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ORIGINAL PAPER

Human health risk assessment related to contaminated land: state of the art

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Abstract Exposure of humans to contaminants from contaminated land may result in many types of health damage ranging from relatively innocent symptoms such as skin eruption or nausea, on up to cancer or even death. Human health protection is generally considered as a major protection target. State-of-the-art possibilities and limitations of human health risk assessment tools are described in this paper. Human health risk assessment includes two different activities, i.e. the exposure assessment and the hazard assessment. The combination of these is called the risk characterization, which results in an appraisal of the contaminated land. Exposure assessment covers a smart combination of calculations, using exposure models, and measurements in contact media and body liquids and tissue (biomonitoring). Regarding the time frame represented by exposure estimates, biomonitoring generally relates to exposure history, measurements in contact media to actual exposures, while exposure calculations enable a focus on exposure in future situations. The hazard assessment, which is different for contaminants with or without a threshold for effects, results in a critical exposure value. Good human health risk assessment practice accounts for tiered approaches and multiple lines of evidence. Specific attention is given here to phenomena such as the time factor in human health risk assessment, suitability for the local situation, background exposure, combined exposure and harmonization of human health risk assessment tools.

Keywords State-of-the-art human health risk assessment · Soil pollution · Exposure assessment · Exposure models · Hazard assessment

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Introduction

Scope

Since humans are constantly surrounded by and in close contact with contaminant-holding materials and matrices, the human body is part of the contaminant cycle. Subsequently, the human body is loaded with contaminants (WWF 2003; Schroijen et al. 2008). The chemical load of the human body can be considered as a chemical footprint of past exposures, including exposure from soil, groundwater and contact media that are in contact with soil or groundwater. Budd et al. (2004) demonstrated on the basis of measurements in tooth enamel of 77 individuals buried in England that humans were exposed to lead from geological sources via their diet, at least since the Neolithic era (about 5000 years ago).

Contaminants have widely differing potentials for causing health damage. Exposure of humans to

contaminants originating for contaminated land may result in many types of health damage ranging from relatively innocent symptoms such as skin eruption or nausea, on up to cancer or even death. Good health is, without any doubt, both literally and figuratively, a priceless asset. Obviously, human health protection is considered as a major protection target, both by decision-makers as well as by the general public. Therefore, human health is widely recognized as the major protection target in the risk-based assessment of soil quality and the management of contaminated sites (Carlon and Swartjes 2007). Although the extent of health damage due to soil contamination is often debated, it is generally accepted that as part of modern civilization people must be safe on the sites where they live, work or recreate. The uncontrollable and generally unobservable nature of soil contamination generally results in a relatively high perceived risk compared to risks from conscious choices (International Programme on Chemical Safety 1999).

Exposure to soil contaminants can occur by oral, inhalation and dermal routes, thus relating to the pathway within the human body through which the contaminants enter the body (the mouth, gullet, stomach; the nose, trachea and lungs; and the skin, respectively).

In Fig. 1, the schematization of the contaminated site management framework (US National Research Council 1983) has been illustrated. In this scheme, which is still a valid basis today, the problem definition and risk management solutions are connected through human health risk assessment (HH RA).

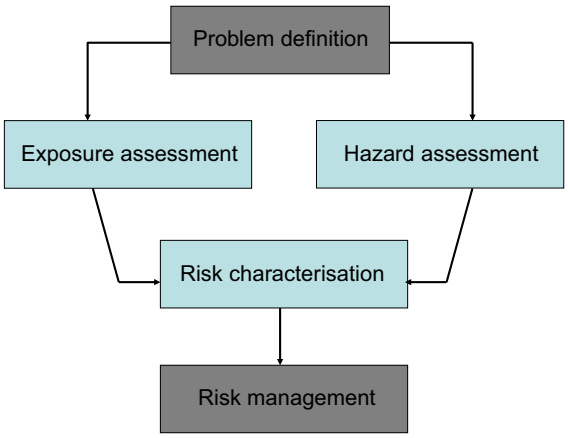

Fig. 1 The contaminated site management framework, in which the problem definition and risk management solutions (*dark shaded rectangles*) are connected through human health risk assessment (*light shaded rectangles*)

HH RA includes two different activities, i.e. the *exposure assessment* and the *hazard assessment*. The combination of these is called the r*isk characterization*, which results in an appraisal of the contaminated site.

The purpose of this paper is to review the state of the art regarding human health risk assessment related to contaminated land and to highlight the main pending critical issues.

Magnitude of health damage from contaminated soil and groundwater

Since the beginning of contaminated land management, in the late 1970s, there has been discussion about the magnitude of health damage from contaminated soil and groundwater. Today, exposure due to contaminated land is considered to have a limited impact on public health at the overall population level (Swartjes and Cornelis 2011). At the local level, however, exposure from a contaminated site can dominate the exposure to specific contaminants and thus pose a significant risk to human health. Su et al. (2010), for example, concluded that exposure to soil-borne arsenic and nickel, next to exposure from cigarette smoking and betel quid chewing, substantially contributed to the development of cancer.

It is interesting to note that a contaminated land map has similarities with the topographic map. This is shown, as an example, for the Netherlands in Fig. 2. In this figure, the distribution of the number of contaminated sites in the Netherlands that has been indicated with a 'need for urgent remediation' is shown versus the topographic map. It is clearly seen that the number of 'urgent remediation sites' corresponds with the size of the towns and cities. This similarity is explained by the fact that most contaminations has been caused by human activity. As a consequence, however, people are in close contact with contaminated land. Moreover, there often is a decreasing contaminant concentration in urban soils with further distance from the city centre as was shown, for example, for lead and chromium concentrations in the upper soils of Karlsruhe, Germany by Norra and Stuben (2003).

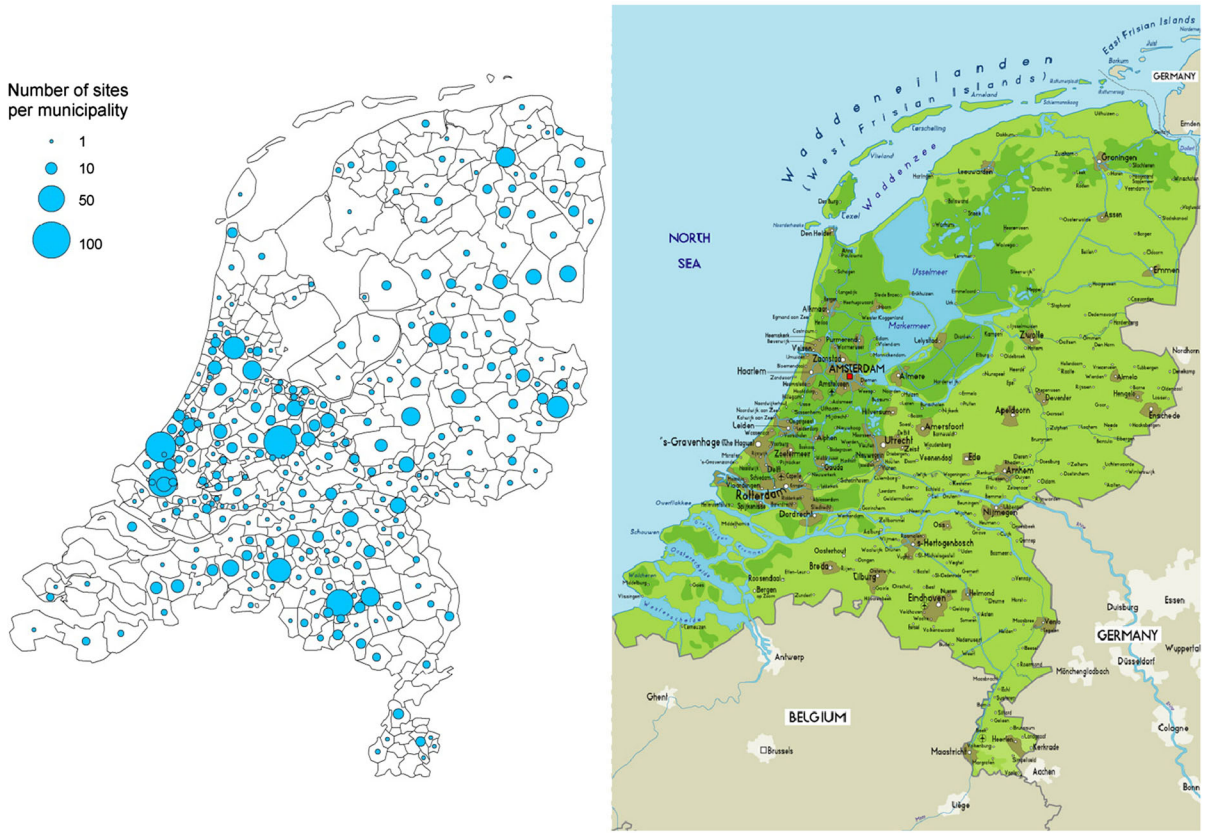

Fig. 2 Contaminated land map, showing the distribution of the number of contaminated sites in the Netherlands that has been indicated with a 'need for urgent remediation' (2013) (*left*) and the topographic map of the Netherlands (*right*)

Exposure assessment

Biomonitoring

The most appropriate exposure measure is the *internal exposure*, represented by the amount of contaminants that accumulates in the body organs, or in case of systemic effects, in the blood. Therefore, the most direct way to assess human exposure from soil contaminants is to *measure* the actual body burden through biomonitoring. In practice, this means sampling and measuring body fluids or body tissue. For ethical and technical reasons, however, these measurements generally offer limited possibilities and are only used in higher tier risk assessments. The best biomonitoring options are the sampling of blood, urine, nails, hair and, in extreme cases, skin tissue. Indirect sampling of human material entails the measurement of volatile compounds in exhaled breath, maternal and umbilical cord blood plasma, the liver function, immune function, neurological impairment, dermatological effects, reproductive pathology and mortality (Swartjes 2011). In general, biomonitoring results in an estimate of accumulated exposure from a past period, ranging from hours (exhaled breath) to years (nails). Drawbacks of biomonitoring are that it is technically difficult, relatively expensive, a reference value for the contaminant concentration in body material is often missing and disturbing non-soil-related background sources are often unknown. Moreover, it might lead to ethical complications. From a practical perspective, a limitation is that biomonitoring cannot anticipate on exposure in future situations. Nevertheless, biomonitoring is applied in specific cases. Among the most popular options is lead monitoring in blood, since it is relatively easy, background sources are often known and there is a reference value available (10 μg/dL). Sceptics,

however, discuss the reference value (e.g. Gilbert and Weiss 2006, who claimed that levels higher than 2 μg/dL do not protect neurobehavioral development). As another criticism, the lead exchange between blood and the bones disturbs the relation between exposure from soil and lead blood levels (e.g. Mushak 2003). Another useful option is arsenic monitoring in hair and nails (e.g. Subhani et al. 2015, who found elevated arsenic concentrations in hairs and nails of Pakistan residents in industrial, urban and even rural areas, related to exposure via dust). The big advantage of this biomonitoring procedure is that the sampling of hair and nails does not imply difficult medical operations and there is a reference value available.

Exposure calculations

Exposure models

A very practical methodological possibility for assessing human exposure is that of *calculating human exposure*, using a so-called *exposure model*. Such an exposure model enables the calculation of the rate of soil contaminants that enter the human body, blood stream or target organs. Exposure models consider direct contact with the soil and intake of so-called contact media that include soil-borne contaminants. Since contaminants enter the body via the mouth, nose or skin (external exposure), the absorption in specific organs has to be specified. Worldwide, several exposure models are available, generally with the same basis structure, including three elements: (1) contaminant distribution over the soil phases; (2) contaminant transfer from (the different phases of) the soil into contact media; and (3) direct and indirect exposure to humans. Input parameters, however, do differ substantially between the different exposure models. Differences between input parameters in different models increase in the order: compound-specific properties; human characteristics; parameters that describe physico-chemical processes; human behaviour factors; geological factors (soil/water); climatic/cultural factors. Moreover, most exposure models include, often implicitly, policy decisions that have a major impact on the exposure calculations. In the Netherlands, for example, the following policy decisions have been included in the CSOIL exposure model: acceptable fractions of vegetables from own garden to total vegetable consumption (impacting the calculation of exposure through consumption of vegetables from contaminated land); the focus on lifelong-averaged exposure (except for lead) (impacting both the calculated exposure, which is calculated as lifelong-averaged daily exposure and the risk characterization, in which this calculated exposure is compared to acceptable lifelong-averaged daily exposure); input parameters based on the reasonable maximal exposure assumption (impacting all exposure calculations, resulting in a realistic high-end estimate of total exposure); and the exclusion of background exposure (resulting in relatively high acceptable exposure values, which is non-conservative).

From a survey focused on the state of the art in the European Union, it was concluded that the most important exposure pathways are exposure through soil ingestion (including soil-borne dust), vegetable consumption and vapour inhalation (Carlon and Swartjes 2007).

Exposure through soil ingestion

Exposure through soil ingestion is controlled by soil and dust ingestion rates, soil and dust concentrations, body weight and the relative bioavailability factor in the human body. The combined soil and dust ingestion rates have been determined mainly by tracer studies, using typical soil constituents as aluminium, silicon, titanium and yttrium in faeces and urine as indicator (e.g. Calabrese et al. 1997; Stanek et al. 2001). Moreover, ingestion rates have been determined from hand-loading studies, both video and real-time observations. In rare cases, biokinetic models and the lead isotope methodology are used to estimate ingestion rates. From tracer studies, combined soil and dust intake rates range from 31 to 195 mg/day (Bierkens et al. 2011). From these studies, using measurements from the period 1986–1997, 100 mg/day seems a reasonable estimate as central tendency estimate. However, since the behaviour of children regarding time use, including time spent outdoors, changed considerable the last two decades, this figure could be an overestimation today. For adults, combined dust and soil intake rates are from 23 to 92 mg/day (Bierkens et al. 2011). Cornelis and Swartjes (2008) varied the ingestion rates outdoors with land use; soil ingestion was, for example, considered lower for residential land use without garden, since for this land use, only a minor part is unpaved and the possibility

for gardening is lacking. For extreme soil ingestion events, representative values are as high as 1000 mg/day for children showing pica behaviour[1] and 50,000 mg/day for geophagy[2] (US Environmental Protection Agency 2011).

For several reasons, it is useful to make a differentiation between soil and (soil-borne) dust ingestion. First, crawling children are in intensive contact with floor dust. Second, soil particles in dust generally are finer than soil particles outside, which might lead to enrichment of contaminants. Lanphear et al. (2003) concluded that for lead exposure to children, indoor dust exposure was the most significant exposure pathway. The fraction of soil in house dust from a number of studies varies between 0.20 and 0.80. Cornelis and Swartjes (2008) used values in between 0.25 and 0.50 for the fraction of soil in house dust, depending on land use. Juhasz et al. (2011) found a lead enrichment in the <50 μm particle size fraction in 16 contaminated sites in urban areas in Australia that was up to five times the concentration observed in the bulk soil. Cornelis and Swartjes (2008), however, derived a much smaller factor of 1.5 for the enrichment factor of the contaminant concentration in soil in household dust compared to the concentration in soil. Siciliano et al. (2009) showed that only the smaller soil fractions, average values ranging from 36 to 105 μm particle size depending on soil type, adheres to the human hand. Moreover, the authors found enrichment in this smaller fraction compared to bulk soil ranging from 110 % for lead up to 810 % for silver, mainly due to surface complexation with carbonates.

The contaminant-specific relative bioavailability factor in the human body (e.g. Cave et al. 2011) is used to cover the difference between intake (external exposure) and uptake (internal exposure) after soil ingestion. It reflects the ratio of the bioavailability in the soil matrix as compared to the bioavailability in a reference matrix (e.g. food, or the matrix on which the toxicological reference value is based). The availability in the human body is dependent on the fraction released from the soil matrix in the stomach during digestion in the gastrointestinal tract (the accessibility), the fraction transported across the intestinal epithelium and reaching the portal vein, and the possible metabolism of the contaminant in the intestinal epithelium and/or in the liver. The major factors that control the oral bioavailability are the concentration in soil and the pH in the stomach (and hence the transient feeding conditions). Moreover, physicochemical behaviour of contaminants, and hence mineralogy, particle size, solid-phase speciation and encapsulation are important parameters. Cox et al. (2013), for example, showed, through solid-phase fractionation, that bioaccessible nickel was associated with calcium carbonate, aluminium oxide, iron oxide and clay-related components, while bioaccessible chromium was associated with clay-related components, in soils overlying basalt in Northern Ireland. This suggests that weathering significantly affects nickel bioaccessibility, but not that of chromium. Juhasz et al. (2011) suggested that the bioaccessibility of lead increased with decreasing particle size, but currently, no quantitative relations between particle size and bioaccessibility exist.

The best model currently available to estimate the bioavailability is the Unified BARGE Method (UBM; Wragg et al. 2009), developed by the Bioaccessibility Research Group of Europe (BARGE) (BARGE 2014). The model showed good results in two recent validation studies (Denys et al. 2012; Van Kesteren et al. 2014).

In particular cases, risks from soil ingestion could be determined in more detail through subdivision of the different factors that control the exposure through soil ingestion. This was done by Swartjes and Janssen (unpublished) for the human HH RA regarding exposure to arsenic from naturally formed clumps of iron ore in a beach setting. To this purpose, the authors used separate values for hand dust cover (Finley et al. 1994), the transfer from hand to mouth (thumb sucking, palm licking and sucking on the upper part of the three middle fingers; Kissel et al. 1998); hand mouth contact frequency (Xue et al. 2007), the surface of thumb, palm and the upper part of the three middle fingers; and relative bioavailability (from an experimental study with Beagles fed with iron ore containing food; Groen et al. 1994). In this study, age group (playing children aged 2–12 years) and residence time (21 days at the beach a year; 4-h playing

[1] Pica is an eating disorder, mostly by children, characterized by an appetite for non-nutritive materials, including soils, which is not part of any cultural practice.

[2] Geophagy is the culturally driven practice of eating soil materials, most often in rural or preindustrial societies in Africa and Asia, in particular among children and pregnant women, partly as nutrient supplement.

with sand and materials per day) were based on expert judgement (discussion within a group of four human exposure experts). This procedure offers opportunities for HH RA in specific situations in which the factors that determine exposure through soil ingestion are different from a residential setting, on which most soil ingestion data in the literature are based. Moreover, it gives space to better underpinning of human health-based soil quality standards in countries or regions with different characteristics than are appropriate for Western culture and a moderate climate.

Exposure through vegetable consumption

Exposure through vegetable consumption is controlled by vegetable consumption rates, the fraction of vegetables that is homegrown, concentration in vegetables, body weight and relative bioavailability correction. For the fraction of vegetables that is homegrown, no decent statistics are available. Therefore, selected values are often based on a policy decision: 'the soil quality must offer the possibility to consume a specific percentage of vegetables from one's own garden'. It is reasonable to differentiate for the contribution from own garden between land uses. For the derivation of Maximal Values[3] in the Netherlands, for example, a value of 10 % was used for residential land use (also as basis for the derivation of the Dutch Intervention Values[4]), 50 % (potatoes) and 100 % for the land use vegetable garden, 25 % (potatoes) and 50 % for a small vegetable garden and 0 % for industrial land use (Swartjes et al. 2012). Not many models include specific values for relative bioavailability correction factors, since this information is generally lacking and the difference between intake and uptake is not as large as it is for soil ingestion. Intawongse and Dean (2006) performed an in vitro gastrointestinal study and showed that metal bioavailability varied widely from metal tot metal and according to different plant types. By far, the most challenging aspect of the calculation of exposure through vegetable consumption is the determination of the *accumulated concentration in vegetables*, at the moment of harvesting.

For *metals,* plant root uptake is very different among vegetables and among contaminants. Plant uptake is highest for cadmium and fast-growing leafy vegetables such as endive, spinach and lettuce. The fraction taken up by plant roots is higher for the more mobile contaminants, such as cadmium, zinc and nickel, than for the stronger sorbing metals such as mercury and lead or the metals forming complexes with organic matter such as copper. The fraction taken up of the first group (mobile metals) could be represented by the fraction extracted by 0.01 M $CaCl_2$ or by 1 M NH_4NO_3, while mercury and copper uptake is represented by the fraction extracted with diluted HNO_3 (Kördel et al. 2013).

In principle, the root uptake of metals in vegetables could be calculated on a mechanistic basis, including three subsequent processes, i.e. speciation in soil, plant root uptake and transport within the plant (see Fig. 3; Swartjes et al. 2013). For decades, studies on speciation have been reported in the literature, resulting in 'an effective pore water concentration' for root uptake, independent of plant type [e.g. based on the procedure of Tessier et al. (1979), still used today]. Subsequently, plant root uptake from pore water could be calculated by considering humic acid as a surrogate for roots, assuming similarities to the functional groups of roots and humic acid, as was done in the Windermere Humic-Aqueous Model (WHAM) model (Tipping 1998; Tipping et al. 2008). More recently, the WHAM model was tested on data from three different experiments (Le et al. 2015). It was concluded that the metal concentration in roots was predicted within one order of magnitude for 95 % of the data points. However, to account for plant specificity, an empirical species-specific correction term has to be used, accounting for the difference in the density between plant roots and humic acid. The third step, i.e. calculating the transport within the plant via xylem and phloem, is a very difficult part of the whole process, mainly because this process is highly plant specific. Massaccesi et al. (2014) showed that the transport of lead from roots to the upper plant parts of lettuce, radish and tomato was mainly attributed to lead complexes with organic acids. However, reliable quantitative relationships to describe transport in plants are currently lacking. Given the large

[3] Maximal Values are used to (1) manage the reuse of soil material after transport and (2) set land use-specific remediation objectives for soil in case of soil remediation.

[4] Exceeding the Intervention Value implies a 'seriously contaminated soil' for which remediation is in principle mandatory, but first the urgency of remediation has to be determined.

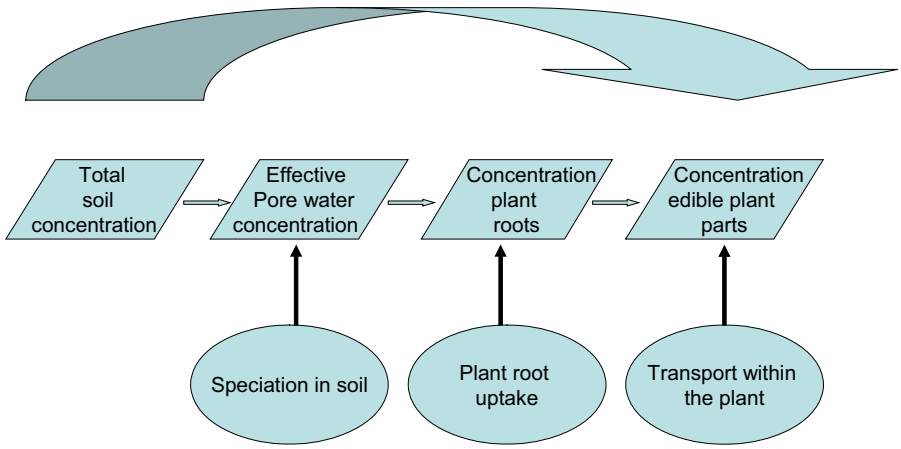

Fig. 3 The three processes that control the metal concentration in the different parts of vegetables (in *ovals*); the *horizontal arrow* illustrates the direct relation between concentration in the edible plant parts and total soil concentration (Swartjes et al. 2013)

uncertainties in the calculation of speciation, root uptake and certainly of the transport within the plant, mechanistic modelling does currently not result in reliable estimates of the accumulated concentration in vegetables.

Alternatively, a generic bioconcentration factor (BCF), i.e. the ratio between the concentration in plant and in soil, for all vegetables and independent on soil concentration and soil properties, is commonly used to calculate accumulation of metals in vegetables. Given the different uptake properties of vegetables, a rather large variation is expected. In Fig. 4, the BCFs for copper from the RIVM dataset ($n = 46$ paired vegetable and soil concentrations; Swartjes et al. 2007) are given, as an example, in which the generic BCF values range from 0.07 up to 1.01. Much variation is explained by the inclusion of different vegetables (potatoes, cauliflower, cabbage, carrot, lettuce and beans), a range of pH values (ranging from 4.9 to 8.4) and a range of organic matter contents (ranging from 0.10 to 0.30). Moreover, the relation between soil and vegetable concentrations is generally curvilinear, which means plant uptake is overestimated at higher soil concentrations when a generic BCF is used.

A more sophisticated way to predict the concentration in vegetables is based on empirical Freundlich-type relations (e.g. Rodrigues et al. 2012, for the description of accumulated mercury in different grasses in agricultural, mining and industrial areas in Portugal). In these relations, the accumulated concentration in vegetables is calculated as a function of the concentration in soil and the soil properties such as pH, organic matter and clay contents. Subsequently, a consumption-weighted concentration in vegetables can be calculated, accounting for an average accumulation in different vegetables and the actual soil properties.

Regarding *organic contaminants*, persistent polar ($\log K_{OW} < 3$) and non-volatile ($K_{AW} < 10^{-6}$) contaminants have the highest potential for accumulation in vegetables from soil; concentrations in leaves may be several hundred times higher than in soil (Trapp and Legind 2011). On the contrary, lipophilic ($\log K_{OW} > 3$) and volatile contaminants show a low accumulation in vegetables. Analogous to metals, plant uptake could be calculated from regression equations, including the Kow as representation of the contaminant. A useful model to estimate accumulation of organic contaminants in vegetables is described in Trapp and Legind (2011). In this model, the accumulated concentration of organic contaminants in roots at equilibrium is calculated based on the concentration in soil, the transpiration rate, the root mass, its first-order growth rate, and the partition coefficients between root and water and water and soil. Plant-specificity is included via the partition coefficients between root and water, which is dependent on the lipid content of the roots (and on the Kow, representing contaminant) (Trapp et al. 1994). In a subsequent step, the accumulated concentration of organic contaminants in the leaves at equilibrium is calculated from the

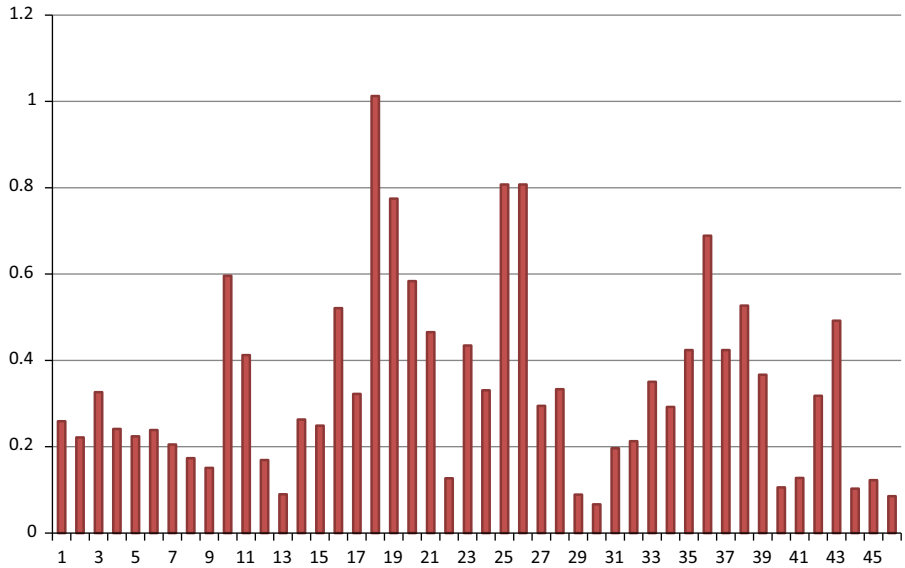

Fig. 4 Bioconcentration factors (BCFs) for 46 paired vegetable and soil concentrations for copper from the RIVM dataset (Swartjes et al. 2007)

concentration of organic contaminants in the roots. The transpiration rate, the partition coefficients between root and water, and the mass of the leaves are influencing the contaminant input into the leaves. A first-order elimination rate, growth dilution and biotic and abiotic (photolysis) degradation processes, determines the contaminant outputs from the leaves. To account for soil particles attached to plant material, an additional term including an attached soil fraction, depending on plant morphology, must be added for leafy vegetables. Li et al. (1994) reported values for this fraction ranging from 1.1 mg soil material per g plant material (dry weight) for cabbage up to 260 mg soil material per g plant material (dry weight) for lettuce. The relevant input parameters for the calculation of the accumulation of organic contaminants in vegetables can be adopted from Trapp and Matthies (1995) for leafy vegetables and from Trapp (2002) for roots.

An alternative to model calculations is *vegetable sampling* and analysis. Based on the criteria 'representativeness of crops in vegetable gardens', 'relative consumption rate', and 'sensitivity for uptake', the most relevant vegetables for sampling must be selected. Sampling should take place at the natural moment of harvesting. Subsequently, these vegetables must be prepared (washing, peeling) following 'a conventional kitchen procedure'. Moreover, measured concentrations in vegetables could be compared to acceptable concentrations in vegetables (i.e., food standards). Alternatively, the resulting concentrations in vegetables could be imported in the calculation of exposure through vegetable consumption, including the calculation of exposure through soil ingestion. Subsequently, exposure must be compared to the critical exposure value.

Exposure through indoor air inhalation

Exposure through indoor air inhalation is controlled by the inhalation rate, the indoor air concentration and body weight. The most challenging aspect of the assessment of exposure through indoor air inhalation is the determination of the indoor air concentration, which is controlled by contaminant fate and transport processes; characteristics of the building such as dimensions, layout and possibilities for building intrusion; and ventilation characteristics of the building. The attenuation factor indoor air concentration to groundwater concentration generally is between 4×10^{-5} and 6×10^{-4} (US Environmental Protection Agency 2012; median values for all investigated sites and all chlorinated hydrocarbons). Basically, two options exist for calculating the indoor air concentration, i.e. using standardized empirical attenuation factors (e.g. US Environmental Protection Agency 2012) or using a vapour intrusion model. These vapour

intrusion models include four processes that determine the indoor air concentration, using the groundwater concentration as starting point. These processes are as follows: (1) convection and diffusion in groundwater and soil; (2) intrusion into buildings; (3) ventilation; and (4) degradation during the whole pathway from soil or groundwater to indoor air. Using a soil concentration as starting point, instead of groundwater concentration, is generally not recommended for assessing subsurface vapour intrusion to indoor air because there are no published studies that clearly show a unique relationship between measured soil concentrations and measured soil gas concentrations (McAlary et al. 2011). The four mentioned processes above are difficult to quantify, and it is generally recognized that this pathway is a weak element in HH RA. Provoost et al. (2009) performed a validation study on vapour intrusion models, including eight exposure models, i.e. Vlier-Humaan (Flanders; BE), Johnson and Ettinger (USA), VOLASOIL (NL), CSOIL (NL), Risc (UK), Dilution model Sweden and Dilution model Norway. Calculated indoor air concentrations were compared with measured concentrations from three sites, for a series of volatile organic contaminants. It was concluded that, although in some cases the models predict too low concentrations, the models have a tendency to overestimate the indoor air concentrations. The differences between predicted and measured indoor air concentrations were the highest at low indoor air concentrations. At indoor air concentration higher than 1 $\mu g/m^3$, the differences between predicted and measured indoor air concentrations were generally within three orders of magnitude. A plausible explanation of the overestimation of the models could be that degradation processes are not included in the models. Picone et al. (2012) demonstrated that the distribution of water in the unsaturated soil layer, which controls the oxygen supply and, hence, degradation, impacts indoor air concentration with up to three orders of magnitude. However, there are more uncertainties in the algorithms and input parameters. Abreu and Johnson (2005, 2006), for example, demonstrated that the position of the groundwater plume, the presence of diffusion obstacles and preferential flow have a high impact on vapour intrusion. The authors showed that a 20-m shift of the border of the groundwater plume from the border of a building, for example, changes the dilution factor indoor air to pore water concentration by 2–5 orders of magnitude. Provoost et al. (2011) showed that the use of a Henry coefficient can overestimate vapour intrusion by a factor of 10. Moreover, preferential flow could play an important role, the 'stack effect' can result in under-pressurization of hundreds of Pascals in taller buildings, and contaminant mass transfer to the water-unsaturated zone can take place due to groundwater fluctuations (McAlary et al. 2011). Turczynowicz et al. (2012) concluded that the importance of subsurface partitioning and transport has been subject to intensive investigation, but that indoor air concentration is also very sensitive to thermal factors on ventilation.

More recently, studies focused on so-called inclusion zones, where proximity to the contaminant might make a building vulnerable to vapour intrusion (Wilson et al. 2012). Within these inclusion zones, which can be considered as an alternative metric to assess the risks from vapour intrusion, additional investigation is necessary to evaluate and manage exposure to the vapours. Verginelli and Baciocchi (2014) developed an analytical solution that allows the prediction of the risk-based vertical exclusion distance for hydrocarbons, considering 1D vapour intrusion, including first-order aerobic biodegradation limited by oxygen availability and the building footprint. This vertical exclusion distance is the distance from the source, above which the potential for vapour intrusion can be considered negligible.

An alternative to model calculations is *indoor air sampling* and analysis. Several passive and active methods for indoor air measuring exist and are often formalized in national standard protocols. Although measurements are often considered to provide the best estimates of environmental parameters, many constraints surround the assessment of indoor air quality applying measurements. These constraints include difficult interpretation due to background contributions from consumer products, building materials and even outdoor air sources; indoor air quality standards that sometimes are lower than typical reporting limits for conventional laboratory methods of analysis; variability of indoor air concentration in time and space, depending on wind, barometric pressure, occupant's activities and heating or air conditioning operations and outdoor concentrations (McAlary et al. 2011). Alternatively, (sub-slab) soil air concentrations could be measured. These concentrations can be considered as conservative estimates for indoor air

concentration or as input parameter for vapour intrusion models. In McAlary et al. (2011), a summary of main benefits and limitations of the various sample collection options (in groundwater, soil air, subslab soil air, or indoor air) is presented.

Traditionally, there has been considerable debate about the accuracy of the assessment of exposure through inhalation. It appears that in most applications, models can provide at best an estimate of indoor air concentrations within one order of magnitude of measured values (Bradley et al. 2009). However, measured indoor air concentrations using 24-h samples can also show up to about one order of magnitude variability (Kuehster et al. 2004).

Exposure through other pathways

Except for the three major exposure pathways described above, other pathways may be of importance in specific situations. Volatile contaminants and metals have minimal potential for dermal uptake due to the likelihood that they will volatilize faster than dermal uptake could occur and a low tendency to partition into skin lipids, respectively. Weschler and Nazaroff (2012), however, concluded that the dermal exposure is comparable to or larger than exposure through inhalation for many semi-volatile organic contaminants. Critical input parameters for estimating dermal uptake from soil include dermal absorption fractions, skin adherence factors and skin surface area exposed (Elert et al. 2011).

In particular cases, exposure through the *inhalation of soil-borne particulate matter* can be of importance, in particular in areas with favourable wind conditions (bare and open surfaces, limited vegetation) and high soil concentrations. The latter conditions might prevail around (former) mining areas, although the oral ingestion of soil-borne particulate matter often results in higher exposure [e.g. Taylor et al. (2014), who found elevated lead blood levels in children, corresponding to high concentrations in surface dust wipes from children playgrounds next to the Broken Hill mining area in Australia, with mean soil lead concentrations of 2450 mg/kg_{DW}]. For the inhalation pathway, the fraction of dust particles smaller than 10 μm (PM10) is the most relevant fraction (Knol and Staatsen 2005). There are models enabling the calculation of the PM10 concentration, as a function of daily average wind speed values, soil texture, soil roughness, vegetation and soil moisture. These models, however, result in unreliable estimates of airborne particulate matter concentrations, due to the dynamic nature of wind speed and lack of strong correlation between the soil and vegetation data and PM10 concentration in air. Moreover, it only includes the impact of wind, not the impact of activities on the ground such as driving cars or playing children. Therefore, Cornelis et al. (2006) used an additional safety factor of 10 when applying such a model. The PM10 concentration has been quantified in VMM (2005) for Flanders, Belgium, and is fairly constant in time. These values are 30–32 μg/m^3 for rural areas and around cities (period 2001–2004), 37–41 and 38–51 μg/m^3 for urban and industrial areas, respectively (period 1996–2004). The proportion of mineral constituents is an indicative measure of the fraction of soil in particulate matter. From the studies performed by Putaud et al. (2004; 24 locations in Europe) and Querol et al. (2004; cities in Austria, Germany, the Netherlands, Spain, Sweden, Switzerland and the UK), it can be concluded that the proportion of mineral constituents in PM10 in central Europe varies between 10 and 15 %. This proportion is higher in northern (Querol et al. 2004) and southern Europe (Almeida et al. 2005), due to the use of winter tiers and road grit in the relatively long winter period and the atmospheric Sahara sand supply, respectively. This part of the mineral constituents, however, does not originate from a contaminated site. Considering the content of PM10 and the proportion of mineral constituents in PM10, the concentration of soil from PM10 is 3–8 μg/m^3. Cornelis and Swartjes (2008) used a value of 5 μg/m^3 PM10, as the product of an average value for the PM10 concentration from the studies mentioned above of 35 μg/m^3 and a rather conservative value for proportion of mineral constituents of 15 %. To account for the impact of the sealed surface fraction to the PM10 concentrations in air, a correction factor was used ranging from 0.2 (residential land use without garden) up to 1.0 (residential land use with garden).

For HH RA of asbestos-contaminated land, exposure calculations are too uncertain. The reason for this is that the relevant exposure is through inhalation of airborne fibres and there are no reliable mechanistic relations between asbestos fibres in soil and asbestos fibres in air, including factors such as type of material (bound, non-bound asbestos), soil type, soil humidity,

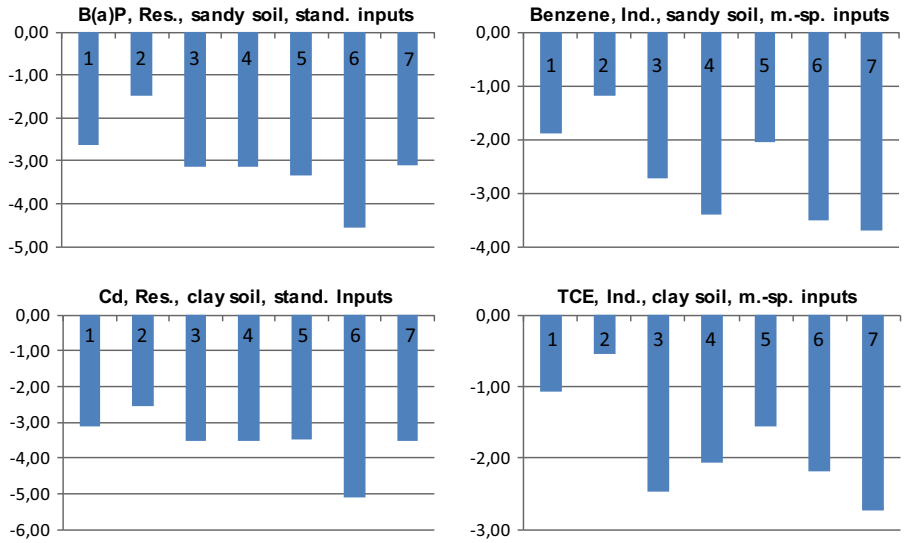

Fig. 5 Calculated exposures (mg/kg_{BW}/day; log-transformed) for four scenarios, using seven different models (models 1–7 in arbitrary order). *Res.* residential land use, *Ind.* industrial land use, *stand. inputs* standardized input parameters, *m.-sp. inputs* model-specific input parameters

wind conditions and activities on the soil surface. Swartjes and Tromp (2008) described a tiered approach for assessing the human health risks from soil-borne asbestos. Tier 1 includes a generic screening value (Intervention Value) of 100 mg/$kg_{soil,dw}$ asbestos equivalents empirically derived from measured asbestos concentrations in soil and air. Tiers 2–4 focus on the probability for emission of asbestos fibres from soil to air, the respirable fraction in the soil and house dust (*potential* site-specific exposure) and a measurement protocol for outdoor and/or indoor air, respectively.

Exposure model comparison

For gaining insight into the variation in calculated human exposures due to soil contamination, Swartjes (2007) investigated the variation in calculated exposures (total exposure and exposures along the separate exposure pathways). Exposure calculation for 40 hypothetical exposure scenarios were carried out using seven exposure models; the models are Cetox-human (DK), CLEA (UK), CSOIL (NL), ROME (IT), Vlier-Humaan (Flanders, BE) and two models without name from France and Sweden. The 40 scenarios are defined by a combination of four factors, i.e. (1) type of contaminant [atrazine, benzene, benzo(a)pyrene (B(a)P), cadmium (Cd) or trichloroethylene (TCE)]; (2) soil type (clay or sand); (3) land use (residential or industrial land use); and (4) selection of input parameters (standardized or model-specific input parameters) (for details, see Swartjes 2007). The concentration of the contaminants was put equal to the Dutch Intervention Values, i.e. atrazine 6 mg/kg_{dw}, benzene 1 mg/kg_{dw}, benzo[a]pyrene 40 mg/kg_{dw}; cadmium 12 mg/kg_{dw} and trichloroethene 60 mg/kg_{dw}. It was concluded that the use of different models could lead to quite different exposures for the same exposure scenarios. This is illustrated in Fig. 5, in which the calculated exposures for four scenarios are shown, as an example, using the seven different exposure models. For these scenarios, the ratio between the highest and lowest calculated total exposure (exposure along all exposure pathways combined) using the seven exposure models ranged from a factor of 149 (TCE, industrial land use, clay soil, model-specific input parameters) and 1235 [B(a)P, residential land use, sandy soil, standardized input parameters].

For better understanding the variation in calculated human exposures due to soil contamination, Swartjes (2009) compared the variation in calculated exposures with the variation in calculated concentrations in contact media and in the soil compartments, along

with the variation in the input parameters using the same exposure model calculations according to the 40 exposure scenarios as described above. This led to the conclusion that most of the variation in exposure through soil ingestion could be explained by differences in the input parameter average daily soil intake. When model-specific input parameters were used, the variation in exposure through vegetable consumption could be explained by differences in the product of total consumption rate and fraction of total consumption rate that is homegrown. When standardized input parameters were used, this variation was comparable to the variation in concentration in root vegetables and in the concentration in leafy vegetables. The variation in exposure through indoor air inhalation was comparable to the variation in concentration in indoor air. This suggests that the parameters that control the variation in concentration in the indoor air, that is, surface and volume of the building and, to a lesser extent, ventilation frequency of the building, also control the variation in exposure through indoor air inhalation.

Hazard assessment

Soil-borne contaminants include substances that are used neither as energy substrates nor as building blocks for biological matrices (Oesch and Arand 1999). The human body has a whole scale of defence mechanisms for eliminating adverse effects of such contaminants that intrude on the human body (Widmaier et al. 2011; Hayes and Kruger 2014). These are physical barriers such as the skin, and internal (lipid) obstacles, a number of defensive molecules such as enzymes and vitamins that neutralize toxic contaminants in the body and specific body organs such as the liver and the kidneys that are specialized in removing contaminants. When the defence system fails and adverse effects result, several repair functions in the human body are able to repair primary damage (Brusick 1999). If, and to what extent, primary damage occurs and repair mechanisms are effective, it is dependent on the toxicity of a contaminant, individual genetic talent, life style, dietary habits, age and the physical condition of a human being.

The toxicity of a contaminant depends on the reactivity in the body and the capability of forming an association of molecules with the body's own molecules. For this reason, toxicity is generally high for contaminants that mimic the body's own molecules such as neurotransmitters or hormones. An important metric in HH RA is the critical exposure (aka: toxicological reference dose). This metric is used to judge about estimated exposure in the stage of risk characterization. A critical exposure value is typically derived in different ways for contaminants with or without a threshold for effects. Generally, genotoxic carcinogens are considered contaminants without a threshold for effects, while other contaminants do have such a threshold.

For genotoxic carcinogens, it is assumed that any interaction of a contaminant with the genetic material in the human body increases the probability of an adverse effect (McMichael and Woodward 1999). To derive a critical exposure value for genotoxic carcinogens, a linear relation between exposure and excess cancer is assumed. The assumption of linearity is debatable, since cancer occurs through a multi-step process and DNA repair mechanisms are able to cope with low levels of DNA damage (EFSA 2005). Moreover, exposure from contaminated land is commonly intermittent, in particular for land uses such as recreation or vegetable gardens. However, estimates for cancer risk are generally derived from the unit risk value, *i.e.* the excess cancer risk per unit of exposure or unit of concentration (dimensionless). The decision on the *acceptable* excess cancer risk is a policy decision. Acceptable excess cancer risk values used in HH RA with regard to contaminated land range worldwide between 1 in 10^4 and 1 in 10^6 lifelong exposed individuals.

For contaminants with a threshold for effects, many options for endpoints exist, such as enzymatic activity, membrane potential, secretion of a hormone, heart rate or muscle contraction. However, there is generally a lack of epidemiological data, for which the exposure conditions are sufficiently known. Therefore, most critical exposure values for contaminants with threshold effects are derived from experimental studies with test animals. From effect data on these test animals, a no-observed-adverse-effect level (NOAEL) or lowest-adverse-effect level (LOAEL) is derived. Examples of endpoints in animal experiments are alteration of morphology, growth, mass or life span. Subsequently, a critical exposure value is derived through division of the NOAEL or the LOAEL by so-called assessment factors, generally ranging from 10 to 1000. These assessment factors cover conversion, extrapolation,

adjustment and uncertainty (Swartjes and Cornelis 2011) and are generally determined by an expert panel. Note that the impact of an additional assessment factor generally has substantially higher impact on the risk characterization than fine-tuning an exposure estimate.

There has been a lot of debate about the use of appropriate assessment factors. Many researchers have criticized the poor scientific foundation and the conservative nature of assessment factors (e.g. Slob 1999). A remarkable consequence of the use of uncertainty factors is that the less epidemiologists know the more at risk the public seems to become (Lindley 2001). In a more sophisticated approach, as proposed by Slob and Pieters (1998), point estimates of assessment factors and NOAELs are replaced by probability density functions. Subsequently, a more realistic distribution of critical exposure values results from Monte Carlo simulations.

Critical exposure values are generally derived for the oral and the inhalation routes, separately. In case of systemic effects, one critical exposure value can be used independently from the exposure route, after correction for differences in bioavailability per route. Critical exposure values for long-term systemic effects through dermal exposure are generally not available, but on occasion can be derived from oral critical exposure values. Several databases with critical exposure values exist, including these from the World Health Organization/the International Programme on Chemical Safety (WHO-IPCS), the International Agency for Research on cancer (IARC), Risk Assessment Reports (RARs) published by the European Chemical Bureau of the European Commission and the US Environmental Protection Agency, Integrated Risk Information System (IRIS).

The interpretation of critical exposure values is cumbersome. A consequence of a limit value for exposure is that some persons exposed above the exposure limit do not respond (the hyposusceptibles) and presumably a small proportion (the hypersusceptibles) will respond at exposures below the exposure limit (Jayjock et al. 2001). These fractions, however, are both unknown. Moreover, exposure limits do generally not give information about the percentage of people protected. They are supposed to protect the vast majority of people, but it is unknown if this is 80, 95 or 99.9 % (Rutkowski 2014). The critical exposure value is generally used to approve estimated exposure that is lower than the critical exposure value. In case the estimated exposure exceeds the critical exposure value, it does not implicitly mean there is a health problem, but it implies that further research after human health risks is warranted. A faulty and misleading situation associated with critical exposure values, in particular those for contaminants without a threshold for effects, is the assumption of zero risk or 'a safe situation' by non-professionals. At least it should be realized that critical exposure values include value-laden, subjective, and last but not least, policy elements.

In a more advanced way, the full dose–response data are used to derive a benchmark dose (BMD). The BMD corresponds to a certain level of effect. The 95 % lower confidence interval (BMDL) is then used as a NOAEL (International Programme on Chemical Safety 2008). For arsenic, for example, in 1983, an estimate of 2.1 $\mu g/kg_{BW}$/day was derived as provisional maximum tolerable daily intake (TDI) for ingested inorganic arsenic from the relation between arsenicism (a disease due to gradual arsenic poisoning) and specific concentrations in water supplies. More recently, however, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) replaced this critical exposure value by a BMDL0.5 (i.e. representing an effect for 0.5 % of the population) of 3.0 $\mu g/kg_{BW}$/day (2.0–7.0 $\mu g/kg_{BW}$/-day), based on the range of estimated total dietary exposures (FAO and WHO 2011). In practical use, a margin of exposure (MOE) between the BMDL and the estimated human exposure is calculated. Based on the size of the MOE, a conclusion is drawn whether or not the health risk is acceptable.

In specific cases, the absorption, distribution, metabolism and excretion of contaminants within the human body can be assessed in detail, using physiologically based toxicokinetic models. Tonnelier et al. (2012), for example, investigated the bioaccumulative potential of contaminants in the human body, using a physiologically based toxicokinetic model, including processes that tend to decrease the concentration of the contaminant such as metabolization.

Good human health risk assessment practice

Procedures

HH RA includes many uncertainties, but is an extremely useful process, when smartly used. A true

cliché is that theoretical knowledge of and experience with HH RA procedures improves the quality of the assessment. Moreover, except for science alone, creativity can improve both the quality and the efficiency of HH RA.

It is generally recognized that one-tier single exposure assessments have limited meaning. Just applying a default exposure calculation, although often done in practical applications driven by budget limitations, might result in an exposure measure without much relation with actual risks. Therefore, two procedural elements are of crucial importance for good HH RA practice, that is, a *tiered approach* and *multiple lines of evidence*.

In a tiered approach, several assessment steps (*tiers*) are followed. In each tier, an assessment is performed with generally two possible outcomes: either a judgment of the absence of unacceptable risks can be given, and the total assessment is finished, or unacceptable risks cannot be excluded, and the assessment has to be continued in the next tier. When the presence of unacceptable risks cannot be reputed in the final tier, unacceptable risks cannot be excluded, and risk management needs to follow the tier-based risk assessment. Given the nature of a tiered approach, in each step, the assessment becomes less conservative, which is based on more site-specific information and, hence, is more complex, time-consuming and often more expensive. The philosophy behind this is: *simple when possible (only the first tier) and more complicated when necessary (higher tiers)*. A tiered approach is an efficient way of risk assessing, without compromising scientific integrity. An example of a tiered approach for assessing the risks from vegetable consumption regarding cadmium-contaminated land, as used in the Netherlands, is given in Fig. 6 (Swartjes et al. 2013). Tier 0 concerns a preliminary qualitative evaluation of the possibilities for experiencing adverse human health effects due to crop consumption. In Tier 1, the actual total soil concentrations (average or relatively high values) are compared with a critical soil concentration, which is derived based on a conservative exposure scenario, including a high-end accumulation in vegetables. Tier 2 offers the possibility for a detailed assessment of the site-specific risks based on calculation. Finally, in Tier 3, a standardized measurement protocol is used, which allows for sampling of a significant number of representative vegetables in the field, for which the edible parts of the plants are treated in the laboratory in analogy with standard kitchen preparation. Subsequently, the measured concentration can be used in an exposure calculation and, when appropriate, compared to acceptable concentrations in vegetables.

Multiple lines of evidence refer to multiple lines of investigation, for which the results are combined to improve the reliability of an assessment. The principle behind the multiple weight of evidence approach is: *when several uncertain results are combined, the overall result is less uncertain*. As an example, multiple lines of evidence need to be investigated for the pathway exposure through indoor air inhalation, i.e. based on calculations and measurements. The reason for this is that both calculation and measuring indoor air concentrations include relatively large uncertainties. Therefore, a vapour intrusion calculation, or the use of standardized attenuation factors, must be combined with indoor air (sub-slab) soil air measurements, with the purpose to reduce uncertainty.

Several other elements need consideration in good HH RA practice. In human exposure modelling, the model user has to deal with many input parameters. It

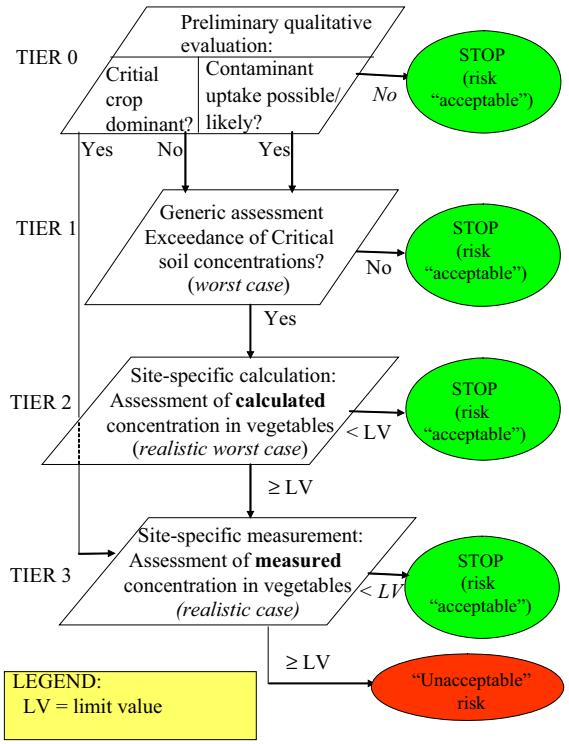

Fig. 6 An example of a tiered approach for assessing the risks from vegetable consumption regarding cadmium-contaminated land, as used in the Netherlands (Swartjes et al. 2013)

is typically not efficient to determine each input parameter with the same degree of precision. In good modelling practice, the model user pays in particular attention to a more detailed identification of the most relevant input parameters. The importance of input parameters follows from the dominant exposure pathways, which depend on contaminant characteristics and land use. Basically, the identification of the most crucial parameters for the specific risk assessment is a matter of experience. To support the identification of relevant input parameters, a sensitivity and uncertainty analysis could be performed.

Since HH RA is characterized by large uncertainties, probabilistic HH RA can offer benefits in specific situations. The basic principle here is to replace point estimates of input parameters with probability density distributions in the stage of exposure assessment. In performing Monte Carlo simulations, values for the input parameters are randomly extracted from these distributions. The result of such a probabilistic HH RA is a distribution of calculated exposures or hazard indices (aka: risk indices). Probabilistic approaches are particularly useful for gaining insight into the variability of exposure. A practical disadvantage of probabilistic human health risk is the time-consuming construction of probability density distributions for a series of input parameters. Moreover, in the stage of risk characterization, a choice must be made for the percentile of the protected population regarding the distribution of calculated exposures or hazard indices.

In the following sections, specific attention is given to phenomena such as the time factor, the suitability for the local situation, the role of background exposure and combined exposure. In a final section, attention is focused on the harmonization of HH RA tools. HH RA-related public perception and ethical issues (see Swartjes (2011) for details) are left out of this overview.

The time factor

In the stage of risk characterization, estimated exposure and critical exposure values should be consistent with regard to duration. This is in particular important for carcinogenic contaminants with latency periods of several decades. Therefore, awareness of the impact of the time factor is a necessity for appropriate risk assessing in the stages of exposure and effect assessment.

Effects do reveal at different moments in time, ranging from acute effects (24 h/14 days), via subacute and sub-chronic (up to 90 days) to chronic (considerably more than 90 days). The phrases ‘acute exposure’ and ‘chronic exposure’ are also often used in the meaning of single exposure and repeated exposure, respectively, but this distinction does not leave much scope for further differentiations with regard to exposure duration. A well-known example of adapting exposure scenarios to the relevant period for effects is the focus on children for human health risks from lead. The toxicologically relevant exposure period can differ for different type of effects. Lead, for example, is well known to cause neurological effects to children, but it can also affect the kidneys (ATSDR 2010) and sperm quality (Alexander et al. 1996) of adults at higher and longer exposure levels. Susceptibility can change with age, and much attention is paid to the susceptibility of children or the elderly for exposure to contaminants (International Programme on Chemical Safety 2006; US Environmental Protection Agency 2006).

A number of pieces of legislation account for the protection of children by performing the risk characterization of threshold contaminants upon exposure during the first years of age. As children will have a higher exposure per unit of body weight, a risk characterization based on children will result in a more stringent risk assessment. Grosse et al. (2002), for example, showed that because of falling lead blood levels, US preschool-aged children in the late 1990s had IQs that were, on average, 2.2–4.7 points higher than they would have been if they had the blood lead distribution observed among US preschool-aged children in the late 1970s.

Exposure periods differ. After calamities, human beings can be exposed over a short period to often high contaminant levels. Analogously, humans are exposed for short periods when they spend a relatively short time at a contaminated site. This is the case, for example, when children play ‘one or two hours’ at a contaminated industrial site or in case of short-stay recreation in a contaminated area. In many other cases, humans are exposed for longer periods and on a more continuous basis, from several years up to their whole lifetime, for example, when they live or work on a contaminated site. The type of effects relevant in a HH RA should correspond with the time span of exposure. Exposure assessments at contaminated land generally

address long-term exposures, in most case of an intermittent nature, thus averaging out any peak exposures occurring at the site. This is generally appropriate for residential or industrial land, as peaks in exposure are not expected. One exception is pica behaviour, particularly by small children, where deliberate ingestion of large amounts of soil particles could result in peak exposures that go well beyond typical assumptions (e.g. Lemanek et al. 2002, who examined the incidence and relationship of pica symptoms and dysfunctional eating patterns in children and adolescents with sickle cell disease).

Regarding the time frame represented by exposure estimates, it should be realized that biomonitoring generally relates to exposure history, measurements in contact media to actual exposures, while exposure calculations enable a focus on exposure in future situations.

Since the frequency humans will spend on a contaminated site is not always known, the definition of the relevant exposure time also is a political issue. A policy requirement, for example, could be that humans must be able to work at a contaminated site for a period of 40 years, 5 days a week and 8 h a day, without experiencing unacceptable adverse effects due to soil contamination. The policy role is even more pronounced for the derivation of screening values. In fact, the exposure time, or the duration that humans perform different tasks at a contaminated site, must be part of the exposure scenarios underlying screening values. According to the Dutch Soil Protection Act, for example, a policy boundary condition for the derivation of the soil screening values (Intervention Values) is that humans must be able to reside their whole lifetime on a contaminated site. Although this is hardly a realistic condition, certainly in case of any land use other than residential, it is believed to represent an acceptable worst-case (conservative) criterion to be used in the first-tier risk assessment. An exception is made for lead for which only the child phase is considered, since human health effects are much more relevant during the child phase.

For commercial land, the United Kingdom and Flanders (Belgium) limit exposure duration and averaging time to a high-end estimate of the duration of a professional career. With regard to non-threshold compounds, the general approach focusses on lifelong average exposure, even if the toxicologically relevant exposure duration is shorter than a lifetime.

Another time frame-related factor regards the representative concentration in soil. Most HH RAs are based on a measured (pseudo-)total soil concentration at a specific moment in time. At contaminated land, however, these concentrations change over time due to leaching, degradation and volatilization. The concentrations of the 2-ring and 3-ring polyaromatic hydrocarbons and petroleum hydrocarbons, for example, decrease significantly by degradation processes (Kördel et al. 2013).

Suitability for the local situation

A pitfall for HH RA is applying exposure principles that are valid under different geological, cultural and/or climatic conditions. The Dutch CSOIL model, for example, includes empirical parameters valid for shallow groundwater tables, representative for the Western part of the Netherlands. Since the calculation of indoor air concentration is sensitive to the depth of the groundwater table, this model may not be used in many parts of the world with deep groundwater tables. Another example is the exposure through vegetable consumption, which in most models is not representative for tropical regions with different (genotypes of) crops, soil and climatic conditions and, hence, transpiration rates, i.e. water flow from the soil through the plant (Melo et al. 2011). A final example relates to soil ingestion rates, which are generally taken from European and North American studies, but are not representative for conditions in many African, Asian and South American regions in which individuals spend more time outdoors; there is generally more uncovered soil surface and a more intensive garden practice for own vegetable production. Moreover, geophagy with substantially higher soil ingestion rates is common in specific regions in Africa, Asia and South America (Eijsackers et al. 2014).

Background exposure

Humans are in constant contact with contaminants. They eat and drink contaminant-holding foods, inhale contaminated air or volatile contaminants from glues, paint, petrol and printed works and use contaminant-holding materials as cosmetics and lotions. From the perspective of exposure from contaminated land, these exposures are considered as background exposure. Falcó et al. (2004), for example, showed a significant

contribution of hexachlorobenzene exposure for the population of Catalonia, Spain, through the consumption of dairy products. Cetin et al. (2003) demonstrated elevated VOC concentrations in ambient air from a petrochemical complex and oil refinery in Izmir, Turkey. It makes an important difference if background exposure is of a voluntary or imposed nature. Humans can control voluntary exposure, such as exposure to cadmium through smoking. Exposure from contaminated land is typically of imposed nature. Obviously, the amount of background exposure is contaminant specific. Moreover, background exposure differs among regions and individuals, depending on factors such as food pattern, lifestyle, traffic density and the proximity of urban or industrialized areas.

Whether or not to include background exposure in risk assessment is basically a policy issue. From a policy perspective, different viewpoints on the role of (imposed) background exposure in HH RA are possible. From a *medical viewpoint*, total exposure is the correct measure in case of contaminants showing threshold effects, since the human body does not distinguish between exposure from background sources or from the contaminated site. As a consequence, exposure from contaminated land may not exceed the critical exposure, reduced by the (imposed) background exposure. From this perspective, reduction of exposure from the contaminated site or from background sources is of equal health importance. From the perspective of risk management, intervention measures should focus on the most effective way of reducing exposure. Often reducing voluntary background exposure is the most promising and effective.

A practical problem is that for some contaminants, the (imposed) background exposure fills up a substantial part of the critical exposure and sometimes even exceeds the critical exposure values (e.g. in case of arsenic exposure; Naujokas et al. 2013; EFSA 2014). In that case, the human health risks due to contaminated land cannot be assessed based on total exposure. This aspect could result in conflicts when setting soil screening values. In some countries, like the UK (Environment Agency 2008) and Germany (Bachmann et al. 1999), the background exposure is limited to a specified proportion of the critical exposure value.

Another principle, which is followed in the Netherlands, for example, in the derivation of Intervention Values (Swartjes et al. 2012), is that the policy on contaminated land can only control exposure from contaminated land and must take the (imposed) background exposure for granted. According to this principle, it is politically defensible to assess only the exposure due to contaminated land. In other words, independent of background exposure and, hence, of the overall effects, the exposure from contaminated land may not exceed the critical exposure value. Since humans may not be fully protected according to this principle, and it would thus not be correct to state that it is safe to reside on the site, a clear communication to that effect is needed to explain the reasoning behind this policy position.

The role of background exposure is different for non-threshold carcinogens. For these contaminants, an acceptable risk level is set, which corresponds to the *excess* risk that is accepted for soil contamination. Therefore, it does not make sense to include background exposure in the risk assessments.

Combined exposure

The great majority of contaminated sites show contamination with more than one contaminant in soil and/or groundwater, sometimes in familiar combinations of contaminants, often as an incoherent cocktail of contaminants. Consequently, humans generally are exposed to several contaminants at the same time.

Non-carcinogenic contaminants can or cannot act independently from each other after exposure. Depending on the composition of the contaminant cocktail, three different possibilities exist for assessing the overall health impact. First, contaminants do not influence the potency of the other contaminants. Second, exposure to several contaminants can enhance the overall effect more than linearly (*synergistic* effects). Third, a less than linear increase in effects is possible (*antagonistic* effects). Quantification of synergy and antagonism is difficult and, therefore, seldom done.

Two types of addition exist, *exposure addition* and *response addition*. For contaminants with the same toxicological endpoint (*e.g.* target organ) that act through a common mode of action, exposure addition is appropriate, if necessary after accounting for differences in potency, and then compared to the critical exposure value. If contaminants have the same toxicological endpoint, but act through a different mode of action, response addition has to be applied. In that case, the responses should be added. In practice,

this means that the combined effect of contaminants showing exposure addition can lead to a negative health risk appraisal, even if the separate exposures do not exceed the critical exposure value. In contrast, the combined effect of contaminants showing response addition will not exert a negative health risk appraisal when the separate exposures do not exceed the critical exposure value (Wilkinson et al. 2000). In that case, attention must be focused on the contaminant that is expected to cause the most serious health effect.

As a simplified approach to deal with combined exposure, the different hazard indices (ratio of estimated exposure to critical exposure value) are added up, while the criterion for 'possible unacceptable human health risk' is that the sum of these indices may not exceed the value of 1. From a toxicological perspective, this procedure is incorrect, since it might result in the consideration of different types of effects on different target organs combined. Moreover, even when the mode of action and the target organs are similar for the different contaminants, it falsely assumes that the risk is linearly related to the risk or hazard index. In spite of the lack of scientific foundation, this procedure offers a practical way to account for an increased risk when more contaminants are present.

In case of effects due to exposure of contaminants with a different endpoint, two or more different threats to the human health risk must be accounted for. However, since there is no standard procedure to quantify the overall effect of two different human health threats, this is rarely done in HH RAs. Generally, attention is focused on the contaminant that is expected to cause the most serious health effect.

Comparable considerations can be made for non-threshold carcinogens. If they act through the same mode of action on the same endpoint, exposure could be combined. However, even with regard to different targets and modes of action, there may be a potential for combined effects (Environment Agency 2008).

An alternative way of dealing with combined exposure is the use of toxicity equivalents (TEQs). The assumption underlying the use of TEQs, often implicitly, is that exposures can be combined, in other words, that the interaction between contaminant and body organ is similar for all contaminants. The toxic potential, however, differs between contaminants. The toxicity profile of one contaminant is put central, usually the most toxic agent, while the toxicity of the other contaminants is scaled in relation to this central contaminant using toxicity equivalent factors (TEFs), usually with values ranging in between 0 and 1. In practical applications, the sum of the multiplication of concentrations and TEFs is tested against the critical exposure value of the central contaminant. The TEQ procedure can be used for contaminants with or without a threshold for effects. TEQs are often used for the assessment of human health risks from dioxins and dioxin-like compounds in which case the 2,3,7,8-TCDD (2,3,7,8-tetrachloro-dibenzo-*p*-dioxine), the most toxic dioxin agent, is put central (with a TEF equal to 1). The TEQ procedure could also be applied for the assessment of risks from a mixture of PAHs, with benzo(a)pyrene as central agent.

Another way of HH RA is based on so-called disability adjusted life years (DALYs). The DALY characterizes severity of exposure, accounting for both mortality (years of life lost due to premature death) and morbidity (state of disease or disability). However, DALYs are often used to assess risks from different compartments (like Lolliet et al. 2003, who compared exposure from different sources, such as air, water, food, agricultural products, performing a life cycle impact assessment methodology) and so far not for contaminated site quality assessment.

Harmonization of human health risk assessment tools

Although the development of risk assessment tools was often based on studying existing HH RA tools, there is a remarkable diversity in tools that are available worldwide for the same purpose. This diversity is partly explained by different geographical, cultural and social conditions, and sometimes due to differences in policy choices. However, lack of scientific consensus also explains an important part of the differences. One of the major challenges in HH RA today is to move towards more consistency in the risk assessment tools used by the European Union member states (Swartjes et al. 2009) or, even better, worldwide. A stronger convergence of risk assessment tools would contribute to scientific integrity, a level playing field and a higher perception of justice among stakeholders. To this purpose, human health-related risk assessment tools that do not include geographical, cultural, social or policy elements should be harmonized (*standardized* risk assessment tools, e.g. physico-chemical

characteristics of contaminants, or reference dose for compounds with a threshold for effects). For risk assessment tools that do include geographical, cultural, social or policy elements, a protocol must be developed allowing a certain level of flexibility so as to account for these elements [*flexible* risks assessment tools, e.g. a vapour intrusion model (dependent on geographical elements such as soil type an depth of groundwater table, and social elements such as type of building construction and ventilation characteristics), or reference dose for compounds with a threshold for effects (dependent on a policy decision)].

Conclusions and recommendations

Conclusions

In this study, the state of the art regarding human health risk assessment related to contaminated sites has been reviewed and the main pending critical issues have been highlighted. The benefits and the limitations of biomonitoring have been outlined. Much attention in this study is paid to exposure calculations, with the emphasis on exposure through soil ingestion (including dust), vegetable consumption and indoor air inhalation. Moreover, inhalation of soil-borne particulate matter and human health risk assessment regarding asbestos-contaminated land are described. Internal exposure through soil ingestion can be predicted reasonably well. The assessment of internal exposure through vegetable consumption strongly depends on the assessment of the accumulated concentration in the edible parts of the crop. For the same metal and metalloids, many different procedures exist for this calculation, ranging in complexity from simple to sophisticated, and resulting in substantially different numbers. Relatively reliable models exist for the assessment of the accumulated concentration of organic contaminants in the edible parts of the crop. Exposure through indoor air inhalation is the most cumbersome pathway. Vapour intrusion models are complex, often not reliable and frequently overestimate indoor air concentration. Measuring indoor air concentrations, however, is also surrounded with constraints. An exposure model comparison study revealed substantial differences in calculated exposure for the same exposure scenarios, in particular for volatile contaminants and, to a lesser extent, mobile contaminants. The procedures for the derivation of critical exposure values for contaminants with or without a threshold for effects are described.

In spite of the many uncertainties, HH RA is an extremely useful process when smartly used. Theoretical knowledge of and experience with HH RA, and creativity, are crucial for good practice. The use of tiered approaches and multiple lines of evidence can substantially improve the quality and efficiency of risk assessments. Moreover, additional focus must be on the time factor, the local situation, background exposure and combined exposure.

Recommendations

In general, the pursuit of a stronger convergence of risk assessment tools must be encouraged among the European Union member states or, even better, worldwide. This could result in s*tandardized* tools for human health-related risk assessment tools that do not include geographical, cultural, social or policy elements. For tools that do include geographical, cultural, social or policy elements, *flexible* risks assessment tools must be developed, based on a protocol allowing a certain level of flexibility so as to account for these elements. In particular, this harmonization should focus on the following elements:

- The relation between the accumulated concentration of metals and metalloids in the edible part of crops, the soil concentration and soil properties. This is in particular important for the frequently found metals cadmium (many different relations available) and lead (impact of foliar uptake) and for arsenic (no clear relation between concentration in vegetables and in soil). Moreover, understanding of and insight into generic bioconcentration factors (the ratio between the concentration in plant and in soil, for all vegetables and independent on soil concentration and soil properties) is crucial, revealing the possibilities and limitations for practical use of this simple and popular metric.
- Ditto, for organic contaminants.
- A protocol for measuring and sampling the 'representative concentration' in vegetables.
- Vapour intrusion modelling, including the impact of the groundwater table, building construction type, position of the groundwater plume with regard to the location of the building and the

relation between oxygen supply and potential for degradation.
- A protocol for measuring and sampling indoor air and (sub-slab) soil gas, accounting for available (national) standard protocols.
- Critical exposure values for contaminants with a threshold for effects.
- Possibilities and limitations of applying a unit risk value in the derivation of critical exposure values for contaminants with a threshold for effects, with particular focus on the extrapolation of responses at low to high exposures and the impact of intermittent instead of continues exposure.

Moreover, further research should relate to:

- Impact of the evolution in time that children spend outdoors during the last two decades on soil ingestion rates.
- Relation between particle size, adherence to the human hand and enrichment of contaminants.
- Relation between particle size and bioaccessibility.
- The impact of the transient feeding conditions (and transient pH in the stomach) on the oral bioavailability of metals and metalloids.
- The possibilities for implementation of the benchmark dose concept (BMDL) and the margin of exposure (MOE), in particular regarding the derivation of screening values.

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