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Advances in Metals Classification Under the United Nations Globally Harmonized System of Classification and Labeling

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ABSTRACT

This article shows how regulatory obligations mandated for metal substances can be met with a laboratory-based transformation/dissolution (T/D) method for deriving relevant hazard classification outcomes, which can then be linked to attendant environmental protection management decisions. We report the results of a ring-test at 3 laboratories conducted to determine the interlaboratory precision of the United Nations T/D Protocol (T/DP) in generating data for classifying 4 metal-bearing substances for acute and chronic toxicity under the United Nations Globally Harmonized System of Classification and Labelling (GHS) criteria with respect to the aquatic environment. The test substances were Ni metal powder, cuprous oxide (Cu_2O) powder, tricobalt tetroxide (Co_3O_4) powder, and cuttings of a NILO K Ni–Co–Fe alloy. Following GHS Annex 10 guidelines, we tested 3 loadings (1, 10, and 100 mg/L) of each substance at pH 6 and 8 for 7 or 28 d to yield T/D data for acute and chronic classification, respectively. We compared the T/DP results (dissolved metal in aqueous media) against acute and chronic ecotoxicity reference values (ERVs) for each substance to assess GHS classification outcomes. For dissolved metal ions, the respective acute and chronic ERVs established at the time of the T/D testing were: 29 and 8 μg/L for Cu; 185 and 1.5 μg/L for Co; and 13.3 and 1.0 mg/L for Fe. The acute ERVs for Ni were pH-dependent: 120 and 68 μg/L at pH 6 and 8, respectively, whereas the chronic ERV for Ni was 2.4 μg/L. The acute classification outcomes were consistent among 3 laboratories: cuprous oxide, Acute 1; Ni metal powder, Acute 3; Co_3O_4 and the NILO K alloy, no classification. We obtained similar consistent results in chronic classifications: Cu_2O, Ni metal powder, and Co_3O_4, Chronic 4; and the NILO K alloy, no classification. However, we observed equivocal results only in 2 of a possible 48 cases where the coefficient of variation of final T/D concentrations masked clear comparisons with ERVs. Results support the validity and interlaboratory precision of the United Nations T/DP in establishing GHS classification outcomes for metals and metal compounds and support its use in regulatory hazard-based systems. Drawing on T/D data derived from laboratory testing of the metal-bearing substance itself, the T/D approach can be applied to establish scientifically defensible decisions on hazard classification proposals. The resulting decisions can then be incorporated into environmental management measures in such jurisdictions as the European Union. Integr Environ Assess Manag 2011;7:559–576. © 2011 SETAC

Keywords: Metals Alloys Transformation/dissolution Aquatic environment Hazard classification

INTRODUCTION

The United Nations (UN) Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UN 2009) and REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (EU 2006) have significant implications for environmental protection, transport, insurance, and market access, both within the European Union (EU) and worldwide. Within the GHS framework, a scheme to classify chemical substances with respect to the hazards they may present to the aquatic environment has been developed (UN 2009, p 213), a section of which has been adapted to enable the classification of metals and metal compounds (UN 2009, p 507).

Data generated by a transformation/dissolution protocol (T/DP) (UN 2009, p 547) may be applied within the framework of the GHS to derive hazard classifications for metals and inorganic metal compounds. The T/DP was developed within the framework of the Organisation for Economic Cooperation and Development (OECD 2001) and is designed to determine the rate and extent to which metals and sparingly soluble metal compounds can produce soluble, available metal species under conditions representative of those generally found in the environment. The T/DP (a detailed Standard Operating Procedure [SOP] that is available in Skeaff et al. 2006) is aimed at standardizing the principal test variables such that the level of the dissolved ion can be directly related to the loading of the substance added to the aqueous medium (UN 2009, p 507). To derive a hazard classification, T/D data, consisting of dissolved metal concentrations in the aqueous test media, are then compared to acute or chronic ecotoxicity reference values (ERVs). If the dissolved metal concentration within a period of 7 d at a 1 mg/L loading exceeds the acute ERV, the metal-bearing substance is classified as Acute 1. If the ERV is exceeded at loadings of 10 or 100 mg/L, the substance is classified as Acute 2 or 3, respectively. If the ERV of the metal ions is more than

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100 mg/L, the substance need not be considered further in the GHS classification scheme (UN 2009, p 511). A comparison of 28-d T/DP concentrations at a loading of 1 mg/L to chronic ERVs may be used to determine chronic classifications. Skeaff et al. (2008) discussed the GHS classification scheme for metals, metal compounds, and alloys in further detail and presented examples of its application to metals and alloys.

The UN requested that the OECD validate the T/DP, because the UN considered it important to have available a reliable laboratory method to examine the T/D behavior of metals and sparingly soluble metal compounds that would yield data for application in aquatic hazard classification. A standardized T/DP validated in round-robin testing would enable laboratories worldwide to apply it in the knowledge that it could yield reproducible, reliable, scientifically defensible data for use in the hazard classification of metals, metal compounds, and alloys. Data users, such as regulatory authorities and industry associations, could be confident that T/D data from a standardized protocol could be reproduced by any properly equipped laboratory, using the same methodology. The hazard classification outcomes would therefore be acceptable to both regulatory authorities and industry associations alike in the interests of environmental protection.

The objective of this study was to assess the agreement among 3 participating laboratories in deriving GHS aquatic hazard classification outcomes based on data that they generated by the application of the T/DP to 4 metal-bearing reference substances. Specifically, the goals were to 1) examine the performance of the T/DP as applied to substances covering a range of anticipated reactivities, 2) determine the extent to which data from the 3 participating laboratories might be in agreement, 3) determine whether the data could be used to derive hazard classification outcomes for the test substances, and 4) determine the extent to which the hazard classification outcomes from each participating laboratory were in agreement with each other.

MATERIALS AND METHODS

Substances

Using T/DP conditions of aqueous media, pH, agitation, loadings, and sample times, we examined the reference substances Ni metal, cuprous oxide (Cu_2O), tricobalt tetroxide (Co_3O_4), and an INVAR Ni–Co–Fe alloy, NILO K. The first 3 substances were in powder form, whereas the alloy was provided as cuttings from a 1-mm diameter wire in lengths ranging from 1 to 3.5 mm. Details on the substances are listed in Table 1. The suppliers shipped the substances to the lead laboratory, CANMET-MMSL, where the Canadian Certified Reference Material Program prepared subsamples under strict quality control and assurance procedures (details available upon request) and then simultaneously shipped the prepared subsamples of each of the 4 substances to the 3 participating laboratories.

We selected the substances for examination so that we could assess the reliability of the T/DP over a range of reactivities covered by 1 metal, 2 metal oxides, and an alloy.

Test scheme

The test scheme provided for 7-d T/D tests to be conducted in triplicate, plus 1 blank, at pH 6 and 8 on the 4 substances at loadings of 1, 10, and 100 mg/L, with the 1 mg/L loadings, including a blank, extending to 28 d. We collected samples at 0, 2, 6, 24, 48, 96, and 168 h for the 7-d tests, and also at 336, 504, and 672 h for the 1 mg/L tests, with 3 samples at each sampling interval except for 2 and 6 h, when we drew single samples. We analyzed the samples from the alloy tests for Ni, Co, and Fe, and those from the other tests for single metals only. In the entire scheme, the total numbers of samples and determinations for each laboratory were 1200 and 1920, respectively.

Methods of agitation and temperature control

CANMET-MMSL. The Canada Centre for Mineral and Energy Technology–Mining and Mineral Sciences Laboratories (CANMET-MMSL), Ottawa, Canada, used (except for the 1 mg/L loadings of the alloy cuttings) a top-loading LabLine Model 3530-1 refrigerated environmental shaker with a 2-inch (5 cm) orbit set at 100 rpm and 21°C to maintain the flow of aqueous medium over the test substance while maintaining its integrity (UN 2009, p 553). The orbital shaker had a capacity of twenty-four 1-L Schott Duran jars.

For T/D tests with 1 mg/L loadings of the alloy cuttings, CANMET-MMSL used 20-L low-density Nalgene polyethylene carboys, all maintained in a room air conditioned in the range 20 to 23 °C. The aqueous medium was agitated in the 20-L carboys using molded glass impellers set at 200 rpm, 10 mm diameter × 50 cm length, with a paddle of diameter 67 mm immersed in the aqueous medium to a depth of approximately 20 cm driven by either a Caframo RZR 50 or a Heidolph RZR 2021 stirring motor.

CIMM. The Centro de Investigación Minera y Metalúrgica (CIMM), Santiago, Chile, used custom-manufactured top-loading orbital shakers with a 2.54-cm (1-inch) orbit set at 100 rpm and with a capacity of three 2-L Ilbamor Erlenmeyer flasks enclosed in a lucite chamber, maintained in a room temperature-controlled in the range 20 to 23°C.

LISEC Environmental Consulting. Sample handling at LISEC Environmental Consulting, Genk, Belgium, was performed with an Invicon type IVC-60 laboratory table shaker with a horizontal displacement amplitude of 5 cm (2 inches) and a horizontal stroke frequency of 100/min, maintained in a temperature-controlled room in the range 20 to 23 °C. The table shaker had a capacity of 2 × 50 kg, or approximately sixty 1-L Schott Duran jars, and proportionately fewer 2- and 5-L jars.

Aqueous media, pH control, and pH and dissolved oxygen measurement

The compositions of the T/DP media for pH 6, 7, 8, and 8.5 (UN 2009, p 553) are based on that of the OECD 203 medium for aquatic ecotoxicity testing (OECD 1992), which contains 294.00, 123.25, 64.75, and 5.75 mg/L of $CaCl_2 \cdot 2H_2O$, $MgSO_4 \cdot 7H_2O$, $NaHCO_3$, and KCl, respectively, with a hardness equal to 250 mg/L $CaCO_3$. Each participating laboratory used certified or analysis grade reagents to make up the aqueous media.

For a target pH of 8, the OECD 203 medium has a calculated pH of 8 when equilibrated with air at 21.5°C (FactSage 2009). The calculated pH of a medium comprising 10× dilute OECD 203 equilibrated at 21.5°C with air containing 0.5% CO_2 is 6.05 (FactSage 2009) prior to metal or alloy additions.

Table 1. Details on metal compounds, metal, and alloy examined for T/D characteristics in this study

Name	Formula	Method of production	Physical form	Composition, analyses	Particle size analysis	Specific surface area, m^2/g		Supplier	Comments
						Calculated[a]	Measured[b]		
Cuprous oxide	Cu_2O	Reaction of CuO and Cu at 800° to 900°C	Powder	Active ingredient: cuprous oxide, 94% inert ingredients: 6%	50%, 16.5 μm (Microtrac)	0.15	0.512	American Chemet Corp., East Helena, Montana 59635, USA	LOLO TINT 97
									Antifouling ingredient for formulating use
									Untreated
									EPA Registration 26883-7
									Lot no.: 42521
									Date: 18 March 2003
Nickel metal	Ni	Decomposition of nickel carbonyl	Powder	Typically 99.9% pure nickel metal	50%, 10 μm (Microtrac)	0.18	0.43	Inco Ltd., 145 King Street West, Suite 1500, Toronto M5H 4B7, Canada	INCO® Type 123
									Lot no.: 3472165
									Date: 24 April 1997
Tricobalt tetraoxide	Co_3O_4	Decomposition of cobalt hydroxide	Powder	71.0% Co minimum	Median, 11 μm		16.12	The Shepard Chemical Co., 4900 Beech Street, Cincinnati, Ohio 45212, USA	Product no.: 1485
				Co_3O_4 is 73.4% Co, so the Co_3O_4 is minimum 97.6% purity	10%, 6.7 μm				Lot no.: 1019232
					90%, 17.8 μm (Microtrac)				Date: May 2002
Ni–Co–Fe alloy		Drawn from rods	Wire	Ni:Fe:Co = 29.5:53:17	1 mm diameter × 1–3.5 mm length; 0.005–0.02 g per cutting (approximate)	0.0007	0.024	EUROFER, Rue de Noyer 211, B-1000, Brussels, Belgium	NILO K alloy

[a]From particle size analysis.
[b]By N_2 adsorption–desorption (BET method).

CANMET-MMSL. To obtain a pH of 6, a specialty-produced gas mixture consisting of 0.5% CO_2 with the balance air was passed into the 10× dilute OECD 203 medium through manifold arrangement consisting of a $1/4 \times 1/16$ inch (0.635×0.159 mm) tube of rubber latex from which the gas passed through 0.023 inch (0.058 mm) i.d. (internal diameter) polyethylene capillaries, 1 for each Schott Duran jar and 2 for each 20-L carboy. The pH can be expected to remain within ±0.2 unit (UN 2009, p 552).

To measure the pH, an Orion 9107BN Thermo Triode electrode with an Orion 250A+ readout meter was used (range: −2.00 to 19.99; resolution: 0.01; accuracy: ±0.02). For dissolved oxygen (DO) readings, an Orion 3 Star portable DO meter was used.

CIMM. CIMM established pH 6 in the 10× dilute medium by metering a flow of pure CO_2 gas into the Lucite chamber, using a Harris model 825 CO_2 regulator and gas flow valves between the regulator and an AGA model 3805 flow meter. The pH values were continuously measured with a Fisher Scientific Accumet 25, with temperature measurement capability and automatic temperature correction (resolution: 0.1 pH units; accuracy: ±0.002), and linked the pH meter to the CO_2 regulator to adjust the flow rate of pure CO_2 into the chamber to maintain the pH. For DO measurements, an Orion DO meter (model 97–08) with automatic temperature correction and a dynamic range of 0 to 14 mg/L was used. This DO meter had a resolution of 0.05 mg/L in the temperature range 0 to 45 °C and a relative accuracy of 2% of full scale.

LISEC Environmental Consulting. To obtain a pH of 6, a specialty-produced gas mixture consisting of air containing 0.5% CO_2 was passed into the 10× dilute OECD 203 medium, using a manifold arrangement consisting of a 0.43×0.28 inch (11×7 mm) tube of polyvinyl chloride from which the gas passed through 0.023 inch (0.058 mm) i.d. polyethylene capillaries, 1 for each Schott Duran jar. The pH can be expected to remain within ±0.2 unit (UN 2009, p 552).

To measure the pH, DO, and temperature, a WTW Multiline P4 readout meter with the corresponding electrodes was used (pH combined electrode with integrated temperature probe SenTix 41: pH range = −2.00 to 16.00; resolution = 0.01; accuracy = ±0.02. The CellOx 325 DO electrode: range = 0–19.99 mg/L; resolution = 0.01 mg/L; accuracy = 0.5% of measured value ±1 digit with ambient temperature 5–30 °C).

Procedure

All 3 laboratories used similar procedures to make the OECD 203 and 10× dilute OECD 203 aqueous media. We made up and maintained volumes of media in 10- or 20-L Nalgene carboys a few days or weeks in advance of use, by adding the weighed reagents to the deionized water and filtering with 90-mm Pall Life Science Supor®-200 0.2-μm filters or equivalent.

Prior to the start of a set of tests in which the target pH was 6, we passed the gas mixture through or over the solutions in each vessel to condition the aqueous media. For CANMET-MMSL, the conditioning gas flow rate through the solutions was approximately 3 L/h for approximately 10 h for each Schott Duran jar. The corresponding conditioning flow rate for CANMET-MMSL for the 20-L carboys was approximately 13 L/h. During the CANMET-MMSL tests, the flow rate through the aqueous medium was approximately 2 L/h for each 1-L Schott Duran jar, and the same as during conditioning for the reaction kettles. For CIMM, the conditioning gas flow rates were approximately 2 to 3 L/min for a minimum of 12 h prior to the addition of the test samples. During the tests, we used a feedback flow control valve connected to the pH meter to control the pH by varying the flow rate of pure CO_2. For LISEC Environmental Consulting, at 1 day before the start of tests at target pH 6, we introduced the 0.5% CO_2-balance air mixture overnight at a flow rate of 10–20 L/h through a fritted glass disk into a 20-L Schott Duran jar containing the 10× dilute OECD medium. During the test, we kept the pH close to 6 (±0.2 unit) by introducing the 0.5% CO_2-balance air mixture into each 1-L Schott Duran jar at flow rates in the range of 1 to 3 L/h.

At each sampling time, the laboratories generally followed the sampling procedure below, or equivalent:

- Measure pH, temperature, and DO of test solution;
- Use a 15 mL syringe to collect the required number of approximately 12-mL solution samples, either 1 or 3, depending on the sample time;
- Filter samples with a 0.8/0.2 μm Acrodisc filter and acidify to pH < 2 with 1 to 2 drops of Fisher Trace Metal grade HNO_3 (68–71%);
- At 24 h and thereafter, replenish the aqueous media with fresh aqueous medium equivalent in volume to that drawn for analysis in order to maintain the surface area loading as constant as possible.

The 3 laboratories determined the concentrations of total dissolved Co, Cu, Fe, and Ni by inductively coupled plasma mass spectrometry or by graphite furnace atomic absorption spectrometry.

The T/DP suggests that for a standard setup of 3 replicate test vessels and 2 replicate samples per test vessel, the within-vessel variation in metal concentration should be 10%, which might be reasonably expected to also apply to 3 replicate samples. In addition, the between-vessel concentration should be less than 20% (UN 2009, p 554). The 3 laboratories routinely included appropriate laboratory blanks and standards to provide quality assurance and quality control.

Table 2. Acute and chronic ecotoxicity reference values, μg/L, for comparison with T/D data

	Co[a]	Cu[b]	Fe[c]	Ni[d]
Acute	185	29	13 000	68 (pH 8)
				120 (pH 6)
Chronic	1.54	8	1000	2.4

[a] William Stubblefield, Oregon State University, Corvallis, OR, USA, personal communication.
[b] Van Sprang et al. 2005.
[c] CEFIC 2004.
[d] NiPERA 2006.

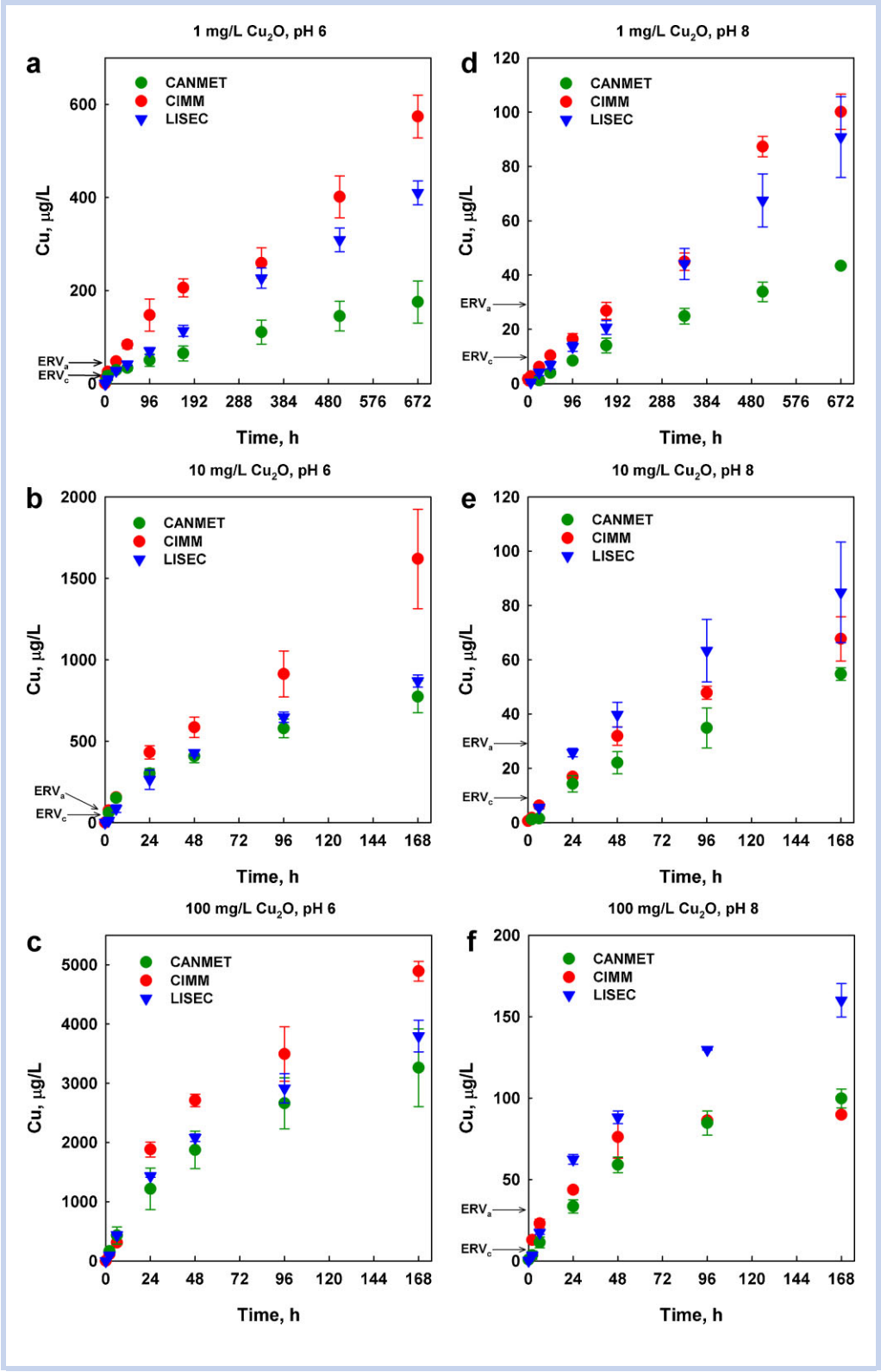


Figure 1. Net T/D data at pH 6 and 8 for 1, 10, and 100 mg/L loadings of Cu_2O powder.

Calculation of net changes in concentration

For each laboratory, the measured metal concentrations for each analyte at each sampling interval were absolute values. For each individual test on each loading, we calculated a within-vessel average concentration as the arithmetic mean of the analytical determinations of the 3 sample solutions drawn at the particular sampling time (except for sampling at 2 and 6 h, when only 1 was drawn), as well as values of σ_w, the standard deviation of the 3-concentration data set, and of $\rho_{w\%}$, the percentage coefficient of variance, which is the quotient $100\sigma_w$/(within-vessel average). For all loadings, $n = 3$ (i.e.,

Table 3. Net average T/D data from the 3 laboratories for Cu_2O, Co_3O_4, and Ni metal powder

	pH 6.0				pH 8.0			
	Ni metal powder							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
Lab	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L
CANMET-MMSL	3262 (20.1)	773 (12.6)	64.8 (24.7)	29	99.4 (5.6)	54.4 (5.4)	13.7 (15.9)	29
CIMM	4891 (3.4)	1619 (18.8)	206 (9.2)	29	85.7 (1.5)	63.7 (12.8)	22.8 (13.5)	29
LISEC	3797 (7.0)	869 (4.3)	113 (10.6)	29	160 (6.4)	84.8 (21.8)	20.7 (12.4)	29
Labs, Average	3983	1087	128		115	67.6	19.1	
Labs, CV%	21	43	56		34	23.0	25.0	
	28-d metal concentration, μg/L (CV%)			Chronic ERV, μg/L	28-d metal concentration, μg/L (CV%)			Chronic ERV, μg/L
CANMET-MMSL			175.4 (25.8)	8			43.4 (1.9)	8
CIMM			574 (7.6)	8			100 (6.5)	8
LISEC			410 (6.1)	8			90.7 (16.4)	8
Labs, Average			386				78	
Labs, CV%			42				39	
	Tricobalt tetroxide, Co_3O_4							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L
CANMET-MMSL	89.7 (16.2)	17.8 (7.4)	2.2 (21.8)	185	3.3 (28)	1.5 (15)	0.34 (9.7)	185
CIMM	183 (8.4)	30.0 (2.3)	3.4 (7.7)	185	3.1 (3.4)	1.6 (4.9)	0.3 (11.2)	185
LISEC	142 (4.6)	31.1 (5.4)	4.0 (21.9)	185	8.3 (14.8)	2.6 (7.8)	0.4 (66.1)	185
Labs, Average	138	26.3	3.2		4.9	1.9	0.3	
Labs, CV%	34	28.1	28.6		60.1	32.0	14.5	
	28-d metal concentration, μg/L (CV%)			Chronic ERV, μg/L	28-d metal concentration, μg/L (CV%)			Chronic ERV, μg/L
CANMET-MMSL			5.9 (14.4)	1.54			0.3 (17.1)	1.54
CIMM			12.4 (9.3)	1.54			0.9 (13.7)	1.54
LISEC			15.8 (6.7)	1.54			1.3 (9.4)	1.54
Labs, Average			11.0				0.8	
Labs, CV%			36.0				60.1	
	Ni metal powder							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L
CANMET-MMSL	541 (1.4)	46 (4.7)	2.5 (93)	120	311 (9.4)	28.5 (14.8)	2.2 (15.1)	68

Table 3. (*Continued*)

	pH 6.0				pH 8.0			
	Ni metal powder							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
Lab	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L
CIMM	694 (3.6)	61.6 (9.9)	4.6 (2.7)	120	415 (1.0)	37.9 (7.0)	2.7 (20.7)	68
LISEC	444 (3.0)	51 (4.0)	2.3 (0.0)	120	420 (0.7)	35 (1.4)	2.3 (0.0)	68
Labs, Average	560	53	3.1		382	34	2.4	
Labs, CV%	23	15	41		16	14	16	
	28-d metal concentration, μg/L (CV%)			Chronic ERV, μg/L	28-d metal concentration, μg/L (CV%)			Chronic ERV, μg/L
CANMET-MMSL			1.8 (98)*	2.4			2.6 (7.1)	2.4
CIMM			6.4 (3.2)	2.4			3.9 (8.4)	2.4
LISEC			3.9 (75)	2.4			0.8 (173)*	2.4
Labs, Average			4.1				2.4	
Labs, CV%			57				65	

*Values are equivocal (see text).

3 replicate jars). For the 7-d procedural blanks run simultaneously with the 10 and 100 mg/L loadings, $n = 2$.

For each laboratory, at each sampling time over the 7 d for each loading, including the procedural blanks, we then calculated a between-vessel average as the arithmetic mean of the average within-vessel values as above. We also calculated between-vessel values of the coefficient of variance, ρ_b, and the between-vessel percent coefficient of variance, $\rho_{b\%}$. To calculate the net average concentration, Me(aq), for each loading at each sampling time, we subtracted the between-vessel average for the procedural blanks from those for the corresponding loaded tests. We then calculated net average among-laboratory metal concentrations, as well as coefficients of variance (CV) and values of $CV_{\%}$ as above.

In many instances, the blank values were below the limit of quantification (LOQ). In such cases, to enable the calculation of net average concentrations and corresponding standard deviations, in the tables for each individual test, we divided by 2 those determinations reported as below the LOQ and subtracted this quotient from the between-vessel average. For instance, if the concentration from a procedural blank for a given analyte at 96 h was <0.61 μg/L and the corresponding average concentration for three 1-mg/L loadings was 3.27 μg/L, then to calculate a net 96-h value, we subtracted 0.61/2 from 3.27 to obtain a net average concentration of 2.96 μg/L at 96 h. This procedure allowed the plotting of the net T/D reaction kinetic data for Co, Cu, Fe, and Ni.

We note that some of the analytical determinations in both the loaded and blank tests were close to the LOQ and that the net differences could therefore be either slightly positive or slightly negative. Relative uncertainties could therefore be very large, although the absolute value of the analytical determinations could be very small. When the net average concentrations were negative or slightly positive, we interpreted these data in the text as also revealing no detectable net average concentrations.

Derivation of GHS hazard classification proposals

The acute and chronic ERVs that were used in comparison with the T/D data to derive GHS hazard classification proposals for the metal, metal compounds, and alloy are given in Table 2 with the sources of the data. However, until the respective chemical safety reports are prepared for the REACH program, these acute and chronic ERVs should be considered as preliminary and the classification outcomes as worked examples for illustrative purposes only. The acute and chronic ecotoxicity data for Cu, Fe, and Ni have been used for classification purposes within the EU, whereas those for Co are from a report to an OECD meeting on the validation of the T/DP.

RESULTS AND DISCUSSION

Cuprous oxide powder

For the 100, 10, and 1 mg/L loadings of the Cu_2O powder at pH 6 and 8, we have plotted the net T/D data from all 3 laboratories in Figure 1 and presented the 7- and 28-d values in Table 3. The concentrations of total dissolved Cu depend on time, loading, and pH; are higher at pH 6 than at pH 8; and increase both with time and loading. Among all 3 laboratories, the average net 100, 10, and 1 mg/L 7-d concentrations at pH 6 were 3983 μg/L ($CV_{\%} = 21$), 1087 μg/L ($CV_{\%} = 43$), and 128 μg/L ($CV_{\%} = 56$), respec-

Table 4. Interlaboratory classification outcomes for Cu_2O, Co_3O_4, and Ni metal powder, based on T/D data from the 3 laboratories

	pH 6.0				pH 8.0			
	Cuprous oxide, Cu_2O							
	Loading, mg/L				**Loading, mg/L**			
	100	**10**	**1**		**100**	**10**	**1**	
Lab	**Acute classification outcome**			**Acute ERV, μg/L**	**Acute classification outcome**			**Acute ERV, μg/L**
CANMET-MMSL	Yes	Yes	Yes	29	Yes	Yes	Yes	29
CIMM	Yes	Yes	Yes	29	Yes	Yes	Yes	29
LISEC	Yes	Yes	Yes	29	Yes	Yes	Yes	29
	Cronic classification outcome			Chronic ERV, μg/L	Chronic classification outcome			Chronic ERV, μg/L
CANMET-MMSL			Yes	8			Yes	8
CIMM			Yes	8			Yes	8
LISEC			Yes	8			Yes	8
	Tricobalt tetroxide, Co_3O_4							
	Loading, mg/L				**Loading, mg/L**			
	100	**10**	**1**		**100**	**10**	**1**	
	Acute classification outcome			**Acute ERV, μg/L**	**Acute classification outcome**			**Acute ERV, μg/L**
CANMET-MMSL	No	No	No	185	No	No	No	185
CIMM	No	No	No	185	No	No	No	185
LISEC	No	No	No	185	No	No	No	185
	Chronic classification outcome			Chronic ERV, μg/L	Chronic classification outcome			Chronic ERV, μg/L
CANMET-MMSL			Yes	1.54			No	1.54
CIMM			Yes	1.54			No	1.54
LISEC			Yes	1.54			No	1.54
	Ni metal powder							
	Loading, mg/L				**Loading, mg/L**			
	100	**10**	**1**		**100**	**10**	**1**	
	Acute classification outcome			**Acute ERV, μg/L**	**Acute classification outcome**			**Acute ERV, μg/L**
CANMET-MMSL	Yes	No	No	120	Yes	No	No	68
CIMM	Yes	No	No	120	Yes	No	No	68
LISEC	Yes	No	No	120	Yes	No	No	68
	Chronic classification outcome			Chronic ERV, μg/L	Chronic classification outcome			Chronic ERV, μg/L
CANMET-MMSL			No*	2.4			Yes	2.4
CIMM			Yes	2.4			Yes	2.4
LISEC			Yes	2.4			No*	2.4

*Classification outcomes are equvocal (see text).

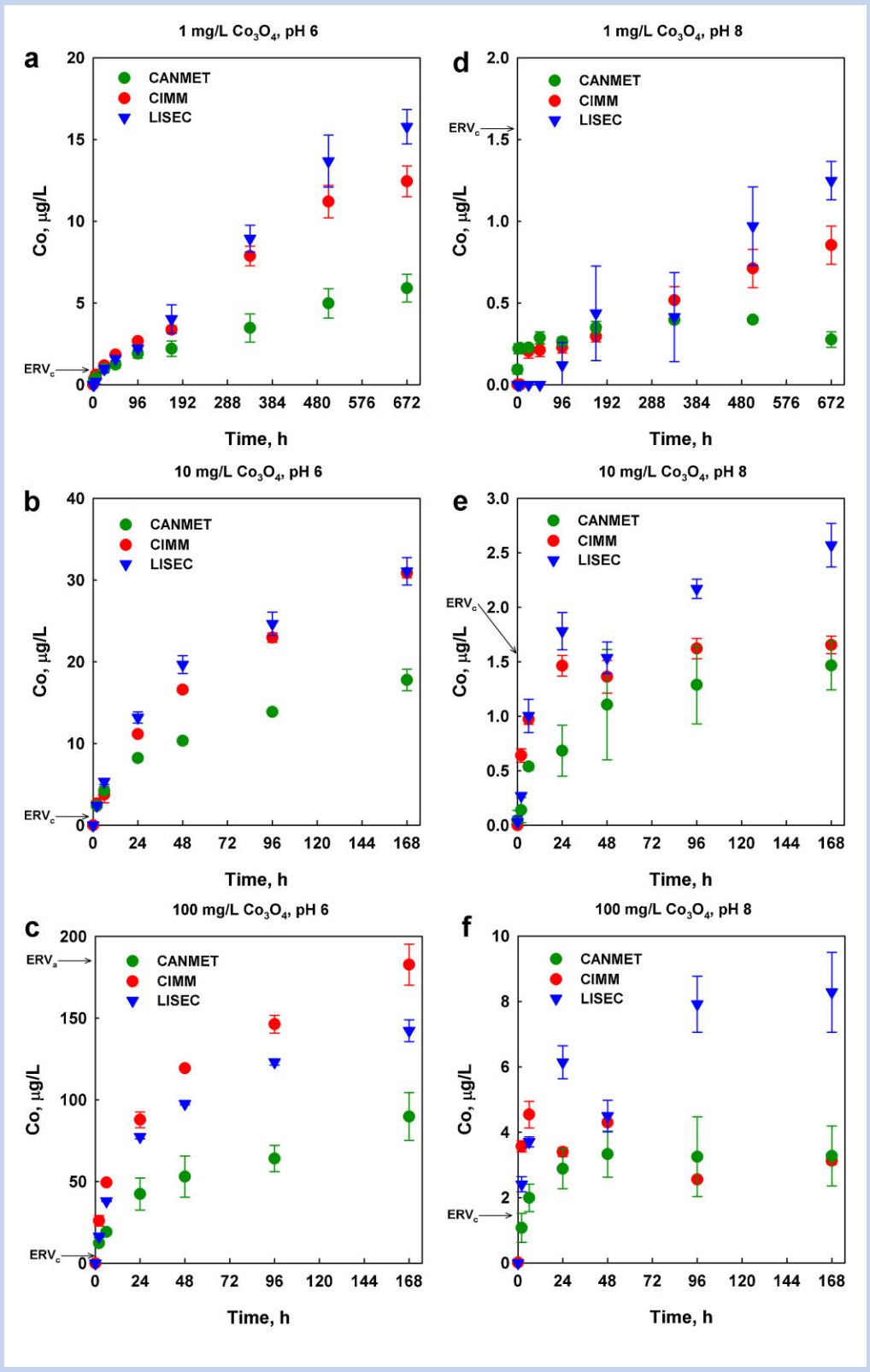


Figure 2. Net T/D data at pH 6 and 8 for 1, 10, and 100 mg/L loadings of Co_3O_4 powder.

tively. The corresponding pH 8 values were 115 µg/L ($CV_{\%} = 34$), 67.6 µg/L ($CV_{\%} = 23.0$), and 19.1 µg/L ($CV_{\%} = 25.0$), respectively. For the 1 mg/L loadings at 28 d, the average concentrations were 386 µg/L ($CV_{\%} = 42$) and 78 µg/L ($CV_{\%} = 39$) at pH 6 and 8, respectively. Also plotted in Figures 1a, b, d, e, and f are ERC_a and ERV_c (the acute and chronic ERVs, respectively) for Cu, against which we can compare the T/D data from each of the 3 laboratories. From Figure 1a and Table 3, the 1 mg/L loading T/D data for all 3 laboratories at pH 6 are in agreement that the Cu_2O would be

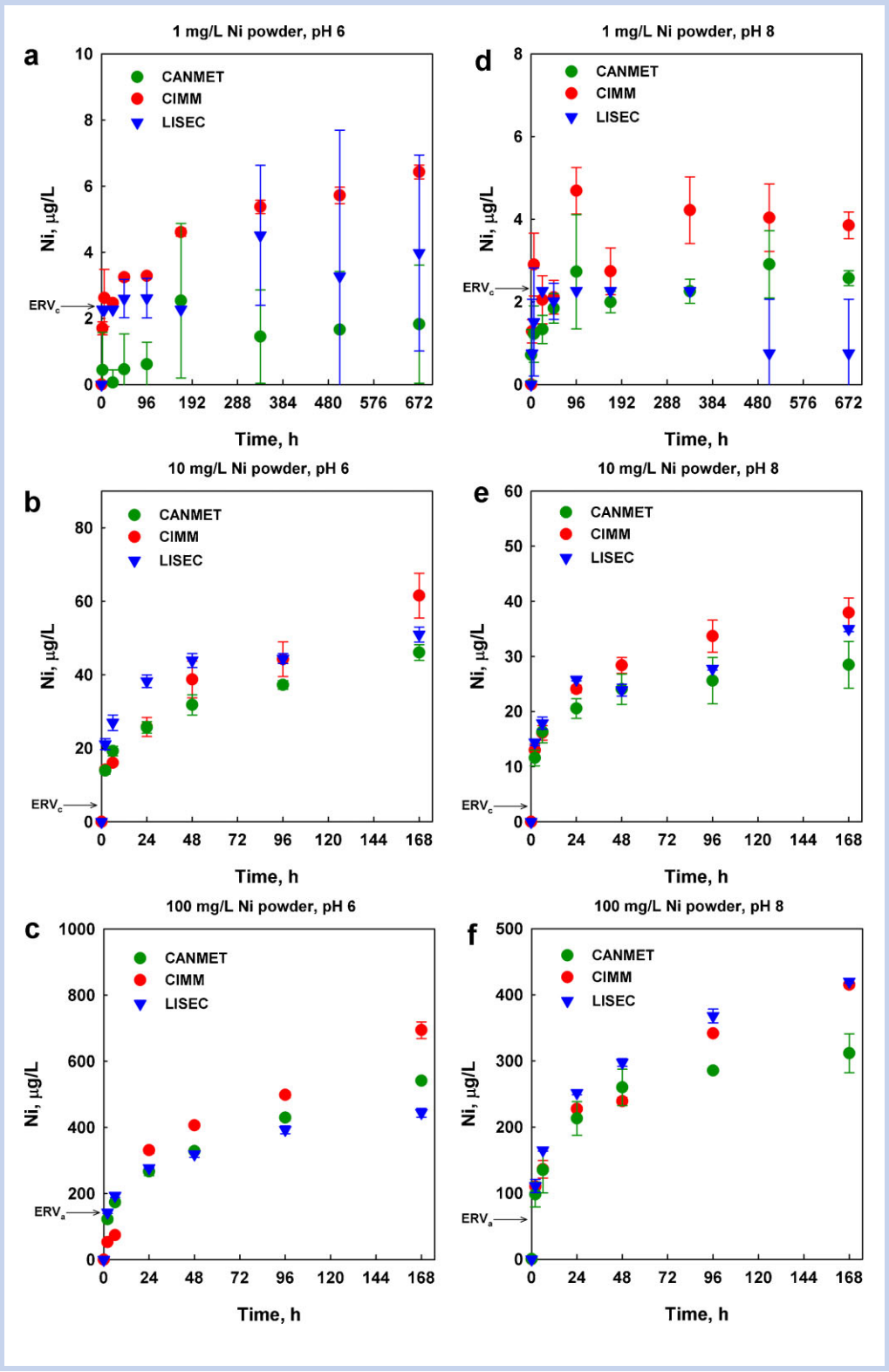


Figure 3. Net T/D data at pH 6 and 8 for 1, 10, and 100 mg/L loadings of Ni metal powder.

classified as Acute 1 (Table 4). However, the 1 mg/L T/D data at pH 8 would classify the Cu_2O as Acute 2, not Acute 1, and because the most severe classification takes precedence, the Cu_2O would be classified as Acute 1. From Figures 1a and d, and Table 3, we note that the Cu T/D data for all 3 laboratories exceed the Cu chronic ERV, so that a Chronic 1 classification would also be applied (Table 4).

The 7-d total dissolved Cu concentrations at pH 6 represent 3 to 4% dissolution of the Cu in the 100 mg/L loadings of the Cu_2O. We propose that the values of $CV_{\%}$ in

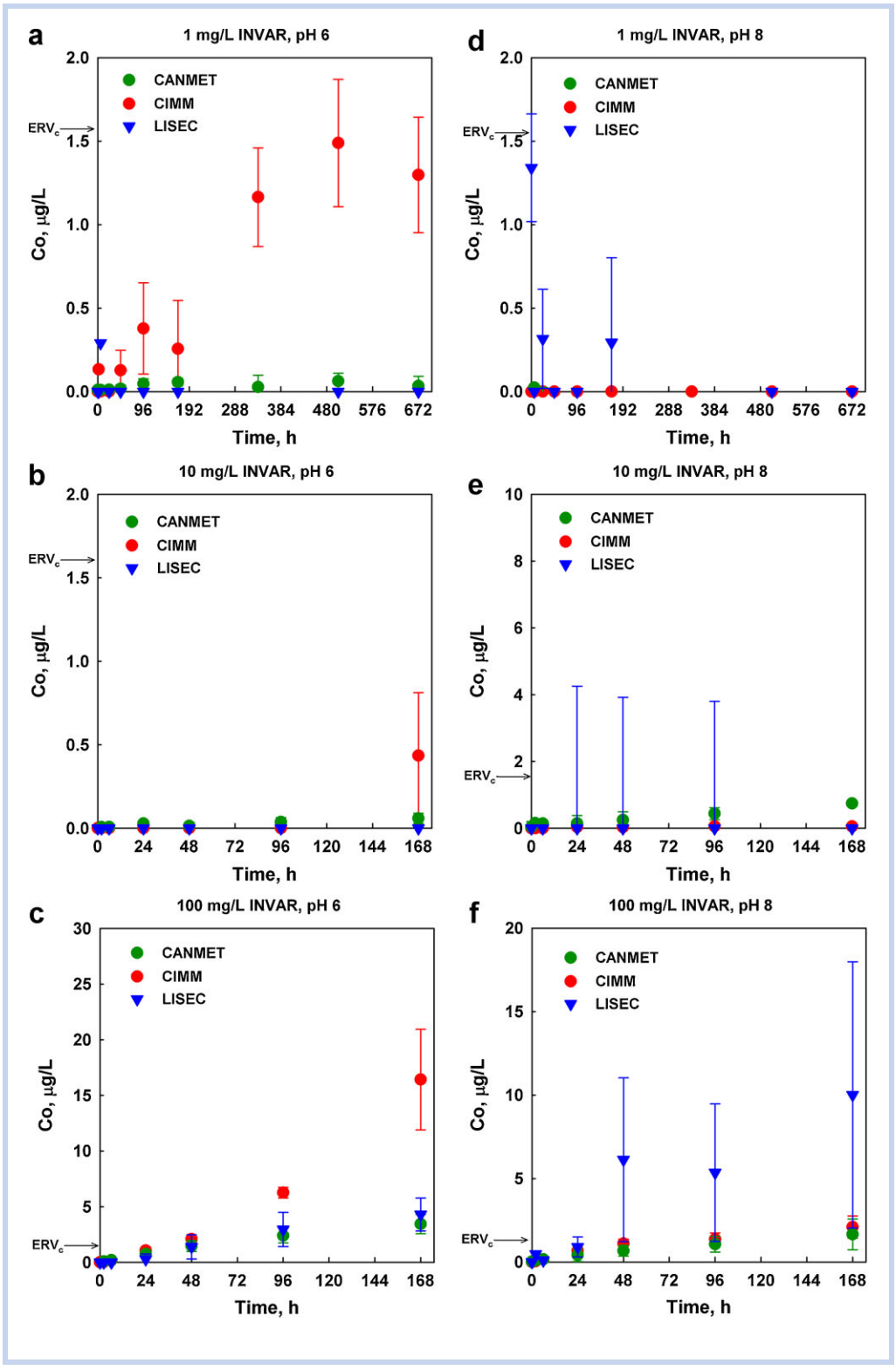


Figure 4. Net T/D data for total dissolved Co at pH 6 and 8 for 1, 10, and 100 mg/L loadings of NILO K alloy.

the range of 21 to 36 among the 3 laboratories are reasonable and acceptable for hazard classification purposes.

Tricobalt tetroxide powder

For Co_3O_4 powder, the net T/D data from all 3 laboratories for the 100, 10, and 1 mg/L loadings are in Figure 2, and the 7- and 28-d values are in Table 3. Similar to Cu_2O, the concentrations of total dissolved Co depend on time, loading, and pH; are higher at pH 6 than at pH 8; and increase both with time and loading. For the 100, 10, and 1 mg/L loadings, the average net concentrations among all 3 laboratories were 138 µg/L ($CV_{\%} = 34$), 26.3 µg/L ($CV_{\%} = 28.1$), and 3.2 µg/L ($CV_{\%} = 28.6$), respectively,

Table 5. T/D data from the 3 laboratories for NILO K alloy

	pH 6.0				pH 8.0			
	NILO K (Co)							
	Loading, mg/L				Loading, mg/L			
	100	10	1	100	10	1		
Lab	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L
CANMET-MMSL	3.4 (25.0)	0.06 (51)	0.06 (39)	185	1.7 (45.8)	0.74 (9.1)	ND	185
CIMM	16.4 (27.5)	0.43 (87)	0.26 (113)	185	2.1(25.9)	0.05 (141)	ND	185
LISEC	4.3 (34.3)	ND	ND	185	10.0 (65.1)	ND	0.29 (141)	185
Labs, Average	8.0	0.2	0.2		4.6	0.40	0.29	
Labs, CV%	94	107	88		101.8	123.5	NA	
	28-d metal concentration μg/L (CV%)			Chronic ERV, μg/L	28-d meal concentration μg/L (CV%)			Chronic ERV, μg/L
CANMET-MMSL			0.03 (174)	1.54			ND	1.54
CIMM			1.3 (26.7)	1.54			ND	1.54
LISEC			ND	1.54			ND	1.54
Labs, Average			0.7				ND	
Labs, CV%			0.9				NA	
	NILO K (Ni)							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, μg/L
CANMET-MMSL	5.5 (37.8)	ND	0.32 (53.9)	120	2.0 (115)	ND	ND	68
CIMM	29.8 (26.7)	1.2 (36.1)	0.33 (173)	120	3.4 (27.5)	ND	ND	68
LISEC	4.2 (86.7)	ND	ND	120	16.7 (85.1)	4.6 (87.3)	ND	68
Labs, Average	13.2	1.2	0.33		7.4	4.6	ND	
Labs, CV%	110	NA	2.2		110	NA	NA	
	28-d metal concentration, μg/L (CV%)			Chronic ERV, μg/L	28-d meal concentratio, μg/L (CV%)			Chronic ERV, μg/L
CANMET-MMSL			ND	2.4			ND	2.4
CIMM			1.74 (27.5)	2.4			0.06 (303)	2.4
LISEC			ND	2.4			ND	2.4
Labs, Average			1.7				0.1	
Labs, CV%			NA				NA	
	NILO K (Fe)							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
	7-d metal concentration, μg/L (CV%)			Acute ERV, mg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, mg/L
CANMET-MMSL	0.87 (278)	1.0 (162)	2.1(20.0)	13.3	ND	ND	1.8 (106)	13.3

Table 5. (*Continued*)

	pH 6.0				pH 8.0			
	NILO K (Fe)							
	Loading, mg/L				Loading, mg/L			
	100	10	1	100	10	1		
Lab	7-d metal concentration, μg/L (CV%)			Acute ERV, mg/L	7-d metal concentration, μg/L (CV%)			Acute ERV, mg/L
CIMM	ND	1.0 (162)	0.70 (140)	13.3	ND	2.0 (319)	ND	13.3
LISEC	ND	ND	ND	13.3	ND	ND	ND	13.3
Labs, Average	0.9	1.0	1.4		ND	2.0	1.8	
Labs, CV%	NA	0.0	0.5		NA	NA	NA	
	28-d metal concentration, μg/L (CV%)			Chronic ERV, mg/L	28-d metal concentration, μg/L (CV%)			Chronic ERV, mg/L
CANMET-MMSL			1.6 (91.5)	1000			0.7 (536)	1000
CIMM			0.08 (1708)	1000			1.1 (583)	1000
LISEC			ND	1000			ND	1000
Labs, Average			0.8				0.9	
Labs, CV%			1.1				0.3	

at pH 6, and 4.9 μg/L ($CV_{\%} = 60.1$), 1.9 μg/L ($CV_{\%} = 32.0$), and 0.3 μg/L ($CV_{\%} = 14.5$), respectively, at pH 8. The 28-d 1 mg/L loading average concentrations were 11.0 μg/L ($CV_{\%} = 36.0$) and 0.8 μg/L ($CV_{\%} = 60.1$) at pH 6 and 8, respectively.

The T/D data in Figure 2 for total dissolved Co from all 3 laboratories for the 100, 10, and 1 mg/L loadings are lower than the acute ERV of 185 μg/L, so that the Co_3O_4 powder would not classify at any Acute level (Table 4). Moreover, because all 3 laboratories report 28-d Co concentrations that are greater than the chronic ERV (Figure 2a), and there was no acute classification, the Co_3O_4 powder would be classified as Chronic 4 (UN 2009, p 512) (Table 4). Similar to those for Cu_2O, the values of $CV_{\%}$ in the range of 14 to 60 among the 3 laboratories are reasonable and acceptable for hazard classification purposes.

With approximately 0.1% Co dissolution of the 100 mg/L loadings at 7 d and pH 6, the Co_3O_4 powder was considerably less reactive than the Cu_2O powder, notwithstanding its considerably greater specific surface area.

Nickel metal powder

The net T/D data from all 3 laboratories for the 100, 10, and 1 mg/L loadings of Ni metal powder are in Figure 3, and the 7- and 28-d values are in Table 3. Similar to the Cu_2O and Co_3O_4 powders, the concentrations of total dissolved Ni depend on time, loading, and pH; are higher at pH 6 than at pH 8; and increase both with time and loading. The average net 100, 10, and 1 mg/L 7-d concentrations among all 3 laboratories at pH 6 were 560 μg/L ($CV_{\%} = 23\%$), 53 μg/L ($CV_{\%} = 15\%$), and 3.1 μg/L ($CV_{\%} = 41\%$), respectively. The corresponding pH 8 values were 382 μg/L ($CV_{\%} = 16\%$), 34 μg/L ($CV_{\%} = 14\%$), and 2.4 μg/L ($CV_{\%} = 16\%$), respectively. For the 1 mg/L loadings at 28 d, the average net concentrations at pH 6 and 8 were 4.1 μg/L ($CV_{\%} = 57\%$) and 2.4 μg/L ($CV_{\%} = 65\%$), respectively.

For all 3 laboratories, the net concentrations of total dissolved Ni at 1 and 10 mg/L at both pHs were significantly less than the acute ERVs of 120 and 68 μg/L at pH 6 and 8, respectively (Figures 3a, b, d, and e; Table 3). However, all 3 laboratories are in agreement that the Ni concentrations exceeded the acute ERVs for the 100 mg/L loadings at pH 6 and 8 by 7 d (Figures 3c and e) and that Ni metal powder would classify as Acute 3 (Table 4). Again, $CV_{\%}$ values in the range of 15 to 65 were reasonable and acceptable for hazard classification purposes.

For the 28-d 1 mg/L loadings at pH 6, the CIMM and LISEC concentrations of Ni, 6.4 and 3.9 μg/L, respectively, exceeded the chronic ERV of 2.4 μg/L, whereas the 1.8 μg/L value of CANMET-MMSL was slightly less. In the case of the pH 8 data, the LISEC value of 0.8 μg/L was slightly less than the chronic ERV, and those of CIMM and CANMET-MMSL, 2.6 and 3.9 μg/L, respectively, were slightly greater. Thus, in these 2 instances, the chronic classification outcomes are equivocal inasmuch that there is no agreement among the 3 laboratories.

The concentrations of total dissolved Ni at both pHs represent 0.4 to 0.7% reaction of the Ni metal powder and dissolution of the Ni cation.

NILO K alloy

All 3 laboratories were in agreement that the net concentrations of Co for all 3 loadings of the NILO K alloy were less than 20 μg/L at both pHs (Figure 4 and Table 5). An increase in Co concentration with time is most notable for the

Table 6. Interlaboratory classification outcomes for NILO K alloy based on T/D data for Co, Ni, and Fe

	pH 6.0				pH 8.0			
	NILO K (Co)							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
Lab	Acute classification outcome			Acute ERV, mg/L	Acute classification outcome			Acute ERV, mg/L
CANMET-MMSL	No	No	No	185	No	No	No	185
CIMM	No	No	No	185	No	No	No	185
LISEC	No	No	No	185	No	No	No	185
	Chronic classification outcome			Chronic ERV, mg/L	Chronic classification outcome			Chronic ERV, mg/L
CANMET-MMSL			No	1.54			No	1.54
CIMM			No	1.54			No	1.54
LISEC			No	1.54			No	1.54
	NILO K (Ni)							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
	Acute classification outcome			Acute ERV, μg/L	Acute classification outcome			Acute ERV, μg/L
CANMET-MMSL	No	No	No	120	No	No	No	68
CIMM	No	No	No	120	No	No	No	68
LISEC	No	No	No	120	No	No	No	68
	Chronic classification outcome			Chronic ERV, μg/L	Chronic classification outcome			Chronic ERV, μg/L
CANMET-MMSL			No	2.4			No	2.4
CIMM			No	2.4			No	2.4
LISEC			No	2.4			No	2.4
	NILO K (Fe)							
	Loading, mg/L				Loading, mg/L			
	100	10	1		100	10	1	
	Acute classification outcome			Acute ERV, μg/L	Acute classification outcome			Acute ERV, μg/L
CANMET-MMSL	No	No	No	13.3	No	No	No	13.3
CIMM	No	No	No	13.3	No	No	No	13.3
LISEC	No	No	No	13.3	No	No	No	13.3
	Chronic classification outcome			Chronic ERV, μg/L	Chronic classification outcome			Chronic ERV, μg/L
CANMET-MMSL			No	1000			No	1000
CIMM			No	1000			No	1000
LISEC			No	1000			No	1000

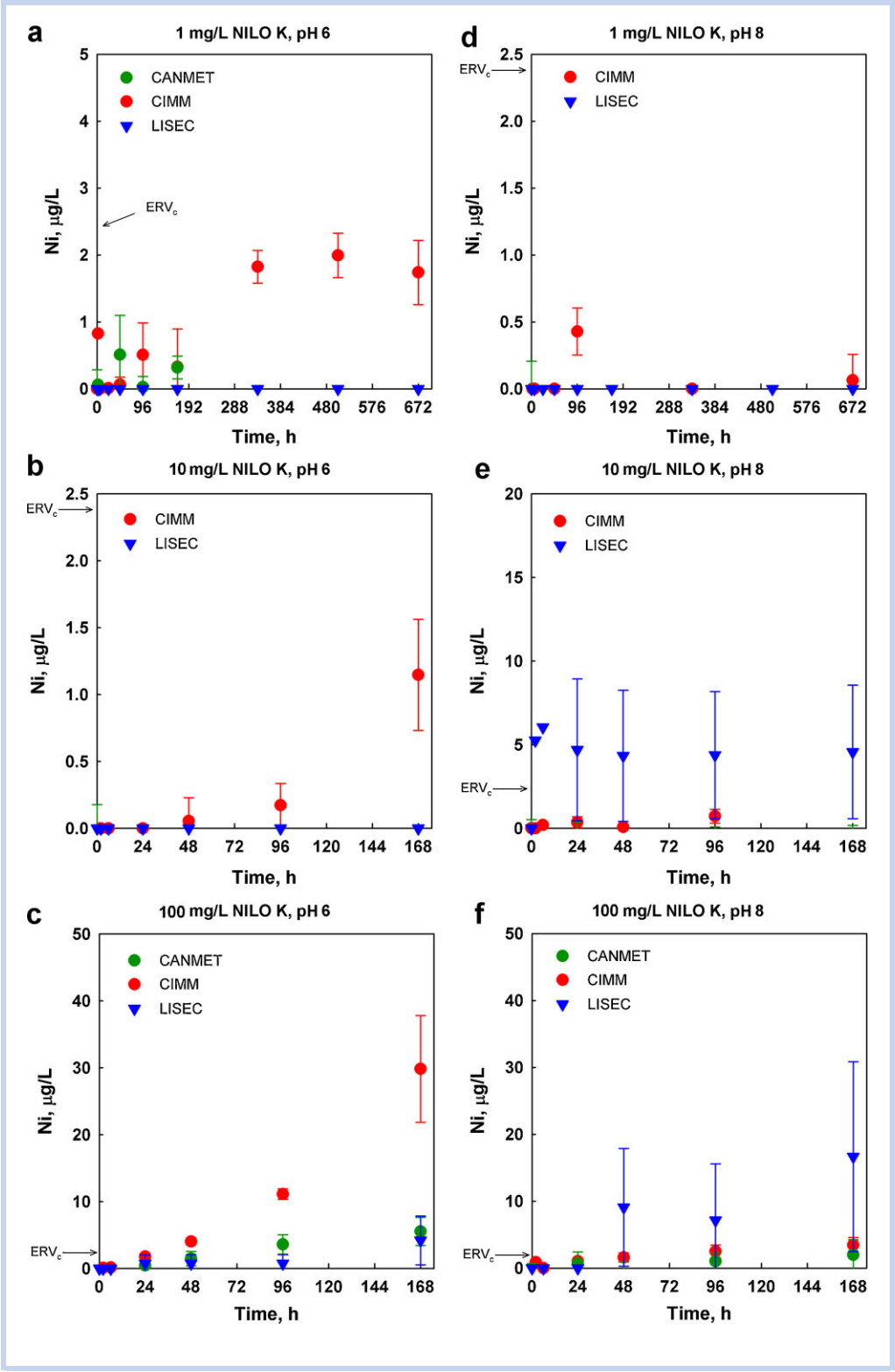


Figure 5. Net T/D data for total dissolved Ni at pH 6 and 8 for 1, 10, and 100 mg/L loadings of NILO K alloy.

100 mg/L loadings, with the LISEC and CANMET-MMSL values of 3 to 4 µg/L and CIMM values of 16 µg/L by 7 d at pH 6. None of the Co concentrations would classify the NILO K alloy at any level (Table 6), because they were all significantly less than the 185 µg/L acute ERV. Moreover, none of the Co concentrations in the 1 mg/L 28-d tests attained the chronic ERV of 1.54 µg/L. The T/D data for Co at all loadings and both pHs demonstrate that Co in the alloy is very nonreactive.

Similar comments apply to the net concentrations of Ni (Figure 5) concerning the classification of the NILO K alloy (Table 6). The values typically reached 4 to 6 µg/L with a

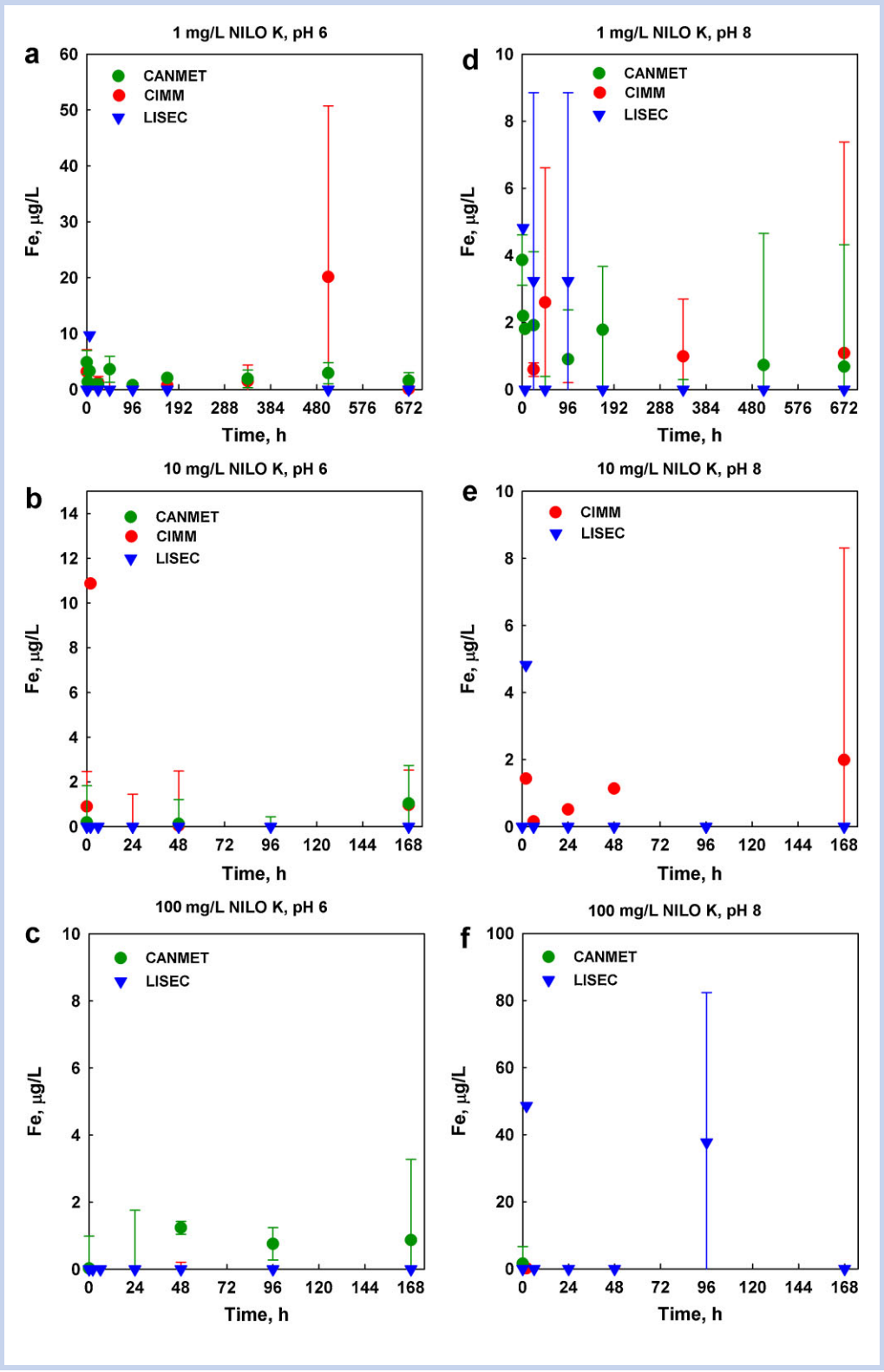


Figure 6. Net T/D data for total dissolved Fe at pH 6 and 8 for 1, 10, and 100 mg/L loadings of NILO K alloy.

maximum of 29.8 µg/L, by 7 d at pH 6 and loadings of 100 mg/L. None of the Ni concentrations exceeded the acute ERVs of 120 µg/L at pH 6 or 68 µg/L at pH 8, or the chronic ERV of 2.4 µg/L for both pHs. The amount of Ni released from the alloy is more than a factor of 40 less than from the Ni powder.

Among all 3 laboratories, the net concentrations of Fe (Figure 6) varied with time, between less than the various

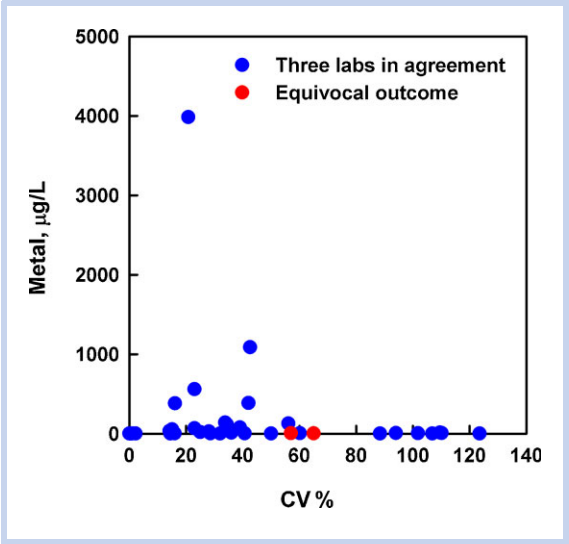


Figure 7. Endpoint metal concentrations as a function of $CV_{\%}$ showing the extent of agreement in classification outcomes among the 3 laboratories.

LOQs and approximately 50 µg/L, and were significantly less than any concentrations that might classify the NILO K alloy (Table 6).

Assessment of classification variability

In Tables 4 and 6, we present comparisons of the acute and chronic classification outcomes based on the supporting T/D data from each of the 3 laboratories. We determined that the 3 laboratories are in agreement in 36 of a possible 36 acute classification outcomes (1 classification outcome for each loading and pH) for Cu_2O, Co_3O_4, Ni metal, and the NILO K alloy.

For the chronic classifications of Cu_2O, Co_3O_4, and Ni metal (Table 4), the 3 laboratories are in agreement in 4 of 6 possible outcomes. The remaining 2 possibilities are equivocal for Ni powder only, because the measured concentrations and chronic ERVs lie within the ranges of the $CV_{\%}$ values at very low levels of micrograms per liter. In the first instance, CANMET-MMSL reported a net 28-d Ni concentration of 1.8 µg/L and an attendant $CV_{\%}$ of 98 at pH 6. Thus, the ERV of 2.4 µg/L lies well within the $CV_{\%}$ range. In the second instance, the net 28-d Ni concentration reported by LISEC was 0.8 µg/L and the $CV_{\%}$ was 173 at pH 8, so once again, the ERV was well within the $CV_{\%}$ range. In these 2 instances, the equivocal classification outcomes are the result of uncertainties in analyses at concentrations close to the LOQ when the chronic ERVs are also close to the analytical LOQs.

Moreover, of 6 possible chronic classification outcomes for the alloy, all 3 laboratories are in agreement that the NILO K would not classify at any chronic level (Table 6).

Thus, of a possible 48 acute and chronic classification outcomes, the 3 laboratories were in agreement 46 times. The 2 instances of equivocal outcomes were the result of the measured concentrations and the acute or chronic ERVs being within the values of $CV_{\%}$ for the measured concentrations.

To assess the potential effect of $CV_{\%}$ on the agreement of classification outcomes among the laboratories, we have plotted in Figure 7 the endpoint concentrations as a function of the 37 values of $CV_{\%}$ in which at least 2 laboratories reported metal concentrations. The 37 values of $CV_{\%}$ varied in the range of 0 to 124. Of these 37, 15 had values of 25% or less. A further 12 $CV_{\%}$ values varied between 25 and 56. The remaining 10 values of $CV_{\%}$ that were 57 or greater were all associated with metal concentrations less than 15 µg/L, reflecting the difficulty in obtaining analyses at these relatively low concentrations that were consistent among the 3 laboratories. Figure 7 reveals that, with the 2 equivocal exceptions, the agreement on the classification outcomes among the 3 laboratories is essentially independent of $CV_{\%}$, notwithstanding some relatively elevated values.

CONCLUSIONS

We set out to assess the interlaboratory reliability and precision of deriving GHS classification proposals based on data from the application of the UN T/DP for metals and sparingly soluble inorganic metal compounds to the reference substances Ni metal powder, Cu_2O powder, Co_3O_4 powder, and cuttings of an INVAR Ni–Co–Fe alloy, NILO K. As a measure of successful application of the T/DP to derive hazard classification proposals, we considered the complete agreement in the classification outcomes among all 3 participating laboratories.

We found that the T/DP was capable of measuring the rate and extent of release of metals from metal-bearing substances with a wide range of reactivities, from Cu_2O, which was the most reactive, to the NILO K alloy, which was the least reactive.

We also found that the T/DP could be applied to generate reliable results for each of the reference substances, and the T/D data could be linked to ERVs to yield consistent GHS hazard classification outcomes for each substance. As an indication of the robustness of the T/DP in generating data for the GHS, the 3 laboratories were in agreement in 46 of a possible 48 classification outcomes. The 2 remaining equivocal outcomes are the result of $CV_{\%}$ values overlapping measured concentrations and ERVs. These 2 equivocal outcomes occurred at metal concentrations close to the analytical limits of quantification. In the few equivocal cases that may arise in general practice, it might be advisable to re-examine the substance under T/D conditions with 5 or even 7 test vessels, in order to provide a more robust statistical analysis and reduce the values of $CV_{\%}$. We also recommend that the analytical limit of detection be developed to ensure that it is a factor of 10 less than the chronic ERV. We observed that the metal substances exhibited a range of reactivities (as expected). It is important to note that the alloy released significantly less metal into solution than when the same metal substances were tested in a nonalloyed form.

This study revealed that properly equipped and operated laboratories can apply the UN T/DP to metal-bearing substances to yield acute and chronic aquatic classification outcomes that are reliable, consistent, and in agreement.

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