CHAPTER 2

Metals, Metallic Compounds, Organic Chemicals, and E-Waste Chemical Mixtures

INTRODUCTION

1. METALS AND METALLIC COMPOUNDS

There are a number of metals and metallic compounds present in electronic devices including lead, cadmium, arsenic, mercury as well as gold, gallium, indium arsenic, selenium, and antimony (Leung, Duzgoren-Aydin, Cheung, & Wong, 2008; Wong, Duzgoren-Aydin, Aydin, & Wong, 2007; Zheng et al., 2013). Some of these elements are highly valuable and extensive efforts are expended to recover them by recyclers, but others such as lead, cadmium, arsenic, and mercury are less valuable and may not be recovered and released into the environment with the resultant human exposures in air, food, and water (Sepúlveda et al., 2010; Wong, Duzgoren-Aydin, et al., 2007). These exposures may hence occur as mixtures of these elements (Cui & Zhang, 2008; Robinson, 2009). The types of effects resulting from mixtures of metallic compounds have been studied in both in vivo (Conner, Yamauchi, & Fowler, 1995; Goering, Maronpot, & Fowler, 1988; Mahaffey, Capar, Gladen, & Fowler, 1981; Whittaker et al., 2011) and in vitro (Aoki et al., 1990; Bustamente, Dock, Vahter, Fowler, & Orrenius, 1997; Fowler, Conne, & Yamauchi, 2005, 2008; Madden & Fowler, 2000, 2002) test systems. In addition, it is important to note that e-waste materials also contain plastics and a number of toxic organic chemical compounds (Robinson, 2009; Wong, Wu, et al., 2007), and possible interactions between metallic and organic constituents of e-waste must also be considered in any risk assessment approach for populations exposed to chemicals released from e-waste. The increasing use of nanomaterials in the fabrication of electronic devices (Caballero-Guzman, Sun, & Nowack, 2015) adds another level of complexity to any risk assessment for populations exposed to e-waste chemicals during recycling processes or released as a result of disposal of electronic devices into landfills or water bodies used for drinking or production of fishery products for human consumption. A more extensive discussion of the mechanisms of toxicity at the cellular level from exposure to a number of these chemical entities on an individual or mixture basis is provided below.

Electronic Waste. http://dx.doi.org/10.1016/B978-0-12-803083-7.00002-0

2. NANOMATERIALS

In the quest to produce smaller, lighter, and faster electronic devices, electronic manufacturers have moved increasingly to nanomaterial-based semiconductors such as particles made of indium arsenide, indium phosphide, and cadmium selenide (Heeres et al., 2007; Landi et al., 2005; Mushonga, Onani, Madiehe, & Meyer, 2012). In addition to metallic nanomaterials, organic nanomaterials containing chemicals derived from plastics (Zhuo & Levendis, 2014) should also be evaluated from a chemical safety perspective. While the behavior of nanomaterials released into the environment has received some attention to date (Klaine et al., 2008; Lowry, Gregory, Apte, & Lead, 2012; Vejerano, Leon, Holder, & Marr, 2014; Walser et al., 2012), further research is clearly needed to assess potential health effects of nanomaterials released into the environment in relation to open air recycling of this new generation of electronic devices containing these materials. Monitoring flows of both metallic and organic nanomaterials through the recycling process (Caballero-Guzman et al., 2015) is clearly an excellent idea from the perspective of both occupational and environmental risk assessment. This is an important and still unresolved area of public health research since it incorporates multimedia exposures, populations at special risk such as children in relation to occupational exposures, and, potentially, dispersion of nanoparticles over large areas.

3. REPRESENTATIVE ORGANIC E-WASTE CHEMICALS

As noted above, e-waste is chemically composed of both inorganic and organic chemicals, which each have their own toxic properties on both an individual or mixture basis. These potential interactive effects are further complicated by the issue of child labor involvement in recycling activities in developing countries. The exposure of children to e-waste chemicals during development may lead to latent health effects such as diabetes or cancer later in life (Heindel, 2003; Jirtle & Skinner, 2007; Perera & Herbstman, 2011; Skinner, Manikkam, & Guerrero-Bosagna, 2011). Common chemicals such as bisphenol A (BPA) (Huang, Zhao, Liu, & Sun, 2014; Matsukami et al., 2015), PBBs, PCBs, PBDEs (Zhao et al., 2009), and styrene (Kiran, Ekinci, & Snape, 2000) are well-known toxic chemicals that are used in the production of electronic devices. Human exposures may occur to these chemicals during recycling via open-pit burning of wiring and circuit boards and incineration of plastic composite computer housings. The overall point is that open-pit incineration of old electronic devices will release a number of toxic chemicals to which persons may be exposed. These chemicals have been shown to include a number of PAHs and PCBs as well as a number of the toxic metals noted above (Tang et al., 2014). In addition, a number of other persistent organic pollutants such as PBDEs, PBBs, dibenzodioxins, and dibenzofurans tetrabromo BPA compounds (Ni, Zeng, Tao, & Zeng, 2010; Shen et al., 2009) may be released from electronic devices during recycling activities. A number of these chemicals have been linked to obesity (Heindel & vom Saal, 2009) and metabolic diseases such as type II diabetes (Heindel & vom Saal, 2009), which may occur via disruption of endocrine regulatory pathways (Heindel & vom Saal, 2009). The main point here is that there are a large number of toxic organic chemicals present in these e-waste recycling sites in addition to toxic metallic compounds. E-waste recycling sites are hence prime examples of organic/metallic chemical mixture exposure situations in both occupational and environmental contexts and may cause important health outcomes. The issue of e-waste chemical mixtures and interactions between chemicals in relation to public health risk assessments is discussed in the following sections.

4. CHEMICAL MIXTURES EXPOSURES IN E-WASTE RECYCLING

As noted above, human exposure to chemicals in e-waste materials will occur as chemical mixtures. These exposures will occur from combinations of a number of metallic compounds and common organic chemicals/plastics released during open-pit burning and dumping not only into arable soils used for growing crops but also into rivers, lakes, and shallow water embayments used for harvesting edible fish and shellfish. Human exposures to these chemicals may hence occur via a number of routes over the lifetime of individuals living in e-waste recycling areas. Since a number of these chemicals are capable of crossing the placenta, the exposures may occur prior to conception, through embryogenesis and fetal development leading to health effects that manifest themselves later in life (Grant et al., 2013) due to altered cellular imprinting (Murphy & Jirtle, 2003; Wilkinson, Davies, & Isles, 2007). In general, interactions among chemicals may occur as additive, antagonistic, or synergistic in nature (Fowler et al., 2005, 2008; Mahaffey et al., 1981; Fig. 2.1) and are not always easily predicable. Further complicating matters is the increasing use of nanomaterials in the production of electronic devices (Cui & Lieber, 2001; Miao, Miyauchi, Simmons, Dordick, & Linhardt, 2010). These materials may greatly alter the absorption, distribution, and elimination of their constituent chemical components, thus further complicating risk assessment predictions.

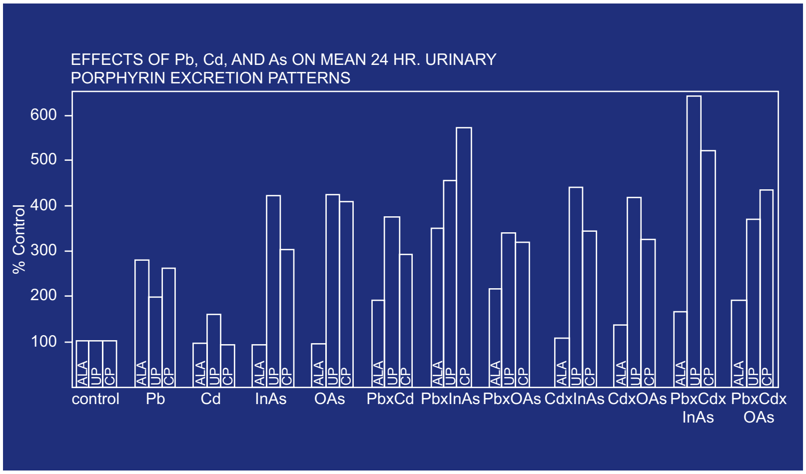


FIGURE 2.1

Urinary porphyrin excretion patterns from rats exposed to inorganic arsenic (As), lead (Pb), cadmium, or organic arsenic compounds (OAs) as arsanilic acid on an individual or mixture basis. *Interactions Fowler, B. A., & Mahaffey, K. R. (1978). Interaction between lead, cadmium and arsenic in relation to porphyrin excretion patterns.* Environmental Health Perspectives, 25*, 87–90.*

5. RISK ASSESSMENT APPROACHES FOR E-WASTE

Given the growing, unique, and evolving nature of the global e-waste problem, it would appear that traditional approaches to chemicals risk assessment will not be sufficient to protect humans or the environment from the untoward effects of chemicals released from e-waste materials during recycling activities. This is particularly true for recycling processing conducted in developing countries with few, if any, environmental or occupational safeguards or child labor laws. Clearly, the challenges of e-waste recycling require the application of newer risk assessment methods capable of evaluating the effects of novel inorganic and organic e-waste chemicals on an individual and mixture basis in populations at special risk in developing countries. These populations may be defined on the basis of age (Fowler, 2013a), gender (Fowler et al., 2005), genetic inheritance (Scinicariello et al., 2007; Fig. 2.2), and nutritional status (Heindel & vom Saal, 2009), resulting in the need for risk assessment approaches capable of integrating these disparate factors to provide credible mode of action (MOA)–based guidance that will hopefully ultimately lead to the development of personalized risk assessment evaluations for sensitive subpopulations at special risk for adverse outcomes.

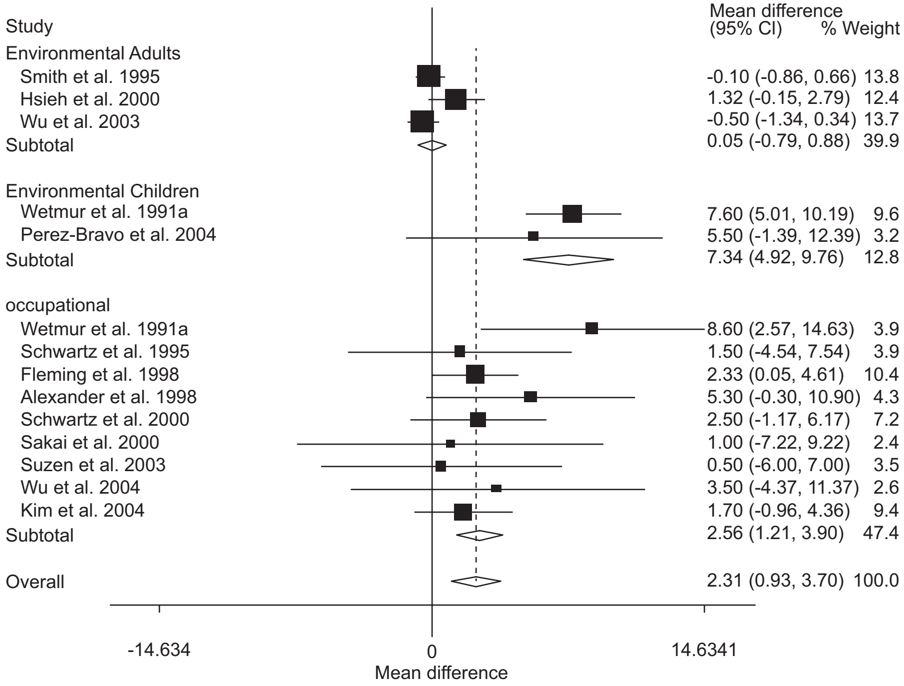


FIGURE 2.2

Metaanalysis of relationships between blood lead values and ALAD1/2 genotypes. *From Scinicariello, F., Murray, H. E., Moffett, D. B., Abadin, H., Sexton, M. J., & Fowler, B. A. (2007). Lead and δ-aminolevulinic acid dehydratase polymorphism: Where does it lead? A meta-analysis.* Environmental Health Perspectives, 115, *35–41.*

Fortunately, there are a number of modern toxicological tools such as molecular biomarkers and computational methodologies that have evolved over the past 20 years, which may be able to address these complex issues if properly applied.

5.1 Molecular Biomarkers

A prior book in this series (Fowler, 2016) has provided an overview of some ways in which molecular biomarkers could be applied to provide more precise risk assessments for chemical exposures arising from e-waste recycling. Biomarker test batteries are becomingly increasingly automated and less expensive so that they may become available for general screening of chemical toxicity in developing countries where a large proportion of e-waste recycling is currently centered (Sthiannopkao & Wong, 2013). There are an increasing array of molecular biomarkers, which include genomic, proteomic, and metabolomics biomarkers, which are discussed in more detail elsewhere (Fowler, 2016).

These biomarkers either alone or in combination can provide useful insights into mechanisms of toxic chemical action and hence help to support MOA risk assessment practice (Cote et al., 2016).

5.2 Computational Toxicology Methodologies

A second essential component for providing cost-effective personalized risk assessments for e-waste chemical exposures is the application of computational toxicology methods capable of integrating large quantities of diverse data to generate an overall risk assessment picture of likely adverse health outcomes in exposed populations at special risk. Such credible information is necessary to formulate wise regulatory decisions. Fortunately, the field of computational toxicology has also evolved in recent years. A relatively recent summary of this field and its potential applications has been published (Fowler, 2013b) as a component of the present three-part series on the application of modern tools of toxicology to risk assessment practice. An example of the value of computational toxicology as a tool in helping to drive MOA risk assessment is via digital image analysis of 2D gels from male or female hamsters exposed to gallium arsenide or indium arsenide particles (Fowler et al., 2005). The images were converted into tabular formats and clearly show marked gender-specific differences in response patterns with regard to gallium arsenide or indium arsenide particles at equal dose levels (see Tables 2.1 and 2.2). These data highlight the value of computational techniques in supporting risk assessments for chemical mixtures on a gender-specific basis. This book is the third volume in this series and represents a real-world case study of how the information in the first two volumes could be applied for addressing the complex and growing problem of e-waste with particular emphasis on the public health aspects.

6. PUBLIC HEALTH IMPLICATIONS AND DIRECTIONS FORWARD

It is clear from the above summary that unregulated releases of toxic metals from e-waste recycling are occurring and that human exposures from air, food, and water are occurring. This situation is further complicated by exposures of children in developing countries without child labor laws and the expanded application of nanomaterials in electronic devices, which can only increase environmental dispersions and exposures of humans and other biota.

6.1 The Current Situation

Based on the brief review of the various aspects of the global e-waste problems stated above, it is clear that there is a growing public health problem with human exposures to chemicals, such as toxic metals, derived from unregulated recycling

Table 2.1 Polypeptides That Exhibit Modulation 30 Days Following Exposure to InAs and GaAs in Hamster Kidney Proximal Tubule Cells

MW Range	Common Spot Number[a]	InAs[b]	GaAs[b]
100–90	1	1.0	2.1[c]
	18	1.0	0.7
89–70	2	–	–
	12	–	1.1
69–50	3	0.90	4.0[c]
	11	–	1.2
	22	–	–
	23	–	–
	25	–	–
	32	–	–
49–40	10	0.85	1.8
	16	1.2	1.6
	26	–	–
	28	–	–
39–30	4	0.79	2.0[c]
	5	1.8	0.5[c]
	6	–	0.1[c]
	7	–	0.3[c]
	8	1.5	3.6[c]
	13	0.9	0.1[c]
	14	0.72	0.6
	15	1.2	1.7
	17	0.74	2.4[c]
	19	–	–
	20	–	–
29–20	30	–	–
	31	–	–

MW, *molecular weight.*
[a] *Spot number denoted on gel.*
[b] *Spot intensity expressed as the ratio of treatment/control.*
[c] *Denotes polypeptides differing by twofold or greater (increasing or decreasing).*
From Fowler, B. A., Conner, E. A., & Yamauchi, H. (2008). Proteomic and metabolomic biomarkers for III-V semiconductors: And prospects for application to nano-materials. Toxicology and Applied Pharmacology, 233*(1), 110–115. http://dx.doi.org/10.1016/j.taap.2008.01.014.*

of electronic devices, which is centered in a number of developing countries. These countries generally do not have the resources or political will to put in place needed regulatory guidelines for protecting the health of citizens dealing with e-waste materials. A key element in improving this situation is the availability of sound scientific information to inform regulatory decision-making.

Table 2.2 Polypeptides That Exhibit Modulation 30 Days Following InAs or GaAs in Female Hamster Kidney Proximal Tubule Cells

MW Range	Common Spot Number[a]	InAs[b]	GaAs[b]
100–90	1	0.92	0.96
	18	0.56	0.17[c]
	29	0.71	0.37[c]
89–70	2	6.60[c]	5.50[c]
	12	0.47[c]	1.20
69–50	3	0.68	1.10
	11	0.51	0.96
	22	0.32[c]	0.78
	23	0.31[c]	0.83
	24	0.26[c]	0.64
	25	0.26[c]	1.26
	32	0.90	0.96
49–40	10	0.43[c]	0.90
	16	2.50[c]	0.57
	26	0.58	0.45[c]
	27	–	1.60
	28	–	10.0[c]
	33	–	1.40
	34	0.43[c]	0.57
39–30	4	–	–
	5	2.00[c]	1.20
	6	0.14[c]	0.70
	7	0.32[c]	0.61
	8	0.39[c]	0.50
	13	0.47[c]	1.20
	14	0.37[c]	1.00
	15	0.76	1.25
	17	1.00	0.96
	19	0.20[c]	1.1
	20	–	0.50
≤29	30	0.84	0.76
	31	0.54	0.68

MW, *molecular weight.*

Thirty-one polypeptides were affected by both InAs or GaAs. The synthesis of 16 polypeptides was altered by InAs by twofold or greater with the synthesis of 3 increasing, 13 decreasing, and 4 absent. After GaAs treatment, 50% of the polypeptides were synthesized at or near control levels. Five polypeptides were changed by twofold or greater, the synthesis of two increased, three decreased, and one was absent.

[a] *Spot number denoted on gel.*

[b] *Spot intensity expressed as the ratio of treatment/control.*

[c] *Denotes polypeptides differing by twofold or greater (increasing or decreasing).*

From Fowler, B. A., Conner, E. A., & Yamauchi, H. (2008). Proteomic and metabolomic biomarkers for III-V semiconductors: And prospects for application to nano-materials. Toxicology and Applied Pharmacology, 233*(1), 110–115. http://dx.doi.org/10.1016/j.taap.2008.01.014.*

6.2 Directions Forward

To make progress on this complex problem area and protect the health of the environment and the public, a number of elements need to be organized in concert.

1. Training and resources need to be marshaled to provide recycling environments that are more efficient and protect the workers and minimize releases of toxic chemicals from electronic devices during the recycling process.
2. Occupational and environmental laws need to be strengthened to encourage safe recycling practices in developing countries.
3. Financial incentives in the form of tax breaks or subsidies need to be provided to companies engaged in the manufacture or recycling of electronic devices to encourage safe recycling and/or refurbishing practices.
4. The utilization of modern approaches to toxicology and risk assessment should be included for evaluation of chemical safety during any phase of e-waste handling to assure that public health is being protected for the most sensitive segments of the population.
5. To be effective and have an impact on public health in developing countries engaged in e-waste recycling, the proposed newer methods must be affordable and cost-effective in developing countries to have an impact on public health issues related to e-waste chemicals. Fortunately, the costs of these evolving tests are declining every year due to incorporation of computer-managed analytical and data management systems. It is reasonable to expect that such evaluations will be practical in even remote areas via incorporation of satellite data telemetry systems to communicate biomarker-based risk assessment data to risk assessors located in more centralized urban locations.

7. SUMMARY AND CONCLUSIONS

From the above discussion, it is clear that metallic elements play essential roles in modern electronic devices and are hence important components of e-waste streams. Some of these elements such as gold are regarded as precious metals and there is considerable effort exerted to recover them. Other metals such as indium and gallium are not only valuable components of semiconductors but also show considerable toxic potential. Elements such as arsenic, cadmium, lead, and mercury are well-known toxicants but financially less valuable, so less effort is exerted to recover them and hence they frequently find their way into air, food, and water where they may produce toxicity on an individual or mixture basis. From the risk assessment perspective, the situation for metallic elements as a class in e-waste is complicated in terms of conducting an accurate evaluation.

This situation is further complicated by concomitant exposures to organic chemicals such as those released by burning insulation from copper wiring and combustion of plastics and flame retardant chemicals. The issue of chemical interactions between metals and organic chemicals in mixture situations is difficult from a risk assessment perspective since these agents may affect different pathways leading to cell injury/cell death or cancer outcomes. In addition, there are biological factors that should be considered in conducting more accurate risk assessments for populations exposed to chemicals released from e-waste recycling activities in developing countries. These include age—the developing fetus exposed to chemicals capable of crossing the placenta, children working in e-waste recycling activities—gender, and intrinsic differences in susceptibility to metal toxicity (Fowler et al., 2005, 2008), and nutritional status. Persons with poor nutritional status are generally less resistant to the effects of toxic chemicals than persons with good nutritional status (Heindel & vom Saal, 2009). Other biological factors such as the presence of infectious diseases (Ortiz et al., 2002) may also play a role in health outcomes since a number of e-waste chemicals produce immune-suppressive effects (Luster et al., 1992). Finally, there is the impact of low socioeconomic status (SES) itself on susceptibility to chemical-induced diseases (Friedman & Lawrence, 2002). Low SES is a major driver for persons in developing countries to engage in the unregulated recycling of e-waste. It is well known that low SES itself is major determinant of decreased longevity (Bassuk, Berkman, & Amick, 2002) for a complex set of reasons, and the impact of this factor coupled with exposure to e-waste chemicals should be considered in future risk assessment paradigm. A diagrammatic overview representation of such an integrative risk assessment approach is presented in Figs. 2.3 and 2.4.

COLLECTION OF DISCARDED ELECTRONIC DEVICES (E-WASTE)
I
CONTAINER SHIP TRANSPORT OF E- WASTE TO DEVELOPING COUNTRIES
I
TRANSFER OF E-WASTE FROM SHIPPING PORT VIA TRUCK TO UN-REGULATED RE-CYCLING SITES
I
DISMANTLING OF E-WASTE DEVICES AND BREAKING OF HARD DRIVES AND CIRCUIT BOARDS BY HAND TOOLS
I - HUMAN EXPOSURES TO PARTICLES AND DUST

MELTING OF METAL AND PLASTIC COMPONENTS IN OPEN AIR CONDITIONS TO RECOVER PRECIOUS METALS WITH VOLATILE RELEASES OF TOXIC METALS AND PLASCTIC COMPONENT CHEMICALS

I - HUMAN EXPOSURES TO VOLATILIZED TOXIC METALLICS AND CHEMICALS FROM PLASTICS

STRIPPING OF INSULATION FROM COPPER WIRNG BY MELTING IN OPEN AIR CONDITIONS WITH RELEASE OF INSULATION CHEMICALS

I – HUMAN EXPOSURES TO VOLATILIZED INSULATION CHEMICALS
I

HUMAN EXPOSURES FOLLOWING DISPOSAL OF UNSALVAGEABLE E-WASTE MATERIALS IN LANDFILLS OR WATER BODIES – CHRONIC RELEASES OF TOXICS CHEMICALS WITH UPTAKE INTO CROPS AND EDIBLE FISHERY PRODUCTS AND HUMAN EXPOSURE FOLLOWING INGESTION

KNOWN POPULATION RISK ASSESSMENT FACTORS

AGE I

GENDER

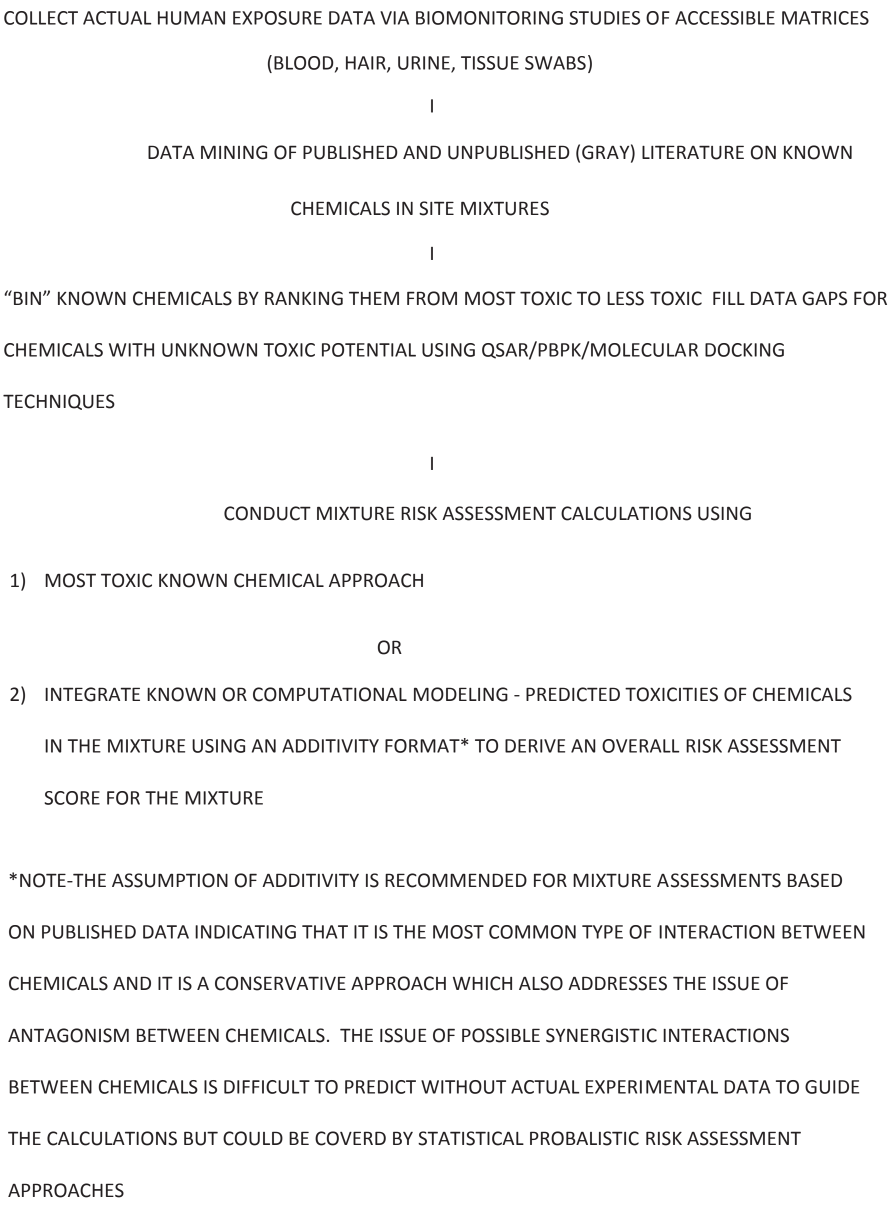
GENETIC SUSCEPTIBILITY >

NUTRITIONAL STATUS

SES I

COLLECT EPIDEMIOLOGICAL DATA ON POPULATION OF INTEREST

FIGURE 2.3
A diagrammatic representation of a possible integrative risk assessment paradigm for evaluating potential health effects from e-waste chemicals in susceptible populations in developing countries.



COLLECT ACTUAL HUMAN EXPOSURE DATA VIA BIOMONITORING STUDIES OF ACCESSIBLE MATRICES (BLOOD, HAIR, URINE, TISSUE SWABS)

I

DATA MINING OF PUBLISHED AND UNPUBLISHED (GRAY) LITERATURE ON KNOWN CHEMICALS IN SITE MIXTURES

I

"BIN" KNOWN CHEMICALS BY RANKING THEM FROM MOST TOXIC TO LESS TOXIC FILL DATA GAPS FOR CHEMICALS WITH UNKNOWN TOXIC POTENTIAL USING QSAR/PBPK/MOLECULAR DOCKING TECHNIQUES

I

CONDUCT MIXTURE RISK ASSESSMENT CALCULATIONS USING

1) MOST TOXIC KNOWN CHEMICAL APPROACH

OR

2) INTEGRATE KNOWN OR COMPUTATIONAL MODELING - PREDICTED TOXICITIES OF CHEMICALS IN THE MIXTURE USING AN ADDITIVITY FORMAT* TO DERIVE AN OVERALL RISK ASSESSMENT SCORE FOR THE MIXTURE

*NOTE-THE ASSUMPTION OF ADDITIVITY IS RECOMMENDED FOR MIXTURE ASSESSMENTS BASED ON PUBLISHED DATA INDICATING THAT IT IS THE MOST COMMON TYPE OF INTERACTION BETWEEN CHEMICALS AND IT IS A CONSERVATIVE APPROACH WHICH ALSO ADDRESSES THE ISSUE OF ANTAGONISM BETWEEN CHEMICALS. THE ISSUE OF POSSIBLE SYNERGISTIC INTERACTIONS BETWEEN CHEMICALS IS DIFFICULT TO PREDICT WITHOUT ACTUAL EXPERIMENTAL DATA TO GUIDE THE CALCULATIONS BUT COULD BE COVERD BY STATISTICAL PROBALISTIC RISK ASSESSMENT APPROACHES

FIGURE 2.4

Diagammatic approach for conducting risk assessments on e-waste chemical mixture exposures among human populations in developing countries.

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