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Worldwide Regulatory Guidance Values Applied to Direct Contact Surface Soil Pesticide Contamination: Part I—Carcinogenic Pesticides

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ABSTRACT: Regulatory agencies worldwide have developed regulatory guidance values (RGVs) for nearly 800 pesticides. Analysis of the residential surface soil guidance values applied to the most frequently regulated current-use agriculture, home, and garden pesticides is presented. Part I concentrates on values applied to atrazine, simazine, and trifluralin. These are unique among commonly used pesticides because they are generally considered to be human carcinogens. Their use has been banned in much of the world, but they are commonly used in the United States. Regulatory guidance values applied to these 3 pesticides vary by 8.6, 5.5, and 5.1 orders of magnitude. Risk model coefficient–bounded set uncertainty analysis is applied to help analyze this variability. Cancer risk model uncertainty bounds appear to contain 36.3%, 43.0%, and 49.5% of the RGVs. Most of the remaining values appear to exceed a lifetime cancer incidence risk of 1×10^{-6} and may not be adequately protective of human health.

KEYWORDS: Soil contamination, environmental regulation, regulatory guidance values, pesticides, cancer risk models, atrazine, simazine, trifluralin

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Introduction

This article presents analysis of the regulatory guidance values (RGVs) applied worldwide to help control the potential health risks of pesticide surface soil contamination. Regulatory guidance values define the concentration at which a soil pollutant triggers some form of regulatory response. These types of standards exist for drinking water, food, air, and soil, although there are very few air pollution values for pesticides. In water, these are often known as maximum contaminant levels (MCLs). Many nations follow European Union (EU) or World Health Organization (WHO) leadership and have adopted similar MCLs. For agricultural commodities, these are generally referred to as maximum residual limits (MRLs). International trade agreements have led many nations to adopt similar MRLs. In soil, there is no unifying factor that has helped establish soil standards and little agreement about what the standards should be called. Names such as action levels, trigger values, screening values, remediation guidelines, maximum permissible concentrations, threshold values, limit values, and intervention values are used. Here, these will all be referred to as RGVs. There is much more variability in soil RGVs than in the MCLs and MRLs applied to the same pollutant.[1] It is true that there are nuances in how RGVs are applied that may not exist for MCLs or MRLs. Some jurisdictions use RGVs as remediation standards. In others, they serve as the starting point for site-specific standard negotiations. However, because RGVs define the concentration at which regulatory concern begins, they all may serve as remediation standards because soil remediated to below the RGV would no longer be of regulatory concern.

Regulatory guidance values also differ from other RGVs because regulatory jurisdictions often promulgate more than one value for each soil pollutant. Some jurisdictions provide values based on the possibility of the pollutant leaching to underlying potable groundwater or contaminating surface runoff that could reach a potable surface water. Regulatory guidance values promulgate specifically for agricultural soils or commercial/industrial sites may also be found. Most of these are based on potential human health impacts, but standards based on ecosystem impacts can also be found. Often developing these standards requires sophisticated fate and transport modeling in addition to human health and ecosystem impact analysis. These RGVs are not considered here. The work presented concentrates on RGVs applied to residential surface soils. These values are generally based on direct surface soil ingestion, inhalation, and dermal contact health impact models applied to children. These are the values often used in the analysis of soil RGVs.

Environmental jurisdictions worldwide have developed soil RGVs. National, regional, provincial, state, city, county, and indigenous peoples in at least 80 United Nations (UN) member states and several multinational organizations have promulgated RGVs. Most provide values to control the cancer and/or noncancer health risks of direct contact with residential surface soil, but there is little agreement about the pollutants that should be regulated or the magnitude of the values that should be used. The RGVs used worldwide for individual pollutants often vary by more than 5 orders of magnitude.

Previous studies at Case Western Reserve University have examined the RGVs applied worldwide to pollutants such as fuel-related benzene, toluene, ethylbenzene, xylenes, and naphthalene[2,3]; individual elements[4–6]; common polycyclic aromatic hydrocarbons[7,8]; and chloromethanes,[9] chloroethanes,[10] chloroethenes,[11] chlorobenzenes,[12] and chlorophenols.[13] Ongoing work is examining values applied to polychlorinated biphenyls, dioxins, and dibenzofurans (PCDDs/PCDFs).

Several other studies have also analyzed soil guidance values. Noteworthy contributions include those of the California Department of Natural Resources,[14] Proctor et al,[15] Schäfer,[16] Bartsch and Dorfman,[17,18] Davis et al,[19] the Science Applications International Corporation,[20] the Association of Environmental Health and Science,[21] the Interstate Technology Regulatory Council,[22] Cavanaga,[23] Provoost et al,[24] Paustenbach et al,[25] Canadian Contaminated Sites Management Working Group,[26] Carlon,[27] Erdal and Carollo,[28] US Environmental Protection Agency (USEPA),[29] Teaf et al,[30] Quinn and Frasier,[31] and Blauvelt and Sweet.[32] However, no previous study has addressed the worldwide scope of pesticide RGVs considered here.

Identifying worldwide pesticide RGVs is challenging. "Pesticides" are a large class of chemicals. Jennings and Li[33] identified RGVs for 739 distinct pesticide compounds regulated using either a chemical nomenclature description or one of the names under which they are marketed. The wide variety of product names expressed in different languages makes it difficult to ensure that the RGVs of comparable compounds are compared.

It is also difficult to identify "current-use" pesticides. Pesticide use is controversial. Many sources are reluctant to release data on specific product use. It is not difficult to identify pesticides that have been approved for use and not difficult to find data on broad category use such as the total amount of herbicides applied, but data on specific products are difficult to acquire. Pesticide manufacturers exert financial and political pressure to protect their markets and shield their products from regulation. Nations are also cautious about releasing pesticide data that might affect agricultural exports. There are also several criteria by which "most commonly used" can be defined. This can refer to the total mass applied or the mass applied per unit surface area, per capita, or per crop.

Based on the available information on current worldwide pesticide use and on the frequency of pesticide soil RGVs,[33] the following 15 pesticides in current common use were selected for analysis; 2,4-D, atrazine, carbaryl, carbofuran, chlorpyrifos, diazinon, dicamba, diuron, glyphosate, malathion, MPCA (2-methyl-4-chlorophenoxyacetic acid), metolachlor, picloram, simazine, and trifluralin. Of these 15 pesticides, the RGVs of 12 are usually based on noncarcinogenic risk considerations. Only atrazine, simazine, and trifluralin are considered to be carcinogenic by the USEPA. This part I article concentrates on defining methods common to both part I and II analysis and on presenting an analysis of atrazine, simazine, and trifluralin RGVs. Part II presents analysis of the RGVs applied to commonly used noncarcinogenic pesticides.

The goal of the work is to examine the variability of the RGVs used to regulate residential surface soil exposures to these pesticides and to determine how much of this variability falls within the span of credible health risk modeling. As has been observed in several of the previous studies, RGVs on the high end of their value distributions may allow for too much human exposure and thus may not be sufficiently protective of human health. Values that are on the low end of the distribution would be more protective of human health but may also impose unnecessary or infeasible remediation obligations. Often these extreme values exist and persist because regulators and the regulated community are simply not aware of where their values fall in the overall distribution of guidance values. The work presented here is intended to clarify this issue for 15 of the most commonly regulated current-use pesticides.

Materials

The materials of this work are the 15 pesticides for which analysis is provided. Detailed information on the toxicology of each may be found in the National Library of Medicine's Hazardous Substances Data Bank,[34] the USEPA-Integrated Risk Information System (USEPA/IRIS),[35] and in Agency for Toxic Substances and Disease Registry (ATSDR)[36] publications. Although this toxicology literature is important, it is only indirectly relevant to the work presented here. Rather than discuss this literature, the following provides information on the origin, typical uses, and use frequency of each pesticide and indicates how the health risks of each have been classified by organizations such as the American Conference of Governmental Industrial Hygienists (ACGIH),[37] the International Agency for Research on Cancer (IARC),[38] the International Labour Organization (ILO),[39] Safe Work Australia,[40] and USEPA.[41] It is how organizations such as these have responded to the toxicology literature in making risk classifications that exerts the greatest influence on RGV development.

Regulatory agencies worldwide have responded to the risk classifications of these pesticides by identifying them as high priority pollutants. Atrazine, malathion, simazine, and trifluralin appear on the United Kingdom "red list" of most dangerous substances.[42] Atrazine, chlorpyrifos, diuron, simazine, and trifluralin appear on the European Commission priority substances list.[43] Atrazine, chlorpyrifos, diuron, and trifluralin also appear on Turkey's list of priority substances.[44] With the exception of glyphosate and picloram, all appear on the ATSDR substance priority list.[45] All except glyphosate and picloram have been found at more than one US national priority "superfund" site, and 2,4-D (the most commonly found) has been identified at 233 sites.[46]

Additional information such as type, International Union of Pure and Applied Chemistry (IUPAC) name, elemental

Table 1. The most frequently regulated of current use pesticides generally considered to be carcinogenic.

NIST[a] REGISTRATION NAME	TYPE	IUPCA[b] NAME	ELEMENTAL COMPOSITION	CAS NO.	NIST NUMBER OF OTHER NAMES
Atrazine	Herbicide	1-chloro-3-ethylamino-5-isopropylamino-2,4,6-triazine	$C_8H_{14}ClN_5$	1912-24-9	91
Simazine	Herbicide	6-chloro-N,N'-diethyl-1,3,5-triazine-2,4-diamine	$C_7H_{12}ClN_5$	122-34-9	64
Trifluralin	Herbicide	2,6-dinitro-N,N-dipropyl-4-(trifluoromethyl) aniline	$C_{13}H_{16}F_3N_3O_4$	1582-09-8	42

[a]NIST – National Institute of Standards and Technology.
[b]IUPCA – International Union of Pure and Applied Chemistry.

composition, chemical abstracts service number (CAS No.) identification for atrazine, simazine, and trifluralin has been summarized in Table 1.

Data are also provided on the number of alternative names under which each has been marketed.

Atrazine

Atrazine is a triazine herbicide developed in the United States and Switzerland in the mid-1950s. It was registered for use in Switzerland in 1956 and in the United States in 1958. It rapidly became one of the most commonly used broadleaf herbicides. It is estimated that 75% of field corn in the United States is treated with atrazine. It is also applied to sorghum, sugarcane, wheat, hay, and pastures.[47] Atrazine is also the most commonly detected pesticide in US drinking water supplies in the Midwest.[48]

The use of atrazine is controversial. It was banned by the EU in 2003 (technically, it was excluded from reregistration because its registrants did not supply sufficient data to demonstrate that it would not contaminate groundwater)[49] even though its major producer is the Swiss corporation Syngenta. Studies have indicated that atrazine is an endocrine disruptor that affects the life cycles of amphibians, and may increase the rates of human breast and prostate cancer, and birth defects.[50,51]

The USEPA reassessed atrazine in 2006 and concluded that it remained eligible for registration.[52] It has been alleged that Syngenta exerted undue influence on the decision and remains aggressively hostile to anyone suggesting problems with atrazine, so its use has remained controversial.[48] This can be seen in the numerous Web pages (including Syngenta's public relations site[53]) touting its benefits or ills.

Atrazine is the second most commonly used agricultural pesticide in the United States.[54] It is also commonly used in New Zealand,[55] Canada,[56] Brazil,[57] South Africa,[58] and Australia[59] and is the fourth largest Chinese pesticide export.[60]

The IARC[38] indicates that Atrazine is "not classifiable as to its carcinogenicity to humans," and the ACGIH[34] indicates that it is "not classifiable as a human carcinogen." Safe Work Australia assigns atrazine risk phrases 48/22, 43, and 50 to 53 indicating that it is dangerous by ingestion or dermal exposure and is harmful to aquatic organisms.[40] The ILO assigns it risk phrases 20/22, 36, 40, and 43 indicating that it is harmful by ingestion, inhalation, and dermal exposure, but that there is "limited evidence of carcinogenic effect."[39] In 2000, USEPA Office of Pesticide Programs (USEPA/OPP) concluded that it was "not likely to be carcinogenic to humans,"[61] but in 2014, the California Office of Environmental Health Assessment issued a notice of intent to list atrazine as a chemical "known to the State to cause reproductive toxicity."[62] The USEPA/IRIS indicates that the cancer risk (CR) evaluation of atrazine "is not available at this time."[35] Nevertheless, although USEPA's RGV calculations are based on both CR and non-CR (NCR) of ingestion and dermal contact, CRs yield the binding value.[63]

Simazine

Simazine is another triazine-derivative herbicide marketed by Syngenta. It was first registered in the United States in 1956 as a preemergence herbicide for broadleaf and grassy weeds control on deep-rooted crops. It is also used for weed control in residential and industrial areas, highway and railroad rights-of-way, and (in combination with pesticides such as Paraquat, Roundup, and Surlflan) on fruit trees, Christmas trees, and ornamental plants. It has also been used to control submerged weeds and algae in ponds, fish hatcheries, swimming pools, and cooling towers, but its use as an algaecide is being discouraged.[64] Similar to atrazine, simazine has been banned by the EU.[65]

Simazine is listed as number 16 of the 25 most commonly used US agricultural pesticides.[54] It is also one of the top 3 herbicides used in Australia.[59]

The IARC indicates that simazine is "not classifiable as to its carcinogenicity to humans."[38] Safe Work Australia associates simazine with risk phrases 40 and 50 to 53 indicating "limited evidence of a carcinogenic effect," but that it is very toxic to aquatic organisms.[38] The ILO also assigns it the risk phrase 40 indicating that there is "limited evidence of carcinogenic effect."[39] Simazine was evaluated by the USEPA/OPP in 2005 which concluded that it was "not likely to be carcinogenic to

humans."[62] The USEPA/IRIS indicates that the risk classification for simazine "is not available at this time."[53] US Environmental Protection Agency bases its RGV calculation on both the CR and NCR of Simazine ingestion and dermal contact, but CR yields the binding value.[63]

Trifluralin

Trifluralin is a selective preemergent fluorinated dinitroaniline herbicide used to control grass and broadleaf weeds. It was patented by Eli Lilly and Company but is currently produced by the Dow Chemical Company. It was registered in the United States in 1963. Trifluralin is used on broccoli, cabbage, onions, leafy green vegetables, beans, tomatoes, potatoes, wheat, soybeans, sugar beets, sugarcane, fruit and nut trees, soybeans, cotton, corn, and wheat. It is also registered for residential and forestry use.[66] All trifluralin registered uses were withdrawn by the EU in 2007.[67]

Trifluralin is number 17 of the 25 most commonly used US agricultural pesticides and is the ninth most commonly used home and garden pesticide.[54] It is also number 15 on the French Agency for Food, Environmental and Occupational Health & Safety[68] list of pesticides commercialized in France, is a high percentage use pesticide in New Zealand,[55] and is number 20 of the agricultural pesticides used in South Africa.[58]

The IARC indicates that trifluralin is "not classifiable as to its carcinogenicity to humans."[38] Safe Work Australia assigns trifluralin the risk phrases 40, 43, and 52 to 53 indicating that there is "limited evidence of a carcinogenic effect," but that it can be toxic by dermal exposure and is harmful to aquatic organisms.[40] The ILO assigns it the risk phrases 36 and 43 indicating that it can cause eye irritation and that dermal exposure can be harmful.[39] Trifluralin was classified as a "Group C-Possible human carcinogen" by USEPA in 1986.[62] The USEPA/IRIS also classifies it as a "possible human carcinogen."[35] The USEPA trifluralin RGV is based on both cancer and noncancer ingestion and dermal contact risks, but CRs yield the binding value.[63]

Methods

Pesticide RGV sources

Pesticide RGVs were recovered from Internet searches of regulatory guidance documents. All values are for residential direct contact surface soil exposures or for the most comparable exposure classification. Identifying RGVs for the 15 pesticides considered in this, and the part II manuscript required translating documents from 21 other languages. This was accomplished with the assistance of native-speaking scholars and translation software. Documenting the RGVs also required extensive use of Internet references. Each RGV is listed in supplemental Table S1 or S2, and a reference is provided for each value. Readers are cautioned that Web pages are often rearranged, and regulatory guidance is frequently updated. If the information is no longer available at the URL listed, it may be located using the word search features (in the appropriate language) available on most Web pages or by contacting the agency directly via the "contact us" feature.

Analysis of RGVs

Pesticide RGV data sets were characterized by the total (N), US-related (N_{US}), and non–US related (N_w) set sizes, plus the set's arithmetic mean (μ), geometric mean (μ_G), $\log_{10}$ mean (μ_L), and $\log_{10}$ standard deviation (σ_L). All values were given equal weight. Statistics based on log-transformed values are included because previous studies have found that RGV distributions often resemble those of lognormal random variables.

Empirical cumulative distributions were constructed from RGV data sets as follows:

$$P(\mathrm{RGV}_r \leqslant \mathrm{RGV}_i) \approx \frac{R_i}{N}; \quad \forall i = 1, N \tag{1}$$

where RGV_r is a known value, RGV_i is a random RGV realization for this same pesticide, and R_i is the ordinal rank of RGV_r in the set of known values. Pearson (r) correlation analysis was applied to examine how empirical distributions correlated with theoretical lognormal random variable cumulative distributions based on identical statistics.

Previous studies have found that RGV distributions often contain clusters of values that are unlikely to have occurred randomly. Apparently, nonrandom clusters were identified as groups of values for which the binomial probability mass function indicated a random occurrence probability of less than .001.

USEPA RGV model calculations

US Environmental Protection Agency RGVs are calculated from CR and NCR models for ingestion, inhalation, and/or dermal contact, although the USEPA does not consider inhalation risks for the pesticides analyzed here. The USEPA models are typical of the formulations used to calculate RGVs and have been used in previous studies to generate uncertainty bounds based on credible variations in risk scenario coefficients. A similar approach is applied here.

The USEPA risk models for ingestion and dermal contact are defined in equations (2) through (7). Each of these is based on an exposure scenario (eg, days per year of exposure and amount of soil ingested per exposure) plus a pollutant toxicology coefficient to calculate the maximum soil concentration that would lead to an acceptable health risk. The chemical-independent exposure scenario coefficients, their current USEPA values (in parentheses),[69] and the range of values (in brackets) used by US states in similar calculations[4] are defined following the equation in which they first appear. The value ranges result from exposure scenario adjustments to account for regional conditions such as winter weather that reduce exposure frequency. The chemical-specific coefficients are also

Table 2. Chemical-specific coefficient values used in US Environmental Protection Agency risk model assessments.

COMMON-USE PESTICIDE	CFS_O—CHRONIC ORAL SLOPE FACTOR, KG D/MG	GIABS—FRACTION ABSORBED IN GASTROINTESTINAL TRACT, UNITLESS	ABS_D—FRACTION ABSORBED DERMALLY FROM SOIL, UNITLESS	RFD_O—CHRONIC ORAL REFERENCE DOSE, MG/KG D
Atrazine	2.3E−01	1.0	0.1	3.5E−02
Simazine	1.2E−01	1.0	0.1	5.0E−03
Trifluralin	7.7E−03	1.0	0.1	7.5E−03

defined following the equation in which they first appear. Their current USEPA values are listed in Table 2. Additional details about these risk models may be found in the USEPA method documentation.[69]

The screening level (SL) based on the CR of incidental soil ingestion is calculated as follows:

$$SL_{res-sol-ca-ing}\left(\text{mg/kg}\right)=\frac{TR\times AT_r\times LT}{CSF_o\times EF_r\times IFS_{adj}\times 10^{-6}} \quad (2)$$

where TR is the target risk (1×10^{-6} unitless), AT_r is the averaging time—resident (365 d/y), LT is the lifetime (70 years) [70-75], CSF_o is the chronic oral slope factor (kg d/mg) (see Table 2), EF_r is the exposure frequency—residential (350 d/y) [143-365], and IFS_{adj} is the resident soil ingestion rate—age-adjusted (114 mg y/kg d) [87-127].

The SL based on the CR of dermal soil contact is calculated as follows:

$$SL_{res-sol-ca-der}\left(\text{mg/kg}\right)=\frac{TR\times AT_r\times LT}{\left(\frac{CSF_o}{GIABS}\right)\times EF_r\times DFS_{adj}\times ABS_d\times 10^{-6}} \quad (3)$$

where GIABS is the fraction of contaminant absorbed in gastrointestinal tract (unitless) (see Table 2), DFS_{adj} is the resident soil dermal contact factor—age-adjusted (360.8 mg y/kg d) [253-1257], and ABS_d is the fraction of contaminant absorbed dermally from soil (unitless) (see Table 2).

The results of equations (2) and (3) are combined as follows to yield the CR RGV:

$$RGV\left(\text{mg/kg}\right)=\frac{1}{\frac{1}{SL_{res-sol-ca-ing}}+\frac{1}{SL_{res-sol-ca-der}}} \quad (4)$$

The SL based on the NCR of incidental soil ingestion is calculated as follows.

The ED_c term of equations (5) and (6) could be canceled but has been retained for consistency with the USEPA documentation:

$$SL_{res-sol-nc-ing}=\frac{THQ\times AT_r\times ED_c\times BW_c}{EF_r\times ED_c\times\left(\frac{1}{RfD_o}\right)\times IRS_c\times 10^{-6}} \quad (5)$$

where THQ is the target hazard quotient (1.0 unitless), ED_c is the exposure duration—child (6 years) [5-7], BW_c is the body weight—child (15 kg) [15-17], RfD_o is the chronic oral reference dose (mg/kg d) (see Table 2), and IRS_c is the resident soil ingestion rate—child (200 mg/d) [100-200].

The SL based on the NCR of dermal soil contact is calculated as follows:

$$SL_{res-sol-nc-der}=\frac{THQ\times AT_r\times ED_c\times BW_c}{EF_r\times ED_c\times\left(\frac{1}{RfD_o\times GIABS}\right)\times SA_c\times AF_cABS_d\times 10^{-6}} \quad (6)$$

where SA_c is the resident soil surface area—child (2800 cm^2) [1750-2960] and AF_c is the resident soil adhesion factor—child (0.2 mg/cm^2) [0.2-1.0].

The results of equations (5) and (6) are combined as follows to yield the NCR RGV:

$$RGV\left(\text{mg/kg}\right)=\frac{1}{\frac{1}{SL_{res-sol-nc-ing}}+\frac{1}{SL_{res-sol-nc-der}}} \quad (7)$$

Although the USEPA models are typical of the formulations used to account for direct contact exposure risks, there are regulatory agencies that consider additional factors when developing their values. For example, there are jurisdictions that adjust their RGVs for different types of soil (sand, silt, and clay),[70,71] different meteorological regimes (<40 in precipitation or >40 in precipitation),[72] site size (<0.5 or >30 acres),[73] site type (regular or hot spot),[74,75] site location (urban or rural),[76,77] site use (residential or allotment),[78,79] or the degree to which site occupants consume on-site–grown produce.[77] Where significant, the presence of an additional consideration has been noted as a "qualifier" in supplemental Tables S1 and S2. However, these extra

considerations yield only minor changes to values dominated by the risks of ingestion and dermal contact and do little to explain the range of RGVs identified for the pesticides considered here.

It should also be noted that USEPA risk models are only used to illustrate the impact that cancer versus determinations and exposure scenario coefficient variability can have RGV calculations. Their use should not be taken to imply that they yield the "correct" values. It is the responsibility of individual regulatory agencies to determine the most appropriate values for their jurisdictions.

Results

A total of 1252 US-related RGVs (74.0% of the total) were identified for the 15 pesticides considered in analysis of parts I and II. These values come from 5 national organizations (USEPA, US Army, National Oceanic and Atmospheric Administration, ATSDR, and the Department of Energy), 43 US states, 2 US territories, 1 county, 1 city, and 6 autonomous Native American tribes. State values were not found for Louisiana, Mississippi, North Dakota, Rhode Island, South Carolina, South Dakota, and Utah.

A total of 439 RGVs (26% of the total) were identified from regulatory jurisdictions in other nations. These include values from 2 multinational organizations (East Africa Community and WHO) and from national, regional, provincial, territorial, or city jurisdictions in 35 other UN member states (Andorra, Argentina, Armenia, Australia, Bahamas, Belarus, Canada, Croatia, Czech Republic, Ecuador, Estonia, Finland, Georgia, Italy, Latvia, Lithuania, Malaysia, Moldova, Montenegro, Bosnia and Herzegovina, the Netherlands, New Zealand, Panama, Poland, Thailand, Russia, Serbia, Singapore, Slovenia, Spain, Tanzania, Turkey, Uzbekistan, Ukraine, and Vietnam). Values were also included from the former *Union of Soviet Socialist Republics* (USSR) because these values are still used in many areas formerly part of the USSR.

Figures 1 to 3 illustrate atrazine, simazine, and trifluralin empirical RGVs' cumulative distributions and illustrate how well they compare with cumulative distributions of lognormal random variables with identical μ_L and σ_L statistics. Results for each pesticide are discussed in the following sections.

The bounds of uncertainty computed from the USEPA CR and NCR models have been indicated as shaded areas on each figure. Regulatory guidance value set statistics are summarized in Table 3. Significant RGV clusters have also been identified on each figure. Typically, there is at least 1 cluster corresponding to the values from US states that have adopted USEPA guidance.

Atrazine

Figure 1 illustrates the empirical cumulative distribution of the 193 atrazine RGVs identified. Of these, 57.5% are from US-related jurisdictions. This is the lowest percentage of the 3 carcinogenic pesticides. The values are well dispersed over more than 8 orders of magnitude. The correlation between the empirical RGV distribution and that of a lognormal random variable is 0.981. This is the highest correlation of any of the carcinogenic pesticides considered here and indicates that there is more scatter in the RGV data, apparently because there are more values from non–US related jurisdictions.

There are 4 value clusters in the atrazine RGV distribution. The largest (47 values, 24.4% of N) at 2.0 to 2.32 mg/kg corresponds to values computed from the USEPA CR model. With the exception of 1 value each from Malaysia and New Zealand, all the RGVs are from jurisdictions associated with the United States. There are also 2 clusters of 9 values each (4.7 % of N) at 470 and 320 mg/kg corresponding to Australian national and regional values for residential sites with gardens or assessable soil and sites with minimal soil access. These have been identified as "Australia clusters" on Figure 1. There is also a cluster of 12 values (6.2% of N) at 0.1 mg/kg made up of RGVs from Canada, Croatia, Georgia, Italy, Montenegro, Bosnia and Herzegovina, Slovenia, and the Ukraine.

The highest atrazine RGV (20 500 mg/kg) is specified by the US Department of Energy, Delaware, and Maine. The lowest value (0.00005 mg/kg) is specified by Poland. The atrazine CR model uncertainty bounds of 1.2 to 7.4 mg/kg contain 70 (36.3% of N) of the RGVs. The atrazine NCR model uncertainty bounds of 1100 to 11 200 mg/kg contain an additional 17 (8.8% of N) of the RGVs.

Simazine

The 135 simazine RGVs identified are illustrated in Figure 2. Of these, 71.1% are from US-related jurisdictions. The values are dispersed over 5.5 orders of magnitude. The correlation between the empirical RGV distribution and that of a lognormal random variable is 0.968.

There are 3 value clusters in the distribution. The cluster of 43 values at 4.0 to 4.6 mg/kg (31.8% of N) corresponds to values computed from the USEPA CR model. With the exception of 1 value from New Zealand (which reiterates the USEPA value in a database of standards) and 1 value from Malaysia (which specifies values nearly identical to those of the USEPA), all of these values come from US-related jurisdictions. The cluster of 11 values at 0.2 mg/kg (8.1% of N) are specified by Armenia, Belarus, Georgia, Lithuania, Moldova, Russia, Russian Tatarstan, Vietnam, and the USSR. This has been characterized as the "USSR cluster" because it is dominated by jurisdictions that were once part of the USSR and that continue to use the USSR 1983 RGV. There is also a small cluster at 0.01 to 0.011 mg/kg made up of 8 values from Idaho, The Nez Perce Tribe, Croatia, Montenegro, Bosnia and Herzegovina, Slovenia, and the Ukraine.

The highest value (2930 mg/kg) is specified by the US Department of Energy, Delaware, and Maine. The lowest

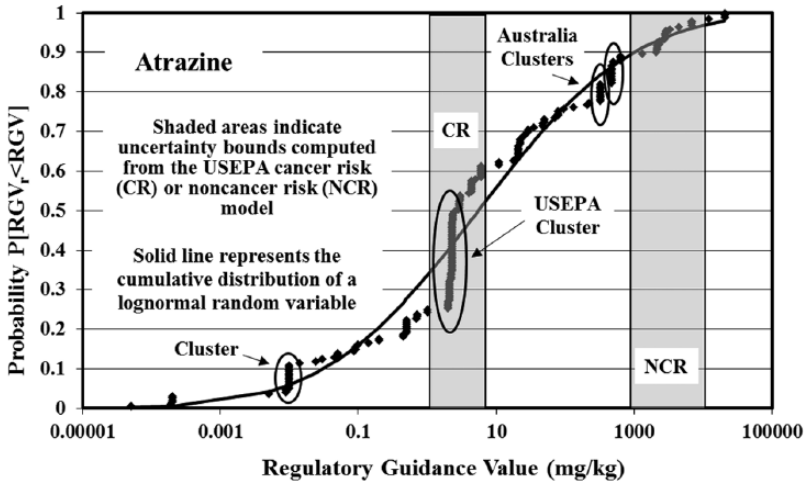

Figure 1. Cumulative distributions of 2,4-D and metolachlor RGVs compared with the cumulative distributions of lognormal random variables. RGV indicates regulatory guidance value; USEPA, US Environmental Protection Agency; USSR, Union of Soviet Socialist Republics; THQ, target hazard quotient.

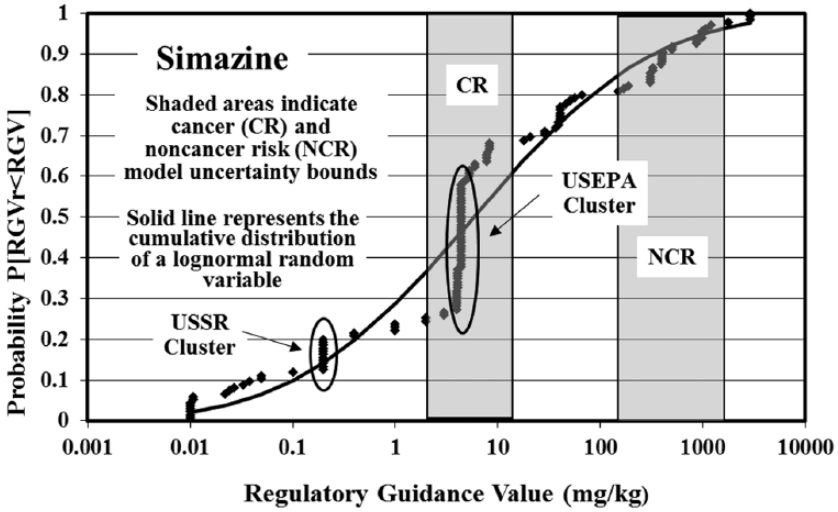

Figure 2. Cumulative distributions of carbofuran and carbaryl RGVs compared with the cumulative distributions of lognormal random variables. RGV indicates regulatory guidance value; USEPA, US Environmental Protection Agency; USSR, Union of Soviet Socialist Republics; THQ, target hazard quotient.

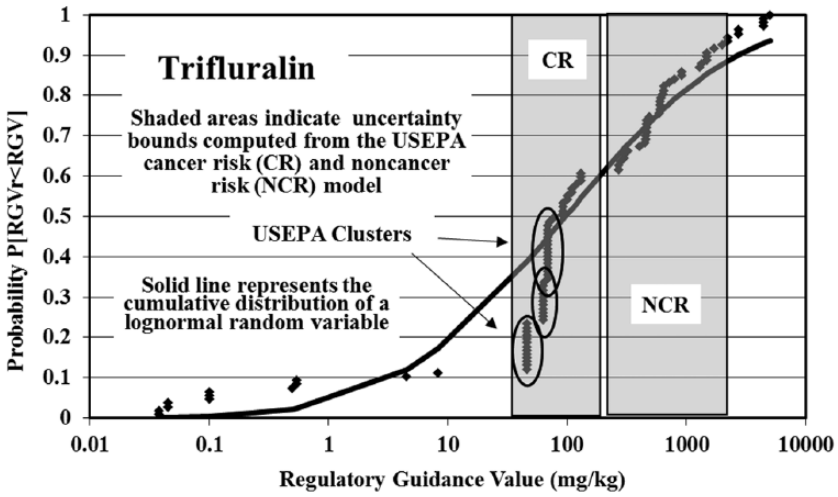

Figure 3. Cumulative distributions of chlorpyrifos and glyphosate RGVs compared with the cumulative distributions of lognormal random variables. RGV indicates regulatory guidance value; USEPA, US Environmental Protection Agency; USSR, Union of Soviet Socialist Republics; THQ, target hazard quotient.

Table 3. Summary of RGV statistics for atrazine, simazine, and trifluralin.

STATISTIC	CURRENT-USE PESTICIDES		
	ATRAZINE	SIMAZINE	TRIFLURALIN
N	193	135	107
N_{US}, % total	111 (57.5)	96 (71.1)	94 (87.9)
N_w, % total	82 (42.4)	39 (28.9)	13 (12.1)
Minimum, mg/kg	0.00005	0.01	0.038
Maximum, mg/kg	20500	2930	5000
Log orders of variation	8.6	5.5	5.1
Mean, mg/kg	737	176.9	529.4
Standard deviation, mg/kg	2840	502.2	984.7
Log mean	0.741	0.768	1.985
Log standard deviation	1.758	1.370	1.132
Geometric mean, mg/kg	5.51	5.86	96.6
Median, mg/kg	2.8	4.4	90
N_{US} (% US RGV) > median	58 (52.2)	58 (60.4)	49 (52.1)
N_w (% worldwide RGV) > median	38 (46.3)	9 (23.1)	4 (30.8)
Correlation with lognormal random variable model	0.981	0.968	0.953

Abbreviation: RGV, regulatory guidance value.

value (0.01 mg/kg) is specified by Croatia, Montenegro, Bosnia and Herzegovina, Slovenia, and the Ukraine. The simazine CR model uncertainty bounds of 2.3 to 14.0 mg/kg contain 58 (43.0%) of the RGVs. The NCR model uncertainty bounds of 150 to 1600 mg/kg contain 23 (17.0%) of the RGVs.

Trifluralin

The 107 trifluralin RGVs identified are illustrated in Figure 3. The percentage of RGVs from US-related jurisdiction (87.9%) is the highest of the pesticides considered here. The values are dispersed over 5.1 orders of magnitude. The correlation between the empirical distribution and that of a lognormal random variable is 0.953, the lowest of the 3 carcinogenic pesticides considered. This appears to result from extreme values at the low end of the distribution.

There are 3 value clusters in the distribution. The cluster of 15 values at 69.0 to 69.2 mg/kg (14.0% of N) corresponds to values computed from the USEPA CR model. The cluster of 13 values at 46 mg/kg (12.1% of N) corresponds to values computed from the USEPA NCR model using a THQ of 0.1. This value is lower than the results of the CR model. There is also a cluster of 11 values (10.3% of N) at 63 mg/kg specified by Texas, Hawaii, Nebraska, Nevada, North Carolina, Vermont, the Commonwealth of the Northern Mariana Islands, Guam, The Hoopa Valley Tribe, Malaysia, and New Zealand. The origin of the 63 mg/kg value is uncertain, but prior to harmonizing standards in 2008, the USEPA had 4 sets of values promulgated by USEPA Regions III, VI, IX, and its Superfund program. The Region IX RGV for trifluralin was 63 mg/kg.

The highest value (5000 mg/kg) is specified by ATSDR. The lowest values (0.045 and 0.038 mg/kg) are specified by Canada's Manitoba and Alberta provinces for coarse and fine-grained soil. The trifluralin CR model uncertainty bounds of 26 to 220 mg/kg contain 53 (49.5% of N) of the RGVs. The trifluralin NCR model THQ = 1.0 uncertainty bounds of 230 to 2400 mg/kg contain 36 (33.6% of N) of the RGVs.

Summary and Conclusions

The pesticides considered here are among the most commonly used in the world. The guidance values used to control their human health risks are important now and will remain important for many years even if use shifts to other formulations. The classification of these pesticides as carcinogens is not universal (USEPA documents are not consistent on their classification), but the current USEPA RGVs for atrazine, simazine, and trifluralin are based on their CRs. These pesticides have been banned by the EU and many other nations. One has to wonder about the wisdom of their continued use.

The RGVs for atrazine, simazine, and trifluralin vary by 8.6, 5.5, and 5.1 orders of magnitude. Atrazine is the most

commonly regulated of the 3, and its RGVs have the largest value span. Its RGVs are well dispersed across the value span, and the correlation between the empirical distribution and that of a lognormal random variable is strong. This high degree of randomness reflects the degree of uncertainty about the safety of continued atrazine use. The value distributions for simazine and trifluralin are not only more compact but also fit the lognormal random variable model. This is typical of the RGVs for most pollutants and indicate how little universal agreement there is on appropriate values. However, there are RGV "consensus" clusters within each distribution, and many values fall within credible risk model uncertainty bounds. The values falling within CR uncertainty bounds account for approximately 36.3%, 43.0%, and 49.5% of the atrazine, simazine, and trifluralin RGVs, respectively.

The atrazine RGV results are most troubling. Although 80 values fall within CR model uncertainty bounds, 123 do not. There are 75 values that exceed the risk model upper uncertainty bound, and 48 that fall below its lower bound. Most of the values that exceed the upper bound come from the United States, although there are also values from Australia, Tanzania, the East Africa Community, Canada, Thailand, and the Netherlands. The 21 values at the top of the distribution (RGVs > 1000 mg/kg) are exclusively from the United States and all appear to be based on NCRs. Of the values that are below the CR model uncertainty bounds (RGV < 1.2 mg/kg), most (39) are from jurisdictions not affiliated with the United States (Finland, Romania, the Netherlands, New Zealand, Moldova, Armenia, Belarus, Russia, USSR, Lithuania, Vietnam, Poland, Panama, Canada, Croatia, Georgia, Italy, Montenegro, Bosnia and Herzegovina, Slovenia, Ukraine, Ecuador, Latvia, and Singapore). It appears that the United States and Australia accept more atrazine health risk than the rest of the world.

Elements of the simazine RGVs distribution are similar to that of atrazine. Of the 43 RGVs that exceed the upper bound of the CR model uncertainty bounds, 38 are from US-related jurisdictions, although there are also values from Canada and the Netherlands. Of the 27 values that exceed 100 mg/kg, all are from US-related jurisdictions, and all appear to be based on NCRs.

The distribution for trifluralin is unusual for several reasons. The results for the USEPA CR and NCR models are close enough (69 and 460 mg/kg, respectively) that if THQ = 0.1 is used, the NCR calculation yields the lowest value (46 mg/kg). It is also unusual that so few values (12) fall below the lower bound of the CR model, and that these are about evenly split between jurisdictions that are and are not affiliated with the United States. The 5 US-related values come from West Virginia, Missouri, the Commonwealth of the Northern Mariana Islands, Guam, and Minnesota. The 7 other values come from Armenia, Belarus, the Ukraine, and Canadian provinces. There are 42 RGVs that exceed the upper bound of CR model calculations. Of these, 1 comes from Canadian British Columbia. The remainder RGVs are from US-related jurisdictions. Most of these values appear to be based on NCR considerations, although Texas, Ohio, and Arizona indicate that their values are based on cancer considerations.

No attempt has been made to identify the "correct" RGVs for these pesticides, and no attempt has been made to explain the origin of values other than those that fall in the vicinity of USEPA risk model results. There are reasons for not attempting to explain the other values. These 3 pesticides yielded 436 RGVs from more than 100 independent jurisdictions. Although some of these jurisdictions document how they arrive at their values, many do not. Furthermore, the explanations for the fraction of jurisdictions that do provide documentation would overwhelm manuscript text limits. In addition, to explain might seem to imply justification, and the authors do not seek to justify any specific RGVs. Rather, the authors would observe that the ranges of RGVs applied to many soil pollutants imply issues of environmental justice on both the high and low sides of the distributions and imply that we have yet to mastered techniques for making risk determinations that are adequately protective of human health.

Although the authors do not seek to explain individual RGVs, we would note that there are considerations that are probably not responsible for the value spans. Some have speculated that differences in soil types or pH, or in hydrologic or meteorological conditions, may be responsible for RGV variability. On the log scales considered here, these factors have little impact. For example, the Missouri Department of Natural Resources promulgates RGVs for sandy, silty, and clayey soils, but for the pesticides considered here, uses the same RGV for each of these soil types. Australian national and regional jurisdictions provide RGVs for 2 classes of residential sites, the atrazine RGVs applied only vary by a factor of 1.5. Similarly, the Alberta Environment and Sustainable Development provides RGVs for coarse and fine-grained soils, but the atrazine RGVs applied only vary be a factor of 1.1 (see Supplemental Data for values and references). The RGVs considered are generic values applied at national or regional scales. They are formulated for widely applicable conditions. Making adjustments for factors such as soil pH, soil type, and climate conditions is best done for site-specific RGV analysis. Furthermore, in the few cases where values are provided for variable conditions or soil types, they vary by less than an order of magnitude. Relative to most RGV set spans, this is not significant.

It has also been suggested that value spans are wide because the physiology of processes such as human gastrointestinal uptake are complex, so the uncertainties involved make it difficult to predict safe exposure levels. It is true that this uncertainty exists, but it is not clear how it affects RGV development because most models do not contain this level of detail. If a mechanistic description of the process is not in the model, it cannot affect the model outcome.

It is also true that the levels of acceptable risk vary among regulatory jurisdictions. Some jurisdictions use lower THQ values to account for exposure to multiple pollutants. Some jurisdictions use higher levels of acceptable CR such as 1×10^{-5} or (very rarely) 1×10^{-4}. However, at most, this should account for 1 or 2 orders of magnitude of RGV variability.

Although there does not appear to be a reasonable explanation for RGVs that vary by 6 or more orders of magnitude, several methods have been suggested to reduce this variability. These include fixing obvious errors, harmonizing value sets, establishing ceiling values, standardizing risk models, standardizing exposure scenarios, standardizing toxicity coefficients, and seeking more aggressive leadership from key organizations. These suggestions have yielded limited success. The USEPA did harmonize what was formerly 4 sets of RGVs in 1 set. Canada has sought to harmonize its provincial standards, and the EU has at least examined this possibility. Unfortunately, evidence indicates that there is still a great deal of variability in the values used worldwide to manage the human health risks of contaminated soil.

It is the responsibility of regulatory jurisdictions to determine the RGVs that will be applied under their authority. One of the reasons RGVs vary so widely appears to be that jurisdictions often determine these values in the absence of information about how the problem has already been assessed in other jurisdictions. This was emphasized when the Qatar Ministry of the Environment first published its soil standards online. The announcement stated that "Since there are no standards for soil quality in the environmental protection law of Qatar, or the US environmental protection agency . . ."[80] Given this perceived lack of USEPA standards, Qatar adopted the 2007 Canadian Soil Quality Guidelines. This was a serious oversight. The USEPA has the largest and best documented soil contamination standards in the world. Qatar officials simply did not have sufficient information to make their determination.

It is the authors' hope that publications such as this will help fill the information gap that contributes to the variability of soil contamination RGVs. Hopefully, if regulatory jurisdictions or the regulated community discovers that their RGVs are at value distribution extremes, it will motivate them to pursue a more rational approach for controlling the risks of soil contamination.

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Author Contributions

Analysed the data: AAJ, ZL. Wrote the first draft of the manuscript: AAJ. Contributed to the writing of the manuscript: ZL. Agree with manuscript results and conclusions: AAJ, ZL. Jointly developed the structure and arguments for the paper: AAJ, ZL. Made critical revisions and approved final version: AAJ. All authors reviewed and approved of the final manuscript.

REFERENCES

1. Li Z. *Analysis of Worldwide Pesticide Regulatory Models and Standards for Controlling Human Health Risk* [dissertation]. Cleveland, OH: Department of Civil Engineering, Case Western Reserve University; 2016.
2. Jennings AA. Statistical analysis of surface soil BTEX regulatory guidance values. *J Environ Eng*. 2009;135:723–736.
3. Jennings AA. Analysis of worldwide naphthalene surface soil regulatory guidance values. *Soil Sediment Contam*. 2012;21:451–497.
4. Jennings AA. Analysis of regulatory guidance values for residential surface soil arsenic exposure. *J Environ Eng*. 2010;136:861–877.
5. Jennings AA. Analysis of worldwide regulatory guidance values for the most commonly regulated elemental surface soil contamination. *J Environ Manage*. 2013;118:72–95.
6. Jennings AA. Analysis of worldwide regulatory guidance values for less frequently regulated elemental surface soil contaminants. *J Environ Manage*. 2013;128:561–585.
7. Jennings AA. Worldwide regulatory guidance values for surface soil exposure to noncarcinogenic polycyclic aromatic hydrocarbons. *J Environ Manage*. 2012;101:173–190.
8. Jennings AA. Worldwide regulatory guidance values for surface soil exposure to carcinogenic polycyclic aromatic hydrocarbons. *J Environ Manage*. 2012;110:82–102.
9. Jennings AA. Worldwide residential soil regulatory guidance values for chlorinated methanes. *J Environ Eng*. 2011;137:416–432.
10. Jennings AA. Worldwide residential soil regulatory guidance values for chlorinated ethanes. *J Environ Eng*. 2011;137:859–879.
11. Jennings AA. Worldwide residential soil regulatory guidance values for chlorinated ethenes. *J Environ Eng*. 2011;137:651–668.
12. Kowalsky ES, Jennings AA. Worldwide regulatory guidance values for chlorinated benzene surface soil contamination. *J Environ Eng*. 2012;138:1085–1105.
13. Hummel MA, Jennings AA. Analysis of regulatory guidance values for six commonly regulated chlorophenols. *Int J Environ Eng*. 2015;7:236–274.
14. California Department of Water Resources. Compilation of Sediment and soil standards criteria and guidelines. http://www.water.ca.gov/pubs/waterquality/municipal_wq_investigations/mwqi_technical_documents/compilation_of_soil_and_sediment_standards_criteria_and_guidelines/compilation_of_soil_and_sediment_standards_criteria_and_guidelines._february_1995.pdf. Published 1995. Accessed December 2, 2015.
15. Proctor DM, Shay EC, Scott PK. Health-based soil action levels for trivalent and 700 hexavalent chromium: a comparison with state and federal standards. *J Soil Contam*. 1997;6(6):595–648.
16. Schäfer KW. *International Experience and Expertise in Registration Investigation, Assessment, and Clean-up of Contaminated Military Sites* (R&D Project 103 40 102/01) Berlin, Germany: Dames & Moore GmbH & Co. KG; 1997. http://www.umweltbundesamt.de/boden-und-altlasten/altlast/web1/berichte/mooreeng/dmeng01.htm. Accessed October 19, 2011.
17. Bartsch C, Dorfman B. Brownfields, VCPs and housing: state-of-the-art information and data. http://nemw.org/NAHBresults.pdf. Published 2000. Accessed January 2, 2008.
18. Bartsch C, Dorfman B. Brownfields, VCPs and housing: how are state VCPs encouraging residential development? http://nemw.org/NAHBresults.pdf. Published 2000. Accessed January 2, 2008.
19. Davis A, Sherwin D, Ditmars R, Hoenke KA. An analysis of soil arsenic records of decision. *Envron Sci Technol*. 2001;35:2401–2406.
20. Science Applications International Corporation. *Compilation and Review of Canadian Remediation Guidelines, Standards and Regulations* (SAIC project number B187-413). http://www.ec.gc.ca/etad.csmwg/pub/comp_rev/en/tablea21_e.htm. Published 2002. Accessed December 20, 2004.
21. Association of Environmental Health and Science. *AEHS Foundation 2003 Survey of States' Soil and Groundwater Cleanup Standards*. http://www.aehsfoundation.org/State-Surveys.aspx. Published 2003. Accessed October 19, 2011.
22. Interstate Technology Regulatory Council. *Examination of Risk-Based Screening Values and Approaches of Selected States*. http://www.itrcweb.org/Documents/RISK-1.pdf. Published 2005. Accessed October 19, 2011.
23. Cavanaga JE. Comparison of soil guideline values used in New Zealand and their derivations. http://ecan.govt.nz/publications/Reports/ComparisonofSoilGuidelineValuesinNewZealand.pdf. Published 2006. Accessed December 2, 2015.

24. Provoost J, Cornelis C, Swartjes F. Comparison of soil clean-up standards fortrace elements between countries: why do they differ? *J Soils Sediment*. 2006;6:173–181.
25. Paustenbach DJ, Fehling K, Scott P, Harris M, Kerger BD. Identifying soil cleanup criteria for dioxins in urban residential soils: how have 20 years of research and risk assessment experience affected the analysis? *J Toxicol Env Health Part B*. 2006;9:87–145.
26. Canadian Contaminated Sites Management Working Group. Compilation and Review of Canadian Remediation Guidelines, Standards and Regulations. http://www.ec.gc.ca/etad/csmwg/pub_rev/en/chap3_e.htm. Published 2007. Accessed December 19, 2007.
27. Carlon C, ed. Derivation methods of soil screening values in Europe. A review and evaluation of national procedures towards harmonization. *EUR 22805, European Commission, Joint Research Centre, Ispra* 2007. http://eusoils.jrc.ec.europa.eu/ESDB_Archive/eusoils_docs/other/EUR22805.pdf. Accessed October 19, 2011.
28. Erdal S, Carollo AN. Assessment of health protectiveness of the risk-based soil remediation standards of the Midwestern states. *Hum Ecol Risk Assess*. 2007;13:543–573.
29. US Environmental Protection Agency (USEPA). Review of state soil cleanup levels for dioxin. https://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=494084. Published 2009. Accessed September 22, 2016.
30. Teaf CM, Covert DJ, Teaf PA, Page E, Starks MJ. Arsenic cleanup criteria for soil in the US and abroad: comparing guidelines and understanding inconsistencies. In: Proceedings of the Annual International Conference on Soils, Sediments, Water, and Energy. Vol. 15, Art. 10; 2010. http://scholarworks.umass.edu/cgi/viewcontent.cgi?article=1146&;context=soilsproceedings. Accessed September 22, 2016.
31. Quinn A, Frasier L. Comparison of international risk-based screening levels. In: Proceedings of the Annual International Conference on Soils, Sediments, Water, and Energy. Vol. 15, Art. 10; 2010. http://scholarworks.umass.edu/cgi/viewcontent.cgi?article=1133&context=soilsproceedings. Accessed September 22, 2016.
32. Blauvelt PR, Sweet M. Interstate comparison of soil remediation standards among six Mid-Atlantic States, USA. *J Environ Prot*. 2014;5:811–818.
33. Jennings AA, Li Z. Scope of the worldwide effort to regulate pesticide contamination in surface soils. *J Environ Manage*. 2014;146:420–443.
34. National Library of Medicine, Hazardous Substances Data Bank (NLM/HSDB). HSDB a toxnet database. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB. Published 2015. Accessed July 1, 2015.
35. US Environmental Protection Agency Integrated Risk Information System (USEPA/IRIS). Integrated Risk Information System. http://www.epa.gov/iris/. Published 2015. Accessed March 19, 2015.
36. Agency for Toxic Substances and Disease Registry (ATSDR). Toxic substances portal. http://www.atsdr.cdc.gov/toxprofiles/Index.asp. Published 2015. Accessed July 2, 2015.
37. About ACGIH, American Conference of Industrial Hygienists 2016. http://www.acgih.org/about-us/about-acgih. Accessed September 22, 2016.
38. International Agency for Research on Cancer (IARC). Agents classified by the IARC Monographs, Volumes 1-111. http://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf. Published 2015. Accessed March 19, 2015.
39. International Labour Organization (ILO). International chemical safety cards (ICSC) database. http://www.ilo.org/dyn/icsc/showcard.listCards2. Published 2011. Accessed March 19, 2015.
40. Safe Work Australia (SWA). Hazardous Substances Information System. http://hsis.safeworkaustralia.gov.au/. Published 2015. Accessed March 19, 2015.
41. US Environmental Protection Agency Integrated Risk Information System (USEPA/IRIS). Integrated risk information system. https://www.epa.gov/iris. Published 2016. Accessed September 22, 2016.
42. Environment Agency (EA). Discharges of concentrated red list substances. https://data.gov.uk/dataset/discharges-of-consented-red-list-substances. Published 2012. Accessed February 24, 2014.
43. European Commission. Priority substances and certain other pollutants according to Annex II of Directive 2008/105/EC. http://ec.europa.eu/environment/water/water-framework/priority_substances.htm. Published 2015. Accessed March 19, 2015.
44. Turkey Ministry of Environment and Urban Planning. Inventory and control of chemicals prepared under regulation. http://www.csb.gov.tr/dosyalar/images/file/1_onceliklist20120710.pdf. Published 2012. Accessed July 2, 2015.
45. Agency for Toxic Substances and Disease Registry (ATSDR). Substance priority list (SPL) resource page. http://www.atsdr.cdc.gov/SPL/resources/. Published 2013. Accessed February 21, 2014.
46. US Environmental Protection Agency Superfund Information System (USEPA/SIS). Superfund Information System. http://cumulis.epa.gov/supercpad/cursites/srchsites.cfm. Published 2015. Accessed March 19, 2015.
47. US Environmental Protection Agency (USEPA). Atrazine background. http://www.epa.gov/pesticides/factsheets/atrazine_background.htm. Published 2012. Accessed July 2, 2015.
48. Sass JB, Colangelo A. European Union bans Atrazine, while the United States negotiates continued use. *Int J Occup Env Heal*. 2006;12:260–267.
49. Australian Pesticides and Veterinary Medicine Authority. Chemicals in the news: Atrazine. http://www.apvma.gov.au/news_media/chemicals/atrazine.php. Published 2011. Accessed March 5, 2014.
50. PAN North America. Atrazine. http://www.panna.org/resources/specific-pesticides/atrazine. Published 2015. Accessed July 2, 2015.
51. Agency for Toxic Substances and Disease Registry (ATSDR). Atrazine CAS # 1912-24-9. http://www.atsdr.cdc.gov/toxfaqs/tfacts153.pdf. Published 2013. Accessed July 2, 2015.
52. US Environmental Protection Agency (USEPA). Decision documents for Atrazine. https://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/red_PC-080803_1-Apr-06.pdf. Published 2006. Accessed September 22, 2016.
53. Syngenta. Atrazine. http://atrazine.com/Atramain.aspx. Published 2014. Accessed March 5, 2014.
54. US Environmental Protection Agency (USEPA). Pesticide industry sales and usage, 2006 and 2007 marked estimates. http://www.epa.gov/opp00001/pestsales/07pestsales/market_estimates2007.pdf. Published 2011. Accessed March 17, 2015.
55. Manktelow D, Stevens P, Walker J, et al. Trends in pesticide use in New Zealand. *Report to the Ministry for the Environment* 2005. http://www.dioxinnz.com/Spray-NZ-Hist/PDF/nz-pesticide-trends.pdf. Accessed September 23, 2016.
56. Health Canada. Pest control product sales report for 2011. http://publications.gc.ca/collections/collection_2014/sc-hc/H111-3-2011-eng.pdf. Published 2011. Accessed March 17, 2015.
57. Brazilian Institute of Environment and Renewable Natural Resources. Pesticides and related products commercialized in Brazil in 2009. http://www.ibama.gov.br/phocadownload/Qualidade_Ambiental/pesticides_commercialized_in_brazil_2009.pdf. Accessed March 17, 2015.
58. Dambrowski MJ, Shadung JM, Wepener V. Prioritizing agricultural pesticides used in South Africa based on their environmental mobility and potential human health effects. *Environ Int*. 2014;62:31–40.
59. Australian Department of the Environment. Indicator: IW-16 Total pesticide use. http://www.environment.gov.au/node/22191. Published 2006. Accessed March 18, 2015.
60. Lin F. China pesticide exports stable in H1 2014. *Agrochemical News*. October 16, 2014. https://agrochem.chemlinked.com/news/news/china-pesticide-exports-stable-h1-2014. Accessed March 18, 2015.
61. US Environmental Protection Agency Office of Pesticide Programs (USEPA/OPP). Chemicals evaluated for carcinogenic potential. http://npic.orst.edu/chemicals_evaluated.pdf. Published October 2, 2014. Accessed March 19, 2015.
62. California Office of Environmental Health Assessment. Notice of intent to list: atrazine, Propazine, Simazine and their chlorometabolites DAC, DEA and DIA. Published 2014. http://oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/noilpkg41Triazines.html. Accessed March 23, 2015.
63. US Environmental Protection Agency (USEPA). Regional screening levels (formerly PRGs)—screening levels for chemical contaminants—RSL tables. http://www.epa.gov/region9/superfund/prg/. Last updated June 2015. Accessed July 2, 2015.
64. US Environmental Protection Agency (USEPA). Basic information about Simazine in drinking water. http://water.epa.gov/drink/contaminants/basicinformation/simazine.cfm. Published 2014. Accessed March 26, 2014.
65. PAN International. Atrazine and simazine banned in the EU but "essential uses" remain in the UK. http://www.pan-uk.org/pestnews/Issue/pn62/pn62p19a.htm. Published 2003. Accessed March 26, 2014.
66. US Environmental Protection Agency (USEPA). Registration eligibility decision (RED), Trifluralin. http://www.epa.gov/pesticides/reregistration/REDs/0179.pdf. Published 1996. Accessed March 26, 2015.
67. European Commission. Review report for the active substance trifluralin. http://ec.europa.eu/food/plant/protection/evaluation/existactive/list_trifluralin.pdf. Published 2007. Accessed March 26, 2015.
68. French Agency for Food, Environmental and Occupational Health & Safety. Exposure of the general population to pesticide residues in France [in French]. http://www.observatoire-pesticides.gouv.fr/upload/bibliotheque/17195921839604387061687505284 7/exposition_population_generale_pesticides_2010_vdef.pdf. Published 2010. Accessed March 17, 2015.
69. US Environmental Protection Agency (USEPA). User's Guide. http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/usersguide.htm. Published June 2015. Accessed July 2, 2015.
70. Missouri Department of Natural Resources. Missouri risk-based corrective action, or MRBCA—Appendix B—default target levels and Tier 1 risk-based target levels. https://dnr.mo.gov/env/hwp/mrbca.htm. Accessed December 17, 2014.
71. Latvian Cabinet of Ministers. Cabinet Regulation No. 804. Regulations on soil and soil quality standards [in Latvian]. http://likumi.lv/doc.php?id=120072. Published 2005. Accessed January 13, 2015.

72. Alaska Department of Environmental Conservation. Oil and other hazardous substances pollution control (18 AAC 75). http://dec.alaska.gov/spar/regulations.htm. Published 2014. Accessed December 10, 2014.
73. Texas Commission on Environmental Quality. TRRP protective concentration levels. https://www.tceq.texas.gov/remediation/trrp/trrppcls.html. Published 2014. Accessed December 22, 2014.
74. Oregon Department of Environmental Quality. Risk-based decision making for the remediation of petroleum-contaminated sites. Table of risk-based concentrations. https://www.oregon.gov/deq/tanks/Pages/Risk-Based-Decision-Making.aspx. Accessed December 19, 2014.
75. Oregon Department of Environmental Quality. Risk-based decision making for the remediation of petroleum-contaminated sites. Table of hot spot concentrations. https://www.oregon.gov/deq/tanks/Pages/Risk-Based-Decision-Making.aspx. Accessed December 19, 2014.
76. Hong Kong Environmental Protection Department. Guidance note for contaminated land assessment and remediation. http://www.epd.gov.hk/epd/english/environmentinhk/waste/guide_ref/contaminated_land.html. Published 2014. Accessed May 5, 2016.
77. New Zealand Ministry for the Environment. Proposed national environmental standard for assessing and managing contaminants in soil. http://www.mfe.govt.nz/nescs/proposed-amendments. Published 2010. Accessed March 17, 2016.
78. United Kingdom Environment Agency. Soil guideline values for dioxins furans and dioxin-like PCBs in soil. https://www.researchgate.net/file.PostFileLoader.html?id=5687ddd97dfbf9dd488b4567&assetKey=AS%3A313454265602050%401451744728991. Published 2009. Accessed September 23, 2016.
79. South Africa Minister of Water and Environmental Affairs. National norms and standards for the remediation of contaminated land and soil quality. http://www.arc.agric.za/arciscw/Documents/Soil%20Remediation%20Workshop%20Files/Norms%20and%20Standards%20for%20Remediation%20of%20Contaminated%20Land%20and%20Soil%20Quality.pdf. Published 2014. Accessed January 20, 2014.
80. Qatar Ministry of the Environment. Ministry of Environment implements a program on soil quality in Qatar for three years. http://www.moe.gov.qa/English/News/Local/pages/Ministry-of-Environment-Implements-a-Program-on-Soil-Quality-in-Qatar-for-Three-Years.aspx. Published 2012. Accessed September 6, 2013.