory mammals
  - Route of exposure
    - Inhalation
    - Oral
    - Dermal (or ocular)
    - Parenteral (these studies will be considered supporting data)
  - Health outcome
    - Death
    - Systemic effects
    - Body weight effects
    - Respiratory effects
    - Cardiovascular effects
    - Gastrointestinal effects
    - Hematological effects
    - Musculoskeletal effects
    - Hepatic effects
    - Renal effects
    - Dermal effects
    - Ocular effects
    - Endocrine effects
    - Immunological effects
    - Neurological effects
    - Reproductive effects
    - Developmental effects
    - Other noncancer effects

Table B-1. Inclusion Criteria for the Literature Search and Screen

Cancer
Toxicokinetics
Absorption
Distribution
Metabolism
Excretion
PBPK models
Biomarkers
Biomarkers of exposure
Biomarkers of effect
Interactions with other chemicals
Potential for human exposure
Releases to the environment
Air
Water
Soil
Environmental fate
Transport and partitioning
Transformation and degradation
Environmental monitoring
Air
Water
Sediment and soil
Other media
Biomonitoring
General populations
Occupation populations

B.1.1 Literature Search

The current literature search was intended to update the draft toxicological profile for molybdenum released for public comment in 2017. The following main databases were searched in January 2018:

- PubMed
- National Library of Medicine's TOXLINE
- Scientific and Technical Information Network's TOXCENTER

The search strategy used the chemical names, Chemical Abstracts Service (CAS) numbers, synonyms, Medical Subject Headings (MeSH) headings, and keywords for molybdenum. The query strings used for the literature search are presented in Table B-2.

The search was augmented by searching the Toxic Substances Control Act Test Submissions (TSCATS), NTP website, and National Institute of Health Research Portfolio Online Reporting Tools Expenditures and Results (NIH RePORTER) databases using the queries presented in Table B-3. Additional databases

were searched in the creation of various tables and figures, such as the TRI Explorer, the Substance Priority List (SPL) resource page, and other items as needed. Regulations applicable to molybdenum were identified by searching international and U.S. agency websites and documents.

Review articles were identified and used for the purpose of providing background information and identifying additional references. ATSDR also identified reports from the grey literature, which included unpublished research reports, technical reports from government agencies, conference proceedings and abstracts, and theses and dissertations.

Table B-2. Database Query Strings

Database search date	Query string
PubMed	
01/2018	((("Molybdenum/toxicity"[mh] OR "Molybdenum/adverse effects"[mh] OR "Molybdenum/poisoning"[mh] OR "Molybdenum/pharmacokinetics"[mh]) OR ("Molybdenum"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Molybdenum"[mh] AND toxicokinetics[mh:noexp]) OR ("Molybdenum/blood"[mh] OR "Molybdenum/cerebrospinal fluid"[mh] OR "Molybdenum/urine"[mh]) OR ("Molybdenum"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Molybdenum"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Molybdenum/antagonists and inhibitors"[mh]) OR ("Molybdenum/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Molybdenum"[mh] AND cancer[sb]) OR ("Molybdenum/pharmacology"[majr])) AND (2013/12/01 : 3000[dp] OR 2014/12/01 : 3000[mhda])) OR (("1317-33-5"[rn] OR "12033-29-3"[rn] OR "12033-33-9"[rn] OR "11098-99-0"[rn] OR "18868-43-4"[rn] OR "1313-27-5"[rn] OR "1313-29-7"[rn] OR "11098-84-3"[rn] OR "27546-07-2"[rn] OR "12054-85-2"[rn] OR "15060-55-6"[rn] OR "7631-95-0"[rn] OR "10102-40-6"[rn] OR "7789-82-4"[rn] OR "12011-97-1"[rn] OR "11119-46-3"[rn] OR "11062-51-4"[rn] OR "10241-05-1"[rn] OR "1309-56-4"[rn] OR "7783-77-9"[rn] OR "13939-06-5"[rn] OR "14221-06-8"[rn] OR "13814-74-9"[rn] OR "12027-67-7"[rn] OR "13106-76-8"[rn]) AND (("Disulfides/toxicity"[mh] OR "Disulfides/adverse effects"[mh] OR "Disulfides/poisoning"[mh] OR "Disulfides/pharmacokinetics"[mh]) OR ("Disulfides/blood"[mh] OR "Disulfides/cerebrospinal fluid"[mh] OR "Disulfides/urine"[mh]) OR ("Disulfides/antagonists and inhibitors"[mh]) OR ("Disulfides/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Disulfides/pharmacology"[majr]) OR ("Chlorides/toxicity"[mh] OR "Chlorides/adverse effects"[mh] OR "Chlorides/poisoning"[mh] OR "Chlorides/pharmacokinetics"[mh]) OR ("Chlorides/blood"[mh] OR "Chlorides/cerebrospinal fluid"[mh] OR "Chlorides/urine"[mh]) OR ("Chlorides/antagonists and inhibitors"[mh]) OR ("Chlorides/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Chlorides/pharmacology"[majr]) OR ("Oxides/toxicity"[mh] OR "Oxides/adverse effects"[mh] OR "Oxides/poisoning"[mh] OR "Oxides/pharmacokinetics"[mh]) OR ("Oxides/blood"[mh] OR "Oxides/cerebrospinal fluid"[mh] OR "Oxides/urine"[mh]) OR

Table B-2. Database Query Strings

Database search date	Query string
	("Oxides/antagonists and inhibitors"[mh]) OR ("Oxides/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Oxides/pharmacology"[majr]) OR (("disulfides"[mh] OR "chlorides"[mh] OR "oxides"[mh]) AND ("environmental exposure"[mh] OR ci[sh])) OR (("disulfides"[mh] OR "chlorides"[mh] OR "oxides"[mh]) AND toxicokinetics[mh:noexp]) OR (("disulfides"[mh] OR "chlorides"[mh] OR "oxides"[mh]) AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR (("disulfides"[mh] OR "chlorides"[mh] OR "oxides"[mh]) AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR (("disulfides"[mh] OR "chlorides"[mh] OR "oxides"[mh]) AND cancer[sb])) AND (2013/12/01 : 3000[dp] OR 2014/12/01 : 3000[mhda])) OR "12027-67-7"[rn] OR ((("7439-98-7"[rn] OR "1317-33-5"[rn] OR "12033-29-3"[rn] OR "12033-33-9"[rn] OR "11098-99-0"[rn] OR "18868-43-4"[rn] OR "1313-27-5"[rn] OR "1313-29-7"[rn] OR "11098-84-3"[rn] OR "27546-07-2"[rn] OR "12054-85-2"[rn] OR "15060-55-6"[rn] OR "7631-95-0"[rn] OR "10102-40-6"[rn] OR "7789-82-4"[rn] OR "12011-97-1"[rn] OR "11119-46-3"[rn] OR "11062-51-4"[rn] OR "10241-05-1"[rn] OR "1309-56-4"[rn] OR "7783-77-9"[rn] OR "13939-06-5"[rn] OR "14221-06-8"[rn] OR "13814-74-9"[rn] OR "12027-67-7"[rn] OR "13106-76-8"[rn]) NOT ("molybdenum"[mh] OR "disulfides"[mh] OR "chlorides"[mh] OR "oxides"[mh])) AND (2013/12/01 : 3000[dp] OR 2014/12/01 : 3000[mhda])) OR (("Ammonium molybdenum sulfide"[tw] OR "Ammonium tetrasulfidomolybdate(2-)"[tw] OR "Ammonium tetrathiomolybdate"[tw] OR "Ammonium thiomolybdate(VI)"[tw] OR "ATTM"[tw] OR "Bis(ammonium)tetrathiomolybdate(2-)"[tw] OR "Calcium molybdate"[tw] OR "Calcium molybdate(VI)"[tw] OR "Calcium molybdenate"[tw] OR "Calcium molybdenum oxide"[tw] OR "Coprexa"[tw] OR "Diammonium tetrakis(sulfido)molybdate(2-)"[tw] OR "Diammonium tetrakis(thioxo)molybdate"[tw] OR "Diammonium tetrasulfidomolybdate"[tw] OR "Diammonium tetrathiomolybdate"[tw] OR "Diammonium tetrathiomolybdate(2-)"[tw] OR "Diammonium tetrathiooxomolybdate(2-)"[tw] OR "Diammonium tetrathioxomolybdate(2-)"[tw] OR "Diammonium thiomolybdate"[tw] OR "Dimolybdenum tetraacetate"[tw] OR "Dimolybdenum trioxide"[tw] OR "Dodecachlorohexamolybdenum"[tw] OR "Hexafluoromolybdenum"[tw] OR "Hexamolybdenum dodecachloride"[tw] OR "MC 400WR"[tw] OR "Molybdate, calcium"[tw] OR "Molybdenite"[tw] OR "Molybdenum anhydride"[tw] OR "Molybdenum carbide"[tw] OR "Molybdenum chloride"[tw] OR "Molybdenum chloride oxide"[tw] OR "Molybdenum dioxide"[tw] OR "Molybdenum fluoride"[tw] OR "Molybdenum hexafluoride"[tw] OR "Molybdenum monocarbide"[tw] OR "Molybdenum oxide"[tw] OR "Molybdenum oxychloride"[tw] OR "Molybdenum oxytrichloride"[tw] OR "Molybdenum sesquioxide"[tw] OR "Molybdenum sulfide"[tw] OR "Molybdenum trichloride monoxide"[tw] OR "Molybdenum trichloride oxide"[tw] OR "Molybdenum trisulfide"[tw] OR "Molybdenum(6+) fluoride"[tw] OR "Molybdenum(II) acetate"[tw] OR "Molybdenum(IV) oxide"[tw] OR "Molybdic acid, calcium salt"[tw] OR "Octachlorohexamolybdenum(4+) tetrachloride"[tw] OR "Tetraacetatodimolybdenum"[tw] OR "tetrakis(acetato)di-Molybdenum"[tw] OR "Tetrakis(acetato)dimolybdenum"[tw] OR "Tetrakis(acetato)molybdenum"[tw] OR "Tetrakis(mu-(acetato-O:O'))dimolybdenum"[tw]

Table B-2. Database Query Strings

Database search date	Query string
	OR "tetrakis(mu-acetato)di-Molybdenum"[tw] OR "Tetrakis(mu-acetato)dimolybdenum"[tw] OR "tetrakis[mu-(acetato-O:O')]di-Molybdenum"[tw] OR "Thiomolybdic acid (H2MoS4), diammonium salt"[tw] OR "Thiomolybdic acid, diammonium salt"[tw] OR "Tiomolibdate diammonium"[tw] OR "Trichlorooxomolybdenum"[tw] OR "Trichlorooxomolybdenum(V)"[tw]) AND (2013/12/01 : 3000[dp] OR 2014/12/01 : 3000[crdat] OR 2014/12/01 : 3000[edat])) OR ((("3N5"[tw] OR "A Powder"[tw] OR "Ammonium dimolybdate"[tw] OR "Ammonium heptamolybdate"[tw] OR "Ammonium heptamolybdate tetrahydrate"[tw] OR "Ammonium molibdate"[tw] OR "Ammonium molibdenum oxide"[tw] OR "Ammonium molybdate"[tw] OR "Ammonium molybdate hydrate"[tw] OR "Ammonium molybdate tetrahydrate"[tw] OR "Ammonium molybdate(VI)"[tw] OR "Ammonium molybdenum oxide"[tw] OR "Ammonium molybdenum sulfide"[tw] OR "ammonium paramolybdate"[tw] OR "Ammonium paramolybdate tetrahydrate"[tw] OR "Ammonium tetrasulfidomolybdate(2-)"[tw] OR "Ammonium tetrathiomolybdate"[tw] OR "Ammonium thiomolybdate(VI)"[tw] OR "Amperit 105.054"[tw] OR "Amperit 106.2"[tw] OR "ATTM"[tw] OR "Bis(ammonium)tetrathiomolybdate(2-)"[tw] OR "Bouen SKN 301"[tw] OR "C-Powder"[tw] OR "Calcium molybdate"[tw] OR "Calcium molybdate(VI)"[tw] OR "Calcium molybdenate"[tw] OR "Calcium molybdenum oxide"[tw] OR "Coprexa"[tw] OR "DAG 206"[tw] OR "DAG 325"[tw] OR "DAG-V 657"[tw] OR "Defric coat HMB 2"[tw] OR "Diammonium dimolybdate"[tw] OR "Diammonium tetrakis(sulfido)molybdate(2-)"[tw] OR "Diammonium tetrakis(thioxo)molybdate"[tw] OR "Diammonium tetrasulfidomolybdate"[tw] OR "Diammonium tetrathiomolybdate"[tw] OR "Diammonium tetrathiomolybdate(2-)"[tw] OR "Diammonium tetrathiooxomolybdate(2-)"[tw] OR "Diammonium tetrathioxomolybdate(2-)"[tw] OR "Diammonium thiomolybdate"[tw] OR "Dimolybdenum tetraacetate"[tw] OR "Dimolybdenum trioxide"[tw] OR "dimolybdenum trisulfide "[tw] OR "Disodium molybdate"[tw] OR "Disodium molybdate dihydrate"[tw] OR "Disodium tetraoxomolybdate"[tw] OR "DM 1 (sulfide)"[tw] OR "DMI 7"[tw] OR "Dodecachlorohexamolybdenum"[tw] OR "Hexaammonium heptamolybdate tetrahydrate"[tw] OR "Hexaammonium molybdate tetrahydrate"[tw] OR "Hexacarbonylmolybdenum"[tw] OR "Hexafluoromolybdenum"[tw] OR "Hexamolybdenum dodecachloride"[tw] OR "JCPDS 35-0609"[tw] OR "Liqui-Moly LM 11"[tw] OR "Liqui-Moly LM 2"[tw] OR "Liqui-Moly Z Powder"[tw] OR "LM 13"[tw] OR "MC 400WR"[tw] OR "MChVL"[tw] OR "MD 40"[tw] OR "Metco 63"[tw] OR "MF 000"[tw] OR "MIPO-M 15"[tw] OR "Mo 1202T"[tw] OR "Mo-1202T"[tw] OR "Moly Fine Powder Y"[tw] OR "Moly Powder B"[tw] OR "Moly Powder C"[tw] OR "Moly Powder PA"[tw] OR "Moly Powder PB"[tw] OR "Moly Powder PS"[tw] OR "Molybdate (Mo2O72-), diammonium"[tw] OR "Molybdate (MoO42-), disodium, dihydrate, (T-4)-"[tw] OR "Molybdate, calcium"[tw] OR "Molybdena"[tw] OR "Molybdenite"[tw] OR "Molybdenum"[tw] OR "Molybdenum anhydride"[tw] OR "Molybdenum bisulfide"[tw] OR "Molybdenum carbide"[tw] OR "Molybdenum carbonyl"[tw] OR "Molybdenum chloride"[tw] OR "Molybdenum chloride oxide"[tw] OR "Molybdenum dioxide"[tw] OR "Molybdenum disulfide"[tw] OR "Molybdenum disulphide"[tw] OR "Molybdenum fluoride"[tw] OR "Molybdenum hexacarbonyl"[tw] OR "Molybdenum hexafluoride"[tw] OR "Molybdenum metallicum"[tw] OR "Molybdenum monocarbide"[tw] OR "Molybdenum oxide"[tw] OR "Molybdenum oxychloride"[tw] OR "Molybdenum oxytrichloride"[tw] OR "Molybdenum pentachloride"[tw] OR "Molybdenum peroxide"[tw] OR "Molybdenum sesquioxide"[tw] OR "Molybdenum sesquisulfide"[tw] OR "Molybdenum sodium oxide"[tw] OR "Molybdenum sulfide"[tw] OR "Molybdenum sulphide"[tw] OR "Molybdenum trichloride monoxide"[tw] OR "Molybdenum trichloride oxide"[tw] OR "Molybdenum trioxide"[tw] OR "Molybdenum trioxide pentamer"[tw] OR "Molybdenum trioxide tetramer"[tw] OR "Molybdenum trisulfide"[tw] OR "Molybdenum(6+) fluoride"[tw] OR "Molybdenum(II) acetate"[tw] OR "Molybdenum(II) chloride"[tw] OR "molybdenum(III)

Table B-2. Database Query Strings

Database search date	Query string
	sulfide"[tw] OR "molybdenum(IV) oxide"[tw] OR "Molybdenum(IV) sulfide"[tw] OR "Molybdenum(V) chloride"[tw] OR "Molybdenum(VI) oxide"[tw] OR "Molybdenum(VI) trioxide"[tw] OR "Molybdenumperoxide"[tw] OR "Molybdic acid (H2Mo2O7), diammonium salt"[tw] OR "Molybdic acid (H2MoO4), calcium salt (1:1)"[tw] OR "Molybdic acid anhydride"[tw] OR "Molybdic acid, ammonium salt"[tw] OR "Molybdic acid, calcium salt"[tw] OR "Molybdic acid, disodium salt"[tw] OR "Molybdic acid, disodium salt, dihydrate"[tw] OR "Molybdic anhydride"[tw] OR "Molybdic oxide"[tw] OR "Molybdic trioxide"[tw] OR "Molycolloid CF 626"[tw] OR "Molyform 15"[tw] OR "Molyhibit 100"[tw] OR "Molyka R"[tw] OR "Molyka R-L 3"[tw] OR "Molyke R"[tw] OR "Molykote"[tw] OR "Molykote Microsize Powder"[tw] OR "Molykote Z"[tw] OR "Molykote Z Powder"[tw] OR "Molysulfide"[tw] OR "MOP-P 100"[tw] OR "Mopol M"[tw] OR "Mopol S"[tw] OR "Motimol"[tw] OR "MVCh 1"[tw] OR "Natural molybdenite"[tw] OR "Natural molybdite"[tw] OR "NeoZ"[tw] OR "Nichimoly C"[tw] OR "Octachlorohexamolybdenum(4+) tetrachloride"[tw] OR "OKS 110"[tw] OR "PA Powder"[tw] OR "Pentachloromolybdenum Molybdenite"[tw] OR "Pigment Black 34"[tw] OR "Pol-U"[tw] OR "Powder PA"[tw] OR "RAC 01"[tw] OR "SGC 15"[tw] OR "Sodium molybdate"[tw] OR "Sodium molybdate dihydrate"[tw] OR "Sodium molybdate(VI)"[tw] OR "Sodium molybdate(VI) dihydrate"[tw] OR "Sodium molybdenate"[tw] OR "Sodium molybdenum oxide"[tw] OR "Sodium tetraoxomolybdate(2-)"[tw] OR "Solvest 390A"[tw] OR "Sumipowder PA"[tw] OR "T-Powder"[tw] OR "Tetraacetatodimolybdenum"[tw] OR "tetrakis(acetato)di-Molybdenum"[tw] OR "Tetrakis(acetato)dimolybdenum"[tw] OR "Tetrakis(acetato)molybdenum"[tw] OR "Tetrakis(mu-(acetato-O:O'))dimolybdenum"[tw] OR "tetrakis(mu-acetato)di-Molybdenum"[tw] OR "Tetrakis(mu-acetato)dimolybdenum"[tw] OR "tetrakis[mu-(acetato-O:O')]di-Molybdenum"[tw] OR "Thiomolybdic acid, diammonium salt"[tw] OR "Tiomolibdate diammonium"[tw] OR "TMOIO"[tw] OR "Trichlorooxomolybdenum"[tw] OR "Trichlorooxomolybdenum(V)"[tw] OR "TsM1"[tw] OR "UP 10"[tw] OR "UP 50"[tw] OR ("Hexaammonium heptamolybdate"[tw] OR "Hexammonium heptamolybdat"[tw] OR "Hexammonium tetracosaoxoheptamolybdate"[tw] OR "Molybdate (Mo7O24), hexammonium"[tw] OR "Molybdate (Mo7O246-), ammonium (1:6)"[tw] OR "Molybdate (Mo7O246-), hexaammonium"[tw] OR "Molybdate, hexaammonium"[tw] OR "Molybdic acid (H6Mo7O24), hexaammonium salt"[tw] OR "Molybdic acid, hexaammonium salt"[tw] OR "Diammonium molybdate"[tw] OR "Diammonium tetraoxomolybdate(2-)"[tw] OR "Molybdate (MoO42-), ammonium (1:2), (T-4)-"[tw] OR "Molybdate (MoO42-), diammonium, (beta-4)-"[tw] OR "Molybdate (MoO42-), diammonium, (T-4)-"[tw] OR "Molybdic acid (H2MoO4), diammonium salt"[tw] OR "Molybdic acid, diammonium salt"[tw])) NOT medline[sb]) AND (2013/12/01 : 3000[dp] OR 2014/12/01 : 3000[crdat] OR 2014/12/01 : 3000[edat]))
Toxline	
01/2018	**Date limit 2013 to present:**
	7439-98-7[rn] OR 1317-33-5[rn] OR 12033-29-3[rn] OR 12033-33-9[rn] OR 11098-99-0[rn] OR 18868-43-4[rn] OR 1313-27-5[rn] OR 1313-29-7[rn] OR 11098-84-3[rn] OR 27546-07-2[rn] OR 12054-85-2[rn] OR 15060-55-6[rn] OR 7631-95-0[rn] OR 10102-40-6[rn] OR 7789-82-4[rn] OR 12011-97-1[rn] OR 11119-46-3[rn] OR 11062-51-4[rn] OR 10241-05-1[rn] OR 1309-56-4[rn] OR 7783-77-9[rn] OR 13939-06-5[rn] OR 14221-06-8[rn] OR 13814-74-9[rn]
	"3N5" OR "Ammonium dimolybdate" OR "Ammonium heptamolybdate" OR "Ammonium heptamolybdate tetrahydrate" OR "Ammonium molibdate" OR "Ammonium molibdenum oxide" OR "Ammonium molybdate" OR "Ammonium molybdate hydrate" OR "Ammonium molybdate tetrahydrate" OR "Ammonium molybdate(VI)" OR "Ammonium molybdenum oxide"

Table B-2. Database Query Strings

Database search date	Query string
	"Ammonium molybdenum sulfide" OR "ammonium paramolybdate" OR "Ammonium paramolybdate tetrahydrate" OR "Ammonium tetrasulfidomolybdate(2-)" OR "Ammonium tetrathiomolybdate" OR "Ammonium thiomolybdate(VI)" OR "Amperit 105.054" OR "Amperit 106.2" OR "ATTM" OR "Bis(ammonium)tetrathiomolybdate(2-)" OR "Bouen SKN 301" OR "C-Powder" OR "Calcium molybdate"
	"Calcium molybdate(VI)" OR "Calcium molybdenate" OR "Calcium molybdenum oxide" OR "Coprexa" OR "DAG 206" OR "DAG 325" OR "DAG-V 657" OR "Defric coat HMB 2" OR "Diammonium dimolybdate" OR "Diammonium tetrakis(sulfido)molybdate(2-)" OR "Diammonium tetrakis(thioxo)molybdate" OR "Diammonium tetrasulfidomolybdate" OR "Diammonium tetrathiomolybdate"
	"Diammonium tetrathiomolybdate(2-)" OR "Diammonium tetrathiooxomolybdate(2-)" OR "Diammonium tetrathioxomolybdate(2-)" OR "Diammonium thiomolybdate" OR "Dimolybdenum tetraacetate" OR "Dimolybdenum trioxide" OR "dimolybdenum trisulfide " OR "Disodium molybdate" OR "Disodium molybdate dihydrate" OR "Disodium tetraoxomolybdate" OR "DM 1 (sulfide)" OR "DMI 7"
	"Dodecachlorohexamolybdenum" OR "Hexaammonium heptamolybdate tetrahydrate" OR "Hexaammonium molybdate tetrahydrate" OR "Hexacarbonylmolybdenum" OR "Hexafluoromolybdenum" OR "Hexamolybdenum dodecachloride" OR "JCPDS 35-0609" OR "Liqui-Moly LM 11" OR "Liqui-Moly LM 2" OR "Liqui-Moly Z Powder" OR "LM 13" OR "M 5" OR "MC 400WR"
	"MChVL" OR "MD 40" OR "Metco 63" OR "MF 000" OR "MFR" OR "MIPO-M 15" OR "Mo 1202T" OR "Mo-1202T" OR "Moly Fine Powder Y" OR "Moly Powder B" OR "Moly Powder C" OR "Moly Powder PA" OR "Moly Powder PB" OR "Moly Powder PS" OR "Molybdate (Mo2O72-), diammonium" OR "Molybdate (MoO42-), disodium, dihydrate, (T-4)-" OR "Molybdate, calcium" OR "Molybdena" OR "Molybdenite"
	"Molybdenum" OR "Molybdenum anhydride" OR "Molybdenum bisulfide" OR "Molybdenum carbide" OR "Molybdenum carbonyl" OR "Molybdenum chloride" OR "Molybdenum chloride oxide" OR "Molybdenum dioxide" OR "Molybdenum disulfide" OR "Molybdenum disulphide" OR "Molybdenum fluoride" OR "Molybdenum hexacarbonyl" OR "Molybdenum hexafluoride"
	"Molybdenum metallicum" OR "Molybdenum monocarbide" OR "Molybdenum oxide" OR "Molybdenum oxychloride" OR "Molybdenum oxytrichloride" OR "Molybdenum pentachloride" OR "Molybdenum peroxide" OR "Molybdenum sesquioxide" OR "Molybdenum sesquisulfide" OR "Molybdenum sodium oxide" OR "Molybdenum sulfide" OR "Molybdenum sulphide" OR "Molybdenum trichloride monoxide"
	"Molybdenum trichloride oxide" OR "Molybdenum trioxide" OR "Molybdenum trioxide pentamer" OR "Molybdenum trioxide tetramer" OR "Molybdenum trisulfide" OR "Molybdenum(6+) fluoride" OR "Molybdenum(II) acetate" OR "Molybdenum(II) chloride" OR "molybdenum(III) sulfide" OR "molybdenum(IV) oxide" OR "Molybdenum(IV) sulfide" OR "Molybdenum(V) chloride"
	"Molybdenum(VI) oxide" OR "Molybdenum(VI) trioxide" OR "Molybdenumperoxide" OR "Molybdic acid (H2Mo2O7), diammonium salt" OR "Molybdic acid (H2MoO4), calcium salt (1:1)" OR "Molybdic acid anhydride" OR "Molybdic acid, ammonium salt" OR "Molybdic acid, calcium salt" OR "Molybdic acid, disodium salt" OR "Molybdic acid, disodium salt, dihydrate" OR "Molybdic anhydride"
	"Molybdic oxide" OR "Molybdic trioxide" OR "Molycolloid CF 626" OR "Molyform 15" OR "Molyhibit 100" OR "Molyka R" OR "Molyka R-L 3" OR "Molyke R" OR "Molykote" OR "Molykote Microsize Powder" OR "Molykote Z" OR "Molykote Z Powder" OR "Molysulfide"

Table B-2. Database Query Strings

Database search date	Query string
	OR "MOP-P 100" OR "Mopol M" OR "Mopol S" OR "Motimol" OR "MVCh 1" OR "Natural molybdenite" OR "Natural molybdite" OR "NeoZ"
	"Nichimoly C" OR "Octachlorohexamolybdenum(4+) tetrachloride" OR "OKS 110" OR "PA Powder" OR "Pentachloromolybdenum Molybdenite" OR "Pigment Black 34" OR "Pol-U" OR "Powder PA" OR "RAC 01" OR "SGC 15" OR "Sodium molybdate" OR "Sodium molybdate dihydrate" OR "Sodium molybdate(VI)" OR "Sodium molybdate(VI) dihydrate" OR "Sodium molybdenate"
	"Sodium molybdenum oxide" OR "Sodium tetraoxomolybdate(2-)" OR "Solvest 390A" OR "Sumipowder PA" OR "T-Powder" OR "Tetraacetatodimolybdenum" OR "tetrakis(acetato)di-Molybdenum" OR "Tetrakis(acetato)dimolybdenum" OR "Tetrakis(acetato)molybdenum" OR "Tetrakis(mu-(acetato-O:O'))dimolybdenum" OR "tetrakis(μ-acetato)di-Molybdenum" OR "Tetrakis(μ-acetato)dimolybdenum"
	"tetrakis[μ-(acetato-O:O')]di-Molybdenum" OR "Thiomolybdic acid, diammonium salt" OR "Tiomolibdate diammonium" OR "TMOIO" OR "Trichlorooxomolybdenum" OR "Trichlorooxomolybdenum(V)" OR "TsM1"
	No date limit:
	"Hexaammonium heptamolybdate" OR "Hexammonium heptamolybdat" OR "Hexammonium tetracosaoxoheptamolybdate" OR "Molybdate (Mo7O24), hexammonium" OR "Molybdate (Mo7O246-), ammonium (1:6)" OR "Molybdate (Mo7O246-), hexaammonium" OR "Molybdate, hexaammonium" OR "Molybdic acid (H6Mo7O24), hexaammonium salt" OR "Molybdic acid, hexaammonium salt" OR 12027-67-7[rn]
	"Diammonium molybdate" OR "Diammonium tetraoxomolybdate(2-)" OR "Molybdate (MoO42-), ammonium (1:2), (T-4)-" OR "Molybdate (MoO42-), diammonium, (beta-4)-" OR "Molybdate (MoO42-), diammonium, (T-4)-" OR "Molybdic acid (H2MoO4), diammonium salt" OR "Molybdic acid, diammonium salt" OR 13106-76-8[rn]
Toxcenter	
01/2018	(FILE 'HOME' ENTERED AT 14:16:56 ON 12 JAN 2018) FILE 'TOXCENTER' ENTERED AT 14:17:07 ON 12 JAN 2018 CHARGED TO COST=EH011.05.LB.02.05 L1 34132 SEA FILE=TOXCENTER 7439-98-7 OR 1317-33-5 OR 12033-29-3 OR 12033-33-9 OR 11098-99-0 OR 18868-43-4 OR 1313-27-5 OR 1313-29-7 OR 11098-84-3 OR 27546-07-2 OR 12054-85-2 OR 15060-55-6 OR 7631-95-0 OR 10102-40-6 L2 523 SEA FILE=TOXCENTER 7789-82-4 OR 12011-97-1 OR 11119-46-3 OR 11062-51-4 OR 10241-05-1 OR 1309-56-4 OR 7783-77-9 OR 13939-06-5 OR 14221-06-8 OR 13814-74-9 L3 1148 SEA FILE=TOXCENTER 12027-67-7 OR 13106-76-8 L4 34486 SEA FILE=TOXCENTER L1 OR L2 L5 636 SEA FILE=TOXCENTER L3 NOT L4 L6 35122 SEA FILE=TOXCENTER L1 OR L2 OR L3 L7 22953 SEA FILE=TOXCENTER L6 NOT PATENT/DT L8 22927 SEA FILE=TOXCENTER L7 NOT TSCATS/FS ACT TOXQUERY/Q --------- L9 QUE (CHRONIC OR IMMUNOTOX? OR NEUROTOX? OR TOXICOKIN? OR BIOMARKER? OR NEUROLOG?) L10 QUE (PHARMACOKIN? OR SUBCHRONIC OR PBPK OR EPIDEMIOLOGY/ST,CT,

Table B-2. Database Query Strings

Database search date	Query string
	IT)
	L11 QUE (ACUTE OR SUBACUTE OR LD50# OR LD(W)50 OR LC50# OR LC(W)50)
	L12 QUE (TOXICITY OR ADVERSE OR POISONING)/ST,CT,IT
	L13 QUE (INHAL? OR PULMON? OR NASAL? OR LUNG? OR RESPIR?)
	L14 QUE ((OCCUPATION? OR WORKPLACE? OR WORKER?) AND EXPOS?)
	L15 QUE (ORAL OR ORALLY OR INGEST? OR GAVAGE? OR DIET OR DIETS OR DIETARY OR DRINKING(W)WATER?)
	L16 QUE (MAXIMUM AND CONCENTRATION? AND (ALLOWABLE OR PERMISSIBLE))
	L17 QUE (ABORT? OR ABNORMALIT? OR EMBRYO? OR CLEFT? OR FETUS?)
	L18 QUE (FOETUS? OR FETAL? OR FOETAL? OR FERTIL? OR MALFORM? OR OVUM?)
	L19 QUE (OVA OR OVARY OR PLACENTA? OR PREGNAN? OR PRENATAL?)
	L20 QUE (PERINATAL? OR POSTNATAL? OR REPRODUC? OR STERIL? OR TERATOGEN?)
	L21 QUE (SPERM OR SPERMAC? OR SPERMAG? OR SPERMATI? OR SPERMAS? OR SPERMATOB? OR SPERMATOC? OR SPERMATOG?)
	L22 QUE (SPERMATOI? OR SPERMATOL? OR SPERMATOR? OR SPERMATOX? OR SPERMATOZ? OR SPERMATU? OR SPERMI? OR SPERMO?)
	L23 QUE (NEONAT? OR NEWBORN? OR DEVELOPMENT OR DEVELOPMENTAL?)
	L24 QUE (ENDOCRIN? AND DISRUPT?)
	L25 QUE (ZYGOTE? OR CHILD OR CHILDREN OR ADOLESCEN? OR INFANT?)
	L26 QUE (WEAN? OR OFFSPRING OR AGE(W)FACTOR?)
	L27 QUE (DERMAL? OR DERMIS OR SKIN OR EPIDERM? OR CUTANEOUS?)
	L28 QUE (CARCINOG? OR COCARCINOG? OR CANCER? OR PRECANCER? OR NEOPLAS?)
	L29 QUE (TUMOR? OR TUMOUR? OR ONCOGEN? OR LYMPHOMA? OR CARCINOM?)
	L30 QUE (GENETOX? OR GENOTOX? OR MUTAGEN? OR GENETIC(W)TOXIC?)
	L31 QUE (NEPHROTOX? OR HEPATOTOX?)
	L32 QUE (ENDOCRIN? OR ESTROGEN? OR ANDROGEN? OR HORMON?)
	L33 QUE (OCCUPATION? OR WORKER? OR WORKPLACE? OR EPIDEM?)
	L34 QUE L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33
	L35 QUE (RAT OR RATS OR MOUSE OR MICE OR GUINEA(W)PIG? OR MURIDAE OR DOG OR DOGS OR RABBIT? OR HAMSTER? OR PIG OR PIGS OR SWINE OR PORCINE OR MONKEY? OR MACAQUE?)

Table B-2. Database Query Strings

Database search date	Query string
	L36 QUE (MARMOSET? OR FERRET? OR GERBIL? OR RODENT? OR LAGOMORPHA OR BABOON? OR CANINE OR CAT OR CATS OR FELINE OR MURINE)
	L37 QUE L34 OR L35 OR L36
	L38 QUE (HUMAN OR HUMANS OR HOMINIDAE OR MAMMALS OR MAMMAL? OR PRIMATES OR PRIMATE?)
	L39 QUE L37 OR L38

	L40 8795 SEA FILE=TOXCENTER L8 AND L39
	L41 1436 SEA FILE=TOXCENTER L40 AND ED>=20141201
	L42 1422 SEA FILE=TOXCENTER L41 AND PY>2012
	L43 184 SEA FILE=TOXCENTER L40 AND L3
	L44 1597 SEA FILE=TOXCENTER L41 OR L43
	L45 0 SEA FILE=TOXCENTER L44 AND MEDLINE/SB
	L46 269 SEA FILE=TOXCENTER L44 AND MEDLINE/FS
	L47 263 SEA FILE=TOXCENTER L44 AND BIOSIS/FS
	L48 1050 SEA FILE=TOXCENTER L44 AND CAPLUS/FS
	L49 15 SEA FILE=TOXCENTER L44 NOT (L46 OR L47 OR L48)
	L50 1425 DUP REM L46 L47 L49 L48 (172 DUPLICATES REMOVED) ANSWERS '1-1425' FROM FILE TOXCENTER
	L*** DEL 269 S L44 AND MEDLINE/FS
	L*** DEL 269 S L44 AND MEDLINE/FS
	L51 269 SEA FILE=TOXCENTER L50
	L*** DEL 263 S L44 AND BIOSIS/FS
	L*** DEL 263 S L44 AND BIOSIS/FS
	L52 234 SEA FILE=TOXCENTER L50
	L*** DEL 1050 S L44 AND CAPLUS/FS
	L*** DEL 1050 S L44 AND CAPLUS/FS
	L53 908 SEA FILE=TOXCENTER L50
	L*** DEL 15 S L44 NOT (L46 OR L47 OR L48)
	L*** DEL 15 S L44 NOT (L46 OR L47 OR L48)
	L54 14 SEA FILE=TOXCENTER L50
	L55 211 SEA FILE=TOXCENTER (L51 OR L52 OR L53 OR L54) AND BIOSIS/FS AND ED>=20141201
	L*** DEL 269 S L44 AND MEDLINE/FS
	L*** DEL 269 S L44 AND MEDLINE/FS
	L56 269 SEA FILE=TOXCENTER L50
	L*** DEL 263 S L44 AND BIOSIS/FS
	L*** DEL 263 S L44 AND BIOSIS/FS
	L57 234 SEA FILE=TOXCENTER L50
	L*** DEL 1050 S L44 AND CAPLUS/FS
	L*** DEL 1050 S L44 AND CAPLUS/FS
	L58 908 SEA FILE=TOXCENTER L50
	L*** DEL 15 S L44 NOT (L46 OR L47 OR L48)
	L*** DEL 15 S L44 NOT (L46 OR L47 OR L48)
	L59 14 SEA FILE=TOXCENTER L50
	L60 826 SEA FILE=TOXCENTER (L56 OR L57 OR L58 OR L59) AND CAPLUS/FS AND ED>=20141201
	L*** DEL 269 S L44 AND MEDLINE/FS

Table B-2. Database Query Strings

Database search date	Query string
	L*** DEL 269 S L44 AND MEDLINE/FS L61 269 SEA FILE=TOXCENTER L50 L*** DEL 263 S L44 AND BIOSIS/FS L*** DEL 263 S L44 AND BIOSIS/FS L62 234 SEA FILE=TOXCENTER L50 L*** DEL 1050 S L44 AND CAPLUS/FS L*** DEL 1050 S L44 AND CAPLUS/FS L63 908 SEA FILE=TOXCENTER L50 L*** DEL 15 S L44 NOT (L46 OR L47 OR L48) L*** DEL 15 S L44 NOT (L46 OR L47 OR L48) L64 14 SEA FILE=TOXCENTER L50 L65 0 SEA FILE=TOXCENTER (L61 OR L62 OR L63 OR L64) NOT (CAPLUS/FS OR MEDLINE/FS OR BIOSIS/FS) AND ED>=20141201 L*** DEL 269 S L44 AND MEDLINE/FS L*** DEL 269 S L44 AND MEDLINE/FS L66 269 SEA FILE=TOXCENTER L50 L*** DEL 263 S L44 AND BIOSIS/FS L*** DEL 263 S L44 AND BIOSIS/FS L67 234 SEA FILE=TOXCENTER L50 L*** DEL 1050 S L44 AND CAPLUS/FS L*** DEL 1050 S L44 AND CAPLUS/FS L68 908 SEA FILE=TOXCENTER L50 L*** DEL 15 S L44 NOT (L46 OR L47 OR L48) L*** DEL 15 S L44 NOT (L46 OR L47 OR L48) L69 14 SEA FILE=TOXCENTER L50 L70 150 SEA FILE=TOXCENTER (L66 OR L67 OR L68 OR L69) NOT ED>=20141201 L71 23 SEA FILE=TOXCENTER L70 AND BIOSIS/FS L72 14 SEA FILE=TOXCENTER L70 NOT (MEDLINE/FS OR BIOSIS/FS OR CAPLUS/FS) L73 82 SEA FILE=TOXCENTER L70 AND CAPLUS/FS L74 52 SEA FILE=TOXCENTER L60 AND ?MOLYB?/TI L75 29 SEA FILE=TOXCENTER L73 AND ?MOLYB?/TI D SCAN L55 L76 37 SEA FILE=TOXCENTER L71 OR L72 D SCAN L76 D SCAN L74 D SCAN L75 L*** DEL 269 S L44 AND MEDLINE/FS L*** DEL 269 S L44 AND MEDLINE/FS L77 269 SEA FILE=TOXCENTER L50 L*** DEL 263 S L44 AND BIOSIS/FS L*** DEL 263 S L44 AND BIOSIS/FS L78 234 SEA FILE=TOXCENTER L50 L*** DEL 1050 S L44 AND CAPLUS/FS L*** DEL 1050 S L44 AND CAPLUS/FS L79 908 SEA FILE=TOXCENTER L50 L*** DEL 15 S L44 NOT (L46 OR L47 OR L48) L*** DEL 15 S L44 NOT (L46 OR L47 OR L48) L80 14 SEA FILE=TOXCENTER L50

Table B-2. Database Query Strings

Database search date	Query string
	L81 1275 SEA FILE=TOXCENTER (L77 OR L78 OR L79 OR L80) AND ED>=20141201 L82 1265 SEA FILE=TOXCENTER L81 AND (L1 OR L2) L83 1012 SEA FILE=TOXCENTER L81 NOT (L55 OR L74) L84 84 SEA FILE=TOXCENTER L70 NOT (L76 OR L75) D SCAN L84 D SCAN L83 (FILE 'HOME' ENTERED AT 20:36:59 ON 14 JAN 2018) FILE 'TOXCENTER' ENTERED AT 20:37:09 ON 14 JAN 2018 CHARGED TO COST=EH011.05.LB.02.05 ACT MOLY1/A --------- L1 (34132)SEA FILE=TOXCENTER 7439-98-7 OR 1317-33-5 OR 12033-29-3 OR 12033-33-9 OR 11098-99-0 OR 18868-43-4 OR 1313-27-5 OR 1313-29-7 OR 11098-84-3 OR 27546-07-2 OR 12054-85-2 OR 15060-55-6 OR 7631-95-0 OR 10102-40-6 L2 (523)SEA FILE=TOXCENTER 7789-82-4 OR 12011-97-1 OR 11119-46-3 OR 11062-51-4 OR 10241-05-1 OR 1309-56-4 OR 7783-77-9 OR 13939-06-5 OR 14221-06-8 OR 13814-74-9 L3 (1148)SEA FILE=TOXCENTER 12027-67-7 OR 13106-76-8 L4 (35122)SEA FILE=TOXCENTER L1 OR L2 OR L3 L5 (22953)SEA FILE=TOXCENTER L4 NOT PATENT/DT L6 (22927)SEA FILE=TOXCENTER L5 NOT TSCATS/FS L7 QUE (CHRONIC OR IMMUNOTOX? OR NEUROTOX? OR TOXICOKIN? OR BIOMARKER? OR NEUROLOG?) L8 QUE (PHARMACOKIN? OR SUBCHRONIC OR PBPK OR EPIDEMIOLOGY/ST,CT, IT) L9 QUE (ACUTE OR SUBACUTE OR LD50# OR LD(W)50 OR LC50# OR LC(W)50) L10 QUE (TOXICITY OR ADVERSE OR POISONING)/ST,CT,IT L11 QUE (INHAL? OR PULMON? OR NASAL? OR LUNG? OR RESPIR?) L12 QUE ((OCCUPATION? OR WORKPLACE? OR WORKER?) AND EXPOS?) L13 QUE (ORAL OR ORALLY OR INGEST? OR GAVAGE? OR DIET OR DIETS OR DIETARY OR DRINKING(W)WATER?) L14 QUE (MAXIMUM AND CONCENTRATION? AND (ALLOWABLE OR PERMISSIBLE)) L15 QUE (ABORT? OR ABNORMALIT? OR EMBRYO? OR CLEFT? OR FETUS?) L16 QUE (FOETUS? OR FETAL? OR FOETAL? OR FERTIL? OR MALFORM? OR OVUM?) L17 QUE (OVA OR OVARY OR PLACENTA? OR PREGNAN? OR PRENATAL?) L18 QUE (PERINATAL? OR POSTNATAL? OR REPRODUC? OR STERIL? OR TERATOGEN?) L19 QUE (SPERM OR SPERMAC? OR SPERMAG? OR SPERMATI? OR SPERMAS? OR SPERMATOB? OR SPERMATOC? OR SPERMATOG?) L20 QUE (SPERMATOI? OR SPERMATOL? OR SPERMATOR? OR SPERMATOX? OR

Table B-2. Database Query Strings

Database search date	Query string
	SPERMATOZ? OR SPERMATU? OR SPERMI? OR SPERMO?)
	L21 QUE (NEONAT? OR NEWBORN? OR DEVELOPMENT OR DEVELOPMENTAL?)
	L22 QUE (ENDOCRIN? AND DISRUPT?)
	L23 QUE (ZYGOTE? OR CHILD OR CHILDREN OR ADOLESCEN? OR INFANT?)
	L24 QUE (WEAN? OR OFFSPRING OR AGE(W)FACTOR?)
	L25 QUE (DERMAL? OR DERMIS OR SKIN OR EPIDERM? OR CUTANEOUS?)
	L26 QUE (CARCINOG? OR COCARCINOG? OR CANCER? OR PRECANCER? OR
	NEOPLAS?)
	L27 QUE (TUMOR? OR TUMOUR? OR ONCOGEN? OR LYMPHOMA? OR CARCINOM?)
	L28 QUE (GENETOX? OR GENOTOX? OR MUTAGEN? OR GENETIC(W)TOXIC?)
	L29 QUE (NEPHROTOX? OR HEPATOTOX?)
	L30 QUE (ENDOCRIN? OR ESTROGEN? OR ANDROGEN? OR HORMON?)
	L31 QUE (OCCUPATION? OR WORKER? OR WORKPLACE? OR EPIDEM?)
	L32 QUE L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31
	L33 QUE (RAT OR RATS OR MOUSE OR MICE OR GUINEA(W)PIG? OR MURIDAE
	OR DOG OR DOGS OR RABBIT? OR HAMSTER? OR PIG OR PIGS OR SWINE
	OR PORCINE OR MONKEY? OR MACAQUE?)
	L34 QUE (MARMOSET? OR FERRET? OR GERBIL? OR RODENT? OR LAGOMORPHA
	OR BABOON? OR CANINE OR CAT OR CATS OR FELINE OR MURINE)
	L35 QUE L32 OR L33 OR L34
	L36 QUE (HUMAN OR HUMANS OR HOMINIDAE OR MAMMALS OR MAMMAL? OR
	PRIMATES OR PRIMATE?)
	L37 QUE L35 OR L36
	L38 (8795)SEA FILE=TOXCENTER L6 AND L37
	L39 (1436)SEA FILE=TOXCENTER L38 AND ED>=20141201
	L40 (184)SEA FILE=TOXCENTER L38 AND L3
	L41 (1597)SEA FILE=TOXCENTER L39 OR L40
	L42 (269)SEA FILE=TOXCENTER L41 AND MEDLINE/FS
	L43 (263)SEA FILE=TOXCENTER L41 AND BIOSIS/FS
	L44 (1050)SEA FILE=TOXCENTER L41 AND CAPLUS/FS
	L45 (15)SEA FILE=TOXCENTER L41 NOT (L42 OR L43 OR L44)
	L46 (1425)DUP REM L42 L43 L45 L44 (172 DUPLICATES REMOVED)
	L47 (269)SEA FILE=TOXCENTER L46
	L48 (234)SEA FILE=TOXCENTER L46
	L49 (908)SEA FILE=TOXCENTER L46
	L50 (14)SEA FILE=TOXCENTER L46
	L51 (211)SEA FILE=TOXCENTER (L47 OR L48 OR L49 OR L50) AND BIOSIS/FS AND ED>=20141201
	L52 (269)SEA FILE=TOXCENTER L46

Table B-2. Database Query Strings

Database search date	Query string
	L53 (234)SEA FILE=TOXCENTER L46 L54 (908)SEA FILE=TOXCENTER L46 L55 (14)SEA FILE=TOXCENTER L46 L56 (826)SEA FILE=TOXCENTER (L52 OR L53 OR L54 OR L55) AND CAPLUS/FS AND ED>=20141201 L57 (52)SEA FILE=TOXCENTER L56 AND ?MOLYB?/TI L58 (269)SEA FILE=TOXCENTER L46 L59 (234)SEA FILE=TOXCENTER L46 L60 (908)SEA FILE=TOXCENTER L46 L61 (14)SEA FILE=TOXCENTER L46 L62 (1275)SEA FILE=TOXCENTER (L58 OR L59 OR L60 OR L61) AND ED>=20141201 L63 1012 SEA FILE=TOXCENTER L62 NOT (L51 OR L57) --------- L64 97 SEA FILE=TOXCENTER L63 AND (MOLYB?/TI OR DIMOLYB?/TI OR DODECACHLOROHEXAMOLYB?/TI OR HEPTAMOLYB?/TI OR HEXACARBONYLMOLY B?/TI OR HEXAFLUOROMOLYB?/TI OR HEXAMOLYB?/TI OR OCTACHLOROHEXA MOLYB?/TI OR PARAMOLYB?/TI) L65 5 SEA FILE=TOXCENTER L63 AND (PENTACHLOROMOLYB?/TI OR TETRAACETAT ODIMOLYB?/TI OR TETRAOXOMOLYB?/TI OR TETRASULFIDOMOLYB?/TI OR TETRATHIOMOLYB?/TI OR TETRATHIOOXOMOLYB?/TI OR THIOMOLYB?/TI OR TRICHLOROOXOMOLYB?/TI) L66 1 SEA FILE=TOXCENTER L63 AND ("3N5"/TI OR "AMMONIUM MOLIBDATE"/TI OR "AMMONIUM MOLIBDENUM OXIDE"/TI OR "AMPERIT 105.054"/TI OR "AMPERIT 106.2"/TI OR "ATTM"/TI OR "BIS(AMMONIUM)TETRATHIOMOLYB DATE(2-)"/TI OR "BOUEN SKN 301"/TI) L67 0 SEA FILE=TOXCENTER L63 AND ("C-POWDER"/TI OR "COPREXA"/TI OR "DAG 206"/TI OR "DAG 325"/TI OR "DAG-V 657"/TI OR "DEFRIC COAT HMB 2"/TI OR "DM 1 (SULFIDE)"/TI OR "DMI 7"/TI OR "JCPDS 35-0609"/TI OR "LIQUI-MOLY LM 11"/TI OR "LIQUI-MOLY LM 2"/TI) L68 0 SEA FILE=TOXCENTER L63 AND ("LIQUI-MOLY Z POWDER"/TI OR "LM 13"/TI OR "MC 400WR"/TI OR "MCHVL"/TI OR "MD 40"/TI OR "METCO 63"/TI OR "MF 000"/TI OR "MIPO-M 15"/TI OR "MO 1202T"/TI OR "MO-1202T"/TI OR "MOLY FINE POWDER Y"/TI) L69 0 SEA FILE=TOXCENTER L63 AND ("MOLY POWDER B"/TI OR "MOLY POWDER C"/TI OR "MOLY POWDER PA"/TI OR "MOLY POWDER PB"/TI OR "MOLY POWDER PS"/TI OR "MOLYCOLLOID CF 626"/TI OR "MOLYFORM 15"/TI OR "MOLYHIBIT 100"/TI OR "MOLYKA R"/TI OR "MOLYKA R-L 3"/TI) L70 0 SEA FILE=TOXCENTER L63 AND ("MOLYKE R"/TI OR "MOLYKOTE"/TI OR "MOLYKOTE MICROSIZE POWDER"/TI OR "MOLYKOTE Z"/TI OR "MOLYKOTE Z POWDER"/TI OR "MOLYSULFIDE"/TI OR "MOP-P 100"/TI OR "MOPOL M"/TI OR "MOPOL S"/TI OR "MOTIMOL"/TI OR "MVCH 1"/TI) L71 0 SEA FILE=TOXCENTER L63 AND ("NEOZ"/TI OR "NICHIMOLY C"/TI OR

Table B-2. Database Query Strings

Database search date	Query string
	"OKS 110"/TI OR "PA POWDER"/TI OR "PIGMENT BLACK 34"/TI OR "POL-U"/TI OR "POWDER PA"/TI OR "RAC 01"/TI OR "SGC 15"/TI OR "SOLVEST 390A"/TI OR "SUMIPOWDER PA"/TI OR "T-POWDER"/TI OR "TIOMOLIBDATE DIAMMONIUM"/TI OR "TMOIO"/TI OR "TSM1"/TI)
	L72 103 SEA FILE=TOXCENTER L64 OR L65 OR L66
	D SCAN L72
	ACT MOLY2/A

	L76 (34132)SEA FILE=TOXCENTER 7439-98-7 OR 1317-33-5 OR 12033-29-3 OR 12033-33-9 OR 11098-99-0 OR 18868-43-4 OR 1313-27-5 OR 1313-29-7 OR 11098-84-3 OR 27546-07-2 OR 12054-85-2 OR 15060-55-6 OR 7631-95-0 OR 10102-40-6
	L77 (523)SEA FILE=TOXCENTER 7789-82-4 OR 12011-97-1 OR 11119-46-3 OR 11062-51-4 OR 10241-05-1 OR 1309-56-4 OR 7783-77-9 OR 13939-06-5 OR 14221-06-8 OR 13814-74-9
	L78 (1148)SEA FILE=TOXCENTER 12027-67-7 OR 13106-76-8
	L79 (35122)SEA FILE=TOXCENTER L76 OR L77 OR L78
	L80 (22953)SEA FILE=TOXCENTER L79 NOT PATENT/DT
	L81 (22927)SEA FILE=TOXCENTER L80 NOT TSCATS/FS
	L82 QUE (CHRONIC OR IMMUNOTOX? OR NEUROTOX? OR TOXICOKIN? OR BIOMARKER? OR NEUROLOG?)
	L83 QUE (PHARMACOKIN? OR SUBCHRONIC OR PBPK OR EPIDEMIOLOGY/ST,CT, IT)
	L84 QUE (ACUTE OR SUBACUTE OR LD50# OR LD(W)50 OR LC50# OR LC(W)50)
	L85 QUE (TOXICITY OR ADVERSE OR POISONING)/ST,CT,IT
	L86 QUE (INHAL? OR PULMON? OR NASAL? OR LUNG? OR RESPIR?)
	L87 QUE ((OCCUPATION? OR WORKPLACE? OR WORKER?) AND EXPOS?)
	L88 QUE (ORAL OR ORALLY OR INGEST? OR GAVAGE? OR DIET OR DIETS OR DIETARY OR DRINKING(W)WATER?)
	L89 QUE (MAXIMUM AND CONCENTRATION? AND (ALLOWABLE OR PERMISSIBLE))
	L90 QUE (ABORT? OR ABNORMALIT? OR EMBRYO? OR CLEFT? OR FETUS?)
	L91 QUE (FOETUS? OR FETAL? OR FOETAL? OR FERTIL? OR MALFORM? OR OVUM?)
	L92 QUE (OVA OR OVARY OR PLACENTA? OR PREGNAN? OR PRENATAL?)
	L93 QUE (PERINATAL? OR POSTNATAL? OR REPRODUC? OR STERIL? OR TERATOGEN?)
	L94 QUE (SPERM OR SPERMAC? OR SPERMAG? OR SPERMATI? OR SPERMAS? OR SPERMATOB? OR SPERMATOC? OR SPERMATOG?)
	L95 QUE (SPERMATOI? OR SPERMATOL? OR SPERMATOR? OR SPERMATOX? OR SPERMATOZ? OR SPERMATU? OR SPERMI? OR SPERMO?)
	L96 QUE (NEONAT? OR NEWBORN? OR DEVELOPMENT OR DEVELOPMENTAL?)
	L97 QUE (ENDOCRIN? AND DISRUPT?)

Table B-2. Database Query Strings

Database search date	Query string
	L98 QUE (ZYGOTE? OR CHILD OR CHILDREN OR ADOLESCEN? OR INFANT?)
	L99 QUE (WEAN? OR OFFSPRING OR AGE(W)FACTOR?)
	L100 QUE (DERMAL? OR DERMIS OR SKIN OR EPIDERM? OR CUTANEOUS?)
	L101 QUE (CARCINOG? OR COCARCINOG? OR CANCER? OR PRECANCER? OR NEOPLAS?)
	L102 QUE (TUMOR? OR TUMOUR? OR ONCOGEN? OR LYMPHOMA? OR CARCINOM?)
	L103 QUE (GENETOX? OR GENOTOX? OR MUTAGEN? OR GENETIC(W)TOXIC?)
	L104 QUE (NEPHROTOX? OR HEPATOTOX?)
	L105 QUE (ENDOCRIN? OR ESTROGEN? OR ANDROGEN? OR HORMON?)
	L106 QUE (OCCUPATION? OR WORKER? OR WORKPLACE? OR EPIDEM?)
	L107 QUE L82 OR L83 OR L84 OR L85 OR L86 OR L87 OR L88 OR L89 OR L90 OR L91 OR L92 OR L93 OR L94 OR L95 OR L96 OR L97 OR L98 OR L99 OR L100 OR L101 OR L102 OR L103 OR L104 OR L105 OR L106
	L108 QUE (RAT OR RATS OR MOUSE OR MICE OR GUINEA(W)PIG? OR MURIDAE OR DOG OR DOGS OR RABBIT? OR HAMSTER? OR PIG OR PIGS OR SWINE OR PORCINE OR MONKEY? OR MACAQUE?)
	L109 QUE (MARMOSET? OR FERRET? OR GERBIL? OR RODENT? OR LAGOMORPHA OR BABOON? OR CANINE OR CAT OR CATS OR FELINE OR MURINE)
	L110 QUE L107 OR L108 OR L109
	L111 QUE (HUMAN OR HUMANS OR HOMINIDAE OR MAMMALS OR MAMMAL? OR PRIMATES OR PRIMATE?)
	L112 QUE L110 OR L111
	L113(8795)SEA FILE=TOXCENTER L81 AND L112
	L114(1436)SEA FILE=TOXCENTER L113 AND ED>=20141201
	L115(184)SEA FILE=TOXCENTER L113 AND L78
	L116(1597)SEA FILE=TOXCENTER L114 OR L115
	L117(269)SEA FILE=TOXCENTER L116 AND MEDLINE/FS
	L118(263)SEA FILE=TOXCENTER L116 AND BIOSIS/FS
	L119(1050)SEA FILE=TOXCENTER L116 AND CAPLUS/FS
	L120(15)SEA FILE=TOXCENTER L116 NOT (L117 OR L118 OR L119)
	L121(1425)DUP REM L117 L118 L120 L119 (172 DUPLICATES REMOVED)
	L122(269)SEA FILE=TOXCENTER L121
	L123(234)SEA FILE=TOXCENTER L121
	L124(908)SEA FILE=TOXCENTER L121
	L125(14)SEA FILE=TOXCENTER L121
	L126(150)SEA FILE=TOXCENTER (L122 OR L123 OR L124 OR L125) NOT ED>=20141
	L127(23)SEA FILE=TOXCENTER L126 AND BIOSIS/FS
	L128(14)SEA FILE=TOXCENTER L126 NOT (MEDLINE/FS OR BIOSIS/FS OR CAPLUS/
	L129(82)SEA FILE=TOXCENTER L126 AND CAPLUS/FS
	L130(29)SEA FILE=TOXCENTER L129 AND ?MOLYB?/TI

Table B-2. Database Query Strings

Database search date	Query string
	L131(37)SEA FILE=TOXCENTER L127 OR L128 L132 84 SEA FILE=TOXCENTER L126 NOT (L131 OR L130) --------- L133 15 SEA FILE=TOXCENTER L132 AND (MOLYB?/TI OR DIMOLYB?/TI OR DODECACHLOROHEXAMOLYB?/TI OR HEPTAMOLYB?/TI OR HEXACARBONYLMOLYB?/TI OR HEXAFLUOROMOLYB?/TI OR HEXAMOLYB?/TI OR OCTACHLOROHEXAMOLYB?/TI OR PARAMOLYB?/TI) L134 0 SEA FILE=TOXCENTER L1L32 AND (PENTACHLOROMOLYB?/TI OR TETRAACETATODIMOLYB?/TI OR TETRAOXOMOLYB?/TI OR TETRASULFIDOMOLYB?/TI OR TETRATHIOMOLYB?/TI OR TETRATHIOOXOMOLYB?/TI OR THIOMOLYB?/TI OR TRICHLOROOXOMOLYB?/TI) L135 0 SEA FILE=TOXCENTER L132 AND ("3N5"/TI OR "AMMONIUM MOLIBDATE"/TI OR "AMMONIUM MOLIBDENUM OXIDE"/TI OR "AMPERIT 105.054"/TI OR "AMPERIT 106.2"/TI OR "ATTM"/TI OR "BIS(AMMONIUM)TETRATHIOMOLYBDATE(2-)"/TI OR "BOUEN SKN 301"/TI) L136 0 SEA FILE=TOXCENTER L132 AND ("C-POWDER"/TI OR "COPREXA"/TI OR "DAG 206"/TI OR "DAG 325"/TI OR "DAG-V 657"/TI OR "DEFRIC COAT HMB 2"/TI OR "DM 1 (SULFIDE)"/TI OR "DMI 7"/TI OR "JCPDS 35-0609"/TI OR "LIQUI-MOLY LM 11"/TI OR "LIQUI-MOLY LM 2"/TI) L137 0 SEA FILE=TOXCENTER L132 AND ("LIQUI-MOLY Z POWDER"/TI OR "LM 13"/TI OR "MC 400WR"/TI OR "MCHVL"/TI OR "MD 40"/TI OR "METCO 63"/TI OR "MF 000"/TI OR "MIPO-M 15"/TI OR "MO 1202T"/TI OR "MO-1202T"/TI OR "MOLY FINE POWDER Y"/TI) L138 0 SEA FILE=TOXCENTER L132 AND ("MOLY POWDER B"/TI OR "MOLY POWDER C"/TI OR "MOLY POWDER PA"/TI OR "MOLY POWDER PB"/TI OR "MOLY POWDER PS"/TI OR "MOLYCOLLOID CF 626"/TI OR "MOLYFORM 15"/TI OR "MOLYHIBIT 100"/TI OR "MOLYKA R"/TI OR "MOLYKA R-L 3"/TI) L139 0 SEA FILE=TOXCENTER L132 AND ("MOLYKE R"/TI OR "MOLYKOTE"/TI OR "MOLYKOTE MICROSIZE POWDER"/TI OR "MOLYKOTE Z"/TI OR "MOLYKOTE Z POWDER"/TI OR "MOLYSULFIDE"/TI OR "MOP-P 100"/TI OR "MOPOL M"/TI OR "MOPOL S"/TI OR "MOTIMOL"/TI OR "MVCH 1"/TI) L140 0 SEA FILE=TOXCENTER L132 AND ("NEOZ"/TI OR "NICHIMOLY C"/TI OR "OKS 110"/TI OR "PA POWDER"/TI OR "PIGMENT BLACK 34"/TI OR "POL-U"/TI OR "POWDER PA"/TI OR "RAC 01"/TI OR "SGC 15"/TI OR "SOLVEST 390A"/TI OR "SUMIPOWDER PA"/TI OR "T-POWDER"/TI OR "TIOMOLIBDATE DIAMMONIUM"/TI OR "TMOIO"/TI OR "TSM1"/TI) D SCAN L133

Table B-3. Strategies to Augment the Literature Search

Source	Query and number screened when available
TSCATS[a]	
01/2018	Compounds searched: 7439-98-7, 1317-33-5, 12033-29-3, 12033-33-9, 11098-99-0, 18868-43-4, 1313-27-5, 1313-29-7, 11098-84-3, 27546-07-2, 12054-85-2, 15060-55-6, 7631-95-0, 10102-40-6, 7789-82-4, 12011-97-1, 11119-46-3, 11062-51-4, 10241-05-1, 1309-56-4, 7783-77-9, 13939-06-5, 14221-06-8, 13814-74-9, 12027-67-7, 13106-76-8
NTP	
01/2018	**14th ROC (https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html):** 7439-98-7 OR 1317-33-5 OR 12033-29-3 OR 12033-33-9 OR 11098-99-0 OR 18868-43-4 OR 1313-27-5 OR 1313-29-7 OR 11098-84-3 OR 27546-07-2 OR 12054-85-2 OR 15060-55-6 OR 7631-95-0 OR 10102-40-6 OR 7789-82-4 OR 12011-97-1 OR 11119-46-3 OR 11062-51-4 OR 10241-05-1 OR 1309-56-4 OR 7783-77-9 OR 13939-06-5 OR 14221-06-8 OR 13814-74-9 OR 12027-67-7 OR 13106-76-8 molybdenum OR molybdate OR molybdic OR dimolybdate OR dimolybdenum OR dodecachlorohexamolybdenum OR heptamolybdate OR hexacarbonylmolybdenum OR hexafluoromolybdenum OR hexamolybdenum OR molibdate OR molibdenum OR octachlorohexamolybdenum OR paramolybdate OR pentachloromolybdenum OR tetraacetatodimolybdenum OR tetraoxomolybdate OR tetrasulfidomolybdate OR tetrathiomolybdate OR tetrathiooxomolybdate OR thiomolybdate OR thiomolybdic OR tiomolibdate OR trichlorooxomolybdenum OR pigment black 34 **NTP Site Search (http://ntpsearch.niehs.nih.gov/home) with Content Types "Reports & Publications", "Systematic Review" or "Testing Status":** 7439-98-7 OR 1317-33-5 OR 12033-29-3 OR 12033-33-9 OR 11098-99-0 OR 18868-43-4 OR 1313-27-5 OR 1313-29-7 OR 11098-84-3 OR 27546-07-2 OR 12054-85-2 OR 15060-55-6 OR 7631-95-0 OR 10102-40-6 OR 7789-82-4 OR 12011-97-1 OR 11119-46-3 OR 11062-51-4 OR 10241-05-1 OR 1309-56-4 OR 7783-77-9 OR 13939-06-5 OR 14221-06-8 OR 13814-74-9 OR 12027-67-7 OR 13106-76-8 molybdenum OR molybdate OR molybdic OR dimolybdate OR dimolybdenum OR dodecachlorohexamolybdenum OR heptamolybdate OR hexacarbonylmolybdenum OR hexafluoromolybdenum OR hexamolybdenum OR molibdate OR molibdenum OR octachlorohexamolybdenum OR paramolybdate OR pentachloromolybdenum OR tetraacetatodimolybdenum OR tetraoxomolybdate OR tetrasulfidomolybdate OR tetrathiomolybdate OR tetrathiooxomolybdate OR thiomolybdate OR thiomolybdic OR tiomolibdate OR trichlorooxomolybdenum OR pigment black 34
Regulations.gov	
01/2018	**Notices or rules:** 7439-98-7, 1317-33-5, 12033-29-3, 12033-33-9, 11098-99-0, 18868-43-4, 1313-27-5, 1313-29-7, 11098-84-3, 27546-07-2, 12054-85-2, 15060-55-6, 7631-95-0, 10102-40-6, 7789-82-4, 12011-97-1, 11119-46-3, 11062-51-4, 10241-05-1, 1309-56-4, 7783-77-9, 13939-06-5, 14221-06-8, 13814-74-9, 12027-67-7, 13106-76-8
NIH RePORTER	
04/2019	**Text Search:** "3N5" OR "Ammonium dimolybdate" OR "Ammonium heptamolybdate" OR "Ammonium heptamolybdate tetrahydrate" OR "Ammonium molibdate" OR "Ammonium molibdenum oxide" OR "Ammonium molybdate" OR "Ammonium molybdate hydrate" OR "Ammonium molybdate tetrahydrate" OR "Ammonium molybdate(VI)" OR "Ammonium molybdenum oxide" OR "Ammonium molybdenum sulfide" OR "ammonium paramolybdate" OR "Ammonium paramolybdate tetrahydrate" OR "Ammonium tetrasulfidomolybdate(2-)" OR "Ammonium tetrathiomolybdate" OR "Ammonium thiomolybdate(VI)" OR "Amperit 105.054" OR "Amperit 106.2" OR

Table B-3. Strategies to Augment the Literature Search

Source	Query and number screened when available
	"ATTM" OR "Bis(ammonium)tetrathiomolybdate(2-)" OR "Bouen SKN 301" OR "C-Powder" OR "Calcium molybdate" OR "Calcium molybdate(VI)" OR "Calcium molybdenate" OR "Calcium molybdenum oxide" OR "Coprexa" OR "DAG 206" OR "DAG 325" OR "DAG-V 657" OR "Defric coat HMB 2" OR "Diammonium dimolybdate" OR "Diammonium tetrakis(sulfido)molybdate(2-)" OR "Diammonium tetrakis(thioxo)molybdate" OR "Diammonium tetrasulfidomolybdate" OR "Diammonium tetrathiomolybdate" OR "Diammonium tetrathiomolybdate(2-)" OR "Diammonium tetrathiooxomolybdate(2-)" OR "Diammonium tetrathioxomolybdate(2-)" OR "Diammonium thiomolybdate" OR "Dimolybdenum tetraacetate" OR "Dimolybdenum trioxide" OR "dimolybdenum trisulfide " OR "Disodium molybdate" OR "Disodium molybdate dihydrate" OR "Disodium tetraoxomolybdate" OR "DM 1 (sulfide)" OR "DMI 7" OR "Dodecachlorohexamolybdenum" OR "Hexaammonium heptamolybdate tetrahydrate" OR "Hexaammonium molybdate tetrahydrate" OR "Hexacarbonylmolybdenum" OR "Hexafluoromolybdenum" OR "Hexamolybdenum dodecachloride" OR "JCPDS 35-0609" OR "Liqui-Moly LM 11" OR "Liqui-Moly LM 2" OR "Liqui-Moly Z Powder" OR "LM 13" OR "MC 400WR" OR "MChVL" OR "MD 40" OR "Metco 63" OR "MF 000" OR "MIPO-M 15" OR "Mo 1202T" OR "Mo-1202T" OR "Moly Fine Powder Y" OR "Moly Powder B" OR "Moly Powder C" OR "Moly Powder PA" OR "Moly Powder PB" OR "Moly Powder PS" OR "Molybdate (Mo2O72-), diammonium" OR "Molybdate (MoO42-), disodium, dihydrate, (T-4)-" OR "Molybdate, calcium" OR "Molybdena" OR "Molybdenite" OR "Molybdenum" OR "Molybdenum anhydride" OR "Molybdenum bisulfide" OR "Molybdenum carbide" OR "Molybdenum carbonyl" OR "Molybdenum chloride" OR "Molybdenum chloride oxide" OR "Molybdenum dioxide" OR "Molybdenum disulfide" OR "Molybdenum disulphide" OR "Molybdenum fluoride" OR "Molybdenum hexacarbonyl" OR "Molybdenum hexafluoride" OR "Molybdenum metallicum" OR "Molybdenum monocarbide" OR "Molybdenum oxide" OR "Molybdenum oxychloride" **(Advanced), Search in: Projects AdminIC: All, Fiscal Year: Active Projects** **Text Search:** "Molybdenum oxytrichloride" OR "Molybdenum pentachloride" OR "Molybdenum peroxide" OR "Molybdenum sesquioxide" OR "Molybdenum sesquisulfide" OR "Molybdenum sodium oxide" OR "Molybdenum sulfide" OR "Molybdenum sulphide" OR "Molybdenum trichloride monoxide" OR "Molybdenum trichloride oxide" OR "Molybdenum trioxide" OR "Molybdenum trioxide pentamer" OR "Molybdenum trioxide tetramer" OR "Molybdenum trisulfide" OR "Molybdenum(6) fluoride" OR "Molybdenum(II) acetate" OR "Molybdenum(II) chloride" OR "molybdenum(III) sulfide" OR "molybdenum(IV) oxide" OR "Molybdenum(IV) sulfide" OR "Molybdenum(V) chloride" OR "Molybdenum(VI) oxide" OR "Molybdenum(VI) trioxide" OR "Molybdenumperoxide" OR "Molybdic acid (H2Mo2O7), diammonium salt" OR "Molybdic acid (H2MoO4), calcium salt (1:1)" OR "Molybdic acid anhydride" OR "Molybdic acid, ammonium salt" OR "Molybdic acid, calcium salt" OR "Molybdic acid, disodium salt" OR "Molybdic acid, disodium salt, dihydrate" OR "Molybdic anhydride" OR "Molybdic oxide" OR "Molybdic trioxide" OR "Molycolloid CF 626" OR "Molyform 15" OR "Molyhibit 100" OR "Molyka R" OR "Molyka R-L 3" OR "Molyke R" OR "Molykote" OR "Molykote Microsize Powder" OR "Molykote Z" OR "Molykote Z Powder" OR "Molysulfide" OR "MOP-P 100" OR "Mopol M" OR "Mopol S" OR "Motimol" OR "MVCh 1" OR "Natural molybdenite" OR "Natural molybdite" OR "NeoZ" OR "Nichimoly C" OR "Octachlorohexamolybdenum(4) tetrachloride" OR "OKS 110" OR "PA Powder" OR "Pentachloromolybdenum Molybdenite" OR "Pigment Black 34" OR "Pol-U" OR "Powder PA" OR "RAC 01" OR "SGC 15" OR "Sodium molybdate" OR "Sodium molybdate dihydrate" OR "Sodium molybdate(VI)" OR "Sodium molybdate(VI) dihydrate" OR "Sodium molybdenate" OR "Sodium molybdenum oxide" OR "Sodium tetraoxomolybdate(2-)" OR "Solvest 390A" OR "Sumipowder PA" OR

Table B-3. Strategies to Augment the Literature Search

Source	Query and number screened when available
	"Tetraacetatodimolybdenum" OR "tetrakis(acetato)di-Molybdenum" OR "Tetrakis(acetato)dimolybdenum" OR "Tetrakis(acetato)molybdenum" OR "Tetrakis(mu-(acetato-O:O'))dimolybdenum" OR "tetrakis(mu-acetato)di-Molybdenum" OR "Tetrakis(mu-acetato)dimolybdenum" OR "tetrakis[mu-(acetato-O:O')]di-Molybdenum" OR "Thiomolybdic acid, diammonium salt" OR "Tiomolibdate diammonium" OR "TMOIO" OR "Trichlorooxomolybdenum" OR "Trichlorooxomolybdenum(V)" OR "TsM1" OR "Hexaammonium heptamolybdate" OR "Hexammonium heptamolybdat" OR "Hexammonium tetracosaoxoheptamolybdate" OR "Molybdate (Mo7O24), hexammonium" OR "Molybdate (Mo7O246-), ammonium (1:6)" OR "Molybdate (Mo7O246-), hexaammonium" **(Advanced), Search in: Projects Admin IC: All, Fiscal Year: Active Projects** **Text Search:** "Molybdate, hexaammonium" OR "Molybdic acid (H6Mo7O24), hexaammonium salt" OR "Molybdic acid, hexaammonium salt" OR "Diammonium molybdate" OR "Diammonium tetraoxomolybdate(2-)" OR "Molybdate (MoO42-), ammonium (1:2), (T-4)-" OR "Molybdate (MoO42-), diammonium, (beta-4)-" OR "Molybdate (MoO42-), diammonium, (T-4)-" OR "Molybdic acid (H2MoO4), diammonium salt" OR "Molybdic acid, diammonium salt" (Advanced), Search in: Projects Admin IC: All, Fiscal Year: Active Projects Text Search: molybdenum OR molybdate OR molybdic OR dimolybdate OR dimolybdenum OR dodecachlorohexamolybdenum OR heptamolybdate OR hexacarbonylmolybdenum OR hexafluoromolybdenum OR hexamolybdenum OR molibdate OR molibdenum OR octachlorohexamolybdenum OR paramolybdate OR pentachloromolybdenum OR tetraacetatodimolybdenum OR tetraoxomolybdate OR tetrasulfidomolybdate OR tetrathiomolybdate OR tetrathiooxomolybdate OR thiomolybdate OR thiomolybdic OR tiomolibdate OR trichlorooxomolybdenum OR pigment black 34 **(Advanced), Search in: Projects AdminIC: All, Fiscal Year: Active Projects**
Other	Identified throughout the assessment process

[a]Several versions of the TSCATS database were searched, as needed, by CASRN including TSCATS1 via Toxline (no date limit), TSCATS2 via https://yosemite.epa.gov/oppts/epatscat8.nsf/ReportSearch?OpenForm (date restricted by EPA receipt date), and TSCATS via CDAT (date restricted by 'Mail Received Date Range'), as well as google for recent TSCA submissions.

The 2018 results were:

- Number of records identified from PubMed, TOXLINE, and TOXCENTER (after duplicate removal): 2,394
- Number of records identified from other strategies: 114
- Total number of records to undergo literature screening: 2,508

B.1.2 Literature Screening

A two-step process was used to screen the literature search to identify relevant studies on molybdenum:

- Title and abstract screen
- Full text screen

Title and Abstract Screen. Within the reference library, titles and abstracts were screened manually for relevance. Studies that were considered relevant (see Table B-1 for inclusion criteria) were moved to the

second step of the literature screening process. Studies were excluded when the title and abstract clearly indicated that the study was not relevant to the toxicological profile.

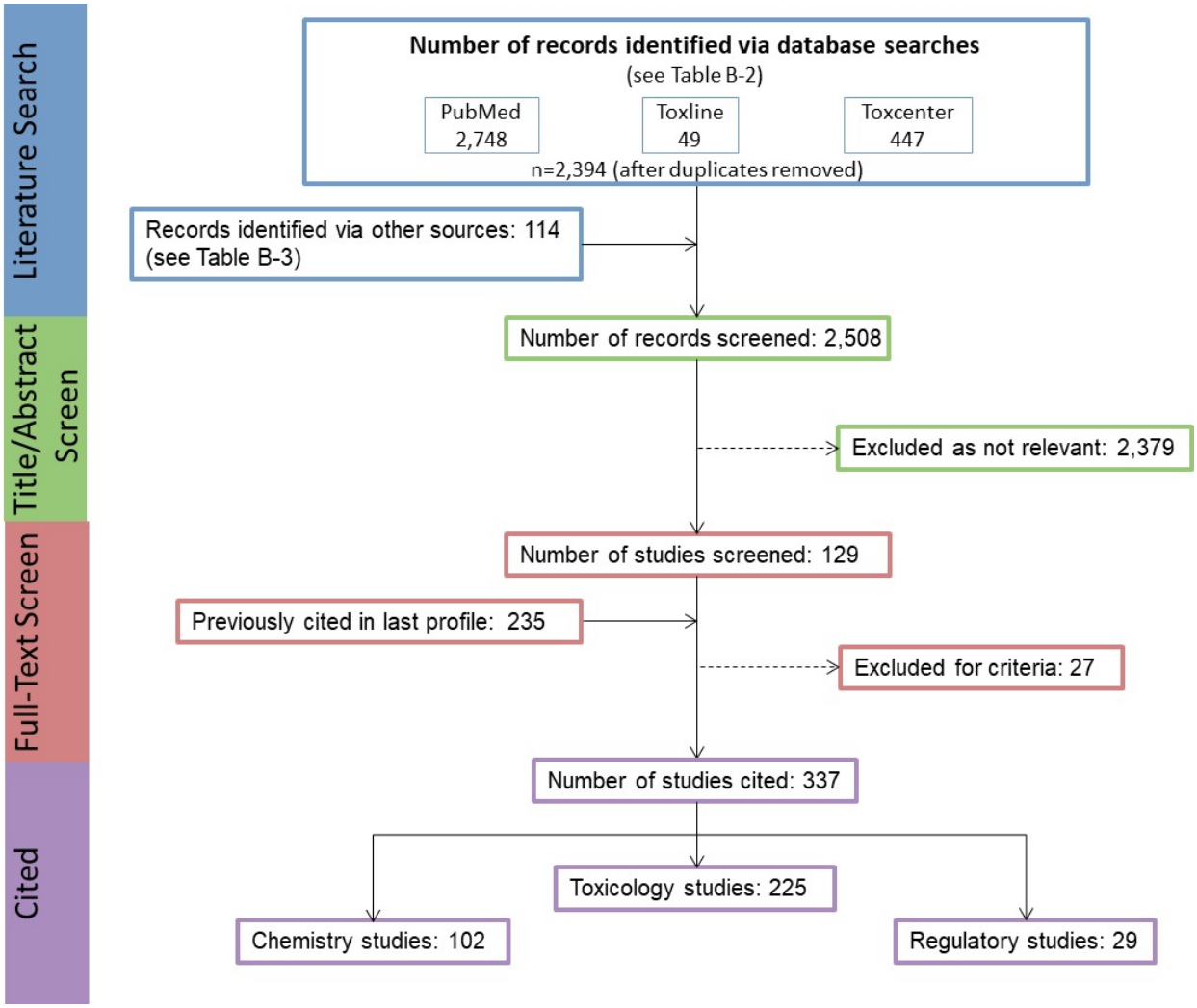
- Number of titles and abstracts screened: 2,508
- Number of studies considered relevant and moved to the next step: 129

Full Text Screen. The second step in the literature screening process was a full text review of individual studies considered relevant in the title and abstract screen step. Each study was reviewed to determine whether it was relevant for inclusion in the toxicological profile.

- Number of studies undergoing full text review: 129
- Number of studies cited in the pre-public draft of the toxicological profile: 235
- Total number of studies cited in the profile: 337

A summary of the results of the literature search and screening is presented in Figure B-1.

Figure B-1. January 2018 Literature Search Results and Screen for Molybdenum



APPENDIX C. FRAMEWORK FOR ATSDR'S SYSTEMATIC REVIEW OF HEALTH EFFECTS DATA FOR MOLYBDENUM

To increase the transparency of ATSDR's process of identifying, evaluating, synthesizing, and interpreting the scientific evidence on the health effects associated with exposure to molybdenum, ATSDR utilized a slight modification of NTP's Office of Health Assessment and Translation (OHAT) systematic review methodology (NTP 2013, 2015; Rooney et al. 2014). ATSDR's framework is an eight-step process for systematic review with the goal of identifying the potential health hazards of exposure to molybdenum:

- Step 1. Problem Formulation
- Step 2. Literature Search and Screen for Health Effects Studies
- Step 3. Extract Data from Health Effects Studies
- Step 4. Identify Potential Health Effect Outcomes of Concern
- Step 5. Assess the Risk of Bias for Individual Studies
- Step 6. Rate the Confidence in the Body of Evidence for Each Relevant Outcome
- Step 7. Translate Confidence Rating into Level of Evidence of Health Effects
- Step 8. Integrate Evidence to Develop Hazard Identification Conclusions

C.1 PROBLEM FORMULATION

The objective of the toxicological profile and this systematic review was to identify the potential health hazards associated with inhalation, oral, or dermal/ocular exposure to molybdenum. The inclusion criteria used to identify relevant studies examining the health effects of molybdenum are presented in Table C-1.

Table C-1. Inclusion Criteria for Identifying Health Effects Studies

Species
Human
Laboratory mammals
Route of exposure
Inhalation
Oral
Dermal (or ocular)
Parenteral (these studies will be considered supporting data)
Health outcome
Death
Systemic effects
Body weight effects
Respiratory effects
Cardiovascular effects
Gastrointestinal effects
Hematological effects
Musculoskeletal effects
Hepatic effects
Renal effects

Table C-1. Inclusion Criteria for Identifying Health Effects Studies

Dermal effects
Ocular effects
Endocrine effects
Immunological effects
Neurological effects
Reproductive effects
Developmental effects
Other noncancer effects
Cancer

Data from human and laboratory animal studies were considered relevant for addressing this objective. Human studies were divided into two broad categories: observational epidemiology studies and controlled exposure studies. The observational epidemiology studies were further divided: cohort studies (retrospective and prospective studies), population studies (with individual data or aggregate data), and case-control studies.

C.2 LITERATURE SEARCH AND SCREEN FOR HEALTH EFFECTS STUDIES

A literature search and screen was conducted to identify studies examining the health effects of molybdenum. The literature search framework for the toxicological profile is discussed in detail in Appendix B.

C.2.1 Literature Search

As noted in Appendix B, the current literature search was intended to update the draft toxicological profile for molybdenum released for public comment in 2017. See Appendix B for the databases searched and the search strategy.

A total of 2,508 records relevant to all sections of the toxicological profile were identified (after duplicate removal).

C.2.2 Literature Screening

As described in Appendix B, a two-step process was used to screen the literature search to identify relevant studies examining the health effects of molybdenum.

Title and Abstract Screen. In the Title and Abstract Screen step, 2,508 records were reviewed; 71 documents were considered to meet the health effects inclusion criteria in Table C-1 and were moved to the next step in the process.

Full Text Screen. In the second step in the literature screening process for the systematic review, a full text review of 92 health effects documents (documents identified in the update literature search and documents cited in older versions of the profile) was performed. From those 92 documents, 115 studies were included in the qualitative review.

C.3 EXTRACT DATA FROM HEALTH EFFECTS STUDIES

Relevant data extracted from the individual studies selected for inclusion in the systematic review were collected in customized data forms. A summary of the type of data extracted from each study is presented in Table C-2. For references that included more than one experiment or species, data extraction records were created for each experiment or species.

Table C-2. Data Extracted From Individual Studies

Citation
Chemical form
Route of exposure (e.g., inhalation, oral, dermal)
Specific route (e.g., gavage in oil, drinking water)
Species
Strain
Exposure duration category (e.g., acute, intermediate, chronic)
Exposure duration
Frequency of exposure (e.g., 6 hours/day, 5 days/week)
Exposure length
Number of animals or subjects per sex per group
Dose/exposure levels
Parameters monitored
Description of the study design and method
Summary of calculations used to estimate doses (if applicable)
Summary of the study results
Reviewer's comments on the study
Outcome summary (one entry for each examined outcome)
No-observed-adverse-effect level (NOAEL) value
Lowest-observed-adverse-effect level (LOAEL) value
Effect observed at the LOAEL value

A summary of the extracted data for each study is presented in the Supplemental Document for Molybdenum and overviews of the results of the studies are presented in Sections 2.2–2.18 of the profile and in the Levels of Significant Exposures tables in Section 2.1 of the profile (Tables 2-1–2-3).

C.4 IDENTIFY POTENTIAL HEALTH EFFECT OUTCOMES OF CONCERN

Overviews of the potential health effect outcomes for molybdenum identified in human and animal studies are presented in Tables C-3 and C-4, respectively. The available human studies examined a limited number of endpoints and reported respiratory, hepatic, endocrine, other systemic (alterations in uric acid levels), reproductive, and developmental effects. Animal studies examined a number of endpoints following inhalation and oral exposure; no dermal exposure studies were identified. These studies examined most systemic endpoints and reported respiratory, gastrointestinal, hematological, musculoskeletal, hepatic, renal, endocrine, dermal, and body weight effects. Additionally, animal studies

Table C-3. Overview of the Health Outcomes for Molybdenum Evaluated In Human Studies

	Body weight	Respiratory	Cardiovascular	Gastrointestinal	Hematological	Musculoskeletal	Hepatic	Renal	Dermal	Ocular	Endocrine	Immunological	Neurological	Reproductive	Developmental	Other Noncancer	Caner
Inhalation studies																	
Cohort		2 1														1 1	1 1
Case control																	
Population																	
Case series																	
Oral studies																	
Cohort														2 2	2 1	1 0	
Case control																	
Population	1 0	1 0	3 2			1 0	1 1			1 1	3 2						2 0
Case series																1 0	
Dermal studies																	
Cohort																	
Case control																	
Population																	
Case series																	

Number of studies examining endpoint	0	1	2	3	4	5-9	≥10	
Number of studies reporting outcome	0	1	2	3	4	5-9	≥10	

APPENDIX C

Table C-4. Overview of the Health Outcomes for Molybdenum Evaluated in Experimental Animal Studies

	Body weight	Respiratory	Cardiovascular	Gastrointestinal	Hematological	Musculoskeletal	Hepatic	Renal	Dermal	Ocular	Endocrine	Immunological[a]	Neurological[a]	Reproductive[a]	Developmental	Other Noncancer	Caner
Inhalation studies																	
Acute-duration	5 5	5 0															
Intermediate-duration		2 0	2 0	2 0	2 0	2 0	2 0	2 0			2 0		2 0	2 0			
Chronic-duration	2 0	2 2	2 0	2 0		2 0	2 0	2 0			2 0		2 0	2 0			2 2
Oral studies																	
Acute-duration	6 2			1 1	1 0	5 4	2 1	2 0						4 3			
Intermediate-duration	41 28	3 0	2 0	3 1	19 6	13 10	8 6	9 6	3 3		8 5		1 0	12 8	12 5	2 0	
Chronic-duration																	
Dermal studies																	
Acute-duration									7 0	4 4		4 0					
Intermediate-duration																	
Chronic-duration																	

Number of studies examining endpoint	0	1	2	3	4	5-9	≥10
Number of studies reporting outcome	0	1	2	3	4	5-9	≥10

[a]Number of studies examining endpoint includes study evaluating histopathology, but not evaluating function.

have reported neurological, reproductive, and developmental effects. Although animal studies have identified a number of affected tissues and systems, interpretation of much of the data is limited by an inadequate amount of copper in the diet. Studies in which the diet did not contain adequate levels of copper or administered ammonium tetrathiomolybdate were carried through Step 3 of the systematic review, but were not considered in the identification of potential health effect outcomes of concern. Additionally, body weight effects were not considered a primary effect especially since most studies did not provide data on food intake; thus, this endpoint was not considered in the assessment of potential human hazards. Studies examining the respiratory, hepatic, renal, uric acid, reproductive, and developmental outcomes were carried through to Steps 4–8 of the systematic review. There were 115 studies (published in 92 documents) examining these potential outcomes were carried through to Steps 4–8 of the systematic review.

C.5 ASSESS THE RISK OF BIAS FOR INDIVIDUAL STUDIES

C.5.1 Risk of Bias Assessment

The risk of bias of individual studies was assessed using OHAT's Risk of Bias Tool (NTP 2015). The risk of bias questions for observational epidemiology studies, human-controlled exposure studies, and animal experimental studies are presented in Tables C-5, C-6, and C-7, respectively. Each risk of bias question was answered on a four-point scale:

- **Definitely low risk of bias (++)**
- **Probably low risk of bias (+)**
- **Probably high risk of bias (-)**
- **Definitely high risk of bias (– –)**

Table C-5. Risk of Bias Questionnaire for Observational Epidemiology Studies

Selection bias
Were the comparison groups appropriate?
Confounding bias
Did the study design or analysis account for important confounding and modifying variables?
Attrition/exclusion bias
Were outcome data complete without attrition or exclusion from analysis?
Detection bias
Is there confidence in the exposure characterization?
Is there confidence in outcome assessment?
Selective reporting bias
Were all measured outcomes reported?

Table C-6. Risk of Bias Questionnaire for Human-Controlled Exposure Studies

Selection bias
Was administered dose or exposure level adequately randomized?
Was the allocation to study groups adequately concealed?
Performance bias
Were the research personnel and human subjects blinded to the study group during the study?
Attrition/exclusion bias
Were outcome data complete without attrition or exclusion from analysis?
Detection bias
Is there confidence in the exposure characterization?
Is there confidence in outcome assessment?
Selective reporting bias
Were all measured outcomes reported?

Table C-7. Risk of Bias Questionnaire for Experimental Animal Studies

Selection bias
Was administered dose or exposure level adequately randomized?
Was the allocation to study groups adequately concealed?
Performance bias
Were experimental conditions identical across study groups?
Were the research personnel blinded to the study group during the study?
Attrition/exclusion bias
Were outcome data complete without attrition or exclusion from analysis?
Detection bias
Is there confidence in the exposure characterization?
Is there confidence in outcome assessment?
Selective reporting bias
Were all measured outcomes reported?

In general, “definitely low risk of bias” or “definitely high risk of bias” were used if the question could be answered with information explicitly stated in the study report. If the response to the question could be inferred, then “probably low risk of bias” or “probably high risk of bias” responses were typically used.

After the risk of bias questionnaires were completed for the health effects studies, the studies were assigned to one of three risk of bias tiers based on the responses to the key questions listed below and the responses to the remaining questions.

- Is there confidence in the exposure characterization? (only relevant for observational studies)
- Is there confidence in the outcome assessment?
- Does the study design or analysis account for important confounding and modifying variables? (only relevant for observational studies)

First Tier. Studies placed in the first tier received ratings of "definitely low" or "probably low" risk of bias on the key questions **AND** received a rating of "definitely low" or "probably low" risk of bias on the responses to at least 50% of the other applicable questions.

Second Tier. A study was placed in the second tier if it did not meet the criteria for the first or third tiers.

Third Tier. Studies placed in the third tier received ratings of "definitely high" or "probably high" risk of bias for the key questions **AND** received a rating of "definitely high" or "probably high" risk of bias on the response to at least 50% of the other applicable questions.

The results of the risk of bias assessment for the different types of molybdenum health effects studies (observational epidemiology, human-controlled exposure studies, and animal experimental studies) are presented in Tables C-8, C-9, and C-10, respectively.

C.6 RATE THE CONFIDENCE IN THE BODY OF EVIDENCE FOR EACH RELEVANT OUTCOME

Confidences in the bodies of human and animal evidence were evaluated independently for each potential outcome. ATSDR did not evaluate the confidence in the body of evidence for carcinogenicity; rather, the Agency defaulted to the cancer weight-of-evidence assessment of other agencies including DHHS, EPA, and IARC. The confidence in the body of evidence for an association or no association between exposure to molybdenum and a particular outcome was based on the strengths and weaknesses of individual studies. Four descriptors were used to describe the confidence in the body of evidence for effects or when no effect was found:

- **High confidence:** the true effect is highly likely to be reflected in the apparent relationship
- **Moderate confidence:** the true effect may be reflected in the apparent relationship
- **Low confidence:** the true effect may be different from the apparent relationship
- **Very low confidence:** the true effect is highly likely to be different from the apparent relationship

Confidence in the body of evidence for a particular outcome was rated for each type of study: case-control, case series, cohort, population, human-controlled exposure, and experimental animal. In the absence of data to the contrary, data for a particular outcome were collapsed across animal species, routes of exposure, and exposure durations. If species (or strain), route, or exposure duration differences were noted, then the data were treated as separate outcomes.

Table C-8. Summary of Risk of Bias Assessment for Molybdenum—Observational Epidemiological Studies

Reference	Risk of bias criteria and ratings: Selection bias — Were the comparison groups appropriate?	Confounding bias — Did the study design or analysis account for important confounding and modifying variables?*	Attrition / exclusion bias — Were outcome data complete without attrition or exclusion from analysis?	Detection bias — Is there confidence in the exposure characterization?*	Detection bias — Is there confidence in the outcome assessment?*	Selective reporting bias — Were all measured outcomes reported?	Risk of bias tier
Outcome: Respiratory effects							
Cohort studies							
Ott et al. 2004	–	–	+	na	+	++	Second
Walravens et al. 1979	–	–	+	+	–	+	Second
Outcome: Hepatic effects							
Cross-sectional studies							
Mendy et al. 2012	+	+	+	+	–	+	Second
Outcome: Alterations in uric acid levels							
Cross-sectional studies							
Koval'sky et al. 1961	–	–	+	–	+	+	Second
Cohort studies							
Walravens et al. 1979	–	–	+	+	–	+	Second
Outcome: Reproductive effects							
Cross-sectional studies							
Lewis and Meeker 2015	na	-	+	+	+	+	First
Meeker et al. 2008	+	+	+	++	++	++	First
Meeker et al. 2010	+	+	++	+	++	++	First

Table C-8. Summary of Risk of Bias Assessment for Molybdenum—Observational Epidemiological Studies

Reference	Risk of bias criteria and ratings: Selection bias — Were the comparison groups appropriate?	Confounding bias — Did the study design or analysis account for important confounding and modifying variables?*	Attrition / exclusion bias — Were outcome data complete without attrition or exclusion from analysis?	Detection bias — Is there confidence in the exposure characterization?*	Detection bias — Is there confidence in the outcome assessment?*	Selective reporting bias — Were all measured outcomes reported?	Risk of bias tier
Outcome: Developmental effects							
Cross-sectional studies							
Vazquez-Salas et al. 2014	+	+	+	+	++	+	First
Shirai et al. 2010	na	–	+	+	+	+	Second

++ = definitely low risk of bias; + = probably low risk of bias; – = probably high risk of bias; – – = definitely high risk of bias; na = not applicable

*Key question used to assign risk of bias tier.

Table C-9. Summary of Risk of Bias Assessment for Molybdenum—Human-Controlled Exposure Studies

Reference	Risk of bias criteria and ratings: Selection bias: Was administered dose or exposure level adequately randomized?	Selection bias: Was the allocation to study groups adequately concealed?	Performance bias: Were the research personnel blinded to the study group during the study?	Attrition/ exclusion bias: Were outcome data complete without attrition or exclusion from analysis?	Detection bias: Is there confidence in the exposure characterization?	Detection bias: Is there confidence in the outcome assessment?*	Selective reporting bias: Were all measured outcomes reported?	Risk of bias tier
Outcome: Alterations in uric acid levels								
Oral acute exposure								
Deosthale and Gopalan 1974	na	+	+	+	+	+	++	First

++ = definitely low risk of bias; + = probably low risk of bias; – = probably high risk of bias; – – = definitely high risk of bias; na = not applicable

*Key question used to assign risk of bias tier.

Table C-10. Summary of Risk of Bias Assessment for Molybdenum—Experimental Animal Studies

Reference	Risk of bias criteria and ratings: Selection bias: Was administered dose or exposure level adequately randomized?	Selection bias: Was the allocation to study groups adequately concealed?	Performance bias: Were experimental conditions identical across study groups?	Performance bias: Were the research personnel blinded to the study group during the study?	Attrition/ exclusion bias: Were outcome data complete without attrition or exclusion from analysis?	Detection bias: Is there confidence in the exposure characterization?	Detection bias: Is there confidence in the outcome assessment?*	Selective reporting bias: Were all measured outcomes reported?	Other bias: Did the study design or analysis account for important confounding and modifying variables?	Risk of bias tier
Outcome: Respiratory effects										
Inhalation acute exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First
Inhalation intermediate exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First
Inhalation chronic exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First
Outcome: Hepatic effects										
Inhalation intermediate exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First
Inhalation chronic exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First

Table C-10. Summary of Risk of Bias Assessment for Molybdenum—Experimental Animal Studies

Reference	Risk of bias criteria and ratings: Selection bias: Was administered dose or exposure level adequately randomized?	Selection bias: Was the allocation to study groups adequately concealed?	Performance bias: Were experimental conditions identical across study groups?	Performance bias: Were the research personnel blinded to the study group during the study?	Attrition/ exclusion bias: Were outcome data complete without attrition or exclusion from analysis?	Detection bias: Is there confidence in the exposure characterization?	Detection bias: Is there confidence in the outcome assessment?*	Selective reporting bias: Were all measured outcomes reported?	Other bias: Did the study design or analysis account for important confounding and modifying variables?	Risk of bias tier
Oral acute exposure										
Bersenyi et al. 2008 (rabbit)	–	+	+	–	++	–	+	+	+	First
Bersenyi et al. 2008 (rabbit)	–	+	+	–	++	–	+	+	+	First
Oral intermediate exposure										
Murray et al. 2014a (rat)	++	+	++	–	++	++	++	++	++	First
Rana and Chauhan 2000 (rat)	–	+	+	–	++	+	–	++	–	Second
Rana and Kumar 1980b (rat)	–	+	+	–	++	–	–	+	–	Third
Rana and Kumar 1980c (rat)	+	+	–	–	++	–	+	++	–	First
Rana and Kumar 1983 (rat)	+	+	–	–	++	+	+	++	–	First
Rana and Prakash 1986 (rat)	–	+	+	–	++	–	+	+	+	First
Rana et al. 1980 (rat)	–	+	+	–	+	–	+	+	+	First
Rana et al. 1985 (rat)	+	+	+	–	++	+	+	+	+	First
Outcome: Renal effects										
Inhalation intermediate exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First

Table C-10. Summary of Risk of Bias Assessment for Molybdenum—Experimental Animal Studies

Reference	Risk of bias criteria and ratings: Selection bias: Was administered dose or exposure level adequately randomized?	Selection bias: Was the allocation to study groups adequately concealed?	Performance bias: Were experimental conditions identical across study groups?	Performance bias: Were the research personnel blinded to the study group during the study?	Attrition/ exclusion bias: Were outcome data complete without attrition or exclusion from analysis?	Detection bias: Is there confidence in the exposure characterization?	Detection bias: Is there confidence in the outcome assessment?*	Selective reporting bias: Were all measured outcomes reported?	Other bias: Did the study design or analysis account for important confounding and modifying variables?	Risk of bias tier
Inhalation chronic exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First
Oral acute exposure										
Bersenyi et al. 2008 (rabbit, males)	–	+	+	–	++	–	+	+	+	First
Bersenyi et al. 2008 (rabbit, females)	–	+	+	–	++	–	+	+	+	First
Oral intermediate exposure										
Bandyopadhyay et al. 1981 (rat)	–	+	+	–	++	–	+	++	++	First
Bompart et al. 1990 (rat)	+	+	+	–	++	+	+	++	+	First
Murray et al. 2014a (rat)	++	+	++	–	++	++	++	++	++	First
Rana et al. 1980 (rat)	–	+	+	–	+	–	+	+	+	First
Rana and Kumar 1980c	+	+	–	–	++	–	+	++	–	First
Rana and Kumar 1983 (rat)	+	+	–	–	++	+	+	++	–	First

Table C-10. Summary of Risk of Bias Assessment for Molybdenum—Experimental Animal Studies

Reference	Risk of bias criteria and ratings: Selection bias: Was administered dose or exposure level adequately randomized?	Selection bias: Was the allocation to study groups adequately concealed?	Performance bias: Were experimental conditions identical across study groups?	Performance bias: Were the research personnel blinded to the study group during the study?	Attrition/ exclusion bias: Were outcome data complete without attrition or exclusion from analysis?	Detection bias: Is there confidence in the exposure characterization?	Detection bias: Is there confidence in the outcome assessment?*	Selective reporting bias: Were all measured outcomes reported?	Other bias: Did the study design or analysis account for important confounding and modifying variables?	Risk of bias tier
Outcome: Alterations in uric acid levels										
Oral intermediate exposure										
Murray et al. 2014a (rat)	++	+	++	-	++	++	++	++	++	First
Outcome: Reproductive effects										
Inhalation intermediate exposure										
NTP 1997 (rat)	++	+	++	+	++	++	++	++	+	First
NTP 1997 (mouse)	++	+	++	+	++	++	++	++	+	First
Oral acute exposure										
Zhang et al. 2013 (mouse)	–	+	++	–	++	– –	+	++	–	First
Zhai et al. 2013 (mouse)	–	+	++	–	++	– –	+	++	+	First
Bersenyi et al. 2008 (rabbit, males)	–	+	+	–	++	–	+	+	+	First
Bersenyi et al. 2008 (rabbit, females)	–	+	+	–	++	–	+	+	+	First
Oral intermediate exposure										
Fungwe et al. 1990 (rat)	+	+	+	–	++	–	+	+	– –	First
Jeter and Davis 1954 (rat, adults)	–	+	+	–	++	–	+	+	–	First

Table C-10. Summary of Risk of Bias Assessment for Molybdenum—Experimental Animal Studies

Reference	Risk of bias criteria and ratings: Selection bias: Was administered dose or exposure level adequately randomized?	Selection bias: Was the allocation to study groups adequately concealed?	Performance bias: Were experimental conditions identical across study groups?	Performance bias: Were the research personnel blinded to the study group during the study?	Attrition/ exclusion bias: Were outcome data complete without attrition or exclusion from analysis?	Detection bias: Is there confidence in the exposure characterization?	Detection bias: Is there confidence in the outcome assessment?*	Selective reporting bias: Were all measured outcomes reported?	Other bias: Did the study design or analysis account for important confounding and modifying variables?	Risk of bias tier
Jeter and Davis 1954 (rat, weanling)	–	+	+	–	++	–	+	+	– –	First
Murray et al. 2014a (rat)	++	+	++	–	++	++	++	++	++	First
Murray et al. 2019 (rat)	++	+	++	–	++	++	++	++	++	First
Pandey and Singh 2002 (rat)	–	+	++	–	++	+	+	++	–	First
Pandey and Singh 2002 (rat fertility study)	–	+	++	–	++	+	+	++	–	First
Outcome: Developmental effects										
Oral intermediate exposure										
Jeter and Davis 1954 (rat, weanling)	–	+	+	–	++	–	+	+	– –	First
Murray et al. 2014b (rat)	++	+	+	–	++	++	+	++	+	First
Pandey and Singh 2002 (rat)	–	+	++	–	++	+	+	++	–	First

++ = definitely low risk of bias; + = probably low risk of bias; – = probably high risk of bias; – – = definitely high risk of bias

*Key question used to assign risk of bias tier.

C.6.1 Initial Confidence Rating

In ATSDR's modification to the OHAT approach, the body of evidence for an association (or no association) between exposure to molybdenum and a particular outcome was given an initial confidence rating based on the key features of the individual studies examining that outcome. The presence of these key features of study design was determined for individual studies using four "yes or no" questions, which were customized for epidemiology, human controlled exposure, or experimental animal study designs. Separate questionnaires were completed for each outcome assessed in a study. The key features for observational epidemiology (cohort, population, and case-control) studies, human controlled exposure, and experimental animal studies are presented in Tables C-11, C-12, and C-13, respectively. The initial confidence in the study was determined based on the number of key features present in the study design:

- **High Initial Confidence:** Studies in which the responses to the four questions were "yes".
- **Moderate Initial Confidence:** Studies in which the responses to only three of the questions were "yes".
- **Low Initial Confidence:** Studies in which the responses to only two of the questions were "yes".
- **Very Low Initial Confidence:** Studies in which the response to one or none of the questions was "yes".

Table C-11. Key Features of Study Design for Observational Epidemiology Studies

Exposure was experimentally controlled
Exposure occurred prior to the outcome
Outcome was assessed on individual level rather than at the population level
A comparison group was used

Table C-12. Key Features of Study Design for Human-Controlled Exposure Studies

A comparison group was used or the subjects served as their own control
A sufficient number of subjects were tested
Appropriate methods were used to measure outcomes (i.e., clinically-confirmed outcome versus self-reported)
Appropriate statistical analyses were performed and reported or the data were reported in such a way to allow independent statistical analysis

Table C-13. Key Features of Study Design for Experimental Animal Studies

A concurrent control group was used
A sufficient number of animals per group were tested
Appropriate parameters were used to assess a potential adverse effect
Appropriate statistical analyses were performed and reported or the data were reported in such a way to allow independent statistical analysis

The presence or absence of the key features and the initial confidence levels for studies examining The presence or absence of the key features and the initial confidence levels for studies examining respiratory, gastrointestinal, renal, dermal, and ocular effects observed in the observational epidemiology, human-controlled exposure, and animal experimental studies are presented in Tables C-14, C-15, and C-16, respectively.

Table C-14. Presence of Key Features of Study Design for Molybdenum—Observational Epidemiology Studies

Reference	Key features: Controlled exposure	Exposure prior to outcome	Outcomes assessed on an individual level	Comparison group	Initial study confidence
Outcome: Respiratory effects					
Cohort studies					
Ott et al. 2004	No	Yes	Yes	No	Low
Walravens et al. 1979	No	No	No	No	Very Low
Outcome: Hepatic effects					
Cross-sectional studies					
Mendy et al. 2012	No	No	Yes	Yes	Low
Outcome: Alterations in uric acid levels					
Cross-sectional studies					
Koval'sky et al. 1961	No	Yes	Yes	No	Low
Cohort studies					
Walravens et al. 1979	No	No	No	No	Very Low
Outcome: Reproductive effects					
Cross-sectional studies					
Lewis and Meeker 2015	No	No	Yes	Yes	Low
Meeker et al. 2008	No	No	Yes	Yes	Low
Meeker et al. 2010	No	No	Yes	Yes	Low

Table C-14. Presence of Key Features of Study Design for Molybdenum—Observational Epidemiology Studies

Reference	Key features: Controlled exposure	Exposure prior to outcome	Outcomes assessed on an individual level	Comparison group	Initial study confidence
Outcome: Developmental effects					
Cross-sectional studies					
Vazquez-Salas et al. 2014	No	No	Yes	Yes	Low
Shirai et al. 2010	No	No	Yes	Yes	Low

Table C-15. Presence of Key Features of Study Design for Molybdenum—Human-Controlled Exposure Studies

Reference	Key feature: Concurrent control group or self-control	Sufficient number of subjects tested	Appropriate methods to measure outcome	Adequate data for statistical analysis	Initial study confidence
Outcome: Alterations in uric acid levels					
Oral acute exposure					
Deosthale and Gopalan 1974	Yes	No	Yes	No	Low

Table C-16. Presence of Key Features of Study Design for Molybdenum—Experimental Animal Studies

Reference	Key feature: Concurrent control group	Sufficient number of animals per group	Appropriate parameters to assess potential effect	Adequate data for statistical analysis	Initial study confidence
Outcome: Respiratory effects					
Inhalation acute exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High
Inhalation intermediate exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High
Inhalation chronic exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High
Outcome: Hepatic effects					
Inhalation intermediate exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High
Inhalation chronic exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High
Oral acute exposure					
Bersenyi et al. 2008 (rabbit, males)	Yes	No	Yes	Yes	Moderate
Bersenyi et al. 2008 (rabbit, females)	Yes	No	Yes	Yes	Moderate
Oral intermediate exposure					
Murray et al. 2014a (rat)	Yes	Yes	Yes	Yes	High
Rana and Chauhan 2000 (rat)	Yes	Yes	No	Yes	Moderate
Rana and Kumar 1980b (rat)	Yes	Yes	No	Yes	Moderate
Rana and Kumar 1980c (rat)	Yes	Yes	No	Yes	Moderate
Rana and Kumar 1983 (rat)	Yes	Yes	No	Yes	Moderate
Rana and Prakash 1986 (rat)	Yes	Yes	No	Yes	Moderate
Rana et al. 1980 (rat)	Yes	Yes	No	No	Low
Rana et al. 1985 (rat)	Yes	Yes	No	Yes	Moderate
Outcome: Renal effects					
Inhalation intermediate exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High

Table C-16. Presence of Key Features of Study Design for Molybdenum—Experimental Animal Studies

Reference	Key feature: Concurrent control group	Sufficient number of animals per group	Appropriate parameters to assess potential effect	Adequate data for statistical analysis	Initial study confidence
Inhalation chronic exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High
Oral acute exposure					
Bersenyi et al. 2008 (rabbit, males)	Yes	No	Yes	Yes	Moderate
Bersenyi et al. 2008 (rabbit, females)	Yes	No	Yes	Yes	Moderate
Oral intermediate exposure					
Bandyopadhyay et al. 1981 (rat)	Yes	No	Yes	No	Low
Bompart et al. 1990 (rat)	Yes	No	Yes	Yes	Moderate
Murray et al. 2014a (rat)	Yes	Yes	Yes	Yes	High
Murray et al. 2019 (rat)	Yes	Yes	Yes	Yes	High
Rana et al. 1980 (rat)	Yes	Yes	No	No	Low
Rana and Kumar 1980c	Yes	Yes	No	Yes	Moderate
Rana and Kumar 1983 (rat)	Yes	Yes	No	Yes	Moderate
Outcome: Alterations in uric acid levels					
Oral intermediate exposure					
Murray et al. 2014a (rat)	Yes	Yes	Yes	Yes	High
Outcome: Reproductive effects					
Inhalation intermediate exposure					
NTP 1997 (rat)	Yes	Yes	Yes	Yes	High
NTP 1997 (mouse)	Yes	Yes	Yes	Yes	High
Oral acute exposure					
Zhang et al. 2013 (mouse)	Yes	Yes	No	Yes	Moderate
Zhai et al. 2013 (mouse)	Yes	Yes	No	Yes	Moderate
Bersenyi et al. 2008 (rabbit, males)	Yes	No	No	Yes	Low
Bersenyi et al. 2008 (rabbit, females)	Yes	No	No	No	Very Low
Oral intermediate exposure					
Fungwe et al. 1990 (rat)	Yes	No	Yes	Yes	Moderate
Jeter and Davis 1954 (rat, adult)	Yes	No	No	No	Very Low
Murray et al. 2014a (rat)	Yes	Yes	Yes	Yes	High
Murray et al. 2019 (rat)	Yes	Yes	Yes	Yes	High
Pandey and Singh 2002 (rat)	Yes	Yes	No	Yes	Moderate
Pandey and Singh 2002 (rat, fertility study)	Yes	Yes	Yes	Yes	High

Table C-16. Presence of Key Features of Study Design for Molybdenum—Experimental Animal Studies

Reference	Key feature: Concurrent control group	Key feature: Sufficient number of animals per group	Key feature: Appropriate parameters to assess potential effect	Key feature: Adequate data for statistical analysis	Initial study confidence
Outcome: Developmental effects					
Oral intermediate exposure					
Jeter and Davis 1954 (rat, weanling)	Yes	No	No	No	Very Low
Murray et al. 2014b (rat)	Yes	Yes	Yes	Yes	High
Murray et al. 2019 (rat)	Yes	Yes	Yes	Yes	High
Pandey and Singh 2002 (rat)	Yes	Yes	Yes	Yes	High

A summary of the initial confidence ratings for each outcome is presented in Table C-17. If individual studies for a particular outcome and study type had different study quality ratings, then the highest confidence rating for the group of studies was used to determine the initial confidence rating for the body of evidence; any exceptions were noted in Table C-17.

Table C-17. Initial Confidence Rating for Molybdenum Health Effects Studies

	Finding	Initial study confidence	Initial confidence rating
Outcome: Respiratory effects (inhalation only)			
Inhalation acute exposure			
Animal studies			
NTP 1997 (rat)	No effect	High	High
NTP 1997 (mouse)	No effect	High	
Inhalation intermediate exposure			
Animal studies			
NTP 1997 (rat)	No effect	High	High
NTP 1997 (mouse)	No effect	High	
Inhalation chronic exposure			
Human studies			
Observational studies			
Ott et al. 2004	Effect	Low	Low
Walravens et al. 1979	Effect	Very Low	

Table C-17. Initial Confidence Rating for Molybdenum Health Effects Studies

	Finding	Initial study confidence	Initial confidence rating
Animal studies			
NTP 1997 (rat)	Effect	High	High
NTP 1997 (mouse)	Effect	High	
Outcome: Hepatic effects			
Inhalation intermediate exposure			
Animal studies			
NTP 1997 (rat)	No effect	High	High
NTP 1997 (mouse)	No effect	High	
Inhalation chronic exposure			
Animal studies			
NTP 1997 (rat)	No effect	High	High
NTP 1997 (mouse)	No effect	High	
Oral acute exposure			
Animal studies			
Bersenyi et al. 2008 (rabbit, males)	Effect	Moderate	Moderate
Bersenyi et al. 2008 (rabbit, females)	Effect	Moderate	
Oral intermediate exposure			
Animal studies			
Murray et al. 2014a (rat)	No effect	High	High
Rana and Chauhan 2000 (rat)	Effect	Moderate	
Rana and Kumar 1980b (rat)	Effect	Moderate	
Rana and Kumar 1980c (rat)	Effect	Moderate	
Rana and Kumar 1983 (rat)	Effect	Moderate	Low
Rana and Prakash 1986 (rat)	Effect	Moderate	
Rana et al. 1980 (rat)	Effect	Low	
Rana et al. 1985 (rat)	Effect	Moderate	
Oral chronic exposure			
Human studies			
Observational studies			
Mendy et al. 2012	Effect	Low	Low
Outcome: Renal effects			
Inhalation intermediate exposure			
Animal studies			
NTP 1997 (rat)	No effect	High	High
NTP 1997 (mouse)	No effect	High	
Inhalation chronic exposure			
Animal studies			
NTP 1997 (rat)	No effect	High	High
NTP 1997 (mouse)	No effect	High	
Oral acute exposure			
Animal studies			
Bersenyi et al. 2008 (rabbit, males)	No effect	Moderate	Moderate
Bersenyi et al. 2008 (rabbit, females)	No effect	Moderate	

Table C-17. Initial Confidence Rating for Molybdenum Health Effects Studies

	Finding	Initial study confidence	Initial confidence rating
Oral intermediate exposure			
Animal studies			
Bandyopadhyay et al. 1981 (rat)	Effect	Low	High
Bompart et al. 1990 (rat)	Effect	Moderate	
Murray et al. 2014a (rat)	Effect	High	
Rana et al. 1980 (rat)	Effect	Low	
Rana and Kumar 1980c	Effect	Moderate	
Rana and Kumar 1983 (rat)	Effect	Moderate	
Murray et al. 2019 (rat)	No effect	High	High
Outcome: Alterations in uric acid levels			
Inhalation chronic exposure			
Human studies			
Observational studies			
Walravens et al. 1979	Effect	Very Low	Very Low
Oral acute exposure			
Human studies			
Controlled exposure			
Deosthale and Gopalan 1974	No Effect	Low	Low
Oral intermediate exposure			
Animal studies			
Murray et al. 2014a (rat)	No effect	High	High
Oral chronic exposure			
Human studies			
Observational studies			
Koval'sky et al. 1961	Effect	Low	Low
Outcome: Reproductive effects			
Inhalation intermediate exposure			
Animal studies			
NTP 1997 (rat)	No effect	High	High
NTP 1997 (mouse)	No effect	High	
Oral acute exposure			
Animal studies			
Zhang et al. 2013 (mouse)	Effect	Moderate	Moderate
Zhai et al. 2013 (mouse)	Effect	Moderate	
Bersenyi et al. 2008 (male, rabbit)	Effect	Low	
Bersenyi et al. 2008 (female, rabbit)	No effect	Very Low	Very low
Oral intermediate exposure			
Animal studies			
Fungwe et al. 1990 (rat)	Effect	Moderate	High
Jeter and Davis 1954 (rat, adult)	Effect	Very Low	
Jeter and Davis 1954 (rat, weanling)	Effect	Very Low	
Pandey and Singh 2002 (rat)	Effect	Moderate	

Table C-17. Initial Confidence Rating for Molybdenum Health Effects Studies

	Finding	Initial study confidence	Initial confidence rating
Pandey and Singh 2002 (rat, fertility study)	Effect	High	
Murray et al. 2014a (rat)	No effect	High	High
Murray et al. 2019 (rat)	No effect	High	
Oral chronic exposure			
Human studies			
Observational studies			
Lewis and Meeker 2015	Effect	Low	
Meeker et al. 2008	Effect	Low	Low
Meeker et al. 2010	Effect	Low	
Outcome: Developmental effects			
Oral intermediate exposure			
Animal studies			
Pandey and Singh 2002 (rat)	Effect	High	High
Jeter and Davis 1954 (rat, weanling)	No effect	Very Low	
Murray et al. 2014b (rat)	No effect	High	High
Murray et al. 2019 (rat)	No effect	High	
Oral chronic exposure			
Human studies			
Observational studies			
Vazquez-Salas et al. 2014	Effect	Low	Low
Shirai et al. 2010	No effect	Low	Low

C.6.2 Adjustment of the Confidence Rating

The initial confidence rating was then downgraded or upgraded depending on whether there were substantial issues that would decrease or increase confidence in the body of evidence. The nine properties of the body of evidence that were considered are listed below. The summaries of the assessment of the confidence in the body of evidence for respiratory, hepatic, renal, alterations in uric acid levels, reproductive, and developmental effects are presented in Table C-18. If the confidence ratings for a particular outcome were based on more than one type of human study, then the highest confidence rating was used for subsequent analyses. An overview of the confidence in the body of evidence for all health effects associated with molybdenum exposure is presented in Table C-19.

Five properties of the body of evidence were considered to determine whether the confidence rating should be downgraded:

- **Risk of bias.** Evaluation of whether there is substantial risk of bias across most of the studies examining the outcome. This evaluation used the risk of bias tier groupings for individual studies examining a particular outcome (Tables C-14, C-15, and C-16). Below are the criteria used to determine whether the initial confidence in the body of evidence for each outcome should be downgraded for risk of bias:
    - No downgrade if most studies are in the risk of bias first tier
    - Downgrade one confidence level if most studies are in the risk of bias second tier
    - Downgrade two confidence levels if most studies are in the risk of bias third tier

Table C-18. Adjustments to the Initial Confidence in the Body of Evidence

	Initial confidence	Adjustments to the initial confidence rating	Final confidence
Outcome: Respiratory effects			
Observational studies (effect)	Low	-1 risk of bias; -1 imprecision	Very low
Animal studies (effect)	High	None	High
Animal studies (no effect)	High	+1 magnitude	High
Outcome: Hepatic effects			
Observational studies (effect)	Low	-1 risk of bias	Very low
Animal studies (effect)	Moderate	-1 indirectness (secondary outcomes);	Moderate
Animal studies (no effect)	High	None	High
Outcome: Renal effects			
Animal studies	High	None	High
Animal studies	High	None	High
Outcome: Alterations in uric acid levels			
Observational studies (effect)	Low	-1 risk of bias	Very low
Controlled exposure studies (no effect)	Low	None	Low
Animal studies (no effect)	High	None	High
Outcome: Reproductive effects			
Observational studies (effect)	Low	None	Low
Animal studies (effect)	High	-1 inconsistency	Moderate
Animal studies (no effect)	High	None	High
Outcome: Developmental effects			
Observational studies (effect)	Low	None	Low
Observational studies (no effect)	Low	None	Low
Animal studies	High	-1 inconsistency	Moderate
Animal studies	High	None	High

Table C-19. Confidence in the Body of Evidence for Molybdenum

	Confidence in body of evidence	
Outcome	Human studies	Animal studies
Respiratory effects	Very low (effect)	High (effect) High (no effect)
Hepatic effects	Very low (effect)	Moderate (effect) High (no effect)
Renal effects	No data	High (effect) High (no effect)
Alterations in uric acid levels	Very low (effect) Low (no effect)	High (effect)
Reproductive Effects	Low (effect)	Moderate (effect) High (no effect)
Developmental effects	Low (effect) Low (no effect)	Moderate (effect) High (no effect)

- **Unexplained inconsistency.** Evaluation of whether there is inconsistency or large variability in the magnitude or direction of estimates of effect across studies that cannot be explained. Below are the criteria used to determine whether the initial confidence in the body of evidence for each outcome should be downgraded for unexplained inconsistency:
    - No downgrade if there is little inconsistency across studies or if only one study evaluated the outcome
    - Downgrade one confidence level if there is variability across studies in the magnitude or direction of the effect
    - Downgrade two confidence levels if there is substantial variability across studies in the magnitude or direct of the effect

- **Indirectness.** Evaluation of four factors that can affect the applicability, generalizability, and relevance of the studies:
    - Relevance of the animal model to human health—unless otherwise indicated, studies in rats, mice, and other mammalian species are considered relevant to humans
    - Directness of the endpoints to the primary health outcome—examples of secondary outcomes or nonspecific outcomes include organ weight in the absence of histopathology or clinical chemistry findings in the absence of target tissue effects
    - Nature of the exposure in human studies and route of administration in animal studies—inhalation, oral, and dermal exposure routes are considered relevant unless there are compelling data to the contrary
    - Duration of treatment in animal studies and length of time between exposure and outcome assessment in animal and prospective human studies—this should be considered on an outcome-specific basis

  Below are the criteria used to determine whether the initial confidence in the body of evidence for each outcome should be downgraded for indirectness:
    - No downgrade if none of the factors are considered indirect
    - Downgrade one confidence level if one of the factors is considered indirect
    - Downgrade two confidence levels if two or more of the factors are considered indirect

- **Imprecision.** Evaluation of the narrowness of the effect size estimates and whether the studies have adequate statistical power. Data are considered imprecise when the ratio of the upper to lower 95% CIs for most studies is ≥10 for tests of ratio measures (e.g., odds ratios) and ≥100 for absolute measures (e.g., percent control response). Adequate statistical power is determined if the study can detect a potentially biologically meaningful difference between groups (20% change from control response for categorical data or risk ratio of 1.5 for continuous data). Below are the criteria used to determine whether the initial confidence in the body of evidence for each outcome should be downgraded for imprecision:
    - No downgrade if there are no serious imprecisions
    - Downgrade one confidence level for serious imprecisions
    - Downgrade two confidence levels for very serious imprecisions

- **Publication bias.** Evaluation of the concern that studies with statistically significant results are more likely to be published than studies without statistically significant results.
    - Downgrade one level of confidence for cases where there is serious concern with publication bias

Four properties of the body of evidence were considered to determine whether the confidence rating should be upgraded:

- **Large magnitude of effect.** Evaluation of whether the magnitude of effect is sufficiently large so that it is unlikely to have occurred as a result of bias from potential confounding factors.
    - Upgrade one confidence level if there is evidence of a large magnitude of effect in a few studies, provided that the studies have an overall low risk of bias and there is no serious unexplained inconsistency among the studies of similar dose or exposure levels; confidence can also be upgraded if there is one study examining the outcome, provided that the study has an overall low risk of bias

- **Dose response.** Evaluation of the dose-response relationships measured within a study and across studies. Below are the criteria used to determine whether the initial confidence in the body of evidence for each outcome should be upgraded:
    - Upgrade one confidence level for evidence of a monotonic dose-response gradient
    - Upgrade one confidence level for evidence of a non-monotonic dose-response gradient where there is prior knowledge that supports a non-monotonic dose-response and a non-monotonic dose-response gradient is observed across studies

- **Plausible confounding or other residual biases.** This factor primarily applies to human studies and is an evaluation of unmeasured determinants of an outcome such as residual bias towards the null (e.g., "healthy worker" effect) or residual bias suggesting a spurious effect (e.g., recall bias). Below is the criterion used to determine whether the initial confidence in the body of evidence for each outcome should be upgraded:
    - Upgrade one confidence level for evidence that residual confounding or bias would underestimate an apparent association or treatment effect (i.e., bias toward the null) or suggest a spurious effect when results suggest no effect

- **Consistency in the body of evidence.** Evaluation of consistency across animal models and species, consistency across independent studies of different human populations and exposure scenarios, and consistency across human study types. Below is the criterion used to determine whether the initial confidence in the body of evidence for each outcome should be upgraded:
    - Upgrade one confidence level if there is a high degree of consistency in the database

C.7 TRANSLATE CONFIDENCE RATING INTO LEVEL OF EVIDENCE OF HEALTH EFFECTS

In the seventh step of the systematic review of the health effects data for molybdenum, the confidence in the body of evidence for specific outcomes was translated to a level of evidence rating. The level of evidence rating reflected the confidence in the body of evidence and the direction of the effect (i.e., toxicity or no toxicity); route-specific differences were noted. The level of evidence for health effects was rated on a five-point scale:

- **High level of evidence:** High confidence in the body of evidence for an association between exposure to the substance and the health outcome
- **Moderate level of evidence:** Moderate confidence in the body of evidence for an association between exposure to the substance and the health outcome
- **Low level of evidence:** Low confidence in the body of evidence for an association between exposure to the substance and the health outcome
- **Evidence of no health effect:** High confidence in the body of evidence that exposure to the substance is not associated with the health outcome
- **Inadequate evidence:** Low or moderate confidence in the body of evidence that exposure to the substance is not associated with the health outcome OR very low confidence in the body of evidence for an association between exposure to the substance and the health outcome

A summary of the level of evidence of health effects for molybdenum is presented in Table C-20.

Table C-20. Level of Evidence of Health Effects for Molybdenum

Outcome	Confidence in body of evidence	Direction of health effect	Level of evidence for health effect
Human studies			
Respiratory effects (inhalation only)	Very low	Health effect	Inadequate
Hepatic effects	Very low	Health effect	Inadequate
Renal effects	No data	No data	No data
Alterations in uric acid levels	Low	Health effect	Inadequate
Reproductive effects	Low	Health effect	Low
Developmental effects	Low	Health effect	Low
Animal studies			
Respiratory effects (inhalation only)	High	Health effect No health effect	High High
Hepatic effects	Moderate	Health effect No health effect	Moderate High
Renal effects	High	Health effect	High
Alterations in uric acid levels	High	No effect	Evidence of no health effect

Table C-20. Level of Evidence of Health Effects for Molybdenum

Outcome	Confidence in body of evidence	Direction of health effect	Level of evidence for health effect
Reproductive effects	Moderate	Health effect No health effect	Moderate High
Developmental effects[a]	Moderate	Health effect No health effect	High Evidence of no health effect

C.8 INTEGRATE EVIDENCE TO DEVELOP HAZARD IDENTIFICATION CONCLUSIONS

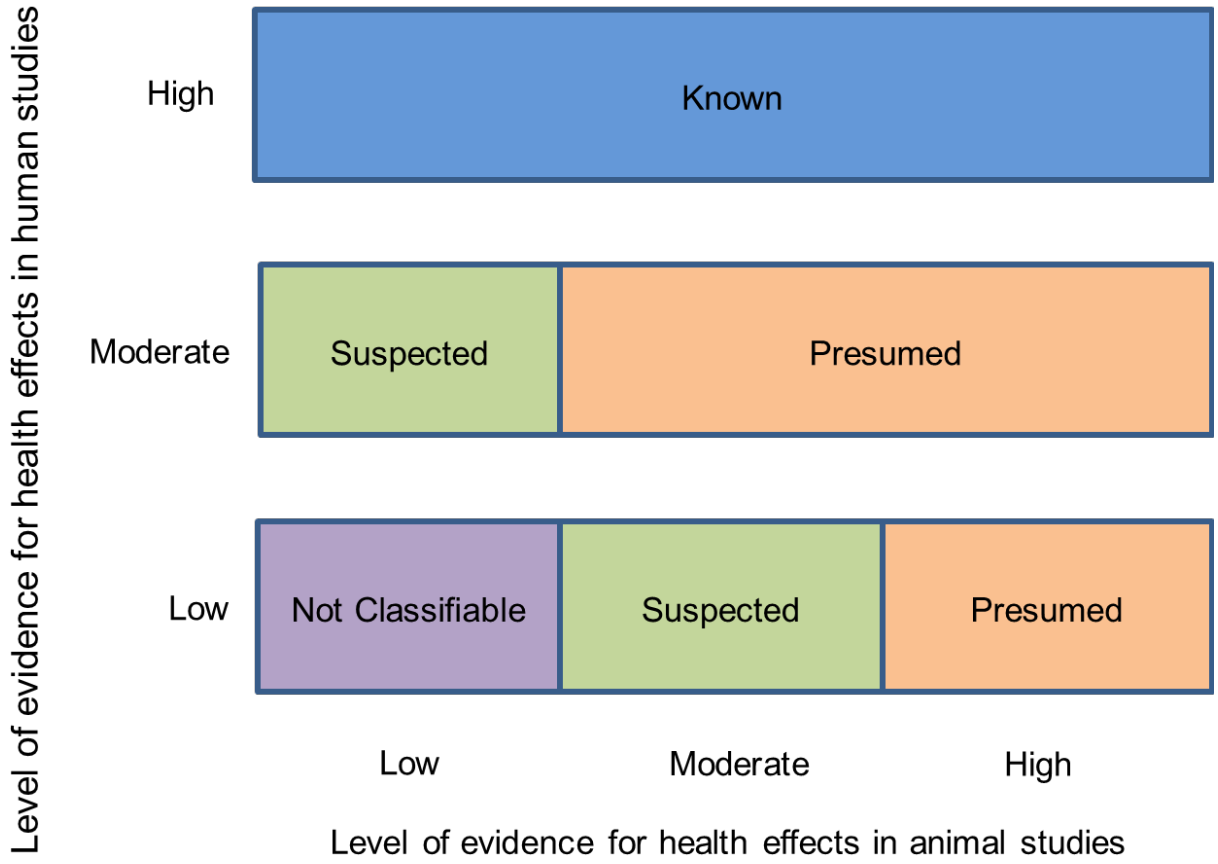
The final step involved the integration of the evidence streams for the human studies and animal studies to allow for a determination of hazard identification conclusions. For health effects, there were four hazard identification conclusion categories:

- **Known** to be a hazard to humans
- **Presumed** to be a hazard to humans
- **Suspected** to be a hazard to humans
- **Not classifiable** as to the hazard to humans

The initial hazard identification was based on the highest level of evidence in the human studies and the level of evidence in the animal studies; if there were no data for one evidence stream (human or animal), then the hazard identification was based on the one data stream (equivalent to treating the missing evidence stream as having low level of evidence). The hazard identification scheme is presented in and described below:

- **Known:** A health effect in this category would have:
  - High level of evidence for health effects in human studies **AND** a high, moderate, or low level of evidence in animal studies.
- **Presumed:** A health effect in this category would have:
  - Moderate level of evidence in human studies **AND** high or moderate level of evidence in animal studies **OR**
  - Low level of evidence in human studies **AND** high level of evidence in animal studies
- **Suspected:** A health effect in this category would have:
  - Moderate level of evidence in human studies **AND** low level of evidence in animal studies **OR**
  - Low level of evidence in human studies **AND** moderate level of evidence in animal studies
- **Not classifiable:** A health effect in this category would have:
  - Low level of evidence in human studies **AND** low level of evidence in animal studies

Figure C-1. Hazard Identification Scheme



Other relevant data such as mechanistic or mode-of-action data were considered to raise or lower the level of the hazard identification conclusion by providing information that supported or opposed biological plausibility.

Two hazard identification conclusion categories were used when the data indicated that there may be no health effect in humans:

- **Not identified** to be a hazard in humans
- **Inadequate** to determine hazard to humans

If the human level of evidence conclusion of no health effect was supported by the animal evidence of no health effect, then the hazard identification conclusion category of "not identified" was used. If the human or animal level of evidence was considered inadequate, then a hazard identification conclusion category of "inadequate" was used. As with the hazard identification for health effects, the impact of other relevant data was also considered for no health effect data.

The hazard identification conclusions for molybdenum are listed below and summarized in Table C-21.

Table C-21. Hazard Identification Conclusions for Molybdenum

Outcome	Hazard identification
Respiratory effects	Presumed health effect following long-term inhalation exposure
Hepatic effects	Not classifiable as a hazard to humans
Renal effects	Presumed health effect
Alterations in uric acid levels	Not classifiable as a hazard to humans
Reproductive effects	Suspected health effect
Developmental effects	Not classifiable as a hazard to humans

Presumed Health Effects

- Respiratory effects following long-term inhalation exposure to molybdenum oxides
  - Inadequate evidence from studies of molybdenum oxide workers (Ott et al. 2004; Walravens et al. 1979).
  - High level of evidence from chronic studies in rats and mice exposed to molybdenum trioxide (NTP 1997). Respiratory effects were not observed following acute- or intermediate-duration inhalation exposure.
- Renal effects
  - No data in humans.
  - High level of evidence of histological alterations in kidneys, alterations in renal function, and/or increased lipid levels in the kidneys in orally exposed rats (Bandyopadhyay et al. 1981; Bompart et al. 1990; Murray et al. 2014a; Rana and Kumar 1980c, 1983; Rana et al. 1980).

Not Classifiable as a Hazard to Humans

- Hepatic effects
  - Inadequate evidence of increased risk of self-reported liver conditions from a cross-sectional study (Mendy et al. 2012).
  - High evidence of no histological alterations following intermediate or chronic inhalation exposure of rats and mice to molybdenum trioxide (NTP 1997), acute oral exposure of rabbits to ammonium heptamolybdate (Bersenyi et al. 2008), or intermediate oral exposure of rats to sodium molybdate (Murray et al. 2014a;).
  - Moderate evidence of increases in clinical chemistry parameters and/or liver lipid levels in rabbits following acute oral exposure (Bersenyi et al. 2008) or rats exposed orally exposed to high doses (Rana and Chauhan 2000; Rana and Kumar 1980b, 1980c, 1983; Rana and Prakash 1986; Rana et al. 1980, 1985).
  - The hazard identification for hepatic effects was downgraded to Not Classifiable because the toxicological significance of the alterations in serum enzyme levels and lipid levels were not known and well-designed inhalation and oral laboratory animal studies have not reported histological alterations.
- Alterations in uric acid levels
  - Low evidence of an effect in cross-sectional studies (Koval'skiy et al. 1961; Walravens et al. 1979).
  - High confidence in an animal study not finding an effect (Murray et al. 2014a).
- Reproductive effects
  - Low level of evidence of male reproductive effects in cross-sectional studies (Lewis and Meeker 2015; Meeker et al. 2008, 2010).

  - Two high-quality, intermediate-duration (Murray et al. 2014a) and 2-generation (Murray et al. 2019) studies have not reported reproductive effects.
  - There is a moderate level of evidence of male and/or female reproductive effects in orally exposed rats (Fungwe et al. 1990; Pandey and Singh 2002), mice (Zhai et al. 2013; Zhang et al. 2013), and rabbits (Bersenyi et al. 2008).
- Developmental effects
  - Low evidence of an effect in a cross-sectional study. Two cross-sectional studies reported no alterations in newborn body weight (Shirai et al. 2010; Vazquez-Salas et al. 2014); one study reported decreases in psychomotor development indices (Vazquez-Salas et al. 2014).
  - Three studies in rats did not find alterations in resorptions, post-implantation losses, or fetal body weights (Jeter and Davis 1954; Murray et al. 2014b, 2019); the initial confidence levels for two of these studies were high and the third study was very low. A fourth study (initial high confidence level) involving male-only exposure found decreases in number of live fetuses and fetal body weights (Pandey and Singh 2002). The animal studies had different study designs (male only, female only, male and female exposure) making a comparison across studies difficult. Additionally, none of the animal studies evaluated potential neurodevelopmental effects, which were observed in an epidemiology study. Thus, the available data were not considered adequate for drawing a conclusion on the potential developmental toxicity of molybdenum in humans.

APPENDIX D. USER'S GUIDE

Chapter 1. Relevance to Public Health

This chapter provides an overview of U.S. exposures, a summary of health effects based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information, and an overview of the minimal risk levels. This is designed to present interpretive, weight-of-evidence discussions for human health endpoints by addressing the following questions:

1. What effects are known to occur in humans?

2. What effects observed in animals are likely to be of concern to humans?

3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

Minimal Risk Levels (MRLs)

Where sufficient toxicologic information is available, ATSDR derives MRLs for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans.

MRLs should help physicians and public health officials determine the safety of a community living near a hazardous substance emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Section 1.2, Summary of Health Effects, contains basic information known about the substance. Other sections, such as Section 3.2 Children and Other Populations that are Unusually Susceptible and Section 3.4 Interactions with Other Substances, provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology that the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the most sensitive endpoint which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen endpoint are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest no-observed-adverse-effect level (NOAEL) that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a

substance-specific MRL are provided in the footnotes of the levels of significant exposure (LSE) tables that are provided in Chapter 2. Detailed discussions of the MRLs are presented in Appendix A.

Chapter 2. Health Effects

Tables and Figures for Levels of Significant Exposure (LSE)

Tables and figures are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species and MRLs to humans for noncancer endpoints. The LSE tables and figures can be used for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of NOAELs, LOAELs, or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE tables and figures follow. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

TABLE LEGEND

See Sample LSE Table (page D-5)

(1) Route of exposure. One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. Typically, when sufficient data exist, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure (i.e., inhalation, oral, and dermal). LSE figures are limited to the inhalation and oral routes. Not all substances will have data on each route of exposure and will not, therefore, have all five of the tables and figures. Profiles with more than one chemical may have more LSE tables and figures.

(2) Exposure period. Three exposure periods—acute (<15 days), intermediate (15–364 days), and chronic (≥365 days)—are presented within each relevant route of exposure. In this example, two oral studies of chronic-duration exposure are reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) Figure key. Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 51 identified NOAELs and less serious LOAELs (also see the three "51R" data points in sample LSE Figure 2-X).

(4) Species (strain) No./group. The test species (and strain), whether animal or human, are identified in this column. The column also contains information on the number of subjects and sex per group. Chapter 1, Relevance to Public Health, covers the relevance of animal data to human toxicity and Section 3.1, Toxicokinetics, contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(5) Exposure parameters/doses. The duration of the study and exposure regimens are provided in these columns. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 51), rats were orally exposed to “Chemical X” via feed for 2 years. For a

more complete review of the dosing regimen, refer to the appropriate sections of the text or the original reference paper (i.e., Aida et al. 1992).

(6) Parameters monitored. This column lists the parameters used to assess health effects. Parameters monitored could include serum (blood) chemistry (BC), behavioral (BH), biochemical changes (BI), body weight (BW), clinical signs (CS), developmental toxicity (DX), enzyme activity (EA), food intake (FI), fetal toxicity (FX), gross necropsy (GN), hematology (HE), histopathology (HP), lethality (LE), maternal toxicity (MX), organ function (OF), ophthalmology (OP), organ weight (OW), teratogenicity (TG), urinalysis (UR), and water intake (WI).

(7) Endpoint. This column lists the endpoint examined. The major categories of health endpoints included in LSE tables and figures are death, body weight, respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, dermal, ocular, endocrine, immunological, neurological, reproductive, developmental, other noncancer, and cancer. "Other noncancer" refers to any effect (e.g., alterations in blood glucose levels) not covered in these systems. In the example of key number 51, three endpoints (body weight, hematological, and hepatic) were investigated.

(8) NOAEL. A NOAEL is the highest exposure level at which no adverse effects were seen in the organ system studied. The body weight effect reported in key number 51 is a NOAEL at 25.5 mg/kg/day. NOAELs are not reported for cancer and death; with the exception of these two endpoints, this field is left blank if no NOAEL was identified in the study.

(9) LOAEL. A LOAEL is the lowest dose used in the study that caused an adverse health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific endpoint used to quantify the adverse effect accompanies the LOAEL. Key number 51 reports a less serious LOAEL of 6.1 mg/kg/day for the hepatic system, which was used to derive a chronic exposure, oral MRL of 0.008 mg/kg/day (see footnote "c"). MRLs are not derived from serious LOAELs. A cancer effect level (CEL) is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases. If no LOAEL/CEL values were identified in the study, this field is left blank.

(10) Reference. The complete reference citation is provided in Chapter 8 of the profile.

(11) Footnotes. Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. For example, footnote "c" indicates that the LOAEL of 6.1 mg/kg/day in key number 51 was used to derive an oral MRL of 0.008 mg/kg/day.

FIGURE LEGEND

See Sample LSE Figure (page D-6)

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) Exposure period. The same exposure periods appear as in the LSE table. In this example, health effects observed within the chronic exposure period are illustrated.

(14) Endpoint. These are the categories of health effects for which reliable quantitative data exist. The same health effect endpoints appear in the LSE table.

(15) Levels of exposure. Concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m^3 or ppm and oral exposure is reported in mg/kg/day.

(16) LOAEL. In this example, the half-shaded circle that is designated 51R identifies a LOAEL critical endpoint in the rat upon which a chronic oral exposure MRL is based. The key number 51 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 6.1 mg/kg/day (see entry 51 in the sample LSE table) to the MRL of 0.008 mg/kg/day (see footnote "c" in the sample LSE table).

(17) CEL. Key number 59R is one of studies for which CELs were derived. The diamond symbol refers to a CEL for the test species (rat). The number 59 corresponds to the entry in the LSE table.

(18) Key to LSE figure. The key provides the abbreviations and symbols used in the figure.

Table 2-X. Levels of Significant Exposure to [Chemical X] – Oral (1)

Figure key[a] (3)	Species (strain) No./group (4)	Exposure parameters (5)	Doses (mg/kg/day) (5)	Parameters monitored (6)	Endpoint (7)	NOAEL (mg/kg/day) (8)	Less serious LOAEL (mg/kg/day) (9)	Serious LOAEL (mg/kg/day) (9)	Effect
CHRONIC EXPOSURE (2)									
51	Rat (Wistar) 40 M, 40 F	2 years (F)	M: 0, 6.1, 25.5, 138.0 F: 0, 8.0, 31.7, 168.4	CS, WI, BW, OW, HE, BC, HP	Bd wt	25.5	138.0		Decreased body weight gain in males (23–25%) and females (31–39%)
					Hemato	138.0			
					Hepatic		6.1[c]		Increases in absolute and relative weights at ≥6.1/8.0 mg/kg/day after 12 months of exposure; fatty generation at ≥6.1 mg/kg/day in males and at ≥31.7 mg/kg/day in females, and granulomas in females at 31.7 and 168.4 mg/kg/day after 12, 18, or 24 months of exposure and in males at ≥6.1 mg/kg/day only after 24 months of exposure
Aida et al. 1992 (10)									
52	Rat (F344) 78 M	104 weeks (W)	0, 3.9, 20.6, 36.3	CS, BW, FI, BC, OW, HP	Hepatic	36.3			
					Renal	20.6	36.3		Increased incidence of renal tubular cell hyperplasia
					Endocr	36.3			
George et al. 2002									
59	Rat (Wistar) 58M, 58F	Lifetime (W)	M: 0, 90 F: 0, 190	BW, HP	Cancer		190 F		Increased incidence of hepatic neoplastic nodules in females only; no additional description of the tumors was provided
Tumasonis et al. 1985									

[a]The number corresponds to entries in Figure 2-x.

(11) [b]Used to derive an acute-duration oral minimal risk level (MRL) of 0.1 mg/kg/day based on the $BMDL_{05}$ of 10 mg/kg/day and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

[c]Used to derive a chronic-duration oral MRL of 0.008 mg/kg/day based on the $BMDL_{10}$ of 0.78 mg/kg/day and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

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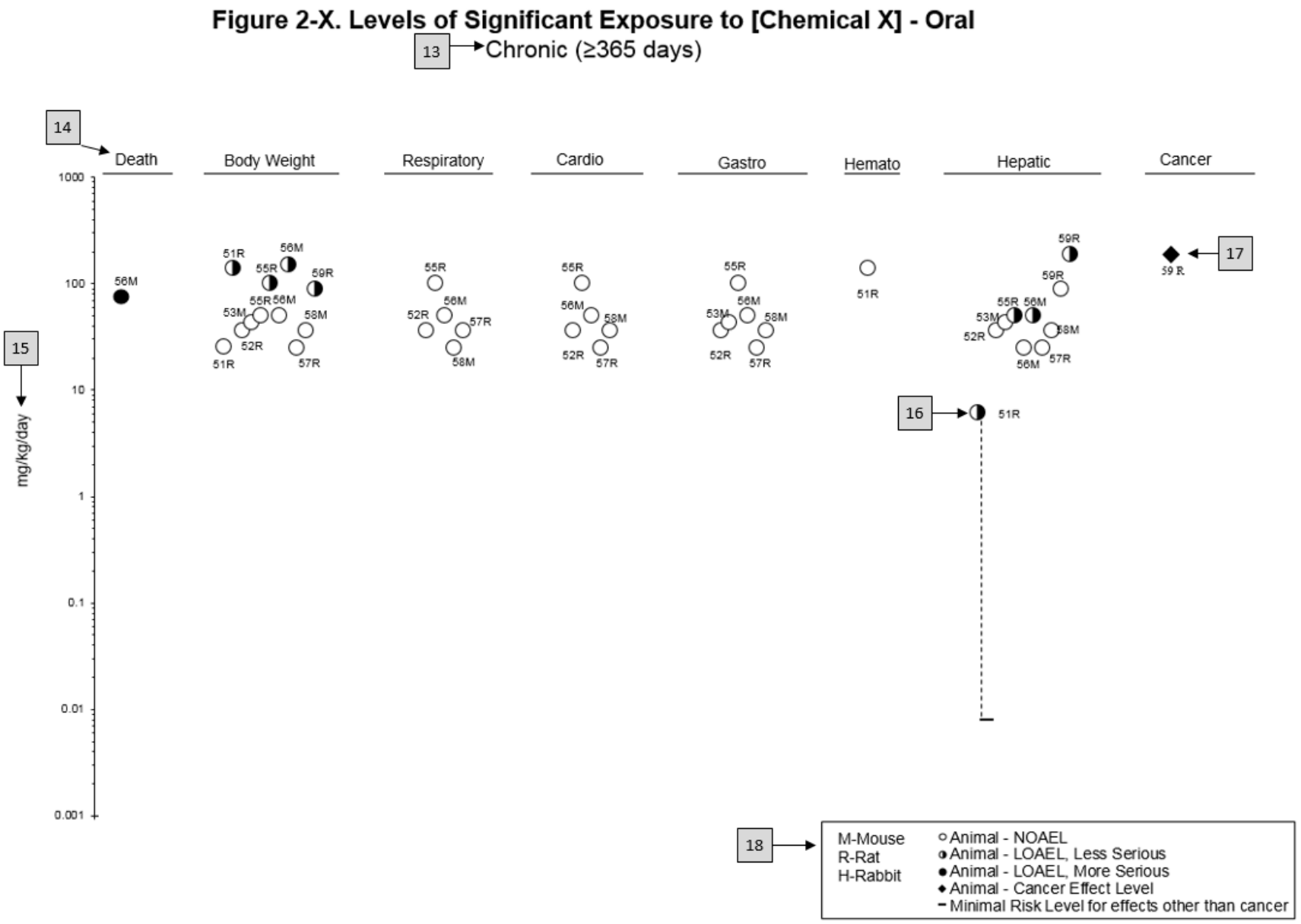
Figure 2-X. Levels of Significant Exposure to [Chemical X] - Oral



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APPENDIX E. QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances may find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

Chapter 1: Relevance to Public Health: The Relevance to Public Health Section provides an overview of exposure and health effects and evaluates, interprets, and assesses the significance of toxicity data to human health. A table listing minimal risk levels (MRLs) is also included in this chapter.

Chapter 2: Health Effects: Specific health effects identified in both human and animal studies are reported by type of health effect (e.g., death, hepatic, renal, immune, reproductive), route of exposure (e.g., inhalation, oral, dermal), and length of exposure (e.g., acute, intermediate, and chronic).
NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting.

Pediatrics:

Section 3.2 Children and Other Populations that are Unusually Susceptible
Section 3.3 Biomarkers of Exposure and Effect

ATSDR Information Center

Phone: 1-800-CDC-INFO (800-232-4636) or 1-888-232-6348 (TTY)
Internet: http://www.atsdr.cdc.gov

The following additional materials are available online:

Case Studies in Environmental Medicine are self-instructional publications designed to increase primary health care providers' knowledge of a hazardous substance in the environment and to aid in the evaluation of potentially exposed patients (see https://www.atsdr.cdc.gov/csem/csem.html).

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident (see https://www.atsdr.cdc.gov/MHMI/index.asp). Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposures*—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs™) provide answers to frequently asked questions about toxic substances (see https://www.atsdr.cdc.gov/toxfaqs/Index.asp).

Other Agencies and Organizations

The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015 • Web Page: https://www.cdc.gov/nceh/.

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 395 E Street, S.W., Suite 9200, Patriots Plaza Building, Washington, DC 20201 • Phone: 202-245-0625 or 1-800-CDC-INFO (800-232-4636) • Web Page: https://www.cdc.gov/niosh/.

The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212 • Web Page: https://www.niehs.nih.gov/.

Clinical Resources (Publicly Available Information)

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact: AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: AOEC@AOEC.ORG • Web Page: http://www.aoec.org/.

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 25 Northwest Point Boulevard, Suite 700, Elk Grove Village, IL 60007-1030 • Phone: 847-818-1800 • FAX: 847-818-9266 • Web Page: http://www.acoem.org/.

The American College of Medical Toxicology (ACMT) is a nonprofit association of physicians with recognized expertise in medical toxicology. Contact: ACMT, 10645 North Tatum Boulevard, Suite 200-111, Phoenix AZ 85028 • Phone: 844-226-8333 • FAX: 844-226-8333 • Web Page: http://www.acmt.net.

The Pediatric Environmental Health Specialty Units (PEHSUs) is an interconnected system of specialists who respond to questions from public health professionals, clinicians, policy makers, and the public about the impact of environmental factors on the health of children and reproductive-aged adults. Contact information for regional centers can be found at http://pehsu.net/findhelp.html.

The American Association of Poison Control Centers (AAPCC) provide support on the prevention and treatment of poison exposures. Contact: AAPCC, 515 King Street, Suite 510, Alexandria VA 22314 • Phone: 701-894-1858 • Poison Help Line: 1-800-222-1222 • Web Page: http://www.aapcc.org/.

APPENDIX F. GLOSSARY

Absorption—The process by which a substance crosses biological membranes and enters systemic circulation. Absorption can also refer to the taking up of liquids by solids, or of gases by solids or liquids.

Acute Exposure—Exposure to a chemical for a duration of ≤14 days, as specified in the Toxicological Profiles.

Adsorption—The adhesion in an extremely thin layer of molecules (as of gases, solutes, or liquids) to the surfaces of solid bodies or liquids with which they are in contact.

Adsorption Coefficient (K_{oc})—The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd)—The amount of a chemical adsorbed by sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Benchmark Dose (BMD) or Benchmark Concentration (BMC)—is the dose/concentration corresponding to a specific response level estimate using a statistical dose-response model applied to either experimental toxicology or epidemiology data. For example, a BMD_{10} would be the dose corresponding to a 10% benchmark response (BMR). The BMD is determined by modeling the dose-response curve in the region of the dose-response relationship where biologically observable data are feasible. The BMDL or BMCL is the 95% lower confidence limit on the BMD or BMC.

Bioconcentration Factor (BCF)—The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Biomarkers—Indicators signaling events in biologic systems or samples, typically classified as markers of exposure, effect, and susceptibility.

Cancer Effect Level (CEL)—The lowest dose of a chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen—A chemical capable of inducing cancer.

Case-Control Study—A type of epidemiological study that examines the relationship between a particular outcome (disease or condition) and a variety of potential causative agents (such as toxic chemicals). In a case-control study, a group of people with a specified and well-defined outcome is identified and compared to a similar group of people without the outcome.

Case Report—A report that describes a single individual with a particular disease or exposure. These reports may suggest some potential topics for scientific research, but are not actual research studies.

Case Series—Reports that describe the experience of a small number of individuals with the same disease or exposure. These reports may suggest potential topics for scientific research, but are not actual research studies.

Ceiling Value—A concentration that must not be exceeded.

Chronic Exposure—Exposure to a chemical for ≥365 days, as specified in the Toxicological Profiles.

Clastogen—A substance that causes breaks in chromosomes resulting in addition, deletion, or rearrangement of parts of the chromosome.

Cohort Study—A type of epidemiological study of a specific group or groups of people who have had a common insult (e.g., exposure to an agent suspected of causing disease or a common disease) and are followed forward from exposure to outcome, and who are disease-free at start of follow-up. Often, at least one exposed group is compared to one unexposed group, while in other cohorts, exposure is a continuous variable and analyses are directed towards analyzing an exposure-response coefficient.

Cross-sectional Study—A type of epidemiological study of a group or groups of people that examines the relationship between exposure and outcome to a chemical or to chemicals at a specific point in time.

Data Needs—Substance-specific informational needs that, if met, would reduce the uncertainties of human health risk assessment.

Developmental Toxicity—The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Dose-Response Relationship—The quantitative relationship between the amount of exposure to a toxicant and the incidence of the response or amount of the response.

Embryotoxicity and Fetotoxicity—Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the effect occurs. Effects include malformations and variations, altered growth, and *in utero* death.

Epidemiology—The investigation of factors that determine the frequency and distribution of disease or other health-related conditions within a defined human population during a specified period.

Excretion—The process by which metabolic waste products are removed from the body.

Genotoxicity—A specific adverse effect on the genome of living cells that, upon the duplication of affected cells, can be expressed as a mutagenic, clastogenic, or carcinogenic event because of specific alteration of the molecular structure of the genome.

Half-life—A measure of rate for the time required to eliminate one-half of a quantity of a chemical from the body or environmental media.

Health Advisory—An estimate of acceptable drinking water levels for a chemical substance derived by EPA and based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH)—A condition that poses a threat of life or health, or conditions that pose an immediate threat of severe exposure to contaminants that are likely to have adverse cumulative or delayed effects on health.

Immunotoxicity—Adverse effect on the functioning of the immune system that may result from exposure to chemical substances.

Incidence—The ratio of new cases of individuals in a population who develop a specified condition to the total number of individuals in that population who could have developed that condition in a specified time period.

Intermediate Exposure—Exposure to a chemical for a duration of 15–364 days, as specified in the Toxicological Profiles.

***In Vitro*—**Isolated from the living organism and artificially maintained, as in a test tube.

***In Vivo*—**Occurring within the living organism.

Lethal Concentration$_{(LO)}$ (LC_{LO})—The lowest concentration of a chemical in air that has been reported to have caused death in humans or animals.

Lethal Concentration$_{(50)}$ (LC_{50})—A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose$_{(LO)}$ (LD_{Lo})—The lowest dose of a chemical introduced by a route other than inhalation that has been reported to have caused death in humans or animals.

Lethal Dose$_{(50)}$ (LD_{50})—The dose of a chemical that has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time$_{(50)}$ (LT_{50})—A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL)—The lowest exposure level of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lymphoreticular Effects—Represent morphological effects involving lymphatic tissues such as the lymph nodes, spleen, and thymus.

Malformations—Permanent structural changes that may adversely affect survival, development, or function.

Metabolism—Process in which chemical substances are biotransformed in the body that could result in less toxic and/or readily excreted compounds or produce a biologically active intermediate.

Minimal Risk Level (MRL)—An estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and duration of exposure.

Modifying Factor (MF)—A value (greater than zero) that is applied to the derivation of a Minimal Risk Level (MRL) to reflect additional concerns about the database that are not covered by the uncertainty factors. The default value for a MF is 1.

Morbidity—The state of being diseased; the morbidity rate is the incidence or prevalence of a disease in a specific population.

Mortality—Death; the mortality rate is a measure of the number of deaths in a population during a specified interval of time.

Mutagen—A substance that causes mutations, which are changes in the DNA sequence of a cell's DNA. Mutations can lead to birth defects, miscarriages, or cancer.

Necropsy—The gross examination of the organs and tissues of a dead body to determine the cause of death or pathological conditions.

Neurotoxicity—The occurrence of adverse effects on the nervous system following exposure to a hazardous substance.

No-Observed-Adverse-Effect Level (NOAEL)—The dose of a chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Although effects may be produced at this dose, they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow})—The equilibrium ratio of the concentrations of a chemical in *n*-octanol and water, in dilute solution.

Odds Ratio (OR)—A means of measuring the association between an exposure (such as toxic substances and a disease or condition) that represents the best estimate of relative risk (risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor). An odds ratio that is greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed group.

Permissible Exposure Limit (PEL)—An Occupational Safety and Health Administration (OSHA) regulatory limit on the amount or concentration of a substance not to be exceeded in workplace air averaged over any 8-hour work shift of a 40-hour workweek.

Pesticide—General classification of chemicals specifically developed and produced for use in the control of agricultural and public health pests (insects or other organisms harmful to cultivated plants or animals).

Pharmacokinetics—The dynamic behavior of a material in the body, used to predict the fate (disposition) of an exogenous substance in an organism. Utilizing computational techniques, it provides the means of studying the absorption, distribution, metabolism, and excretion of chemicals by the body.

Pharmacokinetic Model—A set of equations that can be used to describe the time course of a parent chemical or metabolite in an animal system. There are two types of pharmacokinetic models: data-based and physiologically-based. A data-based model divides the animal system into a series of compartments, which, in general, do not represent real, identifiable anatomic regions of the body, whereas the physiologically-based model compartments represent real anatomic regions of the body.

Physiologically Based Pharmacodynamic (PBPD) Model—A type of physiologically based dose-response model that quantitatively describes the relationship between target tissue dose and toxic endpoints. These models advance the importance of physiologically based models in that they clearly describe the biological effect (response) produced by the system following exposure to an exogenous substance.

Physiologically Based Pharmacokinetic (PBPK) Model—A type of physiologically based dose-response model that is comprised of a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a variety of physiological information, including tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates, and possibly membrane permeabilities. The models also utilize biochemical information, such as blood:air partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

Prevalence—The number of cases of a disease or condition in a population at one point in time.

Prospective Study—A type of cohort study in which a group is followed over time and the pertinent observations are made on events occurring after the start of the study.

Recommended Exposure Limit (REL)—A National Institute for Occupational Safety and Health (NIOSH) time-weighted average (TWA) concentration for up to a 10-hour workday during a 40-hour workweek.

Reference Concentration (RfC)—An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer health effects during a lifetime. The inhalation RfC is expressed in units of mg/m^3 or ppm.

Reference Dose (RfD)—An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily oral exposure of the human population to a potential hazard that is likely to be without risk of deleterious noncancer health effects during a lifetime. The oral RfD is expressed in units of mg/kg/day.

Reportable Quantity (RQ)—The quantity of a hazardous substance that is considered reportable under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). RQs are (1) ≥1 pound or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity—The occurrence of adverse effects on the reproductive system that may result from exposure to a hazardous substance. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Retrospective Study—A type of cohort study based on a group of persons known to have been exposed at some time in the past. Data are collected from routinely recorded events, up to the time the study is undertaken. Retrospective studies are limited to causal factors that can be ascertained from existing records and/or examining survivors of the cohort.

Risk—The possibility or chance that some adverse effect will result from a given exposure to a hazardous substance.

Risk Factor—An aspect of personal behavior or lifestyle, an environmental exposure, existing health condition, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition.

Risk Ratio/Relative Risk—The ratio of the risk among persons with specific risk factors compared to the risk among persons without risk factors. A risk ratio that is greater than 1 indicates greater risk of disease in the exposed group compared to the unexposed group.

Short-Term Exposure Limit (STEL)—A STEL is a 15-minute TWA exposure that should not be exceeded at any time during a workday.

Standardized Mortality Ratio (SMR)—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

Target Organ Toxicity—This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen—A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)—An American Conference of Governmental Industrial Hygienists (ACGIH) concentration of a substance to which it is believed that nearly all workers may be repeatedly exposed, day after day, for a working lifetime without adverse effect. The TLV may be expressed as a Time-Weighted Average (TLV-TWA), as a Short-Term Exposure Limit (TLV-STEL), or as a ceiling limit (TLV-C).

Time-Weighted Average (TWA)—An average exposure within a given time period.

Toxicokinetic—The absorption, distribution, metabolism, and elimination of toxic compounds in the living organism.

Toxics Release Inventory (TRI)—The TRI is an EPA program that tracks toxic chemical releases and pollution prevention activities reported by industrial and federal facilities.

Uncertainty Factor (UF)—A factor used in operationally deriving the Minimal Risk Level (MRL), Reference Dose (RfD), or Reference Concentration (RfC) from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using lowest-observed-adverse-effect level (LOAEL) data rather than no-observed-adverse-effect level (NOAEL) data. A default for each individual UF is 10; if complete certainty in data exists, a value of 1 can be used; however, a reduced UF of 3 may be used on a case-by-case basis (3 being the approximate logarithmic average of 10 and 1).

Xenobiotic—Any substance that is foreign to the biological system.

APPENDIX G. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

AAPCC	American Association of Poison Control Centers
ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ACMT	American College of Medical Toxicology
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AEGL	Acute Exposure Guideline Level
AIC	Akaike's information criterion
AIHA	American Industrial Hygiene Association
ALT	alanine aminotransferase
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BCF	bioconcentration factor
BMD/C	benchmark dose or benchmark concentration
BMD_X	dose that produces a X% change in response rate of an adverse effect
$BMDL_X$	95% lower confidence limit on the BMD_X
BMDS	Benchmark Dose Software
BMR	benchmark response
BUN	blood urea nitrogen
C	Celsius
CAA	Clean Air Act
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
cm	centimeter
CPSC	Consumer Products Safety Commission
CWA	Clean Water Act
DNA	deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
DWEL	drinking water exposure level
EAFUS	Everything Added to Food in the United States
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
ERPG	emergency response planning guidelines
F	Fahrenheit
F1	first-filial generation
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act

FR	Federal Register
FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GGT	γ-glutamyl transferase
GRAS	generally recognized as safe
HEC	human equivalent concentration
HED	human equivalent dose
HHS	Department of Health and Human Services
HPLC	high-performance liquid chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	kilokilogram; 1 kilokilogram is equivalent to 1,000 kilograms and 1 metric ton
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC_{50}	lethal concentration, 50% kill
LC_{Lo}	lethal concentration, low
LD_{50}	lethal dose, 50% kill
LD_{Lo}	lethal dose, low
LDH	lactic dehydrogenase
LH	luteinizing hormone
LOAEL	lowest-observed-adverse-effect level
LSE	Level of Significant Exposure
LT_{50}	lethal time, 50% kill
m	meter
mCi	millicurie
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
MRL	Minimal Risk Level
MS	mass spectrometry
MSHA	Mine Safety and Health Administration
Mt	metric ton
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
NCEH	National Center for Environmental Health
ND	not detected
ng	nanogram

NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NS	not specified
NTP	National Toxicology Program
OR	odds ratio
OSHA	Occupational Safety and Health Administration
PAC	Protective Action Criteria
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PEHSU	Pediatric Environmental Health Specialty Unit
PEL	permissible exposure limit
PEL-C	permissible exposure limit-ceiling value
pg	picogram
PND	postnatal day
POD	point of departure
ppb	parts per billion
ppbv	parts per billion by volume
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure level/limit
REL-C	recommended exposure level-ceiling value
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SD	standard deviation
SE	standard error
SGOT	serum glutamic oxaloacetic transaminase (same as aspartate aminotransferase or AST)
SGPT	serum glutamic pyruvic transaminase (same as alanine aminotransferase or ALT)
SIC	standard industrial classification
SMR	standardized mortality ratio
sRBC	sheep red blood cell
STEL	short term exposure limit
TLV	threshold limit value
TLV-C	threshold limit value-ceiling value
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	uncertainty factor
U.S.	United States

USDA	United States Department of Agriculture
USGS	United States Geological Survey
USNRC	U.S. Nuclear Regulatory Commission
VOC	volatile organic compound
WBC	white blood cell
WHO	World Health Organization

>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
γ	gamma
δ	delta
μm	micrometer
μg	microgram
q_1^*	cancer slope factor
–	negative
+	positive
(+)	weakly positive result
(–)	weakly negative result