Exposure to Toxic Pollutants

Assessing Potential Human Health Risk

By Richard Olawoyin

Human health risk assessment (HHRA) is a systematic tool designed to provide answers to concerning questions in mitigating environmental risks. Depending on the exposure amount of chemicals to humans, beneficial or harmful consequences may ensue. The determination of whether a certain substance or chemical of concern (COC) poses substantial health risk to humans is made using the HHRA method.

Assessing the risks posed by noxious COCs in the environment entails compiling, evaluating and interpreting complex sets of data. Epidemiologic studies are conducted to investigate the connections between toxic chemical exposures and health problems in an area; the goal of these studies is to assess the effects of past chemical exposures in relation to acknowledged health issues in a particular population.

However, HHRAs estimate the impacts of current or future exposures to COCs and associated human health risks in the general population. In this case, since the study plan is to assess risk to human health from substances that will be emitted, HHRA is the appropriate tool to use. Generally, HHRA requires good professional judgment and thorough science, which is a continuously evolving process.

The objectives of an HHRA are to:

- define and determine the scale and proximity of potential adverse effects of several COCs to human health, and human physiological reaction to the COC;
- suggest appropriate mitigation measures and alternatives to the potential risks;
- provide baseline analysis (comparison of all existing conditions including present exposures and possible emerging risks);
- determine the toxicity of materials and potential COCs that might affect human health;
- systematically evaluate COC interactions and documentation of potential human health risks.

Richard Olawoyin, Ph.D., CEP, is an assistant professor in the School of Health Sciences at Oakland University, Rochester, MI, which he joined in January 2014 from Pennsylvania State University. He previously worked in the upstream and downstream sectors of the petroleum industry as a geologist, geophysicist, and safety and environmental health scientist. His research emphases are on human health exposure risk assessment. Other research interests include nanotechnology and statistical techniques in health and safety engineering. Olawoyin serves on the Chemometrics review panel for the National Science Foundation, is a program evaluator for ABET, a reviewer for multiple national and international journals and a recipient of the NASA-funded space grant on nanotechnology. He is also on the disaster response team of the American Red Cross. Olawoyin is a professional member of the International Medical Geology Association, a professional member of ASSE's Greater Detroit Chapter and a member of the Society's Blacks in Safety Engineering Common Interest Group.

Steps Involved in Human Health Risk Assessment

Planning an HHRA should focus on the categories of potential health effects that may ensue from exposures to hazardous COCs; the probability that human health will be negatively affected due to exposures to varying concentrations of hazardous environmental stressors; determination of the magnitude of exposure (dose), frequency and duration of exposure; and assessing the effects of these environmental stressors on vulnerable groups (e.g., job functions with higher exposure rates, body weight of individual exposed, age, gender).

Two basic types of evaluations may be considered when planning an HHRA: hazard-based screening and baseline HHRA (EPA, 2003). However, HHRA mainly involve four steps as illustrated in Figure 1 (p. 42). Each step should be completed in accordance with the guidance provided by EPA (2003). Proper planning toward carrying out an HHRA will help the evaluator gain a better understanding of potential risks to human health from exposures to hazardous COCs. Before proceeding with the HHRA's four steps, it is important to clearly define the aim and scope of the study, so the professional must first conduct an assessment planning and scoping of the human health assessment (HHA).

Assessment Planning (Scoping)

HHRAs may present certain complexities requiring specific strategies pertinent to the characteristic nature of the study site or exposure location (e.g., soil,

water, sediment, surface water, underground water contamination). To guarantee a successful completion of the HHRA, assessment planning is essential to ensure that the risk assessment problem is properly formulated, the assessment is conducted and analyzed, and the risk is adequately characterized.

This step provides guidance for cumulative risk assessment as well as stakeholders' involvement. The planning stage helps create a strategic direction to achieving the global objectives of the process. This facilitates the development of comprehensive sampling and analysis protocols, and streamlines the amount of information relevant to the HHRA process. This stage helps determine the most useful information required for the complete assessment as well as the technical strategy for the entire assessment process. Risk managers, risk assessors and other members of the risk assessment team can clearly define the expectations of the risk assessment process by identifying:

1) motivation for the HHRA (including public safety and concern, regulatory requirements, experimental results and other factors as appropriate);

2) management policies, objectives and concerns that require attention;

3) scope and coverage of team efforts;

4) existing knowledge about the prevalent risk (data availability, type of data, data gap);

5) resource availability and logistics (legal, scientific, economic, social analyses);

6) plans for the dissemination and communication to the public of assessment results upon its completion.

The products that should emerge for the assessment planning process include the conceptual framework and process models with analysis plan and narratives. A visual illustration of the framework will adequately define the ambient concentrations, contaminant sources and potential exposures to the ecosystem that may have adverse effects on human health.

The rationale for the developed conceptual framework may be presented in the associated narrative. Both the narrative and the conceptual framework can be peer-reviewed to provide opportunities for additional insight, modifications and proper structure for the entire process. This is crucial because effective assessment planning will help the risk assessment team understand how the HHRA fits into the environmental decision-making model.

HHRA involves varying degrees of complexities with potential impact on human and environmental health based on the wide range of decisions required at the end of the process. Examples include comprehensive assessments of pollutants, screening-level assessments of emerging COCs and site-specific assessments of hazardous environmental media (soil, water, sediments, air, vegetation). Properly planning the assessment process helps determine the appropriate risk assessment methodology to address the uncertainty and degree of confidence in the risk characterization. For the risk characterization, the decision typology must be integrated with the scope of the risk characterization (Fowle & Dearfield, 2000) to identify the three dimensions (i.e., depth, length, breadth) of the resultant risk assessment.

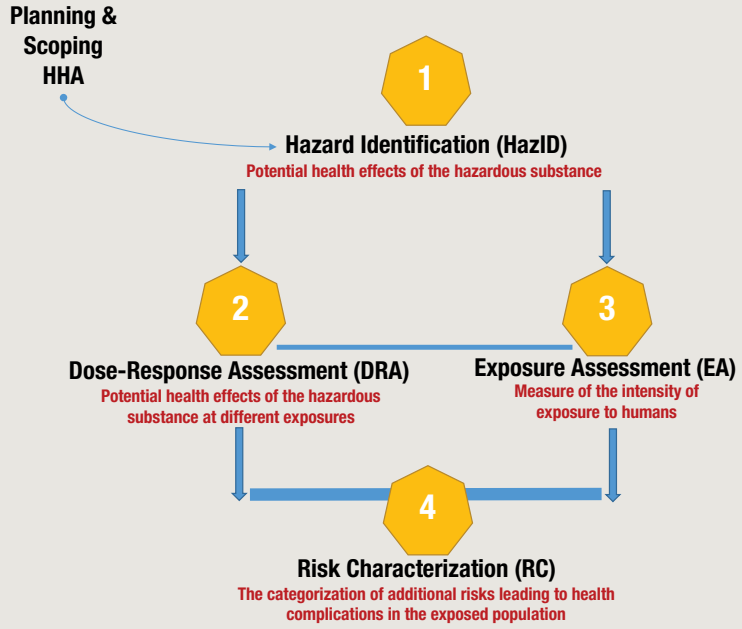
The necessary information for making these decisions and the required efforts to develop the information can be obtained from the decision typology adapted from National Research Council (Stern & Fineberg, 1996), as presented here.

•Unique category: This involves wide-impact, single-time decisions for risk characterizations with some distinctive effect on the health of a large portion of the environment and affecting many people over an extended period.

IN BRIEF

- **Human health risk assessment (HHRA) is designed to evaluate the condition and likelihood of unfavorable health outcomes in people who may or will be exposed to hazardous chemicals through contaminated environmental materials.**
- **HHRA is a well-known method for appraising the potential for unfavorable human health outcomes from exposures or anticipated exposures to toxic materials.**
- **The aim of an HHRA is to evaluate the potential chemicals of concern, possible exposure routes and pathways directly linked to a location of interest.**
- **This article provides the basic information needed to conduct an HHRA for students or entry-level professionals and others with concerns about the potential health effects of hazardous chemicals.**

FIGURE 1
Human Health Risk Assessment Methodology



Note. *Adapted from "Framework for Cumulative Risk Assessment" (EPA/600/P-02/001F), by U.S. EPA, 2003, Washington, DC: Author, Office of Research and Development, National Center for Environmental Assessment.*

•Routine category: This involves narrow-impact decisions for risk characterizations that affect the health of few people over a small geographic location. Examples include the evaluation of circumstances for chemical premanufacturing under the Toxic Substances Control Act using screening-level chemical-specific characterization and the annual air permit decisions made to support smaller facilities, based on thousands of screening-level site-specific characterizations.

•Repeated category: This is similar to the unique category because of the wide-impact on health (of many people and in large geographic locations). However, the unique needs of the current situation are critically considered with emphasis on important issues for the decisions that are not expected to be related to similar risk characterization activities. For the siting of a large waste incineration facility or treatment plant in an area, the repeated risk characterization may be adopted.

•Generic category: The generic risk characterization is similar to the routine category and is used for a particular chemical or for a specific site. It involves the hazard and dose-response decisions for risk characterization, taking into account adequate review of the process and the overall effect of the chemical or site exposure on human health.

HHRA Step 1: Hazard Identification

Hazard identification (HazID) is the process typically used to determine the potential for chemical exposures to result in the prevalence of specific negative health outcomes (e.g., developmental disabilities, cancers, irritations, fatalities). HazID assesses the potential negative health effects that may develop in humans due to exposures to specific toxic pollutants.

Environmental scientists conduct HazID by evaluating all available information on the potential effects of toxic substances on human health. During this stage, a site conceptual model, developed during the assessment planning, is thoroughly reviewed by preparing a graphical representation of the location of concern and identifying the main sources of contaminants and possible exposure pathways that affect humans in the population. HazID determines the availability of scientific data for each COC and it also involves the development of the weight of evidence for the characterization of the cause-and-effect relationship. The better the weight of evidence, the more certain environmental scientists are that a toxic substance/pollutant has a specific effect on human health.

The HazID data may be obtained through quantitative methods or clinical controlled methods. Several studies and analyses are important when applying HazID techniques, such as toxikoninetics and toxicodynamics. Toxicokinetics involves how human body mechanisms and processes function in terms of metabolism, absorption, distribution and elimination of certain toxic chemicals from the human body. Toxicodynamics examines the mechanisms involving the effects that toxic chemicals have on human health.

Human information is lacking for most toxic substances/pollutants, hence scientists mostly use laboratory animals (e.g., rats, mice) for toxicological studies (HHRA Step 2). The effects of a toxic pollutant on humans are extrapolated from the results of these studies. The primary objective of HazID is to evaluate the potential of chemicals to induce unfavorable human health problems, thus it provides the weight of evidence for the chemical effects such as mutagenicity, carcinogenicity and endocrine disruption.

HHRA Step 2: Exposure Assessment

Exposure to toxic pollutants occurs through three primary exposure routes: inhalation, ingestion and dermal absorption. Examples include:

•Ingestion: Accidentally eating soil contaminated with toxic chemicals (Li, Wei, Zhao, et al., 2014; Olawoyin, Oyewole & Grayson, 2012) or drinking contaminated drinking water (Nelson, 2016).

•Inhalation: Breathing of dusts, vapors, fumes, particulates or air contaminated with a toxic substance (Bandowe & Nkansah, 2016; Keshavarzi, Tazarvi, Rajabzadeh, et al., 2015).

•Dermal absorption: Skin contact with contaminated soil or showering in contaminated water containing toxic pollutants (Abdallah, Pawar & Harrad, 2016; Bányiová, Nečasová, Kohoutek, et al., 2015).

Exposure is examined through field collection and laboratory analyses of soil, air, water and biological samples (bodily fluids). Toxic pollutant concentration levels are indicated in the results. Ex-

posure pathways are then evaluated to determine human exposure to specific toxic pollutants in the environment. This often includes assessment of the land use that triggered exposure (commercial, industrial, residential), consideration of underground water used as drinking water source and air quality (e.g., is there a constant release of toxic pollutants of high concentrations in the area?).

This involves the evaluation of the level of contact with the COC based on exposure magnitude, duration, frequency and range for a particular population and also the exposure pathways. Exposure assessment primarily examines the exposure pathway (the path a contaminant follows from the pollution source to the human body) and the exposure route (inhalation, dermal absorption, ingestion).

For exposure assessment, it is important to have a clear understanding of the following:

a) applied dose ($_{a}D$): the amount of COC available at the absorption barrier;

b) potential dose ($_{p}D$): the amount of COC ingested, dermally absorbed or inhaled (if the COC is partially bioavailable, then $_{a}D < {}_{p}D$);

c) absorbed dose ($_{ab}D$) (internal dose): the amount of COC absorbed and available for interactions with human physiological receptors;

d) delivered dose ($_{d}D$): the amount of COC available for interactions with a particular tissue, organ or cell in the human body.

Exposure Factors

When measuring human exposure to a COC, it is essential to determine the extent of contact between the exposed humans and the contaminated environmental material. Each concerning exposure is anticipated to be different with regard to the exposure level at a particular locality due to dissimilarities in rates of intake, body mass, exposure frequencies and durations. This is important and should be considered for all daily intake calculations.

Exposure Quantification

In quantifying exposures using adequate data resources, statistically representative concentrations are calculated for COCs present in the contaminated environmental material. In exposure situations with insufficient samples or data, the maximum concentrations will represent the level of COC. Based on the varying range of exposures to pollutants, individuals may experience either central-tendency (CT_E) or high-end (HE_E) exposures. CT_E is estimated from the average amount of chemicals in the environment, the exposure duration and frequency, and how human health is affected, while HE_E represents the highest dose affecting some subjects in the population, which is often approximated to equate to the 90th percentile exposure classification for individual humans in the population.

Exposures can be quantified through:

- Point of contact measurement (PCM): Measurement is carried out at the point of contact during exposure; the exposure concentration and time of contact are measured and integrated.
- Scenario evaluation (S_{Eval}): Exposure concentration and time of contact are measured independently, then integrated.
- Reconstruction (Recon): Exposures are approximated through the dose after exposure has occurred, and reconstruction can be performed through internal indicators such as human body burden and biomarkers.

HHRA Step 3: Dose-Response Assessment

Dose-response estimates for humans are often based on animal studies. Correlations can be made using the dose-response relationship by examining the magnitude/quantity or condition of exposure (the dose) and the possibility and/or severity of harmful health effects (the response) in humans. The increase in dose invariably results in an increase in the response, therefore at low doses the response may be negligible or not present at all.

Dose response assessment (DRA) involves assessing all available data to report the dose-response relationship of the observed exposure. It also involves extrapolating risk estimates that are beyond the lower range of observation data. DRA is useful in making data-driven decisions and inferences about the starting point of the dose level at which adverse effects in humans are enabled. The human health effects due to accidental ingestion, inhalation and dermal absorption of a COC can be calculated if the chronic daily intake (*CDI*) values are known (ATSDR, 2011).

Nonlinear DRA

Nonlinear DRA assumes the threshold hypothesis, which states that exposure range from zero to a certain finite value can be endured if there is no chance that the organism will express any toxic effect. This is also held valid if the threshold toxicity of the chemical remains where the effects begin to ensue. When the magnitude, severity and frequency of harmful health effects between the exposed population and the appropriate control population are marked by maximum exposure level, with no physiological, biological or statistical significant difference, then a no-observed-adverse-effect level (NOAEL) is established. Reference dose (*RfD*) is the daily exposure of humans to noncarcinogenic compounds that may occur without substantial adverse risk during a lifetime, while the chronic oral reference dose estimates long-term exposure of humans to potentially noncarcinogenic compounds (Olawoyin, et al., 2012).

When calculating the systematic toxicity, it helps to know the chronic exposure level at which a human population is unlikely to have substantial risk of deadly consequences in a lifetime. For the noncarcinogenic effects, the systemic toxicity value is derived by the hazard index (*HI*). The *HI* is calculated for each chemical based on the chronic noncarcinogenic exposure as shown in Equation 1 (p. 44), then the summation of multiple substances exposure is given as the cumulative chronic hazard index (*CHI*) as described in Equation 2 (p. 44).

Equation 1

$$HI = \frac{CDI}{RfD}$$

Equation 2

$$CHI = \sum_{k=1}^{n} \frac{CDI_k}{RfD_k} \quad k = 1 \ldots n$$

Where: *HI* = total hazard index (unitless). This is the likelihood of humans suffering adverse health problems. The level of concern for human health increases when *HI* or *CHI* > 1; *CDI* = chronic daily intake or dose ($mgkg^{-1}.day^{-1}$); CDI_k = *k*th toxicant: chronic daily intake of the ($mgkg^{-1}.day^{-1}$); *RfD* = chronic reference dose ($mgkg^{-1}.day^{-1}$); RfD_k = *k*th toxicant: chronic reference dose ($mgkg^{-1}.day^{-1}$) (Olawoyin, et al., 2012).

Linear DRA

If there is no toxicity threshold, the assessment conducted constitutes a linear DRA, such as for carcinogens. There is no lower theoretical exposure level at which adverse effects may not occur for this COC category, however carcinogenic response may develop. Hence, to ensure health and investigative efficacy, it is essential to consider the balance between the quality of the analysis and effective exposure reduction techniques, where COCs are present. The extrapolation for the assessment excludes uncertainty factors; instead, a linear line is drawn from the origin to the point of observed data departure. The linear line represents the cancer slope factor, which is used to approximate risk at exposure concentration along the linear line.

The lifetime cancer risk can be estimated using Equation 3, which estimates the incremental likelihood of humans with a lifetime exposure to potential carcinogenic substances, while the cumulative total carcinogenic risk (CTR) due to simultaneous exposure to different substances is expressed in Equation 4. The DRA for cancer risk is usually expressed as lifetime incremental cancer risk values, such as x 10^5, meaning that 1 in 100,000 people may develop the cancer risk or x 10^6, meaning that 1 in 1 million people may develop the cancer risk.

Equation 3

$$Total\ cancer\ risk\ (TR) = CDI \times SF$$

Equation 4

$$CTR = \sum_{k=1}^{n} \frac{CDI_k}{SF_k} \quad k = 1 \ldots n$$

Where: *TR* = probability of cancer affecting human health in a lifetime (i.e., child to adult) (unitless); *CDI* = chronic daily intake ($mgkg^{-1}.day^{-1}$); *SF* = oral cancer slope factor ($mgkg^{-1}.day^{-1}$); CTR_k = risk estimate for the *k*th substance; CDI_k = kth toxicant: chronic daily intake ($mgkg^{-1}.day^{-1}$); SF_k = *k*th toxicant: oral slope factor ($mgkg^{-1}.day^{-1}$) (Olawoyin, et al., 2012).

When there is inadequate information on the dose-response of the toxic substance, the default options are adopted as conservative assumptions for the protection of human health. Default assumptions used for the determination of cancer risk include:

- Chemicals that induce cancer in exposed occupational workers are assumed to have the capability to induce cancer in other humans exposed to the toxic chemical.
- Chemicals that induce cancer in exposed animals are assumed to be capable of inducing cancer in humans.
- Short-term exposure to a high dose of a toxic is assumed to be equivalent to a low dose spread over a lifetime.
- The general assumption is that there are no exposures to toxic chemicals with zero risk, and that minimal exposure to a cancer-inducing toxic pollutants can increase the risk of cancer.
- A linear relationship exists between dose and response; for every unit of increase in exposure (dose) there will be a corresponding increase in cancer response.

Default assumptions are also applicable to the level of exposure to toxic chemicals. Take as an example Flint, MI, with high concentrations of lead in the drinking water system. The applicable default assumption when studying the drinking water contaminants could be that the drinking water daily intake for an adult is half gallon (approximately 2 L) for 350 days per year for 30 years.

Human health data collection, toxicological animal studies and the embedded assumptions allow for development of the DRA. Collecting health data, conducting animal studies and making assumptions allow scientists to develop dose-response relationships.

HHRA Step 4: Risk Characterization

Risk characterization (RC) is the final integrative step and an essential element of the HHRA framework. This step integrates information from all preceding steps of the HHRA, and provides and synthesizes conclusions (on the assessed risks) that are informative, complete and valuable for decision making.

The RC process categorizes the conclusions contained in the data obtained during the prior three stages and highlights the circumstances surrounding the nature and extent of the exposure risk examined. This step also describes the resultant human health risks that are expected to occur in the population exposed to the COC. RC must reaffirm the scope of the assessment as established during the HHRA planning phase. The results should be expressed clearly and all significant assumptions and uncertainties observed during the assessment must be properly articulated. As outlined by EPA, a quality RC must ensure transparency through the process and clarity of purpose and methods (e.g., methods and results must be understandable to all, consistency in the process), and assumptions and protocol must be consistent with similarly conducted assessments with the same general scope.

HHRA in Practice

Rahman, Asaduzzaman and Naidu (2013) report that 57 million people were exposed to Arsenic (As) concentration in drinking water exceeding the World Health Organization guideline in Bangladesh. Current national level exposure concentration estimates that 45 million people are exposed to As in the area (Flanagan, Johnston & Zheng, 2012). Extant studies have explored the risk characterization for the population by quantifying the average daily water intake corresponding to each lifetime year involving approximately 400 people in the Bengal basin, including direct (1 to 4 L per day) and indirect (0.5 to 2 L per day) of water intake, based on As exposures by gender and various age groups (Hossain, Rahman, Murrill, et al., 2013; Joseph, Dubey & McBean, 2015).

The CTR based on 85 million population subset (lifetime As exposure in consumed water = 0.01 mg/L) was estimated as 0.41×10^{-6}, for 75 million population subset (lifetime As exposure in consumed water = 0.05 mg/L), was estimated as 0.74×10^{-6}, making the CTR for the total population to be approximately 1.15×10^{-6}.

The potential effects of COCs on human health in the Niger Delta was characterized through the assessment of the lifetime exposure through three pathways: accidental ingestion of soils, inhalation of soil particulate materials and soil-dermal contact (Olawoyin, et al., 2012). This study determined the potential cumulative carcinogenic health effects from heavy metals on lifelong residents of the area as substantial, based on the HHRA methodology used. The accidental soil ingestion and dermal contact for children were determined to be substantially high (*HI* = 5.1). The researchers characterized the risk in the study area and determined that potential lifetime risks exist for children and adults in the Niger Delta area. These studies provide the tools for proper decision making that may include further clinical toxicological studies to determine the specific epidemiological consequences of toxic pollutants on human health, especially for the most vulnerable population.

Conclusion

The potential effects on human health of individual and cumulative contaminants in an area can be assessed through a proper human health risk assessment study. A risk assessment designed by EPA (2003) is useful to calculate the carcinogenic and noncarcinogenic risks due to lifetime exposure through three pathways: accidental ingestion, inhalation of particulate materials and dermal contact of air, soil and water. Health risk assessments help evaluate the benefits and consequences of several alternatives for decreasing anticipated chemical exposures with a major goal of reducing (to an insignificantly low level) the human health risks linked with hazardous chemicals exposure. **PS**

References

Abdallah, M.A-E., Pawar, G. & Harrad, S. (2016). Human dermal absorption of chlorinated organophosphate flame retardants: Implications for human exposure. *Toxicology and Applied Pharmacology*, *291*(15), 28-37.

Agency for Toxic Substances and Disease Registry (ATSDR). (2011). Retrieved from www.atsdr.cdc.gov

Bányiová, K., Nečasová, A., Kohoutek, J., et al. (2015). New experimental data on the human dermal absorption of Simazine and Carbendazim help to refine the assessment of human exposure. *Chemosphere*, *145*, 148-156.

Bandowe, B.A. & Nkansah, M.A. (2016). Occurrence, distribution and health risk from polycyclic aromatic compounds (PAHs, oxygenated-PAHs and azaarenes) in street dust from a major West African metropolis. *Science of the Total Environment*, *553*, 439-449.

EPA. (2003). Framework for cumulative risk assessment (EPA/600/P-02/001F). Washington, DC: U.S. EPA, Office of Research and Development, National Center for Environmental Assessment.

Flanagan, S.V., Johnston, R.B. & Zheng, Y. (2012). Arsenic in tube well water in Bangladesh: Health and economic impacts and implications for arsenic mitigation. *Bulletin of the World Health Organization*, *90*(11), 839-846.

Fowle, J.R. & Dearfield, K.L. (2000). *Risk characterization handbook* (EPA 100-B-00-002). Washington, DC: U.S. EPA, Office of Science Policy.

Hossain, M.A., Rahman, M.M., Murrill, M., et al. (2013). Water consumption patterns and factors contributing to water consumption in arsenic affected population of rural West Bengal, India. *Science of the Total Environment*, *463-464*, 1217-1224.

Joseph, T., Dubey, B. & McBean, E. (2015). Human health risk assessment from arsenic exposures in Bangladesh. *Science of the Total Environment*, *527-528*, 552-560.

Keshavarzi, B., Tazarvi, Z., Rajabzadeh, M.A., et al. (2015). Chemical speciation, human health risk assessment and pollution level of selected heavy metals in urban street dust of Shiraz, Iran. *Atmospheric Environment*, *119*, 1-10.

Li, J., Wei, Y., Zhao, L., et al. (2014). Bioaccessibility of antimony and arsenic in highly polluted soils of the mine area and health risk assessment associated with oral ingestion exposure. *Ecotoxicology and Environmental Safety*, *110*, 308-315.

Stern, P.C. & Fineberg, H.V. (Eds.). (1996). Understanding risk: Informing decisions in a democratic society. Washington, DC: National Research Council, National Academies Press.

Nelson, R. (2016). Crisis in Flint: Lead and Legionnaires' disease. *The Lancet Infectious Diseases*, *16*(3), 298-299.

Olawoyin, R., Oyewole, S.A. & Grayson, R.L. (2012). Potential risk effect from elevated levels of soil heavy metals on human health in the Niger Delta. *Ecotoxicology and Environmental Safety*, *85*, 120-130. doi:10.1016/j.ecoenv.2012.08.004

Rahman, M.M., Asaduzzaman, M. & Naidu, R. (2013). Consumption of arsenic and other elements from vegetables and drinking water from an arsenic-contaminated area of Bangladesh. *Journal of Hazardous Materials*, *262*, 1056-1063.

The potential effects on human health of individual and cumulative contaminants in an area can be assessed through a proper human health risk assessment study.