Available online at www.sciencedirect.com
ScienceDirect
Journal of Hazardous Materials 145 (2007) 296–304
Journal of Hazardous Materials
www.elsevier.com/locate/jhazmat

Quantitative estimation of uncertainty in human risk analysis

G. Sassi [a,*], A. Magnetti Vernai [b], B. Ruggeri [b,a]

[a] Dipartimento di Scienza dei Materiali e Ingegneria Chimica, Politecnico di Torino, Corso Duca degli Abruzzi, 24, 10129 Torino, Italy
[b] Envi-MOD, Environment Park S.p.A., Via Livorno, 60, 10144 Torino, Italy

Received 12 July 2006; received in revised form 10 November 2006; accepted 13 November 2006
Available online 18 November 2006

Abstract

This paper is aimed to candidate the use of an ISO standard procedure (Guide to the Expression of Uncertainty in Measurement, GUM) for quantitative evaluation of uncertainty in Human Risk estimation under chronic exposure to a hazardous chemical compound. Risk was evaluated by using the usual methodologies: the deterministic reasonable maximum exposure (RME) and the statistical Monte Carlo method; in both cases the procedures to evaluate the uncertainty on risk values are detailed.

The paper put in evidence that the procedure is able to single out the variables that contribute mostly to the uncertainty. The obtained results show that the application of GUM procedure is easy and straightforward to estimate the uncertainty value on the results of risk estimation. The procedure is applied to a real case concerning the ingestion of milk contaminated by dioxins in a northern part of Italy; the risk value resulted to be over the minimal threshold of 10^{-6} with 20–80% confidence.

Keywords: Risk assessment; Uncertainty; Variability; Monte Carlo; GUM; Dioxins

1. Introduction

The importance of adequately characterizing uncertainty, in human health and ecological risk assessment has been emphasized in several U.S. EPA documents and activities [1], as well as in the most used guide for risk analysis for contaminated site [2,3] and Italian regulation for risk analysis [4]. Notwithstanding several procedures were proposed [5–9] there is not a standard accepted procedure. It is known that uncertainty about the numerical results of risk estimation, in environmental contest, is generally large (i.e., on the range of at least an order of magnitude or greater) [10]. Consequently, it is not important to reach high precision in quantifying the degree of uncertainty in the risk assessment, but it is very important to identify the key site-related variables and assumptions that contribute most to the uncertainty [10]. Notwithstanding the advancement of techniques able to evaluate risk, the problem of uncertainty estimation in human and ecological risk context is still an open question [11].

This paper shows the application of the procedures reported in the *Guide to the Expression of Uncertainty in Measurement* (GUM) [12] to estimate the uncertainty of health risk and the contribute of each variable to uncertainty. GUM is a standard guide that establishes general rules for evaluating and expressing uncertainty in measurement that are intended to be applicable to a broad spectrum of measurements. It is supported by seven international organizations (BIPM, IEC, IFCC, ISO, IUPAC, IUPAP, OIML; see GUM [12] for extended names) and it is published in their name.

Some confusion exists about terms commonly used to indicate several components of uncertainty; thus a definition of uncertainty is necessary. Following GUM [12] and the international vocabulary of basic and general terms in metrology [13] (VIM), uncertainty is a parameter associated with the results of a measurement, e.g., a risk estimation, that characterizes the dispersion of the values that could reasonably be attributed to the measurand, i.e., the risk. In other words the uncertainty reflects the lack of exact knowledge about the value of the risk [12]. EPA [14] has advised the risk and exposure assessors to distinguish between variability and uncertainty. Following EPA [1]: "Uncertainty represents a lack of knowledge about factors affecting exposure or risk, whereas variability arises from true heterogeneity across people, places or time. In other words, uncertainty can

* Corresponding author. Tel.: +39 0115644625; fax: +39 0112257225.
E-mail address: guido.sassi@polito.it (G. Sassi).

0304-3894/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.jhazmat.2006.11.020

Nomenclature

AT	averaging time
BW	adult male body weight
$c(x)$	sensitivity coefficient of variable X calculated at x
$c^2(x)u^2(x)$	quadratic term of variable X calculated at x
CDF	cumulative density function
$C(K)$	constant distribution
CR	adult milk ingestion rate
C_{ep}	concentration of dioxin in milk
ED	adult exposure duration
EF	exposure frequency
GM	geometric mean
GSD	geometric standard deviation
H	highest value
L	lowest value
LN(M; SD)	lognormal distribution
m	median
mo	mode, i.e., highest frequency value
M	mean
N(M; SD)	normal distribution
PDF	probability density function
R	risk
RME	reasonable maximum exposure
SD	standard deviation
SF	slope factor
TR(H; mo; L)	triangular distribution
TV_o	oral toxicity value (SF for carcinogenic)
$u(x)$	standard uncertainty of variable X calculated at x
$u(x)/x$	relative standard uncertainty of variable X calculated at x
$U(H; L)$	uniform distribution
x	value of variable X
X	variable
$[X]$	units of variable X
X_T	threshold value
z_T	z score of threshold value (values of z score and CDF for normal distribution are tabled)
z_{95}	z score of normal distribution for 95 percentile = 1.645

Greek letters

μ_L	scale parameter of lognormal distribution
μ_N	scale parameter of normal distribution
σ_L	shape parameter of lognormal distribution
σ_N	shape parameter of normal distribution

lead to inaccurate or biased estimates, whereas variability can affect the precision of the estimates and the degree to which they can be generalized."GUM [12] indicates 10 sources of uncertainty where the tenth source deals with variability; the other nine sources deal with the "uncertainty" taken into consideration by EPA definition.

In risk evaluation context the following sources have particular importance: the incomplete definition of risk (i.e., route, target, substances), imperfect realization of the definition (i.e., the model used), the sampling and chemical analysis of contaminated matrixes at the exposure point, the choice of a representative sample of receptors (male, female, children, resident trans-passengers, etc.) and the variation in repeated observations (i.e., variability). In this paper the term uncertainty is used following GUM [12] and VIM [13] and includes variability as a component.

In risk assessment the estimation of uncertainty deals with the estimation of the level of confidence that risk is under a threshold of acceptability. The acceptable level of confidence and the threshold values are still on debate. They depend on regulators and populations involved in such risk estimation procedure; in any case 95% and 10^{-6} are at the moment the main terms of reference in the world, notwithstanding in some specific nation 10^{-5} is used as a threshold [4]. The choice of the appropriate values for level of confidence and threshold is a political decision and it is out of the task of risk evaluators.

This paper concerns the estimation of cancer risk for a population of the northern Italy as a consequence of daily consumption of dioxin contaminated milk. A deterministic approach as well as stochastic ones were followed; the evaluation of uncertainty was performed in each case.

2. Methodology

2.1. Experimental determination of dioxin in milk

The experimental determination concerns the measure of the dioxin concentration in the milk used by the population namely: concentration at the exposition point, without considering any attenuation factor, C_{ep}. Concentration values come from the experimental determination of dioxin in samples of milk of dairy farms located near a steel mill in the northern Italy. Dioxins were measured according to the method suggested by EU directive 2002/69/EC [15] and expressed by toxic equivalent factors defined by WHO [16], as mgTE/kg. Twenty-four samples of milk were collected. They were collected into an area of about 90 km^2 during a period of 4 months. Concentrations used are "upper-bound results" where no-detected congeners were assumed to be present in concentration equal to the detection limit. Values were originally expressed as pgTE per kilogram of milk fat and have been converted to mgTE per kilogram of milk by assuming fat content of 3% by weight. Measured values have been statistically analyzed in order to determinate the characteristic distribution. Test was performed on concentration data using ProUCL Version 3 [17]. C_{ep} distribution resulted to be normal. Type A evaluation of uncertainty [12] was performed. The mean value 8.57×10^{-8} mgTE/kg and the standard deviation 3.92×10^{-8} mgTE/kg represents an estimate respectively of the value of concentration and its standard uncertainty. The relative standard uncertainty is about 46% while the relative uncertainty on single milk sample resulted to be lower than 2%, thus the main source of uncertainty is variability among samples. The distribution for C_{ep} resulted to be $N(8.57 \times 10^{-8}; 3.92 \times 10^{-8})$.

Table 1
Reasonable maximum exposure (RME) values, values and uncertainty

Variable	Units	Reference	RME value	x	$u(x)$
Concentration of dioxin in milk C_{ep}	mgTE/kg	Experimental	1.50×10^{-7}	7.9×10^{-8}	4.6×10^{-8}
Oral toxicity value TV_o, slope factor SF (carcinogens)	kg d/mg	EPA [18], Smith [23], IRIS [24]	SF = 150,000	79,000	46,000
Adult milk ingestion rate CR	kg/d	Turrini et al. [19]	0.332	0.175	0.101
Exposure frequency EF	d/year	EPA [18]	350	184	106
Adult exposure duration ED	year	EPA [18]	30	15.8	9.1
Adult male body weight BW	kg	EPA [18]	70	70	27
Averaging time AT for carcinogenic	d	EPA [18], Smith [23]	25,550	13,400	7800

Table 2
Variability of risk parameters from literature

Parameter	Units	Reference	Distribution
Concentration of dioxin in milk C_{ep}	mgTE/kg	Experimental results	$N(8.57 \times 10^{-8}; 3.92 \times 10^{-8})$
Oral toxicity value TV_o, slope factor SF (carcinogens)	kg d/mg	La Grega et al. [26], Burmaster and von Stackelberg [27]	LN(SF/3.425; SF/2.060)
Adult milk ingestion rate CR	kg/d	Turrini et al. [19]	LN(0.119; 0.120)
Exposure frequency EF	d/year	Smith [23], EPA [20]	TR(180; 345; 365)
Adult exposure duration ED	year	Israeli and Nelson [25], Smith [23], EPA [20]	LN(11.36; 13.72)
Adult male body weight BW	kg	Turrini et al. [19]	$N(75; 10.4)$

2.2. *Values and variability of parameters*

The values of parameters for risk estimation were taken from the specialized literature. Table 1 reports the reasonable maximum exposure (RME) values suggested by EPA [18] for deterministic estimation of risk. Adult milk ingestion rate and dioxins concentrations in milk do not have suggested RME values. The 95th percentile of the distribution of Turrini et al. [19] and the 95th percentile of C_{ep} distribution previously reported were considered as RME value for CR (adult milk ingestion rate) and C_{ep} (dioxins concentration in milk), respectively. The 95th percentile was calculated by equations reported in Table 3.

Table 2 reports the distributions of the parameters proposed in literature. Many distributions are available for body weights [1,19–23] nevertheless median and 95th percentile value of distributions show a spread of about 10% while variability range in 14–25%. Thus, if no specific data about target are available, 10% could be added to variability in order to consider uncertainty coming from the lack of knowledge about the body weight of the target. In this case study the distribution proposed by Turrini et al. [19] is referred to Italy, thus it is specific for the target. Averaging time (AT) is always considered not affected by variability. Figs. 1–6 show the graphical representation of distributions. No information about the way by which distributions were determined is here considered.

3. Risk estimation

In the case study analyzed in this paper the risk evaluation procedure was applied to evaluate the human risk connected to the ingestion of milk produced in farms exposed to an industrial source of dioxins.

Risk equation for a point estimation is assumed to be an expression of all independent variables, namely: the concentration at the exposure point (C_{ep}); toxicological parameter oral toxicity value (TV_o), i.e., slope factor (SF) for carcinogenic as dioxins and reference dose (RfD) for no-carcinogenic; rate of exposure E [2]:

$$R = f(C_{ep}, TV_o, E) \tag{1}$$

An application of the general expression of R (1) is

$$R = C_{ep}\, TV_o \frac{CR\, EF\, ED}{BW\, AT} \tag{2}$$

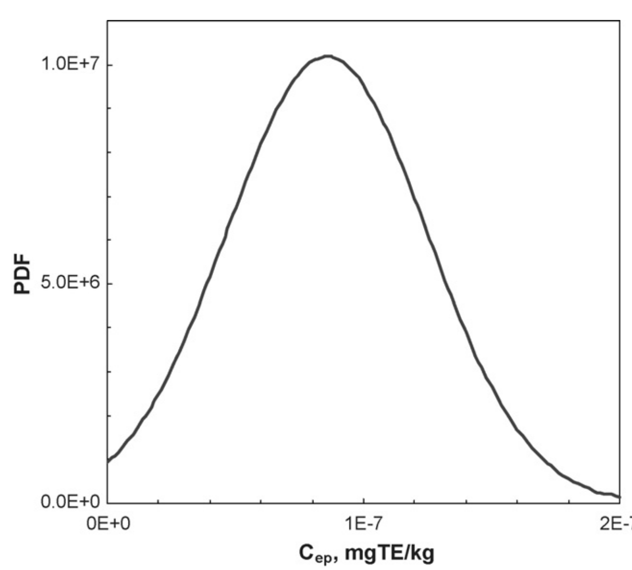

Fig. 1. Dioxins concentration.

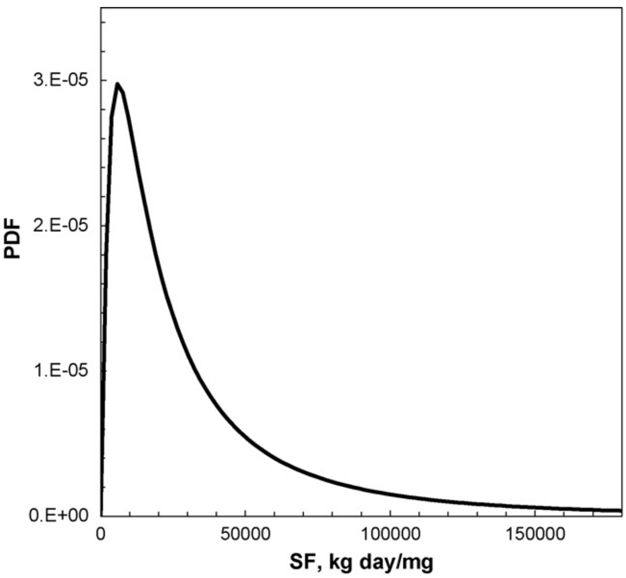

Fig. 2. Oral toxicity value (dioxins).

where CR is the milk ingestion rate (kg/d), EF the exposure frequency (d/year), ED the exposure duration (year), BW the body weight (kg) and AT is the averaging time (year d/year), i.e., the time along which the risk is evaluated. In this study the exposure parameters listed above refer to an adult male receptor.

The risk evaluation in this paper considers the direct ingestion of the milk without any other attenuation factor; thus risk equation is directly or inversely proportional to the variables affecting the risk.

Risk value was calculated by reasonable maximum exposure (RME) deterministic method and Monte Carlo method. The distributions generated by the Monte Carlo simulation were obtained by the commercial program Crystal Ball®, with Monte Carlo sampling technique, performing 100,000 iterations.

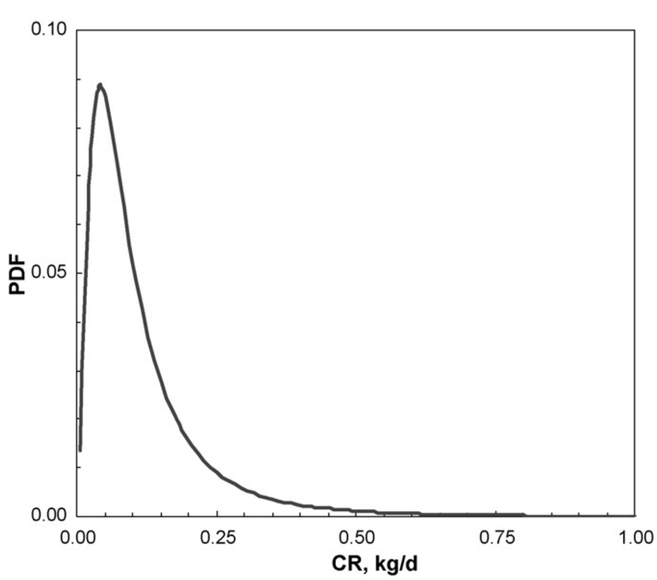

Fig. 3. Adult milk ingestion rate.

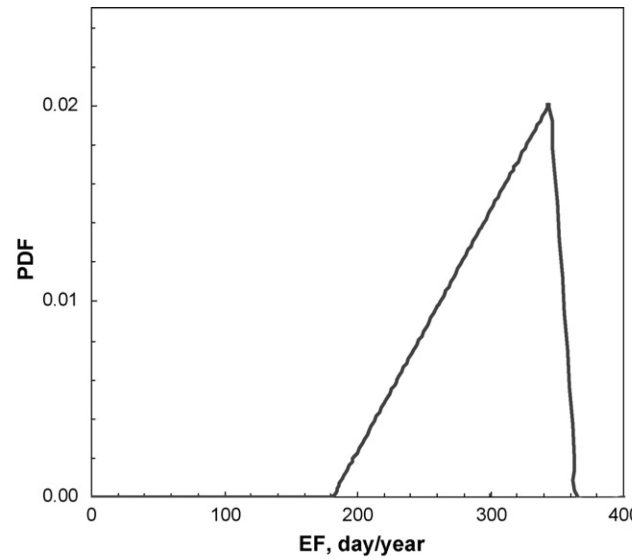

Fig. 4. Exposure frequency.

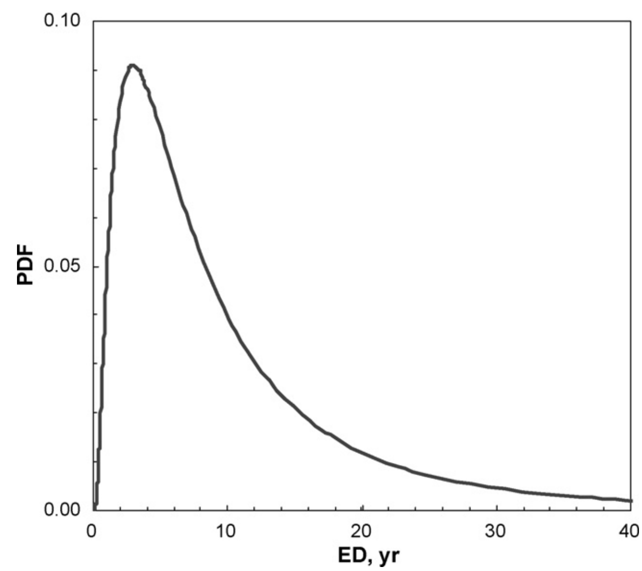

Fig. 5. Exposure duration.

The value of risk calculated by RME deterministic method is $R_{\mathrm{RME}} = 4.39 \times 10^{-5}$. Figs. 7 and 8 report Monte Carlo simulation result, 95th percentile is $R_{95} = 3.33 \times 10^{-6}$.

4. Uncertainty estimation

4.1. GUM procedure

The uncertainty characterizing the value of risk is evaluated by applying the procedure proposed by GUM [12] for combined standard uncertainty for uncorrelated input quantities. More specifically, the standard uncertainty of r, where r is an estimation of the true value of R calculated by Eq. (2) is a combination of the standard uncertainties of the input quantities. In

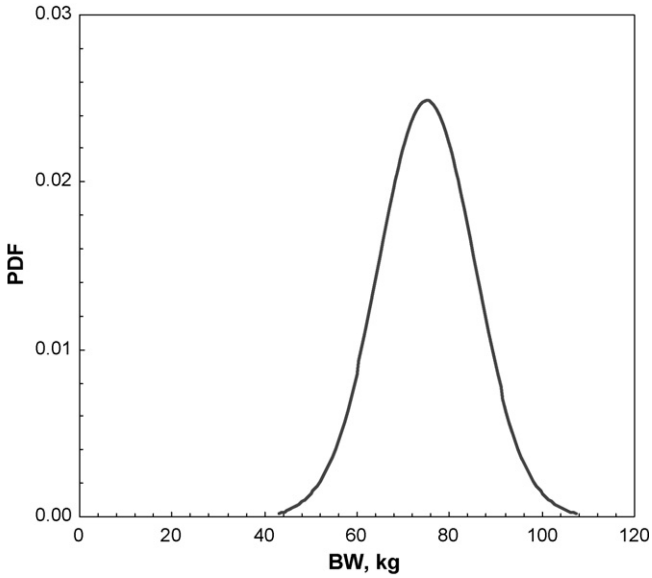

Fig. 6. Adult male body weight.

analytical form from Eq. (2):

$$u_c^2(r) = \sum_{i=1}^{N} \left(\frac{\partial f}{\partial x_i}\right)^2 u^2(x_i) = \sum_{i=1}^{N} c_{x_i}^2 u^2(x_i),$$

$$u_c^2(r) = c_{\mathrm{Cep}}^2 u^2(c_{\mathrm{ep}}) + c_{\mathrm{TV_o}}^2 u^2(\mathrm{tv_o}) + c_{\mathrm{CR}}^2 u^2(\mathrm{cr}) + \cdots + c_{\mathrm{EF}}^2 u^2(\mathrm{ef}) + c_{\mathrm{ED}}^2 u^2(\mathrm{ed}) + c_{\mathrm{BW}}^2 u^2(\mathrm{bw}) + c_{\mathrm{AT}}^2 u^2(\mathrm{at}) \quad (3)$$

where x_i is the ith parameter, $u(x_i)$ the standard uncertainty of the ith input quantities, $(\partial f/\partial x_i)$ the partial derivative by the ith variable, u indicates uncertainties, c indicates the sensitivity coefficients, capital letter indicates variable and small letter indicates value. Eq. (3) is used to estimate the combined uncertainty of risk $u_c(r)$. Sensitivity coefficients are limited to first order Taylor series because of the slight non-linearity of risk expression, i.e., the partial derivatives of Eq. (2) calculated at the point at which risk is evaluated. As an example the partial derivative by BW is reported:

$$c(\mathrm{BW}) = \frac{\partial R}{\partial \mathrm{BW}} = -C_{\mathrm{ep}}\,\mathrm{TV_o}\frac{\mathrm{CR\,EF\,ED}}{\mathrm{BW}^2\,\mathrm{AT}} \quad (4)$$

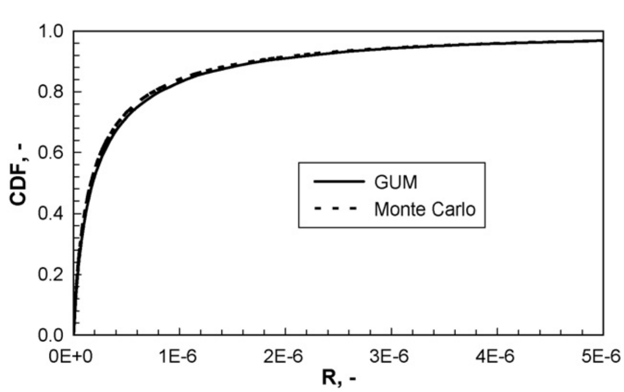

Fig. 7. Monte Carlo and GUM cumulative density functions comparison.

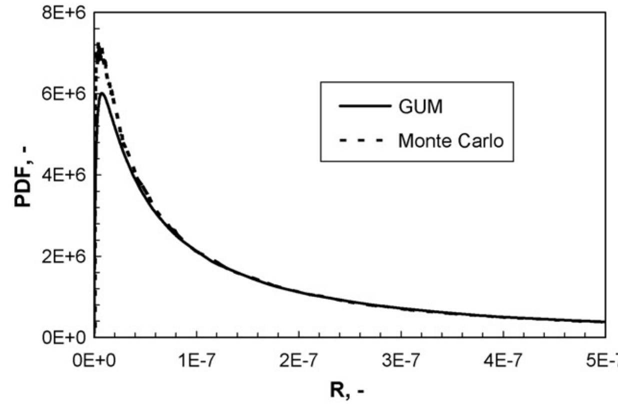

Fig. 8. Monte Carlo and GUM probability density functions comparison.

When non-linearity of the exposure model is significant, higher order terms in the Taylor series expansion must be included in the expression (3) [12].

The GUM procedure permits to create a "budget of uncertainty" which underlines the sources of uncertainty for the risk and gives a classification of the sources, based on their sensitivity coefficients. The budget is a very useful tool to point out how to reduce uncertainty, how to determinate the boundary conditions for the reduction and which are the relevant variables that affect uncertainty.

The budget of uncertainty is a table which summarizes in each row the parameters of a variable. Parameters are: acronym (X), units ([X]), value (x), uncertainty at value x ($u(x)$), relative uncertainty at value x ($u(x)/x$), sensitivity coefficient calculated at values x ($c(x)$), quadratic term ($u^2(x)c^2(x)$), criticism. Last row shows the parameters of the combined quantity, i.e., risk (R).

X and $u(x)$ (excluded last row) are the independent values, all the other values in the table are calculated from them.

Relative uncertainty is calculated as the ratio between standard uncertainty $u(x)$ and the value x for each variable, sensitivity coefficient equations must be analytically determined and are calculated at the values x, quadratic terms are calculated from sensitivity coefficient $c(x)$ and standard uncertainty $u(x)$.

Risk value r is calculated from values x by Eq. (1). The quadratic term of risk is calculated as sum of quadratic terms $u^2(x)c^2(x)$, i.e., Eq. (3). Uncertainty of risk is calculated as the square root of the quadratic term of risk.

Criticism is calculated as the ratio between the quadratic term of the variable and the maximum quadratic term of the summation:

$$\mathrm{criticism} = \frac{c^2(x)u^2(x)}{\max\limits_{i=1,7}(c^2(x_i)u^2(x_i))} \quad (5)$$

Criticism indicates which terms contribute most to the uncertainty, i.e., terms with criticism greater than 0.1. The budget of uncertainty includes and explicates all the calculations used; the needs are a single sheet of a spreadsheet like Excell.

The uncertainty $u(x)$ of each variable, i.e., C_{ep}, $\mathrm{TV_o}$, CR, EF, ED, BW, AT, must be evaluated from all the information available on the estimation of their values x using Type A or Type B evaluation of standard uncertainty [12]. Table 3 reports the equa-

Table 3
Properties of statistical distributions and Type B evaluation of uncertainty

Distribution	Constant	Uniform	Triangular	Normal	Lognormal
Acronym	$C(K)$	$U(H; L)$	TR(H; mo; L)	$N(M; \mathrm{SD})$	LN(M; SD)
Value x	$x=m=K$	$x=M=m=\frac{H+L}{2}$	$x=M=\frac{H+\mathrm{mo}+L}{3}$	$x=M=m=\mu_N$	$x=m=\exp(\mu_L)$
Uncertainty $u(x)$	$u=0$	$u=\frac{H-L}{2\sqrt{3}}$	$u=\frac{H-L}{2\sqrt{6}}$	$u=\sigma_N$	$u=\sigma_L\exp(\mu_L)$
X_{95}	K	$L+0.95(H-L)$	$H-\sqrt{\frac{(H-L)(H-\mathrm{mo})}{20}}$	$M+z_{95}\,\mathrm{SD}$	$\exp(\mu_L+z_{95}\sigma_L)$
Confidence of a threshold X_T	0 if $X_T<K$; 1 if $X_T>K$	$\frac{X_T-L}{H-L}$	$\frac{(X_T-L)^2}{(H-L)(\mathrm{mo}-L)}$	$z_T=\frac{X_T-\mu_N}{\sigma_N}$	$z_T=\frac{\ln(X_T)-\mu_L}{\sigma_L}$
Special properties			$m=H-\sqrt{\frac{(H-L)(H-\mathrm{mo})}{2}}$	$\mu_N=M$, $\sigma_N=\mathrm{SD}$	$\mu_L=\ln(M)-\frac{\sigma_L^2}{2}$, $\sigma_L=\sqrt{\left(\frac{\mathrm{SD}^2}{M^2}\right)+1}$, $\mu_L=\ln(\mathrm{GM})$, $\sigma_L=\ln(\mathrm{GSD})$

Parameters of distribution: $z_{95}=1.645$; M = mean; m = median; SD = standard deviation; GM = geometric mean; GSD = geometric standard deviation; H = highest value; L = lowest value; mo = mode = highest frequency value.

tions that have to be used to calculate uncertainty from statistical distribution parameters. Because of the properties of the asymmetric distributions, the median was chosen as representative value of lognormal distributions [28].

Following GUM [12] prescription, the estimations of uncertainty involving health and safety of humans requires a measure of uncertainty and an evaluation of an interval about the estimation may expected. This is done in order to encompass a large fraction of the distribution of values that could reasonably be attributed to the measurand, i.e., the risk. The additional estimation of uncertainty that meets the requirement is termed by GUM *expanded uncertainty* (U). It is obtained by multiplying the uncertainty (u) by a coverage factor (k). In general coverage factor will be in the range from 2 to 3. Extensive experience with and full knowledge of the uses to which an estimation result will be used can facilitate the selection of the proper value of the coverage factor. Differently the value of the coverage factor may be calculated from a level of confidence, e.g., 95%.

4.2. Uncertainty of deterministic estimation

RME values of $\mathrm{TV_o}$, EF, ED are safeguard values, they are affected by uncertainty due to caution. More precise information about the estimation of RME values is not available, thus a uniform distribution in the range between 0 and RME value with a 95% confidence may be representative of the evaluation. Similar reasoning may apply to C_{ep} and CR. Also for AT it is possible to apply this reasoning.

Table 1 reports the results of Type B evaluation [12] calculated by

$$x=\frac{\mathrm{RME}}{2\times 0.95},\qquad u(x)=\frac{\mathrm{RME}}{2\times 0.95\times\sqrt{3}} \tag{6}$$

For BW the RME is a mean value, it is not known the reason to estimate 70 kg, but a uniform distribution in the range 30–120 with a 95% confidence may be representative of the evaluation. Type B evaluation [12] for BW is

$$\mathrm{bw}=\mathrm{BW_{RME}}=70\,\mathrm{kg},\qquad u(\mathrm{bw})=\frac{120-30}{2\times 0.95\times\sqrt{3}}=27\,\mathrm{kg} \tag{7}$$

If different information is available about RME values estimation, a different set of values may be calculated, but a negligible difference is expected. Table 4 shows the results of uncertainty estimation for RME.

For a measurand bounded from below (risk must be greater than 0) with an uncertainty comparable to or greater than the median an asymmetric distribution could be stated. The lognormal distribution is the simplest asymmetric distribution for risk. By mean of the equations in Table 3, mean and standard deviation can be calculated from the value and the uncertainty; a lognormal distribution LN(1.00×10^{-5}; 2.78×10^{-5}) describes the distribution of risk. Risk results to be lower than RME at 96% confidence, lower than 10^{-6} at 20% confidence, lower than 10^{-4} at 99% confidence.

Table 4
Budget of uncertainty for RME calculation of risk

X	$[X]$	x	$u(x)$	$u(x)/x$ (%)	$c(x)$	$c^2(x)u^2(x)$	Criticism	RME
C_{ep}	mgTE/kg	7.9×10^{-8}	4.6×10^{-8}	58	43	3.82×10^{-12}	0.98	1.50×10^{-7}
SF	kg d/mg	79,000	46,000	58	4.3×10^{-11}	3.88×10^{-12}	1.00	150,000
CR	kg/d	0.175	0.101	58	1.9×10^{-5}	3.82×10^{-12}	0.98	0.332
EF	d/year	184	106	58	1.8×10^{-8}	3.80×10^{-12}	0.98	350
ED	year	15.8	9.1	58	2.1×10^{-7}	3.80×10^{-12}	0.98	30
BW	kg	70	27	39	4.8×10^{-8}	1.70×10^{-12}	0.44	70
AT	d	13,400	7800	58	2.5×10^{-10}	3.88×10^{-12}	1.00	25,550
R	–	3.4×10^{-6}	5.0×10^{-6}	147		2.47×10^{-11}		4.39×10^{-5}

Table 5
Budget of uncertainty for variability

X	$[X]$	x	$u(x)$	$u(x)/x$ (%)	$c(x)$	$c^2(x)u^2(x)$	Criticism
C_{ep}	mgTE/kg	8.57×10^{-8}	3.92×10^{-8}	46	2.17	7.22×10^{-15}	0.16
SF	kg d/mg	22,570	25,990	115	8.23×10^{-12}	4.58×10^{-14}	1.00
CR	kg/d	0.0838	0.0702	84	2.22×10^{-6}	2.42×10^{-14}	0.53
EF	d/year	297	38	13	6.13×10^{-10}	5.37×10^{-16}	0.01
ED	year	7.25	6.87	95	2.56×10^{-8}	3.10×10^{-14}	0.68
BW	kg	75	10.4	14	2.48×10^{-9}	6.64×10^{-16}	0.01
AT	d	25,550	0	0	7.27×10^{-12}	0	0.00
R	–	1.82×10^{-7}	3.24×10^{-7}	178		1.05×10^{-13}	

GUM gives details about the way to express the final result of estimation by a value of the measurand, i.e., the risk, and the expanded uncertainty.

For symmetric distributions mode, median and mean have the same value, but for asymmetric distributions (as lognormal) mode, median and mean have different values and each of them may be considered representative of the value of the risk. Mean was chosen to report the results as the most representative value in the contest of risk analysis.

Generally, the cover factor is chosen between 2 and 3 in calculating expanded uncertainty, nevertheless GUM suggests to choose other values for specific applications (as for strong asymmetric distributions). In the present case, in order to reach the 95% confidence, the cover factor k was stated at 5.6. The results is then $r = 1.0 \times 10^{-5} \pm 2.8 \times 10^{-5}$. Criticism is higher than 0.1 for all variables, it means that all the variables have importance in determining uncertainty.

This is not the only way to calculate uncertainty of RME estimation; a similar result can be reached considering different information sets:

(a) If RME value for risk is considered as a threshold with about 95% confidence and uniform distribution is considered for risk, uncertainty can be calculated by Eq. (6). Expanded uncertainty may be calculated by $k = 1.645$ [12]. It results in $r = 2.2 \times 10^{-5} \pm 2.2 \times 10^{-5}$. Based on this information set, risk is lower than RME at 95% confidence, lower than 10^{-6} at 2% confidence and lower than 10^{-4} at 100% confidence.
(b) If RME value for risk is considered as a threshold with about 95% confidence and normal distribution is considered for risk, standard and expanded uncertainty can be calculated by z score tables. It results again in $r = 2.2\ 10^{-5} \pm 2.2 \times 10^{-5}$. Risk derived from this information set is lower than RME at 95% confidence, lower than 10^{-6} at 6% confidence, lower than 10^{-4} at almost 100% confidence (risk is greater than 10^{-4} at 10^{-7}% confidence).

As a conclusion, different information sets may be used to estimate uncertainty. Nevertheless, because of the congruence of information sets the results are quite similar. Following GUM, the result of RME estimation of risk may be reported in the form: $r = \text{RME} - U$, where RME and U were estimated to be 4.4×10^{-5} and $2.2–2.8 \times 10^{-5}$, respectively, e.g., $r = 4.4 \times 10^{-5} - 2.5 \times 10^{-5}$.

4.3. Uncertainty of statistical estimation

To evaluate variability of risk and uncertainty of statistical method, from the distributions shown in Table 2 value and uncertainty were calculated by the equations reported in Table 3, the budget of uncertainty is reported in Table 5.

For EF and BW criticism is lower than 0.1 thus their variability is negligible and do not affect variability of risk. This means that if relative uncertainty of BW is increased adding 10% to account for the differences among distributions available in literature the result does not change.

No information is considered about the way by which distributions were determined, this source of uncertainty was thus neglected. A deeper analysis should be addressed to that variables which criticism is greater than 0.1. No further information is available for the other variables. Thus, at the light of actual information, variability is completely representative of total uncertainty.

If a lognormal distribution is stated for risk, mean and standard deviation can be calculated from the value r and the uncertainty $u(r)$, a lognormal distribution LN(0.89×10^{-6}; 4.24×10^{-6}) results for risk. Risk is lower than RME at 99.90% confidence, lower than 10^{-6} at 83% confidence, lower than 10^{-4} at almost 99.98% confidence. The 95th percentile is $R_{95} = 3.40 \times 10^{-6}$.

Following the same procedure described in the previous paragraph, cover factor k was stated at 7.75 to reach 95% confidence and risk estimation result may be reported as $r = 0.9\ 10^{-6} \pm 2.5 \times 10^{-6}$.

4.4. Comparison GUM versus Monte Carlo

Figs. 7 and 8 show cumulative distribution function and probability density function, respectively, calculated by both GUM procedure and Monte Carlo simulation.

GUM results show a good fitting of Monte Carlo simulation results. The difference between 95th percentile of risk is lower than 3%.

The result is not surprising, because the risk model has not strong non-linearity that could invalidate the applicability of a first order Taylor series approximation. Nevertheless, when strong non-linearity appears in models, the second order may be used for approximation.

An asymmetric distribution is needed when a below limited variable (risk must be greater than 0) with a relative uncertainty comparable with median is considered. Lognormal is the simplest asymmetric distribution with two parameters. This comparison confirms the validity of the choice of lognormal distribution for risk.

5. Conclusions

The application of GUM procedure to evaluate uncertainty of risk evaluation was detailed. Deterministic and statistic approach to uncertainty assessment were evaluated and discussed. GUM procedure demonstrates that it is possible to treat different kind of information in order to have a quantitative evaluation of risk and its uncertainty. Uncertainty was evaluated for deterministic and statistical evaluations of risk. By GUM procedures it is possible to couple deterministic, statistical and heuristic approaches in order to obtain a total uncertainty value, which account for the main sources of uncertainty and variability.

The result of the application of GUM procedures is the distribution of risk in an analytical form. It is then possible to easily and analytically calculate the level of confidence of all the thresholds, which are interesting for risk analysis.

The proposed procedure is easy and straightforward and the use of a simple spreadsheet program is enough to implement the algorithm. Anyone with a little experience with spreadsheet programs can easily implement the procedure. A simple table is sufficient to implement the complete procedure calculations, i.e., the budget of uncertainty, all calculations are explicitated in the table. GUM procedure does not have any adjusting parameter such as number of iterations, sampling technique, number and width of intervals.

GUM procedures are widely used and accepted by different scientific and technical communities in order to evaluate uncertainty. The calculation, provided by an analytical system of algebraic equations, is straightforward and the reverse ones are simple due to the analytical form of applied equations; it enables in principle, inverse calculations of a threshold of concentration of a carcinogens from a threshold of risk, e.g., 10^{-6}, and a level of confidence of the threshold, e.g., 95%.

In this paper the comparison of GUM procedure and Monte Carlo approach sustains the applicability of the first order Taylor's series approximation to this kind of model of risk. The model is widely suggested by EPA [20] for different situations of risk, i.e., ingestion, inhalation, and dermal contact in residential and industrial land use. Moreover, other kind of models may be tested with GUM procedure comparing results with Monte Carlo simulation. The budget of uncertainty helps in understanding which variable contributes most to the uncertainty. Obviously, information about the source of uncertainty is already present in input data uncertainty, nevertheless criticism gives a tool to judge the direct information managing the possibility of neglecting deeper insight about a variable. Moreover, if a different kind of model is considered (as an example model for soil migrating pollutants, showering models or model considering attenuation phenomena) where the information cannot be easily extracted directly from input variable, the criticism parameter help considerably to addressing uncertainty evaluation and reduction.

Concerning the case study considered in this paper, i.e., the risk to develop a cancer as a consequence of daily ingestion of dioxins contained in milk, the result is that the presence of dioxins in milk is a problem that has to be considered but it is not an immediate hazard.

References

[1] U.S. EPA, Exposure Factors Handbook, EPA/600/P-95/002Fa, U.S. EPA, 1997.
[2] ASTM, Standard Guide for Risk-based-Corrective-Action, Designation E2081-00, ASTM, 2000.
[3] AIHA, American Industrial Hygiene Association White Paper on Risk Assessment and Risk Management, American Industrial Hygiene Association, 2002.
[4] Repubblica Italiana, DECRETO LEGISLATIVO 3 aprile 2006, n.152, Norme in materia ambientale, GU Serie Generale 88, 2006.
[5] J.I. Daniels, K.T. Bogen, L.C. Hall, Procedures for Addressing Uncertainty and Variability in Exposure to Characterize Potential Health Risk from Trichloroethylene Contaminated Ground Water at Beale Air Force Base in California, UCRL-ID-135784 Rev. 1, U.S. Department of Energy, 1999.
[6] K.T. Bogen, Methods for Addressing Uncertainty and Variability to Characterize Potential Health Risk from Trichloroethylene-Contaminated Ground Water at Beale Air Force Base in California: Integration of Uncertainty and Variability in Pharmacokinetics and Dose–Response, UCRL-ID-135978-REV-1, U.S. Department of Energy, 2001.
[7] J.S. Hammonds, F.O. Hoffman, S.M. Bartell, An Introductory Guide to Uncertainty Analysis in Environmental and Health Risk Assessment, ES/ER/TM-35/R1, U.S. Department of Energy, 1994.
[8] U.S. Department of Energy, Final Environmental Impact Statement for the Tank Waste Remediation System: Appendix K Uncertainties Analysis, DOE/EIS-0189, U.S. Department of Energy, 1996.
[9] W.H. Warren-Hicks, D.R.J. Moore, Uncertainty Analysis in Ecological Risk Assessment, SETAC, 1998.
[10] U.S. EPA, Risk Assessment Guidance for Superfund, EPA/540/1-89/002, U.S. EPA, 1989.
[11] D. Guyonnet, D. Dubois, B. Bourgine, B. Come, J.P. Chilès, Uncertainty in risk assessments: combining probabilities and possibilities, Theme B5: Uncertainties, Consoil 2003, Gent, 2003, pp. 378–387.
[12] ISO TAG4, Guide to the Expression of Uncertainty in Measurement (GUM), ISO, Geneve, 1994.
[13] ISO, International Vocabulary of Basic and General Terms in Metrology, 2nd ed., ISO, 1993.
[14] U.S. EPA, Guidance for Risk Characterization, Science Policy Council, Washington, DC, 1995.
[15] Directive 2002/69/EC (OJ L 209, 6.8.2002), Sampling Methods and Methods of Analysis for the Official Control of Dioxins and PCBs, 2002.
[16] M. Van den Berg, L. Birnbaum, T. Bosveld, B. Brunström, P. Cook, M. Feely, J.P. Giesy, A. Hanberg, R. Hasegawa, S.W. Kennedy, T. Kubiak, J.C. Larson, F.X.R. van Leeuwen, A.K. Djien Liem, C. Nolt, R.E. Peterson, L. Pollinger, S. Safe, D. Schrenk, D. Tillit, M. Tysklind, M. Younes, F. Waren, T. Zacharewski, Toxic equivalency factors (TEFs) of PCBs, PCDDs, PCDFs for humans and wildlife, Environ. Health Perspect. 106 (1998) 775–792.
[17] A. Singh, A.K. Singh, R.W. Maichle, ProUCL Version 3.0 User Guide, EPA/600/R04/079, 2004.
[18] U.S. EPA, Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities, EPA530-D-98-001A, U.S. EPA, July 1998.
[19] A. Turrini, A. Saba, D. Perrone, E. Cialfa, A. D'Amicis, Food consumption patterns in Italy: the INN-CA study 1994–96, Eur. J. Clin. Nutr. 55 (7) (2004) 571–588.

[20] U.S. EPA, Quantitative Uncertainty Analysis of Superfund Residential Risk Pathway Models for Soil and Groundwater: White Paper, 1996.
[21] American Industrial Health Council, Exposure Factors Sourcebook. Available from Update Coordinator, American Industrial Health Council, Suite 760, 2001 Pennsylvania Avenue, NW, Washington, DC 20006-1807, May 1994.
[22] Brainard, D.E. Burmaster, Bivariate distributions for height and weight of men and women in the United States, Risk Anal. 12 (1992) 267.
[23] R.L. Smith, Use of Monte Carlo simulation for human exposure assessment at a superfund site, Risk Anal. 14 (4) (1994) 433–439.
[24] IRIS Integrated Risk Information System, http://www.epa.gov/iris.
[25] M. Israeli, C.B. Nelson, Distribution and expected time of residence for U.S. households, Risk Anal. 12 (1992) 65–72.
[26] M.D. La Grega, P.L. Buckingham, J.C. Evans, Hazardous Waste Management, McGraw-Hill, New York, 1994.
[27] D.E. Burmaster, K.E. von Stackelberg, Quantitative Uncertainty Analysis in Exposure and Dose Response Assessment in Public Health Risk Assessment using Monte Carlo Techniques. Superfund'89, Hazardous Materials Control Research Institute, Washington DC 82-85, 1989.
[28] L.R. Bloomfield, D.E. Burmaster, Mathematical properties of the risk equation when variability is present, Hum. Ecol. Risk Assess. 2 (2) (2000) 348–355.