

Lead Science Review

(January – June, 2017)

#	Author and Title	Salient information	Regulatory implications for the industry	Source/link
Environmental publications				
1	DeForest et al., 2017. Development of biotic ligand model (BLM)-based freshwater aquatic life criteria for lead following U.S. EPA guidelines.	The current U.S. EPA water quality criteria for lead for the protection of aquatic life in freshwater are hardness based and were developed in 1984, but recent data suggest that hardness is not the primary factor mitigating lead toxicity in freshwater. The paper presents a set of new acute and chronic lead criteria that have been derived using biotic ligand model, a state of the art bioavailability tool, to replace the existing hardness-based criteria in the US. For a range of representative water conditions, proposed acute BLM-based lead criteria ranged from 20 to 1000 µg/L and chronic BLM-based lead criteria ranged from 0.3 to 40 µg/L. The toxicity datasets presented here are also much more robust than in 1984. The paper concludes that the BLM-based criteria would better account for site-specific lead bioavailability and more consistently achieve the U.S. EPA's target level of aquatic protection over a much broader range of site water conditions.	A milestone introducing bioavailability based Ambient Water Quality Criteria (AWQC) for aquatic life in the U.S., which may help U.S. EPA revise its outdated hardness-based criteria.	Environ. Toxicol. Chem., (In press)
2	Church et al., 2017. Updated species sensitivity distribution	Similarly to freshwater, the current U.S. EPA water quality criteria for lead for the protection of aquatic life in saltwater were developed in 1984. The paper has analyzed	Introducing updated saltwater criteria for the protection of aquatic life in the U.S., which may help U.S.	Environ. Toxicol. Chem. (in press)

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	evaluations for acute and chronic lead toxicity to aquatic life	recent data and presents a set of new acute and chronic lead criteria for saltwater in the US. The proposed updated acute and chronic criteria are 100 and 10 µg/L, respectively (the existing 1984 criteria are 210 and 8.1 µg/L). In addition, the study provides a comparative analysis of the methods used in the U.S. and the European Union for saltwater criteria development.	EPA revise its outdated 1984 criteria.	
3	Ecke et al., 2017. Sublethal lead exposure alters movement behavior in free-ranging Golden Eagles	The study examines blood lead and liver lead and flight performance in scavenging Golden Eagles in Sweden. Lead levels in blood were correlated with progress of the moose hunting season. The analysis of bird tracking data reveals that even sublethal lead concentrations in blood (25 ppb, wet weight), can likely negatively affect movement behavior (flight height and movement rate) of free-ranging scavenging Golden Eagles, which may lead to their death due to reduced hunting skills (starvation) or alertness (poaching). The study highlights lead exposure as a serious threat to wildlife conservation and suggests implementation of bans of lead ammunition for hunting.	Weight of evidence to call for Europe-wide banning of lead uses in ammunition and in particular, accepting the REACH restriction proposal that is currently under discussion for lead ammunition uses in wetlands.	Environ. Sci. Technol. 51: 5729–5736
4	Naidoo et al., 2017. Lead ingestion as a potential contributing factor to the decline in vulture populations in southern Africa	The study explores the relationship between whole blood lead concentrations of captive and wild vulture populations in Southern Africa and lead exposure factors such as mining and soil levels in order to understand the reasons of vulture populations decline. It has been demonstrated that both wild and captive vulture populations in South Africa are being exposed to	Weight of evidence to identify leaded bullets as a threat to wildlife and call for banning of lead uses in ammunition.	Environ. Res., 152: 150 – 156.

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		<p>higher than expected sources of lead. For the captive birds, this is likely linked to the historic use of leaded fuels and mining activities. For the wild birds, ingestion of leaded ammunition is suspected to be the source.</p>		
5	<p>Wiemere et al., 2017. Repeated conservation threats across the Americas: High levels of blood and bone lead in the Andean Condor widen the problem to a continental scale.</p>	<p>The extent and intensity of lead poisoning due to exposure to leaded ammunition for a widely distributed threatened species, the Andean Condor (<i>Vultur gryphus</i>) in south American countries have been presented. As usual, the study uses blood lead and bone lead data in addition to X-ray images to provide evidence of lead poisoning and suggests that lead is a threat to scavenger birds across the Americas.</p>	<p>Weight of evidence to identify leaded bullets as a threat to wildlife and call for banning of lead uses in ammunition.</p>	<p>Environ. Pollut., 220 (A): 672 – 679.</p>
6	<p>Fabian et al., 2017. Quantifying diffuse contamination: method and application to lead in Soil</p>	<p>While local point-source contamination of a metal is easily recognized, quantification of anthropogenic diffuse contamination at the country, continental or global scale is still a challenge. This paper introduces a new method for recognizing and quantifying diffuse contamination with example applications for lead. The method compares distribution of lead with another element of similar geochemical behavior that is not emitted by human activities. Diffuse lead contamination in surface soil is estimated to be <0.5 mg/kg for Australia, 1–3 mg/kg for Europe, and 1–2 mg/kg, or at least <5 mg/kg, for the U.S.A.</p>	<p>The method can be used to efficiently monitor diffuse contamination at the country to regional scale, allowing more efficient analysis of exposure scenarios that are required under regulatory risk assessment frameworks, such as European REACH.</p>	<p>Environ. Sci. Technol. (In press)</p>

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7	<p>Nys et al., 2017. Systematic evaluation of chronic metal-mixture toxicity to three species and implications for risk assessment</p>	<p>This is a meta-analysis to address metal mixtures in risk assessment with identification of appropriate methods and models. Using consistent methodologies, the toxicity of metal mixtures (Ni, Zn, Cu, Cd, and lead) to <i>Daphnia magna</i>, <i>Ceriodaphnia dubia</i>, and <i>Hordeum vulgare</i> was investigated in different waters or soils, totaling 30 different experiments. Some mixtures of different metals, each individually causing <10% inhibition, yielded much larger inhibition (up to 66%) when dosed in combination. In general, independent action approach was most accurate in predicting mixture toxicity, while that for concentration addition was the most conservative. The study reports mixture interactions with implications on metal bioavailability and suggests that the current metal-by-metal approach in risk evaluations may not be conservative enough for metal mixtures.</p>	<p>Metal contamination generally occurs as mixtures, but the current practices of evaluating risks for metals in soil and water are mainly based on metal-by-metal assessments. As a result, mixture toxicity is an emerging issue with anticipation of its incorporation in future risk assessment procedures in the European Union. This study may influence future regulatory deliberations requiring the consideration of mixture effects in risk assessment.</p>	<p>Environ. Sci. Technol. 51: 4615-4623.</p>

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Health publications				
1	Fustinoni et al., 2017 Blood lead levels following consumption of game meat in Italy.	To measure lead levels in blood (PbB) in consumers of game meat, taking into account other possible sources of lead exposure. A spot blood sample was obtained from 95 subjects, and a questionnaire was used to collect general information and data on game meat consumption, hunting, wine drinking, and other possible sources of lead exposure. PbB was not influenced by age, sex, residence in an urban or rural area, consumption of game meat, tobacco smoking, or hobbies associated with potential exposure to lead, and median PbB was 1.7 (5 th to 95 th percentile = 1.0-5.3) µg/dL and 3.4 (0.9-6.1) µg/dL for game meat non-eaters and eaters, respectively. A multiple linear regression analysis found an association with hunting (PbB almost double in hunters) and wine drinking (40% higher in drinkers) but not with consumption of game meat or other parameters.	It was unclear to the authors whether the higher PbB level associated with hunting was due to inhalation of lead fumes while shooting with lead ammunition, to handling lead ammunition, or both, but it appears from the results of this study that game meat consumption did not increase PbB. This study may influence to some extent the regulation (i.e., potential bans or restrictions) of lead shot in Europe and the U.S.	Environ Res. 55:36-41.
2	Prokopowicz et al., 2017 Effect of occupational exposure to lead on new risk factors for cardiovascular diseases.	To determine to what extent chronic exposure to lead affects new risk factors for cardiovascular disease (CVD) development. A cross-sectional study of 231 male volunteers working for at least 2 years in jobs with exposure to lead during the mining and processing of lead-zinc ores. Predictive properties for lead in the blood increased for particular biomarkers in the following order: L-homoarginine, fibrinogen, CRP, and homocysteine. Among the specified groups, significant differences were	Authors concluded that occupational exposure to lead can promote atherosclerosis, particularly in highly exposed individuals. This adds to the body of literature on lead as a CV stressor and may support regulation of lead on the basis of this disease endpoint. However, it is not clear how specific the	Occup Environ Med. 74(5):366-373.

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		observed only between the groups with the most and least exposure to lead.	biomarkers examined in the study are for CVD (vs. other – e.g., kidney – disease; see http://www.era-edta.org/eureca-m/images/clinical_usefulness_of_biomarkers_in_patients_on_hemodialysis%20NRN%202011.pdf).	
3	Reuben et al., 2017 Association of childhood blood lead levels with cognitive function and socioeconomic status at age 38 years and with IQ change and socioeconomic mobility between childhood and adulthood.	To test the hypothesis that childhood lead exposure is associated with cognitive function and socioeconomic status in adulthood and with changes in IQ and socioeconomic mobility between childhood and midlife. A prospective cohort study of a 1972-1973 birth cohort from New Zealand. Observed participants to age 38. Childhood lead exposure ascertained as blood lead levels measured at ages 11 and 38. IQ and socioeconomic status were assessed at age 38. Each 5-µg/dL higher level of blood lead in childhood was associated with a 1.61-point lower score in adult IQ (statistically significant), and each 5-µg/dL higher level of blood lead in childhood was associated with a (statistically significant) 1.79-unit lower score in socioeconomic status.	The degree of association between childhood lead exposure and IQ reported in the present study is far less than that of the association between other factors and IQ; studies have shown that lead exposure accounts for a 1% to 4% amount of variance in cognitive ability, whereas social and parenting factors account for 40% or more. Nonetheless, the findings in this study could be extended to estimate monetary damages associated with childhood lead exposure, as is now being done in the EU under REACH. Findings are not really novel in that more than 10 years ago, Canfield et al. conducted a review of the existing literature on lead exposure during	JAMA 317(12):1244-1251.

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			<p>infancy and childhood and later-life neurodevelopmental consequences (i.e., IQ); and more than 40 papers were cited in this review, many dating to the early 1980's.</p>	
4	<p>Simões et al., 2017 Low-level chronic lead exposure impairs neural control of blood pressure and heart rate in rats.</p>	<p>Wistar rats were exposed to lead acetate for 30 days to investigate the cardiovascular system impact on autonomic nervous system control – heart rate variability (HRV), baroreflex sensitivity, cardiopulmonary reflex, and hemodynamic responses to vagal and sympathetic pharmacological blockade. Rats exposed to lead exhibited a higher blood pressure and reduced HRV in the time domain when compared to the saline-injected group. Methylatropine and atenolol administration suggest increased sympathetic tone and reduced vagal tone on the control of heart rate. Chronic lead exposure decreased the sensitivity of the baroreflex without significantly changing the cardiopulmonary reflex.</p>	<p>Authors claimed that their study demonstrated for the first time in an animal model that cardiovascular changes, such as arterial hypertension, are accompanied by impaired autonomic control of the cardiovascular system, as characterized by reduced baroreflex sensitivity and a sympathovagal imbalance. This adds to the small body of human studies literature and could be used in future regulatory deliberations that consider lead effects on the autonomic nervous system.</p>	<p>Cardiovasc Toxicol. 17(2):190-199.</p>
5	<p>Smith et al., 2017 High-precision (MC-ICPMS) isotope ratio analysis reveals contrasting sources of</p>	<p>A case where MC-ICPMS was applied to isotopically resolve lead sources in human clinical samples. An adult male and his child presented to care with elevated blood lead levels (BLLs) (>200 µg/dL for the adult and 10 µg/dL for the child). Adult subject was a gunshot</p>	<p>There exists a need for robust tools for assessment of lead exposure sources, and the latest generation of MC-ICPMS instrumentation offers the capability of using lead isotopic</p>	<p>Biol Trace Elem Res. 177(1):33-42</p>

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	elevated blood lead levels of an adult with retained bullet fragments, and of his child, in Milwaukee, Wisconsin.	victim who had multiple bullet fragments embedded in soft tissue of his thigh for approximately 10 years. Study compared the high-precision isotopic fingerprints of lead in the adult's and child's whole blood (WB) to a surgically extracted bullet fragment, household paint samples, tap water, and a lead water-distribution pipe removed from servicing a house in the same neighborhood. Lead in the bullet and adult WB were nearly isotopically indistinguishable, indicating that bullet fragments embedded in soft tissue could be the cause of both acute and chronic elevated blood lead levels.	signatures as a tool for environmental source tracking in public health.	
6	Steenland et al., 2017 A cohort mortality study of lead-exposed workers in the USA, Finland and the UK.	To investigate further whether inorganic lead is a carcinogen among adults, or associated with increased blood pressure and kidney damage, via a large mortality study. Mortality study of three cohorts of lead-exposed workers with blood lead (BL) data – in the USA, Finland, and the UK – including over 88,000 workers and over 14,000 deaths. Significant positive trends were found for BL and lung cancer, chronic obstructive pulmonary disease (COPD), stroke, and heart disease, while borderline significant trends were found for bladder cancer, brain cancer and larynx cancer. In external comparisons, significantly elevated standardized mortality ratios (SMRs) were reported for those with BLs >40 µg/dL; for bladder, lung, and larynx cancer; and for COPD.	The authors concluded from their study that it was unlikely that confounding by smoking – for which they had no data for any of the three cohorts – could explain their positive findings, despite the fact that lung cancer, COPD, stroke, and heart disease are all strongly associated with smoking, with decades of literature to support this. The authors claimed that their findings for cancer were concordant with IARC's 2006 determination that lung and brain cancer are two cancers more strongly associated	Occup Environ Med Published Online First: 25 May 2017. doi: 10.1136/oemed-2017-104311.

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			<p>with inorganic lead, but were not concordant regarding stomach cancer. In addition, non-malignant kidney disease, an outcome of <i>a priori</i> interest to the authors, did not show a significant positive trend with lead. As such, it is difficult to make the case that this study adds to the evidence for the disease-causing potential for lead, and it is doubtful that the study will have any influence on the present IARC classification of lead as a probable human carcinogen.</p>	
7	<p>Zhou et al., 2017 Prenatal maternal stress in relation to the effects of prenatal lead exposure on toddler cognitive development.</p>	<p>To evaluate the effects of maternal lead exposure during pregnancy on toddler cognitive development and the potential effect modification by maternal stress. A prospective birth-cohort study in Shanghai from 2010 to 2012 of 225 mother-infant pairs. Mothers were recruited in mid-to-late pregnancy and children were followed up until 24-36 months old. A self-administered Symptom Checklist-90-Revised Scale (SCL-90-R) was used to assess maternal emotional stress during pregnancy. Maternal whole blood lead levels were measured during gestational weeks 28-36. The mean maternal blood lead concentration was 3.30 µg/dL.</p>	<p>Authors concluded that prenatal maternal stress may exacerbate the effects of prenatal exposure to lead on toddler cognitive development. This study provides evidence that effects of lead on cognitive development in children may be confounded by factors such as parental stress.</p>	<p>Neurotoxicology 59:71-78.</p>

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		<p>After adjusting for relevant confounders, no significant associations of maternal blood lead concentrations with toddlers' cognitive levels were observed in all five domains of the Gesell scale, but the interaction between prenatal maternal blood lead and stress was significant in the domains of adaptive behavior, language, and social behavior.</p>		