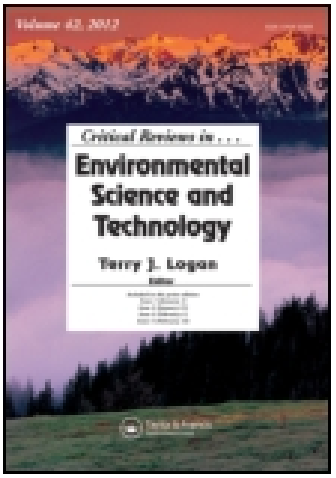

Critical Reviews in Environmental Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/best20

Critical Review: Toxicity of Dietborne Metals to Aquatic Organisms

David K. DeForest[a] & Joseph S. Meyer[b]
[a] Windward Environmental, Seattle, Washington, USA
[b] ARCADIS U.S., Inc., Lakewood, Colorado, USA
Accepted author version posted online: 10 Sep 2014.Published online: 10 Sep 2015.

To cite this article: David K. DeForest & Joseph S. Meyer (2015) Critical Review: Toxicity of Dietborne Metals to Aquatic Organisms, Critical Reviews in Environmental Science and Technology, 45:11, 1176-1241, DOI: 10.1080/10643389.2014.955626

To link to this article: http://dx.doi.org/10.1080/10643389.2014.955626

Critical Reviews in Environmental Science and Technology, 45:1176–1241, 2015

ISSN: 1064-3389 print / 1547-6537 online
DOI: 10.1080/10643389.2014.955626

Critical Review: Toxicity of Dietborne Metals to Aquatic Organisms

DAVID K. DeFOREST[1] and JOSEPH S. MEYER[2]
[1]*Windward Environmental, Seattle, Washington, USA*
[2]*ARCADIS U.S., Inc., Lakewood, Colorado, USA*

This paper reviews dietborne toxicity of 13 metals (Ag, Al, As, B, Cd, Co, Cr, Cu, Mo, Ni, Pb, V, Zn) to aquatic biota. Of those, Ag, As, Cd, Cu, Ni, and Zn have caused dietborne toxicity in laboratory exposures when the dietborne concentrations resulted from exposure of the food to waterborne concentrations near toxicity thresholds. To facilitate merging this laboratory-based effects information with realistic exposure scenarios, concentrations of metals in water and food items should be surveyed in a variety of real-world freshwater and saltwater systems to determine dietborne:waterborne metal ratios and the chemical forms in which the metals occur.

KEY WORDS: dietborne exposure, metals, toxicity

1. INTRODUCTION

For at least four decades, researchers have investigated the uptake and toxicity of metals in the diets of aquatic organisms (Mount, 2005). Although a variety of metals and aquatic organisms have been tested in laboratory and field studies in freshwater or saltwater systems (Handy et al., 2005; Schlekat et al., 2005), the results are still equivocal. It is clear that diet can be an important metal-exposure pathway in aquatic organisms (Luoma and Rainbow, 2008), and diet is the predominant source of metal to some marine predators such as gastropods and fish (Wang, 2013a). However, bioaccumulation of metals by an aqueous or dietary pathway does not necessarily result in toxicity (Luoma and Rainbow, 2005; Adams et al., 2011). In some studies, dietborne metals have caused toxicity at concentrations that occur in the

Address correspondence to David K. DeForest, Windward Environmental, LLC, 200 W. Mercer Street, Suite 401, Seattle, WA 98119, USA. E-mail: DavidD@windwardenv.com

environment; whereas in other studies, toxicity of dietborne metals has not been demonstrated or has appeared to be minor compared to contributions from waterborne metals. Until recently, the most comprehensive review of dietborne-metal toxicity to aquatic organisms was conducted in 2002 and were the results reported in Meyer et al. (2005a). At that time, the reasons for differences among experimental results were uncertain. However, a number of new and potentially key dietborne-metal studies have been published since then. Additionally, Wang (2013a) recently published a narrative, study-by-study analysis of key papers related to dietborne-metal toxicity and future research needs. Supplementing that review, the current paper includes a meta-analysis of a more extensive set of dietborne-metals toxicity literature, identifies remaining uncertainties, and recommends research needed to help decrease those uncertainties.

Investigations of the fate and effects of dietborne metals began with Hg and Se in the 1970s (Matida et al., 1971; Goettl and Davies; 1978; see also reviews in Adams et al., 2005; Handy et al., 2005). However, the dietborne toxicity of other metals was not a major concern until the 1990s and early 2000s (Mount, 2005), when several research groups reported dietborne-metal toxicity to fish and invertebrates in freshwater and saltwater systems (e.g., Woodward et al., 1994, 1995; Hook and Fisher, 2001a, 2001b). Those papers led to numerous studies that continue to investigate accumulation and toxicity of several trace elements (e.g., Ag, As, Cd, Cu, Ni, Pb, Zn) from the diet. Additionally, several types of biodynamic models have been developed to describe the fate and effects of metals in aquatic organisms during dietborne exposure (e.g., Wang and Fisher, 1999; Steen-Redeker and Blust, 2004; Steen-Redeker et al., 2004; Luoma and Rainbow, 2005). That flurry of research and modeling activity and associated concerns about potential ecological risk and regulatory implications spurred the convening of a Society of Environmental Toxicology and Chemistry (SETAC) Pellston Workshop about the toxicity of dietborne metals to aquatic organisms in 2002, during which the most recent comprehensive reviews of the dietborne-metals literature were conducted (Meyer et al., 2005a).

At the time of the 2002 SETAC Pellston Workshop, it was clear that the dietborne-exposure route for at least some metals needs to be considered in (1) evaluating the potential risks posed by those metals in the environment and (2) developing regulatory criteria or guidelines for those metals in aquatic systems. For example, diet is recognized as the most significant exposure pathway for the toxicity of some metals and metalloids like Hg and Se (Wang, 2002; Adams et al., 2005; Chapman et al., 2010); and currently, Hg and Se are the two trace elements for which regulatory actions are primarily being based on dietborne exposure (USEPA, 1997a, 1997b, 2004). However, for cationic metals such as Ag, Cd, Cu, Ni, Pb, and Zn, the toxicological and ecological significance of the dietborne-exposure route is still not always clear. Since 2002, new studies have continued to investigate

the potential dietborne-pathway effects of some of the more-well-studied cationic metals (e.g., Bielmyer et al., 2006; Kolts et al., 2009), and new concerns have emerged for other metals such as As (e.g., Hansen et al., 2004; Erickson et al., 2010). In addition, the higher sensitivity of at least some insect taxa in field-based metal exposures relative to their sensitivity in standard waterborne-metal exposures in the laboratory might in part be due to exposure to dietborne metals in the field (Buchwalter et al., 2007; Brix et al., 2011). Evaluated together, these and other new studies might help place the mechanisms, role, and significance of dietborne-metal toxicity in a clearer perspective.

The following is an update and review of the current understanding of dietborne-metal toxicity. This review consists of two phases. In the first phase, a comprehensive database of dietborne-metal toxicity data are presented; in the second phase, that database is interpreted to address the question of whether water quality guidelines or criteria for metals are underprotective because they do not explicitly account for the dietborne-exposure pathway (see also Wang, 2013a). This latter question is emphasized because it is commonly raised by regulators and thus has important implications for ecological risk assessments, product registration, and guideline or criteria development.

2. MATERIALS AND METHODS

2.1 Phase 1: Development of a Dietborne-Metals Toxicity Database

The dietborne-metals database in the present study builds upon the dietborne-metals toxicity data compiled in Handy et al. (2005), which included 35 publications related to the effects of dietborne metals on the physiology, survival, growth, and reproduction of aquatic organisms (i.e., the effects of primary interest in the current evaluation). The expanded database includes data published since the workshop held in 2002 as well as some older data that were not included in Meyer et al. (2005a). Literature searches were conducted using the Scirus search engine (key words included the metals of interest, toxicity, response, effects, impairment, diet, dietary, dietborne), and dietborne-metal toxicity data were also identified in the US Environmental Protection Agency's (US EPA's) ECOTOX database. The reference sections of papers that were reviewed also led to additional dietborne-metal toxicity papers, and relevant studies were obtained from scientists actively conducting research in the field of dietborne-metal toxicology. This review focused on toxicity endpoints related to survival, growth, development, reproduction, and feeding rate. Review of the physiological effects of dietborne metals was beyond the scope of this evaluation, but overviews can be found in Campbell et al. (2005), Clearwater et al. (2005), and Handy et al. (2005). Although toxicity of dietborne metals was the main focus of our

review, accumulation and toxicity of dietborne metals are intricately linked. Therefore, the following important question was addressed, to try to link accumulation and toxicity: Is dietborne-metal accumulation a strong predictor of dietborne-metal toxicity?

The 13 metals (and metalloids) included in the evaluation are Ag, Al, As, B, Cd, Co, Cr, Cu, Mo, Ni, Pb, V, and Zn. Mercury and Se have recently been reviewed extensively elsewhere (Chapman et al., 2010; Depew et al., 2012) and thus are not included here. Although As and Se are not classified as metals by chemists, they are often included under the umbrella term "metals" in the ecotoxicological literature, and that tradition is followed in this review.

Dietborne-toxicity studies of individual metals and metals mixtures were compiled separately. The database of dietborne toxicity of individual metals was developed in Microsoft Excel® and included the following fields: test species, species type (arthropod, mollusc, fish, etc.), water type [freshwater or saltwater (including estuarine and marine)], age or size of organism at test initiation, exposure duration, diet type (formulated, algae, etc.), dietborne-metal concentration(s), corresponding waterborne-metal concentration(s) (if applicable and/or available), biological endpoint (survival, growth, reproduction, etc.), and toxicity effects data. With the exception of Co, for which only dietborne acute toxicity data were available, chronic dietborne toxicity data were compiled (durations ranged from 4 week to several months for fish and were on the order of weeks for most invertebrate species). Each row in the database describes a single treatment from a toxicity test, and it is noted whether the dietborne-metal treatment resulted in a statistically significant effect relative to the control. In the cases in which statistical significance was not reported, an effect greater than 20% relative to the control was considered "significant" and an effect less than 20% relative to the control was considered "not significant." Although this "operational" choice of significance is somewhat arbitrary, it is consistent with the use of a 20–25% threshold for biologically important differences from control responses in waterborne toxicity tests and allowed discussion of some results for which no clear-cut statement about dietborne-metal toxicity was made by the study authors (e.g., adverse effects could not have been plotted in Figure 1). In addition, for dietborne-toxicity tests in which the metal in the food source was accumulated from water, water chemistry parameters were compiled so the waterborne-metal concentrations could be compared to hardness- or biotic ligand model (BLM)-based ambient water quality criteria (AWQC), probable no effect concentrations (PNECs), or other guideline values, in order to evaluate whether these values would be protective against dietborne-metal toxicity. Unlike Clearwater et al. (2002), we did not derive daily dietborne-metal doses for the toxicity data compiled, because that effort was beyond the scope of this review.

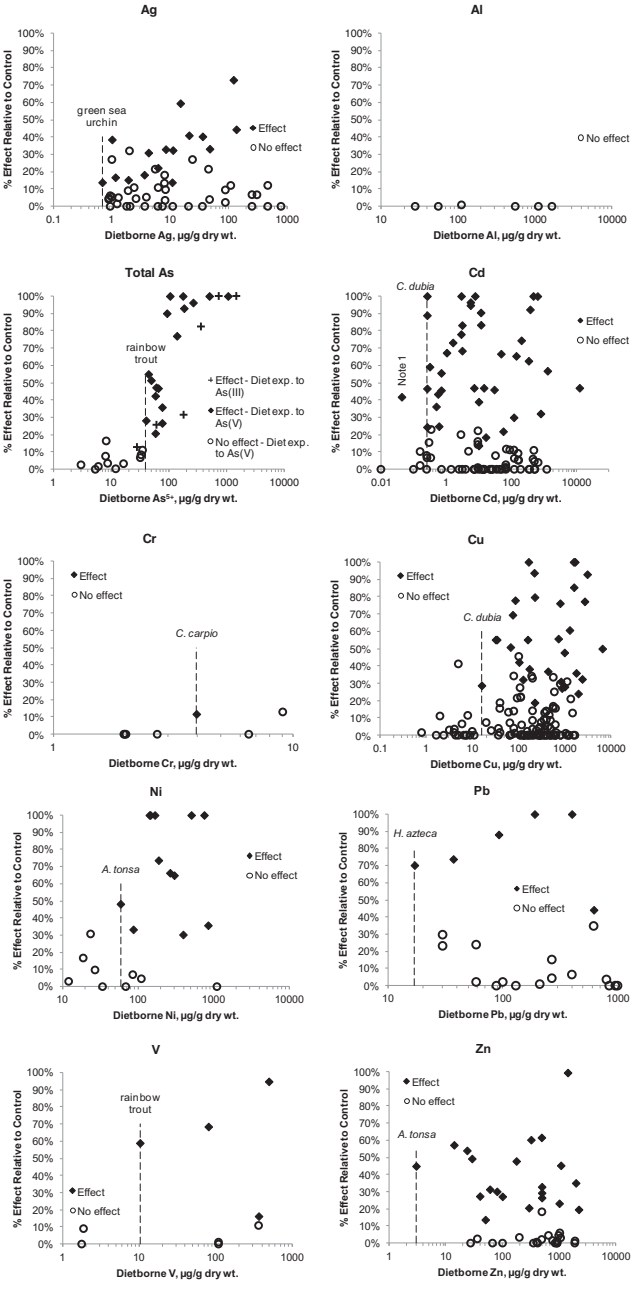

FIGURE 1. Plots of dietborne-metal concentrations associated with significant effects and no significant effects relative to the control based on chronic exposures. Vertical dashed line is the lowest effect concentration, and the associated species is noted. Note 1: For Cd, the lowest dietborne effect concentration of 0.043 μg/g dry wt is for the mayfly *Centroptilum triangulifer* (Xie et al., 2010); however, in two additional tests, dietborne Cd concentrations much greater than this were found to have no significant effects on the mayfly.

The database is included as Table S1 in the Supplemental Material online. Overall, 115 studies were reviewed in developing the dietborne-metals toxicity database for individual metals. The dietborne-metals toxicity database for metals mixtures was compiled separately, with similar information provided. Ten dietborne-toxicity studies with metals mixtures were identified.

2.2 Phase 2: Synthesis and Interpretation of Dietborne-Metals Toxicity Data

The dietborne-metals database was then summarized to describe the amount of toxicity data identified for each metal and the representativeness in terms of the diversity of taxa tested and types of endpoints evaluated. General trends were investigated, such as categories of metals for which dietborne toxicity appeared to be potentially more important or less important than waterborne toxicity, and whether some species or taxa appeared to be more susceptible or less susceptible to dietborne-metal toxicity.

In addition, for dietborne-toxicity studies in which the metal concentrations in a natural diet were caused by the exposure to waterborne metals, the toxicity threshold was compared to existing acute and chronic AWQC or PNECs to evaluate whether those regulatory concentrations are protective against dietborne-metal toxicity. To the extent such data were available, we also evaluated whether there were relationships between the sensitivity of organisms to waterborne-metal exposures and the potential contribution of dietborne-metal toxicity.

The focus of this review was the risk assessment of dietborne metals, including potential implications for regulatory thresholds or guidance. Unless specifically relevant to this topic, this review does not provide details on the identified or hypothesized mechanisms of dietborne-metal toxicity. Readers are referred to the original studies for additional study-specific details, including discussions of mechanisms.

3. RESULTS AND DISCUSSION

3.1 Overview

Of the metals evaluated in this review, Cd, Cu, and Zn have clearly been the most extensively studied, while no to very few dietborne-toxicity studies were identified for Al, B, Co, Mo, Ni, and V (Table 1). The approaches for conducting dietborne-metal toxicity tests are non-standardized, with methods instead developed to answer the specific research questions being asked. In total, dietborne-toxicity data for individual metals were compiled from 115 studies (Table 1). Of those studies, 58% evaluated dietborne-metal toxicity

TABLE 1. Summary of dietborne-metal toxicity studies as a function of diet type, diet-spiking method, and whether test organisms were simultaneously exposed to waterborne metals (studies can fall under more than one category)

Diet type / metals dietborne loading method	Exposure (diet only or diet+water)[a]	Single or mixed species diet	Test species	Al	Ag	As	B	Cd	Co	Cr	Cu	Mo	Ni	Pb	V	Zn	References
			Total no. of study and species combinations[b]:	3	8	6	0	41	3	4	47	0	5	9	3	18	
Formulated diets																	
Spiked	Diet only	—	*Acanthopagrus schlegelii schlegelii* (seabream)								X						Dang et al. (2012b)
			Achatina achatina (snail)											X			Ebenso and Ologhobo (2009)
			Anguilla japonica (Japanese eel)	X													Park and Shimizu (1989)
			Carassius auratus gibelio (Prussian carp)					X									Szczerbik et al. (2006)
			Catla catla (Indian carp)						X								Yaqub and Javed (2012)
			Chelon labrosus (grey mullet)								X						Baker et al. (1998)
			Cirrhina mrigala (mrigal)						X								Yaqub and Javed (2012)
			Clarias gariepinus (African walking catfish)								X						Hoyle et al. (2007)
			Coregonus clupeaformis (lake whitefish)										X				Ptashynski et al. (2002)
			Cyprinus carpio (common carp)							X							Ahmed et al. (2012)
			Cyprinus carpio (common carp)								X						Ajani and Akpoilih (2012)
			Cyprinus carpio (common carp)													X	Jeng and Sun (1981)
			Epinephelus malabaricus (grouper)								X						Lin et al. (2008)

Homarus americanus (lobster)[c]			X				Chou et al. (1987)
Ictalurus punctatus (channel catfish)					X		Murai et al. (1981)
Ictalurus punctatus (channel catfish)					X		Gatlin and Wilson (1986)
Labeo rohita (rohu)				X			Yaqub and Javed (2012)
Labeo rohita (rohu)					X		Jain et al. (1994)
Lateolabrax japonicus (Japanese seabass)			X				Mai et al. (2006)
Limanda limanda (dab)					X		Overnell and McIntosh (1988)
Lytechinus variegatus (green sea urchin)					X		Powell et al. (2010)
Neohelice granulata (crab)[d]					X		Sabatini et al. (2009)
Oncorhynchus kisutch (coho salmon)						X	Bowen et al. (2006)
Oncorhynchus kisutch (coho salmon)						X	Takeda and Shimma (1977)
Oncorhynchus kisutch (coho salmon)						X	Kjoss et al. (2006)
Oncorhynchus mykiss (rainbow trout)		X					Galvez and Wood (1999)
Oncorhynchus mykiss (rainbow trout)		X					Galvez et al. (2001)
Oncorhynchus mykiss (rainbow trout)	X						Handy (1993a)

(*Continued on next page*)

TABLE 1. Summary of dietborne-metal toxicity studies as a function of diet type, diet-spiking method, and whether test organisms were simultaneously exposed to waterborne metals (studies can fall under more than one category) (*Continued*)

Diet type / metals dietborne loading method	Exposure (diet only or diet+water)[a]	Single or mixed species diet	Test species	Al	Ag	As	B	Cd	Co	Cr	Cu	Mo	Ni	Pb	V	Zn	References
			Oncorhynchus mykiss (rainbow trout)			X											Cockell and Hilton (1988)
			Oncorhynchus mykiss (rainbow trout)			X											Cockell et al. (1991)
			Oncorhynchus mykiss (rainbow trout)			X											Cockell et al. (1992)
			Oncorhynchus mykiss (rainbow trout)			X											Cockell and Bettger (1993)
			Oncorhynchus mykiss (rainbow trout)					X									Handy (1993b)
			Oncorhynchus mykiss (rainbow trout)					X									Franklin et al. (2005)
			Oncorhynchus mykiss (rainbow trout)							X							Tacon and Beveridge (1982)
			Oncorhynchus mykiss (rainbow trout)								X						Knox et al. (1984)
			Oncorhynchus mykiss (rainbow trout)								X						Lanno et al. (1985a)
			Oncorhynchus mykiss (rainbow trout)								X						Lanno et al. (1985b)
			Oncorhynchus mykiss (rainbow trout)								X						Julshamn et al. (1988)
			Oncorhynchus mykiss (rainbow trout)								X						Handy (1993b)
			Oncorhynchus mykiss (rainbow trout)								X						Handy et al. (1999)
			Oncorhynchus mykiss (rainbow trout)								X						Kjoss et al. (2006)

Oncorhynchus mykiss (rainbow trout)			X			Kamunde et al. (2001)
Oncorhynchus mykiss (rainbow trout)			X			Kamunde and Wood (2003)
Oncorhynchus mykiss (rainbow trout)			X			Kjoss et al. (2005)
Oncorhynchus mykiss (rainbow trout)				X		Hodson et al. (1978)
Oncorhynchus mykiss (rainbow trout)				X		Ayyat et al. (2010)
Oncorhynchus mykiss (rainbow trout)					X	Hilton and Bettger (1988)
Oncorhynchus mykiss (rainbow trout)					X	Knox et al. (1984)
Oncorhynchus mykiss (rainbow trout)[e]	X					Ng et al. (2009)
Oncorhynchus tshawytscha (Chinook salmon)					X	Richardson et al. (1985)
Oreochromis niloticus × *O. aureus* (tilapia)		X			X	Shiau and Lin (1993)
Oreochromis niloticus (Nile tilapia)			X			Shaw and Handy (2006)
Oreochromis niloticus (Nile tilapia)				X		Dai et al. (2009)
Oreochromis niloticus (Nile tilapia)					X	Eid and Ghonim (1994)

(*Continued on next page*)

TABLE 1. Summary of dietborne-metal toxicity studies as a function of diet type, diet-spiking method, and whether test organisms were simultaneously exposed to waterborne metals (studies can fall under more than one category) (*Continued*)

Diet type / metals dietborne loading method	Exposure (diet only or diet+water)[a]	Single or mixed species diet	Test species	Al	Ag	As	B	Cd	Co	Cr	Cu	Mo	Ni	Pb	V	Zn	References
			Pelteobagrus fulvidraco (yellow catfish)					X									Tan et al. (2010)
			Rana sphenocephala (leopard frog)												X		Rowe et al. (2009)
			Salmo salar (Atlantic salmon)	X													Poston (1991)
			Salmo salar (Atlantic salmon)					X									Lundebye et al. (1999)
			Salmo salar (Atlantic salmon)					X									Berntssen et al. (2003)
			Salmo salar (Atlantic salmon)								X						Berntssen et al. (1999a)
			Salmo salar (Atlantic salmon)								X						Berntssen et al. (1999b)
			Salmo salar (Atlantic salmon)								X						Lundebye et al. (1999)
			Salmo salar (Atlantic salmon)													X	Maage and Julshamn (1993)
			Salmo salar (Atlantic salmon)					X									Berntssen and Lundebye (2001)
			Scophthalmus maximus (turbot)													X	Overnell et al. (1988)
			Sebastes schlegeli (rockfish)					X									Kim et al. (2004) and Kang et al. (2005)
			Sebastes schlegeli (rockfish)								X						Kim and Kang (2004) and Kang et al. (2005)
			Terapon jarbua (grunt)					X									Dang and Wang (2009)

	Diet + water (unmatched)[f]	-	*Danio rerio* (zebrafish)			X			Alsop et al. (2007)
			Morone chrysops×*M. saxatilis* (hybrid striped bass)			X			Bielmyer et al. (2005)
			Oncorhynchus kisutch (coho salmon)					X	Spry et al. (1988)
			Oncorhynchus mykiss (rainbow trout)			X			Kamunde et al. (2002)
Water	Diet + water (matched)[g]		*Hyalella azteca* (amphipod)				X		Besser et al. (2005)
Natural diets									
Water	Diet only	Single sp.	*Acartia* spp. (copepods)	X					Hook and Fisher (2001a)
			Acartia spp. (copepods)		X				Hook and Fisher (2001b)
			Acartia spp. (copepods)					X	Hook and Fisher (2002)
			Acartia tonsa (copepod)	X		X	X	X	Bielmyer et al. (2006)
			Acartia tonsa (copepod)			X			Lauer and Bianchini (2010)
			Anguilla anguilla (eel)		X				Haesloop and Schirmer (1985)
			Ceriodaphnia dubia (cladoceran)	X		X			Kolts et al. (2009)
			Ceriodaphnia dubia (cladoceran)		X				Sofyan et al. (2007a, 2007b)

(*Continued on next page*)

TABLE 1. Summary of dietborne-metal toxicity studies as a function of diet type, diet-spiking method, and whether test organisms were simultaneously exposed to waterborne metals (studies can fall under more than one category) (*Continued*)

Diet type / metals dietborne loading method	Exposure (diet only or diet+water)[a]	Single or mixed species diet	Test species	Al	Ag	As	B	Cd	Co	Cr	Cu	Mo	Ni	Pb	V	Zn	References
			Ceriodaphnia dubia (cladoceran)					X			X						Sofyan et al. (2006)
			Ceriodaphnia silvestrii (cladoceran)								X						Rodgher et al. (2009)
			Chaoborus punctipennis (phantom midge)					X									Munger and Hare (1997)
			Clarias spp. (catfish)					X									Ruangsomboon and Wongrat (2006)
			Crassostrea gigas (Pacific oyster)					X									Ettajani et al. (2001)
			Daphnia magna (cladoceran)					X									Ferard et al. (1983)
			Daphnia magna (cladoceran)								X						De Schamphelaere and Janssen (2004)
			Daphnia magna (cladoceran)								X						De Schamphelaere et al. (2007)
			Daphnia magna (cladoceran)										X				Evens et al. (2009)
			Daphnia magna (cladoceran)[h]										X				Evens et al. (2011)
			Daphnia magna (cladoceran)[h]										X				Evens et al. (2012a)
			Daphnia magna (cladoceran)													X	De Schamphelaere et al. (2004)
			Daphnia magna (cladoceran)													X	De Schamphelaere et al. (2008)
			Daphnia magna (cladoceran)		X												Zhao and Wang (2011)

Haliotis diversicolor (abalone)	X	X			Huang et al. (2010)
Hyalella azteca (amphipod)		X			Ball et al. (2006)
Ictalurus punctatus (channel catfish)		X	X	X	Erickson et al. (2010)
Lytechinus variegatus (green sea urchin)	X				Brix et al. (2012)
Moina macrocopa (cladoceran)		X			Hatakeyama and Yasuno (1981)
Moina mongolica (cladoceran)			X		Wang et al. (2007)
Moina mongolica (cladoceran)		X			Wang et al. (2010)
Oncorhynchus mykiss (rainbow trout)	X				Erickson et al. (2011)
Oncorhynchus mykiss (rainbow trout)		X			Ng and Wood (2008)
Oncorhynchus mykiss (rainbow trout)	X	X	X	X	Erickson et al. (2010)
Oncorhynchus mykiss (rainbow trout)				X	Wood and Alsop (2012)
Palaemonetes pugio (grass shrimp)		X			Wallace et al. (2000)
Peramphithoe parmerong (amphipod)			X		Roberts et al. (2006)

(*Continued on next page*)

TABLE 1. Summary of dietborne-metal toxicity studies as a function of diet type, diet-spiking method, and whether test organisms were simultaneously exposed to waterborne metals (studies can fall under more than one category) (*Continued*)

Diet type / metals dietborne loading method	Exposure (diet only or diet+water)[a]	Single or mixed species diet	Test species	Al	Ag	As	B	Cd	Co	Cr	Cu	Mo	Ni	Pb	V	Zn	References
			Pimephales promelas (fathead minnow)					X			X			X			Erickson et al. (2010)
			Poecilia reticulata (guppy)					X									Hatakeyama and Yasuno (1982)
			Poecilia reticulata (guppy)					X									Hatakeyama and Yasuno (1987)
			Thais clavigera (whelk)					X									Cheung et al. (2006)
		Mixed spp.	*Baetis tricaudatus* (mayfly)					X									Irving et al. (2003)
			Centroptilum triangulifer (mayfly)					X									Xie et al. (2010)
			Hyalella azteca (amphipod)					X									Golding et al. (2011)
	Diet + water (unmatched)[b]	Single sp.	*Americamysis bahia* (mysid)		X												Ward et al. (2006)
			Oncorhynchus mykiss (rainbow trout)			X											Erickson et al. (2011)
			Ceriodaphnia dubia (cladoceran)					X									Sofyan et al. (2007a, 2007b)
			Daphnia magna (cladoceran)					X									Geffard et al. (2008)
			Oncorhynchus mykiss (rainbow trout)					X			X			X		X	Mount et al. (1994)
			Pimephales promelas (fathead minnow)								X						Lapointe et al. (2011)
			Daphnia magna (cladoceran)													X	Evens et al. (2012b)

		Daphnia magna (cladoceran)				X	Evens et al. (2012c)
	Mixed spp.	*Hyalella azteca* (amphipod)	X				Golding et al. (2011)
Diet + water (matched)[c]	Single sp.	*Allorchestes compressa* (amphipod)	X	X		X	Ahsanullah and Williams (1991)
		Cyprinus carpio (common carp)[i]	X				Reynders et al. (2006)
		Acartia tonsa (copepod)		X			Pinho et al. (2007)
		Ceriodaphnia dubia (cladoceran)		X			Kolts et al. (2009)
		Daphnia magna (cladoceran)		X			De Schamphelaere and Janssen (2004)
		Oncorhynchus mykiss (rainbow trout)			X		Wood and Alsop (2012)

[a]In some diet-only exposures (e.g., Evens et al., 2009), the test organism was exposed only to dietborne metal, but the amount of metal that leached from the food into the water was measured and quantified.

[b]Note that some studies are repeated because they included multiple study designs. Kolts et al. (2009), for example, conducted both diet-only and diet+water toxicity tests.

[c]Lobsters in two treatments were provided a formulated diet, while the remaining treatments were provided a crab-based diet amended with vitamins and minerals.

[d]Diet was a combination of rabbit food and algae.

[e]Oligochaete worm pellets were amended with Cd.

[f]Test organism was exposed to a waterborne metal concentration that was different than what it's food item was exposed to.

[g]Test organism was exposed to the same waterborne metal concentration as what it's food item was exposed to.

[h]In some tests, *D. magna* were exposed to dietborne metal via liposomes mixed with a natural algae diet.

[i]Carp and its food were exposed to the same waterborne Cd concentrations except in the highest treatment, in which carp were exposed to a waterborne concentration of 480 μg Cd/L and its food was exposed to 105 μg Cd/L.

by spiking a metal into a formulated diet, whereas 42% evaluated dietborne-metal toxicity using a natural diet such as algae, periphyton, oligochaetes, or brine shrimp.

The majority of the studies that evaluated dietborne-metal toxicity via a natural diet were published since 2000, thus indicating an increased emphasis on understanding the bioavailability and toxicity of biologically incorporated metals. Of those natural-diet toxicity studies, only 13 evaluated simultaneous waterborne-metal exposures; and in only five was the test organism exposed to the same waterborne-metal concentration to which its food was exposed. The latter study design (i.e., exposure of the test organism to "matched" waterborne- and dietborne-metal concentrations) is perhaps most relevant for evaluating the protectiveness of waterborne-metal guidelines, because this is assumed to be a potentially conservative exposure scenario. However, some aquatic receptors might be exposed to non-equilibrated concentrations of metals in water and food. For example, an aquatic receptor might be simultaneously exposed to relatively low waterborne-metal concentrations and relatively high dietborne-metals concentrations that originated from historical sediment contamination; or conversely, an aquatic receptor might be simultaneously exposed to relatively high waterborne-metal concentrations and relatively low dietborne-metal concentrations, if the food item has only been exposed to the waterborne metals for a short time before it is eaten. In concept, these types of exposure scenarios can be accounted for in site-specific risk assessments, but appropriate data about the toxicity of metals in non-equilibrated food would be needed. More recently, some studies have evaluated dietborne-metal toxicity from mixed-species diets, such as complex periphyton communities (Xie et al., 2010). Recent studies have also evaluated the use of alternative dietborne-metal delivery methods, such as liposomes, to help compensate for the lost nutritional quality of food sources that are contaminated with metals (Evens et al., 2011, 2012a).

As a first step in the current review, dietborne-metal concentrations resulting in chronic effects and no effects relative to the control were plotted in Figure 1; and no short-term exposures were included in those plots, to avoid confounding interpretation of the meta-analyses with potential biases due to short exposure times that did not allow dietbore-metal effects to be manifested. Only data for dietborne-metal concentrations expressed on a dry-weight basis were plotted. Unfortunately, some dietborne-metal toxicity data were reported on a wet-weight basis for which the moisture content of the diet could not be reliably estimated, especially in formulated diets that can differ widely in moisture content among studies. These initial summary plots provide a snapshot of how much data are available for each metal and help to identify patterns that warrant further investigation. Not surprisingly, there is substantial overlap between effects and no-effects concentrations for most dietborne metals, because this undoubtedly in part reflects the differential sensitivity among the species included in the plots. However, that overlap

might also be due in part to differences in study design between tests, including diet types, dosages (i.e., daily ingestion rates of the metals), and whether there was simultaneous exposure to waterborne metal.

With the exception of Al, As, and V, the most sensitive species for most metals are small crustaceans (Cd, Cu—*Ceriodaphnia dubia*; Pb—*Hyalella azteca*; Ni, Zn—*Acartia tonsa*) or echinoderm larvae (Ag—*Lytechinus variegatus*). The dietborne-metal food sources in the toxicity studies with *A. tonsa*, *C. dubia*, *Daphnia magna*, *Ly. variegatus*, and rainbow trout (*Oncorhynchus mykiss*) were all based on biologically incorporated metal, in which the food source was exposed to waterborne metal. For As, chronic dietborne-toxicity data (from tests that used formulated and biologically incorporated diets) were only available for rainbow trout. For V, dietborne-toxicity data were only available for rainbow trout and southern leopard frog larvae (*Rana sphenocephala*), and no V studies were conducted with biologically incorporated metal. No adverse effects were observed in any of the dietborne-Al toxicity studies; and no dietborne-B or dietborne-Mo studies were found in the literature.

The following summarizes the dietborne-toxicity data identified for each of the metals in this review, including an overview of the amount and types of data. In addition, as data permit for each metal, comparisons of waterborne- versus dietborne-metal toxicity are provided, along with evaluations of whether water quality guidelines are protective against dietborne-metal toxicity. After the metal-by-metal summaries, observations across metals are synthesized, and recommendations for further research are provided.

3.2 Individual Metals

3.2.1 Aluminum

Dietborne-Al toxicity data were identified for only three species of freshwater fish, in experiments in which either Al chloride or Al sulfate was spiked into a formulated diet (Table 1). None of the dietborne-Al concentrations tested in the three species resulted in adverse effects on growth or survival (Supplemental Data Table S1); hence, over the range of dietborne-Al concentrations tested, no concentration–response relationship can be derived. In Atlantic salmon (*Salmo salar*), no significant effects on weight gain over a 16-week exposure were observed up to a dietborne-Al concentration of 2232 μg/g dry wt, the highest concentration tested (Poston, 1991). Moreover, Handy (1993a) did not observe significant mortality in rainbow trout provided a higher dietborne-Al concentration of 10000 μg/g dry wt for 42 days. No studies were identified that systematically evaluated the relative toxicities of waterborne- and dietborne-Al toxicity during concurrent exposure.

None of the metal-mixture studies in which dietborne-Al concentrations were measured identified Al as a contributing factor to observed dietborne

toxicity (Woodward et al., 1994; Farag et al., 1999). However, much of the Al measured in those macroinvertebrate diets might have been in insoluble mineral forms that were not bioaccessible to the consumer in those studies (westslope cutthroat trout; *Oncorhynchus clarki lewisi*). That does not invalidate the potential utility of such a study for determining whether the diet is toxic, but it does mean that subtle contributions of bioaccumulated Al to dietborne-metal toxicity probably cannot usually be differentiated when feeding undepurated sediment-ingesting prey to a consumer. Rather than being an important contributor to dietborne toxicity, the magnitude of Al concentrations in the diet might be an indicator of mineral levels and hence the bioavailability of other metals in the diet. For example, Farag et al. (1999) measured concentrations of Al, Cu, Pb, Zn, and other metals in two field-collected macroinvertebrate diets that were then fed to westslope cutthroat trout. One of these diets ("South Fork") contained Al, Cu, Pb, and Zn concentrations that were 74%, 40%, 75%, and 10% greater than in the other diet ("Cataldo"). However, after 90-day feeding exposures, whole-body concentrations of Cu, Pb, and Zn in trout fed the Cataldo diet were, respectively, 37%, 37%, and 49% greater than the concentrations in trout fed the South Fork diet. Farag et al. (1999) suggested that the higher Al concentration in the South Fork diet was due to undigested material in the South Fork invertebrates, which provides a bioavailability-based explanation why metals crossed the small intestine of the trout less efficiently from the South Fork diet than from the Cataldo diet.

Based on the limited data available, dietborne-Al toxicity to fish appears to be low and unlikely to be of concern. However, this does not preclude the possibility of dietborne-Al toxicity in invertebrates, which currently is an important data gap that should be addressed. In addition, it is unknown whether the dietborne toxicity of biologically incorporated Al would differ from that observed in the toxicity studies using formulated diets spiked with Al salts. Because the biogeochemistry of Al is complex, with site-specific water chemistry influencing the bioavailability and bioaccumulation potential of Al (Gensemer and Playle, 1999), more research is needed to evaluate whether specific water chemistry conditions favor the bioaccumulation of Al that is then potentially bioavailable to consumer organisms.

As an example of the potential for Al bioaccumulation in food webs, Oberholster et al. (2012) reported that Al concentrations in filtered (1 μm) water from Lake Loskop (South Africa), which has elevated Al concentrations from historical mining, ranged from 60 to 90 μg/L (a range bracketing the USEPA [2009] chronic freshwater criterion of 87 μg/L). In the food web, Al concentrations (μg/g dry wt) ranged from 3,111 to 18,997 in phytobenthos, from 121 to 1,579 in phytoplankton, and from 24 to 386 in undepurated macroinvertebrates. However, it is possible that the algae samples might also have included cofiltered sediment particles. This demonstrates the extreme variability in Al concentrations that can occur in natural food webs.

Given that Al concentrations in at least some food-web components can exceed the highest Al concentrations that have been evaluated in dietborne-Al toxicity tests, more research is needed to fully understand the potential for dietborne-Al toxicity and the conditions under which it might be of concern. Additionally, when possible, Al concentrations should be measured in depurated and undepurated animals so bioaccumulation of Al can be evaluated in depurated animals and the potential for trophic transfer of Al can be evaluated in undepurated animals.

3.2.2 Arsenic

Most of the dietborne-toxicity studies with As, either in chronic "As-only" studies or in metal-mixture studies, have been conducted with fish. Of the six "As-only" studies identified in this review, all were conducted with rainbow trout (Table 1). From those six studies, dietborne-toxicity data are available from studies in which food items exposed to waterborne arsenite [As(III)] and arsenate [As(V)] and from studies that used formulated and natural diets (Supplemental Data Table S1). There is a clear concentration–response relationship for dietborne toxicity of total As [whether the food was exposed to waterborne As(III) or As(V)], even when pooling data from multiple studies and diet types (Figure 1). The lowest total-As dietborne concentrations that caused significant effects relative to the control were 28 and 40 μg/g dry wt in food exposed to waterborne As(III) and waterborne As(V), respectively (Figure 1; Supplemental Data Table S1).

Several of the early dietborne-toxicity studies in which As was a constituent of potential concern were conducted using metal mixtures in invertebrates obtained from, or representative of, the Clark Fork River, Montana, USA (Woodward et al., 1994, 1995; Hansen et al., 2004). In addition to As, key metal constituents in the Clark Fork River invertebrates included Cd, Cu, Pb, and Zn. Woodward et al. (1994, 1995) observed significant effects on growth of rainbow trout and brown trout (*Salmo trutta*) when fed a diet of macroinvertebrates collected from the Clark Fork River, and Hansen et al. (2004) observed significant growth effects when rainbow trout were fed oligochaetes that were cultured in Clark Fork River sediment (Supplemental Data Table S2).

To evaluate the causative agent for the dietborne-metal toxicity observed in the Clark Fork River studies, Erickson et al. (2010) determined the individual toxicities of dietborne As, Cd, Cu, and Zn to juvenile rainbow trout via a diet of live oligochaetes (*Lumbriculus variegatus*). Because rainbow trout growth decreased in a dose-dependent manner when dietborne-As concentration was the predictor of toxicity, those authors concluded that the toxicity observed in the earlier Clark Fork River studies is likely attributable to As. In a follow-up study, Erickson et al. (2011) evaluated the relative toxicity of As(V) to juvenile rainbow trout via water and a live *Lu. variegatus* diet. Overall, growth effects were greater when trout and its oligochaete prey

were exposed to the same waterborne As(V) concentration than when trout were exposed to waterborne As(V) alone.

The lowest total-As dietborne concentrations of 28 and 40 μg/g dry wt that resulted in significant toxicity (decreased growth) relative to the controls were from Erickson et al. (2010) for food exposed to waterborne As(III) or As(V), respectively. However, because both of those treatments were the lowest dietborne-As concentration tested in their respective experiments, the threshold concentrations for dietborne-As(III) and/or dietborne-As(V) toxicity might be lower. In Erickson et al. (2010, 2011), the waterborne-As concentrations to which the live diet was exposed (490–8700 μg As/L) were greater than the USEPA [2009] acute and chronic As criteria (340 and 150 μg As/L, respectively).

The dietborne As concentration–response data for juvenile rainbow trout reported in Cockell and Hilton (1988) and Cockell et al. (1991, 1992) based on formulated diets are consistent with the concentration–response data reported in Erickson et al. (2010, 2011) based on a *Lu. variegatus* diet (which are pooled in Figure 1). In all of these studies, dietborne As treatments that resulted in significant growth reductions in rainbow trout were associated with a reduction in feeding rate. The lowest total-As dietborne concentrations that resulted in significant growth reduction in rainbow trout were 28 and 40 μg/g dry wt for food exposed to waterborne As(III) and As(V), respectively, whereas Zhang et al. (2012) did not observe any significant growth effects in marine juvenile grunt (*Terapon jarbua*) exposed to dietborne As(III) or As(V) concentrations up to 500 μg/g dry wt in a formulated diet for 10 days (data not included in Figure 1 because not a truly chronic exposure). The absence of dietborne-As toxicity in Zhang et al. (2012) was most likely due to the relatively short exposure duration of 10 days, but it might also reflect a difference in species and/or physiology (e.g., freshwater vs. saltwater fish, and possibly faster detoxicification of As by the grunts).

Unfortunately, As speciation in the food has only been determined in one dietborne-As study (Erickson et al., 2011, p. 112). Those authors reported

> absorbed arsenate [As(V)] is largely reduced to arsenite [As(III)], with extracts ranging from 75% to 88% arsenite ($n = 3$), but there was no measurable conversion to organoarsenic species. This conversion from arsenate to arsenite by oligochaetes would explain our earlier findings (Erickson et al., 2010) that growth reductions in fish occurred at similar concentrations of total arsenic in the oligochaete diet whether the oligochaetes had been exposed to arsenite or arsenate.

Therefore, an among-study meta-analysis of the concentration–response relationship between percent effects and dietborne-As concentration is only currently possible for total-As concentration in diets, as in Figure 1. In the future, researchers should speciate the As in food items to help determine

what As species in the food might be contributing to dietborne As toxicity (regardless of the chemical form of As in the water to which the food was exposed).

In addition to the Woodward et al. (1994, 1995) and Hansen et al. (2004) studies noted above, several other studies of the toxicity of dietborne-metal mixtures to fish had As concentrations within the range of effect concentrations reported by Erickson et al. (2010, 2011), including Farag et al. (1999), Boyle et al. (2008), and Dang et al. (2012a), as well as one dietborne-toxicity study with a saltwater shrimp (Rainbow et al. 2006). The combination of data from laboratory studies and field-based metal-mixture studies strongly suggests that analyses of As (including its oxidation state in the diet and the consumer) should be included in evaluations of field-based dietborne-As toxicity studies, even if the waterborne As concentrations to which the food items were exposed appear to be relatively low compared to thresholds for waterborne-As toxicity. For field-collected diets, the speciation should include differentiation between mineral and labile forms of As.

Overall, at least based on toxicity data for rainbow trout, it is apparent that assessment of risks from As exposures is incomplete without considering dietborne exposures (Erickson et al., 2011). Furthermore, it is apparent that As is potentially an important metal to consider when evaluating the toxicity of dietborne-metal mixtures. Currently, there is a data gap in dietborne-As toxicity studies with invertebrates that should be filled in order to evaluate whether any invertebrate species are more sensitive than the fish tested to date.

3.2.3 Boron

No dietborne-B toxicity studies have been conducted for strictly aquatic organisms, such as aquatic invertebrates and fish. Although some studies have evaluated the effects of dietborne-B concentration on frog development, they generally focused on B deficiency. For example, tail resorption was delayed in frogs (*Xenopus laevis*) provided a B-deficient diet containing 0.062 μg B/g compared to frogs fed a diet containing 1.85 μg B/g (Fort et al., 1999). Similarly, highly specific forelimb and hindlimb defects occurred in *X. laevis* larvae fed a B-deficient diet containing 0.045 μg B/g, but no limb defects or other effects occurred in larvae fed a B-supplemented diet containing 1.85 μg B/g (Fort et al., 2000).

For comparison, although not strictly aquatic, dietborne-B toxicity has been investigated in aquatic birds, such as mallards (*Anas platyrhynchos*). Stanley et al. (2006) reported adverse effects on egg weight, egg fertility, and hatching success in adult mallards that were provided a diet supplemented with 900 μg B/g, whereas a diet supplemented with 450 μg B/g did not cause adverse effects. To put those dietborne-B concentrations in context, Saiki et al. (1993) reported a maximum B concentration of 280 μg/g in the food chains of the lower San Joaquin River and its tributaries, which

were considered to have elevated B concentrations. An important question is whether that B concentration can result in dietborne toxicity. The sites in the Saiki et al. (1993) study with the highest B concentrations in detritus and algae had waterborne-B concentrations ranging between 1000 and 2000 μg/L, although elevated B concentrations in algae were also sometimes associated with lower waterborne-B concentrations. For example, one site had a waterborne-B concentration of 120 μg/L with a corresponding B concentration of 92 μg/g dry wt in filamentous algae. Because 120 μg/L is generally considered a safe waterborne B concentration (Loewengart, 2001), an important question is whether dietborne-B concentrations on the order of 92 μg/g dry wt could cause toxicity to strictly aquatic species. This currently represents a data gap. Given that the highest B concentrations in the Saiki et al. (1993) study were measured in detritus and filamentous algae, with concentrations generally decreasing as trophic level increased, it appears that the potential for dietborne-B toxicity would be greatest with primary consumers if primary consumers are generally as sensitive or more sensitive than species in other trophic levels. Therefore, toxicity of diets containing B-contaminated algae and/or plants to invertebrate consumers should be the focus of future dietborne-toxicity studies with B.

3.2.4 Cadmium

Thirty-seven dietborne-Cd toxicity studies were identified, including data for 17 freshwater species (7 invertebrate species and 10 fish species) and 11 saltwater species (8 invertebrate species and 3 fish species) (Table 1). The lowest unequivocal lowest observed effects concentration (LOEC) for dietborne-Cd toxicity is 0.495 μg/g dry wt, based on decreased growth of *H. azteca* provided a Cd-contaminated diet (Ball et al., 2006; Figure 1; Supplemental Data Table S1). In that study, a clear concentration–response relationship between dietborne-Cd concentrations and the wet weight of *H. azteca* was observed; however, Cd concentrations in *H. azteca* did not consistently increase as dietborne-Cd concentration increased (Figure 2). Ball et al. (2006) speculated that the lack of Cd bioaccumulation in *H. azteca* might have been indicative of an indirect effect of Cd, such as behavioral avoidance of the algal food, or of decreased nutritional quality; but they ultimately concluded that they did not have the necessary information to differentiate between direct and indirect effects. As discussed later, similar patterns of apparent dietborne-metal toxicity are not always associated with an increase in the body burden of the metal in the test organism.

The cladoceran *C. dubia* has sensitivity to dietborne Cd similar to *H. azteca*, and there is likewise not a clear relationship between dietborne Cd concentrations, bioaccumulation, and toxicity. Sofyan et al. (2007a, 2007b) fed Cd-contaminated algae (*Pseudokirchneriella subcapitata*) to *C. dubia* in two different tests. In one test, *C. dubia* were exposed only to a series of dietborne-Cd concentrations; while in the other test, *C. dubia* were provided

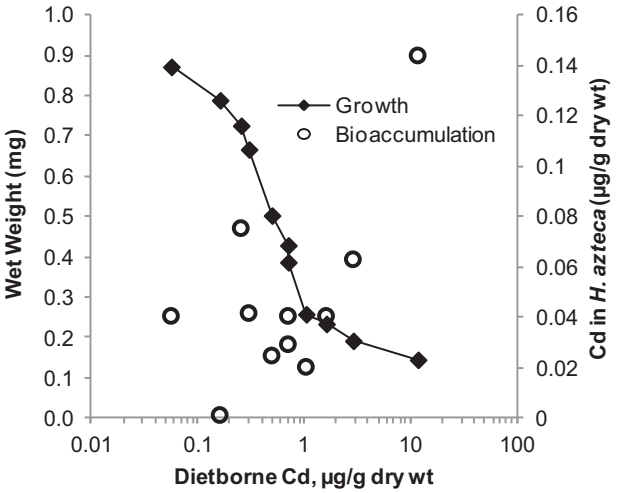

FIGURE 2. Concentration–response relationship for *Hyalella azteca* exposed to dietborne Cd. Data from Ball et al. (2006).

a dietborne-Cd concentration of 0.26 μg/g dry wt along with corresponding waterborne Cd concentrations ranging from 1.1 to 20 μg/L (Supplemental Data Table S1). In a third test, *C. dubia* were only exposed to waterborne Cd. Traditional sigmoid concentration–response relationships based on reproductive toxicity as a function of whole-body Cd concentration in the *C. dubia* were observed in the waterborne-only and waterborne + dietborne-Cd exposures, but not entirely in the dietborne-only Cd exposure (Figure 3). Likewise, whole-body Cd concentrations in *C. dubia* did not increase with

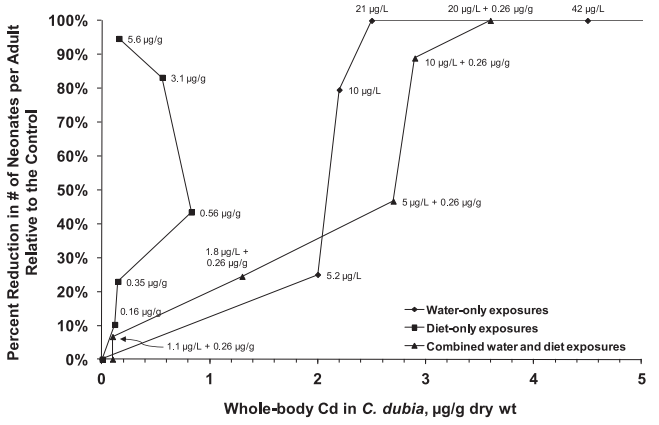

FIGURE 3. Concentration–response relationships for *Ceriodaphnia dubia* exposed to Cd via water only, diet only, and water + diet. Exposure concentrations in water (μg/L) and diet (μg/g) are shown beside the data points. Data from Sofyan et al. (2007a).

each increasing dietborne-Cd concentration (Figure 3). In the dietborne-only Cd test, both reproductive effects and whole-body Cd concentrations increased in the three lowest treatments; whereas in the two highest treatments, reproductive effects increased but the whole-body Cd concentrations decreased (Figure 3). The authors reported a statistically significant ($p < .05$) decrease of the feeding rate at the two highest dietborne-Cd treatments relative to the control, with the effect of Cd on the feeding rate resulting in an indirect effect on reproduction. It is also important to note that the dietborne-Cd concentrations were obtained by exposing algae to waterborne-Cd concentrations of 5.22–61.33 μg/L, which are much greater than the acute and chronic freshwater criteria concentrations of 2.0 and 0.25 μg Cd/L at the nominal reported exposure-water hardness of 100 mg/L as $CaCO_3$ (USEPA, 2001).

Although Sofyan et al. (2007a, 2007b) evaluated chronic Cd toxicity to *C. dubia* via water-only, diet-only, and a combined water + diet exposure, relative Cd toxicity from the three exposure routes could not be compared across the full range of exposure concentrations because the series of waterborne-Cd concentrations was not used to generate dietborne-Cd concentrations for the diet-only and combined water + diet exposures. However, specific treatments could be compared when the waterborne- and dietborne-Cd concentrations were similar (i.e., 4.63–5.22 μg/L in water and 0.26–0.33 μg/g dry wt in the diet; see Figure 7 in Sofyan et al. [2007b]). At those concentrations, reproduction significantly ($p < .05$) decreased in the combined water + diet Cd exposure compared to the water-only and diet-only Cd exposures. In order to better understand the relative toxicity of waterborne and dietborne Cd to *C. dubia*, or other aquatic species, studies are needed in which a common series of waterborne-Cd concentrations is used for both direct waterborne exposures and generation of dietborne-Cd concentrations.

A lower LOEC was identified from other studies, but the reported effects could not be unequivocally attributed to dietborne Cd. For example, a dietborne-Cd concentration as low as 0.043 μg/g dry wt in periphyton was associated with adverse effects when fed to the mayfly *Centroptilum triangulifer* (Xie et al., 2010). However, that study included experiments conducted with natural periphyton grown in three different seasons, with highly variable results reported among experiments and/or seasons. For example in one season (Summer), a waterborne Cd concentration of 0.1 μg/L resulted in a periphyton Cd concentration of 0.043 μg/g dry wt, which corresponded to 57% mayfly survival compared to 98% survival in the controls. Yet in another of those three seasons (Winter), a Cd concentration of 10 μg/L resulted in a Cd concentration of 7.6 μg/g dry wt in periphyton, which corresponded to 75% mayfly survival compared to a mean of 60% survival in the controls. Therefore, there was sufficient variability in the data that neither a waterborne- or a dietborne-Cd effect threshold could be identified for the mayfly. The study by Xie et al. (2010) provides an example of the complexities of evaluating the effects of dietborne-metal exposures to natural

periphyton communities, which are highly complex and seasonally dynamic. However, the study generally demonstrates the importance of periphyton as a sink for Cd, and as a potentially important exposure source to many aquatic insect species.

In several studies, dietborne-Cd concentrations in live food organisms were obtained via exposure to waterborne-Cd concentrations (Supplemental Data Table S3). Those studies allow evaluation of whether existing waterborne guidelines (i.e., AWQC, PNECs) are protective against dietborne-Cd toxicity. Of the 12 freshwater and saltwater species for which this evaluation could be conducted, a marine copepod (*A. tonsa*) and marine cladoceran (*Moina monogolica*) are the only species for which the USEPA's chronic Cd criterion clearly appears to be under-protective of dietborne toxicity (Hook and Fisher, 2001b; Wang et al., 2010), because the waterborne-Cd concentrations that resulted in dietborne toxicity to the saltwater copepod and cladoceran were less than the USEPA's current saltwater chronic Cd criterion of 8.8 μg/L (USEPA, 2001). In addition, for two other species, a freshwater amphipod (*H. azteca*; Ball et al., 2006) and a saltwater amphipod (*Allorchestes compressa*; Ahsanullah and Williams, 1991), the waterborne-Cd concentrations that resulted in dietborne EC10s and EC20s bracketed the USEPA's chronic criteria.

Overall, the dietborne toxicity of Cd to both freshwater and saltwater invertebrate and fish species has been fairly well studied, including a number of studies that evaluated dietborne-Cd toxicity from live diets. However, additional studies are needed to fully elucidate the relative toxicity of waterborne- and dietborne-Cd in sensitive species and in paired experiments in which the test organism is exposed to the same series of Cd concentrations in the same exposure waters. In addition, in terms of evaluating whether waterborne guidelines are protective of dietborne-Cd toxicity, the data for Cd suggest that, when conducting such evaluations, it is equally important to consider whether the toxicity databases used to develop waterborne guidelines include toxicity data for species that are generally known or suspected to be sensitive to metals.

3.2.5 Chromium

Limited dietborne-Cr toxicity data are available for aquatic biota. Growth (weight gain) was significantly reduced in common carp (*Cyprinus carpio*) that were fed a dietborne-Cr(III) concentration of 3.95 μg/g dw for 8 weeks (Ahmed et al., 2012). For comparison, Tacon and Beveridge (1982) and Shiau and Lin (1993) likewise fed rainbow trout (*O. mykiss*) and tilapia (*Oreochromis niloticus* × *Oreochromis aureus*), respectively, formulated diets that were amended with Cr(III); neither study observed statistically significant ($p > .05$) effects on growth at the highest dietborne-Cr concentrations tested, which were 9.07 μg/g dry wt for rainbow trout and 2.01 μg/g dry wt for tilapia. Jain et al. (1994) fed rohu (*Labio rohita*) formulated diets containing nominal Cr concentrations of 10, 20, and

40 μg/g for 30 days, which resulted in 0%, 4%, and 13% reductions in growth (weight) compared to the control, respectively. However, the authors did not analyze statistical significance, Cr concentrations in the diet were not measured, and the form of Cr tested was not reported. The dietborne-Cr toxicity studies identified in this review were focused on the influence of Cr supplementation in formulated fish diets used in aquaculture; more research is needed on biologically incorporated dietborne-Cr toxicity to aquatic organisms in natural systems.

3.2.6 Cobalt

Few data are available regarding dietborne-Co toxicity to aquatic life. Yaqub and Javed (2012) evaluated the acute toxicity of dietborne-Co to three different ages (60, 90, and 120 days) of three carp species: Indian carp (*Catla catla*), rohu, and mrigal (*Cirrhina mrigala*). The diet was a crumbled feed spiked with $CoCl_2$, and the 96-h LC50 values ranged from 155 to 243 mg Co/g diet. Those results are notable for two reasons. First, lethality often is not reported in dietborne-metal studies, much less in only 96-h exposures; and second, the dietborne-Co LC50 values were extremely high (i.e., 15.5–24.3% by weight, which is much higher than most dietborne-metal concentrations). For comparison, the dietborne-Co requirement in fish is in the range of 0.05–1.0 μg Co/g dry wt of food (Watanabe et al., 1997). Research on chronic dietborne-Co toxicity is clearly needed.

3.2.7 Copper

Forty-two dietborne-Cu toxicity studies were identified, including 12 freshwater species (3 invertebrate species and 9 fish species) and 10 saltwater species (5 invertebrate species and 5 fish species) (Table 1). The lowest dietborne-Cu concentration associated with adverse effects was 15.9 μg/g dry wt in algae (*P. subcapitata*) fed to a cladoceran (*C. dubia*) (Sofyan et al., 2006; Figure 1; Supplemental Data Table S1). In fact, the most sensitive species to dietborne Cu that have been tested are small crustaceans (cladocerans, copepods, amphipods) or echinoderm larvae. Fish appear to be relatively insensitive to dietborne-Cu exposures, with the lowest LOEC being 760 μg/g dry wt fed to rainbow trout. This pattern of taxa sensitivity is consistent with the pattern of species sensitivity to waterborne Cu.

Although the lowest dietborne effects concentration for Cu was observed in *C. dubia*, the dietborne-toxicity data for this species is not consistent among studies. As shown in Figure 4, Sofyan et al. (2006) observed a clear relationship between increasing dietborne-Cu concentrations and impaired reproduction, whereas concentration–response relationships were not consistently apparent in the tests conducted by Kolts et al. (2009). In addition, *C. dubia* in the Kolts et al. (2009) tests were clearly less sensitive to dietborne Cu than in the Sofyan et al. (2006) test. The reason for the apparent discrepancy between the two studies is not entirely clear. Both studies used *P. subcapitata*

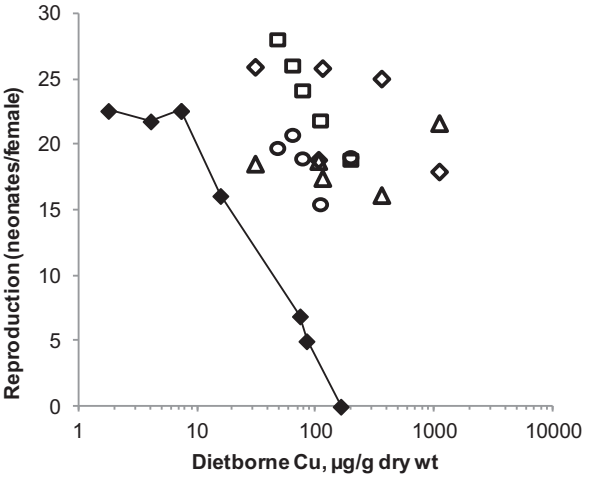

FIGURE 4. Concentration–response relationship for *Ceriodaphnia dubia* exposed to dietborne Cu only (i.e., no concurrent waterborne Cu exposure). Filled diamonds (♦) are from Sofyan et al. (2006) and based on continuous dietborne-Cu exposure. Open symbols are from Kolts et al. (2009): ◊ and □ = 4-hr dietborne exposure followed by feeding of uncontaminated algae and YCT during remainder of test; Δ and ○ = continuous dietborne exposure throughout test.

as the source of dietborne Cu, and both tested continuous dietborne Cu exposures (and Kolts et al. [2009] also tested a 4-h dietborne-Cu exposure followed by feeding with uncontaminated food for the remainder of the test). However, in comparing Sofyan et al. (2006) to the continuous dietborne-exposure tests in Kolts et al. (2009), one potentially important difference is that Sofyan et al. (2006) only fed Cu-contaminated algae (5×10^5 cells/mL) to their *C. dubia*, whereas Kolts et al. (2009) fed a combination of Cu-contaminated algae (2×10^5 cells/mL) plus an uncontaminated mixture of yeast, Cerophyl®, and trout chew (YCT) (0.013 mg solids/mL) to their *C. dubia*. It is possible that the dietborne Cu dose was greater in the Sofyan et al. (2006) test because *C. dubia* (1) were provided Cu-contaminated algae at a higher density and (2) were not able to preferentially feed on uncontaminated YCT. Sofyan et al. (2006) also measured feeding rate and whole-body Cu concentrations in the exposed *C. dubia*, which provides additional information on the Cu dose and dietborne exposure. Those data were not measured in Kolts et al. (2009), so it cannot be confirmed whether differences in the dietborne-Cu dose are responsible for the apparent discrepancy between results shown in Figure 4. This comparison highlights some of the complexities in comparing dietborne-metal toxicity data between studies and how differences in study designs might lead to different conclusions regarding dietborne-metal toxicity.

As noted above, Sofyan et al. (2006) also measured whole-body Cu concentrations in *C. dubia* that were fed dietborne Cu. Whole-body Cu

concentrations increased with increasing dietborne-Cu exposures for all but the highest dietborne treatment of 165 mg/kg dry wt, in which the Cu burden was less than even that in the control organisms. Overall, the relationship between reproductive impairment and a decline in the feeding rate was stronger than its relationship with whole-body Cu burdens. This is consistent with the Cd data from Sofyan et al. (2007a, 2007b) discussed above (see Sofyan et al. [2006] for additional Cd data), which suggests that the reproductive impairment might be a combination of both direct dietborne-Cu toxicity and indirect toxicity due to an influence on the feeding rate (and the relative contribution of each likely varied with the dietborne-Cu concentration).

With regard to the comparative toxicity of waterborne- and dietborne-Cu exposures, three studies tested the toxicity of various combinations of waterborne and dietborne Cu (De Schamphelaere and Janssen, 2004; Kolts et al., 2009; Lauer and Bianchini, 2010). All three were conducted with relatively sensitive species, and all indicated that waterborne-Cu toxicity was more significant than dietborne-Cu toxicity. De Schamphelaere and Janssen (2004) separately exposed *D. magna* to each of three Cu-exposure regimes (waterborne-only, dietborne-only, combined waterborne + dietborne) for 21 days and measured effects on reproduction and growth. The waterborne-Cu concentrations to which the daphnids were exposed in the water-only test were the same as those to which the algal food was exposed for the diet-only and combined water + diet tests. Reproductive or growth effects did not occur when daphnids were exposed to dietborne Cu alone. In general, the combined exposure of daphnids to waterborne-Cu concentrations up to 100 μg/L along with a diet of algae exposed to the same waterborne-Cu concentration resulted in increased growth and reproduction, relative to exposure to either waterborne-Cu or dietborne-Cu alone. However, at a waterborne-Cu concentration of 140 μg/L, there was almost 100% daphnid mortality in the water-only and combined water + diet Cu exposures. Therefore, the chronic toxicity of Cu to *D. magna* appeared to be driven by waterborne Cu. Kolts et al. (2009) similarly reported that exposure of *C. dubia* to various combinations of Cu-contaminated algae and uncontaminated YCT food in the presence of waterborne Cu did not appreciably impair reproduction beyond the impairment in water-only exposures. Finally, Lauer and Bianchini (2010) compared the relative chronic sensitivity of *A. tonsa* to Cu via water-only, diet-only, and combined water + diet exposures at salinities of 5, 15, and 30‰. Like De Schamphelaere et al. (2004) for *D. magna*, they also found that Cu toxicity to *A. tonsa* was greater in water-only exposures across all three salinities. The waterborne-Cu concentrations that resulted in the diet-only and combined water + diet EC20 values were 27.7 and 23.2 μg/L at 5‰ salinity, 30.3 and 36.3 μg/L at 15‰ salinity, and 38.2 and 53.7 μg/L at 30‰ salinity. In contrast, the waterborne EC20 values were 8.3, 18.5, and 27.4 μg/L at salinities of 5, 15, and 30‰, respectively

(i.e., a factor of two or more lower than the combined water + diet EC20 values).

The three studies indicating that waterborne-Cu toxicity is more significant than dietborne-Cu toxicity for three sensitive crustaceans suggest that waterborne-Cu guidelines might be protective against dietborne-Cu toxicity. Several studies in which dietborne-Cu concentrations in live food organisms were obtained via exposure to waterborne Cu can be used to evaluate this further (Supplemental Data Table S3). Of the 27 individual tests with 9 different test species, the waterborne EC20 associated with dietborne-Cu toxicity was less than the corresponding chronic Cu guideline only in a marine copepod (*A. tonsa*) (Bielmyer et al., 2006). In that study, the waterborne EC20 was 1.2 μg/L or approximately 38% of the USEPA's current chronic saltwater criterion of 3.1 μg/L and approximately 23% of the current EU PNEC of 5.2 μg/L.

The toxicity results in Lauer and Bianchini (2010), whether in the diet-only or combined water + diet exposures, differed considerably from the results in Bielmyer et al. (2006). The waterborne EC20s of 8.3 to 27.4 μg Cu/L reported by Lauer and Bianchini (2010; see above) are several-fold greater than the waterborne EC20 of 1.2 μg Cu/L in Bielmyer et al. (2006). The diet-only EC20s from Lauer and Bianchini (2010), expressed as Cu concentration in the diet, were approximately 23 μg/g dry wt at salinities of 5‰ and 30‰ and approximately 31 μg/g dry wt at 15‰ salinity. Interestingly, those are remarkably similar to the diet-only EC20 of 22.3 μg/g dry wt reported by Bielmyer et al. (2006). The differences in the waterborne-Cu thresholds between the two studies might be due to several factors. First, the water chemistry was different between the two studies. Not only did Lauer and Bianchini (2010) test three different salinities, their base water with a salinity of 30‰ had a mean dissolved Cu concentration of 12.9 μg/L and a dissolved organic carbon (DOC) concentration of approximately 5 mg/L (based on data for the same test water provided in Pedroso et al. [2007]), whereas the test water used by Bielmyer et al. (2006) had a background Cu concentration of <1 μg/L and DOC concentration of 1.9 mg/L. Second, the algal diets consisted of different species, because Bielmyer et al. (2006) used *Thalassiosira pseudonana* but Lauer and Bianchini (2010) used *Thalassiosira weissflogii*. The Cu bioconcentration factors (BCFs) for *T. pseudonana* in the Cu treatments near the EC20 in Bielmyer et al. (2006) were approximately 21000 L/kg, whereas the Cu BCFs for *T. weissflogii* near the EC20 values at salinities of 5, 15, and 30‰ in Lauer and Bianchini (2010) ranged from approximately 700 to 900 L/kg. This might simply reflect species differences in Cu bioconcentration from water by the two diatom species. However, it might also reflect other experimental differences. First, diatoms in Bielmyer et al. (2006) were exposed to waterborne Cu for 7 days but those in Lauer and Bianchini (2010) were exposed to waterborne Cu for only 1 day (i.e., the difference in algal exposure durations to Cu might in part explain the

large difference in Cu BCFs between the two studies). Second, the DOC concentrations differed in the two exposure waters, which would have caused Cu bioavailability in the two exposure waters to differ due to differential amounts of Cu complexation at the two different DOC concentrations. The difference in BCFs between the two studies helps explain a large amount of the difference between dietborne EC20s when expressed as the waterborne-Cu concentrations to which the algal diets were exposed. Third, the feeding regimes also differed. Bielmyer et al. (2006) evaluated continuous dietborne exposures, whereas Lauer and Bianchini (2010) provided Cu-contaminated food for 12 hr and then provided uncontaminated food for 12 hr. Comparison of these two studies demonstrates that methodological differences might influence the waterborne-metal concentration that results in dietborne-metal toxicity. However, it is interesting that the dietborne EC20 values from the two studies, expressed as the Cu concentration in the diet, were quite similar.

To summarize, the dietborne toxicity of Cu to aquatic organisms has been fairly well studied for a variety of freshwater and saltwater species, with many studies evaluating dietborne-Cu toxicity from live diets. Based on data for the sensitive freshwater invertebrate *D. magna*, Cu toxicity appears to be greater via the water-only pathway than diet-only or combined water + diet pathways. This suggests that chronic freshwater Cu guidelines should be protective against dietborne-Cu toxicity. For sensitive saltwater invertebrates, such as *A. tonsa*, evidence of whether saltwater Cu guidelines are protective against dietborne-Cu toxicity is less clear. For example, the diet-only data from Bielmyer et al. (2006) suggest current chronic saltwater guidelines might not be protective against dietborne-Cu toxicity to *A. tonsa*, while the data from Lauer and Bianchini (2010) suggest the opposite. When evaluating whether waterborne-Cu guidelines (i.e., AWQC, PNECs) are protective against dietborne-Cu toxicity, the different conclusions derived from these two studies indicate the importance of properly accounting for water chemistry in deriving guidelines (i.e., AWQC, PNECs). For example, the different DOC concentrations in the two studies (2 and 5 mg/L, which are within the range of concentrations that naturally occur in sea water; e.g., Arnold, 2005) would have resulted in different percentages of bioavailable Cu in the waters to which the algal diets were exposed. The different conclusions derived from these studies also emphasize the importance of gaining a better understanding of how test design and choice of food organism(s) can influence the results when trying to relate dietborne-Cu thresholds back to waterborne-exposure concentrations. Future research on dietborne-Cu toxicity should focus on (1) how Cu bioavailability and toxicity in herbivorous consumers varies between different live diets, including different algal species and mixtures, and (2) what the aqueous and algal concentrations of Cu (and other metals) are in a variety of real-world freshwater and saltwater systems.

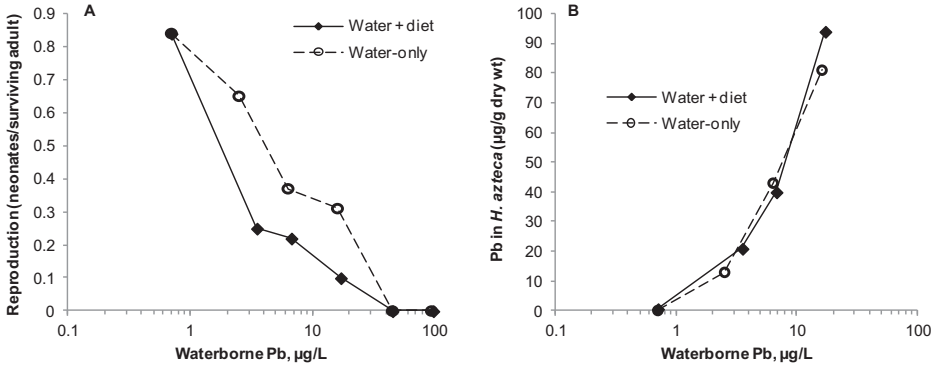

FIGURE 5. Lead toxicity and bioaccumulation in *Hyalella azteca*: (A) reproductive toxicity based on water-only and combined water + diet Pb exposures, and (B) whole-body Pb concentrations based on water-only and combined water + diet Pb exposures. In the combined water + diet exposures, the waterborne-Pb concentrations are also the concentrations with which the diets were equilibrated. Data from Besser et al. (2005).

3.2.8 Lead

Eight dietborne-Pb toxicity studies with freshwater species were identified, with two studies available for invertebrates and six studies for fish (Table 1). No dietborne-toxicity studies for saltwater species were identified. The lowest dietborne-Pb concentration associated with adverse effects was 17 μg/g dry wt in rabbit chow dosed with Pb and fed to an amphipod (*H. azteca*) (Besser et al. 2005; Figure 1). In that study, amphipods were simultaneously exposed to the same waterborne-Pb concentrations to which the food was equilibrated for 14 days. There were clear relationships between increasing waterborne- and dietborne-Pb concentrations and reproductive impairment in *H. azteca*, with the addition of dietborne Pb increasing reproductive toxicity (Figure 5A). Within a given treatment, reproduction, measured as number of neonates per surviving adult, decreased by 41–68% when amphipods were exposed to both dietborne- and waterborne-Pb versus when they were exposed to waterborne-Pb alone. However, addition of dietborne Pb at most only minimally increased Pb concentrations in *H. azteca* compared to water-only exposures (Figure 5B), perhaps suggesting a complex interaction between uptake of waterborne and dietborne Pb. The dietborne LOEC of 17 μg/g dry wt was associated with a corresponding waterborne-Pb concentration of 3.5 μg/L. That Pb concentration is only slightly less than the USEPA's current hardness-based freshwater chronic criterion of 3.6 μg/L at the test hardness of 138 mg/L as $CaCO_3$. It is unclear how the bioavailability of biologically incorporated Pb would compare to Pb in rabbit chow soaked in Pb solutions.

The dietborne toxicity of Pb from a live diet (oligochaetes, *Lu. variegatus*) fed to fish appears to be relatively low, and the long-term effects of dietborne Pb on fish growth might only occur at sites with very high Pb concentrations. For example, dietborne-Pb concentrations of 1000, 956, and 846 μg/g dry wt did not significantly affect ($p > .10$) growth of channel catfish (*Ictalurus punctatus*), rainbow trout, and fathead minnow (*Pimephales promelas*), respectively, during 30-day exposures (Erickson et al., 2010; Supplemental Data Table S3). In a longer 7-week dietborne Pb exposure using rainbow trout, the dietborne no observed effects concentration (NOEC) and LOEC were 268 and 619 μg/g dry wt for specific growth rate when the fish were provided dietborne Pb alone (Wood and Alsop, 2012). When fish were exposed to dietborne Pb and the same waterborne-Pb concentration to which its oligochaete diet was exposed, the waterborne-Pb exposure did not result in increased growth effects. For comparison to those two studies in which Pb-contaminated oligochaete diets were developed in the laboratory, Boyle et al. (2010) evaluated the reproductive performance of zebrafish (*Danio rerio*) fed a diet that was supplemented with a natural Pb-enriched polychaete (*Nereis diversicolor*) collected from either an estuary with high Pb concentrations or a reference estuary with low Pb concentrations. The Pb-enriched polychaete diet, with a whole-body Pb concentration of 33.4 μg/g dry wt, did not result in reproductive effects (the dietborne-Ag dose was also significantly higher in the Pb-enriched diet). This study provides further evidence that dietborne-Pb toxicity in fish might only be observed in water bodies with very high Pb concentrations in either water or sediment.

Finally, for those tests in which dietborne-Pb concentrations were obtained by exposing oligochaetes to waterborne Pb, the waterborne-Pb NOEC values were 576 and 628 μg/L for channel catfish and fathead minnow in Erickson et al. (2010) and 68 μg/L for rainbow trout in Wood and Alsop (2012). Those waterborne-Pb concentrations are much greater than the USEPA's hardness-based freshwater chronic Pb criterion of 1.2 μg Pb/L at the reported water hardness of approximately 50 mg/L as $CaCO_3$ in the Erickson et al. (2010) study and the chronic criterion of 3.6 μg/L in the Wood and Alsop (2012) study at the reported water hardness of approximately 140 mg/L as $CaCO_3$, indicating that current AWQC for Pb are protective against dietborne-Pb toxicity to those fish. In the Wood and Alsop (2012) study, it should be noted that the oligochaetes used in the rainbow trout diets were exposed to waterborne Pb for 28 days; however, in a preliminary 7-week exposure, steady-state Pb concentrations were not reached. Accordingly, lower waterborne-Pb concentrations associated with dietborne toxicity thresholds could be observed if the oligochaete diets are exposed to waterborne Pb for a longer duration. Additional studies with live diets are needed to evaluate whether the above observations for fish are true with sensitive invertebrates like *H. azteca*.

3.2.9 Molybdenum

No data on dietborne-Mo toxicity to aquatic life were identified in this review. Therefore, research on dietborne-Mo toxicity is clearly needed.

3.2.10 Nickel

Five dietborne-Ni toxicity studies were identified, including data for 2 freshwater species (1 fish species and 1 invertebrate species) and 1 saltwater species (an invertebrate species). The lowest dietborne-Ni concentration associated with adverse effects was 58.1 μg/g dry wt in algae (*T. pseudonana*) fed to *A. tonsa* (Bielmyer et al., 2006; Figure 1). *Daphnia magna* appears to be somewhat less sensitive to dietborne Ni delivered via an algal (*P. subcapitata*) diet, with a lowest dietborne-effect concentration of 85.6 μg/g dry wt (Evens et al., 2009). Fish, represented by lake whitefish (*Coregonus clupeaformis*), appear to be much less sensitive, with a dietborne-Ni concentration of 1100 μg/g dry wt not resulting in significant growth effects in a 104-day exposure (Ptashynski et al., 2002). Dietborne concentration–response relationships are apparent for reproductive toxicity in both *A. tonsa* and *D. magna*, although dietborne Ni might cause a maximum level of reproductive impairment less than 100% (Figure 6A). This is most apparent for *D. magna*, in which impaired reproduction remained at 64–70% relative to the control, despite a range of one order of magnitude in the dietborne-Ni concentrations that impaired reproduction. The whole-body Ni concentration in *D. magna* in the highest dietborne-Ni treatment increased by approximately 46% relative to the second-highest dietborne-Ni treatment, with no corresponding increase in reproductive toxicity (Figure 6B). This suggests that whole-body Ni concentrations in *D. magna* might not be a good predictor of the magnitude of dietborne-Ni toxicity, but perhaps might be an indicator of a threshold for toxicity (e.g., greater than 30% reproductive impairment may be expected at whole-body Ni concentration of approximately 54 μg/g dry wt in *D. magna*).

As in other studies with metals, Evens et al. (2009) observed that increasing Ni concentrations decreased the quality of the *P. subcapitata* diet based on measurement of essential omega-3 polyunsaturated fatty acid content and C:P ratio; however, they were unable to conclusively determine whether the shift in nutritional quality affected growth and reproduction. Evens et al. (2011, 2012a) subsequently evaluated the use of liposomes as a means to deliver dietborne Ni to *D. magna*, without the confounding issue of decreased nutritional quality. Nickel delivered by liposomes resulted in significant inhibition of reproduction and growth in *D. magna* when the dietborne dose resulted in daphnid body burdens of 11.9 and 20.0 μg/g dry wt after 7 and 14 days, respectively (Evens et al., 2012a). The authors then noted that the waterborne concentrations of dissolved and bioavailable Ni (i.e., Ni^{2+}) required for an algae diet (without liposomes) to achieve the

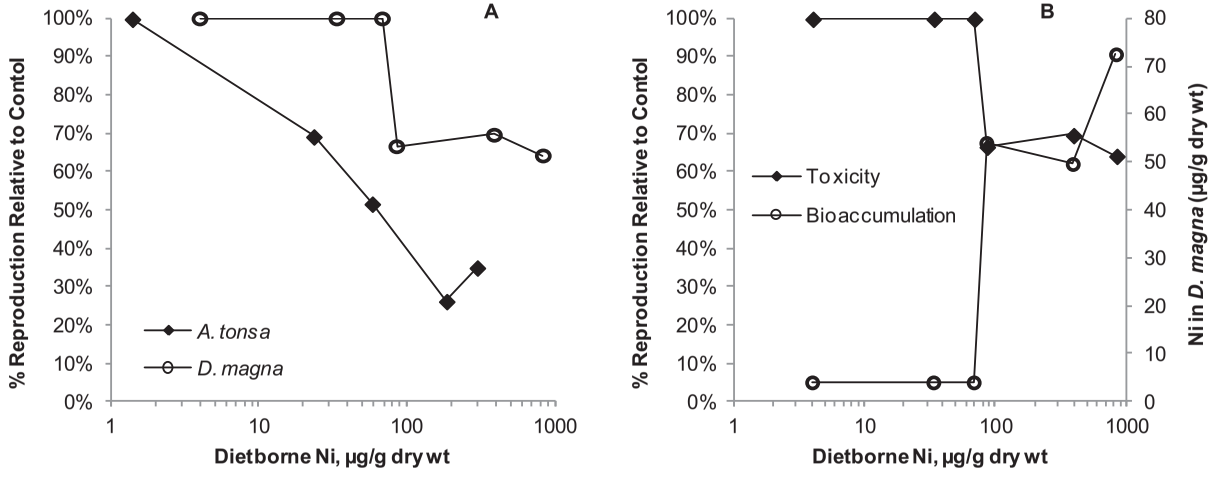

FIGURE 6. Dietborne-Ni toxicity and bioaccumulation: (A) concentration–response relationships for *Acartia tonsa* (Bielmyer et al., 2006) and *Daphnia magna* (Evens et al., 2009), and (B) toxicity and bioaccumulation data for *D. magna*. *A. tonsa* received a dietborne-only Ni exposure, whereas *D. magna* received a combined dietborne + waterborne-Ni exposure.

same Ni body burdens in *D. magna* would need to be 900 and 133 μg/L, respectively. Because these waterborne Ni concentrations are rarely observed in nature (for example, the ambient predicted environmental concentrations [PECs] in the EU risk assessment of Ni ranged from 1.1 to 5.2 μg/L for dissolved Ni [ECB, 2008]), Evens et al. (2012a) concluded that there seems to be limited relevance for dietborne-Ni toxicity to *D. magna* (although Ni concentrations greater than 100 μg/L in surface water are sometimes observed; e.g., Bervoets et al. [2004, 2005]).

The initial dietborne-Ni toxicity data in Evens et al. (2009) are consistent with the conclusion of Evens et al. (2012a) concerning the environmental relevance of dietborne-Ni exposures to *D. magna*. For *D. magna*, the waterborne-Ni concentration associated with the dietborne LOEC of 85.6 μg/g dry wt was 898 μg/L, which is much greater than the USEPA's hardness-based freshwater chronic criterion of 52 μg Ni/L at a hardness of 100 mg/L as $CaCO_3$ (Supplemental Data Table S3). The *D. magna* exposure water contained 4 mg DOC/L. Although the complete chemistry of the water to which the algae were exposed was not reported, Evens et al. (2009) stated that the algal medium was the same as that described in Deleebeeck et al. (2009), in which ethylenediaminetetraacetic acid (EDTA) was replaced by 32 μg/L of Aldrich humic acid. The water hardness of their algal-growth medium would have had to be greater than 2900 mg/L as $CaCO_3$ (i.e., an unrealistically high hardness) for the hardness-based Ni criteria to have not been protective. However, a different conclusion is reached for *A. tonsa*. The waterborne-Ni concentration associated with the dietborne LOEC of 58.1 μg/g dry wt for *A. tonsa* was 7.6 μg/L (Bielmyer et al., 2006), which is slightly less than the USEPA's chronic saltwater criterion of 8.2 μg Ni/L (Supplemental Data Table S3).

It is difficult to directly compare the results of Bielmyer et al. (2006) and Evens et al. (2009) in terms of the waterborne-Ni concentrations that resulted in toxicity, because of the obvious difference in water chemistry between the saltwater and freshwater tests. However, as discussed above for Cu, the species-specific variability in algae BCFs appears to be a contributing factor to the vastly different dietborne-Ni EC20s (expressed as the waterborne-Ni concentration to which algae were exposed), despite the similarity in EC20s when expressed as the Ni concentration in the algae diets. In the *A. tonsa* study, the Ni BCFs for the diatom food (*T. pseudonana*) ranged from approximately 6100 to 12500 L/kg in the Ni treatments; whereas in the *D. magna* study by Evens et al. (2009), the Ni BCFs for the algae food (*P. subcapitata*) ranged from approximately 500–1300 L/kg in the Ni treatments.

To summarize, the data for *A. tonsa* suggest waterborne-Ni concentrations near guideline concentrations could result in dietborne-Ni toxicity, but the data for *D. magna* suggest that very high waterborne-Ni concentrations are required to elicit dietborne-Ni toxicity. In addition to dietborne-Ni toxicity data for additional species and over a wider range of exposure conditions,

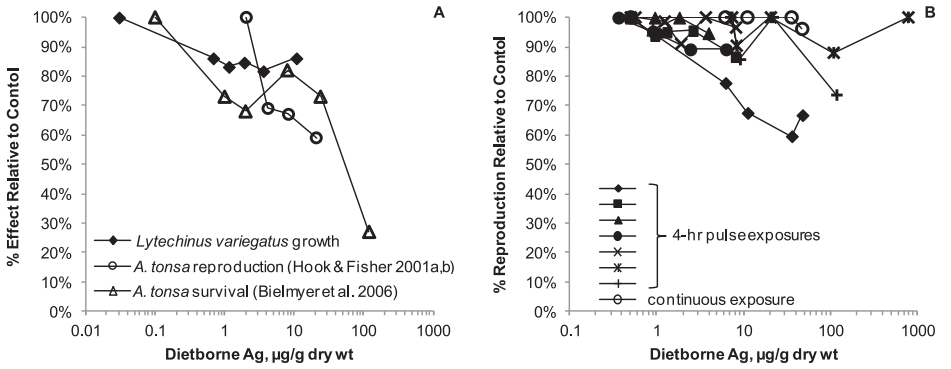

FIGURE 7. Concentration–response relationships for dietborne Ag: (A) sensitive saltwater species: *Lytechinus variegatus* (Brix et al., 2012) and *Acartia* spp. (Hook and Fisher, 2001a, 2001b; Bielmyer et al., 2006), and (B) a freshwater cladoceran *Ceriodaphnia dubia* (Kolts et al., 2009).

data about the aqueous and algal concentrations of Ni in a variety of real-world freshwater and saltwater systems are needed to more fully understand the potential for dietborne-Ni toxicity in nature.

3.2.11 Silver

Eight dietborne-Ag toxicity studies were identified, including three freshwater species (*C. dubia*, *D. magna*, and rainbow trout) and four saltwater taxa (copepods [*Acartia* spp.], mysid [*Americamysis bahia*], abalone [*Haliotis diversicolor*], and green sea urchin [*Ly. variegatus*]) (Table 1). Two studies with rainbow trout were conducted with dietborne Ag provided via a formulated diet, whereas the invertebrates, excluding *Am. bahia*, were provided dietborne Ag via a live algal diet. *Americamysis bahia* was provided a constant dietborne-Ag concentration of 0.043 μg/g dry wt, via a brine shrimp diet, over a series of waterborne Ag concentrations; however, inclusion of dietborne Ag did not result in additional toxicity (based on the most sensitive growth end point) relative to test organisms that were exposed only to waterborne Ag (Ward et al., 2006). Of the remaining invertebrate studies, the lowest dietborne-Ag concentrations associated with adverse effects ranged from 0.68 to 3.57 μg/g dry wt in algae (*Isochrysis galbana*) fed to larvae of the green sea urchin *Ly. variegatus* (Brix et al., 2012; Figure 1; Supplemental Data Table S1). Dietborne-Ag concentrations within this range resulted in a 14–18% reduction in length relative to the controls, suggesting that there might be a dietborne-Ag threshold for growth effects; however, beyond the initial growth decrease, growth did not decrease further as dietborne-Ag concentration increased (Figure 7A). Zhao and Wang (2011) reported a 39% reduction in *D. magna* reproduction in organisms provided a 1.0 μg Ag/g dw diet relative to the controls. Marine copepods (*Acartia* spp.) are similarly

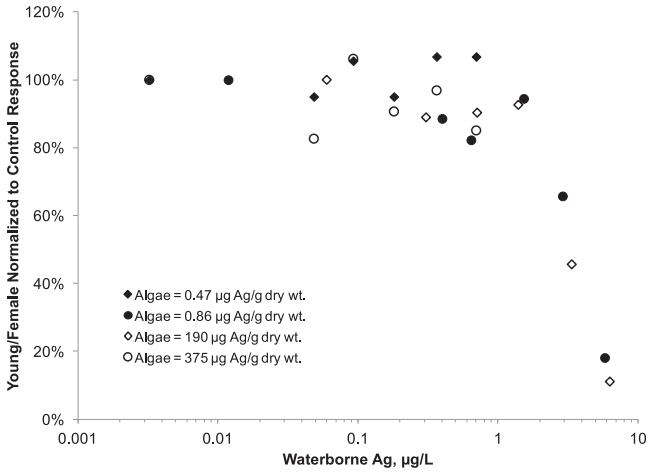

FIGURE 8. Comparison of waterborne-Ag toxicity to *Ceriodaphnia dubia* that were either fed or not fed Ag-contaminated algae. Data from Kolts et al. (2009).

sensitive (Hook and Fisher, 2001a, 2001b; Bielmyer et al., 2006), with overall steeper concentration–response relationships (Figure 7A). On the other hand, Kolts et al. (2009) did not observe concentration–response relationships between dietborne Ag and reproduction in most of the toxicity tests they conducted with a freshwater cladoceran (*C. dubia*; Figure 7B).

The USEPA's current AWQC for Ag (USEPA, 1980) in fresh water and salt water are limited to acute exposures. The acute freshwater criterion is hardness-dependent and equals 2.43 μg Ag/L at a hardness of 85 mg/L as $CaCO_3$ (the approximate hardness used in Kolts et al. [2009]), whereas the acute saltwater criterion is 1.9 μg Ag/L. The waterborne-Ag concentrations resulting in the dietborne-EC20 values for marine copepods (*Acartia* spp.) and the green sea urchin *Ly. variegatus* are approximately 4–48 times less than the acute saltwater-Ag criterion. This might reflect the need for updated saltwater AWQC for Ag, especially establishing chronic criteria (chronic Ag toxicity data were only available for one saltwater organism, a mysid shrimp *A. bahia* [USEPA, 1980]), as much as it reflects the importance of dietborne-Ag toxicity. However, it will also be important to determine the concentrations of Ag in water and algae in a variety of real-world freshwater and saltwater systems, in order to place laboratory-demonstrated effects concentrations for dietborne Ag in appropriate environmental contexts.

Kolts et al. (2009) used three different experimental methods for evaluating dietborne-Ag toxicity to *C. dubia*, one of which was a combined exposure to Ag- or Cu-contaminated algae and uncontaminated YCT in the presence of waterborne metal. Inclusion of Ag-contaminated algae did not appreciably increase the effects of Ag on reproduction (Figure 8). However,

those authors cautioned that different exposure designs could provide different results. For example, they could not exclude the possibility that the *C. dubia* fed preferentially on the uncontaminated YCT (Kolts et al., 2009). On the other hand, preferential feeding might also mimic feeding in the wild, in which the organism might only feed on a single or a few algae species.

In contrast, Hook and Fisher (2001a) reported that the total Ag concentration in water that resulted in dietborne reproductive toxicity to *Acartia* was 1/400 of the total Ag LC50 in an acute 48-h study. However, this might overstate the relative toxicity of dietborne- versus waterborne-Ag toxicity to *Acartia* because (1) chronic reproduction was the endpoint in the dietborne-Ag experiment, whereas acute mortality was the end point in the waterborne-Ag toxicity test, and (2) the copepods were not fed during the acute toxicity test. A more appropriate comparison between dietborne- and waterborne-Ag toxicity would include results from an acute and/or a chronic toxicity test in which the animals were fed the same type and amount of food (but not precontaminated with Ag) that was used in an acute and/or chronic dietborne-exposure experiment. However, because most of the Ag added in such an experiment would bind rapidly to the food particles, such an experiment would be impossible. This again emphasizes how the design of dietborne- and waterborne-metal toxicity studies influences their interpretation when trying to compare results between the two exposure routes. It also emphasizes the need for studies that determine the aqueous and algal concentrations of Ag (and other metals) in a variety of real-world freshwater and saltwater systems.

3.2.12 Vanadium

Dietborne-V toxicity data are limited to three studies with rainbow trout, tilapia (*O. niloticus* × *O. aureus*), and the southern leopard frog (*R. sphenocephala*) fed formulated diets. Rainbow trout appear to be the more sensitive of the three, with a LOEC of <10.2 μg/g dry wt based on a 59% reduction in wet weight relative to the control (Hilton and Bettger, 1988). At the highest dietborne-V concentration of 493 μg/g dry wt of feed, avoidance and increased mortality were observed. The authors noted that carcass concentrations of V increased in the fish as dietborne-V concentration increased, indicating the potential importance of the dietborne-exposure pathway. The dietborne-V concentrations evaluated in the tilapia tests were 1.77 and 1.88 μg/g dry wt based on glucose and starch diets, respectively, which did not result in statistically significant growth effects (Shiau and Lin, 1993). In the leopard frog, significant effects were not observed up to and including the highest tested dietborne-V concentration of 363.2 μg/g dry wt when frogs were fed an *ad libitum* diet (Rowe et al., 2009). However, growth was significantly reduced at that dietborne-V concentration when the frogs were provided a diet at 13% of their body weight. The authors suggested that frogs

in nature may be more sensitive to V when natural diets tend to be more limited.

No dietborne-V toxicity studies were identified in which the test organism was provided a live diet. Likewise, no studies were identified in which the relative contributions of waterborne- and dietborne-V exposures were evaluated.

A PNEC value of 7.6 μg V/L has been developed, which was based on the lowest chronic EC10 of 76 μg/L divided by an assessment factor of 10 (ECHA, 2013). To put this waterborne PNEC for V into perspective relative to the lowest tested dietborne-effect concentration of 10.2 μg/g dry wt, bioaccumulation data for amphipods (*H. azteca*) in Couillard et al. (2008) are relevant. Amphipods, along with natural food items, were deployed for 17 days at six riverine sites affected by metals mining. Dissolved-V concentrations ranged from 0.33 to 0.92 μg/L, or from 4.3% to 12% of the PNEC of 7.6 μg/L. Total-V concentrations in the amphipods, including initial background concentrations, ranged from 0.5 to 2.1 μg/g dry wt. Those concentrations bracket the V concentration of 1.2 μg/g dry wt in the control diet in the dietborne toxicity study with rainbow trout (Hilton and Bettger, 1988) and are lower than the V concentration of 8.2 μg/g dry wt in the control diet in the dietborne-toxicity study with the southern leopard frog (Rowe et al., 2009). Although the bioavailability of V in the amphipods relative to the formulated diets for the rainbow trout and southern leopard frog diets is unknown, this limited analysis indicates that there is not a high likelihood of dietborne-V toxicity near and below thresholds for waterborne-V toxicity.

3.2.13 Zinc

Eighteen dietborne-Zn toxicity studies were identified, including seven freshwater species (one invertebrate species and six fish species) and two saltwater taxa (one invertebrate tax on and one fish species) (Table 1). The lowest dietborne-Zn concentration associated with adverse effects was 3.0 μg/g dry wt in algae (*T. pseudonana*) fed to a marine copepod (*A. tonsa*) (Bielmyer et al., 2006; Figure 1; Supplemental Data Table S1). With the exception of the rainbow trout data from Mount et al. (1994), all the dietborne-Zn studies with fish were based on formulated diets. In contrast, all the dietborne-Zn studies with invertebrates were based on live diets. Dietborne-Zn concentration–response relationships for *A. tonsa* (Bielmyer et al., 2006) and *D. magna* (De Schamphelaere et al., 2004) are similar in shape, i.e., a rapid decline in reproduction that levels out at around 50–60% impairment relative to the controls (Figure 9A). Hook and Fisher (2002) observed a similar relationship in *Acartia* spp. (data not included in Figure 9 because they only reported the waterborne-Zn concentrations to which the algal food was exposed). De Schamphelaere et al. (2004) also measured whole-body Zn concentrations in *D. magna*. As for Ni, whole-body Zn concentrations resulting from dietborne-Zn exposures do not appear to be a good predictor of

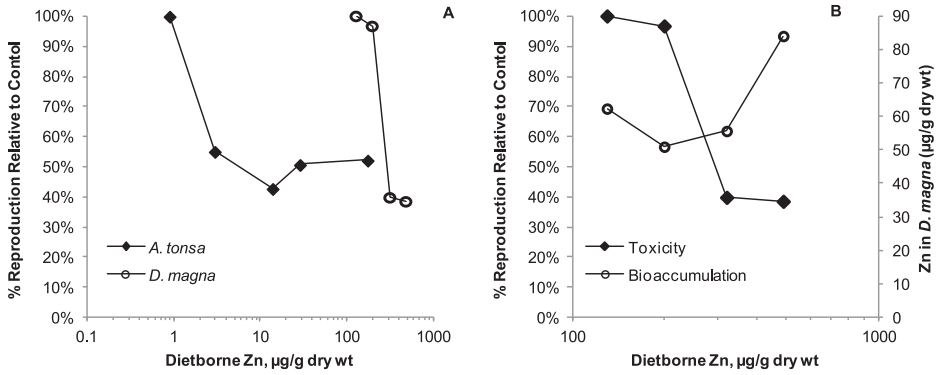

FIGURE 9. Dietborne-Zn toxicity and bioaccumulation: (A) concentration–response relationships for *Acartia tonsa* (Bielmyer et al., 2006) and *Daphnia magna* (De Schamphelaere et al., 2004), and (B) toxicity and bioaccumulation data for *D. magna*.

reproductive toxicity, because the whole-body Zn concentration associated with a 60% reduction in reproduction compared to the control was slightly less than the whole-body Zn concentration in the control (Figure 9B).

In six studies, the food item was exposed to waterborne Zn. In the *Acartia* studies conducted by Hook and Fisher (2002) and Bielmyer et al. (2006), the waterborne-Zn concentrations resulting in the dietborne EC20 values were similar (0.47 and 0.30 μg Zn/L), and each was less than the USEPA's chronic saltwater criterion of 81 μg/L and the European saltwater environmental quality standard (EQS) of 3.27 μg/L (Supplemental Data Table S3). For reference, waterborne-Zn concentrations on the order of 0.30–0.47 μg/L have been commonly measured in coastal marine waters distant from potential point sources of contaminants (DeForest et al., 2012). For *D. magna*, the waterborne-Zn concentration of 24.5 μg/L that resulted in the dietborne EC20 is much less than the USEPA's current hardness-based freshwater Zn criterion of 257 μg/L (based on the test hardness of 250 mg/L as $CaCO_3$), but is only approximately 1/2 of the much lower BLM-based chronic 5th percentile of 44.8 μg/L derived following USEPA guidelines (DeForest and Van Genderen, 2012). The waterborne EC10 of 23.6 μg Zn/L based on dietborne toxicity is greater than the Zn EQS derived using the Bio-Met program (http://www.bio-met.net). Therefore, the USEPA's current hardness-based chronic criterion for Zn clearly appears to be under-protective of dietborne-Zn toxicity, whereas the BLM-based 5th percentile derived following DeForest and Van Genderen (2012) is closer to being protective; and the even lower EQS derived using Bio-Met is protective. This range of outcomes again demonstrates the importance of properly accounting for water chemistry in determining whether waterborne-metal guidelines are protective against dietborne-metal toxicity.

Hook and Fisher (2002) and De Schamphelaere et al. (2004) reported that Zn adversely affected reproduction in *Acartia* spp. and *D. magna*, respectively, but it did not affect other endpoints such as feeding rates and growth. Hook and Fisher (2002) attributed the reproductive effects to disturbance of vitellogenesis, which was apparent due to decreased ovary development and decreased yolk protein content of the eggs. In *D. magna*, De Schamphelaere et al. (2004) did not observe a relationship between reproductive effects and the total body burden of Zn, which suggested that the reproductive effects were due to increased Zn accumulation at specific target sites that might be important for vitellogenesis. A follow-up study by Evens et al. (2012b) evaluated the tissue-specific distribution of Zn following water-only and combined water + diet exposures using synchrotron radiation-based confocal X-ray fluorescence. They found a pronounced increase in Zn concentrations in the eggs that could be attributed to the dietborne-exposure route, thus possibly supporting their hypothesis that dietborne Zn selectively accumulates in reproductive tissue. Additionally, they observed clear toxicity interactions between waterborne- and dietborne-exposure routes and concluded the two exposure routes need to be considered together in risk assessments. Alternatively, Evens et al. (2012c) suggested that reproductive effects of dietborne Zn might be due to a Zn-induced alteration of the P content in the algal diet; and thus, from an ecological perspective, they suggested that the indirect effect of metal-induced shifts in nutritional quality on reproduction might be just as important to consider as direct metal toxicity.

Overall, most studies of the toxicity of dietborne Zn have focused on fish; however, recent studies focused on two invertebrates (*A. tonsa* and *D. magna*) might be the most pertinent. The several studies conducted by De Schamphelaere, Evens, and colleagues have helped identify the potential mechanisms by which dietborne-Zn toxicity occurs in *D. magna*, and have also helped highlight the importance of interactions between waterborne and dietborne exposures and why those pathways should be considered together in ecological risk assessment. The dietborne-Zn studies with *Acartia* have focused on the dietborne pathway alone. Given the apparent extreme sensitivity of *Acartia* to Zn, more research on the combined exposures of waterborne and dietborne Zn is recommended; and it will be important to determine the concentrations of Zn in water and algae in a variety of real-world freshwater and saltwater systems, in order to place laboratory-demonstrated effects concentrations for dietborne Zn in appropriate environmental contexts.

3.3 Metal Mixtures

Nine dietborne-metal toxicity studies of metal mixtures (usually using field-collected food items) were identified, including five freshwater species (all fish species) and two saltwater species (one invertebrate species and one fish

species) (Table 1). Because the food items used in most of those studies were collected from mining-related, metal-contaminated field sites, it is difficult to ascribe toxicity to any specific metal or set of metals. In fact, it is possible that the actual dietborne toxicant(s) might not even have been analyzed in the diet, because the sets of metals reported by study authors depend on their perceptions of the contaminants of concern in the system from which the food items were collected. Moreover, the contribution of a given component of the metal mixture to dietborne toxicity might not be fully appreciated until appropriate studies have been conducted (e.g., see Section 3.2.2).

In addition to the difficulty of identifying the metals that contribute to the toxicity of a dietborne-metal mixture in field-collected food items, results of experiments conducted with field-collected food items should be interpreted with caution because of potential differences in nutritional composition of the food that can alter survival, growth, or reproduction (Campbell et al., 2005). Therefore, especially for dietborne-metal studies that use field-collected food items, it is important to report nutritional analyses of the food (Campbell et al., 2005). However, even when using food items that have been contaminated with metals under controlled conditions in the laboratory, it can be useful to analyze the nutritional composition of the control and treatment diets to help determine whether the metals have a direct, toxic effect on the consumer organisms (via exposure to the metals in the food) or an indirect effect on the quality of the food (e.g., Morris et al., 2003; Evens et al., 2009). As noted above for Ni, one possibility for addressing this issue in toxicity studies in the laboratory is to use liposomes for delivering dietborne metal, which allows for the nutritional quality of an algal diet, for example, to be consistent across dietborne-metal concentrations. However, results of such experiments conducted must still be interpreted cautiously in the context of the bioavailability of metals incorporated into the liposomes relative to the bioavailability of metals incorporated into food items in real-world ecosystems.

3.4 Synthesis

This paper reviewed the state of the science regarding dietborne-metal toxicity to aquatic biota, with a focus on 13 metals: Ag, Al, As, B, Cd, Co, Cr, Cu, Mo, Ni, Pb, V, and Zn. Of those metals, Ag, As, Cd, Cu, Ni, and Zn have been demonstrated to cause dietborne toxicity to aquatic organisms in laboratory exposures. From a regulatory perspective however an important question is whether concentrations of metals near water quality guidelines (e.g., AWQC, EQSs, PNECs) can result in dietborne-metal concentrations that increase the toxicity of the metal(s) beyond that caused by waterborne exposure alone (Wang, 2013a). Because waterborne thresholds based on the species sensitivity distribution (SSD) approach have traditionally been developed based on the fifth percentile of the tested species or taxa, those thresholds are driven

by the sensitivities of the few most sensitive species or taxa that have been tested. Can these waterborne concentrations for the most sensitive tested species result in dietborne concentrations that contribute to added toxicity or otherwise suggest that the waterborne thresholds are not adequately protective? It is apparent that this might be the case for some metals and some species (notably *Acartia*), but unlikely for others (Table 2). In some cases it might also simply suggest that some water quality guidelines are outdated and do not adequately incorporate sensitive species or endpoints. For example, several of the USEPA's AWQC for metals have not been updated since the 1980s. The USEPA's chronic saltwater criterion for Zn is 81 μg/L (USEPA, 2009), whereas a more recently developed chronic saltwater EQS is much lower at 3.27 μg Zn/L (UK Environment Agency, 2009).

Interestingly, two primary sets of studies seem to clearly indicate that current waterborne criteria for some metals are not protective against dietborne-metal toxicity: the studies with *Acartia* conducted by Hook and Fisher (2001a, 2001b, 2002) and Bielmyer et al. (2006). In each of those studies, the exposure water was natural seawater with relatively low DOC concentration (i.e., ~1 mg/L in the Hook and Fisher studies and 1.9 mg/L in the Bielmyer et al. study). The freshwater dietborne-Ag toxicity study by Hook and Fisher (2001a) also suggests that two cladocerans (*Simocephalus* sp. and *C. dubia*) are sensitive at waterborne-Ag concentrations less than the current US EPA freshwater acute criterion of 0.14 μg/L based on the test water hardness of 16 mg/L as $CaCO_3$ (note that the test water also had a low DOC concentration of <0.2 mg/L). Based on draft BLM-based criteria for Ag (HydroQual et al., 2007), BLM-based chronic criteria for a moderately hard water and low DOC would be on the order of approximately 0.0018 μg/L (more than one order of magnitude less than the EC20 of 0.020 μg/L from the test with the mixture of *Simocephalus* sp. and *C. dubia*). The current lack of freshwater and saltwater BLM-based criteria for most metals (except Cu) might in part explain the apparent lack of protection against dietborne-toxicity for some of those metals.

A limited number of studies have systematically compared the toxicity of metals to an organism via water-only, diet-only, and combined water + diet exposures. In general, adverse effects to organisms simultaneously exposed to waterborne and dietborne metal were greater than when exposed to water or diet alone, but this was not always the case. The choice of the combination of waterborne- and dietborne-metal concentrations in an experiment can be crucial to concluding whether one pathway is more important than the other. Unfortunately, information about concurrent concentrations of metals in water and individual food items (and the forms and locations of the metals) in a wide variety of aquatic systems is generally lacking. Because BCFs differ considerably among species and decrease significantly as waterborne-metal concentration increases (McGeer et al., 2003), site-specific accumulations of metals in food items are needed to perform credible site-specific risk

TABLE 2. General summary of whether regulatory waterborne guidelines are protective against dietborne metals toxicity[a]

Metal	May not be protective	May be protective	Conflicting evidence	Comment
Ag	*Acartia* spp. (copepods) *Lytechinus variegatus* (green sea urchin) *Daphnia magna* (cladoceran)	*Haliotis diversicolor* (abalone)	*Simocephalus* sp. and *Ceriodaphnia dubia* (cladocerans)	No data for fish
Al				Insufficient data
As		*Oncorhynchus mykiss* (rainbow trout)	No data for invertebrates	
B				Insufficient data
Cd	*Acartia* spp. (copepods) *Allorchestes compressa* (amphipod) *Moina monogolica* (cladoceran)	*Crassostrea gigas* (Pacific oyster) *Cyprinus carpio* (common carp) *Haliotis diversicolor* (abalone) *Hyalella azteca* (amphipod) *Ictalurus punctatus* (channel catfish) *Oncorhynchus mykiss* (rainbow trout) *Palaemonetes pugio* (grass shrimp) *Pimephales promelas* (fathead minnow)	*Centroptilum triangulifer* (mayfly)	
Co				Insufficient data
Cr				Insufficient data
Cu	*Allorchestes compressa* (amphipod)	*Ceriodaphnia dubia* (cladoceran) *Daphnia magna* (cladoceran) *Ictalurus punctatus* (channel catfish) *Moina mongolica* (cladoceran) *Oncorhynchus mykiss* (rainbow trout) *Peramphithoe parmerong* (amphipod) *Pimephales promelas* (fathead minnow)	*Acartia tonsa* (copepod)	
Mo				Insufficient data
Ni	*Acartia tonsa* (copepod)			No data for fish
Pb		*Ictalurus punctatus* (channel catfish) *Pimephales promelas* (fathead minnow) *Oncorhynchus mykiss* (rainbow trout)		No data for invertebrates
V				Insufficient data
Zn	*Acartia tonsa* (copepod)	*Allorchestes compressa* (amphipod)	*Daphnia magna* (cladoceran)	

[a]Based on the studies in which a live diet was exposed to waterborne metal and then fed to the consumer organism.

assessments; therefore, use of generic BCFs to predict metal concentrations in food items might produce spurious results. Furthermore, several metals (e.g., As, Se) commonly exist in a variety of oxidation states and in a variety of inorganic and organic forms in the water and in food items, making it important to report the percentage composition of the various oxidation states in the exposure media—especially given the apparent importance of dietborne-As toxicity at concentrations in food items that until recently had been overlooked.

Waterborne-metal toxicity studies have generally evolved in a sequence from acute lethality studies used to identify the relative hazards of metals, to longer term studies of sublethal effects, and eventually to more sophisticated studies designed to evaluate geochemical and physiological factors that influence the bioavailability and thus the toxicity of metals. Studies of dietborne-metal toxicity have lagged behind waterborne-metal toxicity, but otherwise have followed a similar pathway. Initial studies tended to focus on whether high metal concentrations, usually in formulated diets, could cause toxicity in aquatic biota (often fish). Dietborne-metal toxicity studies have subsequently progressed toward evaluations of dietborne concentrations resulting from exposures to waterborne concentrations near toxicity-threshold concentrations and toward the use of live diets containing biologically incorporated metals. Although more research is needed to decrease sometimes large uncertainties, those more recent studies are helping to provide information about differences in dietborne-metal bioavailability among diet types.

In much the same way that more caution is now used when applying waterborne-metal toxicity data from one water type to another type having different water chemistry, there is a need to understand how dietborne-metal toxicity from one diet type and/or exposure regime compares to another diet type and/or exposure regime. For example, when a single alga species is exposed to waterborne metal and fed to a consumer, how applicable is this to other diet types given differences in metal bioavailability, as well as differences in metal uptake between algae species and how metals might differentially affect the nutritional quality of the diet? The dietborne-metal concentration itself will not be a good predictor of toxicity outcomes without some understanding of bioavailability. Moreover, the body-weight-normalized rate of consumption of bioavailable metal (i.e., the bioavailable dose, in μg metal/g body weight of consumer/d) might be an even better predictor of dietborne-metal toxicity than is the concentration of bioavailable dietborne metal (Clearwater et al., 2002; Wang, 2013a).

With regard to variable metal accumulation among species, Fisher et al. (2000) reported Ag, Cd, Co, and Zn concentrations in filtered water samples and suspended particles (>0.2 μm) at 10 stations along the Monaco cost. Even though waterborne concentrations of each metal varied by only a factor of 1.6–2.8 across the 10 stations, the BCFs varied by factors of 6,

3, 17, and 10 for Ag, Cd, Co, and Zn, respectively, leading to variability in dietborne-metal concentrations to which consumers of those algae would be exposed. Interspecies differences, the magnitude of the waterborne concentration (BCFs tend to be inversely related to exposure concentration; McGeer et al., 2003), and the exposure-water chemistry influence the magnitude of BCFs and, thus, the propensity of the metal to bioaccumulate in the food web. Furthermore, as Bielmyer et al. (2006) noted, there is uncertainty in the environmental realism of when an organism is fed a single algal species and whether there are adequate levels of essential metals, which might result in unrealistic metal accumulation in the algae and a reduced nutritional value. Finally, the exposure duration of the algal food item to the waterborne-metal concentration has an important influence on whether a given waterborne-metal concentration will result in dietborne-metal toxicity. Both the duration of the algal exposure to waterborne metal and whether algae were exposed to a single initial metal concentration or a renewed metal concentration throughout the exposure can significantly influence metal loading into the algal diet (Brix et al., 2012).

A final step in elucidating or predicting the effects of dietborne metals in aquatic systems is the linkage of metal accumulation in the consumer organism(s) to toxicity (Adams et al., 2011). Biodynamic models (e.g., Luoma and Rainbow, 2005) are available to predict bioaccumulation of metals, but they generally only predict whole-body residues, from which it is difficult to predict toxicity because metals can be stored in various non-toxic forms in organisms (e.g., in metal granules and metal–metallothionein complexes; Luoma and Rainbow, 2008). In contrast, more recent compartmentalized models that explicitly distinguish between biologically inactive metal and biologically active metal (i.e., BIM-BAM models; e.g., Steen-Redeker and Blust, 2004; Steen-Redeker et al., 2004) take into account differences in toxicity of various forms of a metal in an organism and differences in rates of metal incorporation into an organism (e.g., as a result of different daily metal doses), but they require information about pharmacokinetics and pharmacodynamics of metals that generally is lacking in aquatic organisms. Current sub-cellular partitioning methods that involve differential centrifugation of a variety of cellular components can be used to provide approximations of trophically available metal (TAM) concentrations (Wang and Rainbow, 2006). However, as recently addressed by Rainbow et al. (2011) and Wang (2013b), TAM should be considered only as a useful starting hypothesis because TAM will vary among metals, species, and food items. Consequently, the "silver bullet" toxic subcellular compartment(s) have not yet been identified (Adams et al., 2011). For example, analogous to the Buchwalter et al. (2008) analysis of waterborne-Cd exposures, the uptake and depuration rates and subcellular compartmentalization resulting from dietborne-Cd exposures could be determined and related to toxicity and/or detoxification strategies among aquatic organisms.

In this review, relationships between toxicity and whole-body bioaccumulation from dietborne-metal exposures were generally poor. In some cases, the poor correlations might have been due to toxicity in subcellular compartments for which toxicity-related differential accumulations of the metal were not quantified, despite the apparent regulation of metal concentration at the whole-body level; and in other cases, this lack of a relationship might be indicative of indirect effects of the dietborne metal on organismal functions (e.g., effects on feeding rate; Wang, 2013a). Therefore, no studies were identified in the current review that would help link whole-body accumulation of metals to toxicity or that could be used to parameterize BIM–BAM type models. Targeted research could help strengthen this link for understanding and predicting dietborne-metal toxicity.

As a final note, SSDs of dietborne-metal toxicity data were not compiled as part of this review. Given the large variability in test designs for evaluating dietborne-metal toxicity, development of SSDs at this point would be premature and perhaps even provide a misleading impression about relative sensitivity to dietborne metals among species.

4. RECOMMENDATIONS

The potential for dietborne-metal toxicity might be of interest for both waterborne-guideline development and site-specific ecological risk assessment. For waterborne-guideline development, it might be most appropriate to consider a combined exposure to equilibrated waterborne- and dietborne-metal concentrations, because this is assumed to be a potentially conservative exposure scenario. For site-specific ecological risk assessment, the waterborne- and dietborne-metal concentrations should be relevant to the exposure scenario at the site, where metal concentrations in water and food might or might not be in equilibrium. Because the prey species (or type of particle), environmental conditions, and durations of exposure of food items to dissolved metal can greatly alter the amount of metal accumulated in the food (and possibly the chemical forms and physiological compartments in which metals occur in the food), Meyer et al. (2005b, p. 199) recommended to:

> . . . conduct surveys of the concurrent concentrations of metals in the water column, sediments, and food web in a variety of real-world aquatic systems 1) that always have received little or no anthropogenic input, 2) that currently receive anthropogenic input, and 3) that contain residuals from historic inputs of metals. When possible, metal speciation and partitioning should be determined in the foods of various consumers, and stable isotopes [and radio-isotopes] should be used to help identify major trophic interactions.

This is an important research effort that is needed to define the exposure portion of either a generic or a site-specific risk assessment of dietborne metals, in order to better interpret the effects studies that are reviewed herein.

Unfortunately, most surveys of metal concentrations conducted in foodwebs provide only part of the resolution needed, because not all surveys are designed to specifically address questions about dietborne-metal toxicity. For example, it is common to separate macroflora (e.g., macroalgae) and macrofauna (e.g., benthic macroinvertebrates) by species before digesting and analyzing for whole-body metal concentrations. However, microalgae are usually lumped together into "phytoplankton," "epiphytes," "seston," or "biofilm" without sorting by species (e.g., Croteau et al., 2005; Cheung and Wang, 2008; Marín-Guirao et al., 2008). Furthermore, bacteria are almost never even considered although they probably contribute to the "phytoplankton," "epiphytes," "biofilm," "seston," and/or "detritus" (e.g., Barwick and Maher, 2003), and even zooplankton sometimes are not sorted by species (e.g., Barwick and Maher, 2003; Jara-Marini et al., 2009) or are not even included when sampling the aquatic food web (e.g., Pereira et al., 2010). Given that (1) metals incorporated into microalgae are sometimes relatively toxic to invertebrate consumers and (2) metal BCFs vary widely among algae species, this key component for understanding dietborne-metal toxicity remains a black box. Improved resolution of the range of metal concentrations in various algal species in real-world aquatic systems and the contributions of various algal species to the diets of their consumers would help determine whether regulatory criteria/guidelines for waterborne metals are protective against dietborne-metal toxicity; however, analytical techniques are not readily available to accomplish that goal.

Related to increasing the resolution in measuring metal concentrations in foodwebs, it is essential to consider the fraction of metals in mineral material. This is true for all metals, but particularly for Al because its concentration in sediment, for example, can naturally be high. In order to interpret metal concentrations in field-collected food items, whether for comparison to dietborne-toxicity thresholds or to help choose exposure concentrations in dietborne-toxicity studies, it is important to understand the proportion of metal that is chemically incorporated into and thereby not bioaccessible in particles. This will allow for more consistent comparisons and evaluations of dietborne toxicity between studies.

Analogous to those needs in field studies, metal speciation and partitioning (e.g., TAM components) should be determined in the foods used in laboratory studies of dietborne-metal toxicity. Additionally, conceptual and methodological advancements from the bioaccumulation literature can be brought to bear on better designing and executing dietborne-metal toxicity studies. For example, analyses of biodynamics in aquatic organisms demonstrate that metal accumulation can take weeks or longer to achieve steady state (e.g., Xie et al., 2008); and different aquatic organisms use a variety

of ecophysiological strategies of metal uptake/elimination and detoxification (Buchwalter et al., 2008). Therefore, a variety of potential dietborne-metal exposure concentrations and forms can exist within a given ecosystem at a given waterborne-metal concentration (Wang, 2013a), and due consideration should be accorded those possibilities when designing laboratory dietborne-metal toxicity studies.

In general, dietborne-metal studies using invertebrates fed live diets contaminated individually with Al, As, B, Cr, Co, Mo, Pb, or V are needed to expand the understanding of potential aquatic hazards posed by dietborne exposure to these metals. Because small herbivorous organisms such as copepods, cladocerans, and echinoderm larvae appear to be the most sensitive organisms to several metals, study designs that include exposure of algae to waterborne metals, such as the test designs employed by Hook and Fisher (2001a, 2001b), Bielmyer et al. (2006), and Kolts et al. (2009), are encouraged (with inclusion of the waterborne pathway). As a corollary, because algae and periphyton can accumulate dissolved metals relatively rapidly from water, even studies that purport to characterize only waterborne-metal toxicity should report the metal content of abiotic particles and food items (if included in the exposure scenario). Additionally, in all studies in which algae or periphyton is the food, the amount of metal sorbed to the external surface of the cells (usually determined by an EDTA rinse) should be differentiated from the amount of metal otherwise associated with the cells (i.e., internalized or more permanently associated with the cell surface), to help differentiate among possible mechanisms of toxicity.

In addition to the algae-to-herbivorous-invertebrate pathway, research is needed on the toxicity to predators that might be caused by metals in high-bioaccumulation-potential food organisms. For example, although the biomagnification potential of several divalent metals (e.g., Cd, Cu, Pb, Ni, Zn) in aquatic systems is generally low, metals can biomagnify in some discrete marine food chains consisting of bivalves, herbivorous and predatory gastropods, and barnacles (Cardwell et al., 2013). Research to date has focused on the high bioaccumulation potential of metals in these organisms, but to our knowledge no studies have specifically evaluated whether the high metal concentrations in these prey are toxicologically bioavailable to predators. Understanding whether metals in these food chains can cause dietborne toxicity represents a research gap that could have important implications for the regulation and management of metals in some aquatic environments.

More generally, the transfer of metals from sediments into benthic organisms and successive trophic levels is not well understood. Most dietborne-metal studies are conducted without a sediment component; but when sediment has been part of the pathway to load metal into prey organisms, sometimes unexpected and revealing results have been obtained (e.g., Hansen et al., 2004; Erickson et al., 2010). Despite low concentrations

of metals in overlying water and high concentrations of acid volatile sulfides in sediment, some metals can accumulate to high concentrations in benthic invertebrates and fish under field conditions (De Jonge et al., 2009). Therefore, sediment-based food chains might be an important pathway for dietborne-metal exposure (Luoma and Rainbow, 2008).

Choice of prey species is a challenging component in the design of dietborne-metal toxicity studies (Wang, 2013a). Use of multiple algae species for studies with filter-feeding zooplankton, or use of complex periphyton communities in studies with grazing herbivores, such as the mayfly studies conducted by Xie et al. (2010), might help overcome some of the uncertainties in using single-species food sources. However, careful comparison of the metal concentrations in the various food items used in a toxicity test to the concentrations expected in real-world aquatic systems will be needed to appropriately assess the potential for dietborne-metal exposure and toxicity. When conclusions about mechanisms of toxicity are desired, nutritional composition of the control and treatment food should be reported, even if the type of food in a laboratory study is the same in the controls and treatments [except for exposure to the metal(s)]. The studies recently conducted by Evens et al. (2011, 2012a), in which liposomes were used to deliver dietborne metal to reduce the possibility of decreased nutritional content in algae exposed to metals, represent a potentially promising approach for discriminating between direct versus indirect effects of dietborne metals.

Feeding rate should be monitored in dietborne-metal experiments, because this helps elucidate whether effects are due to direct metal toxicity or indirect consequences of the exposure (e.g., metal avoidance). Additionally, the daily dose of a dietborne metal, which is calculated as the mathematical product of the ingestion rate and the dietborne-metal concentration (Clearwater et al., 2002), should be reported to allow more appropriate comparison of exposure than is possible with dietborne-metal concentration alone (Wang, 2013a). A study simply reporting the dietborne-metal concentration is not very useful unless the actual feeding rate is measured (or can be calculated). For example, little toxicity might occur if food containing a high metal concentration is consumed only once or at a low daily dosage.

The above recommendations largely focus on studies relative to dietborne toxicity evaluations of individual metals, because the state-of-the-science with regard to dietborne-metal toxicity is still evolving. However, the growing understanding of dietborne-metal toxicity should be used to help guide dietborne-toxicity studies of metal mixtures, because metals almost always occur in mixtures in nature. Several key studies with field-collected prey organisms have demonstrated the importance of metal-mixture toxicity, and some recent studies have helped identify the key metal of dietborne concern (e.g., As in the Clark Fork River, Montana, USA). However, even more so than for individual metals, much remains to be learned before the

toxicity of dietborne-metal mixtures will be understood and can be predicted accurately.

Finally, as in waterborne-metal toxicity tests, water chemistry must be measured and reported in order to evaluate the toxicity data relative to waterborne thresholds that are adjusted for bioavailability using either hardness-based or BLM-based algorithms. At least in the USA, where AWQC for several metals are now several decades old (e.g., Ag, Cd, Zn), updating the AWQC with the latest toxicity data and properly accounting for water chemistry using the BLM most likely will help make those aged AWQC protective (or at least make them less under-protective) against dietborne-metal toxicity.

ACKNOWLEDGMENTS

We are grateful to Kevin Brix, David Buchwalter, Charles Delos, and David Mount for their thoughtful reviews of an early draft of this manuscript. We also thank the anonymous reviewers for their review of this manuscript.

FUNDING

This research was funded by the Ecotoxicity Technical Advisory Panel of the Metals Industry.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website.

REFERENCES

Adams, W.J., Blust, R., Borgmann, U., Brix, K.V., DeForest, D.K., Green, A.S., Meyer, J.S., McGeer, J.C., Paquin, P.R., Rainbow, P.S., and Wood, C.M. (2011). Utility of tissue residues for predicting effects of metals on aquatic organisms. *Integrated Environmental Assessment and Management* 7, 75–98.

Adams, W.J., Stewart, A.R., Kidd, K.A., Brix, K.V., and DeForest, D.K. (2005). Case histories of dietborne exposure to mercury and selenium in aquatic ecosystems. In J.S. Meyer, W.J. Adams, K.V. Brix, S.N. Luoma, D.R. Mount, W.A. Stubblefield, and C.M. Wood (Eds.), *Toxicity of dietborne metals to aquatic organisms* (pp. 263–274). Pensacola, FL: SETAC Press.

Ahmed, A.R., Jha, A.N., and Davies, S.J. (2012). The efficacy of chromium as a growth enhancer for mirror carp (*Cyprinus carpio* L): An integrated study using biochemical, genetic, and histological responses. *Biological Trace Element Research* 148, 187–197.

Ahsanullah, M., and Williams, A.R. (1991). Sublethal effects and bioaccumulation of cadmium, chromium, copper and zinc in the marine amphipod *Allorchestes compressa*. *Marine Biology* 108, 59–65.

Ajani, E.K., and Akpoilih, B.U. (2012). Growth response and ionic regulation in common carp (*Cyprinus carpio* L.) after chronic dietary copper exposure and recovery. *International Journal of Fisheries and Aquaculture* 4, 13–21.

Alsop, D., Brown, S., and Van Der Kraak, G. (2007). The effects of copper and benzo[a]pyrene on retinoids and reproduction in zebrafish. *Aquatic Toxicology* 82, 281–295.

Arnold, W.R. (2005). Effects of dissolved organic carbon on copper toxicity: Implications for saltwater copper criteria. *Integrated Environmental Assessment and Management* 1, 34–39.

Ayyat, M.S., Safaa, M.S., Fayza, S.A., and El-Marakby, H.I. (2010). Reductions of dietary lead toxicity in Nile tilapia (*Oreochromis nilotius*). Retrieved from http://en.engormix.com/MA-aquaculture/articles/reductions-dietary-lead-toxicity_1502.htm.

Baker, R.T.M., Handy, R.D., Davies, S.J., and Snook, J.C. (1998). Chronic dietary exposure to copper affects growth, tissue lipid peroxidation, and metal composition of the grey mullet, *Chelon labrosus*. *Marine Environmental Research* 45, 357–365.

Ball, A.L., Borgmann, U., and Dixon, D.G. (2006). Toxicity of a cadmium-contaminated diet to *Hyalella azteca*. *Environmental Toxicology and Chemistry* 25, 2526–2532.

Barwick, M., and Maher, W. (2003). Biotransference and biomagnification of selenium, copper, cadmium, zinc, arsenic and lead in a temperate seagrass ecosystsem from Lake Macquarie Estuary, NSW, Australia. *Marine Environmental Research* 56, 471–502.

Berntssen, M.H.G., Hylland, K., Wendelaar Bonga, S.E., and Maage, A. (1999a). Toxic levels of dietary copper in Atlantic salmon (*Salmo salar* L.) parr. *Aquatic Toxicology* 46, 87–99.

Berntssen, M.H.G., and Lundebye, A.-K. (2001). Energetics in Atlantic salmon (*Salmo salar* L.) parr fed elevated dietary cadmium. *Comparative Biochemistry and Physiology Part C Toxicology and Pharmacology* 128, 311–323.

Berntssen, M.H.G., Lundebye, A.-K., and Maage, A. (1999b). Effects of elevated dietary copper concentrations on growth, feed utilization and nutritional status of Atlantic salmon (*Salmo salar* L.) fry. *Aquaculture* 174, 167–181.

Berntssen, M.H.G., Waagbø, R., Toften, H., and Lundebye, A.-K. (2003). Effects of dietary cadmium on calcium homeostasis, Ca mobilization and bone deformities in Atlantic salmon (*Salmo salar* L.) parr. *Aquaculture Nutrition* 9, 175–183.

Bervoets, L., Meregalli, G., De Cooman, W., Goddeeris, B., and Blust, R. (2004). Caged midge larvae (*Chironomus riparius*) for the assessment of metal bioaccumulation from sediments *in situ*. *Environmental Toxicology and Chemistry* 23, 443–454.

Bervoets, L., Voets, J., Covaci, A., Chu, S., Qadah, D., Smolders, R., Schepens, P., and Blust, R. (2005). Use of transplanted zebra mussels (*Dreissena polymorpha*) to assess the bioavailability of microcontaminants in Flemish surface waters. *Environmental Science and Technology* 39, 1492–1505.

Besser, J.M., Brumbaugh, W.G., Brunson, E.L, and Ingersoll, C.G. (2005). Acute and chronic toxicity of lead in water and diet to the amphipod *Hyalella azteca*. *Environmental Toxicology and Chemistry* 24, 1807–1815.

Bielmyer, G.K., Gatlin, D., Isely, J.J., Tomasso, J., and Klaine, S.J. (2005). Responses of hybrid striped bass to waterborne and dietary copper in freshwater and saltwater. *Comparative Biochemistry and Physiology Part C Toxicology and Pharmacology* 140, 131–137.

Bielmyer, G.K., Grosell, M., and Brix, K.V. (2006). Toxicity of silver, zinc, copper, and nickel to the copepod *Acartia tonsa* exposed via a phytoplankton diet. *Environmental Science and Technology* 40, 2063–2068.

Bowen, L., Werner, I., and Johnson, M.L. (2006). Physiological and behavioral effects of zinc and temperature on coho salmon (*Oncorhynchus kisutch*). *Hydrobiologia* 559, 161–168.

Boyle, D., Amlund, H., Lundebye, A.-K., Hogstrand, C., and Bury, N.R. (2010). Bioavailability of a natural lead-contaminated invertebrate diet to zebrafish. *Environmental Toxicology and Chemistry* 29, 708–714.

Boyle, D., Brix, K.V., Amlund, H., Lundebye, A.-K., Hogstrand, C., and Bury, N.R. (2008). Natural arsenic contaminated diets perturb reproduction in fish. *Environmental Science and Technology* 42, 5354–5360.

Brix, K.V., DeForest, D.K., and Adams, W.J. (2011). The sensitivity of aquatic insects to divalent metals: A comparative analysis of laboratory and field data. *Science of the Total Environment* 409, 4187–4197.

Brix, K.V., Gillette, P., Pourmand, A., Capo, T.R., and Grosell, M. (2012). The effects of dietary silver on larval growth in the echinoderm *Lytechinus variegatus*. *Archives of Environmental Contamination and Toxicology* 63, 95–100.

Buchwalter, D.B., Cain, D.J., Clements, W.H., and Luoma, S.N. (2007). Using biodynamic models to reconcile differences between laboratory toxicity tests and field biomonitoring with aquatic insects. *Environmental Science and Technology* 41, 4821–4828

Buchwalter, D.B., Cain, D.J., Martin, C.A., Xie, L., Luoma, S.N., and Garland, T. (2008). Aquatic insect ecophysiological traits reveal phylogenetically based differences in dissolved cadmium susceptibility. *Proceedings of the National Academy of Sciences USA* 10, 8321–8326.

Campbell, P.G.C., Clearwater, S.J., Brown, P.B., Fisher, N.S., Hogstrand, C., Lopez, G.R., Mayer, L.M., and Meyer, J.S. (2005). Digestive physiology, chemistry, and nutrition. In J.S. Meyer, W.J. Adams, K.V. Brix, S.N. Luoma, D.R. Mount, W.A. Stubblefield, and C.M. Wood (Eds.), *Toxicity of dietborne metals to aquatic organisms* (pp. 13–57). Pensacola, FL: SETAC Press.

Cardwell, R.D., DeForest, D.K., Brix, K.V., and Adams, W.J. (2013). Do Cd, Cu, Ni, Pb, and Zn biomagnify in aquatic ecosystems? *Reviews of Environmental Contamination and Toxicology* 226, 101–122.

Chapman, P.M., Adams, W.J., Brooks, M.L., Delos, C.G., Luoma, S.N., Maher, W.A., Ohlendorf, H.M., Presser, T.S., and Shaw, D.P. (Eds.). (2010). *Ecological assessment of selenium in the aquatic environment*. Pensacola, FL: SETAC Press.

Cheung, M.-S., Fok, E.M.W., Ng, T.Y.-T., Yen, Y.-F., and Wang, W.-X. (2006). Subcellular cadmium distribution, accumulation, and toxicity in a predatory gastropod,

Thais clavigera, fed different prey. *Environmental Toxicology and Chemistry* 25, 174–181.

Cheung, M.S., and Wang, W.-X. (2008). Analyzing biomagnifications of metals in different marine food webs using nitrogen isotopes. *Marine Pollution Bulletin* 56, 2082–2105.

Chou, C.L., Uthe, J.F., Castell, J.D., and Kean, J.C. (1987). Effect of dietary cadmium on growth, survival, and tissue concentrations of cadmium, zinc, copper and silver in juvenile American lobster (*Homarus americanus*). *Canadian Journal of Fisheries and Aquatic Sciences* 44, 1443–1450.

Clearwater, S.J., Farag, A.M., and Meyer, J.S. (2002). Bioavailability and toxicity of dietborne copper and zinc to fish. *Comparative Biochemistry and Physiology Part C Toxicology and Pharmacology* 132, 269–313.

Clearwater, S.J., Handy, R.D., and Hogstrand, C. (2005). Interactions of dietborne metals with digestive processes in fishes. In J.S. Meyer, W.J. Adams, K.V. Brix, S.N. Luoma, D.R. Mount, W.A. Stubblefield, and C.M. Wood (Eds.), *Toxicity of dietborne metals to aquatic organisms* (pp. 205–225). Pensacola, FL: SETAC Press.

Cockell, K.A., and Bettger, W.J. (1993). Investigations of the gallbladder pathology associated with dietary exposure to disodium arsenate heptahydrate in juvenile rainbow trout. *Toxicology* 77, 233–248.

Cockell, K.A., and Hilton, J.W. (1988). Preliminary investigation on the comparative chronic toxicity of four dietary arsenicals to juvenile rainbow trout (*Salmo gairdneri* R.). *Aquatic Toxicology* 12, 73–82.

Cockell, K.A., Hilton, J.W., and Bettger, W.J. (1991). Chronic toxicity of dietary disodium arsenate heptahydrate to juvenile rainbow trout (*Oncorhynchus mykiss*). *Archives of Environmental Contamination and Toxicology* 21, 518–527.

Cockell, K.A., Hilton, J.W., and Bettger, W.J. (1992). Hepatobiliary and hematological effects of dietary disodium arsenate heptahydrate in juvenile rainbow trout (*Oncorhynchus mykiss*). *Comparative Biochemistry and Physiology Part C Toxicology and Pharmacology* 103, 453–458.

Couillard, Y., Grapentine, L.C., Borgmann, U., Doyle, P., and Masson, S. (2008). The amphipod *Hyalella azteca* as a biomonitor in field deployment studies for metal mining. *Environmental Pollution* 156, 1314–1324.

Croteau, M.-N., Luoma, S.N., and Stewart, A.R. (2005). Trophic transfer of metals along freshwater food webs: Evidence of cadmium biomagnification in nature. *Limnology and Oceanography* 50, 1511–1519.

Dai, W., Fu, L., Du, H., and Jin, C. (2009). Changes in growth performance, metabolic enzyme activities, and content of Fe, Cu, and Zn in liver and kidney of tilapia (*Oreochromis niloticus*) exposed to dietary Pb. *Biological Trace Element Research* 128, 176–183.

Dang, F., Rainbow, P.S., and Wang, W.-X. (2012a). Dietary toxicity of field-contaminated invertebrates to marine fish: Effects of metal doses and subcellular metal distribution. *Aquatic Toxicology* 120–121, 1–10.

Dang, F., and Wang, W.-X. (2009). Assessment of tissue-specific accumulation and effects of cadmium in a marine fish fed contaminated commercially produced diet. *Aquatic Toxicology* 95, 248–255.

Dang, F., Wang, W.-X., and Rainbow, P.S. (2012b). Unifying prolonged copper exposure, accumulation, and toxicity from food and water in a marine fish. *Environmental Science and Technology* 46, 3465–3471.

DeForest, D., Church, B., and Currie, S. (2012). Ambient background concentrations of trace elements (aluminum, boron, copper, lead, molybdenum, nickel, zinc) and dissolved organic carbon in estuarine, coastal, and open marine waters. Draft report. Prepared for the Ecotoxicity Technical Advisory Panel (ETAP).

DeForest, D.K., and Van Genderen, E.J. (2012). Application of U.S. EPA guidelines in a bioavailability-based assessment of ambient water quality criteria for zinc in freshwater. *Environmental Toxicology and Chemistry* 31, 1264–1272.

De Jonge, M., Dreesen, F., De Paepe, J., Blust, R., and Bervoets, L. (2009). Do acid volatile sulfides (AVS) influence the accumulation of sediment-bound metals to benthic invertebrates under natural field conditions? *Environmental Science and Technology* 43, 4510–4516.

Deleebeeck, N.M.E., De Schamphelaere K.A.C., and Janssen, C.R. (2009). Effects of Mg^{2+} and H^{+} on the toxicity of Ni^{2+} to the unicellular green alga *Pseudokirchneriella subcapitata*: Model development and validation with surface waters. *Science of the Total Environment* 407, 1901–1914.

Depew, D.C., Basu, N., Burgess, N.M., Campbell, L.M., Devlin, E.W., Drevnick, P.E., Hammerschmidt, C.R., Murphy, C.A., Sandheinrich, M.B., and Wiener, J.G. (2012). Toxicity of dietary methylmercury to fish: Derivation of ecologically meaningful threshold concentrations. *Environmental Toxicology and Chemistry* 31, 1536–1547.

De Schamphelaere, K.A.C., Canli, M., Van Lierde, V., Forrez, I., Vanhaecke, F., and Janssen, C.R. (2004). Reproductive toxicity of dietary zinc to *Daphnia magna*. *Aquatic Toxicology* 70, 233–244.

De Schamphelaere, K.A.C., Forrez, I., Dierckens, K., Sorgeloos, P., and Janssen, C.R. (2007). Chronic toxicity of dietary copper to *Daphnia magna*. *Aquatic Toxicology* 81, 409–418.

De Schamphelaere, K.A.C., and Janssen, C.R. (2004). Effects of chronic dietary copper exposure on growth and reproduction of *Daphnia magna*. *Environmental Toxicology and Chemistry* 23, 2038–2047.

De Schamphelaere, K.A.C., Vandenbrouck, T., Muyssen, B.T.A., Soetaert, A., Blust, R., De Coen, W., and Janssen, C.R. (2008). Integration of molecular with higher-level effects of dietary zinc exposure in *Daphnia magna*. *Comparative Biochemistry and Physiology Part D Genomics and Proteomics* 3, 307–314.

Ebenso, I.E., and Ologhobo, A.D. (2009). Effects of lead pollution against juvenile *Achatina achatina* fed on contaminated artificial diet. *Bulletin of Environmental Contamination and Toxicology* 82, 583–585.

ECB (European Chemicals Bureau). (2008). *European Union risk assessment report: Nickel*. Ispra, Italy: European Commission, Joint Research Centre, European Chemicals Bureau.

ECHA (European Chemical Agency). (2013). Divanadium pentaoxide. Ecotoxicological information. Retrieved from http://apps.echa.europa.eu/registered/data/dossiers/DISS-9c7faa0b-a5e9-00e9-e044-00144f67d249/AGGR-ac206e9e-7e3e-408e-8f67-6d172b52447f_DISS-9c7faa0b-a5e9-00e9-e044-00144f67d249.html#AGGR-ac206e9e-7e3e-408e-8f67-6d172b52447f

Eid, A.E., and Ghonim, S.I. (1994). Dietary zinc requirement of fingerling *Oreochromis niloticus*. *Aquaculture* 119, 259–264.

Erickson, R.J., Mount, D.R., Highland, T.L., Hockett, J.R., and Jenson, C.T. (2011). The relative importance of waterborne and dietborne arsenic exposure on survival and growth of juvenile rainbow trout. *Aquatic Toxicology* 104, 108–115.

Erickson, R.J., Mount, D.R., Highland, T.L., Hockett, J.R., Leonard, E.N., Mattson, V.R., Dawson, T.D., and Lott, K.G. (2010). Effects of copper, cadmium, lead, and arsenic in a live diet on juvenile fish growth. *Canadian Journal of Fisheries and Aquatic Sciences* 67, 1816–1826.

Ettajani, H., Berthet, B., Amiard, J.C., and Chevolet, L. (2001). Determination of cadmium partitioning in microalgae and oysters: Contribution to the assessment of trophic transfer. *Archives of Environmental Contamination and Toxicology* 40, 209–221.

Evens, R., De Schamphelaere, K.A.C., Balcaen, L., Wang, Y., De Roy, K., Resano, M., Flórez, M., Boon, N., Vanhaecke, F., and Janssen, C.R. (2012a). The use of liposomes to differentiate between the effects of nickel accumulation and altered food quality in *Daphnia magna* exposed to dietary nickel. *Aquatic Toxicology* 109, 80–89.

Evens, R., De Schamphelaere, K.A.C., Balcaen, L., Wang, Y., De Roy, K., Resano, M., Flórez, M. del R., Van der Meeren, P., Boon, N., Vanhaecke, F., and Janssen, C.R. (2011). Liposomes as an alternative delivery system for investigating dietary metal toxicity to *Daphnia magna*. *Aquatic Toxicology* 105, 661–668.

Evens, R., De Schamphelaere, K.A.C., De Samber, B., Silversmit, G., Schoonjans, T., Vekemans, B., Balcaen, L., Vanhaecke, F., Szaloki, I., Rickers, K., Falkenberg, G., Vincze, L., and Janssen, C.R. (2012b). Waterborne versus dietary zinc accumulation and toxicity in *Daphnia magna*: A synchrotron radiation based X-ray fluorescence imaging approach. *Environmental Science and Technology* 46, 1178–1184.

Evens, R.E., De Schamphelaere, K.A.C., De Laender, F., and Janssen, C. (2012c). The effects of Zn-contaminated diets on *Daphnia magna* reproduction may be related to Zn-induced changes of the dietary P content rather than to the dietary Zn content itself. *Aquatic Toxicology* 110–111, 9–16.

Evens, R.E., De Schamphelaere, K.A.C., and Janssen, C.R. (2009). The effects of dietary nickel exposure on growth and reproduction of *Daphnia magna*. *Aquatic Toxicology* 94, 138–144.

Farag, A.M., Woodward, D.F., Brumbaugh, W., Goldstein, J.N., MacConnell, E., Hogstrand, C., and Barrows, F.T. (1999). Dietary effects of metals-contaminated invertebrates from the Coeur d'Alene River, Idaho, on cutthroat trout. *Transactions of the American Fisheries Society* 128, 578–592.

Ferard, J.F., Jouany, J.M., Truhaut, R., and Vasseur, P. (1983). Accumulation of cadmium in a freshwater food chain experimental model. *Ecotoxicology and Environmental Safety* 7, 43–52.

Fisher, N.S., Stupakoff, I., Sañudo-Wilhelmy, S., Wang, W.-X., Teyssié, J.-L., Fowler, S.W., and Crusius, J. (2000). Trace metals in marine copepods: A field test of a bioaccumulation model coupled to laboratory uptake kinetics data. *Marine Ecology Progress Series* 194, 211–218.

Fort, D.J., Propst, T.L., Stover, E.L., Murray, F.J., and Strong, P.L. (1999). Adverse effects from low dietary and environmental boron exposure on reproduction, development, and maturation in *Xenopus laevis*. *The Journal of Trace Elements in Experimental Medicine* 12, 175–185.

Fort, D.J., Stover, E.L., Rogers, R.L., Copley, H.F., Morgan, L.A., and Foster, E.R. (2000). Chronic boron or copper deficiency induces limb teratogenesis in *Xenopus*. *Biological Trace Element Research* 77, 173–187.

Franklin, N.M., Glover, C.N., Nicol, J.A., and Wood, C.M. (2005). Calcium/cadmium interactions at uptake surfaces in rainbow trout: Waterborne versus dietary routes of exposure. *Environmental Toxicology and Chemistry* 24, 2954–2964.

Galvez, F., Hogstrand, C., McGeer, J.C., and Wood, C.M. (2001). The physiological effects of a biologically incorporated silver diet in rainbow trout (*Oncorhynchus mykiss*). *Aquatic Toxicology* 55, 95–112.

Galvez, F., and Wood, C.M. (1999). The physiological effects of dietary silver sulphide exposure in rainbow trout. *Environmental Toxicology and Chemistry* 18, 84–88.

Gatlin III, D.M., and Wilson, R.P. (1986). Dietary copper requirement of fingerling channel catfish. *Aquaculture* 54, 277–285.

Geffard, O., Geffard, A., Chaumot, A., Vollat, B., Alvarez, C., Tusseau-Vuillemin, M.H., and Garric, J. (2008). Effects of chronic dietary and waterborne cadmium exposures on the contamination level and reproduction of *Daphnia magna*. *Environmental Toxicology and Chemistry* 27, 1128–1134.

Gensemer, R.W., and Playle, R.C. (1999). The bioavailability and toxicity of aluminum in aquatic environments. *Critical Reviews in Environmental Science and Technology* 29, 315–450.

Goettl, Jr., J.P., and Davies, P.H. (1978). Water pollution studies. Colorado Division of Wildlife, Job Progress Report, *Federal Aid Project F-33-R-13*. 45 pp.

Golding, L.A., Borgmann, U., and Dixon, D.G. (2011). Modeling chronic dietary cadmium bioaccumulation and toxicity from periphyton to *Hyalella azteca*. *Environmental Toxicology and Chemistry* 30, 1709–1720.

Haesloop, U., and Schirmer, M. (1985). Accumulation of orally administered cadmium by the eel (*Anguilla anguilla*). *Chemosphere* 14, 1627–1634.

Handy, R.D. (1993a). The effect of acute exposure to dietary Cd and Cu on organ toxicant concentrations in rainbow trout, *Oncorhynchus mykiss*. *Aquatic Toxicology* 27, 1–14.

Handy, R.D. (1993b). The accumulation of dietary aluminium by rainbow trout, *Oncorhynchus mykiss*, at high exposure concentrations. *Journal of Fish Biology* 42, 603–606.

Handy, R.D., McGeer, J.C., Allen, H.E., Drevnik, P.E., Gorsuch, J.W., Green, A.S., Haldorsen, A.-K.L., Hook, S.E., Mount, D.R., and Stubblefield, W.A. (2005). Toxic effects of dietborne metals: Laboratory studies. In J.S. Meyer, W.J. Adams, K.V. Brix, S.N. Luoma, D.R. Mount, W.A. Stubblefield, and C.M. Wood (Eds.), *Toxicity of dietborne metals to aquatic organisms* (pp. 59–112). Pensacola, FL: SETAC Press.

Handy, R.D., Sims, D.W., Giles, A., Campbell, H.A., and Musonda, M.M. (1999). Metabolic trade-off between locomotion and detoxification for maintenance of blood chemistry and growth parameters by rainbow trout (*Oncorhynchus*

mykiss) during chronic dietary exposure to copper. *Aquatic Toxicology* 47, 23–41.

Hansen, J.A., Lipton, J., Welsh, P.G., Cacela, D., and MacConnell, B. (2004). Reduced growth of rainbow trout (*Oncorhynchus mykiss*) fed a live invertebrate diet pre-exposed to metal-contaminated sediments. *Environmental Toxicology and Chemistry* 23, 1902–1911.

Hatakeyama, S., and Yasuno, M. (1981). The effects of cadmium-accumulated *Chlorella* on the reproduction of *Moina macrocopa* (Cladocera). *Ecotoxicology and Environmental Safety* 5, 341–350.

Hatakeyama, S., and Yasuno, M. (1982). Accumulation and effects of cadmium on guppy (*Poecilia reticulata*) fed cadmium-dosed cladocera (*Moina macrocopa*). *Bulletin of Environmental Contamination and Toxicology* 29, 159–166.

Hatakeyama, S., and Yasuno, M. (1987). Chronic effects of Cd on the reproduction of the guppy (*Poecilia reticulata*) through Cd-accumulated midge larvae (*Chironomus yoshimatsui*). *Ecotoxicology and Environmental Safety* 14, 191–207.

Hilton, J.W., and Bettger, W.J. (1988). Dietary vanadium toxicity in juvenile rainbow trout: A preliminary study. *Aquatic Toxicology* 12, 63–71.

Hodson, P.V., Blunt, B.R., and Spry, D.J. (1978). Chronic toxicity of water-borne and dietary lead to rainbow trout (*Salmo gairdneri*) in Lake Ontario water. *Water Research* 12, 869–878.

Hook, S.E., and Fisher, N.S. (2001a). Sublethal effects of silver in zooplankton: Importance of exposure pathways and implications for toxicity testing. *Environmental Toxicology and Chemistry* 20, 568–574.

Hook, S.E., and Fisher, N.S. (2001b). Reproductive toxicity of metals in calanoid copepods. *Marine Biology* 138, 1131–1140.

Hook, S.E., and Fisher, N.S. (2002). Relating the reproductive toxicity of five ingested metals in calanoid copepods with sulfur affinity. *Marine Environmental Research* 53, 161–174.

Hoyle, I., Shaw, B.J., and Handy, R.D. (2007). Dietary copper exposure in the African walking catfish, *Clarias gariepinus*: Transient osmoregulatory disturbances and oxidative stress. *Aquatic Toxicology* 83, 62–72.

Huang, X., Guo, F., Ke, C., and Wang, W.-X. (2010). Responses of abalone *Haliotis diversicolor* to sublethal exposure of waterborne and dietary silver and cadmium. *Ecotoxicology and Environmental Safety* 73, 1130–1137.

HydroQual Inc., EcoTox Inc., and Gorsuch Environmental Management Services, Inc. (2007). *2007 Draft update of ambient water quality criteria for silver. Unpublished report*. East Syracuse, NY: HydroQual Inc., 51 pp.

Irving, E.C., Baird, D.J., and Culp, J.M. (2003). Ecotoxicological responses of the mayfly *Baetis tricaudatus* to dietary and waterborne cadmium: Implications for toxicity testing. *Environmental Toxicology and Chemistry* 22, 1058–1064.

Jain, K.K., Sinha, A., Srivastava, P.P., and Berendra, D.K. (1994). Chromium: An efficient growth enhancer in Indian major carp, *Labeo rohita*. *Journal of Aquaculture in the Tropics* 9, 49–54.

Jara-Marini, M.E., Soto-Jiménez, M.F., and Páez-Osuna, F. (2009). Trophic relationships and transference of cadmium, copper, lead and zinc in a subtropical coastal lagoon food web from SE Gulf of California. *Chemosphere* 77, 1366–1373.

Jeng, S.S., and Sun, L.T. (1981). Effects of dietary zinc levels on zinc concentrations in tissues of common carp. *Journal of Nutrition* 111, 134–140.

Julshamn, K., Andersen, K.-J., Ringdal, O., and Brenna, J. (1988). Effect of dietary copper on the hepatic concentration and subcellular distribution of copper and zinc in the rainbow trout (*Salmo gairdneri*). *Aquaculture* 73, 143–155.

Kamunde, C., Grosell, M., Lott, J.N.A., and Wood, C.M. (2001). Copper metabolism and gut morphology in rainbow trout (*Oncorhynchus mykiss*) during chronic sublethal dietary copper exposure. *Canadian Journal of Fisheries and Aquatic Sciences* 58, 293–305.

Kamunde, C., Grosell, M., Higgs, D., and Wood, C.M. (2002). Copper metabolism in actively growing rainbow trout (*Oncorhynchus mykiss*): Interactions between dietary and waterborne copper uptake. *Journal of Experimental Biology* 205, 279–290.

Kamunde, C., and Wood, C.M. (2003). The influence of ration size on copper homeostasis during sublethal dietary copper exposure in juvenile rainbow trout, *Oncorhynchus mykiss*. *Aquatic Toxicology* 62, 235–254.

Kang, J.-C., Kim, S.-G., and Jang, S.W. (2005). Growth and hematological changes of rockfish, *Sebastes schlegeli* (Hilgendorf) exposed to dietary Cu and Cd. *Journal of the World Aquaculture Society* 36, 188–195.

Kim, S.-G., and Kang, J.-C. (2004). Effect of dietary copper exposure on accumulation, growth and hematological parameters of the juvenile rockfish, *Sebastes schlegeli*. *Marine Environmental Research* 58, 65–82.

Kim, S.-G., Kim, J.-W., and Kang, J.-C. (2004). Effect of dietary cadmium on growth and hematological parameters of juvenile rockfish, *Sebastes schlegeli* (Hilgendorf). *Aquaculture Research* 35, 80–86.

Kjoss, V.A., Grosell, M., and Wood, C.M. (2005). The influence of dietary Na on Cu accumulation in juvenile rainbow trout exposed to combined dietary and waterborne Cu in soft water. *Archives of Environmental Contamination and Toxicology* 49, 520–527.

Kjoss, V.A., Wood, C.M., and McDonald, D.G. (2006). Effects of different ligands on the bioaccumulation and subsequent depuration of dietary Cu and Zn in juvenile rainbow trout (*Oncorhynchus mykiss*). *Canadian Journal of Fisheries and Aquatic Sciences* 63, 412–422.

Knox, D., Cowey, C.B., and Adron, J.W. (1984). Effects of dietary zinc intake upon copper metabolism in rainbow trout (*Salmo gairdneri*). *Aquaculture* 40, 199–207.

Kolts, J.M., Boese, C.J., and Meyer, J.S. (2009). Effects of dietborne copper and silver on reproduction by *Ceriodaphnia dubia*. *Environmental Toxicology and Chemistry* 28, 71–85.

Lanno, R.P., Slinger, S.J., and Hilton, J.W. (1985a). Maximum tolerable and toxicity levels of dietary copper in rainbow trout (*Salmo gairdneri* Richardson). *Aquaculture* 49, 257–268.

Lanno, R.P., Slinger, S.J., and Hilton, J.W. (1985b). Effect of ascorbic acid on dietary copper toxicity in rainbow trout (*Salmo gairdneri* Richardson). *Aquaculture* 49, 269–287.

Lapointe, D., Pierron, F., and Couture, P. (2011). Individual and combined effects of heat stress and aqueous or dietary copper exposure in fathead minnows (*Pimephales promelas*). *Aquatic Toxicology* 104, 80–85.

Lauer, M.M., and Bianchini, A. (2010). Chronic copper toxicity in the estuarine copepod *Acartia tonsa* at different salinities. *Environmental Toxicology and Chemistry* 29, 2297–2303.

Lin, Y.H., Shie, Y.Y., and Shiau, S.Y. (2008). Dietary copper requirements of juvenile grouper, *Epinephelus malabaricus*. *Aquaculture* 274, 161–165.

Loewengart, G. (2001). Toxicity of boron to rainbow trout: A weight-of-the-evidence assessment. *Environmental Toxicology and Chemistry* 20, 796–803.

Lundebye, A.-K., Berntssen, M.H.G., Wendelaar Bonga, S.E., and Maage, A. (1999). Biochemical and physiological responses in Atlantic salmon (*Salmo salar*) following dietary exposure to copper and cadmium. *Marine Pollution Bulletin* 39, 137–144.

Luoma, S.N., and Rainbow, P.S. (2005). Why is metal bioaccumulation so variable? Biodynamics as a unifying concept. *Environmental Science and Technology* 39, 1921–1931.

Luoma, S.N., and Rainbow P.S. (2008). *Metal contamination in aquatic environments: Science and lateral management*. Cambridge: Cambridge University Press.

Maage, A., and Julshamn, K. (1993). Assessment of zinc status in juvenile Atlantic salmon (*Salmo salar*) by measurement of whole body and tissue levels of zinc. *Aquaculture* 117, 179–191.

Mai, K., Li, H., Ai, Q., Duan, Q., Xu, W., Zhang, C., Zhang, L., Tan, B., and Liufu, Z. (2006). Effects of dietary squid viscera meal on growth and cadmium accumulation in tissues of Japanese seabass. *Aquaculture Research* 37, 1063–1069.

Marín-Guirao, L., Lloret, J., and Marin, A. (2008). Carbon and nitrogen stable isotopes and metal concentration in food webs from a mining-impacted coastal lagoon. *Science of the Total Environment* 393, 118–130.

Matida, Y., Kumada, H., Kimura, S., Saiga, Y., Nose, T., Yokote, M., and Kawatsu, H. (1971). Toxicity of mercury compounds to aquatic organisms and accumulation of the compounds by the organisms. *Bulletin of the Freshwater Fish Research Laboratory* 21, 197–227.

McGeer, J.C., Brix, K.V., Skeaff, J.M., DeForest, D.K., Brigham, S.I., Adams, W.J., and Green, A. (2003). Inverse relationship between bioconcentration factor and exposure concentration for metals: Implications for hazard assessment of metals in the aquatic environment. *Environmental Toxicology and Chemistry* 22, 1017–1037.

Meyer, J.S., Adams, W.J., Brix, K.V., Luoma, S.N., Mount, D.R., Stubblefield, W.A., and Wood, C.M. (Eds.). (2005a). *Toxicity of dietborne metals to aquatic organisms*. Pensacola, FL: SETAC Press.

Meyer, J.S., Adams, W.J., Brix, K.V., Luoma, S.N., Mount, D.R., Stubblefield, W.A., and Wood, C.M. (2005b). Workshop summary and conclusions. In J.S. Meyer, W.J. Adams, K.V. Brix, S.N. Luoma, D.R. Mount, W.A. Stubblefield, and C.M. Wood (Eds.), *Toxicity of dietborne metals to aquatic organisms* (pp. 191–201). Pensacola, FL: SETAC Press.

Morris, J.M., Collyard, S.A., and Meyer, J.S. (2003). Effects of chronic copper exposure on the nutritional composition of *Hyalella azteca*. *Aquatic Toxicology* 63, 197–206.

Mount, D.R. (2005). Introduction. In J.S. Meyer, W.J. Adams, K.V. Brix, S.N. Luoma, D.R. Mount, W.A. Stubblefield, and C.M. Wood (Eds.), *Toxicity of dietborne metals to aquatic organisms* (pp. 1–11). Pensacola, FL: SETAC Press.

Mount, D.R., Barth, A.K., Garrison, T.D., Barten, K.A., and Hockett, J.R. (1994). Dietary and waterborne exposure of rainbow trout (*Oncorhynchus mykiss*) to copper, cadmium, lead and zinc using a live diet. *Environmental Toxicology and Chemistry* 13, 2031–2041.

Munger, C., and Hare, L. (1997). Relative importance of water and food as cadmium sources to an aquatic insect (*Chaoborus punctipennis*): Implications for predicting Cd bioaccumulation in nature. *Environmental Science and Technology* 31, 891–895.

Murai, T., Andrews, J.W., and Smith, R.G. (1981). Effects of dietary copper on channel catfish. *Aquaculture* 22, 353–357.

Ng, T.Y.-T., and Wood, C.M. (2008). Trophic transfer and dietary toxicity of Cd from the oligochaete to the rainbow trout. *Aquatic Toxicology* 87, 47–59.

Ng, T.Y.-T., Klinck, J.S., and Wood, C.M. (2009). Does dietary Ca protect against toxicity of a low dietborne Cd exposure to the rainbow trout? *Aquatic Toxicology* 91, 75–86.

Oberholster, P.J., Myburgh, J.G., Ashton, P.J., Coetzee, J.J., and Botha, A.-M. (2012). Bioaccumulation of aluminium and iron in the food chain of Lake Loskop, South Africa. *Ecotoxicology and Environmental Safety* 75, 134–141.

Overnell, J., Fletcher, T.C., and McIntosh, R. (1988). The apparent lack of effect of supplementary dietary zinc on zinc metabolism and metallothionein concentrations in the turbot, *Scophthalmus maximus* (Linnaeus). *Journal of Fish Biology* 33, 563–570.

Overnell, J., and McIntosh, R. (1988). The effect of supplementary dietary copper on copper and metallothionein levels in the fish, dab, *Limanda limanda*. *Marine Environmental Research* 26, 237–247.

Park, C.W., and Shimizu, C. (1989). Quantitative requirements of aluminium and iron in the formulated diets and its interrelation with other minerals in young eel. *Nippon Suisan Gakkashi* 55, 111–116.

Pedroso, M.S., Bersano, J.G.F., and Bianchini, A. (2007). Acute silver toxicity in the euryhaline copepod *Acartia tonsa*: Influence of salinity and food. *Environmental Toxicology and Chemistry* 26, 2158–2165.

Pereira, A.A., van Hattum, B., de Boer, J., van Bodegom, P.M., Rezende, C.E., and Salomons, W. (2010). Trace elements and carbon and nitrogen stable isotopes in organisms from a tropical coastal lagoon. *Archives of Environmental Contamination and Toxicology* 59, 464–477.

Pinho, G.L.L., Pedroso, M.S., Rodrigues, S.C., De Souza, S.S., and Bianchini, A. (2007). Physiological effects of copper in the euryhaline copepod *Acartia tonsa*: Waterborne versus waterborne plus dietborne exposure. *Aquatic Toxicology* 84, 62–70.

Poston, H.A. (1991). Effects of dietary aluminium on growth and composition of young Atlantic salmon. *The Progressive Fish-Culturist* 53, 7–10.

Powell, M.L., Jones, W.T., Gibbs, V.K., Hammer, H.S., Lawrence, J.M., Fox, J., Lawrence, A.L., and Watts, S.A. (2010). Dietary copper affects survival, growth, and reproduction in the sea urchin *Lytechinus variegatus*. *Journal of Shellfish Research* 29, 1043–1049.

Ptashynski, M.D., Pedlar, R.M., Evans, R.E., Baron, C.L., and Klaverkamp, J.F. (2002). Toxicology of dietary nickel in lake whitefish (*Coregonus clupeaformis*). *Aquatic Toxicology* 58, 229–247.

Rainbow, P.S., Luoma, S.N., and Wang, W.-X. (2011). Trophically available metal - a variable feast. *Environmental Pollution* 159, 2347–2349.

Rainbow, P.S., Poirier, L., Smith, B.D., Brix, K.V., and Luoma, S.N. (2006). Trophic transfer of trace metals from the polychaete worm *Nereis diversicolor* to the polychaete *N. virens* and the decapod crustacean *Palaemonetes varians*. *Marine Ecology Progress Series* 321, 167–181.

Reynders, H., Campenhout, K.V., Bervoets, L., De Coen, W.M., and Blust, R. (2006). Dynamics of cadmium accumulation and effects in common carp (*Cyprinus carpio*) during simultaneous exposure to water and food (*Tubifex tubifex*). *Environmental Toxicology and Chemistry* 25, 1558–1567.

Richardson, N.L., Higgs, D.A., Beames, R.M., and McBride, J.R. (1985). Influence of dietary calcium, phosphorus, zinc and sodium phytate level on cataract incidence, growth and histopathology in juvenile Chinook salmon (*Oncorhynchus tshawytscha*). *Journal of Nutrition* 115, 553–567.

Roberts, D.A., Poore, A.G.B., and Johnston, E.L. (2006). Ecological consequences of copper contamination in macroalgae: Effects on epifauna and associated herbivores. *Environmental Toxicology and Chemistry* 25, 2470–2479.

Rodgher, S., Lombardi, A.T., and Melão, M.G.G. (2009). Evaluation onto life cycle parameters of *Ceriodaphnia silvestrii* submitted to 36 days dietary copper exposure. *Ecotoxicology and Environmental Safety* 72, 1748–1753.

Rowe, C.L., Heyes, A., and Hopkins, W. (2009). Effects of dietary vanadium on growth and lipid storage in a larval anuran: Results from studies employing ad libitum and rationed feeding. *Aquatic Toxicology* 91, 179–186.

Ruangsomboon, S., and Wongrat, L. (2006). Bioaccumulation of cadmium in an experimental aquatic food chain involving phytoplankton (*Chlorella vulgaris*), zooplankton (*Moina macrocopa*), and the predatory catfish *Clarias macrocephalus* × *C. gariepinus*. *Aquatic Toxicology* 78, 15–20.

Sabatini, S.E., Chaufan, G., Juárez, Á.B., Coalova, I., Bianchi, L., Eppis, M.R., and del Carmen Ríos de Molina, M. (2009). Dietary copper effects in the estuarine crab, *Neohelice (Chasmagnathus) granulata*, maintained at two different salinities. *Comparative Biochemistry and Physiology Part C Toxicology and Pharmacology* 150, 521–527.

Saiki, M.K., Jennings, M.R., and Brumbaugh, W.G. (1993). Boron, molybdenum, and seleniumin aquatic food chains from the lower San Joaquin River and its tributaries, California. *Archives of Environmental Contamination and Toxicology* 24, 307–319.

Schlekat, C.E., Kidd, K.A., Adams, W.J., Baird, D.J., Farag, A.M., Maltby, L., and Stewart, A.R. (2005). Toxic effects of dietborne metals: Field studies. In J.S. Meyer, W.J. Adams, K.V. Brix, S.N. Luoma, D.R. Mount, W.A. Stubblefield,

and C.M. Wood (Eds.), *Toxicity of dietborne metals to aquatic organisms* (pp. 113–152). Pensacola, FL: SETAC Press.

Shaw, B.J., and Handy, R.D. (2006). Dietary copper exposure and recovery in Nile tilapia, *Oreochromis niloticus*. *Aquatic Toxicology* 76, 111–121.

Shiau, S.-Y., and Lin, S.-F. (1993). Effect of supplemental dietary chromium and vanadium on the utilization of different carbohydrates in tilapia, *Oreochromis niloticus* × *0. aureus*. *Aquaculture* 110, 321–330.

Sofyan, A., Price, D.J., and Birge, W.J. (2007a). Effects of aqueous, dietary and combined exposures of cadmium to *Ceriodaphnia dubia*. *Science of the Total Environment* 385, 108–116.

Sofyan, A., Rosita, G., Price, D.J., and Birge, W.J. (2007b). Cadmium uptake by *Ceriodaphnia dubia* from different exposures: Relevance to body burdens and toxicity. *Environmental Toxicology and Chemistry* 26, 470–477.

Sofyan, A., Shaw, J.R., and Birge, W.J. (2006). Metal trophic transfer from algae to cladocerans and the relative importance of dietary metal exposure. *Environmental Toxicology and Chemistry* 25, 1034–1041.

Spry, D.J., Hodson, P.V., and Wood, C.M. (1988). Relative contributions of dietary and waterborne zinc in the rainbow trout, *Salmo gairdneri*. *Canadian Journal of Fisheries and Aquatic Sciences* 45, 32–41.

Stanley, Jr., T.R., Smith, G.J., Hoffman, D.J., Heinz, G.H., and Rosscoe, R. (2006). Effects of boron and selenium on mallard reproduction and duckling growth and survival. *Environmental Toxicology and Chemistry* 15, 1124–1132.

Steen-Redeker, E., Bervoets, L., and Blust, R. (2004). Dynamic model for the accumulation of cadmium and zinc from water and sediment by the aquatic oligochaete *Tubifex tubifex*. *Environmental Science and Technology* 38, 6193–6200.

Steen-Redeker, E., and Blust, R. (2004). Accumulation and toxicity of cadmium in the aquatic oligochaete *Tubifex tubifex*: A kinetic modeling approach. *Environmental Science and Technology* 38, 537–543.

Szczerbik, P., Mikołajczyk, T., Sokołowska-Mikołajczyk, M., Socha, M., Chyb, J., and Epler, P. (2006). Influence of long-term exposure to dietary cadmium on growth, maturation and reproduction of goldfish (subspecies: Prussian carp *Carrassium auratus gibelio* B.). *Aquatic Toxicology* 77, 126–135.

Tacon, A.G.J., and Beveridge, M.M. (1982). Effects of dietary trivalent chromium on rainbow trout. *Nutrition Reports International* 25, 49–56.

Takeda, H., and Shimma, Y. (1977). Effects of toxic amounts of dietary zinc on the growth and body components of rainbow trout at two levels of calcium. *Bulletin of Freshwater Fisheries Research Laboratory* 27, 103–109.

Tan, X.-Y., Luo, Z., Zhang, G.-Y., Liu, X.-J., and Jiang, M. (2010). Effect of dietary cadmium level on the growth, body composition and several hepatic enzymatic activities of juvenile yellow catfish, *Pelteobagrus fulvidraco*. *Aquaculture Research* 41, 1022–1029.

UK Environment Agency. (2009). *Interim report on derivation of a marine environmental quality standard for zinc*. Almondsbury, Bristol, UK, 31 pp.

USEPA (U.S. Environmental Protection Agency). (1980). *Ambient water quality criteria for silver. EPA 440/5-80-071*. Washington, DC: U.S. Environmental Protection Agency, Office of Water.

USEPA (U.S. Environmental Protection Agency). (1997a). *Mercury study report to Congress. Volume III: Fate and transport of mercury in the environment. EPA-452/R-97-005*. Washington, DC, USA: U.S. Environmental Protection Agency Office of Air Quality Planning and Standards, and Office of Research and Development.

USEPA (U.S. Environmental Protection Agency). (1997b). *Mercury study report to Congress. Volume VII: Characterization of human health and wildlife risks from mercury exposure in the United States. EPA-452/R-97-009*. Washington, DC, USA: U.S. Environmental Protection Agency Office of Air Quality Planning and Standards, and Office of Research and Development.

USEPA (U.S. Environmental Protection Agency). (2001). *2001 update of ambient water quality criteria for cadmium. EPA-822-R-01-001*. Washington, DC, USA: U.S. Environmental Protection Agency Office of Water.

USEPA (U.S. Environmental Protection Agency). (2004). *Draft aquatic life water quality criteria for selenium – 2004. EPA-822-D-04-001*. Washington, DC, USA: U.S. Environmental Protection Agency Office of Water.

USEPA (U.S. Environmental Protection Agency). (2009). *National recommended water quality criteria*. Washington, DC, USA: U.S. Environmental Protection Agency Office of Water. Retrieved from http://water.epa.gov/scitech/swguidance/standards/current/

Wallace, W.G., Brouwer, T.M.H., Brouwer, M., and Lopez, G.R. (2000). Alterations in prey capture and induction of metallothioneins in grass shrimp fed cadmium-contaminated prey. *Environmental Toxicology and Chemistry* 19, 962–971.

Wang, W.-X. (2002). Interactions of trace metals and different marine food chains. *Marine Ecology Progress Series* 243, 295–309.

Wang, W.-X. (2013a). Dietary toxicity of metals in aquatic animals: Recent studies and perspectives. *Chinese Science Bulletin* 58, 203–213.

Wang, W.-X. (2013b). Prediction of metal toxicity in aquatic organisms. *Chinese Science Bulletin* 58, 194–202.

Wang, W.-X., and Fisher, N.S. (1999). Delineating metal accumulation pathways for marine invertebrates. *Science of the Total Environment* 237–238, 459–472.

Wang, W.-X., and Rainbow, P.S. (2006). Subcellular partitioning and the prediction of cadmium toxicity to aquatic organisms. *Environmental Chemistry* 3, 395–399.

Wang, Z., Yan, C., and Hyne, R.V. (2010). Effects of dietary cadmium exposure on reproduction of saltwater cladoceran *Moina monogolica* Daday: Implications in water quality criteria. *Environmental Toxicology and Chemistry* 29, 365–372.

Wang, Z.-S., Kong, H.-N., and Wu, D.-Y. (2007). Reproductive toxicity of dietary copper to a saltwater cladoceran, *Moina monogolica* Daday. *Environmental Toxicology and Chemistry* 26, 126–131.

Ward, T.J., Boeri, R.L., Hogstrand, C., Kramer, J.R., Lussier, S.M., Stubblefield, W.A., Wyskiel, D.C., and Gorsuch, J.W. (2006). Influence of salinity and organic carbon on the chronic toxicity of silver to mysids (A*mericamysis bahia*) and silversides (*Menidia beryllina*). *Environmental Toxicology and Chemistry* 25, 1809–1816.

Watanabe, T., Kiron, V., and Satoh, S. (1997). Trace metals in fish nutrition. *Aquaculture* 151, 185–207.

Wood, C.M., and Alsop, D.H. (2012). *Evaluating the relative contributions of waterborne and dietary lead to toxicity in rainbow trout*. Hamilton, ON: McMaster University. Prepared for the International Lead Zinc Research Organization, Durham, NC, USA.

Woodward, D.F., Brumbaugh, W.G., DeLonay, A.J., Little, E.E., and Smith, C.E. (1994). Effects on rainbow trout fry of a metals-contaminated diet of benthic invertebrates from the Clark Fork River, Montana. *Transactions of the American Fisheries Society* 123, 51–62.

Woodward, D.F., Farag, A.M., Bergman, H.L., Delonay, A.J., Little, E.E., Smith, C.E., and Barrows, F.T. (1995). Metals-contaminated benthic invertebrates in the Clark Fork River, Montana: Effects on age-0 brown trout and rainbow trout. *Canadian Journal of Fisheries and Aquatic Sciences* 52, 1994–2004.

Xie, L., Funk, D.H., and Buchwalter, D.B. (2010). Trophic transfer of Cd from natural periphyton to the grazing mayfly *Centroptilum triangulifer* in a life cycle test. *Environmental Pollution* 158, 272–277.

Xie, L., Lambert, D., Martin, C.A., Cain, D.J., Luoma, S.N., and Buchwalter, D.B. (2008). Cadmium biodynamics in the oligochaete *Lumbriculus variegatus* and its implications for trophic transfer. *Aquatic Toxicology* 86, 265–271.

Yaqub, S., and Javed, M. (2012). Acute toxicity of water—borne and dietary cadmium and cobalt for fish. *International Journal of Agriculture and Biology* 14, 276–280.

Zhang, W., Huang, L., and Wang, W.-X. (2012). Biotransformation and detoxification of inorganic arsenic in a marine juvenile fish *Terapon jarbua* after waterborne and dietborne exposure. *Journal of Hazardous Materials* 221–222, 162–169.

Zhao, C.-M., and Wang, W.-X. (2011). Comparison of acute and chronic toxicity of silver nanoparticles and silver nitrate to *Daphnia magna*. *Environmental Toxicology and Chemistry* 30, 885–892.