CALCUL ET DEVELOPPEMENT D'INDICATEURS BIOCIDES / BEREKENNING EN ONTWIKKELING VAN INDICATOREN VOOR BIOCIDEN / CALCULUS AND DEVELOPMENT OF BIOCIDES INDICATORS

BIOCIDES PT18

Scientific Support to Policy

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1 Scope of the study

This study handles the impact assessment of indicators for PT18 biocides, which involve insecticides, acaricides and products to control arthropods. The main purpose is to develop indicators for the Belgian situation in order to use the deliverables as guidelines for the biocides' reduction plan of the Belgian policy. For example, the federal reduction program (KB 22/02/05) intends to decrease the risk associated with biocides (product category EU-8-14-18) by about 50% over the next 10 years using 2001 as a reference year.

More specifically, the objectives of the research project were set out to address the following questions:

- Which environmental parameters should be included as indicators in an assessment of the environment and/or health toxicity?
- What are the human and environmental exposures? How should these impacts be assessed, scored and interpreted?
- What are the uncertainties related to the indicator values?
- Which indicators are relevant to register effects on specific or integrated environmental variables?

In pursuit of its goal, the project was structured around three research themes, each addressing a number of specific issues

1.1 Theme 1: Quality assessment of the NIJS Algorithm

Theme 1 is concerned with the validation of the NIJS algorithm using PT18 biocides as target compounds (Goeyens et al., 2006). This algorithm is an updated version of indicators elaborated by ECOLAS for both ecological and health risk assessments (Callebaut et al., 2004). It used R-phrases and expert judgment to define risk classes and to assign score values. It can either be used as reference levels and/or as starting points for the search of alternative indicators (see Theme 2). The research developed here aims at an improved assessment of the scoring process and quantification of the related uncertainty. Special attention is paid to the rapid computation of indicator values for 2001 and 2005, for which sales data are available (personal communication, Philippe Ruelle, Risk Management Service, FPS Public health). The outcome provides a rapid and affordable approach to test compliance with the Belgian Biocide Reduction Plan.

1.2 Theme 2: Proposal for Biocides Indicator in BELgium (BIBEL)

Central to this theme are the scenarios used for the estimation of the indicator values. To make the model run, several determining parameters or variables are required. They are largely based on the earlier gathered experience of UGent with the PRIBEL indicator, a multi-component indicator system to assess the occupational risk to agricultural pesticides (Vergucht

et al., 2006). A risk index (RI) is the quotient of the estimated human or environmental exposure and a toxicological reference dose. In the case of BIBEL, the reference dose was calculated with a scoring process, equivalent to the one used in the Nijs algorithm, while exposure was estimated using scenario development based on the European Technical Notes for Guidance (TNGs, 2006). Calculations were made for PT18 biocides. A statistical assessment (uncertainty and sensitivity analyses) of the BIBEL approach was performed. The uncertainty analysis aims at identifying the main sources of uncertainty among all inputs by giving an estimate of the overall/combined uncertainty on the final indicator response (precision of the indicator). The aim of the sensitivity analysis is to test the functioning of the impact indicators, and to identify key parameters / variables that contribute to the highest variations in the outputs.

1.3 Theme 3: Comparison between the NIJS and BIBEL approach

The Nijs and BIBEL approaches have been compared. The difference mainly concerns the calculations of human and environmental exposures. Yet both indicators showed comparable temporal risk trends. While this may increase their credibility, it primarily indicates that the indicators are driven by the same variable, namely the sales data.

2 Quality assessment of the NIJS Algorithm

2.1 Introduction

In its final report (Goeyens, 2006), the “Biocide Indicator” working group recommended to evaluate the indicator elaborated by E. Nijs (personal communication, Risk Management Service, FPS Public health). Two different formulae have been proposed. RI(1) merely based on a sum of scores, and RI(2) based on a sum of a product of scores:

$$\begin{aligned} RI(1) &= Q \cdot \left(HumTox + HumExp + EcoTox + EcoExp\right) = Q \cdot \sum Z_i \\ RI(2) &= Q \cdot \left(\left(HumTox \cdot HumExp\right) + \left(EcoTox \cdot EcoExp\right)\right) = Q \cdot \sum \prod Z_i \end{aligned} \qquad (2.1.1)$$

where Q is the estimated amount of use (sales data), HumTox = composite score for the human toxicity, HumExp = composite score for the human exposure, EcoTox = composite score for the ecotoxicology, EcoExp = composite score for the environmental exposure and Σz_i & $\Sigma \Pi z_i$ = the sum of scores and the sum of products of scores, respectively .

Specific objectives were (i) to compute indicator values that can be used as starting points or references for further indicator development & improvement, (ii) to assess the unpredictability of the Nijs algorithm, (iii) to investigate the optimal scaling factor(s) to be used in the scoring process, and the way of merging them, and (iv) to compare the estimation behaviour of RI(1) *vs.* RI(2).

2.2 Sources of unpredictability

Indicator values are unpredictable because of the joint influence of variability and uncertainty. Variability is a property of the sets of entities (e.g. the group of PT18 biocides represents at least 170 products) or events (e.g. scoring distribution for the human exposure) that differ in some significant way. Variability may be observed and estimated but it cannot be reduced, because it is an inherent and objective property of the system. The response to variability is to use a probability distribution function, so that “objectivist” concepts and “frequentist” methods dominate its analysis (Sutter, 2007).

Uncertainty is the lack of knowledge about a system. Unlike variability, it can be reduced by obtaining additional information (better data, better models). The responses to uncertainty are beliefs or suspended judgements until data or model(s) can be generated. In probabilistic analyses, beliefs like variability should be expressed as distribution functions (Hattis and Burmaster, 1993; Frey and Burmaster, 1999). However, uncertainty concerning variables and forms of mathematical models is a difficult issue that may result in the use of subjective assessment, an expression which here can be used synonymously with “intuitive probability” and “credibility” (Good, 1982). Although it is recognised that subjective probabilities vary from one person to another, and even from time to time for a single person, they are not arbitrary as they are influenced by common sense, by expert knowledge and sometimes by earlier experiments and observations. For example, assessing uncertainty on the scoring process is a typical problem of this nature. Classifying the PT18 biocides according to risk phrases induces a

loss of quantitative information that is partially restored through scoring and/or ranking but under the form of discrete distributions.

Example 2.2.1 - The lethal dose (LD50) of chlorpyrifos that causes death of half (50%) of a test bird population was estimated around 11 milligrams per kilogram with an expanded uncertainty range of 6 to 22 mg/kg (95% confidence level). This indicates that it takes 6 to 22 mg of chlorpyrifos for each kg of body weight to kill 50 percent of the experimental animals tested. Let assume the following coding and scoring systems:

Criteria	Risk-phrase	Score	Score range[(1)]	Uncertainty
<= 1 mg/kg	RX1	3	a = 3-2	0.2
<= 10 mg/kg	RX2	2	a = 3-1	0.4
<= 100 mg/kg	RX3	1	a = 2-1	0.2

[(1)] The range of a score is defined by the absolute value of the difference between the scores surrounding the score in the same category of effect (class of risk).

According to these data, chlorpyrifos will be classified as RX3 (10 < mean LD50 < 100 mg/kg) with score 1. However, in a number of test results chlorpyrifos should be classified as RX2 (test results for which LD50 was <= 10mg/kg) with score 2. One can even estimate that this would occur in 40% of the observations, which is far from being negligible. Thus there is an uncertainty associated with coding and scoring that can be quantified knowing the probability distribution function of the test results.

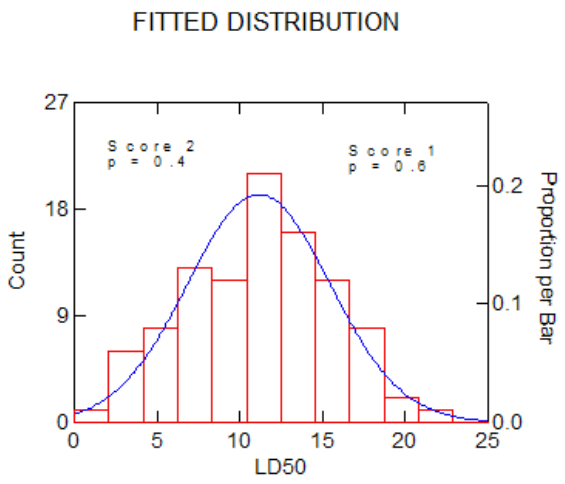

Figure 2.2.1: Observed (bars) and fitted (line) distributions of LD50-value (mg/L) for chlorpyrifos (see example 2.2.1).

In practice, however, the latter information is not (directly) available. If the labelling of chlorpyrifos is quoted RX3, we just feel that the mean LD50 of the product could be anywhere in between 10 and 100 mg/kg, with no idea of whether any part of the range is more likely than another. Under these conditions, an estimate of uncertainty on scoring can be made in the form of **a score range** described by a triangular distribution according to the EURACHEM / CITAC Guide CG4 (2000).

2.3 Quantification of the uncertainty on the scoring process

The uncertainty u(z) related to a triangular distribution is given by:

$$u(z) = \frac{a}{2 \cdot \sqrt{6}} \tag{2.3.1}$$

where a is the score range (see example 2.2.1). This standard procedure can be extended even in case of “intuitive probability” and “credibility” (e.g. based on expert judgement). It merely assumes that it is less likely to observe data in the margins of the distribution near the bounds represented by the lower and upper score values than in the centre corresponding to the assigned score value.

Following the estimation of individual component uncertainty on scores, the next stage is to calculate the combined standard uncertainty using one of the procedures described below.

For models involving only a sum of scores, the combined standard uncertainty is given by:

$$u(\Sigma z_i) = \sqrt{u(z_1)^2 + u(z_2)^2 + \cdots} \tag{2.3.2}$$

For models involving only a product of scores, the combined standard uncertainty is given by:

$$u(\Pi z_i) = \Pi z_i \cdot \sqrt{\left(\frac{u(z_1)}{z_1}\right)^2 + \left(\frac{u(z_2)}{z_2}\right)^2 + \cdots} \tag{2.3.3}$$

For mixed models involving a sum of a product of scores, the combined standard uncertainty is given by:

$$u(\Sigma \Pi z_i) = \Sigma \Pi z_i \cdot \sqrt{\frac{\Sigma u(z_j)^2}{\left(\Sigma z_j\right)^2} + \frac{\Sigma u(z_k)^2}{\left(\Sigma z_k\right)^2} + \cdots} \tag{2.3.4}$$

2.4 Human toxicity (HumTox)

The scoring system for HumTox is based on the use of Risk Phrases (R-phrases), as defined in Annex III of the European Union Directive 67/548/EEC, and updated in Directive 2001/59/EC. Special attention was given to chronic effects with a strengthening factor of 5 when compared to acute effects. The uncertainty on scoring is determined as described in section 2.3.

Table 2.4.1: R-phrases, scores, uncertainty and frequency distribution for the HumTox variable (PT18 biocides). Regular font = acute effects, bold font = chronic effects

Code	R-phrases	Score	Uncert.	Freq. %
None	NC: not classified	0.1	-	34
None	R10: Flammable	1	0.4	7
F	R11: Highly flammable	3	0.4	1
F+	R12: Extremely flammable	3	0.4	15
F+	R15/29: Contact with water liberates toxic, extremely flammable gases	3	0.4	1
Xi	R36: Irritating to eyes	10	2	3
Xi	R38: Irritating to skin	10	2	5
Xn	R20: Harmful by inhalation	20	4	1
Xn	R22: Harmful if swallowed	20	4	2
Xn	R65: Harmful: may cause lung damage if swallowed			
	R34: Causes burns	20	4	4
C	R24: Toxic in contact with skin	30	6	< 1
T	R25: Toxic if swallowed	30	6	< 1
T	R26: Very toxic by inhalation	30	6	< 1
T+	R28: Very toxic if swallowed	50	4	2
T+	R32: Contact with acids liberates very toxic gas	50	4	1
T+		50	4	1
Xi	**R43: May cause sensitisation by skin contact**	50	10	17
Xn	**R40: Limited evidence of a carcinogenic effect**	100	20	1
Xn	**R68: Possible risk of irreversible effects**	100	20	1
T	**R60: May impair fertility**	150	10	1
T	**R61: May cause harm to the unborn child**	150	10	1

It appears that:

- Up to 34% of the PT18 biocides were not classified (NC) having a minimum score of 0.1.
- About 24% of the products displayed only physico-chemical properties (flammable to extremely flammable) with scores ranging from 1 to 3.
- About 42% of the products exhibit health effects (harmful to very toxic) with scores ranging from 10 to 50 for acute effects and 50 to 150 for chronic effects.

Note that these products can cumulate several R-phrases (e.g. group of R26, 28, 32) or fit in several risk classes (e.g. F, Xi, T).

The frequency distribution function of HumTox can be approximated with an exponential distribution (Figure 2.4.1).

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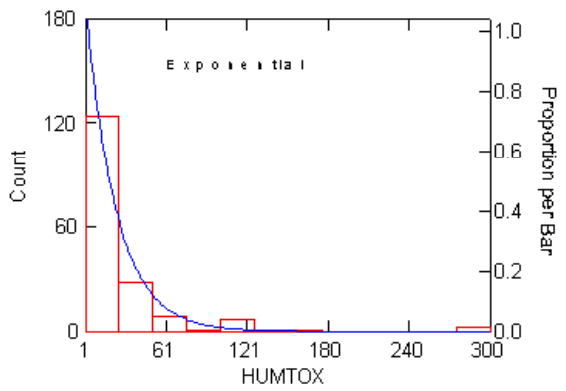


Descriptive statistics

Number of products	173
Minimum	1
Maximum	300
Median	3
First quartile (P25%)	1
Third quartile (P75%)	50
IQR(P75% P25%)	49
P95%	110

Figure 2.4.1: Observed (bars) and fitted (line) distributions for HumTox.

The median value for the relative uncertainty on HumTox is around 20%.

2.5 Human exposure (HumExp)

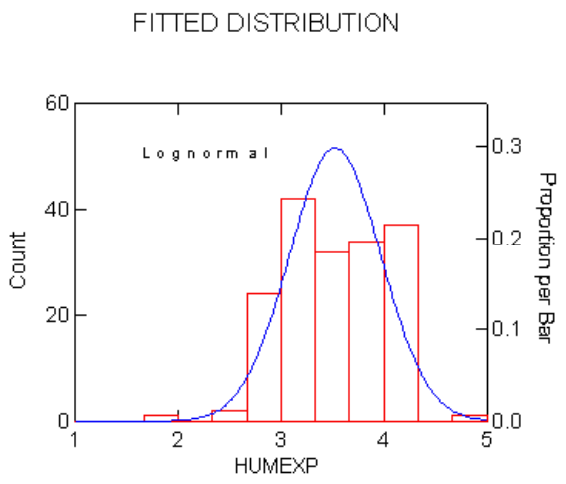
The scoring system for HumExp is based on expert judgement. The PT18 biocides were classified according to their mode of application (e.g. space spraying, electrical evaporator…). Special attention was given to primary (e.g. user) and secondary (e.g. children…) exposure (dermal, oral and inhaling) with scores ranging from 1 to 3. Depending on the frequency of use (e.g. 1x/day, 1x/month…) the sum of scores for the primary and secondary exposure is expanded by a factor 1 to 6 (Table 2.5.1). For example, the use of an electrical evaporator 1x per week yields a score of 54 (4 x 9) with a standard uncertainty of 2.4 (4 x 0.6). Yet, a distinction is made according to professional and non-professional applications thanks to expert judgement.

Table 2.5.1: Scores and uncertainty u(z) distribution for the HumExp variable (PT18 biocides)

Product application	Primary						Secundary						HumExp	
	Inh.	U(z)	Der	U(z)	Ora	U(z)	Inh.	U(z)	Der	U(z)	Ora	U(z)	Σ	U(z)
Spuittoepassingen (gebruiksklaar-targeted spot)	2	0.41	1	0.20	1	0.20	1	0.20	2	0.41	1	0.20	8	0.7
Spuittoepassingen (gebruiksklaar - naden/kieren)	2	0.41	1	0.20	1	0.20	1	0.20	1	0.20	1	0.20	7	0.6
Spuittoepassingen (gebruiksklaar - oppervlakte)	3	0.20	2	0.41	1	0.20	1	0.20	2	0.41	1	0.20	10	0.7
Spuittoepassingen (gebruiksklaar - ruimte)	3	0.20	2	0.41	1	0.20	2	0.41	2	0.41	1	0.20	11	0.8
Spuittoepassingen (niet gebruiksklaar - targeted spot)	2	0.41	2	0.41	2	0.41	1	0.20	2	0.41	1	0.20	10	0.9
Spuittoepassingen (niet gebruiksklaar - naden/kieren)	2	04.1	2	0.41	2	0.41	1	0.20	1	0.20	1	0.20	9	0.8
Spuittoepassingen (niet gebruiksklaar - oppervlakte)	3	0.20	3	0.20	2	0.41	1	0.20	2	0.41	1	0.20	12	0.7
Spuittoepassingen (niet gebruiksklaar - ruimte)	3	0.20	3	0.20	2	0.41	2	0.41	2	0.41	1	0.20	13	0.8
Verdamping uit strips en cassettes	3	0.20	1	0.20	1	0.20	2	0.41	1	0.20	1	0.20	9	0.6
Electrische verdampers	3	0.20	1	0.20	1	0.20	2	0.41	1	0.20	1	0.20	9	0.6
Lokmiddelen	1	0.20	2	0.41	1	0.20	1	0.20	1	0.20	1	0.20	7	0.6
Strooipoeders	2	0.41	3	0.20	2	0.41	1	0.20	2	0.41	1	0.20	11	0.8
Gassen en vernevelaars	3	0.20	1	0.20	1	0.20	2	0.41	1	0.20	1	0.20	9	0.6
Textielbiociden	2	0.41	1	0.20	1	0.20	1	0.20	3	0.20	1	0.20	9	0.6
Halsbanden	1	0.20	3	0.20	1	0.20	1	0.20	2	0.41	1	0.20	9	0.6
Shampoos en lotions	1	0.20	3	0.20	1	0.20	1	0.20	2	0.41	1	0.20	9	0.6

Frequency of use	1x/day	3months/year	1x/week	1x/month	1x/3 months	1x/year
Strengthening factor	6	5	4	3	2	1

The uncertainty on scoring is determined as described in section 2.3. The frequency distribution function of HumExp is fitted to a lognormal distribution (Figure 2.5.1).



Descriptive statistics

Number of products	173
Minimum	7
Maximum	109
Median	35
First quartile (P25%)	25
Third quartile (P75%)	50
IQR(P75%-P25%)	25
P95%	61

Figure 2.5.1: Frequency (bars) and fitted (line) distributions for log of HumExp.

The median value for the relative uncertainty on HumExp is around 10%

2.6 Ecological toxicity (EcoTox)

The scoring system for EcoTox is based on the use of Risk Phrases (R-phrases).

Table 2.6.1: R-phrases, scores, uncertainty and frequency distribution for the EcoTox variable (PT18 biocides).

R-phrases	Score	Uncert.	Freq. %
NC: not classified	1	-	19
R52: Harmful to aquatic organisms	10	2	1
R52/53: Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment	20	4	4
R51/53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment	30	4	8
R50: Very toxic to aquatic organisms	40	4	3
R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment	50	2	51
R57: Toxic to bees	30	6	3

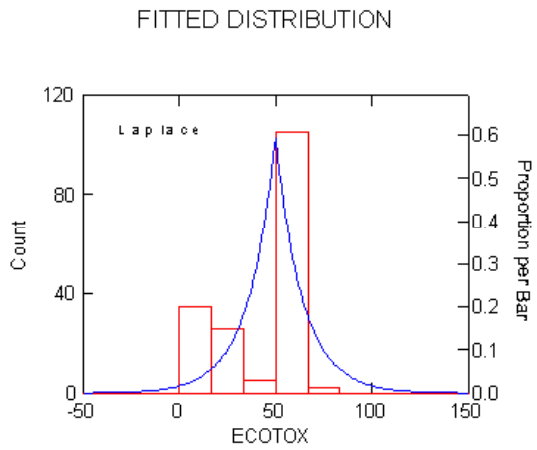
It appears that:

- Up to 19% of the PT18 biocides were not classified (NC) having a minimum score of 1.
- About 67% of the products displayed hazard effects (harmful to very toxic) towards aquatic organisms with scores ranging from 10 to 50.

- Only 3% of the products are toxic to bees with a unique score of 30.

Note that these products can combine R57 with R50, R50/53 and/or R51/53. The uncertainty on scoring is determined as described in section 2.3.

The frequency distribution function of EcoTox looks like a Laplace distribution (Figure 2.6.1).



Descriptive statistics

Number of products	173
Minimum	1
Maximum	80
Median	50
First quartile (P25%)	20
Third quartile (P75%)	50
IQR(P75% P25%)	30
P95%	50

Figure 2.6.1: Frequency (bars) and fitted (line) distributions for EcoTox.

The median value for the relative uncertainty on EcoTox is around 4%.

2.7 Ecological exposure (EcoExp)

The scoring system for EcoExp is based on expert judgement (Philippe Ruelle, Risk Management Service, FPS Public health).

Table 2.7.1: Scores, uncertainty and frequency distribution for the EcoExp variable (PT18 biocides).

Expert judgement	Score	Uncert.	Freq. %
No impact	1	0.2	2
Weak impact (dust, rubbish)	2	0.4	52
Significant impact (water, air, soil)	3	0.4	30
Global impact (trophic level, biodiversity)	4	0.2	3

It appears that:

Most of the PT18 biocides (up to 80%) exhibit weak to significant ecological impacts via waste or local contamination of water, air and soil sources. The uncertainty on scoring is determined

as described in section 2.3. The frequency distribution function of EcoTox is approximated with a binomial distribution (Figure 2.7.1).

Descriptive statistics

Number of products	173
Minimum	1
Maximum	4
Median	2
First quartile (P25%)	2
Third quartile (P75%)	3
IQR(P75% P25%)	1
P95%	3

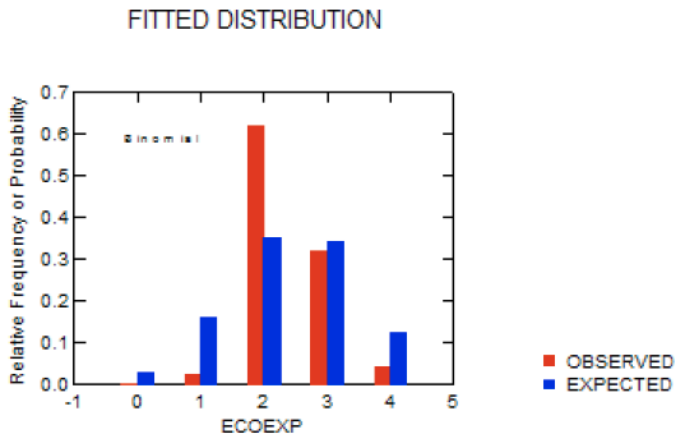


Figure 2.7.1: Frequency and fitted distributions for HumExp.

The median value for the relative uncertainty on HumExp is around 20%.

2.8 Composite score function

As shown by Eq. (2.1.1), a composite score over all the used variables (HumTox, HumExp, EcoTox and EcoExp) is computed using either additive (Σz_i) and/or multiplicative ($\Sigma\Pi z_i$) expressions. Subsequently, it should be investigated (i) whether these formulae may influence the interpretation of data, and (ii) how the uncertainty depends upon the composite score value. If so a functional relationship should be evaluated.

Table 2.8.1: Comparison between additive and/or multiplicative expressions in computing a composite score for PT18 biocides (see Eq. 2.1.1)

Composite score expression	Σz_i	$\Sigma\Pi z_i$
Minimum	12	10
Maximum	382	7936
Median	91	181
First quartile (P25%)	61	78
Third quartile (P75%)	120	1000
IQR (P75% - P25%)	59	1114
P95%	193	4014
Skewness	1.9	2.6

Comparing both distributions, it can be stated that there are substantial differences regarding the range, percentile and skewness values (the degree of asymmetry of a distribution around its mean). The total number of permutation in the ranking of the products amounts to 139, but the

number of significant permutations (a shift > 10 places) is less than 51. These concern mainly products located in the centre of the distributions between the first (P25%) and third (P75%) quartiles. For data beyond P75%, there are only two significant permutations. Overall the Spearman rank order correlation coefficient is 0.95 ($p < 0.001$) suggesting that 90% of the variation in either distribution is explained by its correlation with the other (Figure 2.8.1).

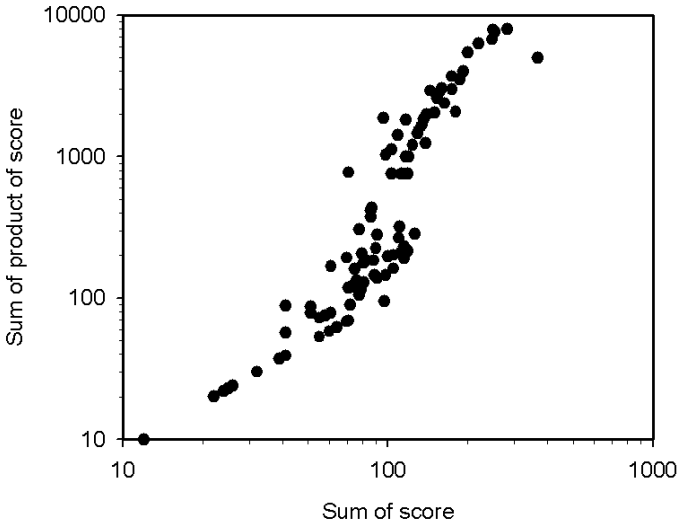


Figure 2.8.1: Comparison between additive and/or multiplicative expressions in computing a composite score for PT18 biocides.

The functional relationship between the uncertainty and the composite score function was investigated according to the International Standard (ISO 5725-2: 1994). Three types of relationship have been considered:

- A straight line through the origin: u(z) = az
- A straight line with a positive intercept: u(z) = az + b
- An exponential type relationship: $u(z) = az^b$

As shown in Figure 2.8.2, all three of these relationships yield practically equivalent fits, but the exponential model should be preferred because at highest scores it is more accurate. The fitted lines (regression coefficient ± SE) are then given by:

$$u(\Sigma z_i) = (0.14 \pm 0.03) \cdot \Sigma z_i^{(0.84 \pm 0.05)}$$
$$u(\Sigma \Pi z_i) = (1.0 \pm 0.2) \cdot \Sigma \Pi z_i^{(0.77 \pm 0.02)} \qquad (2.8.1)$$

On average the precision on scoring (median value for the relative uncertainty) for Σz_i and $\Sigma \Pi z_i$ is around 12 and 30%, respectively.

From a statistical viewpoint, both approaches yield comparable outcomes, i.e. the estimation behaviour of Σz_i and $\Sigma \Pi z_i$ does not significantly differ. We are, therefore, confident that the composite score function does not deeply influence data analysis. Yet within a risk assessment

perspective $\Sigma\Pi z_i$ should be preferred because it is closer to the risk index formulation usually defined as the ratio of an exposure (human or environmental) to a toxicological reference dose. Hence $\Sigma\Pi z_i$ was chosen, hereafter for further assessments.

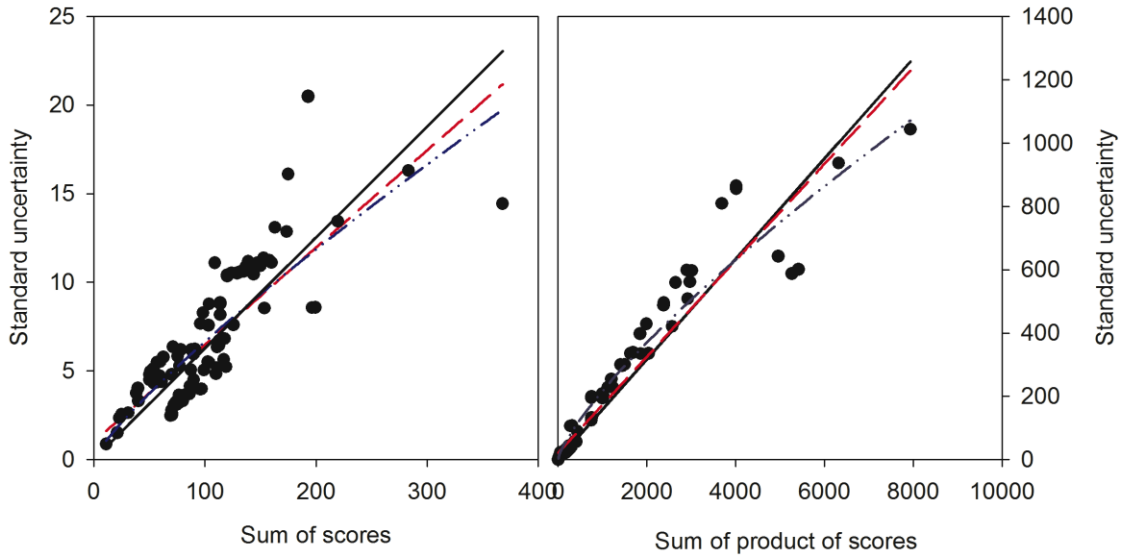


Figure 2.8.2: Functional relationship between precision (uncertainty) and the composite score values (solid line = straight line model; medium dash line = straight line model + positive intercept; Dash-dot-dot line = exponential model)

2.9 Sales data (Q)

In Eq. (2.1.1) it is assumed that the amount of PT18 biocides (Q), which is applied in Belgium, can be approximated with sales data. Missing values in the data sets gathered for years 2000 to 2005 are summarized in Table 2.9.1:

Table 2.9.1: % of data not available, missing or equal to 0 for the years 2000-2005.

Year	2000	2001	2002	2003	2004	2005
Not available (na)	13%	9%	5%	5%	4%	1%
Missing data (md)	18%	22%	26%	26%	6%	7%
Zero value	21%	13%	13%	14%	26%	26%

There are at least three reasons why the data were missing or equal to 0. First, because for a given year, a product may not yet be commercially available or taken out from the market. Under these conditions the data are not actually missing but flagged as “non available” (**na**). Alternatively, data may be missing because computer malfunctioning or because the data were not transmitted correctly. For PT18 biocides, these data may be classifiable as “missing at random” (**md**). This means that the probability of a missing value does not depend on a given

product or to the sales data of any other products. Finally, a zero value was assigned to the data when they were available but not sold for a given period.

We have to decide how to deal with missing values (md) since they can drastically bias data analysis and treatment. There are a number of possible alternatives. By far the most common approaches are “mean substitution” and “interpolation”. Yet these are not very wise choices and should be relegated to the past. By substituting a value that is perfectly “predictable” from other data, we do not add new information but merely increase the sample size and reduce the standard error of estimate. This reduction is spurious and should be avoided, especially with data missing at random (MAR) (Marcantonio and Pechnyo, 2004). Moreover, whenever several successive values are missing, mean substitution and interpolation becomes totally subjective.

The simplest unbiased approach is to omit those cases with missing values and to run analyses on what remains. This approach is often called “**listwise deletion**” or “complete case analysis”. In this study, listwise deletion would results in a substantial decrease in the sample size available for data analysis from 984 to 636. Yet the method does have some important advantages. In particular with MAR data, it leads to unbiased parameter estimates, and can therefore be used for uncertainty quantification (see below). Modern approaches are those, which rely on maximum likelihood solutions, and those, which involve multiple imputations. Here we used the maximum likelihood estimators, based on the **EM (Expectation-Maximization) algorithm** available in SYSTAT Software. An excellent discussion of the EM algorithm and its solution is provided by McLachlan and Kridhnzn, 1996; Borman, 2004).

2.10 Uncertainty on sales data

Listwise deletion was used to estimate the uncertainty related to the missing value imputation. Data were arranged using matrix notation with PT18 biocides on rows and years on column. Omitting cases with missing data lead to a matrix dimension of 106 x 6. Exploratory data analysis (EDA) revealed that the variance is non-constant or unstable. Variance stabilization was achieved with a logarithmic transformation x = log (y + c), where c is a constant required to avoid numerical problems. The value of c is arbitrarily chosen to be 1. Random deletions were then performed in the 106 x 6 matrix to simulate missing data in the same proportions as those reported in Table 2.9.1. These data were then reconstructed using the EM method and the imputed values were compared with the original ones (Figure 2.10.1).

The performance of the EM method is evaluated using the standard error of estimate (residual standard deviation):

$$S_{residual} = \sqrt{\frac{\sum_{i=1}^{n}\left(OBS_i - EMV_i\right)^2}{n-p}} \qquad (2.10.1)$$

where OBS_i is the observed value, EMV_i the imputed value, n the sample size, p the number of missing data. The relative uncertainty on the imputation is then computed by Eq. (2.10.2). The results are shown in Table 2.10.1

$$RSU = 100 \cdot \frac{S_{residual}}{mean} \qquad (2.10.2)$$

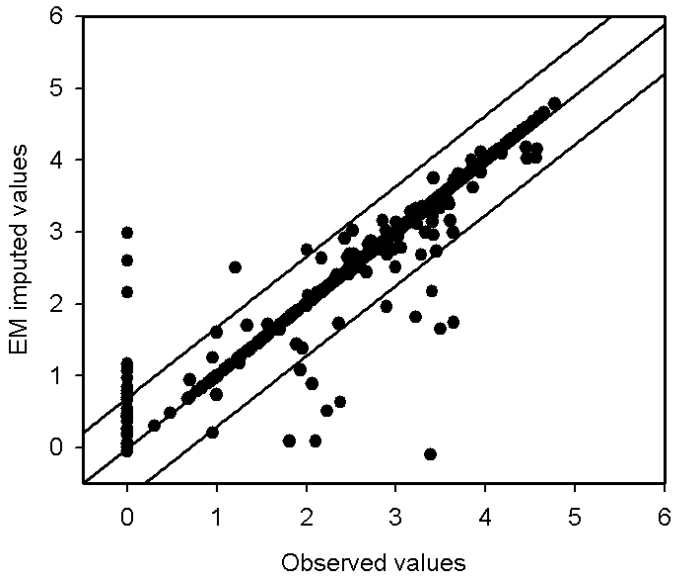


Figure 2.10.1: Scatterplot of observed *vs.* EM imputed values. The continuous lines represent the 95% prediction interval and the regression. The prediction interval (or confidence interval for the population) describes the range where the data values will fall a percentage of the time for repeated observations.

Table 2.10.1: Relative standard uncertainty (RSU) on imputed sales data.

Year	2000	2001	2002	2003	2004	2005	Median
Missing data %	18	22	26	26	6	7	20
RSU %	18	21	23	23	10	10	19

As expected, the relative uncertainty on the imputed value is a function of the missing data. It increases with the number of imputations to be carried out. Overall for the whole period (2000-2005), the uncertainty on the reconstructed data is around 19%. These uncertainties are reasonable approximations to estimate the loss of information due to missing data

2.11 NIJS Indicator Values (NIV)

The indicator values for PT18 biocides can now be computed using (i) the risk index represented by the composite score function $\Sigma\Pi z_i$ and (ii) the frequency of use represented by the sales data. The observed distribution ranges from 0 to 4.1 10^8 with a median value of 6.3 10^4 and an interquartile range (IQR) of 8.1 10^5. Data analysis is improved when results are fairly symmetrically distributed and have fairly uniform variances. Hence, data that vary more than a ten-fold are often logarithmically transformed before the analysis (Eriksson et al. 2006).

To avoid numerical problems (zero values), variance stabilization was achieved with a logarithmic transformation x = log (y + c), where c is arbitrarily chosen to be 0.1. Transformed NIVs for years 2000 to 2005 follow a continuous probability distribution with two different modes. These appear as distinct peaks (local maxima) in the probability density function, as shown in Figure 2.11.1.

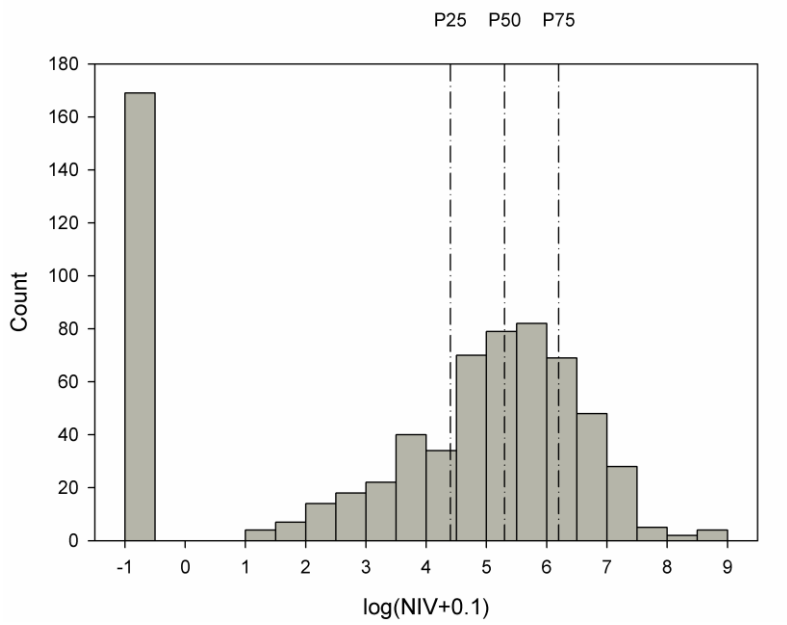


Figure 2.11.1: Transformed NIV for years 2000 to 2005. Sample size n = 701. Dash-dot lines indicate percentiles for the NIV > 0 distribution.

This bimodal distribution arises as a mixture of two different unimodal distributions; data for which NIV > 0, which are log-normally distributed (Kolmogorov-Smirnov test) and the others for which sales data = 0 (see Table 2.9.1). Descriptive statistics on the transformed scale are given in Table 2.12.1.

Table 2.12.1: Descriptive statistics for the NIV > 0 distribution (log transformed data)

Year	Sample size	Missing*	Range	Median	P25%	P75%
2000	152	48	1.5 to 8.0	5.4	4.7	6.1
2001	152	47	1.3 to 8.5	5.3	4.3	6.2
2002	152	47	1.3 to 8.5	5.3	4.6	6.1
2003	152	46	1.3 to 8.6	5.5	4.5	6.2
2004	152	16	1.6 to 8.6	5.3	4.4	6.2
2005	152	13	1.5 to 8.5	5.3	4.2	6.3

* Data not available and missing at random see Table 2.9.1

From these results, it appears that the differences in the median values among the “year groups” are not large enough to exclude that the difference is due to random variability. There is not a statistically significant difference among groups (Kruskal-Wallis, p = 0.454). Note that this does not mean that there are no systematic differences between year groups, only that they have not been demonstrated. Yet, as shown by Table 2.12.1 the proportion of missing data is far from being negligible, and may therefore affect the yearly trend of NIV.

To better appreciate risks within acceptable limits, transformed NIV results have been re-scaled (see Van Bol, 20070927 meeting report). We developed an algorithmic to address this task. The NIV data, which have been log transformed to obtain uniform variance, were rescaled according to the following "membership function":

$$NNIV = \begin{cases} 0 & if \quad \log(NIV) < 1.7 \\ 0.139 \cdot \log(NIV + 0.1) - 0.237 & if \quad 1.7 \le \log(NIV) < 8.9 \\ 1 & if \quad \log(NIV) \ge 8.9 \end{cases} \qquad (2.11.1)$$

Figure 2.11.2 illustrated the relationship between log(NIV + 0.1) and the NNIV. The LWL (lower warning limit) and UWL (upper warning limit) are calculated with robust statistics, and are not very sensitive to extreme values. For example, they are not affected by a value that lies beyond the lower and upper quartile ranges (Massart et al. 1997). Calculations are performed making use of the interquartile range (IQR):

$$\begin{cases} IQR = P75 - P25 \\ LWL = P25 - 1.5 \cdot IQR \\ UWL = P75 + 1.5 \cdot IQR \end{cases} \qquad (2.11.2)$$

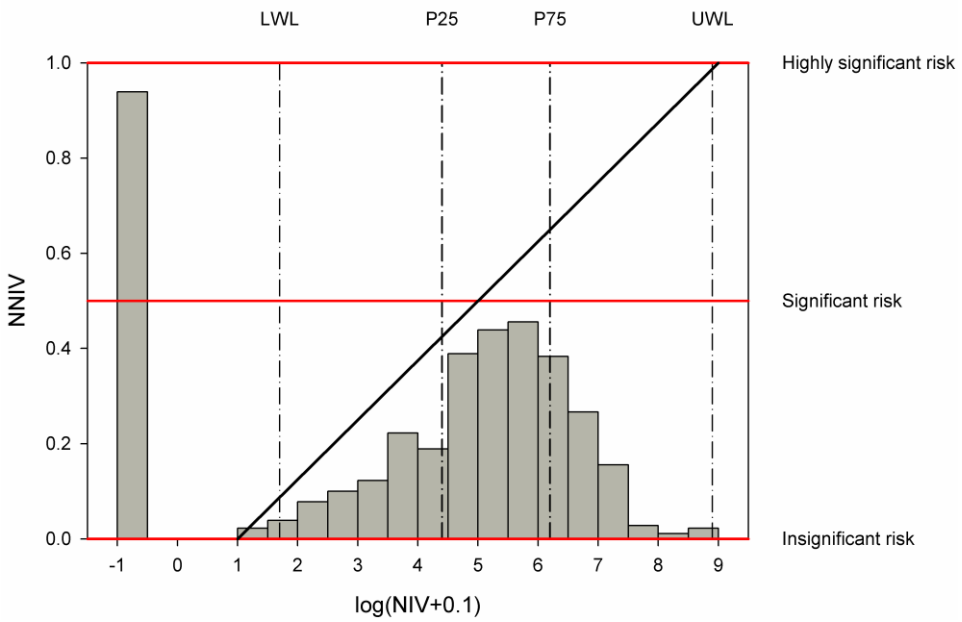


Figure 2.11.2: Rescaled NIV

The rescaling procedure allows us to use the Nijs algorithm as reference levels for the search of alternative indicators (see section 3). The normalisation implies that the range of the indicator response is restricted to lie between zero and one providing intuitive risk awareness: 0 ≤ NNIV ≤ 0.5 insignificant to significant risks; 0.5 < NNIV ≤ 1 significant to highly significant risks.

2.12 Unpredictability on NIV

As indicated in section 2.2, the variability / uncertainty dichotomy has become conventional in risk assessment (Sutter, 2007). The variability on NIV (log scale) is given by the inter-quartile

range (IQR) of the transformed distributions (see Table 2.12.1). We need to calculate the uncertainty by combining the uncertainty on the composite score function (see Figure 2.8.2, the right one) and on the sales data (see Table 2.10.1). The values are combined as relative standard uncertainties:

$$\frac{u(NIV)}{NIV} = \sqrt{\left(\frac{u(\Sigma\Pi z)}{\Sigma\Pi z}\right)^2 + \left(\frac{u(Q)}{Q}\right)^2} \tag{2.12.1}$$

The uncertainty on the log transformed scale (2.12.2) and rescaled NIV (2.12.3) can then be approximated using error propagation formulas based on a Taylor series expansion:

$$\begin{aligned} u(\log(NIV+0.1)) &= \frac{d(\log(NIV+0.1))}{dNIV} \cdot u(NIV) = 0.434 \cdot \frac{u(NIV)}{(NIV+0.1)} \\ &\approx 0.434 \cdot \sqrt{\left(\frac{u(\Sigma\Pi z)}{\Sigma\Pi z}\right)^2 + \left(\frac{u(Q)}{Q}\right)^2} \end{aligned} \tag{2.12.2}$$

$$u(NNIV) = \begin{cases} 0 & if \quad NNIV = 0 \\ 0.060 \cdot \sqrt{\left(\frac{u(\Sigma\Pi z)}{\Sigma\Pi z}\right)^2 + \left(\frac{u(Q)}{Q}\right)^2} & if \quad 0 < NNIV \leq 1 \end{cases} \tag{2.12.3}$$

The functional relationship between the uncertainty and NNIV (for all values > 0) was investigated according to the International Standard (ISO 5725-2: 1994). Two types of relationships have been considered:

- A straight line with a positive intercept
- An exponential type relationship

As shown in Figure 2.12.1, both relationships yield practically equivalent fits, and in such case the first relationship was preferred because of its simplicity

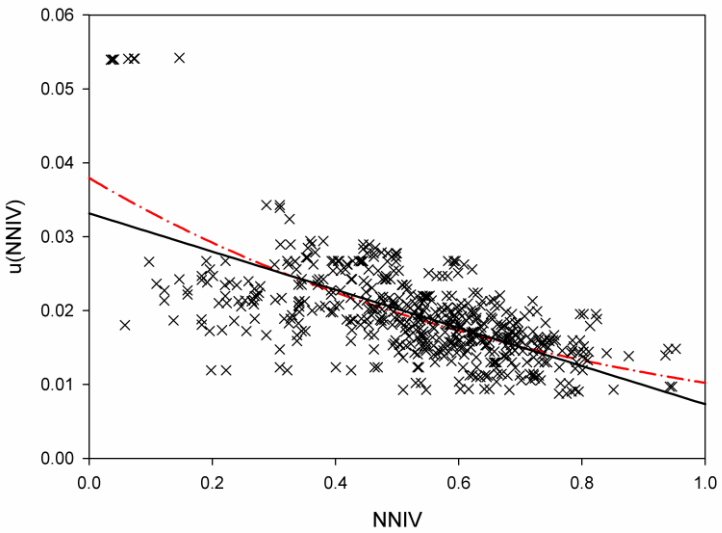


Figure 2.12.1: Functional relationship between precision (uncertainty) and NNIV (for all values > 0). Black solid line = straight line model; red dash-dot line = exponential model).

The fitted lines (regression coefficient ± SE) are given by:

$$u(NNIV) = (0.033 \pm 0.001) - (0.026 \pm 0.001) \cdot NNIV \qquad (2.12.4)$$

Transforming and rescaling data lead to an intuitive perception of the risk. The uncertainty (precision) on NNIV is rather satisfactory and much less than the variability observed for the whole PT18 biocide populations. This uncertainty quantification will enable us to perform significance tests, i.e. to decide whether the difference between indicator values in 2001 and other years can be accounted merely by chance or not (see section 2.13).

2.13 Significance tests

The NNIV data can also be used to illustrate how to calculate a significance test and its related uncertainty. As the term implies, this approach tests whether the difference between results for NNIV during years 2000 to 2005 are statistically significant. Yet, systematic differences between "year groups" could not be demonstrated comparing mean/median results because of the large population variance. These tests were apparently not "fit for purpose".

Risk aggregation can be calculated at different levels per individual products, per group of products (type of formulation, type of mitigating measures, range of active substance…) or for the whole population. For example, it is assumed that the total risk for the whole PT18 biocide population can be calculated as the sum of NNIV for each product during one year.

$$Risk_{PT18} = \sum_{i=1}^{n} NNIV_i \qquad (2.13.1)$$

From (2.12.4), the uncertainty on $Risk_{PT18}$ is then calculated according to:

$$u(Risk_{PT18}) = \begin{cases} 0 & if \quad Risk_{PT18} = 0 \\ 0.033 \cdot n - 0.026 \cdot Risk_{PT18} & if \quad Risk_{PT18} > 0 \end{cases} \qquad (2.13.2)$$

The NNIV data for years 2000 to 2005 are used to illustrate these calculations (Table 2.14.1).

Table 2.13.1: The aggregated NIJS risk for PT18 biocides

Risk	2000	2001	2002	2003	2004	2005
$Risk_{PT18}$ n	35 ± 2.5 104	41 ± 2.2 105	41 ± 2.4 105	42 ± 2.4 106	48 ± 3.2 136	48 ± 3.2 139
Averaged-$Risk_{PT18}$	0.34 ± 0.02	0.39 ± 0.02	0.39 ± 0.02	0.40 ± 0.02	0.35 ± 0.02	0.35 ± 0.02
Simulation experiment*	49 ± 3.1	58 ± 3.1	61 ± 3.2	62 ± 3.2	52 ± 3.4	54 ± 3.5

**In the simulation experiment, the missing data were replaced by the median NNIV-value of 0.5*

Significant difference between years will be observed whenever:

$$\left| Risk_{200x} - Risk_{200y} \right| > 2 \cdot \sqrt{u(Risk_{200x})^2 + u(Risk_{200y})^2} \qquad (2.13.3)$$

For example, the value calculated for years 2000 and 2005 (48 – 35 = 13) is greater than the expanded uncertainty (= 8.3) calculated using a coverage factor of 2, which gives a level of confidence of approximately 95% (EURACHEM/CITAC Guide, 2000).

Note that equation (2.13.3) is a generic test that can be used to compare individual products (one by one), group(s) of products or the whole population as shown in Table 2.13.1.

According to results of Table 2.13.1, there is a clear increasing risk trend from 2000 to 2005. It merely follows the number of product taken into account in the calculations (from 104 in 2000 to 139 in 2005). Yet this tendency is not supported by the "averaged risk", who does not exhibit statistically significant difference among year groups. As earlier mentioned, the proportion of missing data is far from being negligible, especially during 2001/02/03, and may therefore affect the yearly risk trend. In a simulation experiment, we substituted the "missing data" (md) by 0.5, which represents the median risk-value. Under these conditions, the risk increases dramatically for year 2001-03 and gradually decreases towards 2004-05.

Remark: The correlation matrix (Spearman Rank Order Correlation) indicates relative high correlation for pair of variables such as 2000/01; 2001/02; 2002/03; 2003/04; and 2004/05. This tendency to be alike in sequential data suggests serial dependence or autocorrelation.

Table 2.14.2: Spearman Rank Order Correlation for NNIV

	2001	2002	2003	2004	2005
2000	**0.742**	0.759	0.494	0.527	0.482
2001		**0.795**	0.512	0.510	0.504
2002			**0.788**	0.741	0.625
2003				**0.910**	0.768
2004					**0.824**

2.14 Summary and remarks

The methodology for the Nijs Algorithm was presented during the PRPB meeting of 01.02.07. It included the design of the indicator, the uncertainty and sensitivity analysis. Calculations were performed for biocides type EU-18, but can in principle be extended to other type products. The data are available in Excel spreadsheet (2010NIJSPT18.xls). Main criticisms concern scoring and exposure scenarios. For scoring, the question was raised whether or not is it relevant to strengthen chronic *versus* acute effects. With respect to exposure calculations, the lack of traceability was emphasised, especially regarding the distinction made between professional and non-professional use. Improvements were suggested and implemented in the next section (Proposal for biocide Indicator in BELgium-BIBEL).

3 Proposal for Blocides Indicator in BELgium (BIBEL)

3.1 General introduction

Within the framework of the HAIR project, Ghent University developed a set of indicators in order to assess the occupational risk to pesticides. The risk for human exposure and environment exposure is assessed by the use of risk indices. A risk index (RI) is the quotient of the estimated human exposure and a toxicological reference dose (AOEL, Acceptable Operator Exposure Level).

$$RI = \frac{Exposure}{Effect} \tag{3.1.1}$$

The global process of the assessment of risks to humans exposed to pesticides is represented in diagram form (Fig. 3.1.1.).

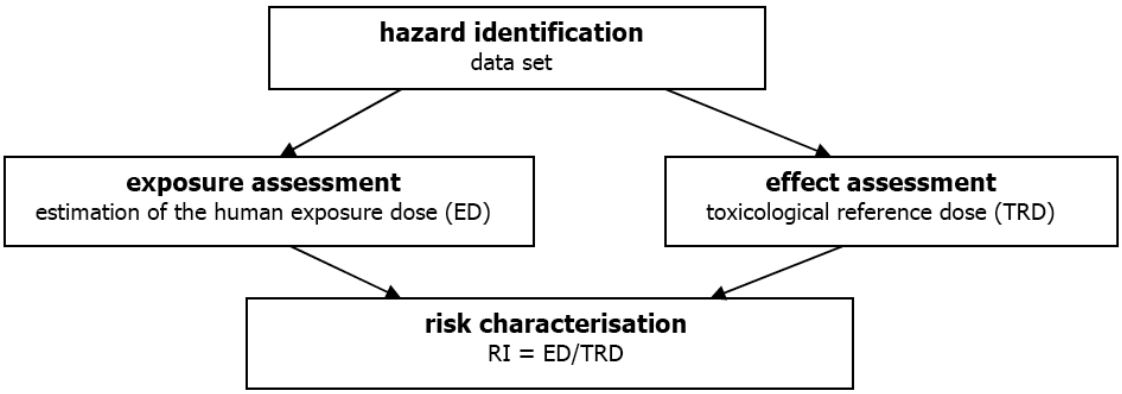


Figure 3.1.1: Risk evaluation of pesticides: principle for computing the worker indicators

This basic risk indicator corresponds closely to the first tier regulatory procedures approved by the European Union. The output of the Risk indices is expected to comply with the endpoints set in Annex VI of the European Union Directive 91/414 and the most recent Guidance document from the European Commission. It consists of

- Two parts: human exposure – environmental exposure
- Two levels: one single application – aggregation for Belgium

There are several possibilities to aggregate: single product – per group of products (type of formulations…) – for the whole population of PT18 biocides

Given the difficulty to define an Acceptable Operator Exposure Level (AOEL) for biocides, it was suggested to use a scoring approach similar to the one elaborated by E. Nijs (see also section 2).

3.2 Refinement of HumTox

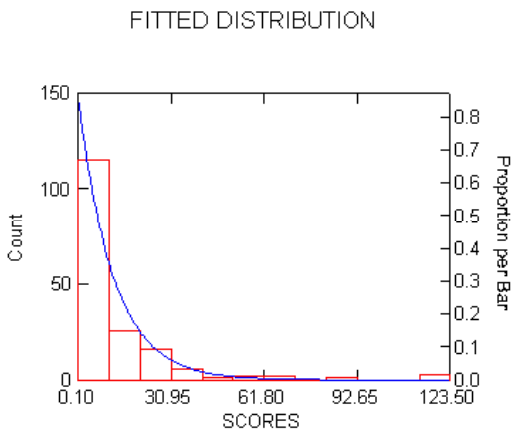
The initial scoring approach proposed by E. Nijs (PRPB meeting 01.02.07) was refined by the expert judgement of C. Vleminckx (PRPB meeting 03.05.07). The following scoring system was proposed (Table 3.2.1).

Table 3.2.1: R-phrases, scores, uncertainty and frequency distribution for the HumTox variable (PT18 biocides)

Code	R-phrases	Score	Uncert.	Freq. %
None	NC: not classified	0.1	-	34
None	R10: Flammable	1	0.1	7
F	R11: Highly flammable	1.5	0.2	1
F+	R15: Contact with water liberates toxic, extremely flammable gases	1.5	0.2	1
F+	R12: Extremely flammable	2	0.1	15
Xi	R36: Irritating to eyes	5	3	3
Xi	R38: Irritating to skin	5	3	5
Xi	R43: May cause sensitisation by skin contact	20	5	17
Xn	R20: Harmful by inhalation	20	5	1
Xn	R22: Harmful if swallowed	20	5	2
Xn	R40: Limited evidence of a carcinogenic effect	20	5	1
Xn	R65: Harmful: may cause lung damage if swallowed	20	5	4
Xn	R68: Possible risk of irreversible effects	20	5	1
C	R34: Causes burns	30	4	< 1
T	R24: Toxic in contact with skin	30	4	< 1
T	R25: Toxic if swallowed	30	4	< 1
T	R60: May impair fertility	30	4	1
T	R61: May cause harm to the unborn child	30	4	1
T+	R26: Very toxic by inhalation	40	2	2
T+	R28: Very toxic if swallowed	40	2	1
T+	R32: Contact with acids liberates very toxic gas	40	2	1

The frequency distribution function of HumTox can be approximated with an exponential distribution (Figure 3.2.1).

For the PT18 population, the median value for the relative uncertainty on HumTox is around 23%.



Descriptive statistics

Number of products	173
Minimum	0.1
Maximum	123.5
Median	2
First quartile (P25%)	0.1
Third quartile (P75%)	20
IQR (P75%- P25%)	19.9
P95%	45

Figure 3.2.1: Observed (bars) and fitted (line) distributions for HumTox.

3.3 Development of HumExp

The indicator for human exposure is based on the most recent Guidance document from the European Commission (TNsG, 2002) (Figure 3.3.1).

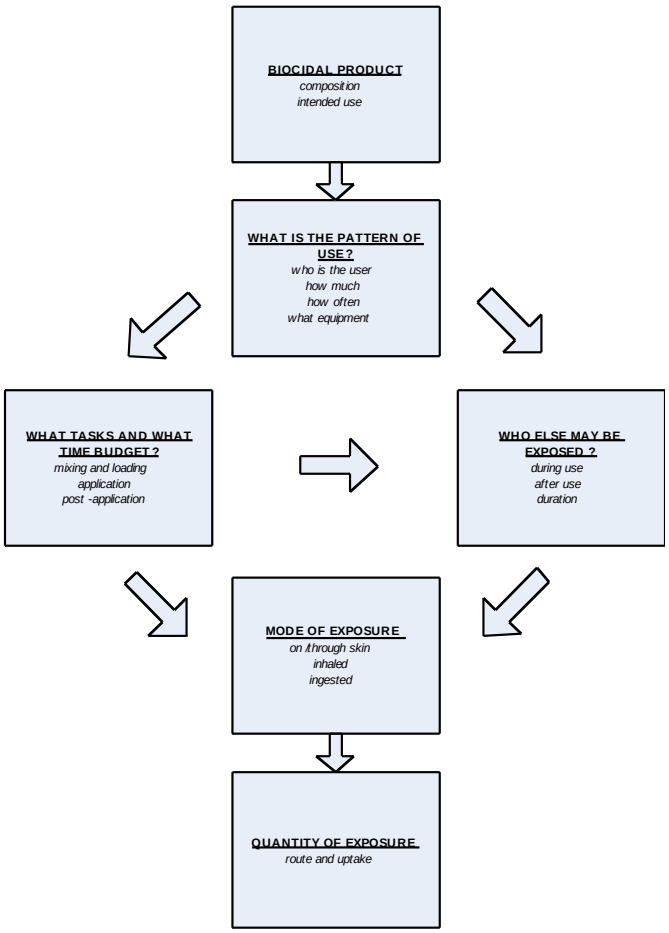


Figure 3.3.1: Scenario development based on the European Technical Notes for Guidance (TNsG).

3.4 Scenario development based on the European Technical Notes for Guidance (TNsG)

The principles for human exposure assessment are the development of a range of human exposure situations that could occur from the use of a biocidal product and to consider all routes of exposure. The exposure assessment process therefore requires determination of the patterns of use, identification of the exposed population, establishing the pathways of exposure and quantification of potential chemical intake. The following survey is a short overview of the approach applied in theTechnical Notes for Guidance on Human Exposure to Biocidal Products (TNsG, June 2002)

3.4.1 Patterns of Use

The patterns of use form the basis of exposure assessments and their information is essential to ascertain how exposure will arise and to whom it will occur. Information on the pattern of use can only be gathered through surveys or generic data from similar products.

The TNsG include a matrix to inform the collection of pattern of use information and also sets out default patterns of use for most of the professional and consumer biocidal products.

The pattern of use information is used to develop exposure scenarios, which are then evaluated to derive quantitative exposure estimates. The essential pattern of use information required for deriving exposure scenarios include information on:

- The product (physical state, concentration, vapour pressure)
- Where and how the product will be used (location, method of application)
- By whom the product will be used (primary exposure)
- Tasks, frequency and duration for each stage of use
- Expected exposure controls
- Who else may be exposed (secondary exposure)

3.4.2 Exposed Populations

Humans may be exposed to biocidal products in the workplace, from the use of consumer products and indirectly via the environment. The exposure assessment process therefore requires determination of the patterns of use, identification of the exposed population, establishing the pathways of exposure, quantification of potential exposure, and estimation of systemic intake. The first step in the exposure assessment process is to determine the likelihood of exposure of the various populations to the biocidal product under consideration. If this initial screening step indicates that exposure to one or more of the human populations do not occur, no further assessment is needed and the conclusion can be mentioned in the risk assessment phase. If potential exposure has been identified, a quantitative exposure assessment will be required.

The exposed human populations can be categorised by the nature of the exposure i.e. primary exposure and secondary exposure. Primary exposure to biocidal products occurs to the individual who actively uses the products containing biocides i.e. the user. Secondary exposure occurs to non-users or bystanders; these are individuals who do not actively use the biocidal products but are indirectly exposed to biocides released during or after product use by another person (the user). It is important to note that the user of a product may be subject to both primary and secondary exposure whereas the non-user or bystander will only experience secondary exposure. Primary exposures are invariably higher than secondary exposures, however, some specific subgroups of the population may experience higher secondary exposures because of their specific behaviour (e.g. children crawling on the floor). In addition, secondary exposure can be experienced over a much longer time-period than primary exposure, particularly for persistent products.

3.4.3 Primary exposure group

The primary user group is relatively simple to identify. Primary exposure is that of the user performing the task. The user may be a professional at work or a non-professional. Professional users differ from non-professional users in a number of aspects and a distinction between the two is necessary in exposure assessments.

Professional users

The professional user is subject to worker protection legislation and has residual risk controlled through control measures which may include the use of Personal Protective Equipment (PPE) if that is necessary for the normal work. Some professional users will have limited knowledge and skills to handle hazardous biocidal products - particularly if the use of biocidal products is not routinely required in the workplace (e.g. incidental use of insecticides PT18 or wood treatment products PT8, etc.). There are also specialised professional users, who will probably have expert knowledge and skill in handling hazardous biocidal products and their pattern of use will show greater frequency and/or duration of use.

Non-professional users (consumers)

The non-professional user is the consumer, i.e. a member of the general public who may primarily be exposed to biocides by using a consumer product. The consumer is unlikely to take informed measures to control exposure and to exactly follow the description of use. In addition, the non-professional pattern of use is expected to show lesser frequency and/or duration of use.

The consumer exposure assessment should normally address the intended uses of the product. However, since consumers may not accurately follow instructions for use of products or articles, a separate assessment of other reasonably foreseeable uses should be made. For example, consumers will experience relatively high exposures when they use biocidal products in poorly vented indoor areas. When use under these circumstances is foreseeable, an exposure assessment for this situation should be carried out.

Another important aspect of consumer practice is the very limited use of PPE to control exposure. Consumers will not normally use PPE unless it is convincingly recommended by the

manufacturer and provided with the product. As a result only typical clothing should be assumed when carrying out consumer exposure assessments.

3.4.4 Secondary exposure group

The groups at risk through secondary exposure are less easy to identify. However, the intended location of use (e.g. indoors, outdoors, industrial, residential recreational) will provide useful indicators. The location of use will help to determine the population (e.g. ancillary workers, general public, residents/children) at potential risk through secondary exposure and suggest the frequency/duration of exposure as well as their exposure routes.

Some individuals may be exposed to higher concentrations than others because of differences in their behaviour and physiological parameters. Young children, for instance, may be exposed to higher levels than adults due to their distinct (hand to mouth or crawling) behaviour and relatively lower body weights. The exposure scenarios therefore need to take such factors, specific to the exposed sub-population, into consideration.

3.4.5 Pathways of Exposure

Human exposure follows through any or all of three potential exposure routes: inhalation, dermal contact and ingestion. The second step in the exposure assessment process is therefore to determine the likelihood of the biocides to enter the body by being breathed in (inhalation), by passing through the skin (dermal), or swallowing (ingestion). If in this second step it is indicated that exposure via one or more of the pathways does not occur, no further assessment is needed for that route of exposure and the conclusion can be mentioned in the risk assessment phase. Where one or more routes of exposure have been identified then each will require a quantitative exposure assessment.

The ultimate choice of exposure estimates should be made on the basis of the robustness/representativeness of the measured and/or modelled data for the situation/use scenario/conditions under consideration. This will require substantial expert judgement and should always be based on reasoned arguments.

Inhalation exposure is often a small component of total exposure to biocides but can in some cases become the predominant route of exposure (e.g. use of a volatile material in an enclosed space). Inhalation exposure is usually derived from the airborne concentration of the breathing zone of the exposed individual. It may refer to the active substance or to the product in use and is expressed as mg/m^3 as a time weighted average concentration over a stipulated period of time.

3.4.5.1 Dermal exposure

Exposure of and via the skin is usually a significant aspect of human exposure to biocides and can be subdivided into potential or actual dermal exposure. Potential dermal exposure is the amount that deposits on the clothes and on exposed skin over some defined period of time. The

most common metric for measurement for biocides is the amount of biocide product that deposits per unit time (mg/min) or task (mg/cycle). Actual dermal exposure is an estimate of the amount of contamination that actually reaches the skin. It is dependent on the efficiency and effectiveness of clothing and is often expressed simply as a weight of biocide product on skin (mg on skin).

3.4.5.2 Ingestion exposure

This is the amount entering the mouth other than that which is inhaled. There are no standard methods for quantifying exposure by ingestion but it can be inferred from biological monitoring studies. It is expressed as mg per event or mg/day.

3.4.5.3 Systemic exposure

The estimates of exposure, via the three routes, outlined above relate to external exposure i.e. the amount of the substance ingested, the amount in contact with the skin and/or the amount inhaled. For risk characterisation purposes it is necessary to calculate internal (systemic) body burdens from these values. This conversion is based on the selection and use of a variety of physiological default values (body weight, breathing rate etc) for specific situations. In addition, absorption data for the different routes of exposure are often not available. Therefore the calculation of systemic body burdens is subject to a high degree of uncertainty and requires expert judgement. In a first approach worst case default values are used (such as 100% for inhalation exposure; 10% for dermal exposure, etc.)

3.4.6 Quantifying Human Exposure

The pattern of use information is used to identify the range of possible exposure scenarios, which are then evaluated to derive quantitative exposure estimates. An exposure scenario is the set of information and/or assumptions that tell us how the contact between the person and the biocide takes place. It describes a specific use of a substance with a set of specific parameters, which characterise the biocidal product's uses and the control measures.

The exposure scenarios for exposure estimation must be well-documented, realistic and, in the absence of good data, work on reasonable worst cases. Although all exposure scenarios that are reasonably foreseeable must be assessed, exposure as a result of accidents or from abuse does not need to be included.

3.4.6.1 Primary exposure scenarios

Primary exposure is experienced by professionals and non-professionals (consumers) who use/apply a biocidal product. It is related to the task and the overall exposure scenario will consist of a series of tasks that can be allocated to 3 distinct phases of use:

- Mixing & loading	Include the tasks involved in delivery and handling of bulk ready-for-use and concentrate products, dilution of concentrates and/or the introduction of product to the application apparatus/system.
- Application	Involves all uses of biocidal products, including application by hand, by hand-held tool, by dipping, by spraying, handling treated articles, and in machining. This phase of use can lead to the exposure of people who are present during the product application (secondary exposure).
- Post-application	Includes exposure through separately cleaning and maintaining process equipment and tools.

The contribution to each route of exposure may vary considerably between these phases with any given active substance, given that mixing and loading can reflect exposure to a concentrate, application to a dilute product, post-application to vapour or dried residue and removal to waste material (e.g. removing and disposing of a preserved coating). In practice, exposure data often relates to full-shift sampling and therefore includes all three phases of use. However, it is important to ensure that each phase of use has been accounted for in the exposure assessment.

3.4.6.2 Secondary exposure scenarios

Secondary exposure is all that is not primary and describes the exposure of people who receive a dose of a biocide through being present during an application task (performed by another person) or being present in places where a biocide had been applied or during use/handling of materials treated with biocidal products. These exposures can include dermal contact of contaminated surfaces, inhalation of residues in air and ingestion from hand to mouth contact. A key feature is that secondary exposure occurs without the exposed person being aware or having control over that exposure and the exposure can occur over a long time period.

A tasked based approach does not apply to secondary exposure assessments, as there are no well-defined tasks for the post use situation. Instead, a reference scenario approach is proposed for estimating secondary exposures. It is important to note that both acute (short-term) and chronic (long-term) exposure potential needs to be considered when developing secondary exposure scenarios

Using the pattern of use information, it is possible to ‘invent’ reasonably foreseeable exposure scenarios that will involve reasonable worst case for secondary exposures of adults and children through inhalation, via the skin and ingestion. These scenarios are termed “Reference Scenarios” and examples of possible Reference Scenarios are presented in Part 2 and Part 3 of the TNsG.

3.4.6.3 Evaluating exposure scenarios

Having established the relevant exposure scenario(s) the next step is to identify the tasks that need to be considered as well as the approximate time budgets for each task. Task analysis will then lead to the identification of suitable exposure data that can be used to calculate the potential exposure for the proposed use based on the time budget information.

3.4.7 Exposure Data

In addition to the pattern of use information, which is used to describe the nature of human exposure there is a need for quantified exposure data to allow estimates of exposure to be calculated. In view of the uncertainties associated with assessing exposure in human populations, preference should always be given to obtaining good representative measured exposure data. Where this is unavailable, it will be necessary to model exposure using generic (analogous/surrogate) data or mathematical models.

Generic exposure data describes measured exposure data from similar operations utilising similar biocidal products. The data is collected from exposure surveys of worker or, in the case of consumers, from simulation studies using analogous products. This data is used to develop simple (generic) database exposure models for particular product types and specific use scenarios.

Generic exposure modelling is a useful regulatory tool in this scheme because of the capability to predict the likely levels of occupational exposure of users of biocides before widespread use and for the ability to estimate the effect of changes in conditions of use on exposure. Where representative generic data and a suitable model exist modelling is the initial and often the only basis for the exposure assessment. Generic exposure models may also be used instead of or as well as exposure data for the specific product if there is significant uncertainty associated with the quality and/or quantity of this data.

The TNsG have collated the available generic models that are considered adequate for human exposure assessment to biocides. These models, for exposure assessment, are based on databases of relevant studies representative of particular biocidal use areas. The ultimate choice of exposure estimates should be made on the basis of the robustness/representativeness of the measured and/or modelled data for the situation/use scenario/conditions under consideration. This will require substantial expert judgement and should always be based on reasoned arguments.

Based on these assumptions, following stepwise procedure is used;

- Selection of appropriate model in TGsN (ex. CSDM1;1)
- Selection of default values from model: percentile, body weight, respiration rate,
- Selection of variable default values in function of:
    - Amateur versus professional
    - RMM (Risk management measures e.g. protective equipment, …

- Expressed as product (not as active substance)

The evaluation scores allocated to the data depending on their quality are summarized in Table 3.4.7.1

Table 3.4.7.1: Criteria evaluation scores of the data quality

Score	Value
9	Ample and good quality data
8	Good quality data
7	Quality and number of studies satisfactory
6	Usable, but open for improvement
5	Little data, parameter value is usable as default value
4	Single data source supplemented with expert judgement, parameter value doubtful as default value
3	Single data source supplemented with expert judgement, parameter value not reliable as default value
2	Educated guess from similarities with other products
1	Educated guess, no data

3.4.8 Survey of exposure scenario's for PT18

3.4.8.1 Consumer spraying and dusting

In the TNsG on the human exposure to biocide products, the "Consumer Spraying and Dusting model (CSDM)" is used for calculating human exposure during the application of aerosols, triggers and dusting powders by non-professionals. Those products are mainly used to kill crawling and flying insects in and around the house.

In general, the use of this type of products will be limited to the actual control of any plague, that is, the product will not be used if there are no pests. Therefore, it is expected that the use of the products mainly take place in the summer months (+/- 3 months per year), since it is usually in this period that invertebrates appear.

A distinction is made between the large group of products, based on the method of application and the formulation of the product (Figure 3.4.8.1.1):

- ***Space spraying***

This includes non-professional space spraying insecticides in a small sealed room with trigger spray (or pumped sprays) or aerosol cans. It is supposed that the user stands in the middle of the room and sprays upwards towards the corners of the room during a few seconds. The products are ready-to-use, so no dilution or other pre-use actions (mixing/loading) are necessary.

The exposure occurs at the moment of application. Small droplets are formed which fall down on the skin (dermal exposure) or which can be inhaled (inhaling exposure). After application, it is supposed that the room is ventilated before re-entering. Secondary exposure occurs when children play on the floor of the treated room. Part of the spray cloud will fall from the air and will reach the ground.

- **Surface (or targeted spot) spraying**

This includes non-professional surface spraying insecticides, indoors, on soft furnishings, carpets, skirting boards and shelves with dust applicators, trigger sprays and aerosol cans. Models are derived from simulated volunteer studies:

- Crack and crevice treatment for ants in a kitchen (skirting, shelves, horizontal laminate floors) using a fine powder and broadcast flea treatment (carpet) using coarse granules
- Crack and crevice treatment (skirting, shelves, horizontal/vertical laminate surfaces) using ready for use liquid spray
- Broadcast treatment of small room (sofa, skirting dining chairs and carpet) using liquid spray

This scenario is based on a private user who sprays an object from close by. It is also assumed that the spraying is carried out indoors. Targeted spot treatment can take place anywhere in the house, per target. This will often involve plants on the window, sill in the living room, …, but also treating the cat in the kitchen or spraying an ant trail along the window or behind the refrigerator falls in this category.

Opposite to space spraying, surface spraying is (mostly) a downward spraying on a small surface. Dermal and inhaling exposures are to be considered together with secondary exposure for children playing on the treated surface.

Figure 3.4.8.1.1: Pictures of some consumer spraying and dusting products

Table 3.4.8.1.1: Selected model depending on the application model (source : TNsG)

Selected models	Application Method	Indicative Exposures	Uncertainty
Non-professional **space spraying** insecticide in a small room with trigger sprays, pumped sprayers and aerosol cans. *Consumer Spraying and Dusting Model 1 TNsG part 2, p 194*	CSDM1;1 Hand-held trigger sprayer	Hand/forearm 136 mg/min Legs/feet/face 42.4 mg/min Inhalation 90.2 mg/m^3	Uncertainty is *moderate.* 90% C.I. for 75th are 95-194 (hands), 22-82 (legs), 69-118 (inhalation).
	CSDM1;2 Hand-held pumped spray	Hand/forearm 98.4 mg/min Legs/feet/face 22.7 mg/min Inhalation 76.3 mg/m^3	Uncertainty is *moderate.* 90 % C.I. for 75th are 36-271 (hands), 19-28 (legs), 65-90 (inhalation).
	CSDM1;3 Aerosol can	Hand/forearm 156 mg/min Legs/feet/face113 mg/min Inhalation 234 mg/m^3	Uncertainty is *moderate.* 90 % C.I. for 75th are 114-214 (hands), 83-153 (legs), 175-312 (inhalation).
Non-professional **surface spraying** insecticide, indoors, on soft furnishings, carpets, skirting boards and shelves with dust applicators trigger sprays and aerosol cans *Consumer Spraying and Dusting Model 2 TNsG part 2, p 197*	CSDM2;1. Hand-held flexible duster CSDM2;1dc = dogs and cats CSDM2;1i = crawling insects CSDM2;1a = ants	Hand/forearm 2.73 mg/min Legs/feet/face 2.74 mg/min Inhalation 2.47 mg/m^3	Uncertainty is *moderate.* 90 % C.I. for 75th are 1.9-3.9 (hands), 1.7-4.4 (legs), 1.5-4.2 (inhalation).
	CSDM2;2. Hand-held trigger spray	Hand/forearm 36.1 mg/min Legs/feet/face 9.7 mg/min Inhalation 10.5 mg/m^3	Uncertainty is *moderate.* 90 % C.I. for 75th are 26-50 (hands), 7.6-12.4 (legs), 9.0-12.2 (inhalation).
	CSDM2;3. Pre-pressurised aerosol spray can	Hand/forearm 64.7 mg/min Legs/feet/face 45.2 mg/min Inhalation 55.9 mg/m^3	For hands and inhalation uncertainty is *moderate.* 90 % C.I. for 75th are 37-114 (hands), 31-43 (inhalation). Uncertainty for legs is *high* – highest exposure out of 6 used.

PRIMARY EXPOSURE Spraying and Dusting

$$EXP_{primary} = EXP_{dermal1} + EXP_{inhalatory1} + EXP_{oral1} \quad (mg\ kg^{-1}\ d^{-1})$$

Dermal exposure ($EXP_{dermal1}$)

$$EXP_{dermal1} = \frac{(X_{body} * RP_{clothes} + X_{hands} * RP_{gloves} + X_{feet} * RP_{shoes}) * N_{day} * T_{appl}}{BW}$$

where:

X_{body}	= product on body rate (mg min^{-1})
X_{hand}	= product on hand rate (mg min^{-1})
X_{feet}	= product on feet rate (mg min^{-1})
$RP_{clothes}$	= relative penetration of clothes (%)
RP_{gloves}	= relative penetration of gloves (%)
RP_{shoes}	= relative penetration of shoes (%)
N_{day}	= number of applications per day (d^{-1})
T_{appl}	= duration of 1 application (min)
BW	= body weight (kg)

Inhalatory exposure ($EXP_{inhalatory1}$)

$$EXP_{inhalatory1} = \frac{X_{inhal} * RP_{mask} * RR * T_{appl} * N_{day}}{BW}$$

where:

X_{inhal}	= product in air concentration (mg m^{-3})
RP_{mask}	= relative penetration of protective mask (%)
RR	= respiratory rate (m^3 min^{-1})
T_{appl}	= duration of 1 application (min)
N_{day}	= number of applications per day (d^{-1})
BW	= body weight (kg)

Oral exposure (EXP_{oral1}) Negligible

<u>SECONDARY EXPOSURE Spraying and Dusting</u>

$EXP_{secondary} = EXP_{dermal2} + EXP_{inhalatory2} + EXP_{oral2}$ (mg kg^{-1} d^{-1} m^{-2})

$$EXP_{dermal2} = \frac{(T_{appl} / A_{room}) * R_{product} * F_{accumul} * F_{deposit} * F_{dislodg} * TC * T_{exp}}{A_{child} * BW_{child}}$$

Dermal exposure ($EXP_{dermal2}$)

where:

T_{appl}	= duration of 1 application (min)
$R_{product}$	= amount of product released per time unit (g min^{-1})
$F_{accumul}$	= accumulation rate (-)
$F_{deposit}$	= amounted of sprayed volume deposited on the floor (%)
$F_{dislodg}$	= amount of product that is dislodgeable (%)
TC	= transfer contact surface (m^2 h^{-1})
T_{exp}	= exposure time (h d^{-1})
A_{child}	= body contact area (m^2)
BW_{child}	= body weight child (kg)
A_{room}	= surface room (m^2)

Inhalatory exposure ($EXP_{inhalatory2}$): Negligible

Oral exposure (EXP_{oral2})

$$EXP_{oral2} = EXP_{dermal2} * T_{hand-mouth}$$

where: $EXP_{dermal2}$ = secondary dermal exposure (mg kg^{-1} d^{-1} m^{-2})

$T_{hand-mouth}$ = transfer coefficient hand – mouth (%)

DEFAULT VALUES Spraying and Dusting

Table 3.4.8.1.2: Default value for each parameter in the formulae and for different TNsG scenarios

Scenario *		CSDM 1;3	CSDM**** 2;1dc 2;1i 2;1a	CSDM 1;1	CSDM 2;2	CSDM 2;3	*Q***
X_{body}	mg min^{-1}	113	2.74	42.4	9.7	45.2	*na*
X_{hand}	mg min^{-1}	156	2.73	136	36.1	64.7	*na*
X_{feet}	mg min^{-1}	0	0	0	0	0	*na*
X_{inhal}	mg m^{-3}	234	2.47	90.2	10.5	35.9	*na*
$RP_{clothes}$	%	50	$50/10^{p}$	50	50	50	*na*
RP_{gloves}	%	100	$100/10^{p}$	100	100	100	*na*
RP_{shoes}	%	50	$50/10^{p}$	50	50	50	*na*
RP_{mask}	%	100	100	100	100	100	*na*
RR	m^3 min^{-1}	0.0208	0.0208	0.0208	0.0208	0.0208	
N_{day}	d^{-1}	1	$1/8^{p}$	1	1	1	
T_{appl}	min	0.33	5	4	4	10	*6/4/6/6/6*
BW	kg	65	65	65	65	65	*9*
$R_{product***}$	g min^{-1}	20	12	21	39	39	*6/4/6/6/6*
$F_{accumul}$	-	4	1	1	1	1	*na*
$F_{deposit}$	%	100	100	100	100	100	*na*
$F_{dislodg}$	%	30	30	30	30	30	*na*
TC	m^2 h^{-1}	0.6	0.6	0.6	0.6	0.6	*na*
T_{exp}	h d^{-1}	1	1	1	1	1	*6*
A_{child}	m^2	0.45	0.45	0.45	0.45	0.45	*7*
BW_{child}	kg	10	10	10	10	10	*9*
$T_{hand-mouth}$	%	10	10	10	10	10	*na*
A_{room}	m^2	22	1	2	2	22	*9/5/6/6/9*

(*) Consumer Spraying and Dusting Models : see table 3.4.8.1.1. (**) Quality of data : see table 3.4.7.1. (***) Source: Pest Control Products Fact Sheet, RIVM-report 613340 003/2002. (****) Second values indicated with “p” are the default values for professional use

3.4.8.2 Electrical Evaporator

(Source: Pest Control Products Fact Sheet, RIVM-report 613340 003/2002)

Electrical evaporators are used to kill insects, in particular flies and mosquitoes. An electrical evaporator is plugged into an electrical socket; the solvent and active ingredients are heated, resulting in evaporation. Once in the colder air of the room, the solvent condenses and the active ingredient almost immediately and completely turns into droplets, which rise to the ceiling due to the warmer air (e.g. Matoba *et al.* (1994) calculated that 12 hours after the start of the

application, the amount of pyrethroid on the floor and on the walls was approximately 0.01% of the amount that was present on the ceiling, and was approximately 1% of the amount in the air).

Figure 3.4.8.2.1: Pictures of electrical evaporators

The assumption here is that the active ingredients used in an electrical evaporator at room temperature are negligibly volatile. The active ingredient will only be evaporated slowly due to heating.

The equipment is mainly used in the evening in a bedroom. The calculations are based on the application of an electrical evaporator in a bedroom for 8 hours a day for 5 month per year. With regard to the exposure after application, a child (10.5 months) is assumed who crawls over the floor for 1 hour a day.

PRIMARY EXPOSURE Electrical Evaporator

$$EXP_{primary} = EXP_{dermal1} + EXP_{inhalatory1} + EXP_{oral1} \quad (\text{mg kg}^{-1}\ \text{d}^{-1})$$

Dermal exposure ($EXP_{dermal1}$): Negligible

Inhalatory exposure ($EXP_{inhalatory1}$)

$$EXP_{inhalatory1} = \frac{C_{room} * T_{appl} * RR * N_{day}}{BW_{child}}$$

where: C_{room} = concentration of product in the room (mg min^{-1})

$$= \frac{R_{product} * T_{appl}}{V_{room}}$$

$R_{product}$ = amount of product released per time unit (mg min^{-1})

T_{appl} = duration of 1 application (min)

V_{room} = room volume (m³)
RR = respiratory rate (m³ min^{-1})
T_{appl} = duration of 1 application (min)
N_{day} = number of applications per day (d^{-1})
BW_{child} = body weight child (kg)

Oral exposure (EXP_{oral1}): Negligible

SECONDARY EXPOSURE Electrical evaporator

$$EXP_{secondary} = EXP_{dermal2} + EXP_{inhalatory2} + EXP_{oral2} \text{ (mg kg}^{-1}\text{ d}^{-1}\text{)}$$

Dermal exposure ($EXP_{dermal2}$)

$$EXP_{dermal2} = \frac{(C_{room} / A_{room}) * F_{accumul} * F_{deposit} * F_{dislodg} * TC * T_{\exp}}{A_{child} * BW_{child}}$$

where: C_{room} = concentration of product in the room (mg min^{-1})

$$= \frac{R_{product} * T_{appl}}{V_{room}}$$

A_{room} = surface room (m^2)
$F_{accumul}$ = accumulation rate (-)
$F_{deposit}$ = amounted of sprayed volume that is deposited on the floor (%)
$F_{dislodg}$ = amount of product that is dislodgeable (%)
TC = transfer contact surface (m² h^{-1})
T_{exp} = exposure time (h d^{-1})
A_{child} = body contact area (m²)
BW_{child} = body weight child (kg)

Inhalatory exposure ($EXP_{inhalatory2}$): Negligible

Oral exposure (EXP_{oral2})

$$EXP_{oral2} = EXP_{dermal2} * T_{hand-mouth}$$

where: $EXP_{dermal2}$ = secondary dermal exposure (mg kg^{-1} d^{-1})

$T_{hand-mouth}$ = transfer coefficient hand – mouth (%)

DEFAULT VALUES Electrical evaporator

Table 3.4.8.2.1: Default value for each exposure parameter in the formulae

			*Q**
$R_{product}$	mg min^{-1}	1.3	*6*
T_{appl}	Min	480	*5*
V_{room}	m^3	16	*9*
RR	m^3 min^{-1}	0.00208	
N_{day}	d^{-1}	1	*5*
BW_{child}	Kg	10	*9*
$F_{accumul}$	-	4	*na*
$F_{deposit}$	%	1	*na*
$F_{dislodg}$	%	30	*6*
TC	m^2 h^{-1}	0.6	*6*
T_{exp}	h d^{-1}	1	
A_{child}	m^2	0.45	*7*
$T_{hand\text{-}mouth}$	%	10	*na*
A_{room}	m^2	7	*9*

*see table 3.4.7.1.

3.4.8.3 Evaporation from strips and cassettes

(Source: Pest Control Products Fact Sheet, RIVM-report 613340 003/2002)

Biocides that evaporate from strips and cassettes are mainly used to control moths, carpet beetle larvae and flying insects. The active substance is trapped in a solid matrix, paper or plastic strip or is present in cassettes (Figure 3.4.8.3.1).

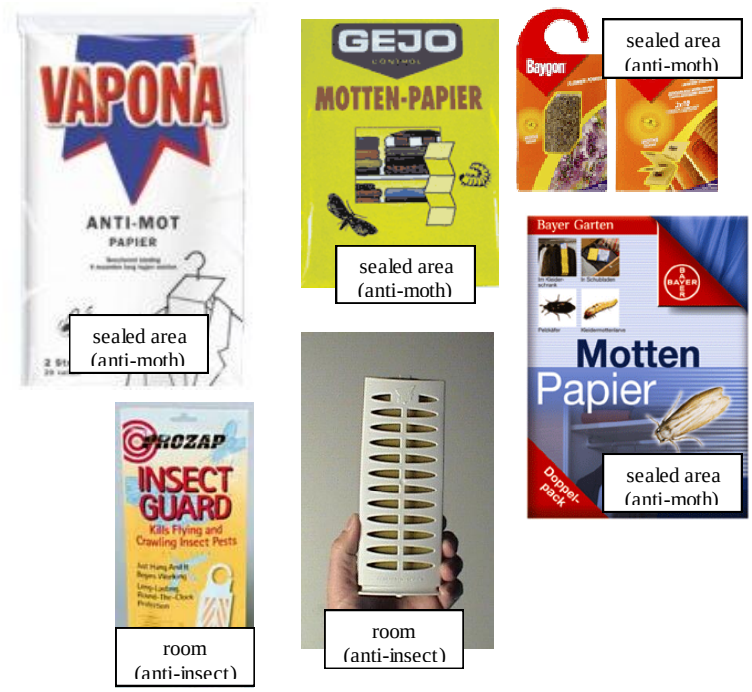


Figure 3.4.8.3.1: Pictures of strips and cassettes

The products can be split in two groups, depending on the exposure:

- Products for use in a small “sealed” area (closet/trunk/suitcase). The insecticide evaporates slowly and spread throughout the small area
- Products for use in a room. This mainly concerns products to control flying insects.

In all cases, the product is sealed until the moment of use; evaporation of the product starts when it is opened.

In the first application group, the two subcategories listed below can be distinguished with regard to the exposure.

- Moth paper supplied in the form of individual sheets. In general, these sheets are sufficient for an area of approximately 1 m³ and must be cut into pieces for smaller areas such as a closet or suitcase.
- Strips pieces of paper or plastic strips that are ready-to-use and supplied in a cassette from which you can take as much as you want. There are also cassettes that should be hung in the closet after opening, in their entirety.

The second application group is in the form of strips and cassettes, both of which are used in a room to control flying insects. The product is hung in a room and the insecticide is supposed to get into the air of the whole room. In this way, all people present in the room are continuously exposed.

Table 3.4.8.3.1: exposure scenarios for strips and cassettes

exposure	**sealed area**		**room**
	paper strips	**strips/cassettes**	**cassettes**
Mixing/loading			
Dermal	contact duration = time of folding, cutting, positioning	short (hanging up the strip)	not applicable
Inhalatory	evaporation in preparatory stage	evaporation in preparatory stage	
Application			
Dermal	not applicable		not applicable
Inhalatory	- the saturated air in small sealed areas results in a brief high concentration - leakage from the sealed area		long term contact
Oral	not applicable		food
After application			
	not applicable		not applicable

PRIMARY EXPOSURE Strips and Cassettes

$$EXP_{primary} = EXP_{dermal1} + EXP_{inhalatory1} + EXP_{oral1} \quad (mg\ kg^{-1}\ d^{-1})$$

Dermal exposure ($EXP_{dermal1}$)

$$EXP_{dermal1} = \frac{C_{strip} * T_{strip-hand} * N_{day}}{BW}$$

where: C_{strip} = amount of product in the strip/cassette/paper (mg)
N_{day} = number of applications per day (d^{-1})
$T_{strip\text{-}hand}$ = transfer coefficient strip/cassette/paper – hand (%)
BW = body weight (kg)

Inhalatory exposure ($EXP_{inhalatory1}$)

$$\frac{C_{strip} * T_{appl}}{Rt * V_{room}}$$

where: C_{room} = concentration of product in the room (mg m^{-3})
$$= \frac{C_{strip} * T_{appl}}{Rt * V_{room}}$$
C_{strip} = amount of product in the strip/cassette/paper (mg)
T_{appl} = duration of 1 application (min)
Rt = release time of the strip/cassette/paper (min)
V_{room} = room volume (m^3)
RR = respiratory rate (m^3 min^{-1})
T_{appl} = duration of 1 application (min)
N_{day} = number of applications per day (d^{-1})
BW = body weight (kg)

Oral exposure (EXP_{oral1}) : Negligible

<u>SECONDARY EXPOSURE Strips and Cassettes</u>

$$EXP_{secondary} = EXP_{dermal2} + EXP_{inhalatory2} + EXP_{oral2} \text{ (mg kg}^{-1}\text{ d}^{-1}\text{)}$$

Dermal exposure ($EXP_{dermal2}$): Negligible

Inhalatory exposure ($EXP_{inhalatory2}$)

$$EXP_{inhalatory2} = \frac{C_{room2} * RR_{child} * T_{exp} * N_{day2}}{BW_{child}}$$

where: C_{room2} = concentration of product in the room (mg m^{-3})
$$= \frac{C_{strip} * T_{appl}}{Rt * V_{room2}}$$
C_{strip} = amount of product in the strip/cassette/paper (mg)
T_{appl} = duration of 1 application(min)
Rt = release time of the strip/cassette/paper (min)
V_{room2} = room volume (m^3)
RR_{child} = respiratory rate child (m^3 min^{-1})
T_{exp} = exposure duration(min)
N_{day2} = number of applications per day (d^{-1})
BW_{child} = body weight child(kg)

Oral exposure (EXP_{oral2}) (! Only in case of “room” application !)

$$EXP_{oral2} = \frac{C_{strip} * I_{food}}{Rt * \rho_{food} * BW}$$

where:

C_{strip}	= amount of product in the strip/cassette/paper (mg)
I_{food}	= food intake child (kg)
Rt	= release time of the strip/cassette/paper (min)
ρ_{food}	= food density (kg m³)
BW	= body weight (kg)

DEFAULT VALUES Strips and cassettes

Table 3.4.8.3.2: Default value for each exposure parameter of the formulae

		room	sealed area	*Q***
C_{strip}	mg	100	100	
V_{room}	M³	1	1	*5*
N_{day}	d^{-1}	1	1	*3*
$T_{strip\text{-}hand}$	%	0	0.5	
BW	kg	65	65	*9*
T_{appl}	min	10	10	*3*
Rt	d	120	120	
RR	$m^3\ min^{-1}$	0.0208	0.0208	
V_{room2}	m³	58	1.5	*8/5*
T_{exp}	min	480	5	*6/3*
RR_{child}	$m^3\ min^{-1}$	0.0028	0.0028	
N_{day2}	d^{-1}	1	1	*3*
I_{food}	kg	0.5	nr*	
ρ_{food}	kg m³	1	nr*	
BW_{child}	kg	10	10	*8*

(*) nr = not relevant. (**) see Table 3.4.7.1.

3.4.8.4 Baits

(Source: Pest Control Products Fact Sheet, RIVM-report 613340 003/2002)

Figure 3.4.8.4.1: Pictures of baits products

In case of type-18 biocides, baits are used to kill ants and/or cockroaches. The products are placed at the appropriate places; the animals eat or come in contact with some of the product and die.

Ant and cockroach bait stations are entirely closed boxes (made of metal or plastic) in which the user only has to make a small hole to be able to use it. The ants take the product out of the box and back to their nest, so that they die in the nest. It takes several days before the whole nest is wiped out. This is why the bait station should remain in the same place for at least one week. One bait station is enough for a small room. The bait will cease to be effective after about 1 month, due to the contents being removed by the ants and by drying out.

The vapour pressure of the active substances used in this type of baits is very low. Evaporation of these substances will be so small that the inhalatory exposure is considered to be negligible.

Some dermal exposure could occur when making the hole in the bait station. In addition, an extremely small, mainly dermal exposure could occur by ants or cockroaches taking the substance out of the bait station, after which people come into contact with it. For the time being, the exposure due to the use of ant and cockroach bait stations is considered to be negligible. Accidents (swallowing, children who open bait stations) do not form part of a standard assessment and are thus not considered in this study.

PRIMARY EXPOSURE Baits

$$EXP_{primary} = EXP_{dermal1} + EXP_{inhalatory1} + EXP_{oral1} \quad (mg\ kg^{-1}\ d^{-1})$$

Dermal exposure ($EXP_{dermal1}$): Negligible

Inhalatory exposure ($EXP_{inhalatory1}$): Negligible

Oral exposure (EXP_{oral1}): Negligible

SECONDARY EXPOSURE Baits

$$EXP_{secondary} = EXP_{dermal2} + EXP_{inhalatory2} + EXP_{oral2}\ (mg\ kg^{-1}\ d^{-1})$$

Dermal exposure ($EXP_{dermal2}$): Negligible

Inhalatory exposure ($EXP_{inhalatory2}$): Negligible

Oral exposure (EXP_{oral2}): Negligible

3.4.8.5 Spraying (mixing : loading)

Most products, belonging to this category, are for professional use only. They are used to control insects, not only in domestic areas, but also in public areas (e.g. schools, nursery homes, restaurants, hospitals), in industrial buildings and stables.

The liquids or powders have to be diluted with water and poured into the sprayer (mixing/loading). Application occurs in- and outdoors in overhead or downward direction, mostly by a hand-held low-pressure sprayer.

The exposure values as suggested in the TNsG include exposure during mixing/loading and application. As well dermal, as inhaling as body exposure might occur. The secondary exposure is considered to be negligible.

PRIMARY EXPOSURE Spraying

$$EXP_{primary} = EXP_{dermal1} + EXP_{inhalatory1} + EXP_{oral1} \quad (mg\ kg^{-1}\ d^{-1})$$

Dermal exposure ($EXP_{dermal1}$)

$$EXP_{dermal1} = \frac{(X_{body} * RP_{clothes} + X_{hands} * RP_{gloves} + X_{feet} * RP_{shoes}) * N_{day} * T_{appl}}{BW}$$

where:
- X_{body} = product on body rate (mg min^{-1})
- X_{hand} = product on hand rate (mg min^{-1})
- X_{feet} = product on feet rate (mg min^{-1})
- $RP_{clothes}$ = relative penetration of clothes (%)
- RP_{gloves} = relative penetration of gloves (%)
- RP_{shoes} = relative penetration of shoes (%)
- N_{day} = number of applications per day (d^{-1})
- T_{appl} = duration of 1 application (min)
- BW = body weight (kg)

Inhalatory exposure ($EXP_{inhalatory1}$)

$$EXP_{inhalatory1} = \frac{X_{inhal} * RP_{mask} * RR * T_{appl} * N_{day}}{BW}$$

where:
- X_{inhal} = product in air concentration (mg m^{-3})
- RP_{mask} = relative penetration of protective mask (%)
- RR = respiratory rate (m^3 min^{-1})
- T_{appl} = duration of 1 application (min)
- N_{day} = number of applications per day (d^{-1})
- BW = body weight (kg)

Oral exposure (EXP_{oral1}): Negligible

SECONDARY EXPOSURE Spraying: Negligible

DEFAULT VALUES Spraying

Table 3.4.8.5.1: Default values of exposure parameters for professional and non-professional users

		Professional	Non-professional	*Q***
X_{body}	mg min^{-1}	92	92	*na*
X_{hand}	mg min^{-1}	10.7	10.7	*na*
X_{feet}	mg min^{-1}	0	0	*na*
X_{inhal}	mg m^{-3}	104	104	*na*
$RP_{clothes}$	%	30	50	*na*
RP_{gloves}*	%	100	100	*na*
RP_{shoes}	%	10	50	*na*
RP_{mask}	%	10	100	*na*
RR	m³ min^{-1}	0.0208	0.0208	
N_{day}	d^{-1}	1	1	
T_{appl}	min	40	40	
BW	kg	65	65	*9*

(*) Exposure values hands (X_{hand}) represents in-glove exposure. (**) : see table 3.4.7.1.

3.4.8.6 Fogging

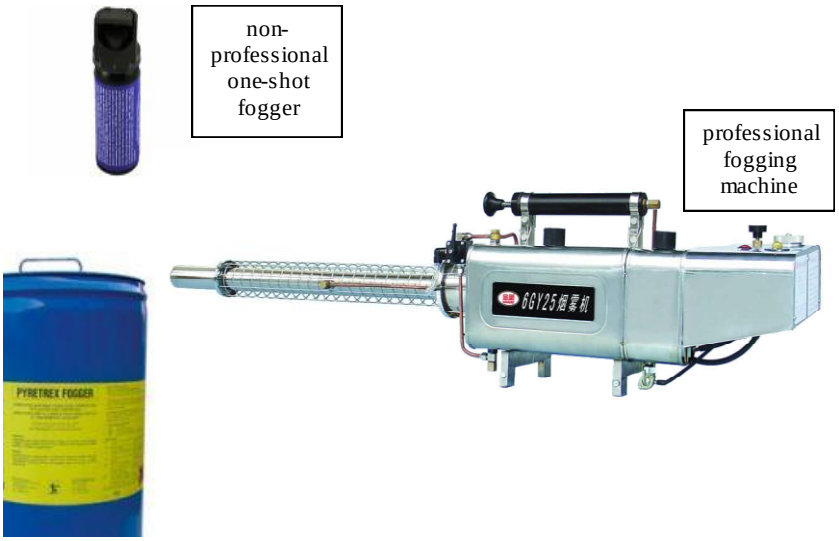


Figure 3.4.8.6.1: Pictures of fogging apparatus

PRIMARY EXPOSURE Fogging

$$EXP_{primary} = EXP_{dermal1} + EXP_{inhalatory1} + EXP_{oral1} \quad (mg\ kg^{-1}\ d^{-1})$$

Dermal exposure ($EXP_{dermal1}$)

$$EXP_{dermal1} = \frac{(X_{body} * RP_{clothes} + X_{hands} * RP_{gloves} + X_{feet} * RP_{shoes}) * N_{day} * T_{appl}}{BW}$$

where:

X_{body}	= product on body rate (mg min^{-1})
X_{hand}	= product on hand rate (mg min^{-1})
X_{feet}	= product on feet rate (mg min^{-1})
$RP_{clothes}$	= relative penetration of clothes (%)
RP_{gloves}	= relative penetration of gloves (%)
RP_{shoes}	= relative penetration of shoes (%)
N_{day}	= number of applications per day (d^{-1})
T_{appl}	= duration of 1 application (min)
BW	= body weight (kg)

Inhalatory exposure ($EXP_{inhalatory1}$)

$$EXP_{inhalatory1} = \frac{X_{inhal} * RP_{mask} * RR * T_{appl} * N_{day}}{BW}$$

where:

X_{inhal}	= product in air concentration (mg m^{-3})
RP_{mask}	= relative penetration of protective mask (%)
RR	= respiratory rate (m^3 min^{-1})
T_{appl}	= duration of 1 application (min)
N_{day}	= number of applications per day (d^{-1})
BW	= body weight (kg)

Oral exposure (EXP_{oral1}) Negligible

SECONDARY EXPOSURE Fogging: Negligible

DEFAULT VALUES Fogging

Table 3.4.8.6.1: default values of exposure parameters for professional and non-professional users

		Professional	**Non-professional**	***Source***	***Q****
X_{body}	mg min^{-1}	21.8	21.8	*1*	*na*
X_{hand}	mg min^{-1}	0.2	0.2	*1*	*na*
X_{feet}	mg min^{-1}	0	0	*1*	*na*
X_{inhal}	mg m^{-3}	70.2	70.2	*1*	*na*
$RP_{clothes}$	%	30	50	*4*	*na*
RP_{gloves}	%	10	100	*4*	*na*
RP_{shoes}	%	10	50	*4*	*na*
RP_{mask}	%	10	100	*4*	*na*
RR	m^3 min^{-1}	0.0208	0.0208		
N_{day}	d^{-1}	8	1		
T_{appl}	min	30	1		
BW	kg	65	65	*2*	*9*

(*) see table 3.4.7.1.

3.4.8.7 Pouring

liquid for pouring
(ready-to-use,
no dilution)

Figure 3.4.8.7.1: Picture of a pouring product

For this type of products, no mixing/loading is required. The product is delivered as a ready-to-use liquid. During application, a few drops of the product are poured on places where insects occur or the nest is wetted.

Exposure only occurs during application. The most important exposure route is the dermal exposure. Oral and inhaling exposures are negligible. Secondary exposure is also negligible.

PRIMARY EXPOSURE Pouring

$$EXP_{primary} = EXP_{dermal1} + EXP_{inhalatory1} + EXP_{oral1} \quad (mg\ kg^{-1}\ d^{-1})$$

Dermal exposure ($EXP_{dermal1}$)

$$EXP_{dermal1} = \frac{(X_{body} * RP_{clothes} + X_{hands} * RP_{gloves} + X_{feet} * RP_{shoes}) * N_{day} * T_{appl}}{BW}$$

where:
- X_{body} = product on body rate (mg min^{-1})
- X_{hand} = product on hand rate (mg min^{-1})
- X_{feet} = product on feet rate (mg min^{-1})
- $RP_{clothes}$ = relative penetration of clothes (%)
- RP_{gloves} = relative penetration of gloves (%)
- RP_{shoes} = relative penetration of shoes (%)
- N_{day} = number of applications per day (d^{-1})
- T_{appl} = duration of 1 application (min)
- BW = body weight (kg)

Inhalatory exposure ($EXP_{inhalatory1}$) Negligible

Oral exposure (EXP_{oral1}) Negligible

SECONDARY EXPOSURE Pouring: Negligible

DEFAULT VALUES Pouring

Table 3.4.8.7.1: Default values of exposure parameter for non-professional users

		non-professional	*Q**
X_{body}	mg min^{-1}	0	*na*
X_{hand}	mg min^{-1}	3.2	*na*
X_{feet}	mg min^{-1}	0	*na*
X_{inhal}	mg m^{-3}	0	*na*
$RP_{clothes}$	%	50	*na*
RP_{gloves}	%	100	*na*
RP_{shoes}	%	50	*na*
RP_{mask}	%	100	*na*
RR	m^3 min^{-1}	0.0208	
N_{day}	d^{-1}	1	
T_{appl}	min	1	
BW	kg	65	*9*

(*) see table 3.4.7.1.

3.5 Calculation of the human exposure (HumExp)

The HumExp values for professional (Table 3.5.1) and amateur use (Table 3.5.2) are given as:

- acute exposure after one application
- chronic exposure for weekly applications (by multiplying the acute exposure with a factor 52/365)
- chronic exposure for monthly applications (x 12/365)
- chronic exposure for yearly application (x 1/365)
- chronic exposure for daily applications during three months (x 90/365)

Table 3.5.1.: List of HumExp values for professional use (the secondary exposure is here not relevant)

	Dermal	Inhalation	TOTAL EXPOSURE*
ACUTE			
3.4.6.1. Spraying (duster) surface	0.34	0.032	0.369
3.4.6.4. Baits	0.000	0.000	0.000
3.4.6.5. Spraying (mixing/loading included)	23.569	0.133	23.702
3.4.6.6. Fogger	24.222	0.539	24.761

(*) : mg product/kg body weight for acute exposure; mg product/kg bw/dag voor chronic exposure

Table 3.5.2.: List of HumExp values for amateur use

	PRIMARY		SECUNDARY child		TOTAL EXPO-SURE*
(CSDM n°)	**dermal**	**Inhala-tion**	**dermal**	**Oral**	
ACUTE					
Spraying (aërosol) surface (2;3)	13.431	0.115	0.319	0.032	13.897
Spraying (duster) surface (2;1)	0.315	0.004	1.08	0.108	1.507
Spraying (trigger) surface (2;2)	2.520	0.013	1.404	0.14	4.078
Spraying (trigger) air space (1;1)	9.674	0.115	0.756	0.076	10.621
Spraying (aërosol) air space (1;3)	1.079	0.025	0.022	0.002	1.127
Electrical evaporator	0.000	5.99	0.000	0.000	5.991
Baits	0.008	0.007	0.000	0.000	0.014
Evaporation from strips and cassettes (sealed area)	0.008	0.000	0.000	0.000	0.008
Evaporation from strips and cassettes (room)	0.000	0.000	0.000	0.001	0.001
Spraying (mixing/loading included)	34.892	1.331	0.000.	0.000	36.224
Fogger	0.171	0.022	0.000	0.000	0.193
Pouring	0.049	0.000	0.000	0.000	0.049

(*): mg product/kg body weight for acute exposure; mg product/kg bw/dag voor chronic exposure

3.6 Sensitivity and uncertainty analysis of the TNsG scenarios

Mathematical formulae that have been used to assess the uncertainty on TNsG scenarios are summarized in Appendix A: Uncertainty on TNsG scenarios. Scenarios are calculated with the help of model equations that are specific for a biocide formulation and/or type of exposure (see section 3.4). Generally model scenarios are multiplicative expressions of the form:

$$y = \frac{a \cdot b \cdots}{i \cdot j \cdots} \tag{3.6.1}$$

where a, b, i, j, … are independent parameters/variables (e.g. body weight, exposure time, relative penetration of gloves…) for which default values were found in literature.

Any modification of the parameter-values in the denominator or numerator will immediately affect the exposure term, and hence the risk index in a same proportion.

For example, the generic expression to calculate a “combined uncertainty” (propagation of standard deviation/uncertainty through model scenario) for an equation like 3.6.1 is given by :

$$\frac{u(y)}{y} = \sqrt{\left(\frac{u(a)}{a}\right)^2 + \left(\frac{u(b)}{b}\right)^2 + \left(\frac{u(i)}{i}\right)^2 + \left(\frac{u(j)}{j}\right)^2 + \cdots} \tag{3.6.2}$$

From (3.6.2) it appears that the relative standard uncertainty in the final result is not much larger than the largest standard deviation used to calculate it. This is mainly a consequence of the squaring of the relative standard uncertainties and illustrates two important general points:

1. Any efforts to improve the precision on model scenarios need to be directed towards improving the precision of the least precise values. As a corollary to this, there is no point in wasting effort in increasing the precision of the most precise values.
2. Because the number of parameters/variables is elevated in the model scenario (up to 10), uncertainty propagation in the final result could be high, i.e. a factor 2 to 3 (Table 3.6.1).

Table 3.6.1: Uncertainty propagation factor per application and median value

Applications	Uncertainty propagation factor
Space spraying aerosol	1.7
Surface spraying duster	2.2
Surface spraying trigger	1.4
Electrical evaporator	2.4
Evaporation from strips and cassettes	2.1
Spraying	2.0
Fogging	2.2
Pouring	2.2
Median propagation factor	**2.0**

Note that the median value for the uncertainty propagation factor is around 2.

Example 3.6.1 – The default values for the surface spraying duster model (dogs and cats) are:

	symbol	units	value
Duration of 1 application	Tapp	min	5
Amount of product released per time	Rpro	mg/min	12
Accumulation rate	Facc	-	1
Amount of product deposited on floor	Fdep	%	100
Amount of product dislodged	Fdis	%	30
Transfer contact surface	TC	m^2/h	0.6
Exposure time	Texp	h/d	1
Child body weight	BWchi	kg	10
Room area	Aroo	m^2	1

The following results were obtained assuming a precision of 10% on each parameter value: DermExp = 1.1 ± 0.25 mg product per kg body weight and per day. The relative standard uncertainty is 22%. This indicates that about 95% of the dermal exposure for children (prediction interval) should lie between 0.6 and 1.6 mg of product / (kg day). Let now suppose that the transfer contact surface is known with a precision of 0.6 ± 0.3 m^2/h (RSD = 50%). This gives a result of 1.1 ± 0.6 mg product / (kg day) with a relative uncertainty of 57%. As mentioned above, the uncertainty in the final result is not much larger than the largest relative standard deviation used to calculate it. Hence there is no point in wasting effort in increasing the precision of the most precise values, if one parameter cannot accurately be determined or known. Also this would mean that about 95% of the results (prediction interval) should lie in the range 0 – 2.3 mg product / (kg day). The uncertainty on HumExp is a description of the imperfection in knowledge of the true value of a particular parameter and/or its real variability. It is reducible by gathering additional information or analysis activities (better data, better model equations), but inescapable. **It is therefore crucial to carefully check the default values chosen for TNsG scenario and related uncertainty**.

To estimate the standard uncertainty (RSU) associated with the default values (chosen in model scenarios) we used the “criteria evaluation scores” for data quality assessment as reported in

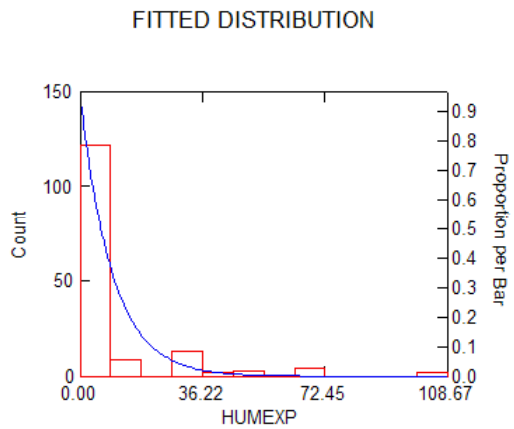
the Technical Notes for Guidance (see Table 3.4.1). At each score, a RSU-value ranging from 1 to 50% depending on the data quality was ascribed.

Table 3.6.2.: Criteria evaluation scores and RSU (%)

Criteria / evaluation	Score	RSU %
Ample and good quality data	9	1
Good quality data	8	5
Quality and number of studies satisfactory	7	10
Usable, but open for improvement	6	20
Little data, parameter value is usable as default value	5	25
Single data source supplemented with expert judgement, parameter value not reliable as default value	3	50
Data Not available	na	50
Expert source	exp	Var.
Median RSU		**12.5**

These assigned RSU-values are rather arbitrary, but can be revised according to expert judgement. Currently in the absence of judgement of this type, we used the median value of 12.5% for our computations. This implies that with a median propagation factor of 2 (see above) and

The frequency distribution function of HumExp for PT18 can be approximated with an exponential distribution (Figure 3.6.1).



Descriptive statistics

Number of products	155
Minimum	0.001
Maximum	109
Median	1.5
First quartile (P25%)	0.01
Third quartile (P75%)	5.2
IQR(P75%- P25%)	5.2
P95%	50

Figure 3.6.1: Observed (bars) and fitted (line) distributions for HumExp.

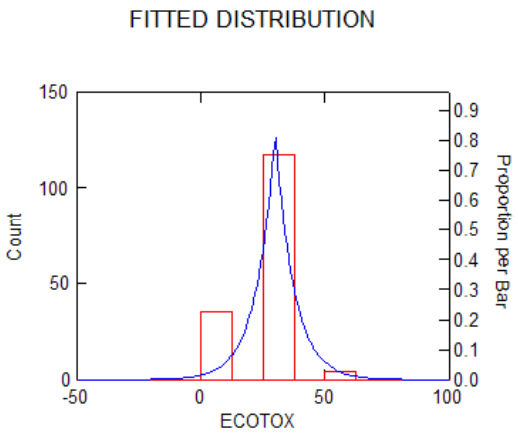
3.7 Refinement of EcoTox

The initial scoring approach proposed by E. Nijs (PRPB meeting 01.02.07) was refined by the expert judgement of C. Vleminckx (PRPB meeting 03.05.07). The following scoring system was proposed (Table 3.7.1).

Table 3.7.1: R-phrases, scores, uncertainty and frequency distribution for the EcoTox variable (PT18 biocides).

Environmental Risk	R-phrases	Score	Uncert.	Freq. %
	NC: not classified	0.1	-	17
Aquatic environment	R52: Harmful to aquatic organisms	10	4	<1
	R52/53: Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment	30	4	8
	R51/53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment	30	4	9
	R50: Very toxic to aquatic organisms	30	4	3
	R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment	30	4	58
Terrestrial environment	R57: Toxic to bees	30	6	4

The frequency distribution function of EcoTox looks like a Laplace distribution (Figure 3.7.1).



Descriptive statistics

Number of products	155
Minimum	0.1
Maximum	60
Median	30
First quartile (P25%)	30
Third quartile (P75%)	30
IQR (P75%- P25%)	0
P95%	30

Figure 3.7.1: Frequency (bars) and fitted (line) distributions for EcoTox

The median value for the relative uncertainty on EcoTox is around 13%.

3.8 Development of EcoExp

3.8.1 Selection of environmental compartments of concern

Because of the special conditions of biocide PT18 use some particular issues are determined. These are defined as follows:

Two types of exposure are applicable depending on their application site:

- Outdoor use in the field (wasp control; ant control, …) is specified for some typical uses

- Indoor use is the main application site for most Type 18 biocides.

Because most PT18 are applied and/or used indoor some environmental “receptor” compartments and effects developed in the POCER-indicator approach are not relevant and can be eliminated. Therefore the following routes and/or effects can be eliminated:

- Negligible routes of entry: groundwater
- Negligible effects: persistence, beneficial arthropods, birds, bees, soil organisms.

This results in the following remaining compartments of concern for indoor use of PT18:

- Indoor use: surface water and air compartments
- Outdoor use: for outdoor use of PT18 is advised to apply risk assessment with the POCER II or PTIBEL methodology which are developed for risk assessment of plant protection products and theit outdoor use.

3.8.2 Construction of operational database

- Application of POCER algorithms for selected compartments of concern
- Selection of default values POCER algorithms for each application type
- Selection of variable default values (Table 3.8.1.) in function of RMM (Risk management measures)

Surface water exposure (SWEXP): idem as POCER but with following default values:

The emission by direct losses: as 0.005*application rate (POCER)

The emission by drift: 0.0005*application rate (POCER). Because this limited impact of drift from indoor uses this value is used for all scenario’s as a worst case approach (thus also for baits and pouring applications.

SWEXP is sum of both effects = 0.0055*application rate of one treatment (as amount of formulation)

Air (AIREXP):

In FOCUS Air the highest deposition of 0.05% of the applied rate at 5 m distance from an indoor application was considered to be a worst case approach for high or low volume applications. Triggers and other droplet applications are high volume treatments.

In FOCUS Air 0.2% is proposed in the case of an ultra low volume application technique. Evaporators, fogging and aerosols are considered to be ULV.

A threshold value for pesticide residues in air from volatilisation is proposed by FOCUS air: there is no volatilisation from soil if the vapour pressure (Vp) > or = 10^{-4} Pa (20°C) and from plants if the vapour pressure (Vp) > or = 10^{-5} Pa (20°C). In Table 3.8.2 a list of low volatile pesticides is given. Baits and pouring applications have no air exposure for

because the active ingredients in these formulations are considered to be of low volatility.

Total ECOEXP:

For indoor use: ECOEXP = SWEXP + AIREXP

For outdoor use: ECOEXP = apply POCER II or PRIBEL approach

Table 3.8.1: SWEXP and AIREXP factors for different applications

	SWEXP	AIREXP
AEROSOL / SPACE SPRAYING	0.0055	0.002
DUSTING / a = ants ; dc = dogs&cats ; i = crawling insects (prof / amateur)	0.0055	0.0005
TRIGGER / SPACE SPRAYING	0.0055	0.0005
TRIGGER / SURFACE SPRAYING	0.0055	0.0005
AEROSOL / SURFACE SPRAYING	0.0055	0.002
ELECTRICAL EVAPORATOR	0.0055	0.002
BAITS	0.0055	0
SPRAYING	0.0055	0.0005
FOGGING	0.0055	0.002
POURING	0.0055	0
STRIPS & CASSETTES	0.0055	0.002

Table 3.8.2: list of low volatile pesticides. Pesticides with Vp >10^{-4} Pa at 20-25°C; those with Vp >10^{-3} Pa are highlighted in Italic and Gray. (Richard Bromilow, Rothamsted Research, 2007).

acephate	*acetochlor*	*alachlor*	*aldicarb*
allethrin	ametryn	amitraz	azinphos-ethyl
azinphos-methyl	benalaxyl	*bendiocarb*	*benfluralin*
benfuresate	benoxacor	bensultap	bentazone
benzoximate	bifenox	*bioallethrin*	*bioresmethrin*
bromobutide	*buprofezin*	butachlor	*butamifos*
butorcarboxim	butoxycarboxim	butralin	*sec-butylamine*
butylate	*cadusafos*	*chloramben*	*chlordane*
chlorethoxyfos	chlorfenvinphos	chlorflurenol-methyl	*chlormephos*
chloropicrin	chlorpropham	*chlorpyrifos*	*chlorpyrifos-methyl*
chlorthal-dimethyl	chlorthiamid	*cinmethylin*	*clomazone*
clopyralid	*cyanophos*	*cycloate*	cymoxanil
cyphenothrin	cyprodinil	*daminozide*	dazomet
demeton-S-methyl	*diazinon*	*dicamba*	*dichlobenil*
dichlormid	*1,3-dichloropropene*	*dichlorvos*	diclocymet

diclofop-methyl	dicloran	*dicrotophos*	*diethofencarb*
diflumetorim	*dikegulac*	dimepiperate	*dimethachlor*
dimethametryn	*dimethenamid*	*dimethirimol*	dimethoate
dimethylvinphos	*diniconazole*	dinitramine	*dinoterb*
disulfoton	dithiopyr	*DNOC*	dodemorph
empenthrin	endosulfan	*esprocarb*	*ethalfluralin*
ethiofencarb	ethion	ethirimol	ethofumesate
ethoprophos	*ethylene dibromide*	*etridiazole*	fenamiphos
fenclorim	*fenitrothion*	*fenobucarb*	fenothiocarb
fenpropathrin	*fenpropidin*	*fenpropimorph*	fenthion
fenuron	*fluazinam*	*fluchloralin*	flumioxazin
fluometuron	*fluoroimide*	*flurenol*	flurochloridone
fosthiazate	*gamma–HCH*	*heptachlor*	*heptenophos*
hexachlorobenzene	*hydroprene*	*hymexazol*	imazalil
iprobenfos	isofenphos	*isoprocarb*	*isoprothiolane*
kinoprene	*malathion*	*MCPA-thioethyl*	mecoprop
metalaxyl	*methamidophos*	methidathion	methomyl
methoprene	*methyl bromide*	*methyl isothiocyanate*	metobromuron
metolachlor	*metolcarb*	*metoxuron*	*mevinphos*
molinate	monocrotophos	*monolinuron*	myclobutanil
naled	napropamide	*nicotine*	*nitrapyrin*
nonanoic acid octhilinone	*omethoate*	*orbencarb*	*oxydemeton-methyl*
parathion	parathion-methyl	*pebulate*	pefurazoate
penconazole	*pendimethalin*	*pentachlorophenol*	*phenthoate*
phenylmercury acetate	*2-phenylphenol*	*phorate phosphamidon*	*phosphine*
phoxim	*piperalin*	pirimicarb	*pirimiphos-methyl*
pretilachlor	prochloraz	*procymidone*	profenofos
prometon	prometryn	*propachlor*	propaphos
propetamphos	*propham*	*propisochlor*	*propoxur*
prosulfocarb	prothiofos	pyrazophos	pyributicarb
pyridaben	*pyrifenox*	*pyrimethanil*	pyroquilon
quinalphos	*quintozene*	*spiroxamine*	*sulfotep*
sulfuryl fluoride	*tebupirinfos*	*tebutam*	tebuthiuron
tecnazene	*tefluthrin*	*terbufos*	terbumeton
terbuthylazine	terbutryn	tetraconazole	*tetramethrin*
thiazopyr	*thiobencarb*	*thiodicarb*	*thiofanox*
thiometon	*thiram*	*tiocarbazil*	*tolclofos-methyl*
tolylfluanid	transfluthrin	*tri-allate*	triazamate
triazophos	tribufos	trichlorfon	triclopyr
tridemorph	triflumizole	*trifluralin*	*triforine*
trimethacarb	*trinexapac-ethyl*	*uniconazole*	*vernolate*
vinclozolin	*xyly*		

3.9 Uncertainty evaluation of EcoExp

Calculations of environmental exposure are related to the POCER methodology (see section 3.8). It involves the calculations of:

- A surface water exposure (SWEXP) for which the emission by direct losses and by drift is given by: 0.0055 x the application rate of one treatment (g / application)
- An air exposure (AIREXP) for which the emission is given by: air coefficient x exclusion factor x the application rate of one treatment (g / application).

Unless otherwise stated, the uncertainty calculation is limited herein to the “application rate” since the uncertainty on a physical constant/coefficient is *a priori* negligible. The application rate is calculated as the product of the time of application by the amount of product released per time unit (g / application). In the absence of expert judgement we assumed that the relative uncertainty on these variables (time of application and amount of released product) is close to 10% (Table 3.9.1).

Table 3.9.1: Uncertainty calculation on EcoExp.

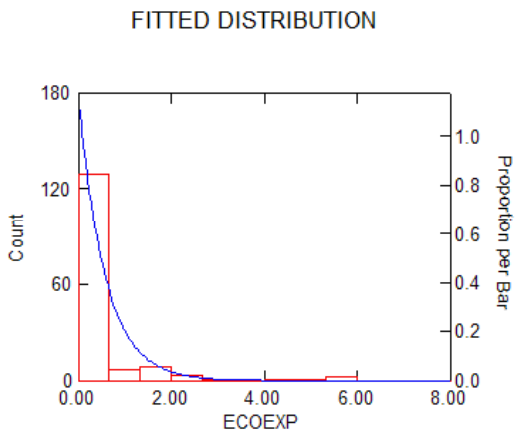
Application	Ap. Rate*	Uncert.	SWEXP	Uncert.	Air Coef.	AIREXP	Uncert.	EcoExp	Uncert.	RSU %
Aerosol sp. spraying	7	0.99	0.039	0.0054	0.002	0.014	0.0020	0.053	0.008	15
Dusting	60	8.5	0.33	0.047	0.0005	0.03	0.0042	0.36	0.066	18
Trigger	79.2	11.2	0.44	0.062	0.0005	0.040	0.0056	0.48	0.087	18
Aerosol su. spraying	390	55.2	2.15	0.30	0.002	0.78	0.11	2.9	0.43	15
Electrical evaporator	0.624	0.09	0.0034	0.0005	0.002	0.0012	0.00018	0.0047	0.0007	15
Baits	12	1.2	0.066	0.0066	0	0	0	0.066	0.0093	20
Spraying	100	10	0.55	0.055	0.0005	0.05	0.005	0.6	0.078	18
Fogging	97.2	14	0.54	0.076	0.002	0.19	0.027	0.73	0.11	15
Pouring	20	2	0.11	0.011	0	0	0	0.11	0.016	20
Evaporation from strips/ cassettes	0.1	0.01	0.0006	0.0001	0.002	0.0002	0.00002	0.0008	7.7E-05	15
Median RSU										**17**

* The application rate is calculated as the product of the time of application by the amount of product released per time unit (g / application)

From the aforementioned results, it appears that the median value for the propagated uncertainty on EcoExp is about 17%, i.e., the error amplification factor being 1.7. Accordingly, the RSU on EcoExp can be approximated with:

$$RSU_{EcoExp} \approx 2 \cdot RSU_{Appl.rate} \qquad (3.8.1)$$

The frequency distribution function of EcoExp can be approximated with an exponential distribution (Figure 3.9.1).



Descriptive statistics

Number of products	155
Minimum	0.001
Maximum	8
Median	0.1
First quartile (P25%)	0.7
Third quartile (P75%)	0.44
IQR (P75%- P25%)	0.37
P95%	2

Figure 3.9.1: Frequency (bars) and fitted (line) distributions for EcoExp

3.10 Risk index

As shown by Eq. (3.1.1), a risk index can be computed within a health (HumRisk) and/or an environmental (EcoRisk) risk assessment perspective. Descriptive statistics for these data are given in Table 3.10.1

Table 3.10.1: Descriptive statistics for HumRisk and EcoRisk.

Risk index	HumRisk	EcoRisk
Minimum	7.6E-5	5.5E-5
Maximum	2752	88
Median	0.4	2
First quartile (P25%)	0.0056	0.26
Third quartile (P75%)	3.6	13
IQR (P75% - P25%)	3.6	13
P95%	759	22
Skewness	4.7	3.6

Risk indices are heavily tailed distributions that vary significantly from the pattern expected if the data were draw from populations with lognormal distributions (Kolmogorov-Smirnov test).

The functional relationship between the uncertainty and risk indices was investigated according to the International Standard (ISO 5725-2: 1994). Three types of relationships have been considered:

- A straight line through the origin: $u(z) = az$
- A straight line with a positive intercept: $u(z) = az + b$
- An exponential type relationship: $u(z) = az^b$

As shown in Figure 3.10.1, all three of these relationships yield practically equivalent fits, and in such case the first relationship should be preferred because it permits the following simple statement: “the coefficient of variation (100 u(z)/b) is a constant for all levels”.

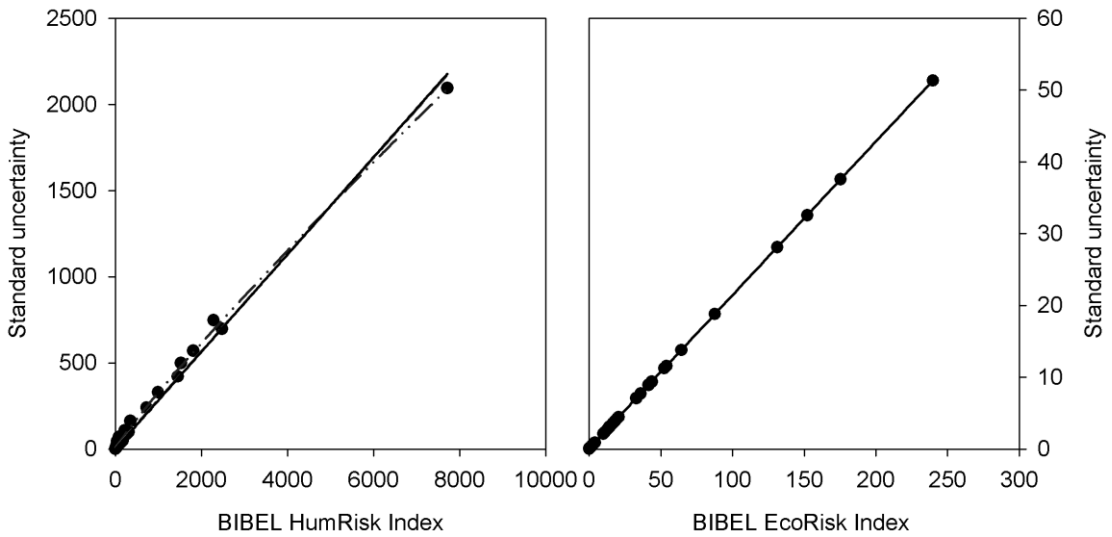


Figure 3.10.1: Functional relationship between precision (uncertainty) and the risk indices (solid line = straight line model; medium dash line = straight line model + positive intercept; Dash-dot-dot line = exponential model)

The fitted lines (regression coefficient ± SE) are given by:

$$u(z) = (0.28 \pm 0.002) \cdot HumRisk$$
$$u(z) = (0.21 \pm 0.001) \cdot EcoRisk \qquad (3.9.1)$$

Accordingly, the coefficient of variation (relative uncertainty) on HumRisk and EcoRisk is around 28 and 21%, respectively.

During the PRBP committee meeting of 27.09.07, the question was raised whether or not we have to consider the uncertainty on the scoring process in computing the risk index (Van Bol, 20070927 meeting report). Cancelling the uncertainty on scoring simplifies the calculations and increases the predictability of the indicator. It should be noted that the uncertainty on scoring is not clearly tied to mechanisms related to variability in human or environmental toxicity. Put in another way, the uncertainty on scoring is due to a loss of information when making a class or group, but it does not modify our perception of the risk; R-phrases being defined in Annex III of European Union Directive 67/548/EEC. On the other hand, we clearly demonstrated (see section 2.2) that there is an inherent uncertainty associated with coding and scoring, and there are no objective reasons to cancel it, except within a risk management perspective.

During the PRBP committee meeting of 04.12.07, the consensus of the steering members was to withdraw the uncertainty calculation on scoring at least in a first tier approach. Under these conditions, the coefficient of variation on HumRisk and EcoRisk decreases to 25 and 17%, respectively.

3.11 Calculation of frequency of use

Frequency of use can be determined in several ways such as:

- Total use in Belgium (kg) / number of habitants (or users)
- Total use in Belgium (kg) / application dose (kg per treatment)

For this study the application dose is estimated in function of the application method (according to type of PT18). Therefore default values are taken for each type of application:

Frequency (F) = total amount per year / unit dose per treatment

3.12 Determination of unit application dose for biocides

The application dose for biocides is difficult to determine. The only relevant data on this aspect can be found in the Technical Notes for Guidance and some RIVM publications, which are used as basic default input values for EUSES and other Calculation Sheets.

A survey of these values is proposed as default values for unit dose per treatment (Table 3.12.1):

Table 3.12.1: Default values for unit dose for the different applications

Application	Type	TNsG scenario's	Unit Dose One event *g/application*	Application one event characteristics
CONSUMER SPRAYING AND DUSTING				
1. Space spraying	1. Trigger	CSDM1;1	79.2	4 min*0.33 g/sec and 0.7 g/ml
	2. Aerosol	CSDM1;3	6.6	20 sec*0.35 g/sec and 0.7 g/ml
2. Surface spraying	1. Dusting	CSDM2;1dc dogs+cats CSDM2;1i Crawling insects CSDM2;1a ants	60	5 min * 12 g/min
	2. Trigger	CSDM2;2	79.2	4 min*0.33 g/sec and 0.7 g/ml
	3. Aerosol	CSDM2;3	390	10 min * 0.65 g/sec and 0.7 g/m
ELECTRICAL EVAPORATORS				
			0.624	480 min * 1.3 mg/min and 0.8 g/cm³
STRIPS and CASSETTES				
1. Paper strips			0.1	content of 1 strip/cassette = 100 mg
2. Strips in cassettes			0.1	content of 1 strip/cassette = 100 mg
3. Cassettes			0.1	content of 1 strip/cassette = 100 mg
BAITS				
			12	1 bait = 12 g
SPRAYING (HANHELD SPRAYER – KNAPSACK SPRAYER)				
			100	100 ml product per application
FOGGING				
1. One shot applicator			97.2	1 min * 1.62 g/sec
2. Fogging machine			97.2	1 min * 1.62 g/sec
POURING				
			20	20 g/application

3.13 Data base of biocides uses in Belgium

Fundamental to any realistic outcome for the development of indicators of biocide impact on the environment, users or consumers is meaningful data on the use of biocides as an input.

Biocide usage data come in many forms and levels of sophistication. While some countries have no statistics on biocide consumption, most do have sales statistics, which may vary in

complexity from tonnage of broad biocide groups (e.g. Product Type, active ingredients, etc..), through more detailed groupings (e.g. aerosols, baits etc.) to detailed data at the level of individual active substances. Confounding these figures is sometimes the confusion between recording sales of formulated product or active substance, while comparisons between countries are often confounded by classification and nomenclature, with some biocides, often in the high usage category (e.g. desinfectants etc.) being classified into different major biocide groups by different countries, or not classified as a biocide in some countries despite accounting for a considerable amount of use by weight in others.

Sales data are rarely, if ever, attributed or even readily attributable, to the specific applications for which they were ultimately applied. Indeed, for many active substances, the use of individual countries' approvals registers affords little assistance in apportioning usage where a broad spectrum of approvals exists. In these cases, expert judgement may be required to provide some approximation of use amongst approved crops.

In some countries, however, detailed surveys of biocide use are undertaken from usage records providing a more accurate assessment of how biocides are actually used in practice. There is thus a range of data available on biocide use, showing wide-ranging levels of sophistication and parameter availability.

In order for sales data to be converted into a meaningful data set be useful within the indicator proposal, each of the following parameters must be taken into consideration and an appropriate value derived.

Year

This will be based on the year for which the sales data apply but some thought should be given to the level of carryover from year to year. In one year, some biocides will come onto the market which was present and stored from the previous year's sales. Similarly, some of the current year's sales will not be used and carry over to the next year. It may be prudent to consider a rolling three-year mean as the best estimate of usage in any one year from sales in that year and the years before and after it.

Region

It may be possible to derive a regional breakdown from regional patterns and regional expert knowledge of usage patterns. It would be anticipated, however, that the level of data manipulation necessary would be too time consuming and costly to develop the sales data any further than at a national level.

Application

Fundamental to apportionment of sales data to usage on individual items will be the country's approval regulations, which will stipulate for which purpose each biocide has approval for use. This approach, of course, precludes any illegal use which may well be occurring and would be picked up by appropriate usage surveys.

Apportionment of sales of actives to individual uses should be approached in two ways.

1. For biocides whose use is restricted to certain applications, for example ant control, it will be appropriate to apportion all sales to use on that use.
2. However, where biocides have a wide spectrum of use on which their use is approved, expert judgment will be required to give a meaningful estimate. This knowledge can be obtained from the distributors or other relevant sources

Method of application

The method of application has importance for several indicators and should be estimated by expert judgement from knowledge of the biocides commonly used in the country. It does not need to be exhaustive with regard to the detail of the type used and need only cover categories such as aerosol, triggers, baits, evaporators, etc.. As sales data are likely to be available only at the active substance level, these forms in which each biocide is sold should be estimated and apportioned from a knowledge of the products approved and a kind of expert knowledge of what consumers normally purchase and use because each product (application type) has its own commercial unique name.

Application rate

While the application rate for any biocide is more or less stipulated on the label it would be inappropriate to assume the exact label rate has been used in every case. In the absence of an exact dose an expert opinion has to be taken for default estimates. Such default application rates can be obtained from the so-called “Fact Sheets” (VROM) which are used in the CONSEXPO model.

Mitigation

The human risk assessment for PT18 is mainly focused on the non-professional user or the consumer, i.e. a member of the general public who may primarily be exposed by using a consumer product. The consumer is unlikely to take informed measures to control exposure and to follow exactly the instructions for using the biocidal product. On the other hand, the non-professional pattern of use is expected to show a lower frequency and/or duration of use. The consumer is not taking much care to the control of his exposure by personal protective equipment (PPE). Consumers will not normally use PPE unless it is convincingly recommended by the manufacturer and provided with the product. As a result only typical clothing should be assumed when carrying out consumer exposure assessment. While consumers may wear overalls, gloves or even dust masks, such usage cannot be assured and must nor be assumed in exposure estimations.

3.14 BIBEL Indicator Value (BIV)

By analogy with NIV (Nijs Indicator Value), the BIV for PT18 biocides was computed using either (i) the risk index represented by HumRisk or EcoRisk, and (ii) the frequency of use represented by the sales data. The dataset was upgraded and enclosed now a list of 267 products. As earlier mentioned (Table 2.9.1, section 2.9), sales data were labelled with:

- “na” whenever a product is not yet commercially available or taken out from the market

- “md” when missing at random
- “0” if a product is available but not sold for a given period

Table 3.14.1: % of data not available (na), missing (md) or equal to 0 for years 2000-2007

Year	2000	2001	2002	2003	2004	2005	2006	2007
na %	35	33	30	30	30	25	13	1
md %	16	18	21	20	8	7	2	7
0 %	13	10	10	10	16	20	31	36

The calculation procedure for BIV is identical to the one followed for the NIJS algorithmic (see section 2.11) and is outlined in sections 3.15 and 3.16.

3.15 BIV for HumRisk (BIV_{HR})

1) Generic expression: $BIV_{HR} = Q_{sales} \cdot HumRisk_{Index}$

2) Variance stabilization: $Y = \log(BIV_{HR} + 0.1)$

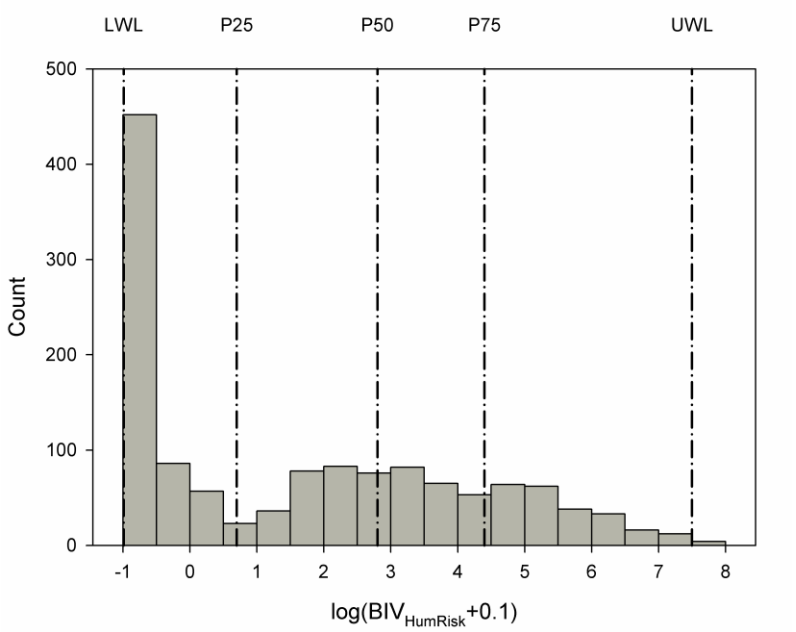


Figure 3.15.1: Transformed BIV for years 2000 to 2007. Sample size n = 1320. Dash-dot lines indicates percentiles for the distribution of $BIV_{HumRisk} > 0$

3) Rescaling process: The transformed BIV results were rescaled between 0 and 1 using the following membership function:

$$NBIV_{HR} = \begin{cases} 0 & if \quad \log(BIV_{HR}+0.1) = -1 \\ 0.115 \cdot \log(BIV_{HR}+0.1) + 0.115 & if \quad -1 < \log(BIV_{HR}+0.1) < 7.7 \\ 1 & if \quad \log(BIV_{HR}+0.1) \geq 7.7 \end{cases}$$

The lower warning limit was defined at log (BIV_{HR} + 0.1) = -1. The upper warning limit was taken equal to P99.9. Note that the median value of 0.5 was assigned to each of the missing data.

4) Uncertainty quantification:

a) Relative uncertainty on BIV: $\frac{u(BIV_{HR})}{BIV_{HR}} = \sqrt{\left(\frac{u(Q)}{Q}\right)^2 + \left(\frac{u(HumRisk_{Index})}{HumRisk_{Index}}\right)^2}$,

where $100 \cdot u(HumRisk_{Index}) / HumRisk_{Index} = 25\%$ (see section 3.10) and $100 \cdot u(Q)/Q$ is taken equal to the md-values given in Table 3.14.1

b) Standard uncertainty on transformed BIV: $u(\log(BIV_{HR}+0.1)) = 0.434 \cdot \frac{u(BIV_{HR})}{BIV_{HR}+0.1}$

c) Standard uncertainty on rescaled BIV:

$$u(NBIV_{HR}) = \begin{cases} 0 & if \quad NBIV_{HR} = 0 \\ 0.050 \cdot \frac{u(BIV_{HR})}{BIV_{HR}+0.1} & if \quad 0 < NBIV_{HR} \leq 1 \end{cases}$$

5) Relationship between the relative uncertainty on NBIV calculations and NBIV results:
From (4c) the empirical relationship between the expected uncertainty (RSU%) and $NBIV_{HR}$ (for all values > 0) is illustrated in Figure 3.15.2 and given by: $RSU\% = \frac{37 \pm 1}{1 + (22 \pm 1) \cdot NBIV_{HR}}$

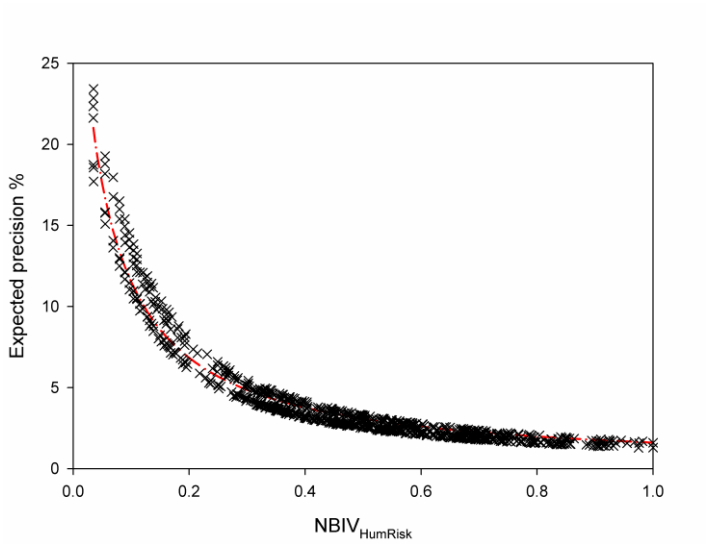


Figure 3.15.2: Functional relationship between RSU% and $NBIV_{HR}$

6) Generic expression for risk aggregation: $BIBELPT18_{HR,n} = \sum_{i=1}^{n} NBIV_{HR,i}$

Risk aggregation can be calculated at different levels per individual products, per group of products (type of formulation, type of active substance…) or for the whole population (see section 3.17)

7) Uncertainty on BIBELPT18$_{[HR,n]}$:

From (5), the uncertainty on BIBELPT18$_{[HR,n]}$ is calculated according to:

$$u\left(BIBELPT18_{[HR,n]}\right) = \begin{cases} 0 & if \quad BIBELPT18_{[HR,n]} = 0 \\ \dfrac{0.37 \cdot n \cdot BIBELPT18_{[HR,n]}}{n + 22 \cdot BIBELPT18_{[HR,n]}} & if \quad BIBELPT18_{[HR,n]} > 0 \end{cases}$$

3.16 BIV for EcoRisk (BIV$_{ER}$)

1) Generic expression: $BIV_{ER} = Q_{sales} \cdot EcoRisk_{Index}$

2) Variance stabilization: $Y = \log\left(BIV_{ER} + 0.1\right)$

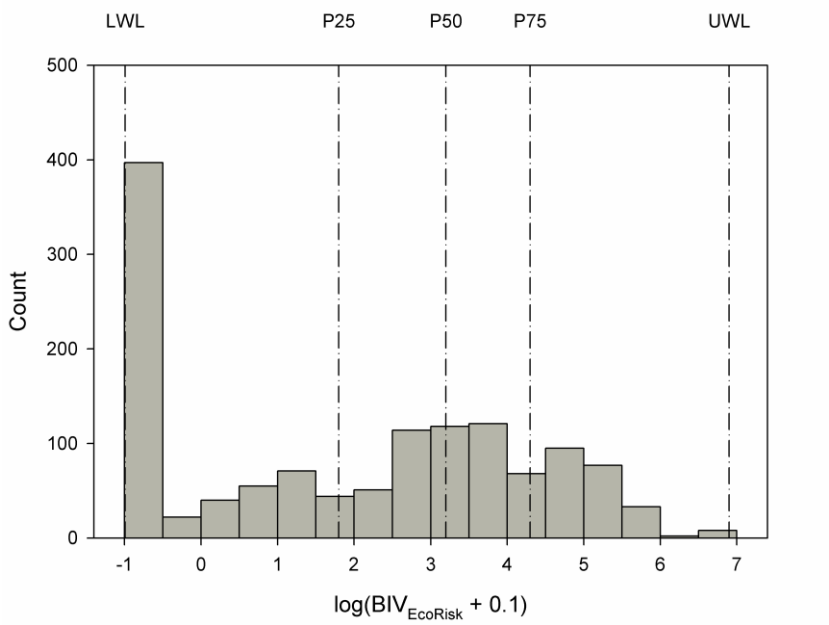


Figure 3.16.1: Transformed BIV for years 2000 to 2007. Sample size n = 1320. Dash-dot lines indicates percentiles for the distribution of BIV$_{EcoRisk}$ > 0

3) Rescaling process: The transformed BIV results were rescaled between 0 and 1 using the following membership function:

$$NBIV_{ER} = \begin{cases} 0 & if \quad \log(BIV_{ER} + 0.1) = -1 \\ 0.127 \cdot \log(BIV_{ER} + 0.1) + 0.127 & if \quad -1 < \log(BIV_{ER} + 0.1) < 6.9 \\ 1 & if \quad \log(BIV_{ER} + 0.1) \geq 6.9 \end{cases}$$

The lower warning limit was defined at log (BIV$_{ER}$ + 0.1) = -1. The upper warning limit was taken equal to P99.9. Note that the median value of 0.5 was assigned to each of the missing data.

4) Uncertainty quantification:

a) Relative uncertainty on BIV: $\frac{u(BIV_{ER})}{BIV_{ER}} = \sqrt{\left(\frac{u(Q)}{Q}\right)^2 + \left(\frac{u(EcoRisk_{Index})}{EcoRisk_{Index}}\right)^2}$, where $100 \cdot u(EcoRisk_{Index}) / EcoRisk_{Index} = 17\%$ (see section 3.10) and $100 \cdot u(Q)/Q$ is taken equal to the md-values given in Table 3.14.1

b) Standard uncertainty on transformed BIV: $u(\log(BIV_{ER} + 0.1)) = 0.434 \cdot \frac{u(BIV_{ER})}{BIV_{ER} + 0.1}$

c) Standard uncertainty on rescaled BIV:

$$u(NBIV_{ER}) = \begin{cases} 0 & if \quad NBIV_{ER} = 0 \\ 0.055 \cdot \frac{u(BIV_{ER})}{BIV_{ER} + 0.1} & if \quad 0 < NBIV_{ER} \leq 1 \end{cases}$$

5) Relationship between the precision/uncertainty on NBIV calculations and NBIV results:
From (4c) the empirical relationship between the expected uncertainty (RSU%) and $NBIV_{ER}$ (for all values > 0) is illustrated in Figure 3.16.2 and given by: $RSU\% = \frac{23 \pm 1}{1 + (18 \pm 1) \cdot NBIV_{ER}}$

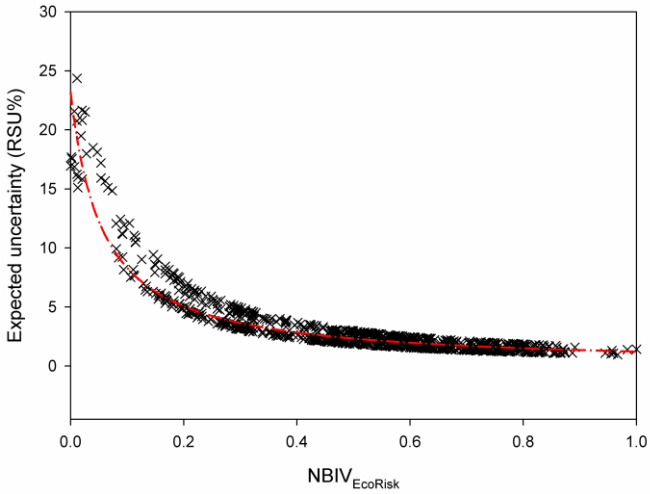


Figure 3.16.2: Functional relationship between RSU% and $NBIV_{ER}$

6) Generic expression for risk aggregation: $BIBELPT18_{[ER,n]} = \sum_{i=1}^{n} NBIV_{ER,i}$ Risk aggregation can be calculated at different levels per individual products, per group of products (type of formulation, type of active substance…) or for the whole population (see section 3.17)

7) Uncertainty on $BIBELPT18_{[EcoRisk,n]}$:
From (5), the uncertainty on $BIBELPT18_{[ER,n]}$ is calculated according to:

$$u(BIBELPT18_{[ER,n]}) = \begin{cases} 0 & if \quad BIBELPT18_{[ER,n]} = 0 \\ \frac{0.23 \cdot n \cdot BIBELPT18_{[ER,n]}}{n + 18 \cdot BIBELPT18_{[ER,n]}} & if \quad BIBELPT18_{[ER,n]} > 0 \end{cases}$$

3.17 Risk aggregation for BIBELPT18

As early mentioned, risks can be calculated at different levels, i.e., per individual products (e.g., $BIBELPT18_{[ER,\ Aquapy]}$), per group of products involving type of formulation (e.g., $BIBELPT18_{[HR,\ Aerosol]}$), type of active substance (e.g., $BIBELPT18_{[ER,\ Permethrin]}$)… or for the whole population (e.g., $BIBELPT18_{[HR,\ \Sigma products]}$). Examples of results are summarized in Table 3.17.1.

Using the generic test defined by Equation 2.13.3, one can compare the risk-values obtained for a given year with those obtained for the reference year "2001" and decide whether the difference is statistically significant or not.

Table 3.17.1: Risk aggregation for BIBELPT18

BIBELPT18	2000	2001	2002	2003	2004	2005	2006	2007
[HR, Σproducts]	63 ± 3	68 ± 3	72 ± 3	74 ± 3	63 ±3	66 ± 3	66 ± 3	74 ± 4
[HR, Permethrin]	20 ± 1*	24 ± 1	24 ± 1	24 ± 1	20 ± 1*	21 ± 1*	22 ± 1	25 ± 1
[HR, Aerosol]	15 ± 1	17 ± 1	20 ± 1*	20 ± 1*	21 ± 1*	21 ± 1*	18 ± 1	19 ± 1
[ER, Σproducts]	70 ± 2	76 ± 2	82 ± 2	83 ± 2*	75 ± 2	75 ± 2	79 ± 3	89 ± 3*
[ER, Permethrin]	22 ± 1*	26 ± 1	25 ± 1	26 ± 1	23 ± 1*	23 ± 1*	26 ± 1	30 ± 1*
[ER, Aerosol]	15± 0.3*	16± 0.3	18± 0.4*	18± 0.4*	18± 0.4*	19± 0.5*	16± 0.4	17± 0.4

Cells that show a statistically significant difference ($p < 0.05$) with regard to the reference year 2001 are labelled with*

3.17.1 Data analysis

Results of calculations shown in Table 3.17.1 are readily obtained using the Excel spreadsheets (2010BIBELPT18HR and 2010BIBELPT18ER). Following statements can be given in relation to these outcomes:

a) Multivariate analysis indicates that the risk trends for both [HR, Σproducts] and [ER, Σproducts] are explained by the fluctuations of two independent variables: (i) the averaged volume of sales data per year (Q_{sales}) and (ii) the available number of product per year (n). Figure 3.17.1 illustrates the behaviour of these variables between 2000 and 2007. Note that for the sake of confidentiality, Q_{sales} was rescaled between 0 and 1.

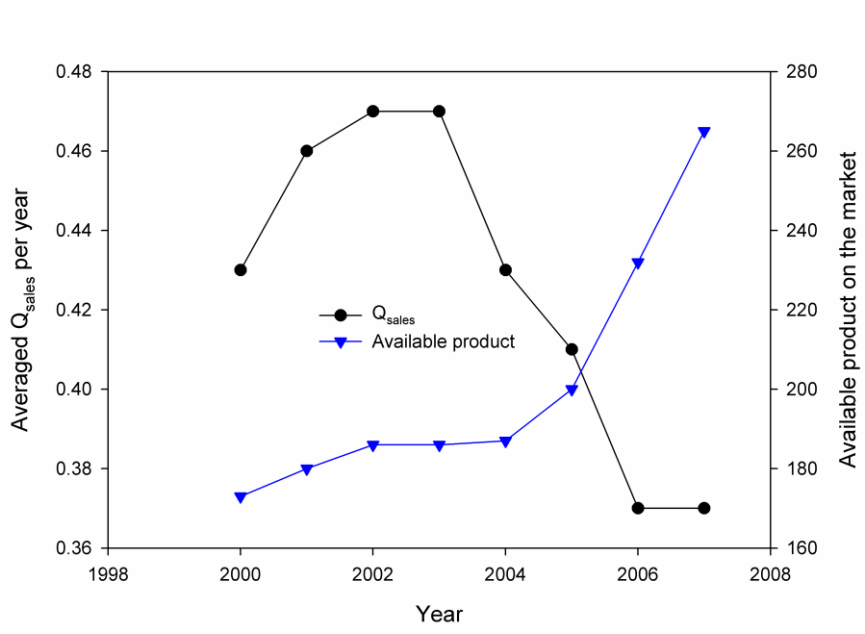


Figure 3.17.1: Averaged sales data per year and available products on the market between 2000 and 2007.

b) Products involving “Permethrin” as active substance represent more than 30% of the aggregated risk for both HR and ER, whereas aerosol type products contribute to about 25%.

c) The risk index (RI) provides information on the risk per unit of sold product (usually in kg). Its value was rescaled between 0 and 1 with a median of 0.5 assigned to the averaged RI for the reference year 2001. Figure 3.17.2 shows that RI for both [HR, Σproducts] and [ER, Σproducts] remains remarkably stable over the investigated period, but that RI for products containing Permethrin or aerosol type products display considerably higher RI-values.

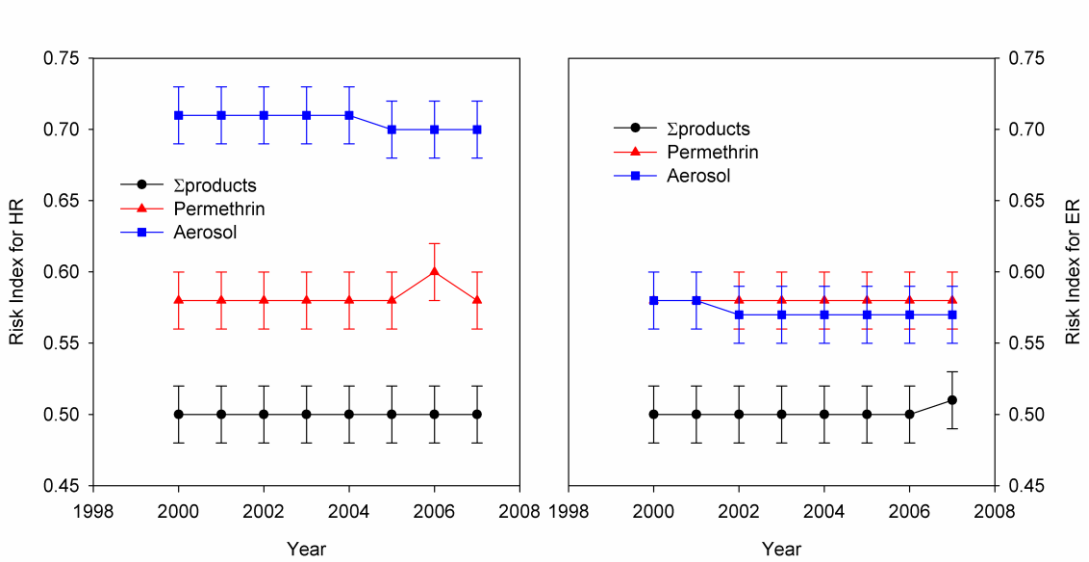


Figure 3.17.2: Risk Index for BIBELPT18

3.18 Summary and remarks

The BIBEL methodology was presented during the PRPB meeting of 27.09.07. It included the design of the indicator, the uncertainty and sensitivity analysis. Calculations were performed for biocides type EU-18, but can in principle be extended to other type products (see Theme 4: Development of a BIBEL indicator for wood preservatives). The data are available in Excel spreadsheets (2010BIBELPT18HR and 2010BIBELPT18ER). Examples of applications are given in Table 3.17.1. The question was raised whether or not it is relevant to consider the uncertainty on scoring. The general consensus was to withdraw these calculations at least within a first tier approach. Under these conditions, the uncertainty decreased from 28 to 25% for HumRisk and from 25 to 21% for EcoRisk. With respect to the exposure calculations, traceability was clearly improved, especially regarding the distinction made between professional and non-professional use (see 3.4.2.1.). Yet it is crucial to carefully check the **default values** chosen in the scenarios of the European Technical Notes for Guidance. It should be noted that BIV for PT18 biocides was computed using the risk index represented by the HumRisk or the EcoRisk and the frequency of use represented by the sales data. However, sales data are rarely, if ever, attributed to a specific biocide application. Propositions to upgrade the calculation of a frequency of use and to build-up a data base of biocides uses in Belgium are discussed in sections 3.11 to 3.13.

4 Assessing the difference of the NIJS and BIBEL approach

The two indicators have to be compared in order to identify:

- What kind of differences may exist between the indicators?
- At which levels the differences are to be found?
- What is the overall impact on the final indicator value?

The results are illustrated in Figures 4.1 and 4.2 and can be summarized as follows:

4.1 Variable: HumTox

Despite different scores with respect to acute and chronic effects, both scoring (NIJS and BIBEL) yielded essentially similar results. The Spearman's rank correlation coefficient or Spearman's rho, which assesses how well an arbitrary monotonic function could describe the relationship between two variables, without making any assumptions about the frequency distribution of the variables, is around 0.96. Accordingly, it can be stated that about 92% of the variation in either scoring was explained by its correlation with the other (Fig. 4.1A). Only in the upper 95 percentiles, some differences were detected, but those concern a few biocides on a total of 152. We are therefore confident that the scoring process cannot deeply bias the risk assessment.

4.2 Variable: HumExp

The Spearman's rank correlation coefficient is around 0.38. Both variables tend to increase together ($p < 0.0001$) but less than 14% of the variation in either variable is explained by its correlation with the other. The interpretation of these results is complicated by the fact that the scaling between NIJS and BIBEL is dissimilar (Figure 4.1B). To understand these differences, robust statistical methods, based on ranking and making use of percentiles (P25, P50 and P75) were applied to the data. Under these conditions, we identified five main contrasting behaviours:

- Category I: Products < P25 for NIJS but > P75 for BIBEL
- Category II: Products < P25 for NIJS but P50 ≤ Products ≤ P75 for BIBEL
- Category III: Products > P75 for NIJS but P25 ≤ Products ≤ P50 for BIBEL
- Category IV: Products < P25 for BIBEL but P50 ≤ Products ≤ P75 for NIJS
- Category V: Products > P75 for BIBEL but P25 ≤ Products ≤ P50 for NIJS

Detail on these groups are presented in Table 4.2.1

Following remarks can be given in relation to these contrasting groups:

- Cat. I concerns aerosols with multiple active ingredients
- Cat. II is mainly dusting powders and solutions ready to use
- Cat. V is mainly solutions ready to use

Table 4.2.1: List of product name, code, active substance, user and its application ordered by category.

Product name	Code	Active substance	User*	application
Group I				
Bolfo Fleegard Spray	1699	Cyfluthrine (0.04%) Pyriproxyfen (0.05%)	NP	Spraying, aerosol
Insecticide Kapo Special Mites et Larves	776	d-phenothrine (0.10%) permethrine (0.15%) tetrametrine (0.10%)	NP	Spraying, trigger
Insecticide Kaporex tous insectes rampants	1200	Cypermethrine (0.20%) d-phenothrine (0.13%) tetrametrine (0.15)	NP	Spraying, Trigger
Group II				
Bio Kill Pets	3498	Permethrine (2.2g/L)	NP	Solution ready to use
Canitex Powder	1582	Permethrine (1.2%)	NP	Dusting powder
Flamingo Antiparasiet halsband	3400	Permethrine (10%)	NP	Collar
Kadox spray	398	Chlorpyriphos (2g/L) Fenoxycarbe (0.2g/L)	NP	Ready to use solution, pouring
Mafu Mothbag	4699	Transfluthrine (0.42%)	NP	Strips and cassettes
Max Poudre Insecticide	1698	Permethrine (1%)	NP	Dusting Powder
Poudre Antipuces	5384	Permethrine (1.2%)	NP	Dusting Powder
Pulvex Spot	692	Permethrine (65%)	NP	Solution ready to use
Pyrethro Pure Spray	2704	Pyrethrine (0.25%)	NP	Spraying, trigger
Solution Antipuces et Antitiques	5897	Piperonyl butoxide (1g/L) Pyrethrine (0.25g/L)	NP	solution ready to use
Total Insecticide	2301	Permethrine (0.28%)	NP	solution ready to use
Vermikill Vlooienpoeder	9083	Pyrethrine (0.75%)	NP	Dusting powder
Vitakraft Insecticide Vlooienpoeder	1596	Pyrethrine (0.75%)	NP	Dusting powder
Youcky vlooienpoeder hond/kat	5299	Pyrethrine (0.75%)	NP	Dusting powder
Zerox One Shot	3599	Piperonyl butoxide (2.4%) Pyrethrine (0.3%)	NP & P	Trigger 1 shot
Detrans CIK	500	Deltamethrine (0.02%)	NP	Trigger
Group III				
Kapo insecticide tous insectes volants	3496	d-phenothrine (0.15%) tetramethrine (0.25%)	NP	Solution ready to use
KO Spray insects volants	2701	d-phenothrine (0.15%) tetramethrine (0.3%)	NP	Spraying, trigger
Responsar Sc 125	2497	Beta-cyfluthrine (125g/L)	P	Concentrated solution
Zerox P.A.	3579	Piperonyl butoxide (1.12%) Pyrethrine (0.14%)	NP	Spraying, trigger
Group IV				
Ezalo liquid	4197	Esbiothrine (1.7%)	NP	Electrical evaporator
Vapona Tablet	1680	Allethrine (4.3%) Piperonyl butoxide (4.2%)	NP	Evaporation from strips and cassettes

Group V Bieva Spray	793	Bioresmethrine (0.2g/L) Piperonyl butoxide (15g/L) Permethrine (2g/L)	NP & P	Solution ready to use
Collieer Anti-puces pour chat Friskies	3486	Permethrine (8%)	NP	Collar
Diagnose insecticide spray	1300	Permethrine (1%)	NP	Spraying, trigger
Natura shampooing anti-parasitaire	4901	Permethrine (1%)	NP	Solution ready to use (shampooing)
Pedigree Care Vlooienspray	6605	Permethrine (1%)	NP	Solution ready to use (spraying)
Pet star vlooienshampoo hond/kat	2897	Permethrine (1%)	NP	Solution, ready to use (shampooing)
Pinto	9387	Piperonyl butoxide (1.2%) Pyrethrine (0.5%)	NP	Solution, ready to use
Pyretrex fogger	1296	Piperonyl butoxide (24g/L) Pyrethrine (3g/L)	P	Nebulisator solution
Shampooing Antipuces	4497	Permethrine (0.1%)	NP	Solution, ready to use (shampooing)
Vapona mierenstop	2302	Cyphenothrine (0.1%) d-trans-tetramethrine (0.1%)	NP	Spraying, trigger
Vermikill Insecticide Spray	3399	Permethrine (1%)	NP	Spraying, trigger

** P : Professional; NP : Non-Professional*

It is obvious that the BIBEL-approach is giving much attention to the different application scenarios (see Table 3.4.8.1.1) and this is reflecting in the product categories.

4.3 Variable: EcoTox

The Spearman's rank correlation coefficient is around 0.75. Both variables tend to increase together ($p < 0.0001$) and about 50% of the variation in either scoring was explained by its correlation with the other.

4.4 Variable: EcoExp

The Spearman's rank correlation coefficient is around 0.48. Both variables tend to increase together ($p < 0.0001$) but less than 25% of the variation in either variable is explained by its correlation with the other. This poor correlation is merely explained by the fact that the probability distribution functions (pdf) for NIJS (discrete binomial type distribution) and BIBEL (Continuous exponential type distribution) are totally different; the data range for BIBEL (0.0008 to 8) far exceeding the four NIJS categories.

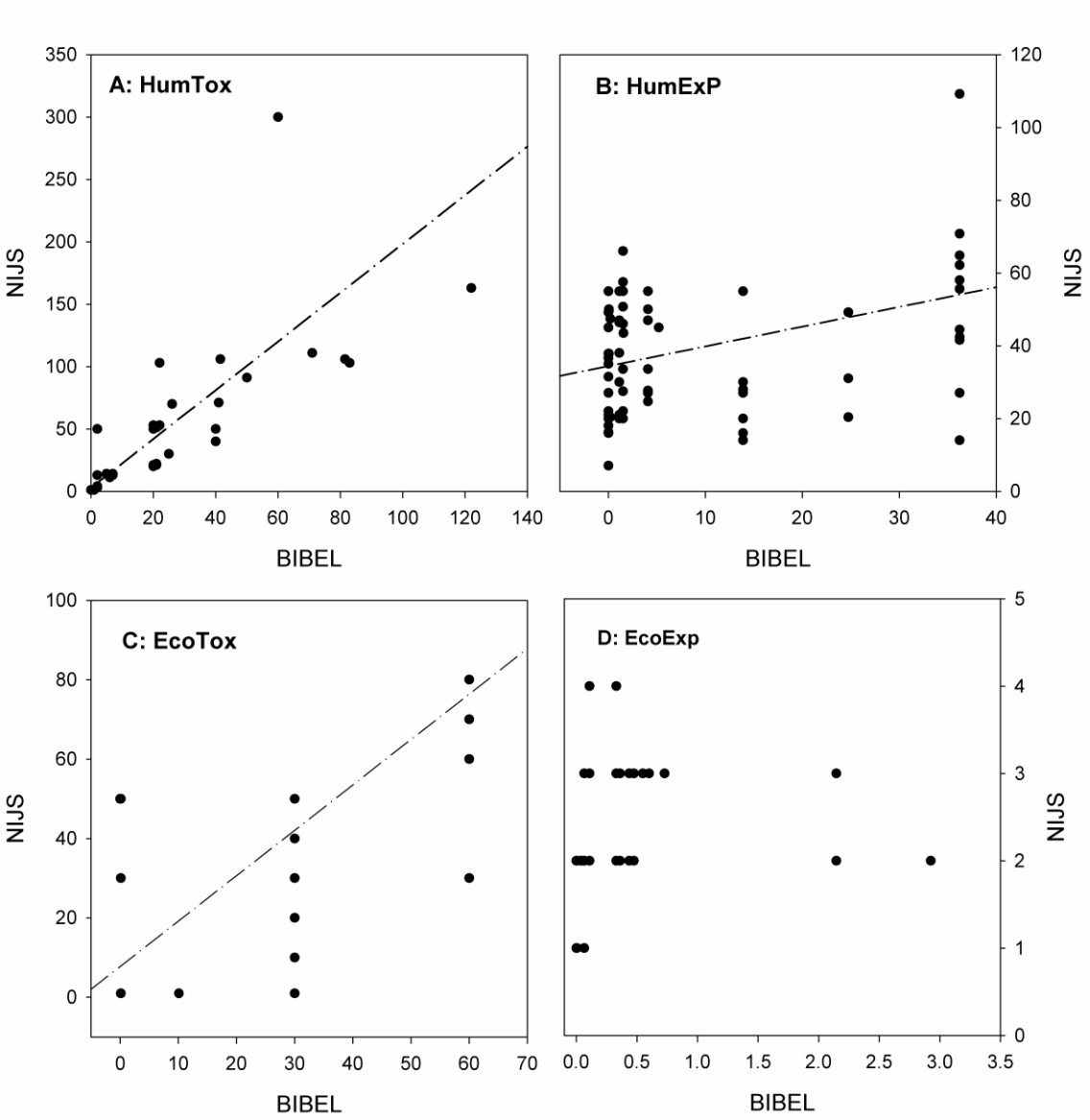


Figure 4.1: Relationships between NIJS and BIBEL for variables HumTox, HumExp, EcoTox and EcoExp.

4.5 Risk indexes

The risk index was computed within a health (HumRisk) and an environmental (EcoRisk) risk assessment perspective (Figure 4.2):

- For HumRisk, the Spearman's rank correlation coefficient is around 0.67. Both variables tend to increase together ($p < 0.0001$) and about 45% of the variation in either scoring was explained by its correlation with the other.
- For EcoRisk, the Spearman's rank correlation coefficient is around 0.68. Both variables tend to increase together ($p < 0.0001$) and about 45% of the variation in either scoring was explained by its correlation with the other.

These results are not surprising given the Spearman's rank correlation values that were obtained individually for each variable HumTox, HumExp, EcoTox and EcoExp.

4.6 NIJS and BIBEL Indicator values

- For HumRisk, the Spearman's rank correlation coefficient is around 0.85. Both variables tend to increase together ($p < 0.0001$) and about 72% of the variation in either scoring was explained by its correlation with the other.
- For EcoRisk, the Spearman's rank correlation coefficient is around 0.82. Both variables tend to increase together ($p < 0.0001$) and about 67% of the variation in either scoring was explained by its correlation with the other.

Overall, the introduction of the sales data within the computations tends to attenuate the differences between both algorithmic.

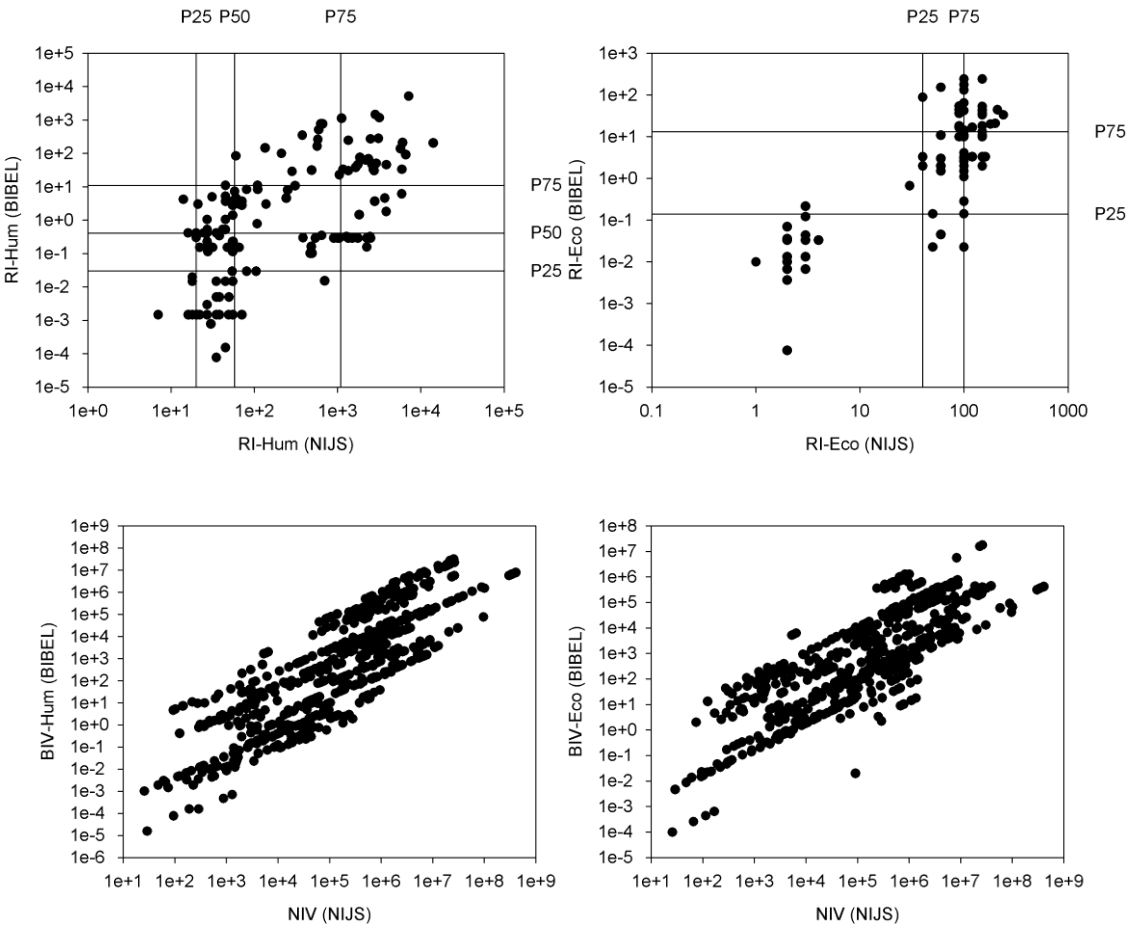


Figure 4.2: Relationships between NIJS and BIBEL for the risk index and risk indicator

5 Conclusions

Risk per se is rather a theoretical concept than a concrete variable, and is therefore not measurable in the real world. Hence, validation of risk indicators has to be carried out indirectly. This has been done by different complementary approaches:

- Statistic approach: We investigated the robustness of the risk indicators through sensitivity and uncertainty analyses. The objective was to focus on the examination of variation in temporal risk trends and the sensitivity of trends to variability in input data. While this approach provides useful information about statistic soundness, it does not clarify the meaningfulness or reliability of the indicator.
- Comparing indicators: We compared the BIBEL and NIJS approaches. Both indicators showed comparable temporal risk trends. While this may increase their credibility, it primarily indicates that they are driven by the same variables but does not necessarily prove the indicator accuracy.
- Scoring and normalisation: It is generally accepted that scores are not to be introduced too early in the aggregation process, and that scores includes risk management decisions, which are not a scientist responsibility. This brings to the distinction between aggregation with our without valuation. However, scoring can be avoided for some of the possible questions but not for all; as an example some of the questions from OECD (2002).

“Aggregate effects of biocides for human and environmental exposure”, and “Can this number be used to show trends over the last 5-10 years?”

“Has a particular policy significantly reduced health and/or environmental risks”?

These questions involves aggregation across components, time and possibly also across hazards and substances, simultaneously. In consequence valuation and techniques like scoring or fuzzy logic are necessary to answer part of the questions that we can foresee. We suggested a normalisation/scoring, based on a “membership function” of the following form:

$$Risks = \begin{cases} 0 & for \quad x < LWL \\ a \cdot x + b & for \quad LWL \le x \le UWL \\ 1 & for \quad x > UWL \end{cases} \tag{3.5.1}$$

where LWL and UWL are lower and upper warning limits determined using robust statistical methods. This normalisation/scoring implies that the range of the indicator response is restricted to lie between zero and one providing intuitive risk awareness: 0 ≤ NNIV ≤ 0.5 insignificant to significant risks; 0.5 < NNIV ≤ 1 significant to highly significant risks. This avoids part of the problems that appears when non-continuous scores or classes are combined in an aggregation process. Further more, the idea of classes is to be maintained, there are tools that define this classes by fuzzy sets, avoiding also the problems with the non-continuous classes and that at the same time are user friendly and easily understandable by most users.

6 Appendix A: Uncertainty on TNsG scenarios

This section summarizes the formulae used to assess the uncertainty on model scenarios as recommended by the Technical Notes for Guidance.

6.1 Surface / Space spraying

Primary exposure

$$EXP_P = EXP_{D1} + EXP_{I1}$$
$$\sigma^2_{EXP_P} = \sigma^2_{EXP_{D1}} + \sigma^2_{EXP_{I1}}$$

Dermal exposure

$$EXP_{D1} = \frac{\left(X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho}\right) \cdot N_{day} \cdot T_{app}}{BW}$$
$$\sum = X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho}$$
$$\sigma^2_{EXP_{D1}} = EXP_{D1}{}^2 \cdot \left(\left(\frac{\sigma_\Sigma}{\Sigma}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{BW}}{N_{BW}}\right)^2 \right)$$
$$\sigma^2_\Sigma = \left(X_{bod} \cdot RP_{clo}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{bod}}}{X_{bod}}\right)^2 + \left(\frac{\sigma_{RP_{clo}}}{RP_{clo}}\right)^2 \right) + \left(X_{han} \cdot RP_{glo}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{han}}}{X_{han}}\right)^2 + \left(\frac{\sigma_{RP_{glo}}}{RP_{glo}}\right)^2 \right)$$
$$+ \left(X_{fee} \cdot RP_{sho}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{fee}}}{X_{fee}}\right)^2 + \left(\frac{\sigma_{RP_{sho}}}{RP_{sho}}\right)^2 \right)$$

Inhalatory exposure

$$EXP_{I1} = \frac{X_{inh} \cdot RP_{mas} \cdot RR \cdot T_{app} \cdot N_{day}}{BW}$$
$$\sigma^2_{EXP_{I1}} = EXP_{I1}{}^2 \cdot \left(\left(\frac{\sigma_{X_{inh}}}{X_{inh}}\right)^2 + \left(\frac{\sigma_{RP_{mas}}}{RP_{mas}}\right)^2 + \left(\frac{\sigma_{RR}}{RR}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{BW}}{BW}\right)^2 \right)$$

Secondary exposure

$$EXP_S = EXP_{D2} + EXP_{O2}$$
$$\sigma^2_{EXP_S} = \sigma^2_{EXP_{D2}} + \sigma^2_{EXP_{O2}}$$

Dermal exposure

$$EXP_{D2} = \frac{T_{app} / A_{roo} \cdot R_{pro} \cdot F_{acc} \cdot F_{dep} \cdot F_{dis} \cdot TC \cdot T_{\exp}}{A_{chi} \cdot BW_{chi}}$$

$$\sigma^2_{EXP_{D2}} = EXP_{D2}{}^2 \cdot \left(\begin{array}{l} \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{A_{roo}}}{A_{roo}}\right)^2 + \left(\frac{\sigma_{R_{pro}}}{R_{pro}}\right)^2 + \left(\frac{\sigma_{F_{acc}}}{F_{acc}}\right)^2 + \left(\frac{\sigma_{F_{dep}}}{F_{dep}}\right)^2 + \left(\frac{\sigma_{F_{dis}}}{F_{dis}}\right)^2 \\ + \left(\frac{\sigma_{TC}}{TC}\right)^2 + \left(\frac{\sigma_{T_{\exp}}}{T_{\exp}}\right)^2 + \left(\frac{\sigma_{A_{chi}}}{A_{chi}}\right)^2 + \left(\frac{\sigma_{BW_{chi}}}{BW_{chi}}\right)^2 \end{array} \right)$$

Oral exposure

$$EXP_{O2} = EXP_{D2} \cdot T_{h-m}$$

$$\sigma^2_{EXP_{O2}} = EXP_{O2}{}^2 \cdot \left(\left(\frac{\sigma_{EXP_{D2}}}{EXP_{D2}}\right)^2 + \left(\frac{\sigma_{T_{h-m}}}{T_{h-m}}\right)^2 \right)$$

6.2 Electrical evaporator

Primary exposure

$$EXP_P = EXP_{I1}$$

$$\sigma^2_{EXP_P} = \sigma^2_{EXP_{I1}}$$

Inhalatory exposure

$$EXP_{I1} = \frac{C_{roo} \cdot T_{app} \cdot RR \cdot N_{day}}{BW_{chi}}$$

$$\sigma^2_{EXP_{I1}} = EXP_{I1}{}^2 \cdot \left(\left(\frac{\sigma_{C_{roo}}}{C_{roo}}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{RR}}{RR}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{BW_{chi}}}{BW_{chi}}\right)^2 \right)$$

$$C_{roo} = \frac{R_{pro} \cdot T_{app}}{V_{roo}}$$

$$\sigma^2_{C_{roo}} = C_{roo}{}^2 \cdot \left(\left(\frac{\sigma_{R_{pro}}}{R_{pro}}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{V_{roo}}}{V_{roo}}\right)^2 \right)$$

Secondary exposure

$$EXP_S = EXP_{D2} + EXP_{O2}$$

$$\sigma^2_{EXP_S} = \sigma^2_{EXP_{D2}} + \sigma^2_{EXP_{O2}}$$

Dermal exposure

$$EXP_{D2} = \frac{T_{app}/A_{roo} \cdot R_{pro} \cdot F_{acc} \cdot F_{dep} \cdot F_{dis} \cdot TC \cdot T_{\exp}}{A_{chi} \cdot BW_{chi}}$$

$$\sigma^2_{EXP_{D2}} = EXP_{D2}{}^2 \cdot \left(\begin{array}{l} \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{A_{roo}}}{A_{roo}}\right)^2 + \left(\frac{\sigma_{R_{pro}}}{R_{pro}}\right)^2 + \left(\frac{\sigma_{F_{acc}}}{F_{acc}}\right)^2 + \left(\frac{\sigma_{F_{dep}}}{F_{dep}}\right)^2 + \left(\frac{\sigma_{F_{dis}}}{F_{dis}}\right)^2 \\ + \left(\frac{\sigma_{TC}}{TC}\right)^2 + \left(\frac{\sigma_{T_{\exp}}}{T_{\exp}}\right)^2 + \left(\frac{\sigma_{A_{chi}}}{A_{chi}}\right)^2 + \left(\frac{\sigma_{BW_{chi}}}{BW_{chi}}\right)^2 \end{array} \right)$$

Oral exposure

$$EXP_{O2} = EXP_{D2} \cdot T_{h-m}$$

$$\sigma^2_{EXP_{O2}} = EXP_{O2}{}^2 \cdot \left(\left(\frac{\sigma_{EXP_{D2}}}{EXP_{D2}}\right)^2 + \left(\frac{\sigma_{T_{h-m}}}{T_{h-m}}\right)^2 \right)$$

6.3 Evaporation from strips and cassettes

Primary exposure

$$EXP_P = EXP_{D1} + EXP_{I1}$$

$$\sigma^2_{EXP_P} = \sigma^2_{EXP_{D1}} + \sigma^2_{EXP_{I1}}$$

Dermal exposure

$$EXP_{I1} = \frac{C_{str} \cdot T_{s-h} \cdot N_{day}}{BW}$$

$$\sigma^2_{EXP_{I1}} = EXP_{I1}{}^2 \cdot \left(\left(\frac{\sigma_{C_{str}}}{C_{str}}\right)^2 + \left(\frac{\sigma_{T_{s-h}}}{T_{s-h}}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{BW}}{BW}\right)^2 \right)$$

Inhalatory exposure

$$EXP_{I1} = \frac{C_{roo} \cdot T_{app} \cdot RR \cdot N_{day}}{BW}$$

$$\sigma^2_{EXP_{I1}} = EXP_{I1}{}^2 \cdot \left(\left(\frac{\sigma_{C_{roo}}}{C_{roo}}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{RR}}{RR}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{BW}}{BW}\right)^2 \right)$$

$$C_{roo} = \frac{C_{str} \cdot T_{app}}{Rt \cdot V_{roo}}$$

$$\sigma^2_{C_{roo}} = C_{roo}{}^2 \cdot \left(\left(\frac{\sigma_{C_{str}}}{C_{str}}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{Rt}}{Rt}\right)^2 + \left(\frac{\sigma_{V_{roo}}}{V_{roo}}\right)^2 \right)$$

Secondary exposure

$$EXP_S = EXP_{I2} + EXP_{O2}$$
$$\sigma^2_{EXP_S} = \sigma^2_{EXP_{I2}} + \sigma^2_{EXP_{O2}}$$

Inhalatory exposure

$$EXP_{I2} = \frac{C_{roo} \cdot T_{\exp} \cdot RR_{chi} \cdot N_{day}}{BW_{chi}}$$
$$\sigma^2_{EXP_{I2}} = EXP_{I2}{}^2 \cdot \left(\left(\frac{\sigma_{C_{roo}}}{C_{roo}} \right)^2 + \left(\frac{\sigma_{T_{\exp}}}{T_{\exp}} \right)^2 + \left(\frac{\sigma_{RR_{chi}}}{RR_{chi}} \right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}} \right)^2 + \left(\frac{\sigma_{BW_{chi}}}{BW_{chi}} \right)^2 \right)$$
$$C_{roo} = \frac{C_{str} \cdot T_{app}}{Rt \cdot V_{roo}}$$
$$\sigma^2_{C_{roo}} = C_{roo}{}^2 \cdot \left(\left(\frac{\sigma_{C_{str}}}{C_{str}} \right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}} \right)^2 + \left(\frac{\sigma_{Rt}}{Rt} \right)^2 + \left(\frac{\sigma_{V_{roo}}}{V_{roo}} \right)^2 \right)$$

Oral exposure

$$EXP_{O2} = \frac{C_{str} \cdot I_{foo}}{Rt \cdot \rho_{foo} \cdot BW_{chi}}$$
$$\sigma^2_{EXP_{O2}} = EXP_{O2}{}^2 \cdot \left(\left(\frac{\sigma_{C_{str}}}{C_{str}} \right)^2 + \left(\frac{\sigma_{I_{foo}}}{I_{foo}} \right)^2 + \left(\frac{\sigma_{Rt}}{Rt} \right)^2 + \left(\frac{\sigma_{\rho_{foo}}}{\rho_{foo}} \right)^2 + \left(\frac{\sigma_{BW_{chi}}}{BW_{chi}} \right)^2 \right)$$

6.4 Baits

Primary exposure Negligible

Secondary exposure Negligible

6.5 Spraying

Primary exposure

$$EXP_P = EXP_{D1} + EXP_{I1}$$
$$\sigma^2_{EXP_P} = \sigma^2_{EXP_{D1}} + \sigma^2_{EXP_{I1}}$$

Dermal exposure

$$EXP_{D1} = \frac{\left(X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho}\right) \cdot N_{day} \cdot T_{app}}{BW}$$

$$\sum = X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho}$$

$$\sigma^2_{EXP_{D1}} = EXP_{D1}{}^2 \cdot \left(\left(\frac{\sigma_\Sigma}{\Sigma}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{BW}}{N_{BW}}\right)^2 \right)$$

$$\sigma^2_\Sigma = \left(X_{bod} \cdot RP_{clo}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{bod}}}{X_{bod}}\right)^2 + \left(\frac{\sigma_{RP_{clo}}}{RP_{clo}}\right)^2 \right) + \left(X_{han} \cdot RP_{glo}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{han}}}{X_{han}}\right)^2 + \left(\frac{\sigma_{RP_{glo}}}{RP_{glo}}\right)^2 \right)$$
$$+ \left(X_{fee} \cdot RP_{sho}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{fee}}}{X_{fee}}\right)^2 + \left(\frac{\sigma_{RP_{sho}}}{RP_{sho}}\right)^2 \right)$$

Inhalatory exposure

$$EXP_{I1} = \frac{X_{inh} \cdot RP_{mas} \cdot RR \cdot T_{app} \cdot N_{day}}{BW}$$

$$\sigma^2_{EXP_{I1}} = EXP_{I1}{}^2 \cdot \left(\left(\frac{\sigma_{X_{inh}}}{X_{inh}}\right)^2 + \left(\frac{\sigma_{RP_{mas}}}{RP_{mas}}\right)^2 + \left(\frac{\sigma_{RR}}{RR}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{BW}}{BW}\right)^2 \right)$$

Secondary exposure Negligible

6.6 Fogging

Primary exposure

$$EXP_P = EXP_{D1} + EXP_{I1}$$
$$\sigma^2_{EXP_P} = \sigma^2_{EXP_{D1}} + \sigma^2_{EXP_{I1}}$$

Dermal exposure

$$EXP_{D1} = \frac{\left(X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho}\right) \cdot N_{day} \cdot T_{app}}{BW}$$

$$\sum = X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho}$$

$$\sigma^2_{EXP_{D1}} = EXP_{D1}{}^2 \cdot \left(\left(\frac{\sigma_\Sigma}{\Sigma}\right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}}\right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}}\right)^2 + \left(\frac{\sigma_{BW}}{N_{BW}}\right)^2 \right)$$

$$\sigma^2_\Sigma = \left(X_{bod} \cdot RP_{clo}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{bod}}}{X_{bod}}\right)^2 + \left(\frac{\sigma_{RP_{clo}}}{RP_{clo}}\right)^2 \right) + \left(X_{han} \cdot RP_{glo}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{han}}}{X_{han}}\right)^2 + \left(\frac{\sigma_{RP_{glo}}}{RP_{glo}}\right)^2 \right)$$
$$+ \left(X_{fee} \cdot RP_{sho}\right)^2 \cdot \left(\left(\frac{\sigma_{X_{fee}}}{X_{fee}}\right)^2 + \left(\frac{\sigma_{RP_{sho}}}{RP_{sho}}\right)^2 \right)$$

Inhalatory exposure

$$EXP_{I1} = \frac{X_{inh} \cdot RP_{mas} \cdot RR \cdot T_{app} \cdot N_{day}}{BW}$$

$$\sigma^2_{EXP_{I1}} = EXP_{I1}{}^2 \cdot \left(\left(\frac{\sigma_{X_{inh}}}{X_{inh}} \right)^2 + \left(\frac{\sigma_{RP_{mas}}}{RP_{mas}} \right)^2 + \left(\frac{\sigma_{RR}}{RR} \right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}} \right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}} \right)^2 + \left(\frac{\sigma_{BW}}{BW} \right)^2 \right)$$

Secondary exposure Negligible

6.7 Pouring

Primary exposure

$$EXP_P = EXP_{D1}$$

$$\sigma^2_{EXP_P} = \sigma^2_{EXP_{D1}}$$

Dermal exposure

$$EXP_{D1} = \frac{\left(X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho} \right) \cdot N_{day} \cdot T_{app}}{BW}$$

$$\sum = X_{bod} \cdot RP_{clo} + X_{han} \cdot RP_{glo} + X_{fee} \cdot RP_{sho}$$

$$\sigma^2_{EXP_{D1}} = EXP_{D1}{}^2 \cdot \left(\left(\frac{\sigma_{\Sigma}}{\Sigma} \right)^2 + \left(\frac{\sigma_{N_{day}}}{N_{day}} \right)^2 + \left(\frac{\sigma_{T_{app}}}{T_{app}} \right)^2 + \left(\frac{\sigma_{BW}}{N_{BW}} \right)^2 \right)$$

$$\sigma^2_{\Sigma} = \left(X_{bod} \cdot RP_{clo} \right)^2 \cdot \left(\left(\frac{\sigma_{X_{bod}}}{X_{bod}} \right)^2 + \left(\frac{\sigma_{RP_{clo}}}{RP_{clo}} \right)^2 \right) + \left(X_{han} \cdot RP_{glo} \right)^2 \cdot \left(\left(\frac{\sigma_{X_{han}}}{X_{han}} \right)^2 + \left(\frac{\sigma_{RP_{glo}}}{RP_{glo}} \right)^2 \right)$$
$$+ \left(X_{fee} \cdot RP_{sho} \right)^2 \cdot \left(\left(\frac{\sigma_{X_{fee}}}{X_{fee}} \right)^2 + \left(\frac{\sigma_{RP_{sho}}}{RP_{sho}} \right)^2 \right)$$

Secondary exposure Negligible

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