UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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SUBJECT: Calculating fold factors for uncertain worker exposures to mixed metal oxide (MMO) cathode active materials (CAMs) that contain cobalt

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Background

Under TSCA Section 5, the New Chemicals Division (NCD) is responsible for conducting risk assessment of new chemical substances submitted to determine whether these chemicals pose an unreasonable risk to the human health and the environment. NCD receives approximately 500 new chemical submissions each year that cover a variety of industry sectors. In recent years, NCD has received new chemical submissions for mixed metal oxides (MMO) in cathode active materials (CAMs) used in electric vehicles. MMO CAMs are crystallized metal oxides typically composed of some combination of lithium, cobalt, nickel, and other additional modifier metal oxides. This memorandum focuses on cobalt-containing CAMs as these types of MMO CAMs are the most common in the New Chemicals Program.

Additionally, this memorandum focuses on the hazards and worker exposures via the inhalation route. MMO CAM substances are known to induce adverse respiratory effects at low exposure concentrations based on 90-day inhalation studies in rats. In addition, the individual metal components are well-studied and induce adverse health effects such as pulmonary fibrosis, asthma

and lung cancer. Cobalt is the most potent carcinogenic component of the CAM metals. As a result, the percent composition of cobalt in the CAM is important for quantifying worker risks. A combination of engineering controls and respiratory protection is typically utilized to protect workers from these substances. To inform this decision process, EPA has subsequently developed a method for calculating fold factors for worker inhalation exposures for MMO CAMs that contain cobalt. The fold factor is the amount that the exposure exceeds the benchmark margin of exposure (MOE). The options for mitigating risks when exposure exceeds the acceptable MOE include 1) reducing exposures, 2) providing respiratory protection with an appropriate Assigned Protection Factor (APF), or a combination of both options 1 and 2.

To quantify inhalation risks for cobalt-containing CAMs, EPA currently uses a benchmark concentration lower bound ($BMCL_{1SD}$) of 8.4E-3 mg/m^3 as the point of departure (POD) which is based on respiratory effects (i.e., increased lung weight, macroscopic changes in the lung, and histopathological changes in the respiratory tract) in a 90-day inhalation study in rats (OECD TG 413) for an analogue substance; this analogue substance is a CAM containing aluminum cobalt lithium nickel oxide[1].

EPA is not able to accurately quantify worker inhalation exposures for some scenarios involving the manufacturing or processing of CAM materials due to uncertainties of control technologies at facilities that have not yet been constructed. Therefore, EPA has calculated a generic fold factor for different air concentrations of cobalt-containing CAMs to identify the appropriate worker protection mitigation strategy. The fold factor ranges provided herein correspond to commonly used cutoffs for determining the appropriate APF.

Analysis Approach

1. As previously mentioned, NCD typically uses a $BMCL_{1SD}$ of 8.4E-3 mg/m^3 to quantify non-cancer effects to MMO CAMs. Since an Inhalation Unit Risk (IUR) is not available for a MMO CAM to quantitatively assess cancer risks, NCD uses an IUR for cobalt and adjusts for the percent composition of cobalt in the new chemical substance. To determine the maximum percent composition of cobalt for which the $BMCL_{1SD}$ is protective for both cancer and non-cancer effects, EPA calculated New Chemical Exposure Limits (NCELs; represents the maximum airborne concentration of a new chemical substance in air that is allowable without the use of personal protection equipment) using either the $BMCL_{1SD}$ for aluminum cobalt lithium nickel oxide for non-cancer respiratory effects or the cobalt IUR for lung cancer. The $BMCL_{1SD}$ of 8.4E-3 mg/m^3 yields a NCEL of 3.28E-5 mg/m^3 (see Table 1) and the IUR of 7.7E-3 $(\mu g/m^3)^{-1}$ yields a NCEL of 3.29E-5 mg/m^3 for a target risk level of 1 in 10,000 when the percent of cobalt is 79% of the new chemical substance (see Table 2). The calculations demonstrate that when the cobalt composition is < 80% in the MMO CAM, the $BMCL_{1SD}$ is more protective than the IUR for setting occupational exposure limits.

[1] Study available upon request

Table 1. NCEL calculation based on the BMCL for aluminum cobalt lithium nickel oxide

POD Human (aka Human Equivalent Concentration, HEC) Calculation																				NCEL Calculation		
POD Animal Study BMCL (mg/m^3)		Blood:Air Partition coefficient ratio (PCanimal / PChuman)		Animal Experiment Daily Duration (hrs/day)		Animal Exposure Frequency (days/wk)		Duration of Workshift (hrs/day)		Weekly Frequency of Workshift (days/wk)		Adjust resting breathing volume (5.2 m^3/8hrs) to working breating rate (10 m^3/8hrs)		Structural Alert as % of New Chemical Substance		POD Human (mg/m^3)		Uncertainty Factor[2] (unitless)		**NCEL, 8h Time Weighted Avg (mg/m^3)**
8.40E-03	x	1	x	6	x	5	÷	8	÷	5	x	0.52	÷	100%	=	0.003276	÷	100	=	**3.28E-05**

Table 2. NCEL calculation based on Cobalt IUR

NCEL Calculations Cancer Endpoint, Rat Cancer Inhalation Unit Risk based on Cobalt IUR for insoluble compounds																		
Target Risk Level		Inhalation Unit Risk (per $\mu g/m^3$)		Structural Alert as % PMN		µg/mg		Permissible Air Concentration[1] (mg/m^3)		Average Daily Adult Inhalation Rate (m^3/day)		Permissible Amt per Person per Day (mg/day)		Air vol. inhaled in 8 hr work shift[2] (m^3)		**NCEL, 8h Time Weighted Avg (mg/m^3)**
1E-04	÷	7.70E-03	÷	79%	÷	1000	=	2E-05	x	20	=	0.0003288	÷	10	=	**3.29E-05**
1E-05	÷	7.70E-03	÷	79%	÷	1000	=	2E-06	x	20	=	3.288E-05	÷	10	=	**3.29E-06**
1E-06	÷	7.70E-03	÷	79%	÷	1000	=	2E-07	x	20	=	3.288E-06	÷	10	=	**3.29E-07**

2. Using the $BMCL_{1SD}$, EPA calculated the worker exposure concentrations that correspond to commonly used respiratory APFs. The calculations in Table 3 demonstrate that exposure concentrations of 3.09E-1 mg/m^3, 3.09E-2 mg/m^3, 1.54E-3 mg/m^3, and 3.09E-4 mg/m^3 result in fold factors of 10,000, 1,000, 50, and 10, respectively.

Table 3. Worker inhalation risk calculation using the $BMCL_{1SD}$

Worker Margin of Exposure (MOE) Calculations using Animal Inhalation POD and Engineering Report PDR															
	Animal or Human POD			Worker Exposure				Human Breathing Rates						Benchmark MOE	Endpoint Type
Exposure Route	POD Conc. mg/m^3	POD Period hrs/day	POD Frequency days/wk	Exposure mg/day Potential Dose Rate (PDR)	Total Worker Breathing Volume for PDR Exposure Period m^3	Worker Exposure Duration Hours/Day	Exposure Frequency Days/Wk	Default	Worker	Structural Alert as % of PMN	POD Conc - Duration & Breathing Rate Correction $Scenario_{HEC}$ mg/m^3	Exposure TWA mg/m^3	**Margin of Exposure MOE**	100	BMCL
Inhalation	8.4E-03	6.00	5	3.09E+00	10.0	8.00	5	4.90	10.00	100%	3.1E-03	3.09E-01	**0.01**	Fold Factor =	10000
Inhalation	8.4E-03	6.00	5	3.09E-01	10.0	8.00	5	4.90	10.00	100%	3.1E-03	3.09E-02	**0.1**	Fold Factor =	1000
Inhalation	8.4E-03	6.00	5	1.54E-02	10.0	8.00	5	4.90	10.00	100%	3.1E-03	1.54E-03	**2**	Fold Factor =	50
Inhalation	8.4E-03	6.00	5	3.09E-03	10.0	8.00	5	4.90	10.00	100%	3.1E-03	3.09E-04	**10**	Fold Factor =	10

Conclusion

Based on the $BMCL_{1SD}$ of 8.4E-3 mg/m^3 and a benchmark MOE of 100, EPA calculated the corresponding fold factor for 4 different exposure ranges. The results of these calculations are presented in Table 4. The calculated fold factors utilizing the $BMCL_{1SD}$ instead of the IUR are protective for both cancer and non-cancer respiratory effects, when the cobalt composition is less than 80% in the MMO CAM.

Table 4. Fold factors corresponding to worker inhalation exposures to cobalt-containing MMO CAMs

Calculated Fold Factor When the Calculated MOE Is Below the Benchmark MOE	Anticipated Worker Exposure Range (mg/m^3)	Anticipated Worker Exposure Range (µg/m^3)
>1,000 to 10,000	**> 3.09E-02 to 3.09E-01**	**> 3.09E+01 to 3.09E+02**
>50 to 1,000	**>1.54E-03 to 3.09E-02**	**> 1.54E+00 to 3.09E+01**
>10 to 50	**> 3.09E-04 to 1.54E-03**	**> 3.09E-01 to 1.54E+00**
≤10	**≤ 3.09E-04**	**≤ 3.09E-01**