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Schematic Characterization of Human Health Impact of Toxic Chemicals for Sustainable Design and Manufacturing

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Abstract—A schematic method to characterize the human health impact of toxic chemicals is presented. This schematic method uses a streamlined three-tiered hierarchy process which includes intake, toxicity and persistence of a chemical release for its impact characterization. The human health impact of a chemical is represented by its position in a two-dimensional characterization plot, which enables the benchmarking of chemicals to be easily made by comparing the relative positions of the chemicals in the characterization plot. A case study is performed on 12 toxic chemicals commonly used as solvents by the manufacturing industry. The reliability of this schematic method is checked and confirmed by comparing its benchmarked results with that of the conventional Human Toxicity Potential (HTP) method. With an explicit model structure and a visual representation, this schematic method increases the transparency of the human impact assessment and can facilitate decision-making in the material screening and benchmarking of toxic chemicals for implementation of sustainable design and manufacturing strategies.

Index Terms—Human health impact, toxic chemicals, schematic characterization, benchmarking.

I. INTRODUCTION

Wide applications of toxic chemicals in product design and manufacturing have caused grave concerns due to their toxic effects and potential impact on human health. For monitoring and controlling the industrial releases of toxic chemicals, the U.S. EPA has established the Toxic Release Inventory (TRI) program to collect the facility level of toxic chemical releases information from manufacturing and seven related industrial sectors [1]. Based on the TRI data, about 2 billion pounds of toxic chemicals were released from the manufacturing industry in the United States in 2001 alone [1]. For such an enormous release, approximately 47% were air emissions; 12% were surface water discharges; 9% were injected underground, and 32% were solid land wastes [1]. Besides the United States, such inventory programs have also been established in many other countries including European Union nations, Australia, Canada, Japan, Korea, etc. [2-3].

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The potential human health impact of a toxic chemical release needs to be properly assessed to provide decision support for industry to benchmark and screen such chemical materials to achieve sustainable design and manufacturing. Human health impact assessment of a toxic chemical release is a complicated issue as it needs to quantify the amount of emissions, track the fate and transport of the chemical in the environment, and evaluate the final risk of the chemical on the exposed population in the model environment.

Human toxicity potential (HTP), proposed by Guinée and Heijungs [4] and later extended by Hertwich et al [5], is the metric currently used for human health impact assessment of toxic chemicals. HTP is a computed weighting index which reflects the potential harm of a released chemical on exposed human beings in the model environment [5]. The HTP values of toxic chemicals are generally calculated by using multimedia environmental fate, exposure and risk analysis models based on the inherent toxicity and final dose delivered from the toxic release to an individual in the model environment [5][6].

However, HTP is limited in practical use due to its complex structure and the lack of transparency [7]. In current HTP calculations, dozens of exposure pathways are employed for tracking the chemicals' release pattern, degradation, partitioning, transport and transformations under specific environmental and demographic conditions, which requires a wide range of data inputs on both the chemical's material properties and the environmental conditions, including physical-chemical properties, partition coefficients, landscape parameters, media-specific degradation rates, etc., which creates difficulties in applying the methodology to a wide variety of chemicals due to data scarcity and model complexity. Currently, HTP values are only calculated for 330 toxic chemicals for the U.S. region [5], while there are approximately 100,000 chemicals in commercial use in the United States [8].

In order to facilitate decision-making in material screenings and benchmarking of toxic chemicals for sustainable design and manufacturing, streamlined and transparent tools are greatly needed, particularly for organizing the impact assessment information into an explicit structure to improve the transparency of the impact process and to discern the impact mechanisms of toxic chemicals on human beings for identifying improving opportunities [9].

In this paper, we present a schematic method to characterize and benchmark the human health impact of toxic chemicals by following the general risk-based analysis principles as described in [10]. This schematic method successfully transfers

the complicated impact assessment process into an explicit visual representation, which provides decision-makers with a system thinking of the human health impact mechanism and can increase their understanding of the human health impact processes. In particular, this schematic method offers a way for promoting trust and consensus among group decision-makers by sketching out the key process parameters of human health impact and accordingly can improve the material selection efficiency of toxic chemicals for sustainable design and manufacturing.

II. METHOD

In current practice, the human health impact of a toxic chemical release is assessed based on risk assessment principles by using a five-tiered hierarchy process: mass, toxicity, persistence, concentration and intake [11-14]. In the five-tiered hierarchy, the mass of chemical emissions is directly correlated to its concentration in the environmental media, which in turn dictates its potential exposure and intake among a population under specific meteorological and geological conditions. In this point, mass and concentration of a chemical release can be regarded as two embedded factors in the intake determination. As a result, the impact assessment framework of toxic chemicals can be reduced to a three-tiered hierarchy which includes intake, toxicity and persistence.

Toxicity is an inherent material property of a chemical substance. Chemical materials are very different from each other and the differences between toxicities of chemicals can be as large as seven orders of magnitude [15]. Evaluation of toxicity is typically made through material equivalency approach by using threshold values obtained from dose-response modeling in public health studies. Typically used toxicity indicators in human health impact assessment include the Threshold Limit Value [15], Permissible Exposure Limit [16], Human Limit Value [17], Acceptable Daily Intake [18], etc.

Persistence of a chemical in the environment is an important indicator in its exposure and risk assessment because the same intake over different time periods has different damaging effects. Persistence of chemicals has been systematically investigated by researchers in the past decade, and various methods have been developed for its calculations [19-24]. Those chemicals which have longer persistence in the environment have a higher long-range transport potential, and accordingly, pose higher risks to the population in the model environment. Persistence of a chemical in the environment is determined by both the material's properties and environmental conditions. Materials' half-life was widely used as an indicator of the persistence in the regulatory context, while recent research results found that overall persistence should be used since it integrates both single media half-lives and phase partitioning of a chemical in various environmental media [25].

Intake of a chemical release is calculated as the product of the chemical's concentrations in the environmental media and an intake factor (for inhalation and ingestion) or an uptake factor (for dermal contact) of the environmental media which the population is exposed to [22].

In this paper, we characterize the human health impact of a toxic chemical by using the three-tiered hierarchy process

which includes intake, toxicity and persistence. The final impact is characterized as a function of the three process parameters. Like current human health impact assessment methods, this schematic method is developed to evaluate the chronic impact of toxic chemicals on human health only.

The overall intake of a released chemical by an exposed population is largely related to the persistence of the chemical material in the environment. However, the potential health impacts induced by the exposure are determined by the periodic intake of an individual, instead of the overall intake of the whole population. In this method, we define an individual daily intake as the intake indicator, which measures the intake of a chemical material by an average person under a 24-hour exposure time period. In the calculations, we employ intake fraction, IF, to obtain the overall intake of a chemical release by the exposed population. Intake fraction is a well defined concept for expressing the source-to-intake relationship of an environmental emission [26]. For steady-state release and exposure conditions, intake fraction can be calculated as the ratio of the rate of intake to the rate of release, both in the same units of mass per time [26]. The intake fraction concept is independent of material species, environmental media and exposure pathways, and accordingly, offers broad potential applicability in exposure assessment and risk characterization of toxic chemicals [26]. As a result, the average individual daily intake of a chemical release can be calculated through:

$$D = \frac{E \times IF \times 10^6}{N \times BW \times T} \quad (1)$$

Where D is the average individual daily intake with units of mg/kg bw/day; E is the released amount of the chemical material, with unit of kg; IF is the intake fraction of the chemical; N is the total number of people exposed to the release; BW is the average body weight of an individual, typically at 70 kg; and T is the overall persistence of the chemical in the environment, which is generally calculated by means of [20]:

$$T = \frac{\sum M_j}{\sum M_j k_j} \quad (2)$$

Where M_j is the mass in environmental compartment j, and k_j is the decay rate of the chemical in compartment j.

In this method, the toxicity of chemical material is assessed by using ADI, a chronic toxicity indicator which stipulates the threshold dose amount of a toxic substance on human beings without an appreciable health risk during a lifetime of exposure. ADI is widely adopted by the Council of Europe, WHO, U.S.FDA, etc., in human risk and exposure analysis. By using the ADI toxicity indicator as a standard weighting factor, various types of chemical materials are assessed on the same toxicity benchmark. In this paper, a dimensionless individual daily risk ratio, R, defined as the ratio of the individual daily intake to the acceptable daily intake of a chemical substance, is used to quantify the health risk posed to an individual by a chemical release during an average 24-hour exposure time period, as shown below:

$$R = \frac{D}{ADI} \quad (3)$$

With the intake and toxicity being combined into a single risk factor, the human health impact of a chemical substance, i,

can be characterized through two independent parameters: the individual daily risk ratio, R_i , and the persistence time, T_i , as expressed below:

$$I_i = f(R_i, T_i) \quad (4)$$

In this method, we use equation (4) as the basic function to assess the human health impact of toxic chemical releases. One of the advantages of Equation (4) is that it can be transformed into a schematic characterization which can effectively facilitate the benchmarking of various chemical materials. The impact characterization concept is as follows: for a toxic chemical release, its potential impact on human health is jointly determined by the individual daily risk ratio R and persistence time T . Schematic demonstration of the impact characterization concept is shown by three chemicals i, j, k , in Figure 1. The potential human health impact of a chemical is represented by its position in the plot. Due to the large differences of the R and T values, both axes of the plot are set in logarithmic scales. As a result, benchmarking of chemicals can be made by comparing the relative positions of the chemical materials in the impact characterization plot. In Figure 1, the impact characterization plot area is divided into eight regions according to the relative significance of the T and R values of the chemicals, so as to facilitate the benchmarking efficiency of the characterized toxic chemicals.

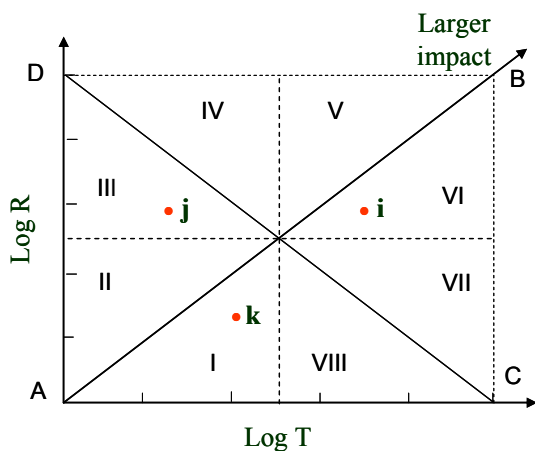


Fig.1 Human health impact characterization concept

The potential human health impact of a chemical material, I_i , is directly proportional to its R_i and T_i values. An increase of R and T values will increase the potential impact of a chemical material on human health, as indicated by line AB in Figure 1. In this schematic characterization method, the basis of the benchmarking principle is that a chemical with a higher risk ratio and a longer persistence time has more potential impact on human health than a chemical with a lower risk and a shorter persistence. Mathematical expression of this characterization principle, as demonstrated on two chemical materials, m, n , is shown as follows: when $R_m \geq R_n$ and $T_m \geq T_n$, then

$$I_m = f(R_m, T_m) \geq I_n = f(R_n, T_n) \quad (5)$$

This characterized relationship indicates that chemicals characterized in regions V and VI in Figure 1 have more potential impact on human health than those in regions I and II .

In the cases where m and n are positioned with a negative slope value, further analysis is needed to assess the tradeoffs between the risk ratio and persistence time. Here we benchmark the two chemicals by comparing the magnitude ratios of the two evaluation factors, as shown in table I below:

Condition		Result
If $R_m > R_n$ and $T_m > T_n$		$I_m > I_n$
If $R_m > R_n$ and $T_m < T_n$	$\frac{R_m}{R_n} > \frac{T_n}{T_m}$	$I_m > I_n$
	$\frac{R_m}{R_n} = \frac{T_n}{T_m}$	$I_m = I_n$
	$\frac{R_m}{R_n} < \frac{T_n}{T_m}$	$I_m < I_n$
If $R_m = R_n$ and $T_m > T_n$		$I_m > I_n$
If $R_m > R_n$ and $T_m = T_n$		$I_m > I_n$

The benchmarking scenarios presented in table I could be transformed to the assessment of the slope value, $S_{m,n}$, between chemical m, n in the impact characterization plot, as shown below:

$$S_{m,n} = \frac{\text{Log}R_n - \text{Log}R_m}{\text{Log}T_n - \text{Log}T_m} \quad (6)$$

If $S_{m,n} > 0$, then $I_m > I_n$, as shown in Figure 2(a); if $S_{m,n} = -1$, then $I_m = I_n$, as shown in Figure 2(b); when $S_{m,n} < -1$, then $I_m > I_n$, as shown in figure 2(c); when $0 > S_{m,n} > -1$, then $I_m < I_n$, as shown in Figure 2(d). For special cases like $S_{m,n}$ valued at zero or infinity, the two chemicals would have either the same R or T values. So the benchmarking can be made by comparing the value of the other factor.

As demonstrated in fig. 2(b), the chemicals positioned in a line with a slope value of -1 have the same impact on human health. Accordingly, in the schematic characterization plot, the magnitude of the human health impact can be geometrically represented by the vector distance from the chemical's position to a line with a slope value of -1, as shown by equation (7). A larger vector distance means a larger human health impact.

$$I_i \propto \frac{\text{Log}(T_i) + \text{Log}(R_i) + m}{\sqrt{2}} \quad (7)$$

Where m is a constant representing the position of the line with a slope of -1.

Regarding applications of the schematic method, it is important to point out here that the final benchmarked results are not influenced by the scales of the R and T coordinates since the relative positions of the chemicals are fixed in the impact characterization plot (as determined by the absolute values of R and T).

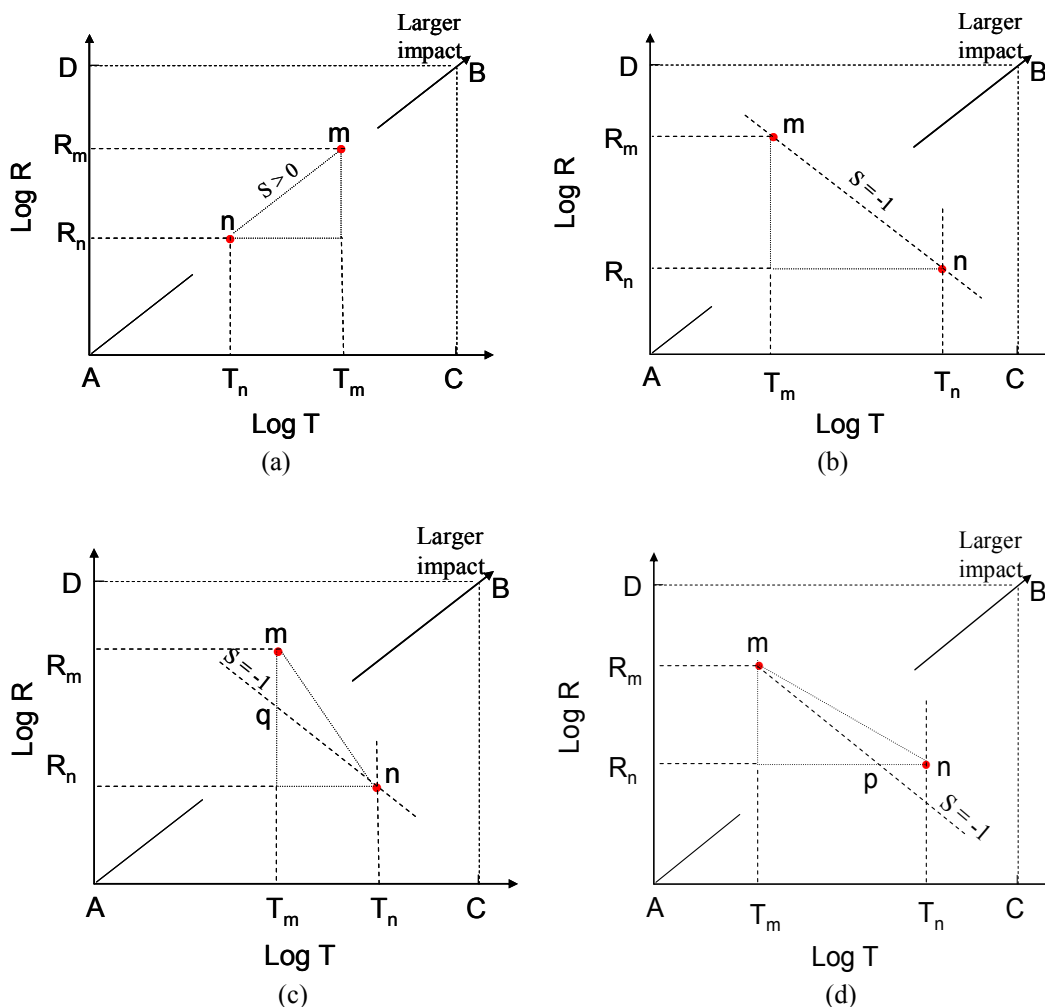


Fig. 2 Schematic benchmarking of human health impact of two chemicals. The potential human health impact of chemical m, n : (a) $I_m > I_n$; (b) $I_m = I_n$; (c) $I_m > I_n$; (d) $I_m < I_n$.

III. RESULTS

In order to illustrate the application of the schematic characterization method, we have studied 12 toxic chemicals which are commonly used as solvents in various manufacturing operations. In the manufacturing industry, solvents are a major source of toxic chemical release [27]. Based on a 1 kg emission to the air in the U.S. region, human health impacts of these 12 chemicals are schematically characterized in Figure 3. In the assessment, intake fraction (IF) values are obtained from [28]. Persistence time of each chemical is calculated through the CalTOX model [18]. Like conventional HTP method, here we also assume the U.S. region a closed system and the whole U.S. population is subject to the exposure of these toxic releases. The U.S. population used is 304.6 million and the average body weight is taken to be 70 kg [5]. The characterization process parameters of these 12 chemicals are shown in table II below.

In Figure 3, three parallel lines with slope values of -1 are drawn as reference lines to facilitate the benchmarking of these 12 toxic chemicals. The magnitude of the chemicals' impact is represented by the vector distance between the chemical's position and a reference line with a slope value of -1. Rankings

of the 12 chemicals in terms of their human health impact are shown by the red numbers in the impact characterization plot.

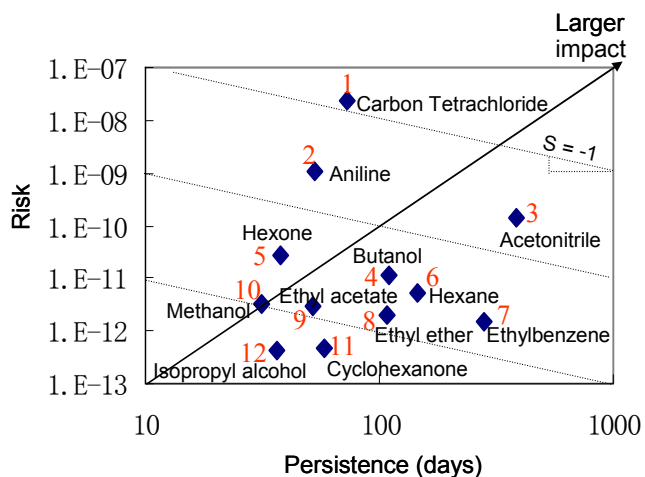


Fig. 3. Schematic characterization of human health impact of 12 chemicals used as solvents in manufacturing industry.

TABLE II
Schematic characterization parameters of 12 chemicals used as solvents in manufacturing industry

Chemical	Individual daily intake (mg/kg/day)	ADI (mg/kg/day)	Individual daily risk (R)	Persistence (T, days)
Carbon tetrachloride	1.63E-11	0.0007	2.33E-08	73.4
Aniline	3.14E-13	0.000286	1.10E-09	53.4
Acetonitrile	2.50E-12	0.0171	1.46E-10	384.5
Butanol	1.11E-12	0.1	1.11E-11	108.9
Hexone	5.95E-13	0.0229	2.60E-11	37.6
Hexane	3.06E-13	0.057	5.37E-12	145.3
Ethylbenzene	4.13E-13	0.286	1.44E-12	279.5
Ethyl ether	4.13E-13	0.2	2.06E-12	107.9
Ethyl acetate	2.56E-12	0.9	2.84E-12	51.9
Methanol	9.22E-12	2.857	3.23E-12	31.5
Cyclohexanone	2.32E-12	5	4.64E-13	58
Isopropyl alcohol	8.65E-13	2	4.33E-13	36.2

As shown in Figure 3, the chemical, Carbon tetrachloride, has the most significant impact on human health among these twelve chemical substances, while Isopropyl alcohol has the least potential impact on human health. From the plot, Aniline and Acetonitrile have a very comparable impact on human health even though their risk ratios and persistence times are completely different. Aniline has an R value 7.5 times that of Acetonitrile while Acetonitrile has a T value 7.2 times that of Aniline. As a result, Aniline has a bit higher impact on human health than Acetonitrile.

IV. RELIABILITY

In order to check the reliability of the schematic characterization method, here we compare the schematically benchmarked results with that of the conventional HTP method on these 12 toxic chemicals [5]. In the HTP assessment, the human health impacts of toxic chemicals are calculated for their carcinogenic and non-carcinogenic effect, separately [5]. In order to benchmark the toxic chemicals on their overall human health impact, we have the cancer and non-cancer effects combined into a single HTP value by weighting cancer risk 10^6 times of non-cancer effect, by following the suggestions in [5].

As for these 12 toxic chemicals used as solvents in manufacturing, carbon tetrachloride and aniline have both cancer and non-cancer effects while the other ten chemicals only have non-cancer effects [5]. Based on the assessment, the benchmarked results of the conventional HTP method and the schematic characterization method are exactly the same on these 12 solvent chemicals, as demonstrated in figure 4.

Beyond these 12 chemicals, we have studied and compared the benchmarked results of the schematic method and the HTP method on 102 toxic chemicals as covered in [5]. The study leads to a very high correlation coefficient $r=0.987$ on the benchmarked results of the 102 chemicals between these two methods, which indicates that this schematic method is reliable for use in characterizing and benchmarking the human health impact of toxic chemicals. Moreover, this schematic method characterizes the human health impact of a toxic chemical

release through a two dimensional visual representation which increases the transparency of the human health impact assessment method and also provides a convenient way to facilitate decision-making in material selection of toxic chemicals for sustainable design and manufacturing.

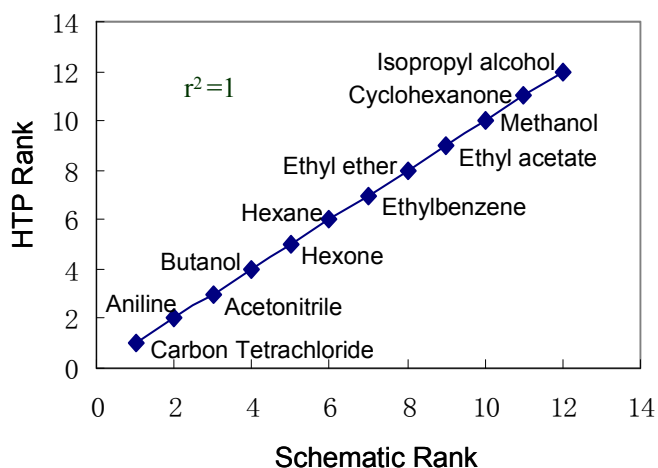


Fig. 4. Correlation of the impact rank of 12 chemicals by HTP and schematic method.

V. CONCLUSIONS

A schematic method is presented in this paper to characterize the human health impact of toxic chemicals. This method uses a reduced three-tiered hierarchy process which uses intake, toxicity and persistence of a chemical release for its impact characterization. This schematic method is straightforward, transparent, and convenient to use. With an explicit model structure and a streamlined characterization process, this schematic method can improve the understanding of the intrinsic factors behind the human health impact of a toxic chemical release, and can be used for rapid benchmarking of various chemical materials by facilitating decision-making in industrial implementation of sustainable design and manufacturing strategies.

A simplified individual daily intake is used in this schematic characterization method which makes the intake of a chemical release independent of its persistence in the environment. It should be noted here that this schematic characterization method uses ADI as the toxicity weighting factor of various toxic chemicals, and accordingly, cannot apply to those chemicals which have zero ADI values. As the toxicity indicator is used in this method only to address the relative differences of various chemicals in their inherent toxicities, other threshold toxicity indicators like Reference Dose (RfD), or benchmarked toxicity indicator like ED10 could also be used in this schematic characterization method, which will be investigated in our future work.

In the assessment of the human health impact, the schematic characterization method does not specifically address the release differences between various environmental media as that is reflected separately in the intake and persistence of the chemical materials. As a result, chemicals released to different environmental media can be benchmarked on the same plot through this schematic method. Like the conventional HTP method, severity of human health damages is not addressed in this schematic method either.

A case study is performed on 12 toxic chemicals commonly used as solvents by the manufacturing industry. The human health impact of these 12 chemicals are benchmarked and ranked through their individual daily risk and environmental persistence values. The results show that the chemical Carbon tetrachloride has the most significant impact on human health among these twelve chemicals, while Isopropyl alcohol has the least potential impact.

Reliability of the schematic characterization method is checked by comparing the benchmarked results of the 12 toxic chemicals with that of the conventional HTP method. Based on the assessment, the benchmarked results of the conventional HTP method and the schematic characterization method are exactly the same for these 12 solvent chemicals. Beyond these 12 chemicals, a larger group of 102 chemicals are characterized and benchmarked through the schematic method. With a correlation coefficient $r=0.987$ obtained on these two methods, the schematic method is confirmed for its reliability on human health impact characterization and benchmarking of toxic chemicals.

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