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Validation of Monte Carlo models for estimating pesticide intake of Dutch infants

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SUMMARY

In the EU project Monte Carlo probabilistic methods for exposure assessment have been developed for additives, nutrients and pesticides. This report describes the validation of the pesticide model by comparing Monte Carlo (MC) model results, based on Dutch monitoring data, with the exposure estimated from a duplicate diet study in 250 Dutch infants, and with the traditional point estimate IESTI (International estimate of short-term intake) calculated from the same data.
In the duplicate diet study, the six selected pesticides occurred in 3-9 out of the 250 samples (1.2-3.6 %).

The basic Monte Carlo model was enhanced by including information on processing factors, variability between units within composite samples, and by applying the precautionary principle to measurements below the limit of reporting (i.e. the limit of reporting was used for nondetects in the calculations for all 64 measured products in the monitoring database).

The Monte Carlo model was considered to be validated for the intended application (fit for purpose), if the predicted 99th percentile (p99) of the exposure distribution was higher than the estimate from the duplicate diet study, but lower than the traditional point estimate.

For five pesticides (chlorfenvinphos, chlorpyrifos, iprodione, methamidophos and pirimiphos-methyl) the validation of the enhanced model (MC vn or MC pvn) was unambiguous (non-overlapping 95 % confidence intervals of the percentile estimates). In the case of pirimicarb, the p99 estimates were also in the right order, but the confidence interval of the duplicate diet estimate (0.04-1.55) did overlap somewhat with the confidence interval of the MC model (1.16-2.94). A direct comparison of the two models in one bootstrap procedure would enable a more sensitive statistical comparison and probably a clear validation, but such a test could not be executed with the current software.
Similar conclusions were obtained for lower tail percentiles (p90, p95, p97.5). For higher percentiles (p99.9, p99.99) the estimates were still in the right order, but there was overlap in the 95% confidence intervals of the MC model estimate and the IESTI for some food products. In this report we also give results for the median exposure (p50), but we do not consider these as trustworthy estimates, because there is not any empirical information about this percentile in the actual data. In general, we conclude that the most precise validation is possible for percentiles in the actually observed region (p99 and sometimes p97.5 in this study).

The main conclusion is, that the traditional point estimate (IESTI) gives an enormous overestimation of the actual exposure as measured in the duplicate diet study. The Monte Carlo model provides much more realistic estimates, these estimates being still conservative in comparison with the duplicate diet results. Therefore the Monte Carlo results are still in accordance with the precautionary principle, and are validated for the investigated cases.

1 INTRODUCTION

This report describes a validation study of a stochastic (or Monte Carlo) model for the assessment of acute risks due to the intake of pesticides from food. The model combines food consumption survey data and pesticide concentration data from monitoring programs. The model allows for effects of food processing between monitoring and ingestion, it can model unit variability, and it uses information on limit of reporting to check whether nondetects present a source of uncertainty.
The current paper is only concerned with single-pesticide risk modelling. Multiple-compound cumulative assessments are outside the scope of the current model.

2 METHODS

2.1 Monte Carlo modelling of pesticide intake

The basic Monte Carlo (MC) model for estimating pesticide intake is

$$y_{ij} = \frac{\sum_{k=1}^{p} x_{ijk}\ c_{ijk}}{bw_i}$$

where y_{ij} is the intake by individual i on day j (in µg pesticide per kg body weight), x_{ijk} is the consumption by individual i on day j of food commodity k (in g), c_{ijk} is the concentration of the pesticide in commodity k eaten by individual i on day j (in mg/kg, 'ppm'), and bw_i is the body weight of individual i (in kg). Finally, p is the number of food commodities accounted for in the model.
Note that the definition of 'commodity' is flexible: it may represent a raw agricultural commodity (RAC), e.g. 'apple', but it may also be a processing-related subdivision, e.g. 'apple, peeled' or 'apple, juiced'.

In the stochastic model the quantities x_{ijk}, bw_i and c_{ijk} are assumed to arise from probability distributions for individual food consumption and weight, $p(x_1,\ldots,x_p,bw)$, and for pesticide concentrations in each food commodity, $p_k(c)$. In principle these probability distributions may be parametric (e.g. completely defined by the specification of some parameter values) or empirical (e.g. only implicitly and roughly defined by the availability of a representative sample). In this paper only empirical distributions are used in the MC model.

The empirical distribution of food consumption and body weight was collected in a dietary study of 250 Dutch non-breast-fed infants (one-day diary). A recipe database has been used to convert the amounts of food as consumed to amounts of commodities ($x_1,\ldots,x_p$) which are used in the model.

The empirical distribution of chemical residues in raw agricultural commodities (RACs), based on monitoring programs, is available from the Quality Programme for Agricultural Products (KAP database, van Klaveren 1999). This database records the frequency of positive results in the monitoring data, as well as the actual measurement values of the positives.

Given these probability distributions (or estimates thereof) of consumption and residue concentrations Monte Carlo simulations have been used to generate an estimate of the probability distribution $p(y_{ij})$ to assess acute (short-term) risks by intake of the pesticide.

There are several optional features that may be added to the basic model, in order to deal with some important aspects of reality:

1. processing factors (p): chemical concentrations are multiplied with processing factors, depending on pesticide, commodity and processing type. The list of processing factors available for this study is given in Appendix 1, Table 10.
2. variability factors (v): residue concentrations used in the MC model have been measured in composite samples (consisting of n_u units), whereas a consumer typically eats individual units of parts thereof. Therefore it may be realistic to include information about the variability of residue concentrations between individual units. However, in this study such information was not available. We restrict the attention to the worst case assumption, that the variability in the composite sample was maximal, with one unit containing a residue concentration that is n_u times higher than the measured concentration, and the remaining units that have no residue. This is approach 3c as described in Appendix 3. In the simulations, for each whole or partial unit that is consumed, any residue concentration drawn from the empirical distribution of composite sample concentrations, is multiplied by n_u (with probability n_u^{-1}) , or by 0 otherwise. The number of units in a composite sample (n_u) depend on the unit weight of the raw agricultural commodities (see Appendix 1, Table 11). n_u equals 5 for unit weights above 250 g, it is 7 for unit weights between 25 and 250 g, and it is set to 1 (no variability) for unit weights up to 25 g and also when the processing type is 9 (juicing). For further discussion on variability factors see Appendix 3.
3. nondetects replacement (n): Chemical concentrations are only reported above certain levels. These levels are called the limit of reporting (LOR), often also indicated as limit of detection (LOD) or quantification (LOQ), although such indications are incorrect. LOR values are given in Appendix 1, Table 12. For chemical nondetects we do not know whether the pesticide was really absent, or that is was present in a concentration below LOR (censored observations). In this study we only consider the worst-case assumption that all nondetects really had a concentration equal to the LOR.

In this paper we use the MC model as implemented in the software developed in the EU research project Monte Carlo by the Department of Mathematics of Trinity College Dublin, Ireland (Monte Carlo Project Team 2002).

Models will be coded with the letters given in parentheses, for example the *MC pvn* model runs a Monte Carlo simulation with all three options, whereas the *MC vn* model includes variability factors and nondetect replacement, but no processing factors.

2.2 Statistical methods for validation

Validation is, according to the definition of the International Standard on quality management systems (ISO 9000) *the confirmation through the provision of objective evidence that the requirements for a specific intended use or application have been fulfilled*. Therefore different

intended uses require different validation studies, and we will first detail the intended use of the MC model which underlies this validation study.

In the validation study described her, the intended use of the MC model is the assessment of the dietary exposure of non-breast-fed Dutch infants to 6 specific pesticides, based on the dietary records in an empirical sample of 250 infants, and the chemical concentration data from the national Quality Programme for Agricultural Products monitoring. The interest is particularly in the upper percentiles of the exposure distribution because these are of concern for the risk evaluation of pesticides. A further particular requirement follows from the precautionary principle in risk assessment: we don't want the MC model to underestimate the true exposure, although we can accept some overestimation due to conservative assumptions in the case of lack of information. On the other hand, fitness-for-purpose requires that the MC model should provide more realistic (i.e. lower) estimates than the deterministic estimation (IESTI) method currently in use by the FAO and WHO experts.

The true intake of the 6 pesticides has been estimated with a duplicate diet study for the same group of infants whose dietary records were used as an input to the MC model. Duplicate portions of the diets consumed (and recorded) were collected in a container, and subsequently analysed in the laboratory. This permits the estimation of true intake.

In the following three sections we describe in more detail how percentiles of the intake distribution have been estimated with a: the Monte Carlo model (section 2.3), b: the duplicate diet data (section 2.4), and c: the IESTI approach (section 2.5). In section 2.6 we describe how to compare these percentile estimates.

2.3 Estimating the intake distribution with the MC model

The MC model developed in the Monte Carlo EU project (Monte Carlo 2002) was used for each of the 6 pesticides with the following specifications:

- the subject set (250 subjects) was replicated four times;
- this enlarged set of 1000 subjects was resampled 1000 times, giving rise to 1000 bootstrap sets apart from the original set;
- results were collected for the percentiles p50, p90, p95, p97.5, p99, p99.9 and p99.99 in the form of the mean values of the 1001 bootstrap sets, and the central 95 % confidence interval;
- the program was first run in a basic version (no special options used); in this version (**MC basic** model) only the products were included for which at least one chemical concentration had been found in the monitoring program. Percentiles were also collected for the intake distributions from individual products;
- in a second and third version of the program processing factors were applied, variability of units was accounted for, and nondetect concentration measurements were replaced with the value of the LOR; one version included only the products for which positive measurements were found (**MC pvn pos** model), the other version used all 64 products recorded in the infant diets which were measured at all, reasoning that even products with no positive pesticide measurements can contribute to the intake if nondetect measurements

are replaced by the LOR (**MC pvn all** model). For the products with positive pesticide measurements also the individual intake distributions were collected.

2.4 Estimating the true intake distribution from a duplicate diet study

In principle, an empirical duplicate diet study with n individuals (n=250 here) provides an empirical distribution of n intake values. The true exposure is estimated by

$$y_i = \frac{c_i \sum_{k=1}^{p} x_{ik}}{bw_i}$$

where y_i is the intake by individual i (in µg pesticide per kg body weight), x_{ik} is the consumption by individual i of food commodity k (in g), c_i is the concentration of the pesticide in the duplicate diet (in mg/kg, 'ppm'), and bw_i is the body weight of individual i (in kg). p is the number of food commodities. In the duplicate diets of the 250 infants there were 67 food commodities. In this study we only consider the 64 commodities for which monitoring was available (ignoring the three minor commodities rose hip, elderberry, bean sprouts).

However, in the case of pesticide intake the estimated distribution will typically consist of very many nondetect measurements and only a few (3-9 in this study) positive values. Nondetects are censored observations: we only know that

$$y_i < \frac{LOR \sum_{k=1}^{p} x_{ik}}{w_i}$$

where LOR denotes the limit of reporting (in mg/kg), which is minimum pesticide concentration value that will be reported by the laboratory.

With only very few positive measurements available, the inference on percentiles of the distribution becomes very crude if only the empirical data are used. Therefore it was decided to develop a more accurate model under the additional assumption that the intake distribution is lognormal.
This model, which is fully described in Appendix 2, applies a nonparametric bootstrap procedure to the full set of intake observations (observed and nondetects). For each bootstrap sample it then fits a lognormal distribution to the observed and censored intake observations using maximum likelihood. After adjusting the estimates such that the percentage observed values in the bootstrap sample is correct, percentiles are calculated. The procedure therefore gives a bootstrap distribution for each requested percentile.

The primary results do not incorporate all aspects of the measurement uncertainty of the analytical measurements. There are indications that the recovery is substantially less than 100 %, and it is suitable to correct the results (and the LOR) for lower recovery in the validation of the MC model. A simple procedure to do this is described in Appendix 4.

The results presented here for the duplicate diet study are corrected according to this model.

The method used to estimate percentiles with confidence intervals depends on the assumption of log-normality for the distribution of all intakes. We know that this is only an approximation to the truth. Therefore the results should be interpreted with care. This is especially true for the percentile estimates that depend on extrapolation: with n=250 subjects and m=3-9 positively measured intakes all percentiles lower than p98.8 (m=3) or p96.4 (m=9), as well as all percentiles higher than p99.6 are extrapolations. Consequently we propose that with the current data p99 is the most relevant percentile on which to base the validation.

2.5 Estimating the intake using the IESTI approach

The current official method (JMPR 2001, FAO 2002) for short-term dietary risk assessment for pesticide residues in food involves the calculation of the IESTI (for International Estimate of Short-Term Intake), which can be written as

$$IESTI = (HR \text{ or } HRP) \cdot \frac{\min(wu, x_{97.5}) \cdot v + \max(0, x_{97.5} - wu)}{bw_{mean}}$$

where:

- $x_{97.5}$ is the large-portion consumption of the commodity (in practice the 97.5th percentile from the consumption data distribution);
- wu is the unit weight of one commodity;
- HR is the maximum value from the composite sample residue level distribution.
- bw_{mean} is the mean body weight of the chosen (sub)population;
- $HRP = f_{processing} HR$ is the high residue value accounting for processing; $f_{processing}$ is a factor accounting for processing and/or edible portions; the use of this factor is optional;
- v is the variability factor; in this study there were insufficient empirical data for estimating v. Therefore we follow the FAO/WHO Expert Consultation recommendation to assume (conservatively) that all residue in a composite sample is present on one unit. Under this assumption v equals the number of units in the composite sample. If Codex sampling protocols are used, then the number of units per composite sample depends on the unit weight. In this study we used, in accordance with JMPR (2001), variability factors 5 for large crops (unit weight > 250 g) and 7 for medium crops (unit weights 25-250 g). For small crops (unit weight < 25 g) no variability factor was applied (v = 1).

Intake assessment based on IESTI clearly is a conservative approach: it is assumed that a large portion of a maximally contaminated product has been consumed. IESTI can only be calculated for each commodity separately. Because of the inherent conservatism, summing over commodities would be the equivalent of assuming that large portions of *all* commodities are consumed in one and the same day, which is clearly a nonsensical assumption. Therefore, this part of the validation will be performed by comparing MC model predictions with IESTI values per commodity.

In principle the IESTI methodology applies to only one commodity and one type of processing. We calculated IESTI per commodity in two ways:

1. Ignoring the processing; in this case the variability factor was based on the unit weight only (even if part of the consumption was actually in a blended form, e.g. apple juice). This type of IESTI was used in the comparison with the basic MC model.
2. Averaging over processing types: the IESTI was calculated as the weighted average of the processing type specific IESTIs with the total amount of consumption in the dietary data set as weights. In this case the variability factor for blended products (e.g. fruit juice) was set to v=1. This type of IESTI was used in comparison with the MC pvn model.

The IESTI can be calculated conditional upon the available data for consumption and residue levels. However, in this validation study the uncertainty due to the availability of only limited data is (at least partially) accounted for by the use of bootstrap methodology. Therefore the bootstrap was also applied to the IESTI calculation: $x_{97.5}$ and bw_{mean} were calculated from bootstrap samples of the consumption data set, and HR was calculated from bootstrap samples of the residue concentration data set.
Note: in the second type of IESTI estimation, the bootstrap was only applied to the separate IESTIs per processing type. Weighted averages were made of the estimates themselves and of the lower and upper limits of the bootstrap uncertainty intervals.

There is a conceptual problem for the validation of the MC model against IESTI: which percentiles of the estimated intake distribution should be considered for comparison with IESTI? There is no clear answer to this question, because the IEST I is fundamentally a deterministic estimate based on worst-case assumptions. Although a 97.5 percentile is used for estimating a large portion, other elements in the equation (maximum of residue data, assumptions concerning variability) have no clear stochastic interpretation. We will therefore compare IESTI with the whole range of estimated percentiles (up to p99.99).

2.6 Validation of the MC models by comparing the estimates

For the validation of the MC model the two-sided 95 % confidence interval based on the bootstrap distributions were used. This is not statistically optimal for a comparison of any two models; it would have been better to use the same bootstrap samples for both models, and then calculate the bootstrap distribution for the ratio of the exposure estimates. However, such an approach is only practical when the models to be compared (MC and duplicate diet, or MC and IESTI) are available in one computational setting. This was not true in the current project, and therefore we will base our conclusions upon the separately calculated bootstrap distributions.

We looked separately at the validation status of the MC models with respect to the duplicate diet results and the IESTI. In each case we distinguished three categories (indicated in Table 7 and Table 8 with +, (+) and -, respectively):

- The MC model was considered fully validated if the MC estimate was higher than the estimate from the duplicate diet study or lower than IESTI, and moreover the bootstrap 95 % confidence intervals were completely disjunct.
- The MC model was considered tentatively validated if the MC estimate was higher than the estimate from the duplicate diet study or lower than IESTI, but with overlap of the bootstrap 95 % confidence intervals. In these cases we looked in more detail at the amount of overlap.
- The MC model was considered invalid if the MC estimate was lower than the estimate from the duplicate diet study or higher than IESTI.

3 RESULTS

3.1 General results of validation

The percentile estimates (duplicate diet and MC model) and IESTI values are reported in Tables 1-6, together with the lower and upper limits of their 95% confidence intervals. In these tables we have omitted products for which even the highest estimate (the upper confidence limit of p99.99) is less than 1 µg/kg BW/day (exception: for chlorfenvinphos we included all four products on which the residue has been found).
The results of Tables 1-6 are visualised in the sections on the six separate substances. In this section we concentrate on the implications for the validation of the MC models.

The validation results are summarized in Table 7 (comparison with duplicate diet results) and Table 8 (comparison with IESTI). As shown in the captions of these tables we distinguished three categories. The model was completely validated if the MC result was higher than the DD result or lower than the IESTI, with non-overlapping 95 % confidence intervals. In a second category the estimates were in the right order, but the 95 % confidence intervals were overlapping. Finally, the estimates in the third category were wrong (lower than the DD estimate or higher than the IESTI), so that the MC model was invalidated for these situations. In these tables we have emphasized the 99th percentile, because, as explained earlier, this is the percentile for which the empirical information is best (no extrapolation).

The results allow the following conclusions:

1. In general, the MC models are validated for estimating the intermediate percentiles in the upper tail of the exposure distribution, e.g. p97.5 or p99. However, there are some exceptions (see below).
2. As explained earlier, the duplicate diet estimates of percentiles which are far outside the empirically observed part of the distribution are questionable. Consequently, the estimation of median exposure (p50) by the MC models cannot be properly validated by comparison with duplicate diet results.
3. For this study, we propose to concentrate on the 99th percentile of exposure (p99). For this percentile, all models are validated (fit for purpose) with the exception of the basic MC model for pirimiphos-methyl.
4. In general the exposure levels were low (for example p99 estimates from the duplicate diet model were between 0.04 and 0.24 µg/kg BW/day, p99 estimates from the MC models were between 0.05 and 9 µg/kg BW/day).
5. The deterministic estimate of acute exposure currently used by the FAO/WHO experts (IESTI) was typically much higher than the exposure as estimated from either the duplicate diet model or the MC model, with values up to 624 µg/kg BW/day (for iprodione in endive).
6. At low levels of exposure the treatment of nondetects (measurements below the limit of reporting LOR) becomes crucial. Negative validation results were obtained with the MC basic model (which treats nondetects as real zero observations) whenever the estimated p99 of the exposure distribution was below 0.12 µg/kg BW/day; because of this, for pirimiphos-methyl even the p99 was estimated too low in comparison with the duplicate diet value.
7. Both the MC (p)vn model variants (pos and all) give percentiles higher than the duplicate diet percentiles (with exception of p50, see above), and may be considered fit for purpose. Of

course, the more conservative variant (pvn all) has less cases of overlapping confidence intervals (only for pirimicarb).

8. All MC models clearly improve upon the IESTI values. However, for the extreme percentiles p99.9 and p99.99 confidence intervals overlap fairly often, perhaps reflecting the fact that with n=250 there is no empirical information on these percentiles.
9. In some cases (methamidophos MC basic model, pirimicarb all MC models, and pirimiphos-methyl MC vn pos model) there are overlapping confidence intervals for p99, so that it is advisable to apply a more precise statistical comparison using one simultaneous bootstrap procedure on the ratio of the two p99 estimates (this requires the integration of the MC model and the duplicate diet model in one program).

Table 1. Chlorfenvinphos.

Percentiles of estimated intake distribution (μg/kg BW/day) from duplicate diet study (DD) and Monte Carlo models (MC), and IESTI estimates.
Entries in each cell of the table are mean, lower and upper limit of 95 % confidence interval, based on 1000 bootstrap samples.
Empty cells correspond with values < 0.0005.

model	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
DD	0.010	0.038	0.055	0.075	0.109	0.236	0.447	
	0.000	0.006	0.015	0.027	0.043	0.044	0.033	
	0.437	0.227	0.205	0.208	0.279	1.284	6.092	
MC basic		0.176	0.437	0.822	1.672	4.041	4.917	
		0.116	0.323	0.582	1.074	2.641	3.197	
		0.235	0.549	1.128	2.523	5.999	6.865	
MC vn pos		0.306	0.614	1.384	3.042	11.568	17.563	
		0.255	0.427	0.878	1.915	4.557	5.665	
		0.427	0.876	2.058	4.4	24.586	34.006	
MC vn all	0.766	1.243	1.456	2.09	3.73	13.048	19.488	
	0.745	1.2	1.343	1.646	2.65	5.361	6.768	
	0.783	1.289	1.646	2.673	5.266	26.554	35.345	
MC basic								
mandarin						0.027	0.22	10.00
						0	0	7.30
						0.462	1.314	10.70
carrot		0.174	0.434	0.817	1.669	4.041	4.917	33.70
		0.115	0.321	0.581	1.071	2.641	3.197	21.80
		0.234	0.547	1.107	2.523	5.999	6.865	34.30
celeriac						0.001	0.007	0.33
						0	0	0.11
						0.016	0.043	0.36
parsley						0.007	0.086	0.76
						0	0	0.01
						0.027	0.487	0.76
MC vn								
mandarin			0.001	0.094	0.182	0.234	0.556	10.01
			0	0.03	0.139	0.202	0.217	7.05
			0.024	0.139	0.202	0.461	4.735	10.61
carrot		0.295	0.603	1.374	3.028	11.548	17.555	33.43
		0.247	0.415	0.873	1.901	4.466	5.665	21.29
		0.34	0.86	2.058	4.4	24.582	34.006	34.35
celeriac				0.004	0.018	0.045	0.053	0.33
				0	0.014	0.02	0.045	0.11
				0.014	0.02	0.048	0.115	0.35
parsley						0.012	0.086	0.76
						0	0.004	0.01
						0.027	0.487	0.76

Table 2. Chlorpyrifos

Percentiles of estimated intake distribution (μg/kg BW/day) from duplicate diet study (DD) and Monte Carlo models (MC), and IESTI estimates.
Entries in each cell of the table are mean, lower and upper limit of 95 % confidence interval, based on 1000 bootstrap samples.
ARfD = 100 μg/kg BW/day (JMPR 1999). Empty cells correspond with values < 0.0005.

model	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
DD	0.015	0.042	0.056	0.072	0.097	0.177	0.292	
	0.002	0.009	0.013	0.017	0.022	0.035	0.048	
	0.106	0.197	0.250	0.315	0.427	0.892	1.788	
MC basic		0.026	0.317	0.610	1.061	3.028	4.386	
		0.000	0.208	0.454	0.758	1.443	1.630	
		0.101	0.438	0.789	1.495	5.764	8.494	
MC pvn pos	0.208	0.734	1.040	1.554	2.348	7.296	10.924	
	0.181	0.684	0.885	1.277	1.801	3.664	4.648	
	0.236	0.799	1.259	1.802	3.630	13.608	26.576	
MC pvn all	1.160	1.865	2.094	2.295	3.077	7.865	11.206	
	1.114	1.810	2.037	2.157	2.452	4.265	5.112	
	1.193	1.938	2.148	2.477	4.333	13.919	26.368	
MC basic								
grapefruit						0.375	0.829	16.690
						0.000	0.000	4.960
						1.128	1.860	16.690
mandarin				0.012	0.362	1.276	1.746	21.030
				0.000	0.091	0.649	0.826	13.570
				0.123	0.645	2.516	2.895	22.050
orange			0.065	0.360	0.713	1.602	2.081	30.090
			0.000	0.213	0.506	1.013	1.154	15.390
			0.196	0.517	1.001	2.630	3.872	32.350
apple					0.016	0.387	0.562	4.670
					0.000	0.160	0.219	3.730
					0.148	0.713	1.146	5.210
peach						0.275	1.185	36.150
						0.000	0.000	6.100
						2.611	5.633	38.400
nectarine						0.179	0.520	11.030
						0.000	0.000	1.390
						1.495	1.579	11.970
grape					0.013	0.854	1.849	37.910
					0.000	0.157	0.289	8.500
					0.142	3.366	7.388	39.900
spinach						0.926	2.732	6.910
						0.000	0.000	5.260
						5.521	7.398	7.210

Table (continued)

MC pvn								
grapefruit					0.017	0.562	1.636	16.690
					0.000	0.104	0.241	4.958
					0.104	1.951	7.919	16.690
mandarin			0.002	0.148	0.379	2.439	4.612	21.030
			0.000	0.035	0.232	0.670	0.954	13.000
			0.027	0.232	0.672	6.592	12.699	22.120
orange		0.146	0.313	0.510	1.052	5.017	7.906	12.960
		0.087	0.247	0.395	0.621	1.906	2.643	6.566
		0.191	0.385	0.662	1.774	10.508	17.267	13.440
apple	0.023	0.434	0.562	0.677	1.125	1.574	1.975	2.945
	0.007	0.392	0.511	0.625	0.894	1.429	1.429	2.254
	0.046	0.480	0.620	0.992	1.429	2.490	4.361	3.061
peach				0.070	0.314	0.949	2.710	32.220
				0.000	0.140	0.487	0.726	5.427
				0.141	0.488	3.992	16.587	34.000
nectarine				0.001	0.239	0.460	1.248	11.030
				0.000	0.000	0.345	0.347	1.398
				0.000	0.345	1.588	10.041	11.970
grape		0.041	0.152	0.202	0.281	1.321	3.447	13.680
		0.000	0.112	0.190	0.209	0.379	0.379	2.336
		0.085	0.190	0.210	0.379	4.869	17.245	14.68
spinach			0.149	0.355	0.438	1.386	3.067	6.793
			0.000	0.278	0.424	0.450	0.587	4.463
			0.278	0.424	0.450	5.521	7.398	7.140

Table 3. Iprodione

Percentiles of estimated intake distribution (μg/kg BW/day) from duplicate diet study (DD) and Monte Carlo models (MC), and IESTI estimates.
Entries in each cell of the table are mean, lower and upper limit of 95 % confidence interval, based on 1000 bootstrap samples.
Empty cells correspond with values < 0.0005.

model	**p50**	**p90**	**p95**	**p97.5**	**p99**	**p99.9**	**p99.99**	IESTI
DD	0.011	0.025	0.031	0.038	0.048	0.077	0.113	
	0.002	0.009	0.013	0.018	0.023	0.026	0.025	
	0.082	0.072	0.074	0.081	0.101	0.225	0.514	
MC basic		0.371	1.043	2.615	6.137	19.200	32.877	
		0.251	0.719	1.566	3.816	9.665	12.082	
		0.509	1.500	3.933	9.064	61.445	91.886	
MC pvn pos	0.261	0.734	1.816	4.131	8.918	39.001	81.067	
	0.241	0.636	1.245	2.624	5.492	14.131	17.870	
	0.284	0.879	2.549	6.094	13.824	99.749	384.526	
MC pvn all	0.521	0.983	2.031	4.280	9.008	39.275	77.420	
	0.510	0.888	1.487	2.868	5.820	13.568	17.760	
	0.533	1.108	2.789	6.051	13.159	106.760	323.854	
MC basic								
apple						1.213	3.089	52.260
						0.000	0.000	47.780
						5.566	11.129	58.280
pear						2.669	5.808	109.700
						0.000	0.000	21.000
						9.599	14.782	115.500
apricot					0.002	4.001	8.786	69.810
					0.000	0.001	0.190	2.100
					0.000	16.485	19.449	73.300
peach					0.005	2.963	6.654	149.900
					0.000	0.002	0.745	21.100
					0.001	7.986	23.620	158.900
plum						1.340	3.973	98.780
						0.000	0.000	17.600
						6.226	15.688	104.200
nectarine						1.642	5.362	139.100
						0.000	0.000	14.900
						4.565	18.565	150.900
grape				0.034	0.782	3.831	6.045	72.660
				0.000	0.225	1.513	2.061	40.500
				0.292	1.573	8.841	14.439	76.800
strawberry					0.059	2.916	5.705	23.940
					0.000	0.403	0.950	7.860
					0.441	7.985	20.111	24.660
raspberry						2.202	5.265	17.980
						0.000	0.000	3.630
						7.872	15.334	17.980
currant					1.044	7.959	10.375	16.220
					0.000	3.226	4.752	7.760
					3.098	12.162	16.413	17.280

Table (continued)

kiwi fruit				0.001	0.283	0.974	1.181	10.290
				0.000	0.000	0.554	0.680	2.880
				0.000	0.538	1.441	1.644	10.550
Carrot		0.001	0.184	0.381	0.641	1.271	1.571	10.810
		0.000	0.112	0.267	0.477	0.833	0.949	5.720
		0.002	0.255	0.491	0.851	2.042	2.240	11.050
Tomato					0.009	0.567	0.852	11.590
					0.000	0.107	0.297	6.230
					0.126	1.216	1.521	11.890
courgette						0.294	0.956	26.740
						0.000	0.000	1.960
						1.372	4.263	28.280
red cabbage						0.051	0.401	16.750
						0.000	0.000	0.330
						1.141	2.279	18.140
curly kale						0.070	0.399	15.590
						0.000	0.000	0.810
						0.800	1.853	16.990
Cabbage lettuce						0.880	4.351	151.300
						0.000	0.000	122.700
						7.382	27.233	223.100
Endive					0.134	11.262	27.830	623.900
					0.000	1.250	2.739	174.000
					1.381	61.432	91.886	660.000
Spinach						0.358	1.788	10.150
						0.000	0.000	1.590
						2.653	7.622	10.560
Chicory						1.285	5.470	136.900
						0.000	0.000	100.600
						13.780	16.012	143.700
turnip tops						0.539	2.913	15.520
						0.000	0.000	0.000
						11.416	11.416	15.520
green beans						0.185	0.474	1.314
						0.000	0.000	0.945
						0.918	1.150	1.423
MC pvn								
apple	0.024	0.199	0.250	0.340	0.515	2.061	7.029	41.590
	0.013	0.191	0.232	0.258	0.400	0.616	0.616	34.580
	0.032	0.213	0.258	0.451	0.616	7.172	38.855	43.640
pear		0.162	0.229	0.276	0.330	4.171	13.690	104.200
		0.153	0.211	0.257	0.301	0.431	0.431	20.840
		0.177	0.251	0.301	0.431	17.224	73.467	109.400
apricot				0.001	0.077	6.937	19.986	65.160
				0.000	0.007	0.236	0.490	1.939
				0.008	0.235	39.757	68.322	65.560
peach				0.030	0.183	4.783	14.120	133.600
				0.000	0.056	0.302	0.781	23.400
				0.069	0.302	22.212	49.603	141.000
plum				0.004	0.072	2.084	8.577	98.780
				0.000	0.032	0.148	0.149	19.870
				0.032	0.096	11.015	51.794	103.300

Table (continued)

nectarine			0.001	0.103	2.463	10.524	139.100
			0.000	0.000	0.139	0.139	13.920
			0.000	0.139	18.855	118.879	150.900
grape	0.021	0.074	0.140	1.042	8.105	16.038	78.560
	0.000	0.062	0.084	0.263	2.281	3.620	36.100
	0.039	0.081	0.336	2.278	20.775	48.062	82.410
strawberry		0.004	0.061	0.188	2.872	5.710	22.970
		0.000	0.017	0.085	0.349	0.893	7.015
		0.017	0.097	0.410	8.284	19.936	24.170
raspberry				0.012	2.224	5.124	13.440
				0.000	0.060	0.107	3.337
				0.061	7.872	15.447	13.440
currant			0.024	1.072	8.113	10.553	16.220
			0.000	0.033	3.402	5.151	8.340
			0.033	3.326	12.199	16.316	17.450
kiwi fruit	0.096	0.136	0.162	0.346	2.377	4.219	10.240
	0.084	0.118	0.152	0.173	0.639	0.898	2.848
	0.109	0.152	0.182	0.657	6.727	9.819	10.500
carrot	0.162	0.248	0.496	1.140	4.388	6.138	10.720
	0.150	0.216	0.330	0.653	1.977	2.516	5.535
	0.185	0.312	0.698	2.025	8.870	11.462	11.050
celeriac			0.002	0.012	0.061	0.225	3.275
			0.000	0.009	0.014	0.030	0.9334
			0.009	0.014	0.203	1.124	3.463
onion	0.003	0.019	0.028	0.036	0.365	0.978	4.082
	0.000	0.015	0.023	0.029	0.045	0.045	2.709
	0.008	0.022	0.029	0.045	1.823	3.482	4.232
tomato	0.074	0.128	0.158	0.183	1.008	2.305	11.390
	0.065	0.111	0.144	0.169	0.186	0.289	6.003
	0.087	0.144	0.169	0.186	4.049	8.576	11.700
sweet pepper		0.000	0.019	0.037	0.083	0.253	5.965
		0.000	0.003	0.026	0.042	0.054	1.525
		0.003	0.026	0.042	0.268	1.473	6.172
courgette		0.001	0.059	0.119	0.559	1.858	26.740
		0.000	0.001	0.089	0.178	0.303	1.882
		0.000	0.089	0.179	2.584	8.716	28.210
red cabbage				0.013	0.172	0.982	17.360
				0.000	0.053	0.111	5.600
				0.053	1.143	11.374	17.360
curly kale				0.055	0.319	0.867	15.590
				0.000	0.178	0.258	1.517
				0.178	0.880	5.065	16.990
cabbage lettuce					1.387	7.871	151.300
					0.000	0.034	83.200
					10.403	57.923	151.300
endive		0.003	0.106	0.343	19.063	60.160	623.900
		0.000	0.059	0.178	1.626	4.375	149.300
		0.025	0.178	1.568	83.740	384.243	659.700
spinach		0.060	0.143	0.175	0.567	2.059	9.978
		0.000	0.111	0.170	0.180	0.235	1.435
		0.111	0.170	0.180	4.797	7.866	10.360

Table (continued)

chicory		0.001	0.123	0.201	2.186	12.021	136.900
		0.000	0.001	0.175	0.218	0.220	101.500
		0.000	0.175	0.218	15.594	97.792	142.600
turnip tops				0.001	0.604	3.043	15.520
				0.000	0.001	0.187	0.003
				0.000	11.416	11.416	15.520
green beans	0.048	0.118	0.176	0.214	0.323	0.516	1.227
	0.041	0.096	0.149	0.187	0.228	0.249	0.825
	0.056	0.134	0.187	0.229	0.918	1.154	1.371
bleach-celery			0.003	0.037	0.143	0.256	1.695
			0.000	0.016	0.050	0.136	0.857
			0.016	0.050	0.151	1.459	1.783

Table 4. Methamidophos

Percentiles of estimated intake distribution (μg/kg BW/day) from duplicate diet study (DD) and Monte Carlo models (MC), and IESTI estimates.
Entries in each cell of the table are mean, lower and upper limit of 95 % confidence interval, based on 1000 bootstrap samples.
Empty cells correspond with values < 0.0005.

model	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
DD	0.030	0.035	0.037	0.038	0.040	0.044	0.048	
	0.008	0.011	0.011	0.012	0.013	0.014	0.014	
	0.117	0.118	0.121	0.123	0.127	0.140	0.156	
MC basic				0.001	0.147	0.833	1.116	
				0.000	0.000	0.334	0.460	
				0.000	0.340	1.505	1.561	
MC vn pos	0.009	0.085	0.112	0.139	0.238	1.502	2.912	
	0.000	0.076	0.103	0.125	0.145	0.422	0.645	
	0.013	0.093	0.125	0.145	0.457	4.352	9.770	
MC vn all	0.250	0.386	0.424	0.447	0.527	1.669	2.991	
	0.244	0.380	0.409	0.438	0.458	0.632	0.861	
	0.255	0.399	0.438	0.458	0.656	4.314	9.779	
MC basic								
nectarine						0.260	0.652	10.550
						0.000	0.000	2.880
						1.430	1.510	11.450
tomato						0.043	0.114	3.675
						0.000	0.000	3.275
						0.219	0.263	3.841
broccoli						0.196	0.373	3.675
						0.000	0.000	3.275
						0.529	0.937	3.841
endive						0.018	0.153	6.637
						0.000	0.000	4.804
						0.441	1.020	7.070
green beans						0.350	0.662	1.577
						0.000	0.056	0.536
						1.101	1.417	1.699
MC vn								
nectarine					0.050	0.392	1.381	10.550
					0.000	0.069	0.069	2.803
					0.069	1.529	9.624	11.450
tomato		0.037	0.062	0.077	0.088	0.116	0.257	1.899
		0.033	0.055	0.072	0.081	0.093	0.093	1.645
		0.043	0.070	0.085	0.093	0.264	1.391	1.960
sweet			0.000	0.010	0.020	0.346	1.077	17.900
pepper			0.000	0.005	0.017	0.028	0.028	7.173
			0.002	0.017	0.028	1.435	5.315	18.530
melon				0.025	0.047	0.333	1.162	7.581
				0.000	0.031	0.058	0.064	3.594
				0.032	0.057	1.959	5.679	8.009
broccoli		0.020	0.042	0.063	0.098	0.339	0.837	3.675
		0.007	0.040	0.053	0.081	0.164	0.164	3.245
		0.028	0.046	0.083	0.164	1.548	3.534	3.832
endive			0.001	0.045	0.093	0.132	0.398	6.637
			0.000	0.029	0.050	0.103	0.112	4.803

		0.013	0.050	0.103	0.441	2.485	7.116
green beans	0.024	0.060	0.090	0.110	0.350	0.644	1.473
	0.021	0.048	0.075	0.103	0.125	0.125	0.440
	0.028	0.075	0.103	0.125	1.071	1.389	1.635

Table 5. Pirimicarb

Percentiles of estimated intake distribution (μg/kg BW/day) from duplicate diet study (DD) and Monte Carlo models (MC), and IESTI estimates.
Entries in each cell of the table are mean, lower and upper limit of 95 % confidence interval, based on 1000 bootstrap samples.
Empty cells correspond with values < 0.0005.

model	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
DD	0.064	0.133	0.164	0.197	0.243	0.377	0.542	
	0.010	0.021	0.026	0.031	0.038	0.059	0.083	
	0.422	0.854	1.048	1.255	1.552	2.433	3.554	
MC basic		0.093	0.296	0.54	1.017	2.945	4.59	
		0.041	0.22	0.394	0.689	1.499	1.841	
		0.149	0.384	0.713	1.556	5.735	14.191	
MC pvn pos	0.077	0.23	0.401	0.793	1.837	7.136	12.415	
	0.072	0.208	0.336	0.537	1.068	2.832	3.496	
	0.082	0.265	0.519	1.197	2.94	17.003	34.456	
MC pvn all	0.249	0.415	0.543	0.899	1.859	6.716	11.75	
	0.242	0.399	0.466	0.666	1.156	2.882	3.712	
	0.256	0.43	0.646	1.305	2.944	15.587	31.84	
MC basic								
orange						0.014	0.064	2.257
						0	0	1.570
						0.155	0.287	2.455
apple		0.015	0.204	0.399	0.729	1.903	2.626	23.330
		0	0.136	0.289	0.512	1.05	1.352	16.690
		0.063	0.285	0.537	1.049	3.269	5.005	25.990
pear					0.034	0.477	0.648	6.785
					0	0.211	0.319	3.380
					0.226	0.851	1.229	7.139
plum						0.032	0.111	2.577
						0	0	1.148
						0.224	0.413	2.695
strawberry					0.003	0.479	1.042	7.183
					0	0.041	0.121	1.230
					0.042	1.366	5.182	7.450
tomato						0.027	0.104	2.576
						0	0	2.312
						0.221	0.334	2.661
oxheart						0.005	0.057	2.160
						0	0	0.027
						0.066	0.296	2.313
cabbage lettuce						0.022	0.186	6.335
						0	0	6.834
						0.19	1.054	9.344
endive					0.072	2.315	4.101	99.550
					0	0.44	0.852	28.100
					0.516	5.333	14.19	105.500
spinach						0.057	0.247	1.079
						0	0	0.282
						0.533	0.854	1.119

Table (continued)

MC pvn								
orange		0.024	0.049	0.066	0.088	0.117	0.18	1.436
		0.01	0.039	0.056	0.077	0.101	0.113	1.017
		0.036	0.056	0.077	0.101	0.164	0.943	1.497
apple	0.011	0.121	0.255	0.5	1.215	4.84	7.771	13.810
	0.007	0.104	0.199	0.327	0.716	2.027	2.588	8.305
	0.016	0.141	0.318	0.768	2.035	10.986	18.7	14.530
pear		0.082	0.118	0.143	0.19	0.957	1.996	6.446
		0.077	0.108	0.131	0.155	0.226	0.349	3.235
		0.089	0.131	0.155	0.244	3.099	5.665	6.815
plum				0.002	0.035	0.097	0.277	2.577
				0	0.016	0.048	0.072	0.999
				0.016	0.048	0.288	1.848	2.695
strawberry			0.002	0.028	0.063	0.493	1.109	6.891
			0	0.008	0.042	0.137	0.137	1.120
			0.008	0.042	0.137	1.569	5.242	7.240
tomato		0.036	0.062	0.077	0.088	0.109	0.244	2.532
		0.033	0.055	0.072	0.081	0.093	0.093	2.200
		0.043	0.07	0.081	0.093	0.279	1.55	2.613
oxheart					0.005	0.104	0.189	2.160
					0	0.022	0.099	0.027
					0.022	0.109	1.46	2.313
cabbage lettuce						0.052	0.384	6.335
						0	0.017	4.586
						0.511	4.087	6.335
endive			0.002	0.055	0.159	4.138	9.698	99.550
			0	0.029	0.089	0.704	1.327	26.140
			0.029	0.096	0.636	14.383	34.265	106.300
spinach			0.03	0.071	0.088	0.16	0.304	1.061
			0	0.056	0.085	0.09	0.117	0.252
			0.056	0.085	0.09	0.556	0.849	1.108

Table 6. Pirimiphos-methyl

Percentiles of estimated intake distribution (μg/kg BW/day) from duplicate diet study (DD) and Monte Carlo models (MC), and IESTI estimates.
Entries in each cell of the table are mean, lower and upper limit of 95 % confidence interval, based on 1000 bootstrap samples.
Empty cells correspond with values < 0.0005.

model	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
DD	0.050	0.078	0.089	0.099	0.113	0.148	0.185	
	0.014	0.027	0.032	0.036	0.041	0.052	0.059	
	0.180	0.227	0.249	0.274	0.311	0.425	0.577	
MC basic					0.052	0.732	1.653	
					0.000	0.169	0.248	
					0.167	2.920	4.420	
MC vn pos		0.146	0.169	0.220	0.260	1.316	3.683	
		0.134	0.162	0.186	0.241	0.299	0.417	
		0.154	0.176	0.241	0.299	4.271	21.394	
MC vn all	0.498	0.769	0.838	0.885	0.965	2.006	4.238	
	0.487	0.747	0.816	0.860	0.907	1.098	1.098	
	0.510	0.782	0.859	0.907	1.098	4.808	21.663	
MC basic								
Mandarin						0.128	0.738	31.540
						0.000	0.000	3.900
						1.454	4.139	33.300
Orange						0.442	1.147	33.100
						0.000	0.044	4.900
						1.651	4.045	35.500
MC vn								
mandarin			0.001	0.062	0.122	0.255	1.516	31.540
			0.000	0.016	0.093	0.134	0.145	4.026
			0.016	0.093	0.134	2.030	12.814	33.300
orange		0.049	0.100	0.137	0.187	0.752	2.395	21.060
		0.020	0.087	0.120	0.168	0.229	0.229	2.865
		0.071	0.120	0.168	0.229	3.278	14.681	21.750
nectarine					0.098	0.140	0.194	1.439
					0.000	0.138	0.139	1.236
					0.138	0.140	1.243	1.561
grape		0.018	0.062	0.081	0.102	0.169	0.386	3.632
		0.000	0.045	0.076	0.084	0.134	0.150	2.238
		0.038	0.076	0.084	0.134	0.357	2.783	3.908
kiwi fruit		0.093	0.124	0.151	0.166	0.265	0.549	1.706
		0.082	0.113	0.143	0.154	0.175	0.186	1.634
		0.102	0.143	0.160	0.173	0.998	1.591	1.757
sweet pepper			0.000	0.019	0.037	0.103	0.320	4.534
			0.000	0.003	0.026	0.055	0.055	0.426
			0.003	0.026	0.048	0.411	1.639	4.686

Table 7. Validation Monte Carlo (MC) models against duplicate diet (DD) results.

Legend:
+ DD < MC with disjunct 95% confidence intervals;
(+) DD < MC with overlapping 95 % confidence intervals;
- DD ≥ MC.

Substance	MC model	p50	p90	p95	p97.5	p99	p99.9	p99.99
clfv	basic	-	(+)	+	+	+	+	+
	vn pos	-	+	+	+	+	+	+
	vn all	+	+	+	+	+	+	+
clpf	basic	-	-	(+)	+	+	+	+
	pvn pos	+	+	+	+	+	+	+
	pvn all	+	+	+	+	+	+	+
ipro	basic	-	+	+	+	+	+	+
	pvn pos	+	+	+	+	+	+	+
	pvn all	+	+	+	+	+	+	+
meth	basic	-	-	-	-	(+)	+	+
	vn pos	-	(+)	(+)	+	+	+	+
	vn all	+	+	+	+	+	+	+
pica	basic	-	-	(+)	(+)	(+)	(+)	(+)
	pvn pos	(+)	(+)	(+)	(+)	(+)	+	+
	pvn all	(+)	(+)	(+)	(+)	(+)	+	+
pime	basic	-	-	-	-	-	(+)	(+)
	vn pos	-	(+)	(+)	(+)	(+)	(+)	(+)
	vn all	+	+	+	+	+	+	+

MC models: basic = basic model; (p)vn = model with (processing,) variability, nondetect replacement ;
pos/all: nondetect replacement only for products with positive results in the database / for all consumed products

Table 8. Validation Monte Carlo (MC) models against IESTI results.
Legend:
+ MC < IESTI with disjunct 95% confidence intervals for all products;
(+) MC < IESTI with overlapping 95 % confidence intervals for listed products;
- MC ≥ IESTI for listed products.

Substance	MC model	p50	p90	p95	p97.5	p99	p99.9	p99.99
clfv	basic	+	+	+	+	+	(+) parsley	(+) parsley
	vn	+	+	+	+	+	(+) carrot, parsley	(+) carrot, parsley
clpf	basic	+	+	+	+	+	(+) nectarine, spinach	(+) nectarine, spinach
	pvn	+	+	+	+	+	(+) orange, apple, nectarine, grape, spinach	(+) grapefruit, orange, apple, peach, nectarine, grape, spinach
ipro	basic	+	+	+	+	+	(+) strawberry, raspberry, currant, red cabbage, spinach, turnip tops	(+) peach, nectarine, strawberry, raspberry, currant, courgette, red cabbage, curly kale, endive, spinach, turnip tops, green beans
	pvn	+	+	+	+	+	(+) apricot, nectarine, strawberry, raspberry, currant, kiwi fruit, carrot, courgette, spinach, turnip tops, green beans	(+) apple, pear, apricot, peach, plum, nectarine, grape, strawberry, raspberry, currant, kiwi fruit, carrot, celeriac, onion, tomato, courgette, red cabbage, curly kale, endive, spinach, turnip tops, green beans, bleach celery
meth	basic	+	+	+	+	+	(+) green beans	(+) green beans
	vn	+	+	+	+	+	(+) green beans	(+) nectarine, melon, broccoli, green beans
pica	basic	+	+	+	+	+	(+) strawberry, oxheart, spinach	(+) strawberry, oxheart, spinach
	pvn	+	+	+	+	+	(+) apple, strawberry, oxheart, spinach	(+) apple, pear, plum, strawberry, oxheart, endive, spinach
pime	basic	+	+	+	+	+	+	(+) mandarin
	vn	+	+	+	+	+	(+) orange	(+) mandarin, orange, nectarine, grape, sweet pepper
MC models: basic = basic model; (p)vn = model with (processing,) variability, nondetect replacement								

3.2 Chlorfenvinphos (clfv)

In the residue database, chlorfenvinphos was found in 4 of the 64 products in the diet of any of the infants in the duplicate diet study: mandarin/tangerines (1 positive value), carrot (39 values), celeriac (1 value) and parsley (2 relatively high concentrations).

In the duplicate diet study 3 out of 250 infants had a measured positive intake (after recovery correction 0.028, 0.464 and 0.769 µg/kg BW/day). For the other 247 infants the censoring limit varied between 0.007 and 0.149 µg/kg BW/day (mean 0.065 µg/kg BW/day).

There is only 1 reported processing factor (carrot, peeled). This combination did not occur in the consumption data. No processing factors were therefore applied in the model calculations. We will therefore consider the validation of the MC basic and the MC vn models. The MC-vn model was run based on the 4 products on which positive residuals have been found (MC vn pos), and based on all 64 consumed products (MC vn all).

Figure 1 shows an example of the bootstrap distribution (for p99.9 in this figure) obtained with the basic MC model. The results of the validation of the MC models are summarized in Table 1 and visualized in Figure 2 - Figure 5.

The upper-tail MC percentiles of the basic MC model are higher than the percentiles estimated from the duplicate diet, by factors between 5 and 17. The uncertainty intervals are disjunct for percentiles p95 and higher, so that we may conclude that the MC model will not produce too low values. The model is not validated for the estimation of the median intake (p50). However, also the duplicate diet estimate is here of questionable value and very much dependent on the assumption of a lognormal intake distribution.

The predictions from the MC vn models are much higher than that of the basic model. Runs with the MC n and MC v models show that replacements of nondetects is responsible for the increase of the lower percentiles, and use of the variability factors for increase of the upper percentiles (see Table 9 and Figure 6).

The IESTI values are higher than even the p99.99 percentiles of individual commodities by a factor between 1.6 and 47. The estimated percentiles of MC-vn are still lower than the IESTI values, but the bootstrap distributions overlap for the higher percentiles.

The MC models calculate a p99 between 1.7 and 3.7 µg/kg BW/day. Note that IESTIs for carrot and mandarin are still much higher (33 and 10 µg/kg BW/day), whereas the p99 estimated from the duplicate diet study is much lower (0.07 µg/kg BW/day).

According to the MC models carrot is clearly the commodity that contributes most to the exposure (p99 is 3.0 µg/kg BW/day according to the MC vn model), with only a minor contributions from mandarin (p99 of 0.2 µg/kg BW/day).

Conclusion for chlorfenvinphos: The MC models are unambiguously validated for estimation of the p95, p97.5 and p99.

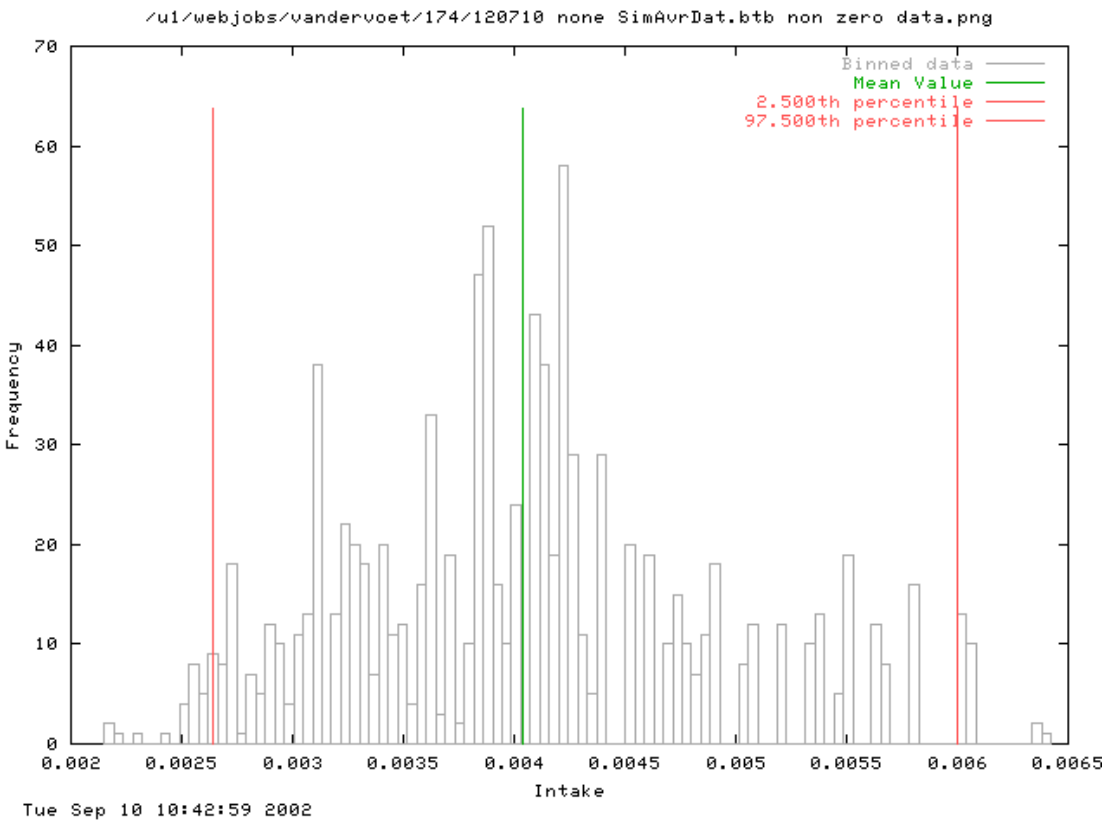
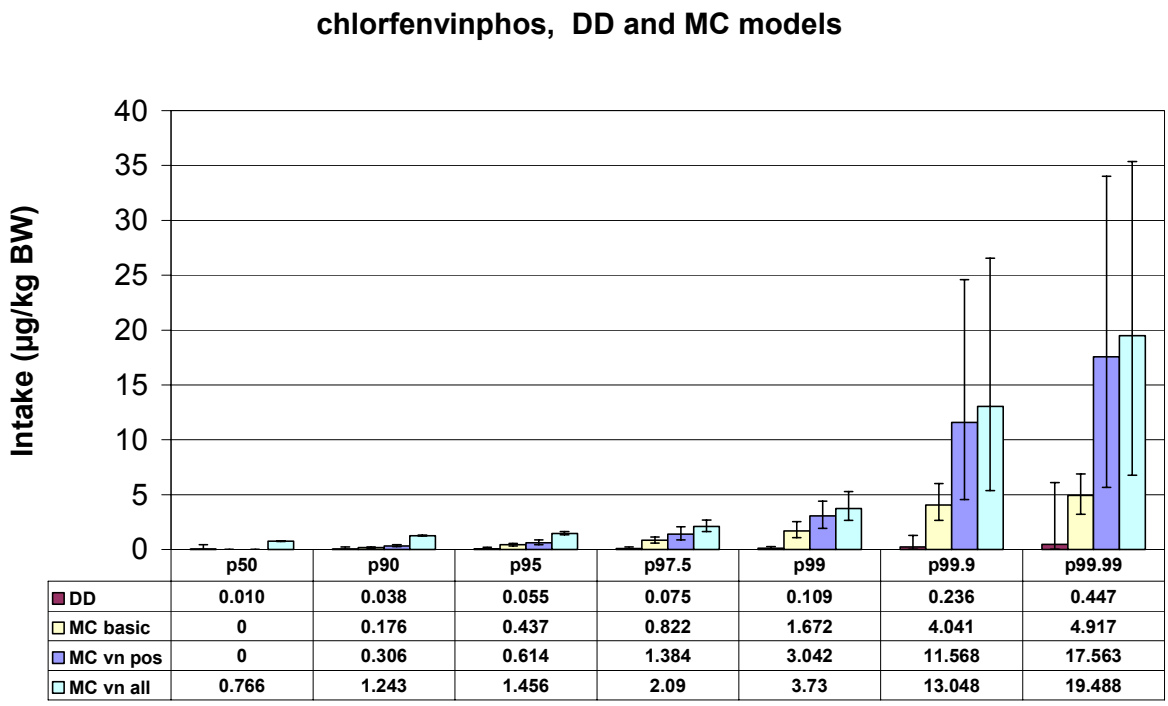
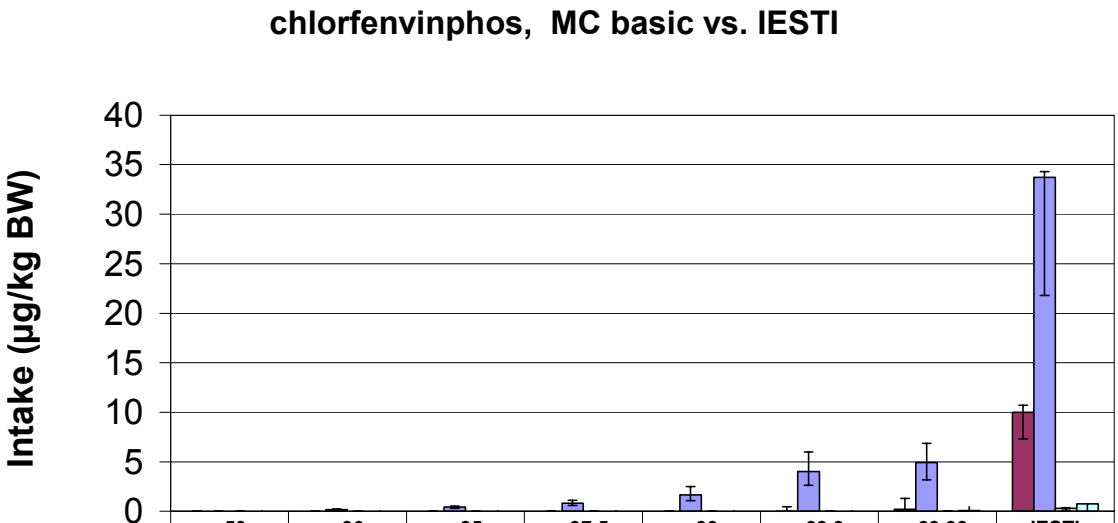


Figure 1. Chlorfenvinphos intake (mg/kg BW/day). Bootstrap distribution for p99.9.



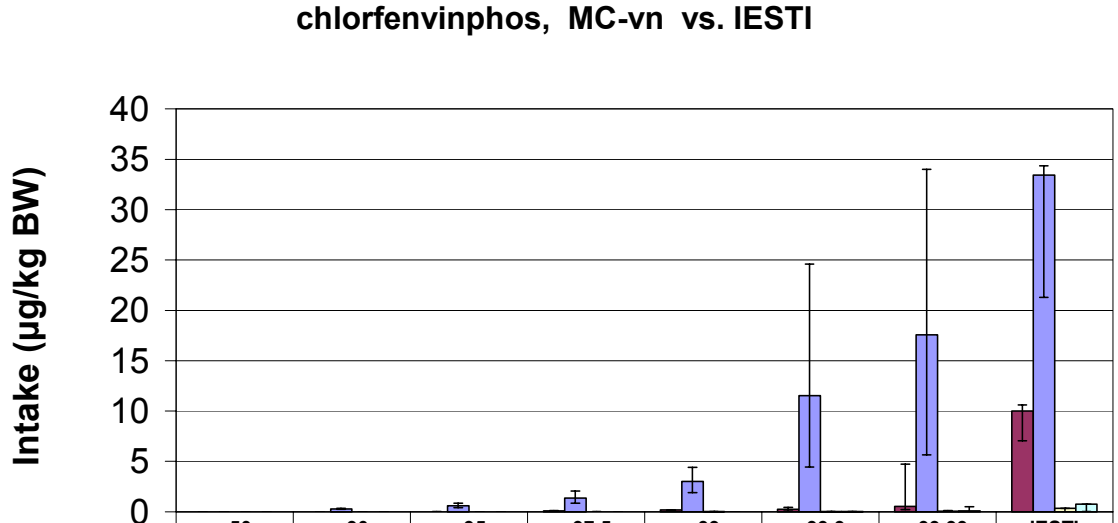
	p50	p90	p95	p97.5	p99	p99.9	p99.99
DD	0.010	0.038	0.055	0.075	0.109	0.236	0.447
MC basic	0	0.176	0.437	0.822	1.672	4.041	4.917
MC vn pos	0	0.306	0.614	1.384	3.042	11.568	17.563
MC vn all	0.766	1.243	1.456	2.09	3.73	13.048	19.488

Figure 2. Validation MC models against duplicate diet results.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
mandarin	0	0	0	0	0	0.027	0.22	10.00
carrot	0	0.174	0.434	0.817	1.669	4.041	4.917	33.70
celeriac	0	0	0	0	0	0.001	0.007	0.33
parsley	0	0	0	0	0	0.007	0.086	0.76

Figure 3. Validation MC basic model against IESTI for the four products with positive concentrations.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
mandarin	0	0	0.001	0.094	0.182	0.234	0.556	10.01
carrot	0	0.295	0.603	1.374	3.028	11.548	17.555	33.43
celeriac	0	0	0	0.004	0.018	0.045	0.053	0.33
parsley	0	0	0	0	0	0.012	0.086	0.76

Figure 4. Validation MC model with variability and replacement of nondetects by LOR against IESTI for the four products with positive concentrations.

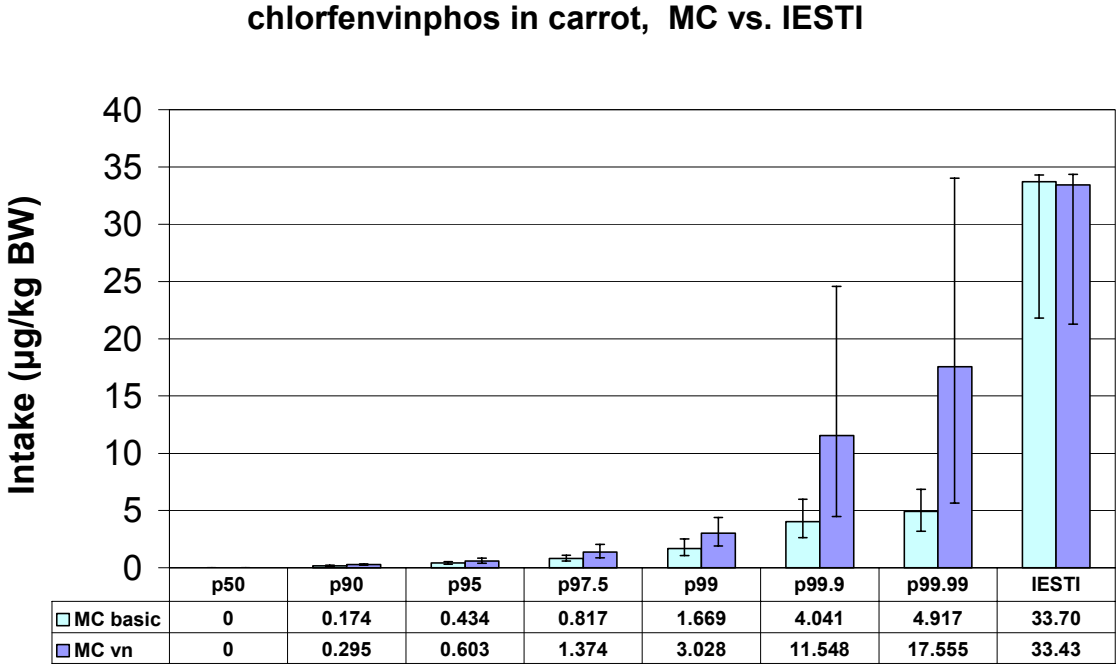


Figure 5. Comparison of exposure estimates (µg/kg BW/day) from MC basic and vn models and two types of IESTI in carrot.

Table 9. Comparison of several variants of the MC model.

Percentiles of estimated intake distribution (μg/kg BW/day) from Monte Carlo models with variability factors (MC v), nondetect replacement (MC n), both (MC vn).
Entries in each cell of the table are mean, lower and upper limit of 95 % confidence interval, based on 1000 bootstrap samples.
Nondetect replacement (n) increases the lower percentiles, whereas the inclusion of variability factors (v) increases the higher percentiles.

model	Product	p50	p90	p95	p97.5	p99	p99.9	p99.99
MC basic	All		0.176	0.437	0.822	1.672	4.041	4.917
			0.116	0.323	0.582	1.074	2.641	3.197
			0.235	0.549	1.128	2.523	5.999	6.865
MC n	All	0.763	1.212	1.351	1.607	2.337	4.648	5.471
		0.744	1.163	1.315	1.466	1.774	3.148	3.681
		0.778	1.249	1.418	1.814	3.131	6.491	7.363
MC v	All		0.204	0.599	1.369	3.008	12.173	18.331
			0.130	0.409	0.879	1.880	4.370	5.898
			0.287	0.835	2.023	4.472	26.884	34.652
MC vn	All	0.766	1.243	1.456	2.09	3.73	13.048	19.488
		0.745	1.2	1.343	1.646	2.65	5.361	6.768
		0.783	1.289	1.646	2.673	5.266	26.554	35.345

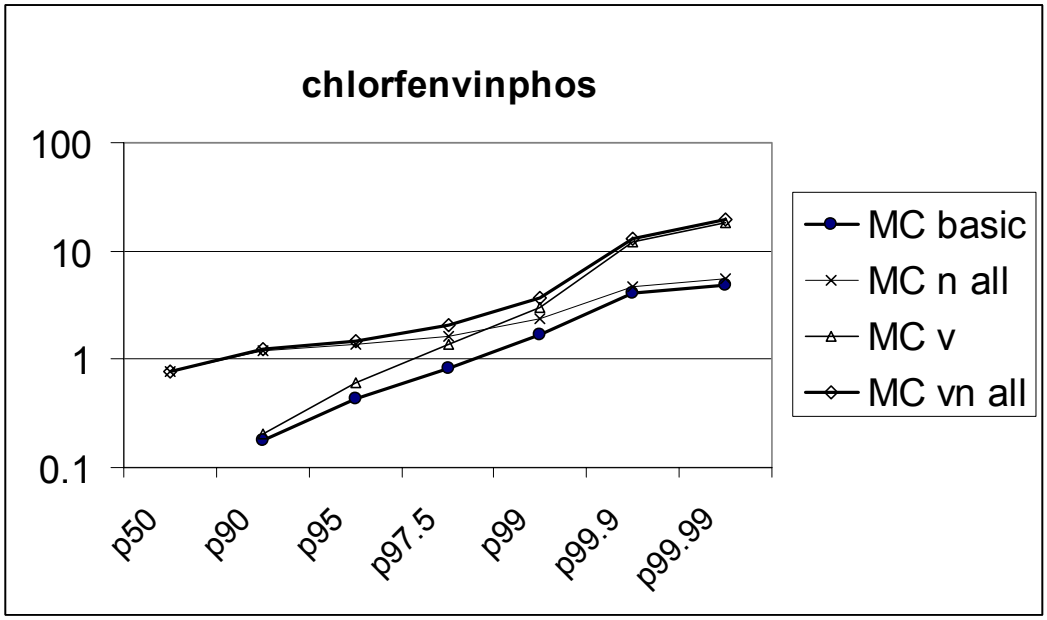


Figure 6. Percentiles of exposure (ug/kg BW/day) to chlorfenvinphos for four different MC models.

3.3 Chlorpyrifos (clpf)

In the residue database, chlorpyrifos was found in 15 of the 64 products in the diet of any of the infants in the duplicate diet study.

In the duplicate diet study 6 out of 250 infants had a measured positive intake (after recovery correction 0.046, 0.085, 0.109, 0.186, 0.191 and 0.691 µg/kg BW/day). For the other 244 infants the censoring limit varied between 0.008 and 0.185 µg/kg BW/day (mean 0.081 µg/kg BW/day). The acute reference dose (ARfD) is 100 µg/kg BW/day.

The MC pvn model was run based on the 15 products on which positive residuals have been found (MC pvn pos), and based on all 64 consumed products (MC pvn all). The results of the validation of the MC models are summarized in Table 2 and visualized in Figure 7 - Figure 13.

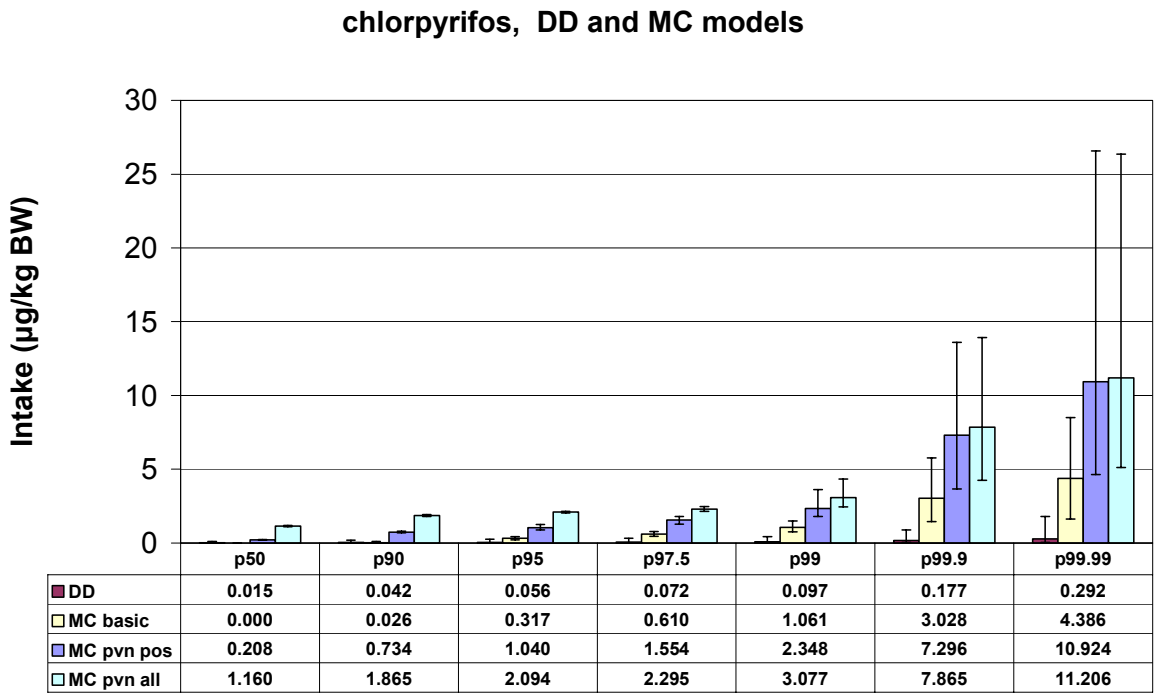
The 50th and 90th percentiles of the basic MC model are lower than the percentiles estimated from the duplicate diet. The basic MC model is thus not validated for the estimation of the median intake (p50) or relative low percentiles. However, also the duplicate diet estimate is here of questionable value and very much dependent on the assumption of a lognormal intake distribution. For percentiles p95 and higher the basic MC model is higher than the duplicate intake percentiles by factors between 6 and 17. The uncertainty intervals are disjunct for percentiles p97.5 and higher, so that we may conclude that the MC model will not produce too low values.

The IESTI values of the basic MC model are higher than even the p99.99 percentiles of individual commodities by a factor between 2.5 and 31. Compared with the estimated 99.99th percentiles of MC pvn these factors vary between 1.5 and 12.

The estimated percentiles of exposure to chlorpyrifos are always not always below the ARfD of 1o0 µg/kg BW/day. The MC models calculate a p99 between 1.1 and 3.1 µg/kg BW/day. The p99 estimated from the duplicate diet study (0.07 µg/kg BW/day) is far below the ARfD level.
Note that IESTI (calculated with processing factors) are also below the ARfD level (highest values are peach 32, mandarin 21, grapefruit 17, grape 14, orange 13, nectarine 11 µg/kg BW/day).

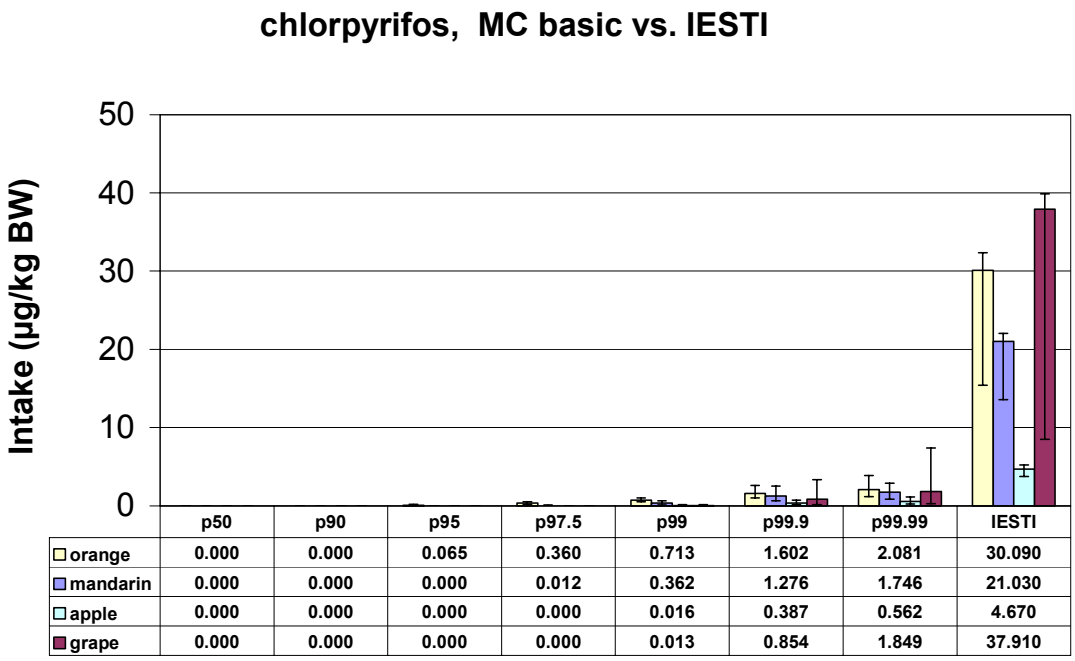
According to the basic MC model orange and mandarin are the commodities that contribute most to the exposure (p99 0.71 and 0.36 µg/kg BW/day). If we allow for processing, unit variability and replace nondetects with LOR, then the contribution of apple is more clearly noticed (p99 1.12 µg/kg BW/day, vs. 1.05 for orange and 0.38 for mandarin).

Conclusion for chlorpyrifos: the MC models were easily validated, at least for estimation of percentiles p97.5 and p99. For lower percentiles the basic model may be too simple, but the estimation of p90, p95, p97.5 and p99 with the MC pvn model is unambiguous.



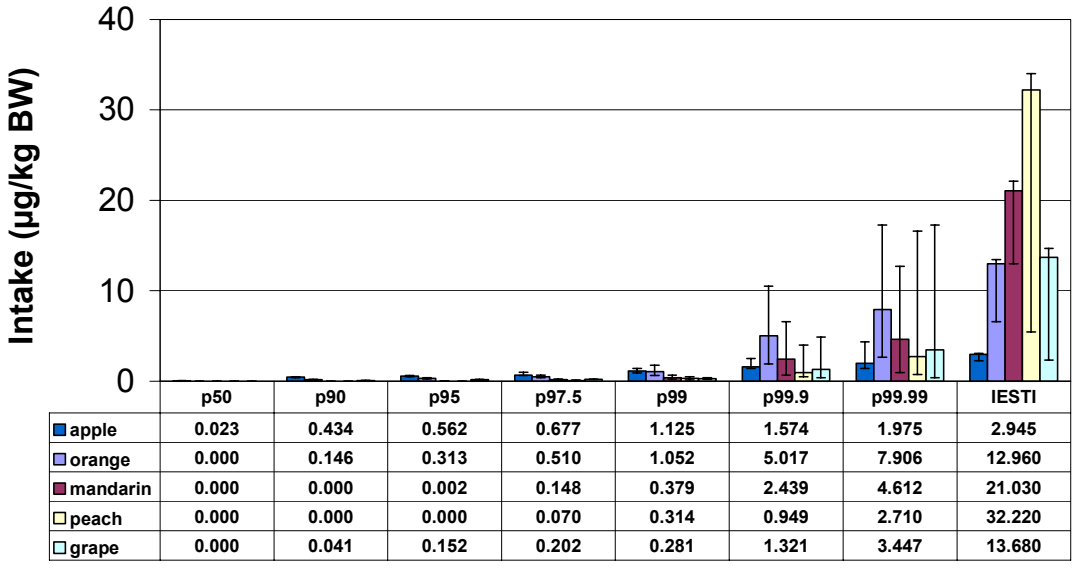
	p50	p90	p95	p97.5	p99	p99.9	p99.99
DD	0.015	0.042	0.056	0.072	0.097	0.177	0.292
MC basic	0.000	0.026	0.317	0.610	1.061	3.028	4.386
MC pvn pos	0.208	0.734	1.040	1.554	2.348	7.296	10.924
MC pvn all	1.160	1.865	2.094	2.295	3.077	7.865	11.206

Figure 7. Validation MC models against duplicate diet.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
orange	0.000	0.000	0.065	0.360	0.713	1.602	2.081	30.090
mandarin	0.000	0.000	0.000	0.012	0.362	1.276	1.746	21.030
apple	0.000	0.000	0.000	0.000	0.016	0.387	0.562	4.670
grape	0.000	0.000	0.000	0.000	0.013	0.854	1.849	37.910

Figure 8. Validation basic MC model against IESTI for the four products with highest p99.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
apple	0.023	0.434	0.562	0.677	1.125	1.574	1.975	2.945
orange	0.000	0.146	0.313	0.510	1.052	5.017	7.906	12.960
mandarin	0.000	0.000	0.002	0.148	0.379	2.439	4.612	21.030
peach	0.000	0.000	0.000	0.070	0.314	0.949	2.710	32.220
grape	0.000	0.041	0.152	0.202	0.281	1.321	3.447	13.680

Figure 9. Validation of MC model with processing, variability and nondetects replaced by LOR against IESTI for the five products with highest p99.

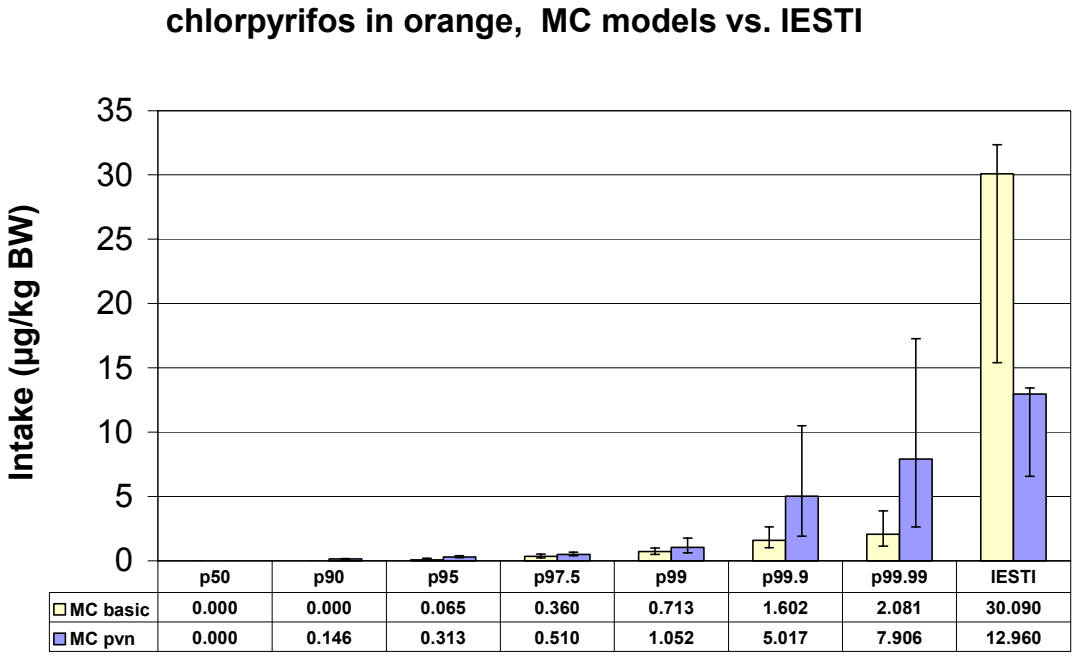


Figure 10. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in orange.

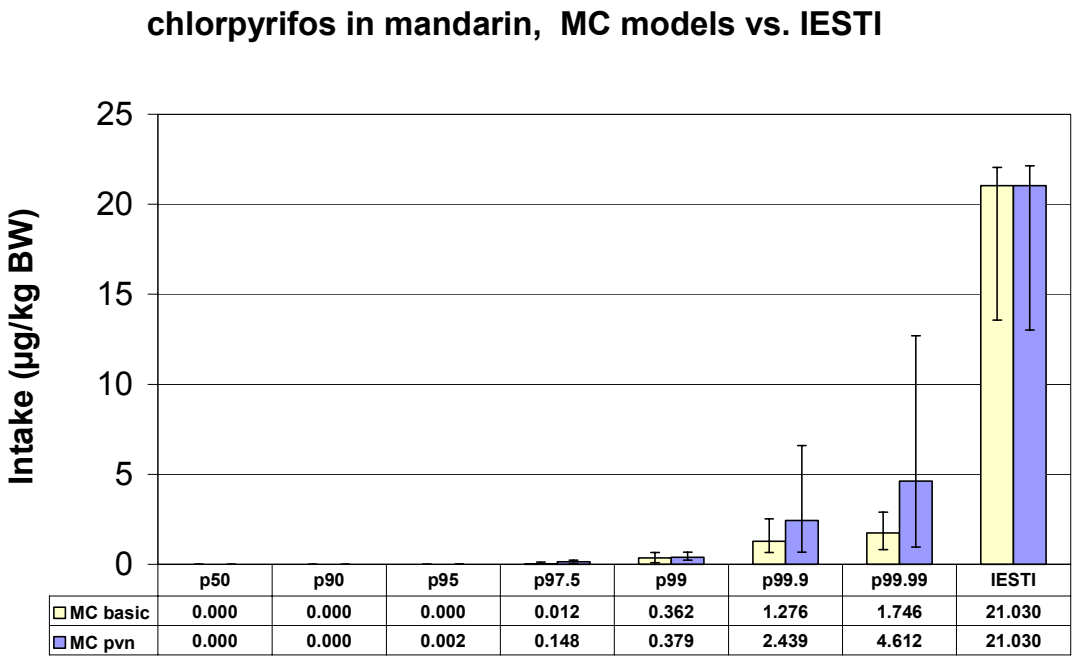
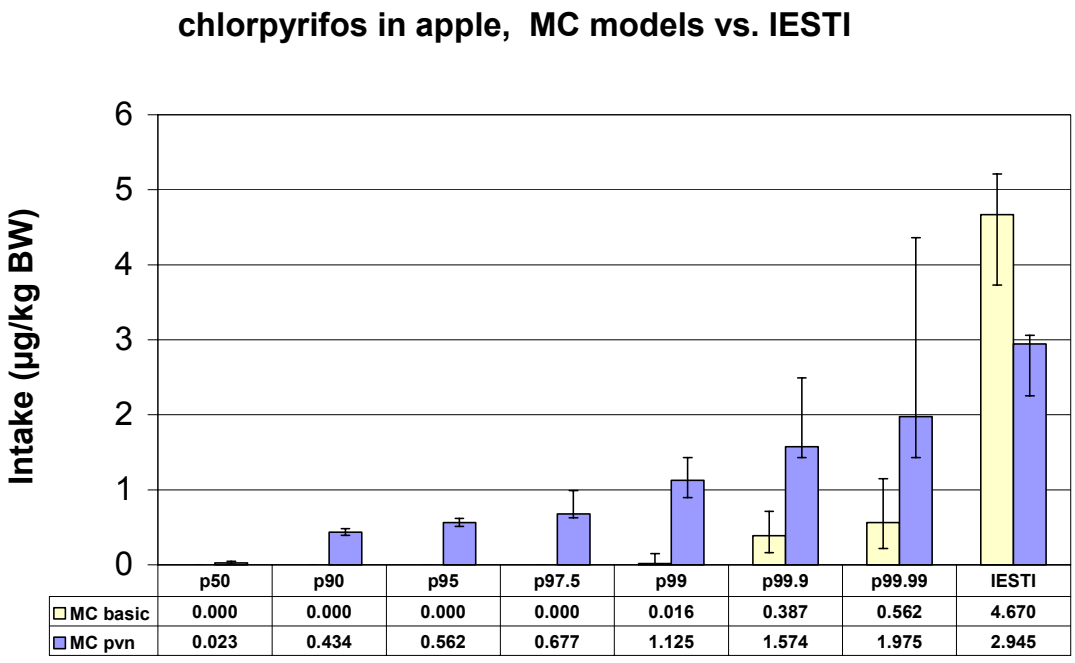
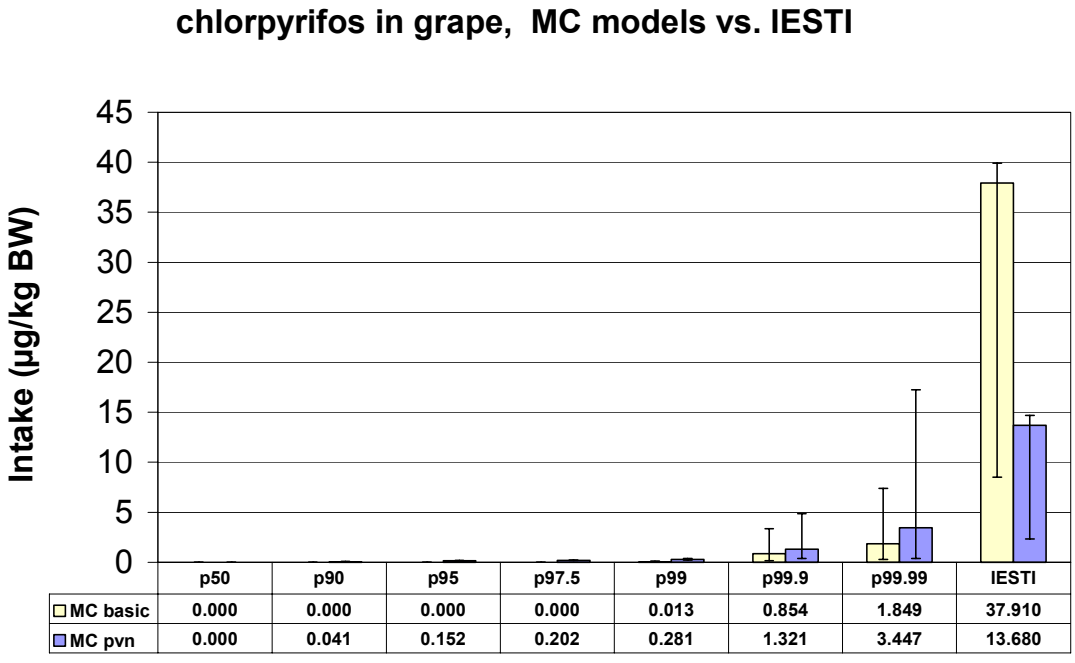


Figure 11. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in mandarin.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.000	0.016	0.387	0.562	4.670
MC pvn	0.023	0.434	0.562	0.677	1.125	1.574	1.975	2.945

Figure 12. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in apple.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.000	0.013	0.854	1.849	37.910
MC pvn	0.000	0.041	0.152	0.202	0.281	1.321	3.447	13.680

Figure 13. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in grape.

3.4 Iprodione (ipro)

In the residue database, iprodione was found in 33 of the 64 products in the diet of any of the infants in the duplicate diet study.

In the duplicate diet study 4 out of 250 infants (1.6 %) had a measured positive intake (after recovery correction 0.033, 0.174, 0.188 and 0.241 µg/kg BW/day). For the other 246 infants (98.4 %) the censoring limit varied between 0.005 and 0.106 µg/kg BW/day (mean 0.047 µg/kg BW/day).

The MC pvn model was run based on the 33 products on which positive residuals have been found (MC pvn pos), and based on all 64 consumed products (MC pvn all). The results of the validation of the MC models are summarized in Table 3 and visualized in Figure 14 - Figure 21.

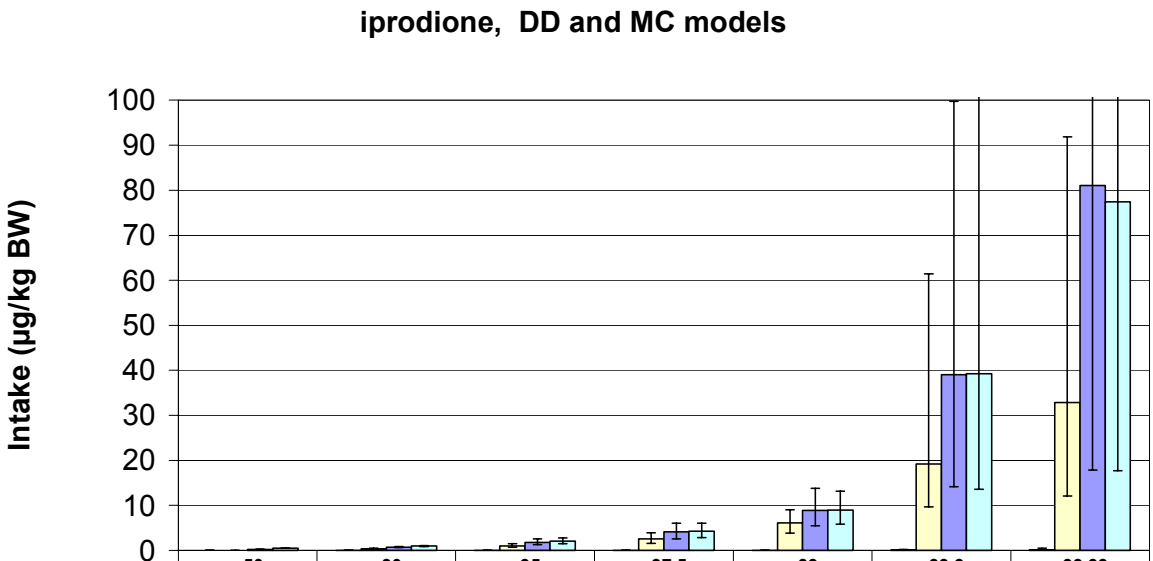
The 50th percentile of the basic MC model is lower than the percentile estimated from the duplicate diet. The basic MC model is thus not validated for the estimation of the median intake (p50). However, also the duplicate diet estimate is here of questionable value and very much dependent on the assumption of a lognormal intake distribution. For percentiles p90 and higher the basic MC model percentiles are higher than the duplicate intake percentiles by factors between 15 and 291. The uncertainty intervals are disjunct, so that we may conclude that the MC model will not produce too low values. Indeed, for iprodione the above factors are much higher than for the other substances.

The IESTI values of the basic MC model are higher than even the p99.99 percentiles of individual commodities by a factor between 1.6 and 42. Compared with the estimated 99.99th percentiles of MC pvn these factors are between 1.5 and 24.

The MC models calculate a p99 between 6.1 and 9.0 µg/kg BW/day. The p99 estimated from the duplicate diet study is 0.05 µg/kg BW/day

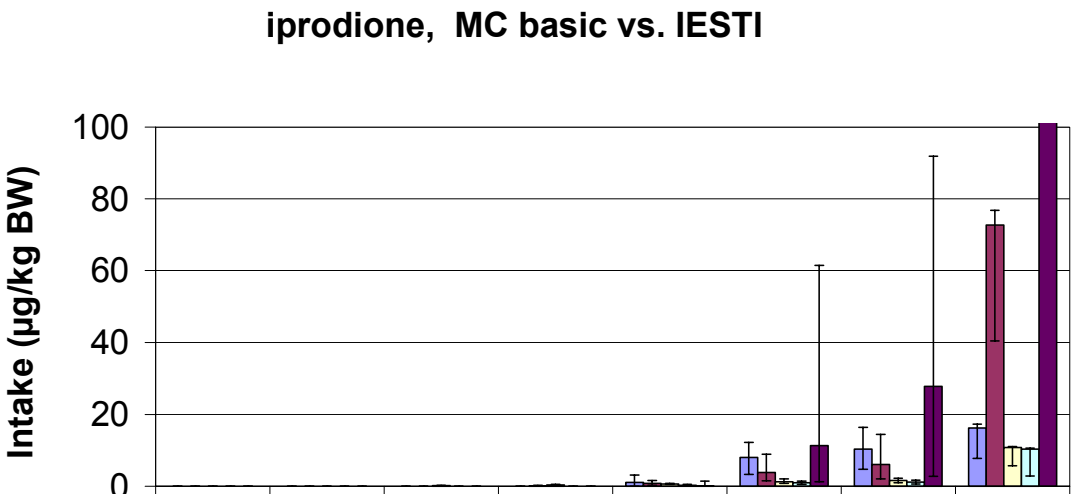
According to the basic MC model currant, grape and carrot are the commodities that contribute most to the exposure (p99 1.04, 0.78 and 0.64 µg/kg BW/day). If we allow for processing, unit variability and replace nondetects with LOR, then the contributions are in the order carrot, currant and grape (p99 1.14, 1.07 and 1.04 µg/kg BW/day).

Conclusion for iprodione: the exposure as estimated by the MC models is very high when compared with the duplicate diet data. Still the estimates were still far below IESTI levels, and thus the MC models were unambiguously validated for estimation of all upper-tail percentiles (with the usual caveat about extrapolation upon the very high percentiles p99.9 and p99.99).



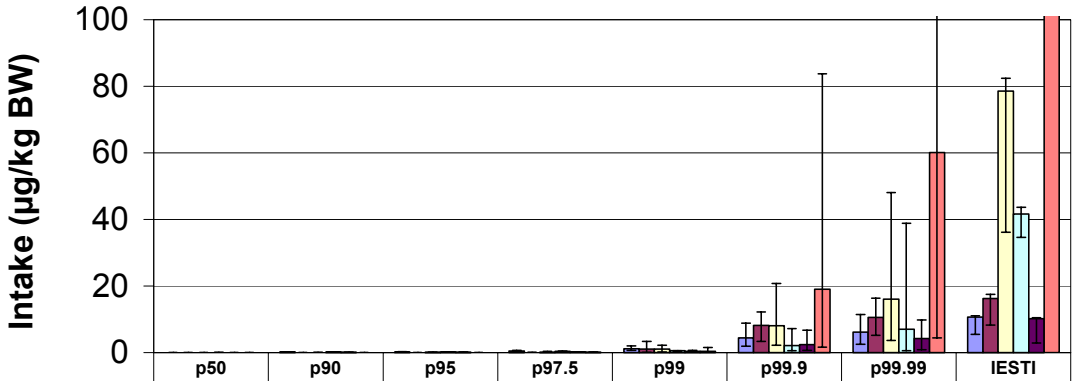
	p50	p90	p95	p97.5	p99	p99.9	p99.99
DD	0.011	0.025	0.031	0.038	0.048	0.077	0.113
MC basic	0.000	0.371	1.043	2.615	6.137	19.200	32.877
MC pvn pos	0.261	0.734	1.816	4.131	8.918	39.001	81.067
MC pvn all	0.521	0.983	2.031	4.280	9.008	39.275	77.420

Figure 14. Validation MC models against duplicate diet.



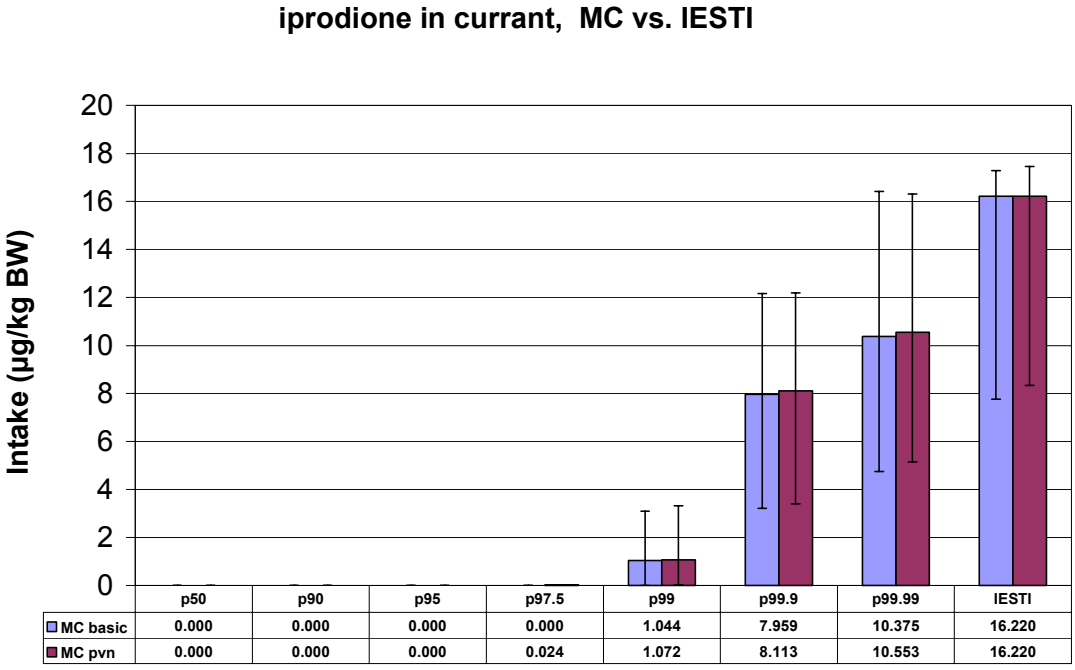
	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
currant	0.000	0.000	0.000	0.000	1.044	7.959	10.375	16.220
grape	0.000	0.000	0.000	0.034	0.782	3.831	6.045	72.660
carrot	0.000	0.001	0.184	0.381	0.641	1.271	1.571	10.810
kiwi fruit	0.000	0.000	0.000	0.001	0.283	0.974	1.181	10.290
endive	0.000	0.000	0.000	0.000	0.134	11.262	27.830	623.900

Figure 15. Validation MC basic model against IESTI for the five products with highest p99.



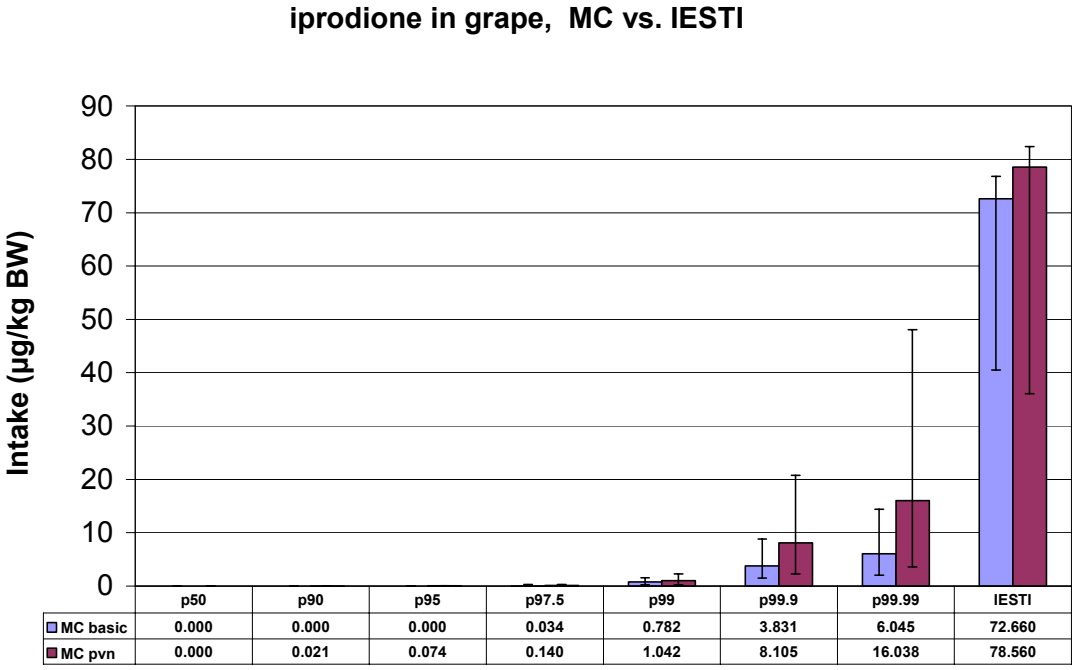
	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
carrot	0.000	0.162	0.248	0.496	1.140	4.388	6.138	10.720
currant	0.000	0.000	0.000	0.024	1.072	8.113	10.553	16.220
grape	0.000	0.021	0.074	0.140	1.042	8.105	16.038	78.560
apple	0.024	0.199	0.250	0.340	0.515	2.061	7.029	41.590
kiwi fruit	0.000	0.096	0.136	0.162	0.346	2.377	4.219	10.240
endive	0.000	0.000	0.003	0.106	0.343	19.063	60.160	623.900

Figure 16. Validation of MC model with processing, variability and nondetects replaced with LOR against IESTI for the six products with highest p99.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.000	1.044	7.959	10.375	16.220
MC pvn	0.000	0.000	0.000	0.024	1.072	8.113	10.553	16.220

Figure 17. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in currant.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.034	0.782	3.831	6.045	72.660
MC pvn	0.000	0.021	0.074	0.140	1.042	8.105	16.038	78.560

Figure 18. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in grape.

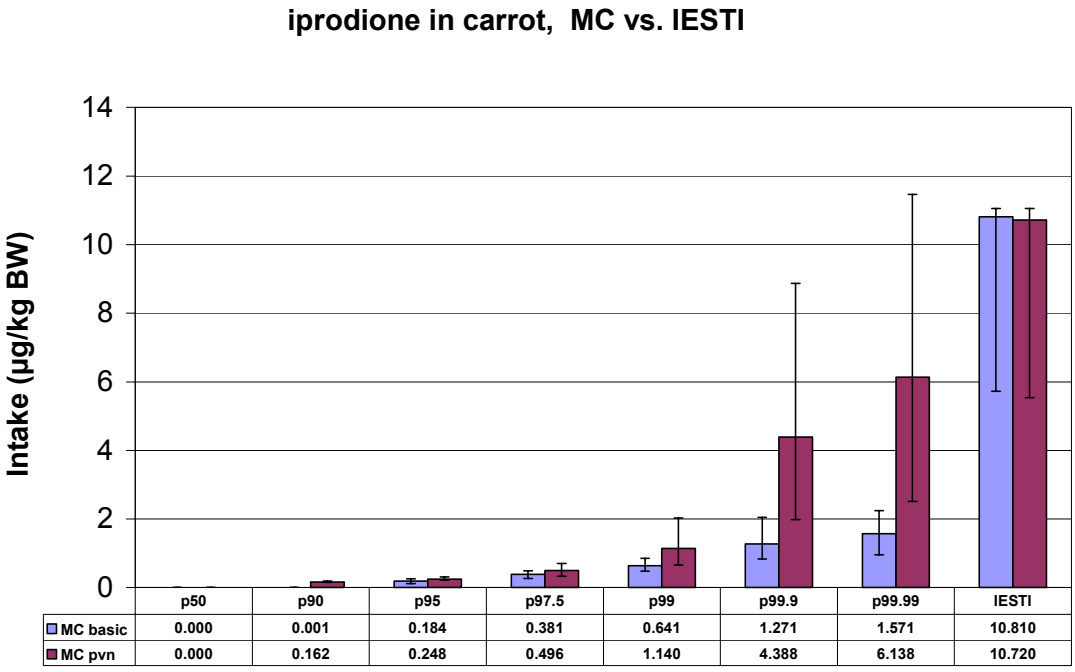


Figure 19. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in carrot.

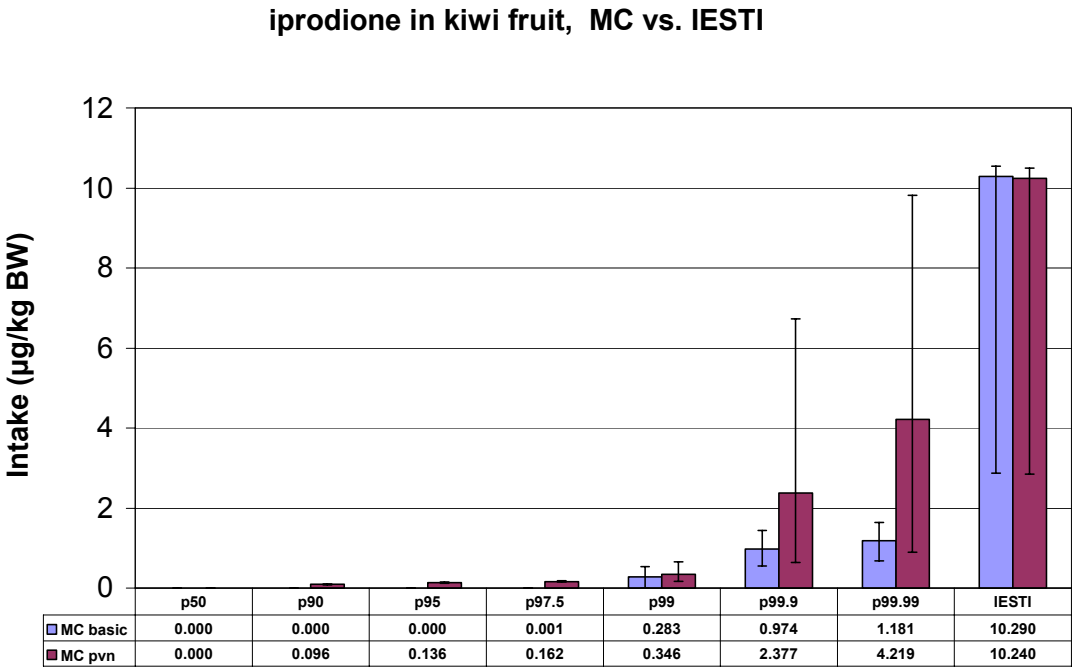


Figure 20. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in kiwi fruit.

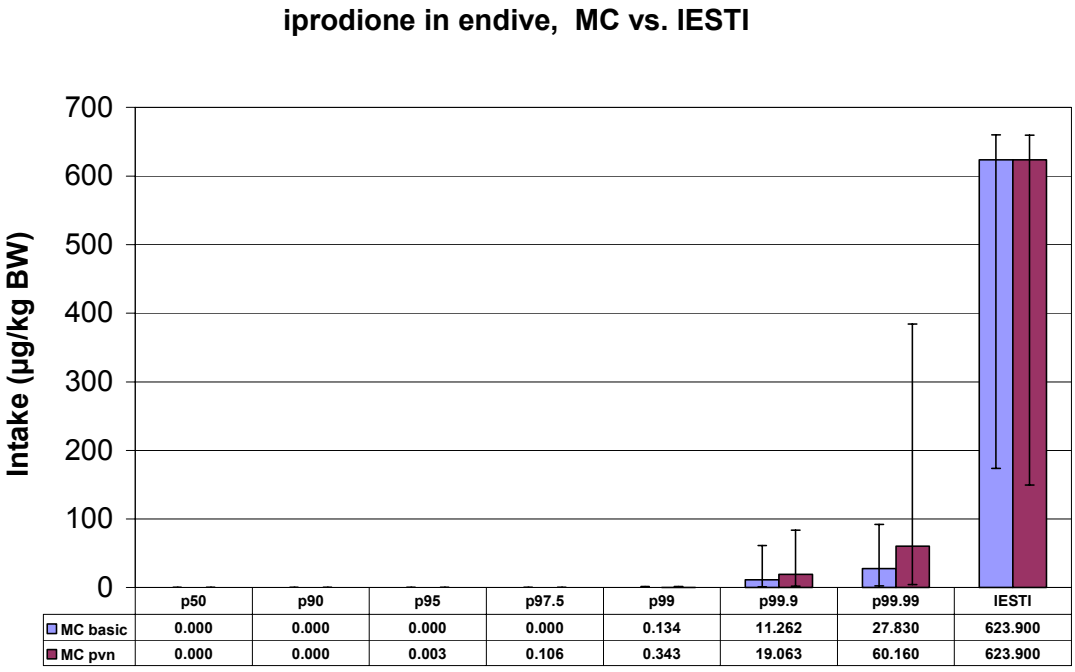


Figure 21. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in endive.

3.5 Methamidophos (meth)

In the residue database, methamidophos was found in 10 of the 64 products in the diet of any of the infants in the duplicate diet study.

In the duplicate diet study 3 out of 250 infants (1.2 %) had a measured positive intake (after recovery correction 0.037, 0.051 and 0.052 µg/kg BW/day). For the other 247 infants (98.8 %) the censoring limit varied between 0.004 and 0.100 µg/kg BW/day (mean 0.044 µg/kg BW/day).

No processing factors were available for methamidophos. The MC vn model was run based on the 10 products on which positive residuals have been found (MC vn pos), and based on all 64 consumed products (MC vn all). The results of the validation of the MC models are summarized in Table 4 and visualized in Figure 22 - Figure 28.

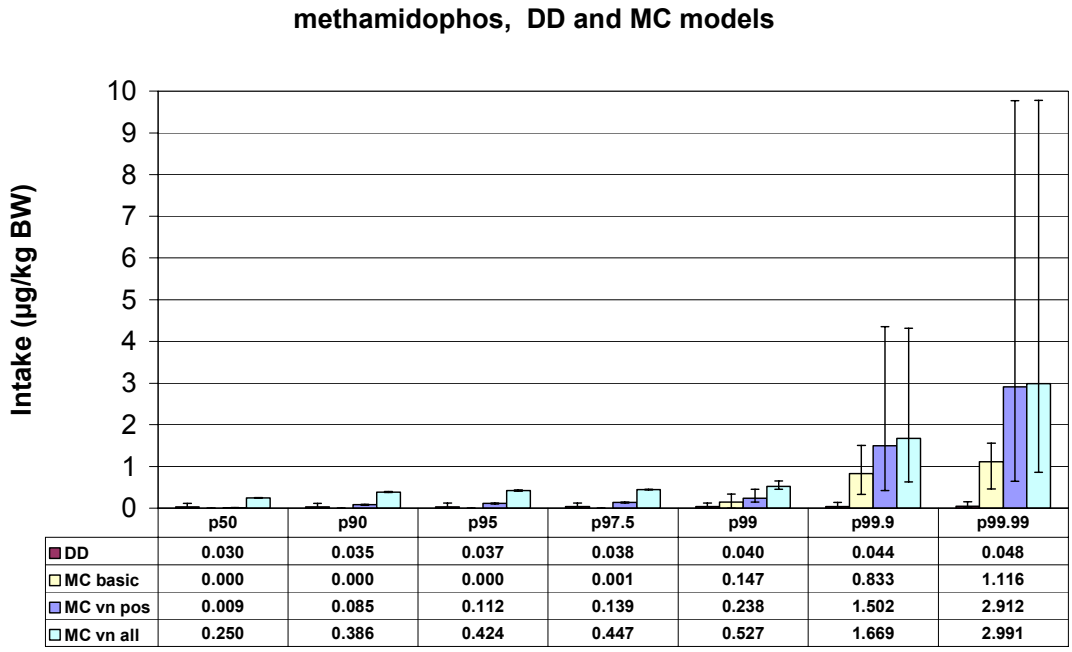
The 50th, 90th, 95th, and 97.5th percentile of the basic MC model and the 50th percentile of the MC vn pos model are all lower than 0.08 µg/kg BW/day and also lower than the percentile estimated from the duplicate diet. The basic MC model is thus not validated for the estimation of these very low exposures. For percentiles p99 and higher the basic MC model percentiles are higher than the duplicate intake percentiles by factors between 4 and 23. Similar factors vary between 6 and 61 for the MC vn pos model, and between 13 and 62 for the MC vn all model. For p99 the uncertainty intervals of MC basic and duplicate diet do overlap so that we must be cautious when concluding that the basic MC model will not produce too low values. A further statistical analysis comparing the basic MC model and the duplicate diet results in one bootstrap procedure is advisable.
The uncertainty intervals of both MC vn models and the duplicate diet model are disjunct for percentiles p97.5 and higher, so that these models are validated.

The IESTI values of the basic MC model are higher than even the p99.99 percentiles of individual commodities by a factor between 2.4 and 44. Compared with the estimated 99.99th percentiles of MC vn these factors are between 2.3 and 17.

The MC models calculate a p99 between 0.15 and 0.53 µg/kg BW/day. The p99 estimated from the duplicate diet study is 0.04 µg/kg BW/day. The highest IESTI values are: sweet pepper 18, nectarine 11, melon 8, endive 7 µg/kg BW/day.

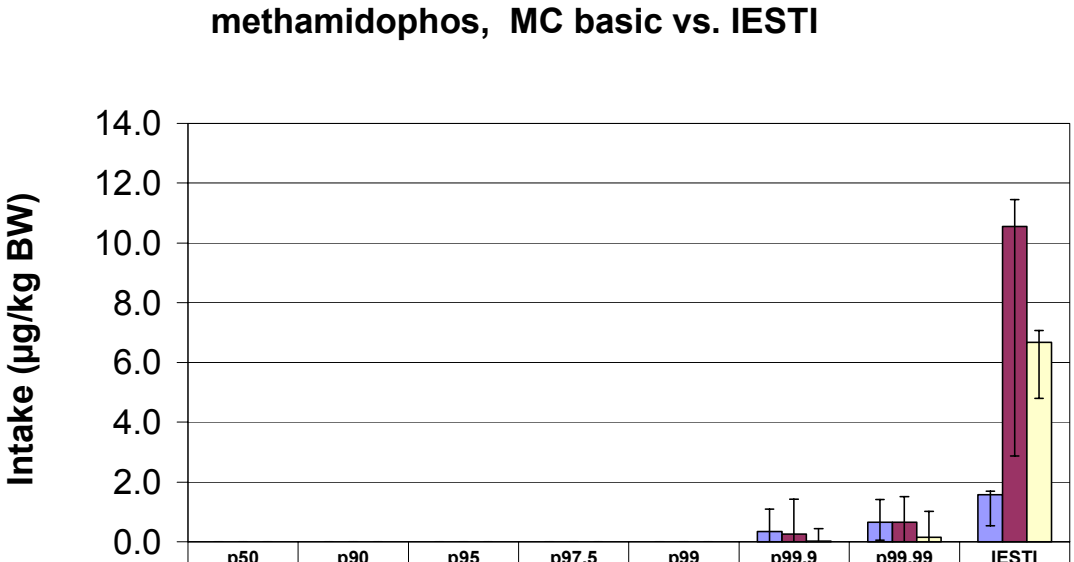
According to the basic MC model green beans, nectarine and endive are the commodities that contribute most to the exposure (p99 all below 0.001 µg/kg BW/day, p99.9 0.35, 0.26 and 0.02 µg/kg BW/day). If we allow for unit variability and replace nondetects with LOR, then the contributions are in the order green beans, broccoli, endive, tomato (p99 estimates 0.11, 0.10, 0.09 and 0.09 µg/kg BW/day).

Conclusion for methamidophos: the exposure as estimated by the MC models is very low. Still, the estimation of p99 with the MC models seems valid (although a further confirmation in the case of the MC basic model is desirable). The estimation of upper-tail percentiles with the MC vn model is unambiguously validated.



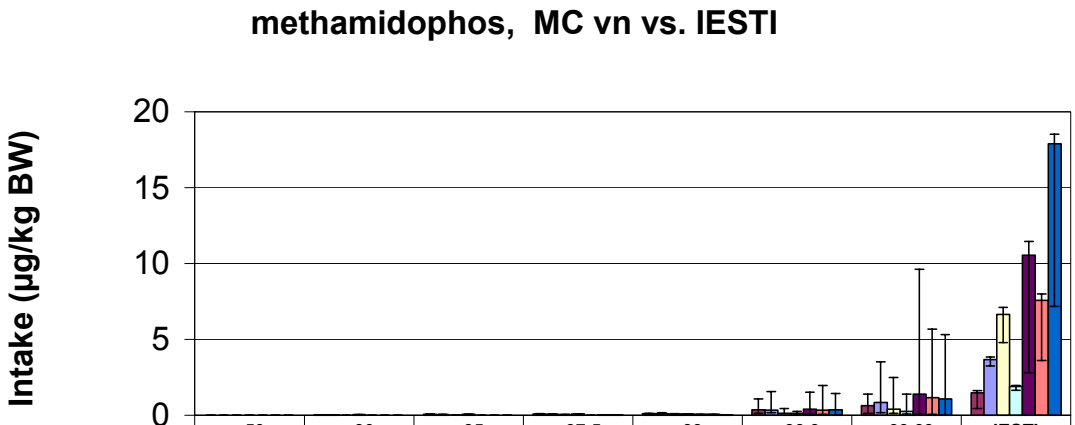
	p50	p90	p95	p97.5	p99	p99.9	p99.99
DD	0.030	0.035	0.037	0.038	0.040	0.044	0.048
MC basic	0.000	0.000	0.000	0.001	0.147	0.833	1.116
MC vn pos	0.009	0.085	0.112	0.139	0.238	1.502	2.912
MC vn all	0.250	0.386	0.424	0.447	0.527	1.669	2.991

Figure 22. Validation MC models against duplicate diet.



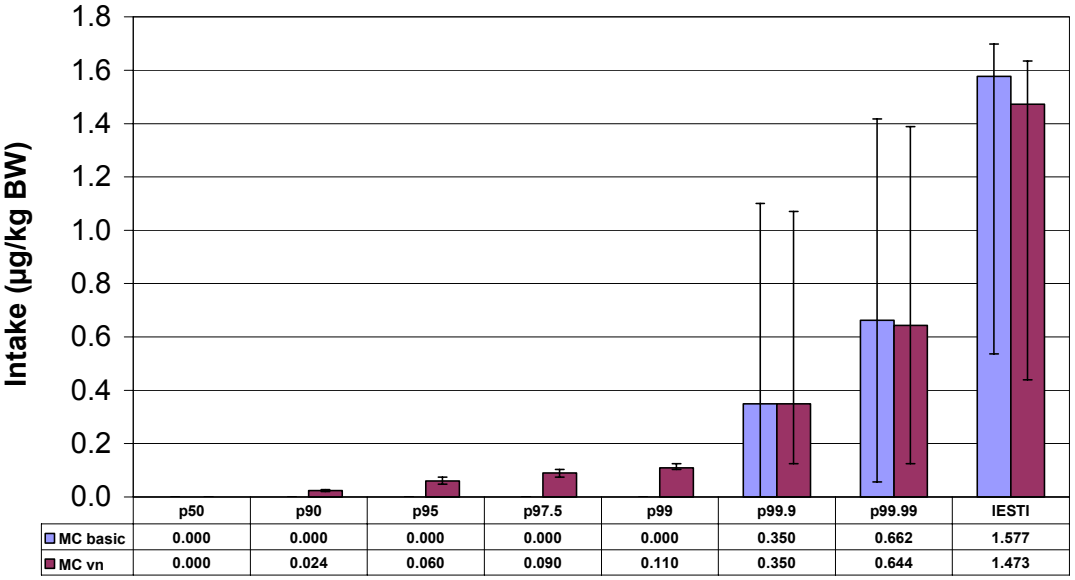
	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
green beans	0.000	0.000	0.000	0.000	0.000	0.350	0.662	1.577
nectarine	0.000	0.000	0.000	0.000	0.000	0.260	0.652	10.550
endive	0.000	0.000	0.000	0.000	0.000	0.018	0.153	6.670

Figure 23. Validation MC basic model against IESTI for the three products with the highest p99.9.



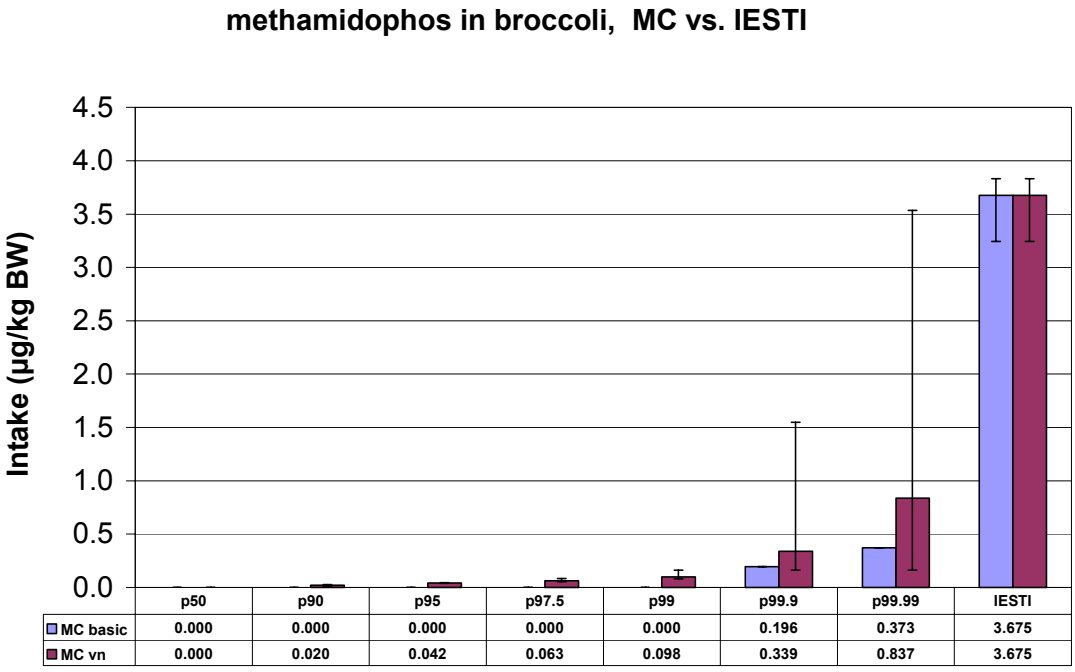
	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
green beans	0.000	0.024	0.060	0.090	0.110	0.350	0.644	1.473
broccoli	0.000	0.020	0.042	0.063	0.098	0.339	0.837	3.675
endive	0.000	0.000	0.001	0.045	0.093	0.132	0.398	6.637
tomato	0.000	0.037	0.062	0.077	0.088	0.116	0.257	1.899
nectarine	0.000	0.000	0.000	0.000	0.050	0.392	1.381	10.550
melon	0.000	0.000	0.000	0.025	0.047	0.333	1.162	7.581
sweet pepper	0.000	0.000	0.000	0.010	0.020	0.346	1.077	17.900

Figure 24. Validation MC model with variability and replacement of nondetects by LOR against IESTI for the seven products with the highest p99.



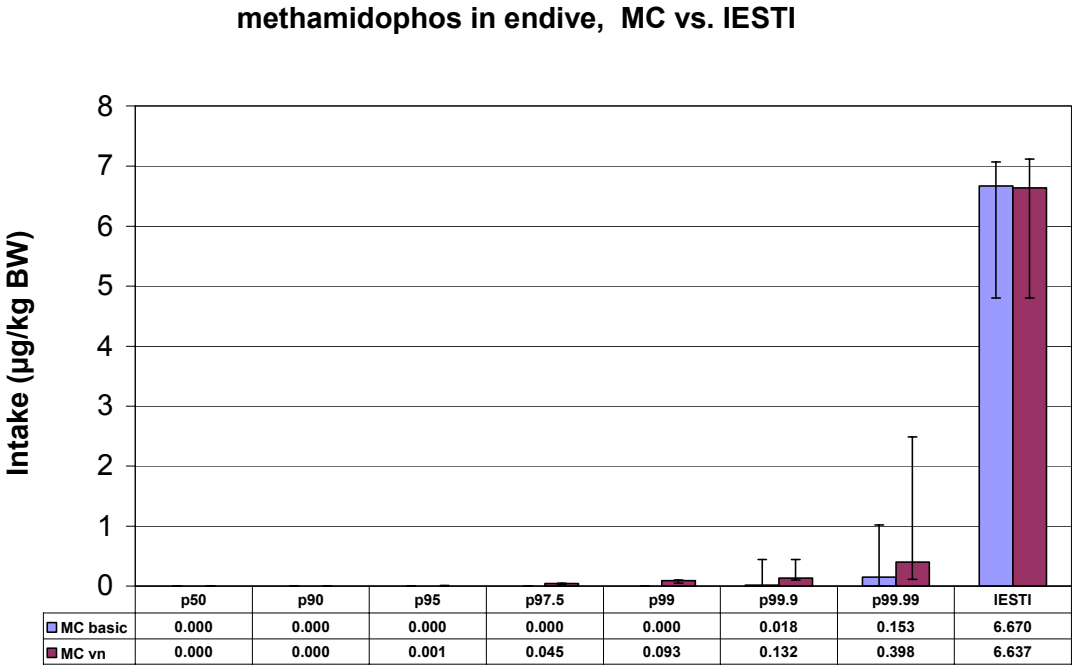
	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.000	0.000	0.350	0.662	1.577
MC vn	0.000	0.024	0.060	0.090	0.110	0.350	0.644	1.473

Figure 25. Comparison of exposure estimates (µg/kg BW/day) from MC basic and vn models and two types of IESTI in green beans.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.000	0.000	0.196	0.373	3.675
MC vn	0.000	0.020	0.042	0.063	0.098	0.339	0.837	3.675

Figure 26. Comparison of exposure estimates (µg/kg BW/day) from MC basic and vn models and two types of IESTI in broccoli.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.000	0.000	0.018	0.153	6.670
MC vn	0.000	0.000	0.001	0.045	0.093	0.132	0.398	6.637

Figure 27. Comparison of exposure estimates (µg/kg BW/day) from MC basic and vn models and two types of IESTI in endive.

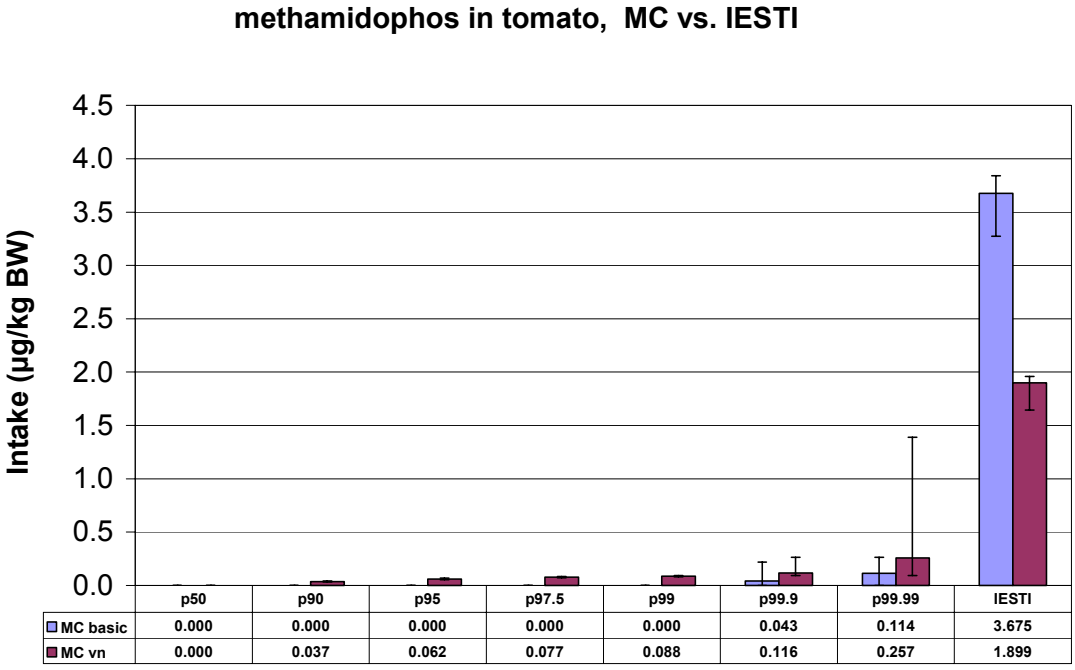


Figure 28. Comparison of exposure estimates (µg/kg BW/day) from MC basic and vn models and two types of IESTI in tomato.

3.6 Pirimicarb (pica)

In the residue database, pirimicarb was found in 20 of the 64 products in the diet of any of the infants in the duplicate diet study.

In the duplicate diet study 9 out of 250 infants (3.6 %) had a measured positive intake (after recovery correction 0.150, 0.167, 0.183, 0.267, 0.268, 0.486, 0.524, 0.647 and 0.691 µg/kg BW/day). For the other 241 infants (96.4 %) the censoring limit varied between 0.020 and 0.455 µg/kg BW/day (mean 0.200 µg/kg BW/day).

The MC pvn model was run based on the 20 products on which positive residuals have been found (MC pvn pos), and based on all 64 consumed products (MC pvn all). The results of the validation of the MC models are summarized in Table 5 and visualized in Figure 29 - Figure 34.

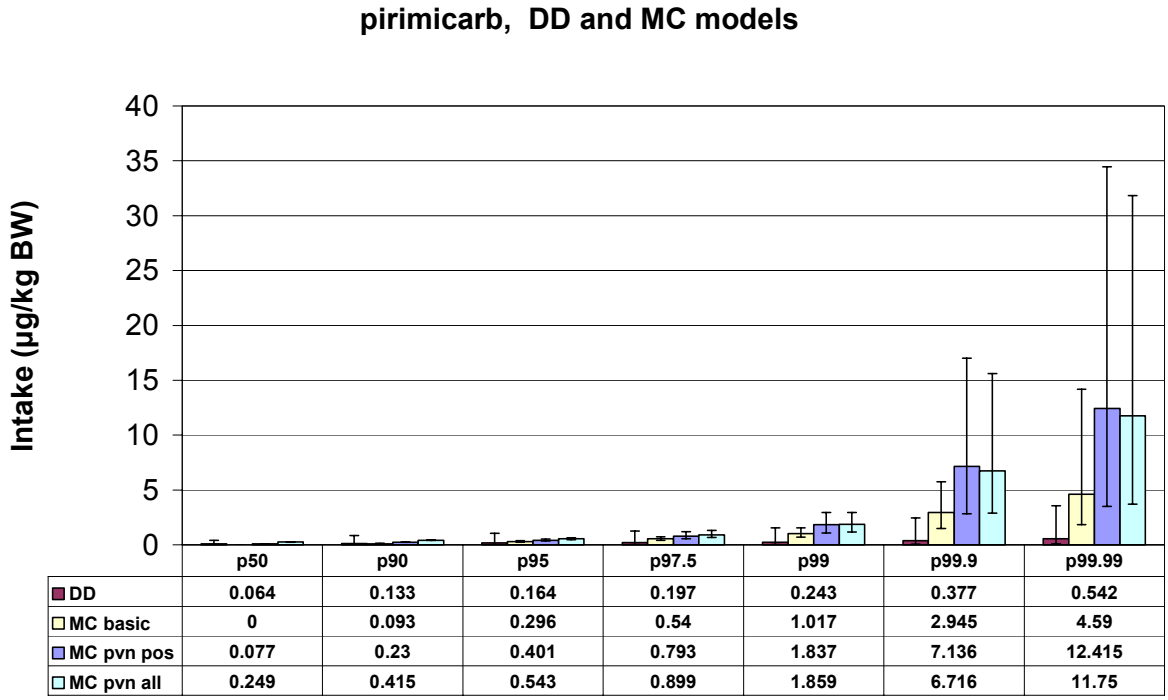
The 50th and 90th percentiles of the basic MC model are lower than 0.1 µg/kg BW/day and also lower than the percentile estimated from the duplicate diet. The basic MC model is thus not validated for the estimation of these very low exposures. For percentiles p90 and higher the basic MC model percentiles are higher than the duplicate intake percentiles by factors between 1.8 and 8. Similar factors vary between 2.4 and 23 for the MC vn pos model, and between 4 and 59 for the MC vn all model. For almost all percentiles the uncertainty intervals of the MC models and duplicate diet do overlap so that we must be cautious when concluding that the MC models will not produce too low values. A further statistical analysis comparing the MC models and the duplicate diet results in one bootstrap procedure is advisable.

The IESTI values of the basic MC model are higher than even the p99.99 percentiles of individual commodities by a factor between 2.1 and 104. Compared with the estimated 99.99th percentiles of MC pvn these factors are between 1.8 and 24.

The MC models calculate a p99 between 1.0 and 1.9 µg/kg BW/day. The p99 estimated from the duplicate diet study is 0.24 µg/kg BW/day. The highest IEST is, for endive, 100 µg/kg BW/day.

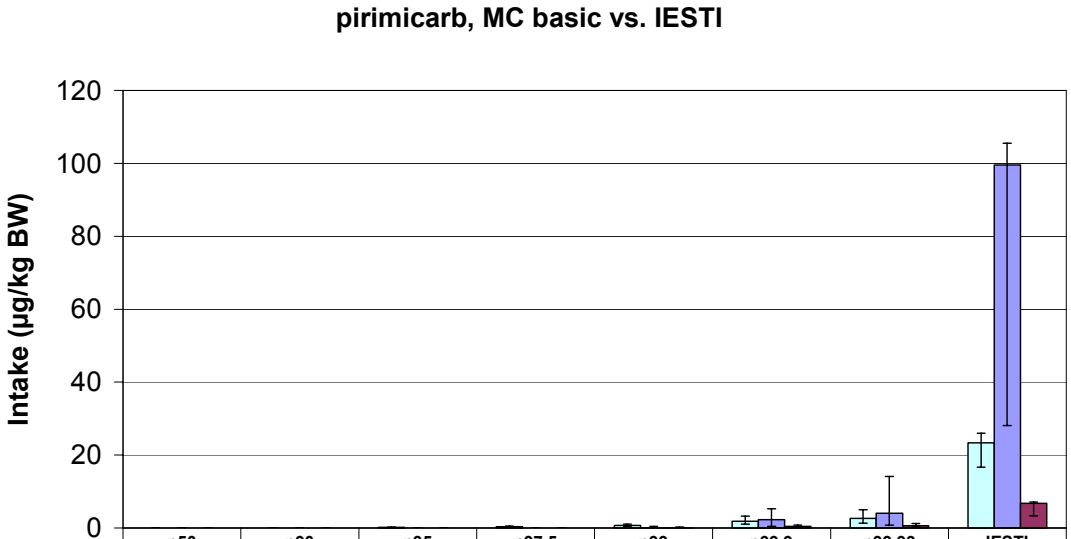
According to the basic MC model apple, endive and pear are the commodities that contribute most to the exposure (p99 estimates 0.73, 0.07 and 0.03 µg/kg BW/day). If we allow for processing, unit variability and replace nondetects with LOR, then the contributions are in the order apple, pear, endive (p99 estimates 1.22, 0.19 and 0.16 µg/kg BW/day).

Conclusion for pirimicarb: The MC models seem valid for most of the percentiles, but the estimates are relatively close to the duplicate diet estimates (and therefore significance is hard to prove). This may be due to the fact that the duplicate diet estimates have been corrected for recovery losses by a factor, which was estimated as 5.00 (much higher than for the other substances). No information was available about the possible need to correct also the residue databank concentrations for recovery losses.



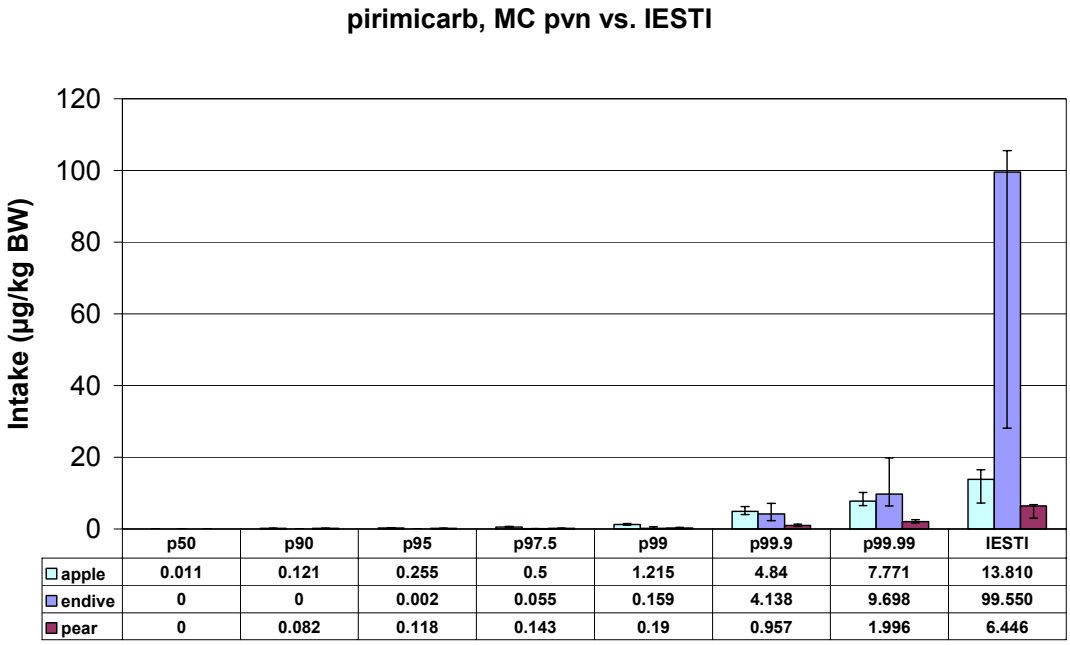
	p50	p90	p95	p97.5	p99	p99.9	p99.99
DD	0.064	0.133	0.164	0.197	0.243	0.377	0.542
MC basic	0	0.093	0.296	0.54	1.017	2.945	4.59
MC pvn pos	0.077	0.23	0.401	0.793	1.837	7.136	12.415
MC pvn all	0.249	0.415	0.543	0.899	1.859	6.716	11.75

Figure 29. Validation MC models against duplicate diet results.



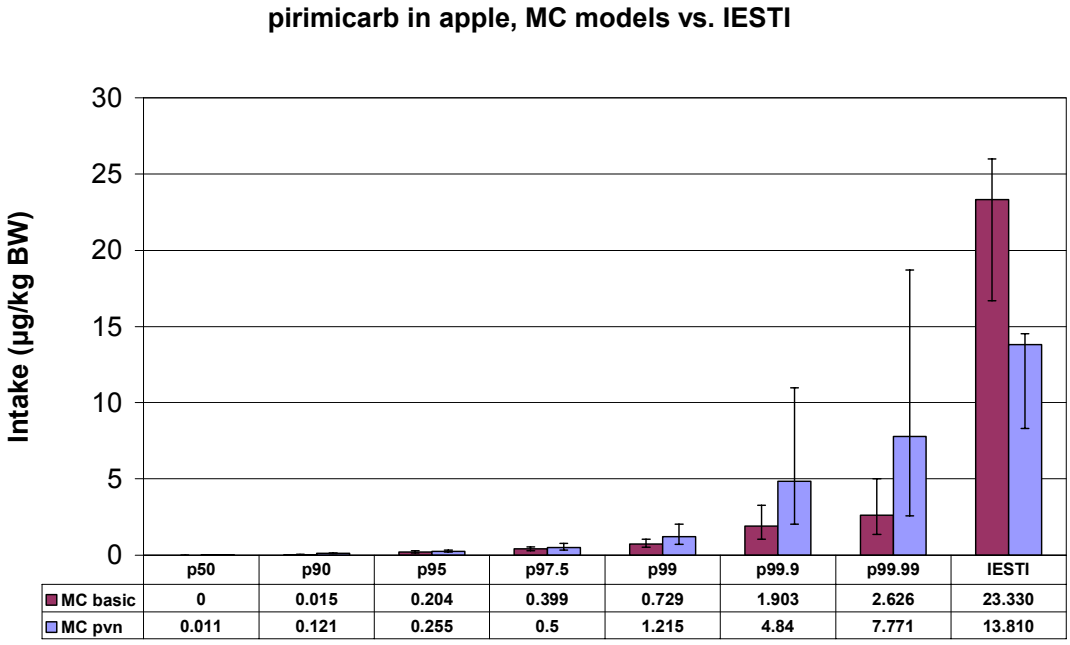
	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
apple	0	0.015	0.204	0.399	0.729	1.903	2.626	23.330
endive	0	0	0	0	0.072	2.315	4.101	99.550
pear	0	0	0	0	0.034	0.477	0.648	6.785

Figure 30. Validation MC basic model against IESTI for three products with highest p99**.**



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
apple	0.011	0.121	0.255	0.5	1.215	4.84	7.771	13.810
endive	0	0	0.002	0.055	0.159	4.138	9.698	99.550
pear	0	0.082	0.118	0.143	0.19	0.957	1.996	6.446

Figure 31. Validation of MC model with processing, variability and nondetect replacement with LOR against IESTI for three products with highest p99.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0	0.015	0.204	0.399	0.729	1.903	2.626	23.330
MC pvn	0.011	0.121	0.255	0.5	1.215	4.84	7.771	13.810

Figure 32. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in apple.

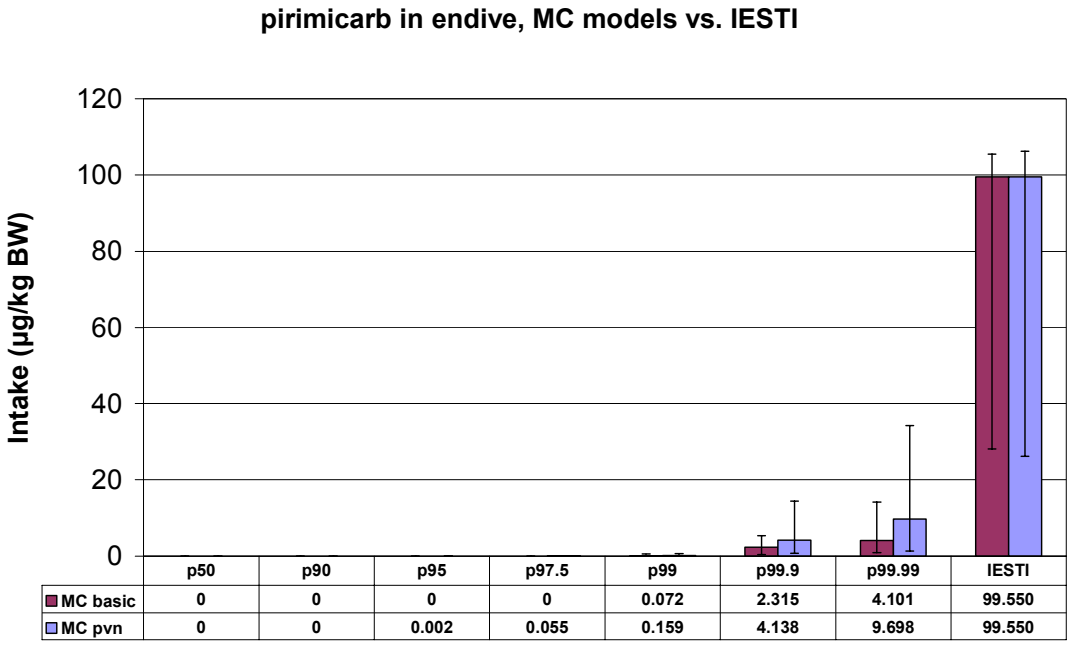


Figure 33. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in endive.

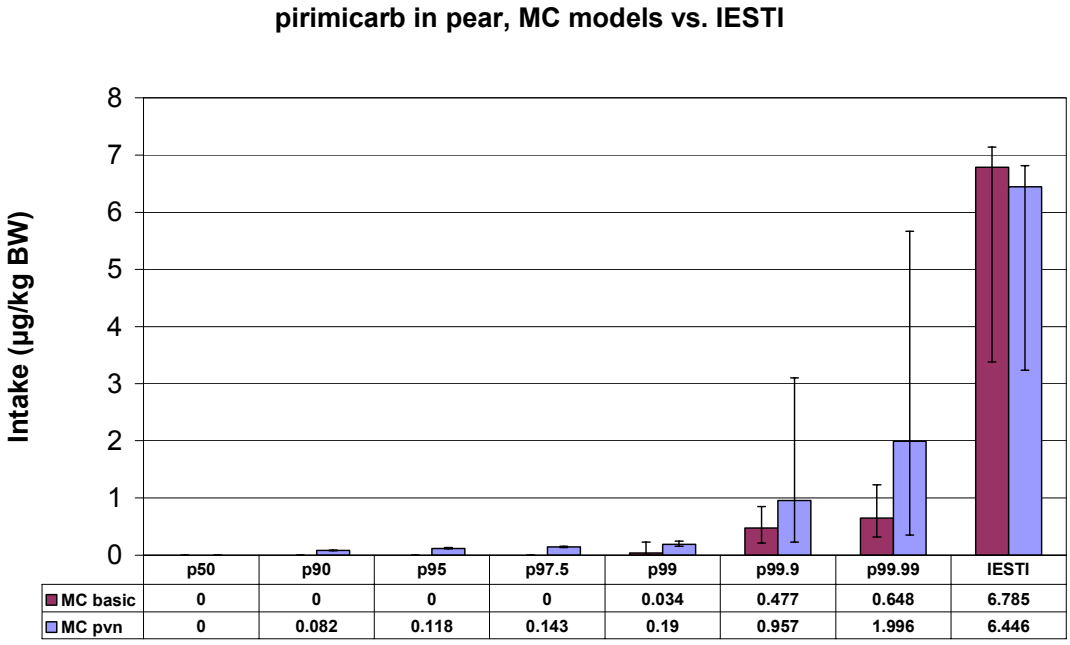


Figure 34. Comparison of exposure estimates (µg/kg BW/day) from MC basic and pvn models and two types of IESTI in pear.

3.7 Pirimiphos-methyl (pime)

In the residue database, pirimiphos-methyl was found in 7 of the 64 products in the diet of any of the infants in the duplicate diet study.

In the duplicate diet study 4 out of 250 infants (1.6 %) had a measured positive intake (after recovery correction 0.150, 0.227, 0.265 and 0.448 µg/kg BW/day). For the other 246 infants (98.4 %) the censoring limit varied between 0.012 and 0.266 µg/kg BW/day (mean 0.117 µg/kg BW/day).

There is only 1 reported processing factor (carrot, peeled). This combination did not occur in the consumption data. No processing factors were therefore applied in the model calculations. We will therefore consider the validation of the MC basic and the MC vn models. The MC vn model was run based on the 7 products on which positive residuals have been found (MC vn pos), and based on all 64 consumed products (MC vn all). The results of the validation of the MC models are summarized in Table 6 and visualized in Figure 35 - Figure 39.

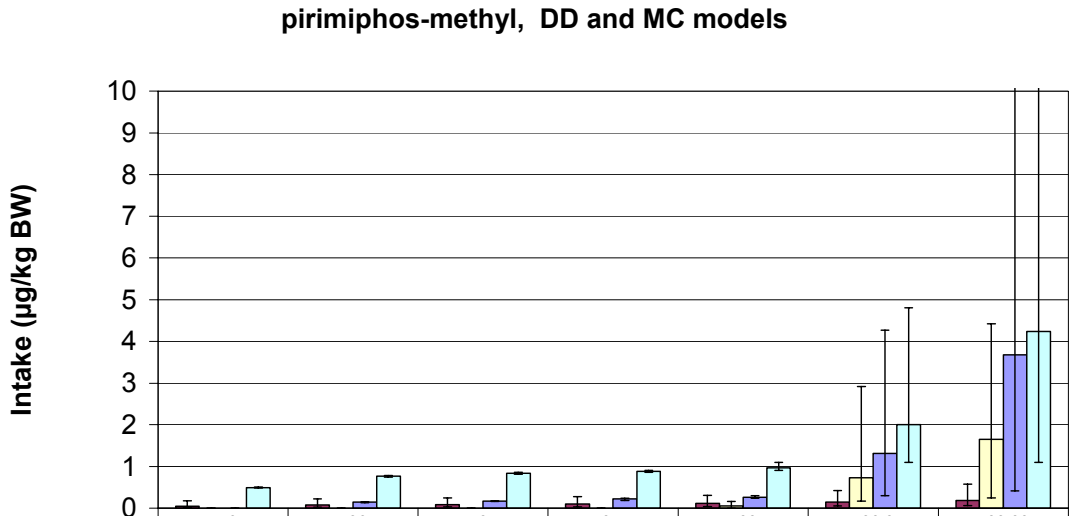
The 50th, 90th, 95th, 97.5th and 99th percentiles of the basic MC model and the 50th percentile of the MC vn pos model are all lower than 0.1 µg/kg BW/day and also lower than the percentile estimated from the duplicate diet. The basic MC model is thus not validated for the estimation of these very low exposures. Note that this is the only case where the estimation of p99 was invalid. For percentiles p99.9 and p99.99 the basic MC model percentiles are higher than the duplicate intake percentiles by factors 5 and 9. For percentiles p90 and higher the duplicate diet estimates are lower than the MC vn models by a factor between 1.9 and 20 (for the MC vn pos model), and between 9 and 23 (for the MC vn all model). For all percentiles p90 and higher the uncertainty intervals of the MC vn pos model and duplicate diet do overlap so that we must be cautious when concluding that the MC vn pos model will not produce too low values. A further statistical analysis comparing the MC model and the duplicate diet results in one bootstrap procedure is advisable.
The uncertainty intervals for the percentiles of the MC vn all model are disjunct from those of the duplicate diet model, so that this model is validated beyond doubt.

The IESTI values of the basic MC model are higher than even the p99.99 percentiles of individual commodities by a factor between 29 and 43. Compared with the estimated 99.99th percentiles of MC pvn these factors are between 3 and 21.

The MC models calculate a p99 between 0.05 and 0.96 µg/kg BW/day. The p99 estimated from the duplicate diet study is 0.11 µg/kg BW/day. The highest IESTI level is, for mandarin, 32 µg/kg BW/day.

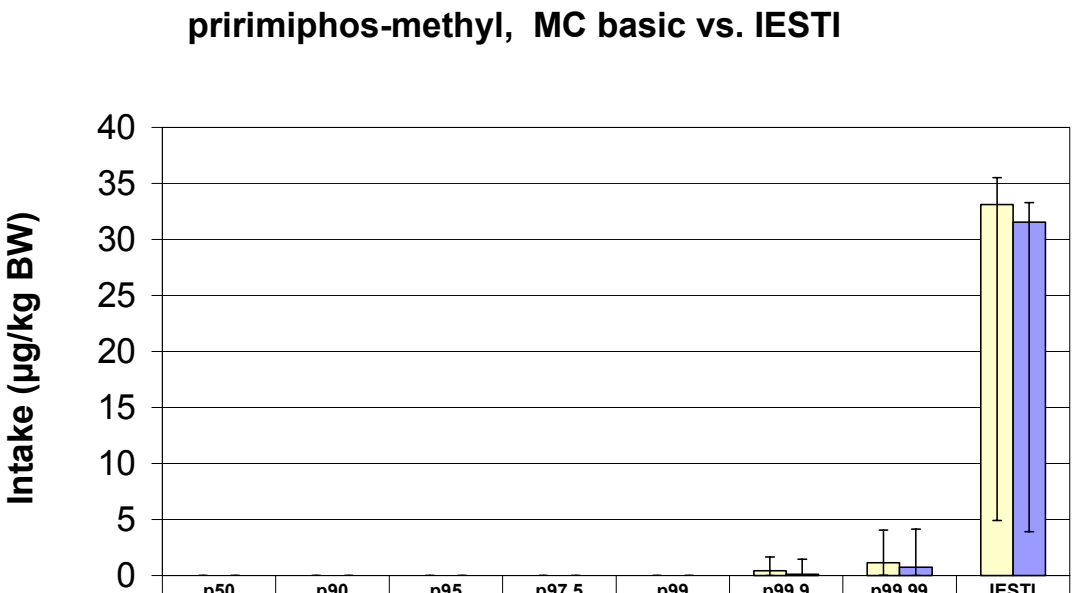
According to the basic MC model orange and mandarin are the commodities that contribute most to the exposure (p99 estimates below 0.001, p99.9 estimates 0.44 and 0.13 µg/kg BW/day). If we allow for unit variability and replace nondetects with LOR, then the contributions are in the order orange, kiwi fruit, mandarin and pear (p99 estimates 0.19, 0.17, 0.12 and 0.10 µg/kg BW/day).

Conclusion for pirimiphos-methyl: the exposure as estimated by the MC models was very low. This was the only case where the estimation of a 99th percentile by the MC model was invalidated (only the basic model). The MC vn all model was unambiguously validated for percentiles between p90 and p99.



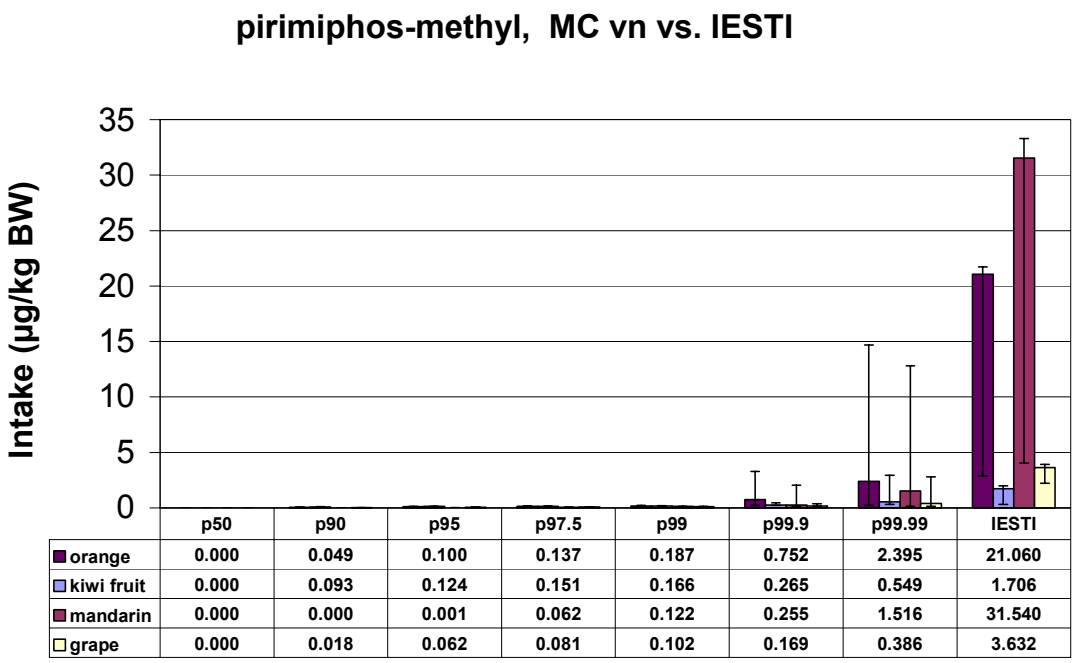
	p50	p90	p95	p97.5	p99	p99.9	p99.99
DD	0.050	0.078	0.089	0.099	0.113	0.148	0.185
MC basic	0.000	0.000	0.000	0.000	0.052	0.732	1.653
MC vn pos	0.000	0.146	0.169	0.220	0.260	1.316	3.683
MC vn all	0.498	0.769	0.838	0.885	0.965	2.006	4.238

Figure 35. Validation MC models against duplicate diet.



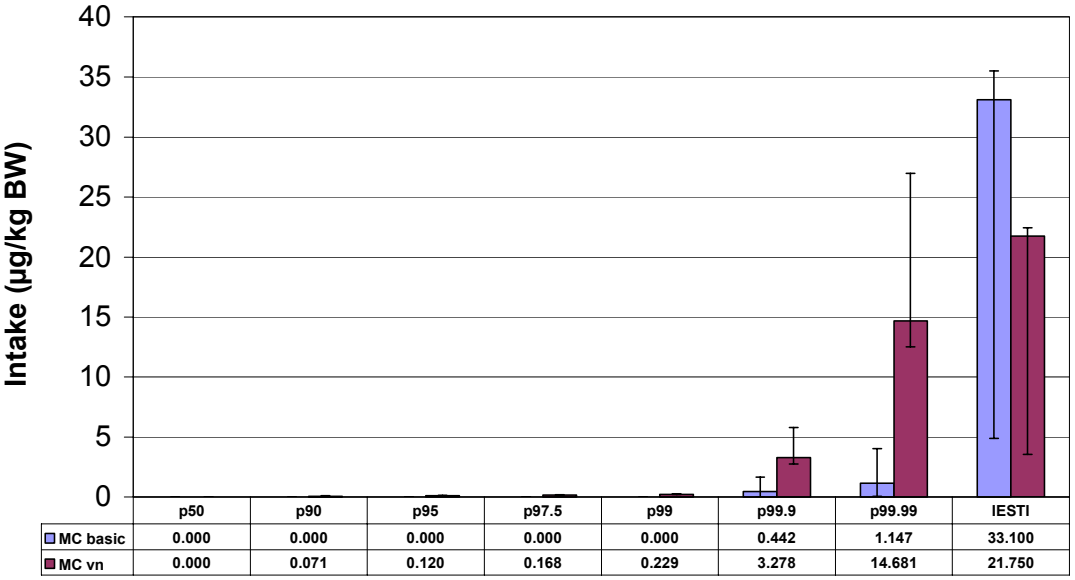
	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
orange	0.000	0.000	0.000	0.000	0.000	0.442	1.147	33.100
mandarin	0.000	0.000	0.000	0.000	0.000	0.128	0.738	31.540

Figure 36. Validation MC basic model against IESTI for two products with highest p99.9.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
orange	0.000	0.049	0.100	0.137	0.187	0.752	2.395	21.060
kiwi fruit	0.000	0.093	0.124	0.151	0.166	0.265	0.549	1.706
mandarin	0.000	0.000	0.001	0.062	0.122	0.255	1.516	31.540
grape	0.000	0.018	0.062	0.081	0.102	0.169	0.386	3.632

Figure 37. Validation MC model with variability and replacement of nondetects by LOR against IESTI for four products with highest p99.



	p50	p90	p95	p97.5	p99	p99.9	p99.99	IESTI
MC basic	0.000	0.000	0.000	0.000	0.000	0.442	1.147	33.100
MC vn	0.000	0.071	0.120	0.168	0.229	3.278	14.681	21.750

Figure 38. Comparison of exposure estimates (µg/kg BW/day) from MC basic and vn models and two types of IESTI in orange.

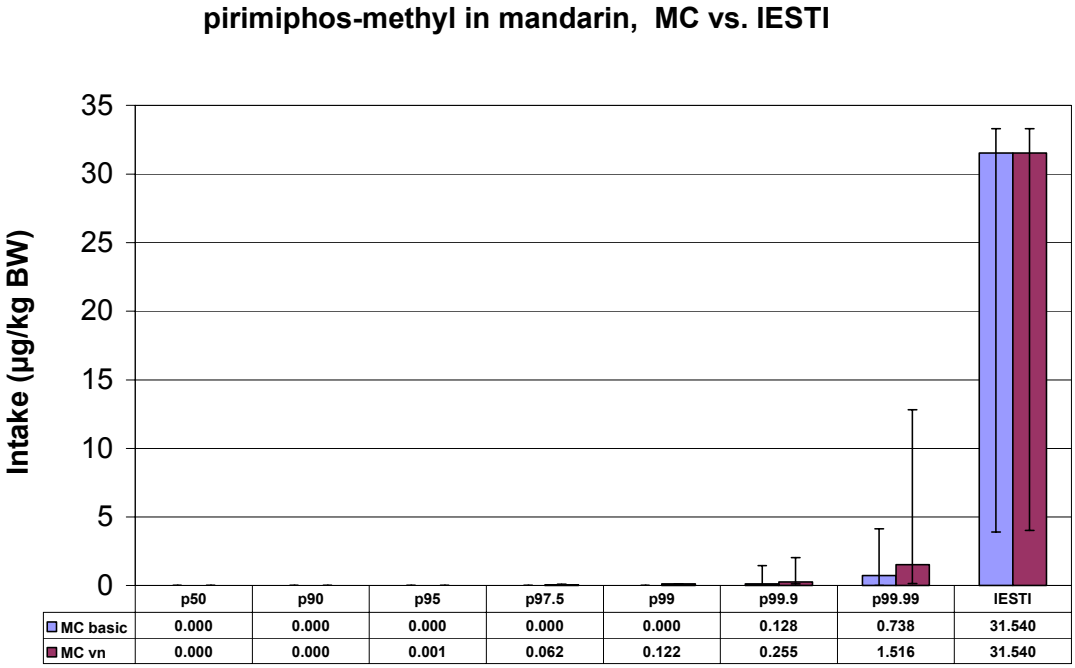


Figure 39. Comparison of exposure estimates (µg/kg BW/day) from MC basic and vn models and two types of IESTI in mandarin.

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APPENDICES

Appendix 1. Processing factors, unit weights, limits of reporting

Table 10. Processing factors used in the MC model.

pest_ code	pest_ name	rac_ code	RAC_ name	proc_ code	proc_ name	proc_upp[1]	references
120712	chlorpyrifos	103001	apple	2	peeling	1	PSD (1998), Zabik et al. (2000)
				3	cooking/boiling	0.03	Zabik et al. (2000)
				9	juicing	0.27	Zabik et al. (2000), FAO/WHO (2001), Newsome et al. (2000)
				13	sauce/puree	0.34	FAO/WHO (2001), Newsome et al. (2000)
		106002	banana	2	peeling	0.69[2]	Hasegawa et al. (1991), PSD (1998), Zabik et al. (2000)
		101001	grapefruit	9	juicing	0.49[3]	FAO/WHO (2001)
		101002	lemon	9	juicing	0.49[3]	FAO/WHO (2001)
		101004	mandarin, tangerines	9	juicing	0.49[3]	FAO/WHO (2001)
		101005	orange	2	peeling	0.69[2]	Hasegawa et al. (1991), PSD (1998), Zabik et al. (2000)
				9	juicing	0.49[3]	FAO/WHO (2001)
		105001	grape	7	drying	0.24	FAO/WHO (2001)
				9	juicing	0.52[3]	FAO/WHO (2001)
		502099	potato	2	peeling	0.69[2]	Hasegawa et al. (1991), PSD (1998), Zabik et al. (2000)
		203001	tomato	13	sauce/puree	0.3[4]	FAO/WHO(2001)
110501	iprodione	201002	carrot	9	juicing	1	Burchat et al. (1998)
				15	washing w water	0.64[5]	Burchat et al. (1998), Cabras et al. (1998)
		105001	grape	7	drying	2.63	Cabras et al. (1998)
				15	washing w water	0.64[5]	Burchat et al. (1998), Cabras et al. 1998)
		203001	tomato	15	washing w water	0.64[5]	Burchat et al. (1998), Cabras et al. (1998)
120314	pirimicarb	103001	apple	2	peeling	0.63[3]	Celik et al. (1995)
				15	washing w water	1[3]	Celik et al. (1995)
		203002	sweet pepper	15	washing w water	1[3]	Celik et al. (1995)
		203001	tomato	15	washing w water	1[3]	Celik et al. (1995)

[1] In principle we used upper confidence limits roughly estimated as $m+2s$ with m and s the mean and standard deviation calculated from basic values found in the references. If there was >1 reference for one product and >1 value in any of the references, we applied the calculation to the mean values of the references. The limits were restricted to a maximum value of 1 except for drying. We pooled the information across products if values were similar.

[2] Pooled from values for apple, banana, orange and potato.

[3] Only one value was available. For s we used the pooled standard deviation of all other available cases (0.23).

[4] Maximum value as reported in the reference.

[5] Pooled from values for carrot, grape and tomato.

Table 11. Unit weights of raw agricultural commodities (RACs).
Small commodities (<25 g, where no variability applies) are coded with -25

RAC_code	RAC_name	unit weight (g)
101001	GRAPEFRUIT	160
101002	LEMON	67
101004	MANDARIN, TANGERINES	100
101005	ORANGE	160
103001	APPLE	112
103002	PEAR	150
104001	APRICOT	39
104003	PEACH	110
104004	PLUM, INCLUDING DAMSON	55
104005	NECTARINE	149
105001	GRAPE	500
105003	STRAWBERRY	-25
105007	RASPBERRY	-25
105010	CURRANT (RED, WHITE, BLACK)	-25
105013	ELDERBERRY	-25
105015	ROSE HIP	-25
106002	BANANA	100
106005	KIWI FRUIT	75
106008	MANGO	375
106011	PASSIONFRUIT	45
106012	PINEAPPLE	150
106014	GUAVE	-25
201001	BEETROOT	35
201002	CARROT	80
201003	CELERIAC	189
201008	RADISH	-25
201009	SCORZONERA OR BLACK SALSIFY	-25
201011	SWEDE	500
201016	BLACK RADISH	-25
202002	ONION, INCLUDING PEARL/COCKTAIL ONION	150
202003	SHALLOT	26
203001	TOMATO	85
203002	SWEET PEPPER	160
203003	AUBERGINE/EGG PLANT	480
203005	CUCUMBER	60
203007	COURGETTE	114
203009	MELON	322
203013	SWEET CORN	215
204001	BROCCOLI	74
204002	CAULIFLOWER	780
204004	BRUSSELS SPROUTS	-25
204006	RED CABBAGE	540
204007	OXHEART/CONICAL CABBAGE	540
204008	WHITE CABBAGE	540
204009	SAVOY CABBAGE	540
204010	CHINESE CABBAGE	540
204011	CURLY KALE	165
205003	CABBAGE LETTUCE, COS LETTUCE	558
205004	ENDIVE	558

205005 PURSLANE	-25
205006 SPINACH	-25
205010 CHICORY	153
205013 PARSLEY	-25
205014 CELERY	-25
205015 TURNIP TOPS/GREENS	-25
206010 BEAN, (SCARLET/STRING/FRENCH)	-25
206011 GREEN BEANS (FRESH)	-25
206012 LEGUME (FRESH)	-25
206021 BROAD BEAN	-25
206030 GREEN/(GARDEN) PEAS (FRESH)	-25
207003 BLEACH-CELERY	30
207004 FENNEL	-25
207006 LEEK	140
207007 RHUBARB	100
207008 BEAN SPROUTS	-25
208002 MUSHROOM	-25
502099 POTATOES	216

Table 12. Limits of Reporting (LOR) for pesticides in the monitoring program and duplicate diet study.

pesticide code	pesticide name	LOR (mg/kg)	
		monitoring program	duplicate diet study
110501	IPRODIONE	0.02	0.001
120314	PIRIMICARB	0.01	0.001
120710	CHLORFENVINPHOS	0.03	0.001
120712	CHLORPYRIFOS	0.05	0.001
120753	METHAMIDOPHOS	0.01	0.001
120764	PIRIMIPHOS-METHYL	0.02	0.001

Appendix 2. Percentile and percentile confidence interval estimation of heavily censored lognormal data using the nonparametric bootstrap

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Suppose we have a sample of n values y_i from a lognormal distribution, but that these values are only known when $y_i \geq Ly_i$, where the Ly_i denote censoring limits (which in general may be different for each observation y_i). We will consider the situation where n is fairly large (e.g. n = 250), but where the number of uncensored observations ($y_i \geq Ly_i$) is small (e.g. n_{det} = 10). Our interest is in estimating upper percentiles of the lognormal distribution (point estimates) and in estimating confidence intervals of these percentiles (interval estimates).

Let μ and σ^2 denote the mean and variance of the normal distribution of $x_i = \ln(y_i)$. Percentiles $y_{(p)}$ corresponding with cumulative percentages p are then given by

$$y_{(p)} = \exp\left(x_{(p)}\right) = \exp\left(\mu + z_p \sigma\right)$$

where z_p is the corresponding percentage point of the standard normal distribution (e.g. z_{95} = 1.645).

In the absence of censoring the estimation of μ and σ^2 is straightforward, using for example the maximum likelihood (ML) estimators $\bar{x} = \left(\sum_{i=1}^{n} x_i\right)/n$ and $s^2 = \sum_{i=1}^{n}\left(x_i - \bar{x}\right)^2/n$. For the point estimation of percentiles it is sensible to apply an unbiased estimator for σ (see e.g. Johnson et al. (1994), p. 127), multiplying the ML estimate s with a factor a_n given by

$$a_n = \frac{\Gamma\left[(n-1)/2\right]}{\sqrt{(2/n)}\,\Gamma\left(n/2\right)}$$

which can be approximated by

$$a_n = 1 + \frac{0.75}{n-1}.$$

With censored data points it is possible to obtain ML estimates of μ and σ^2 starting from the likelihood equation

$$Lik\left(\mu, \sigma^2 \middle| x\right) = \prod_{nondetects}\left[\Phi\left(L_i\right)\right] \cdot \prod_{detects}\left[\phi\left(x_i\right)\right]$$

where $L_i = \ln(Ly_i)$ are the censoring limits transformed to the logarithmic scale, and where $\Phi(\cdot)$ and $\phi(\cdot)$ denote the cumulative normal probability function and normal probability density, respectively. Iterative computations are necessary to optimise this likelihood, and several methods have been described in the literature, e.g. by using the EM algorithm or iterative least squares (see e.g. Aitkin, 1981). It is also possible to use tabulated values (Cohen, 1959). In our method we apply a Newton-Raphson optimisation as provided in the FITNONLINEAR procedure of Genstat to minimize the deviance, which equals –2 ln(*Lik*). We use μ and $\ln(\sigma)$ as parameters in the optimisation algorithm.

Commonly, ML based methods are only advocated for relatively low amounts of censoring. For example, the US Environmental Protection Agency has given guidelines for analysing data with nondetects (US-EPA, 1998, p. 4.7-1). In short, these guidelines are to use simple substitution method for percentages of nondetects up to 15 %, to use statistical methods such as Cohen's method (which is based on ML) for percentages of nondetects between 15 % and 50 %, and to use tests for proportions (that is, ignore the numerical character of the data) when the percentage of nondetects is between 50 % and 90 %. For still higher percentages of nondetects in the data, only a vague allusion to the Poisson distribution is made.

In this paper we extend the use of ML estimation methods to situations with very high percentages of nondetects, e.g. 95 % when the sample size is e.g. 250. To this end we apply the nonparametric bootstrap (Efron & Tibshirani 1993) and use ML estimation on each of the bootstrap samples. This provides us with a bootstrap distribution of percentile estimates, which can be used for constructing confidence intervals or testing.

We need the assumption of log normality to arrive at these results. Admittedly, the procedure will fail if this assumption fails. It is the price we pay in order to be able to make inference from so few data. Only by complementing the relatively scarce data with prior knowledge it is possible to obtain confidence statements about the percentiles we are interested in.

The procedure works as follows:

1. Transform all observations y and censoring limits Ly to the logarithmic scale:
$$x_i = \ln(y_i); \quad L_i = \ln(Ly_i)$$
2. Calculate the mean censoring limit $\overline{L} = \left(\Sigma_{i=1}^{n} L_i\right)/n$.
3. Calculate the approximate percentage point $z_{max,n}$ corresponding with the maximum in a sample of n observations (see e.g. David, 1970):
$$z_{\max,n} = \Phi^{-1}\left[(n-\alpha)/(n-2\alpha+1)\right]$$
where $\alpha = 0.315065 + 0.05797u - 0.009776u^2$, and $u = {}^{10}\log(n)$.
4. Select B independent bootstrap samples, each drawn with replacement from the data . The value of B should be large enough for accurate confidence interval estimation (e.g. B=1000).
5. For each bootstrap sample calculate percentile estimates as follows:

5.1. Calculate the number n_{det} of values $x_i \geq L_i$.

5.1.1. Only if n_{det} = 0, estimate μ with the logarithm of a random value from the uniform distribution on the interval between 0 and the geometric mean censoring limit:
$$\hat{\mu} = \ln(u); \quad u \sim U\left(0, \exp\left(\overline{L}\right)\right),$$
and choose σ such that the mean censoring limit corresponds to the percentage point expected for the maximum of n values.
$$\hat{\sigma} = \left(\overline{L} - \hat{\mu}\right)/z_{\max,n}.$$

5.2. If n_{det} > 0, apply ML estimation:

5.2.1. Initial values for the parameters are based on the percentage points corresponding with the fraction of nondetects and the maximum observation:
$$\hat{\sigma} = \left(\max(x_i) - \overline{L}\right)/\left(z_{\max,n} - z_{pnondetect}\right)$$
$$\hat{\mu} = \overline{L} - z_{pnondetect}\hat{\sigma}$$
where $z_{pnondetect} = \Phi^{-1}\left(1 - n_{\det}/n\right)$.

5.2.2. ML is carried out by optimising $\hat{\mu}$ and $\ln(\hat{\sigma})$ in a Newton-Raphson minimization of the deviance function $D = \sum_{detects}\left(2\ln(\hat{\sigma}) + \frac{x_i - \hat{\mu}}{\hat{\sigma}}\right) - 2 \cdot \sum_{nondetects} \ln\left[\Phi\left(\frac{\overline{L} - \hat{\mu}}{\hat{\sigma}}\right)\right]$.

5.2.3. The ML estimate of σ is corrected for bias assuming that it is effectively based on n_{det} degrees of freedom, and the estimate of μ is adapted to in order to have the correct percentage point for the percentage of nondetects:

$$\hat{\sigma} = \hat{\sigma}_{ML} \cdot \left(1 + 0.75 / n_{\text{det}}\right)$$

$$\hat{\mu} = \overline{L} - z_{pnondetect}\hat{\sigma}$$

5.3. Calculate any percentile that we are interested in as

$$x_{(p),b} = \hat{\mu} + z_p \hat{\sigma}$$

6. The results $x_{(p),b}$, b=1,...,B from all B bootstrap samples together constitute the bootstrap distribution of the percentile. From this we may obtain a point estimate by taking the median $x_{(p)}$, or a 95 % confidence interval ($x_{(p),low}$,$x_{(p)upp}$) by estimating the 2.5th and 97.5th quantile.
7. (testing) If percentiles $x_{(p)}$ are to be compared in a statistical test with other estimates $\tilde{x}_{(p)}$ which are (at least partly) based on the same set of individuals, then it may be sensible to use the same B bootstrap samples for both calculations. It will then be useful to calculate the bootstrap distribution of $d_{(p)} = x_{(p)} - \tilde{x}_{(p)}$. The position of 0 in this distribution can be used for a bootstrap significance test.
8. Results are transformed back to the original scale

Simulations with the model

Although, technically, the method works with at least one observation greater than or equal to the censoring limit in the original data set, it was not expected to have good statistical properties unless there would be a reasonable number of positive values. Some simulations were performed to investigate the bias of the point estimators and the coverage of the confidence intervals.

Throughout we used a sample size n=250. Complete data x_i were drawn from a standard normal distribution. For some percentages q (10 %, 95 %, 97.5 %, 99 %) of nondetects in the population, the corresponding percentage point z_q was used as a censoring limit in the simulations. The number of bootstrap iterations was between B=100 in some simulations and B=1000 in other. Bootstrap distributions were calculated for percentiles p equal to 50, 90, 95, 97.5, 99, 99.9 and 99.99 %. Of course the true values of these percentiles are z_p because we are simulating from the standard normal distribution.

Simulations were repeated a large number of times (between n_{sim}=100 and n_{sim}=1000).The bias was quantified by comparing the median of medians in the bootstrap distribution with the true value (Table 1). The variability of the bootstrap estimators is quantified using the median bootstrap standard deviation (Table 2). The coverage of empirical 95 % confidence intervals shows how often these intervals included the true percentiles z_p (Table 3).

Preliminary conclusion is that the estimators have no significant bias. The standard deviations are smallest for the percentile corresponding with the true % nondetects, and of course they increase with increasing true % of nondetects. Coverage is fair (>85%) except for p50, p99.9 and p99.99 when 99% is censored.

Preliminary results

Table 1. Median point estimates for percentiles in standard normal distribution.

percentile	true value	10 % nondetects n_{sim}=100, n=250, B=1000	95 % nondetects n_{sim}=500, n=250, B=1000	97.5 % nondetects n_{sim}=200 (198), n=250, B=1000	99 % nondetects n_{sim}=200 (187), n=250, B=1000
p50	0.000	0.004	-0.009	-0.065	0.107
p90	1.282	1.290	1.291	1.316	1.428
p95	1.645	1.651	1.628	1.671	1.771
p97.5	1.960	1.961	1.936	1.943	2.084
p99	2.326	2.326	2.324	2.318	2.353
p99.9	3.090	3.089	3.121	3.174	3.270
p99.99	3.832	3.723	3.765	3.881	3.924

Table 2. Bootstrap standard deviation for percentiles in standard normal distribution.

percentile		10 % nondetects n_{sim}=100, n=250, B=100	95 % nondetects n_{sim}=500, n=250, B=1000	97.5 % nondetects n_{sim}=200 (198), n=250, B=1000	99 % nondetects n_{sim}=200 (187), n=250, B=100
p50	0.000	0.088	0.490	0.932	1.311
p90	1.282	0.105	0.210	0.462	0.696
p95	1.645	0.115	0.161	0.336	0.528
p97.5	1.960	0.126	0.153	0.258	0.395
p99	2.326	0.139	0.187	0.224	0.260
p99.9	3.090	0.170	0.331	0.359	0.353
p99.99	3.832	0.197	0.476	0.598	0.626

Note: with uncensored data the standard deviation of p50 is $1/\sqrt{250} = 0.063$.

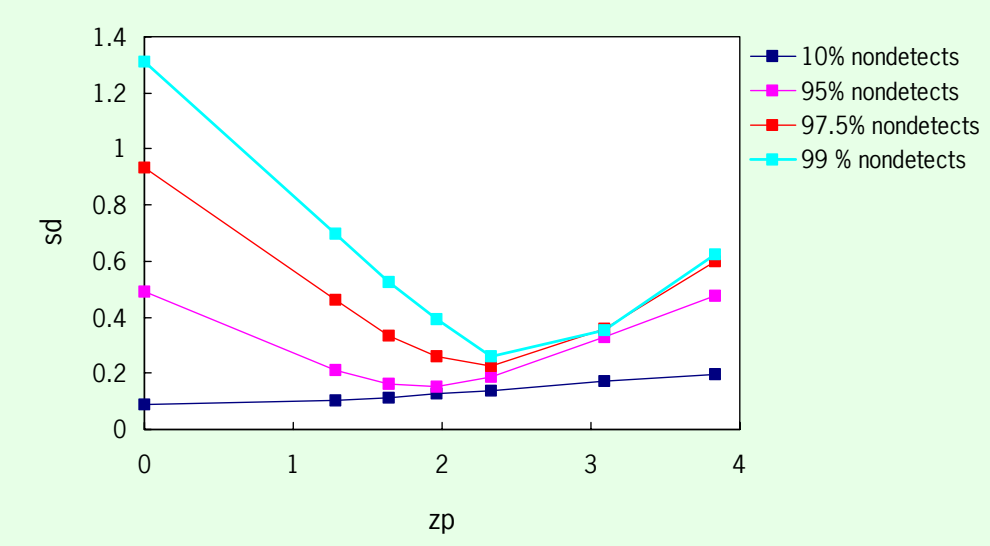
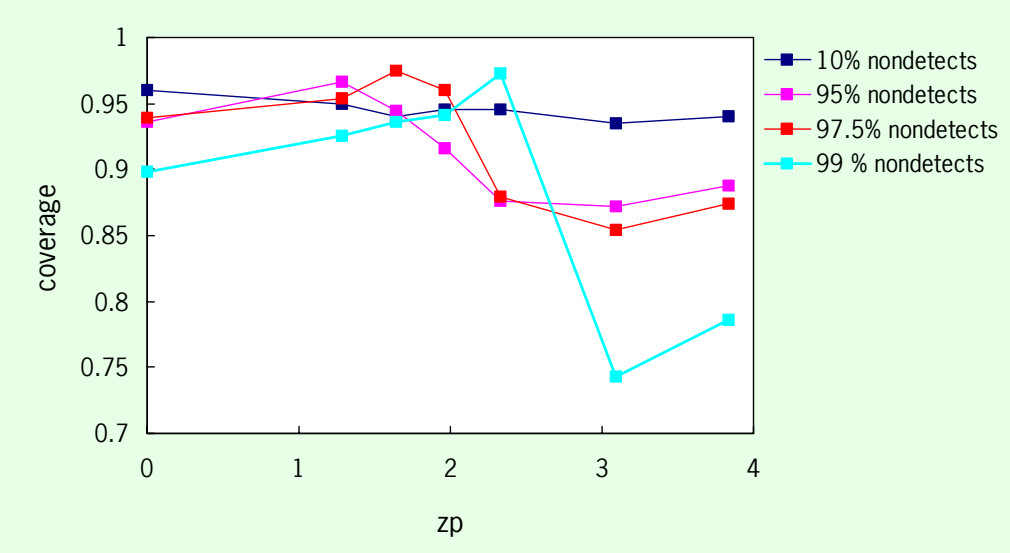


Table 3. Coverage of 95 % confidence intervals for percentiles.

percentile	10 % nondetects n_{sim}=500, n=250, B=100	95 % nondetects n_{sim}=500, n=250, B=1000	97.5 % nondetects n_{sim}=200 (198), n=250, B=1000	99 % nondetects n_{sim}=200 (187), n=250, B=1000
p50	0.960	0.936	0.939	0.898
p90	0.950	0.966	0.954	0.925
p95	0.940	0.944	0.975	0.936
p97.5	0.945	0.916	0.960	0.941
p99	0.945	0.876	0.879	0.973
p99.9	0.935	0.872	0.854	0.743
p99.99	0.940	0.888	0.874	0.786



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Appendix 3. Unit variability in probabilistic models for pesticide exposure assessment

Variability in residue concentrations between individual units is a relevant factor in the assessment of short-term dietary exposure to pesticide residues. It should be addressed separately because available data on residue levels are commonly obtained from composite samples, both in controlled field trials and in food monitoring programs. The FAO/WHO Geneva Consultation therefore recommended to include a *variability factor* (*v*) in the non-probabilistic calculation of an international estimate of short-term intake (*IESTI*) (FAO/WHO 1997, Crossley 2000). The *IESTI* has been adopted by the Joint Meeting of FAO and WHO experts on Pesticide Residues in food in 1999, and was modified in 2000 to reflect that the supply for actual consumption on a given day is likely to be derived from a single lot (JMPR 1999, 2000). In both the original and the modified definition the variability factor is used in a similar way. The basic idea is that the residue concentration for the first unit eaten is multiplied by *v*, whereas this factor is not applied for any remaining part of the daily consumption.

In the original presentation *v* was meant to reflect "*the ratio of a highest level of residue in the individual commodity unit to the corresponding residue level seen in the composite sample*" (FAO/WHO 1997). It was not clearly stated what was meant with "*a highest level*". Should this be the maximum level found or should it be a high percentile, e.g. p95 or p97.5? In practical terms this did not matter too much, because little data were available. Therefore the FAO/WHO Consultation recommended to take *initial* values of *v* equal to "*the number of commodities in the composite sample as given in Codex sampling protocols*". This will provide a conservative estimate of the residue concentration in the first unit, based on the assumption that all of the residues present in the composite sample are present in this single unit. This conservative approach gives $v = 5$ for large crops (unit weight > 250 g) and $v = 10$ for medium-sized crops (unit weight 25 – 250 g). The Consultation specifically recommended to replace these default values with more realistic values obtained from studies on actually measured units.

A working group of the International Conference on Pesticide Residues Variability and Acute Dietary Risk Assessment held in York in 1998 suggested to define *v*, for samples taken from controlled trials, as the 97.5th percentile of the unit levels divided by the sample mean (Harris et al. 2000).

How should variability between units be incorporated in probabilistic modelling? In probabilistic modelling we will generate consumption amounts and residue concentrations which will be multiplied and summed over products to estimate the intake. However, the residue concentration c_m will usually be derived from a distribution based on measurements on composite samples. Assume that a batch of product contains N units (N large, for the statistics we assume infinite). The monitoring measurement c_m is made on a composite sample of n_m units (for example, $n_m = 5$). These units are assumed to be representative of the batch.
Unit concentrations c are to be simulated for one or more units from this batch that will be part of a consumption portion in the Monte Carlo simulation.
Basically, there are three possibilities depending on the availability of data:
use actual measurement data on individual units;
use variability factors or other summary statistics based on measured individual units;

use conservative assumptions.

1.
The first approach has been pioneered in the context of a large UK survey on pesticides in fruit (Hamey 2000). The survey involved measurements on composite samples in 289 batches of fruit from retail sale points. In the 12 batches where carbaryl was detected, additional measurements were made on 100 individual fruits. A probabilistic model was made (the 'individual fruit model') where in each iteration residue levels were independently selected from the individual fruit data of one batch for each fruit (whole or part) in the total amount consumed.

2.
When variability factors based on empirical studies are available, these can be used in a probabilistic model by assuming a parametric form for the unit-to-unit variability within a batch. First of all, it should of course be clear which definition has been used in calculating the variability factors: 97.5th percentile divided by mean, 95th percentile divided by mean, maximum value divided by mean (in that case it is also necessary to know the number of individual measurements), or any of these with the median instead of the mean in the denominator. Using the appropriate definition the variability factor and the value of the batch mean can be used to parameterise a two-parameter distribution.
Here we have two possibilities for modelling:

- 2a. Simulate concentrations for a new unit in the batch: in this case there is no upper limit to the residue level that can be present, and we might choose for example the lognormal distribution for modelling;
- 2b. Simulate concentrations for a unit in the actual composite sample on which the measurement was made: in this case the residue level of an individual unit can never be higher than the monitoring measurement multiplied by the number of units in the composite sample. A beta distribution on the interval (0, c_{max}) can be used as a model for this situation. Note, that we now use two bits of information: the number of units in the composite sample (n_{mon}) to define the upper limit c_{max}, and the variability factor v to estimate the variability within the interval (0, c_{max}). This implies that v should be lower than n_{mon} (at least for the definitions of v with the mean in the denominator).

3.
Unfortunately, often neither method 1 or 2 can be applied due to lack of data, and the exposure assessment has to be based on a default variability factor. First we should handle the question how to translate the concept of conservatism to the probabilistic model. In a non-probabilistic model a higher value of v gives a higher *IESTI*, but in a stochastic model a higher variability means more spread around a central value. In general this means that higher values, but also lower values can be generated. In order to retain an overall conservatism it is therefore necessary to replace all simulated values below the monitoring level (c_m) with c_m itself.
Depending on the status of the default v value there are two possibilities:

- 3a/b. The default variability factor may be defined in the same way as a data-based variability factor (e.g. 97.5th percentile/mean). For example, it may be an expert opinion based on seeing many actual data sets from trials, that a certain value v can be used as a conservative value for other situations (see e.g. Table 1 in Harris et al. 2000). Then we might use the same models as in 2 (lognormal (3a) or beta(3c)), but we must censor these

distributions at c_m to guarantee conservative behaviour. Note again that the beta model cannot be used if $v \geq n_{mon}$.

- 3c. If the default variability factor is defined as the number of units in the composite sample ($v = n_{mon}$), then we have no bound on the residue levels of new units in the batch, and the lognormal model cannot be used. The only workable model in this case is the beta model on the interval (0, c_{max}) with maximal variance and with censoring at c_m. This simplifies to just a Bernoulli distribution with probability $(n_m - 1)/n_m$ for the value c_m and probability $1/n_m$ for the value $c_{max} = n_m \cdot c_m$. For example, with $v = 5$, there will be 80 % probability at $c = c_m$ and 20 % probability at $c = c_{\max.}$.

References

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Appendix 4. Incorporating variable recovery of the analytical method used in the duplicate diet study

Pesticide concentrations in duplicate diets are typically lower than in single hazardous ingredients. Therefore the analytical method was optimized to the measurement of very low concentrations down to 1 µg/kg (see Appendix 1). However, at these low levels the performance of the analytical method is less than optimal. Both systematic errors and random errors may be substantial.

A limited amount of quality control data is available to evaluate the analytical errors. Basically the recovery of the pesticides has been measured in 7 series of measurements (see Table 1).

Table 1. Recovery (%) of pesticides in QC samples.

Pesticide	Series 1	Series 2	Series 3	Series 4	Series 5	Series 6	Series 7
Chlorfenvinphos	40	49	61	77	64	128	43
Chlorpyrifos	*	115	31	49	34	108	22
Iprodione	65	64	85	152	62	100	102
Methamidophos	136	136	113	150	33	66	74
Pirimicarb	39	35	7	12	8	73	19
Pirimiphos-methyl	27	28	27	44	31	90	22

From these data we may calculate the geometric mean recovery (*Rec*, exponent of the mean of the ln(recovery) values), and standard deviation of the ln(recovery) values ($s_{ln(f)}$, which is approximately equal to the coefficient of variation in the recovery values). We can also test for the significance of the bias (deviation of ln(*Rec*) from ln(100)), using a *t* test assuming a normal distribution for the logarithms of the recoveries.

Table 2. Significance of bias, and bias correction factors.

Pesticide	mean recovery (%)	*t* test : recovery < 100 % significant?	correction factor	sd for added uncertainty in ln(concentration) and ln(intake)
	Rec		*f*	$s_{ln(f)}$
Chlorfenvinphos	61	$p < 0.01$	1.63	0.43
Chlorpyrifos	49	$p < 0.05$	2.03	0.74
Iprodione	86	*n.s.*	1.17	0.35
Methamidophos	91	*n.s.*	1.10	0.58
Pirimicarb	20	$p < 0.01$	5.00	0.94
Pirimiphos-methyl	34	$p < 0.001$	2.92	0.51

It turns out that for 4 of the 6 pesticides the mean recovery is significantly lower than 100 %. The method may thus be expected to underestimate the real concentrations, and therefore also the real intakes (calculated intakes are directly proportional to the measured concentrations in the duplicate diet). It is necessary to correct the measurement results for recovery. It was decided to do this for all pesticides, including the ones where the recovery was only moderately and not significantly lower than 100 %.

During future development of the analytical method it should be investigated how to apply these correction factors: are recoveries variable between series but constant within series? Then it may be sensible to introduce a calibration factor for each series separately. Or are recoveries varying between samples without clear differences between series? Currently there is no information on this, and moreover there were no recovery factors established for all series comprising the 250 duplicate diet analyses. Therefore it was decided to apply for each pesticide one general correction factor equal to the inverse of mean recovery (seeTable 2). E.g. for the 99th percentile:

$$p99_{corr} = p99 \cdot f$$
$$f = 100 / Rec$$

The correction factor shift the complete distribution of intakes to higher values, and therefore all percentiles should be corrected with the same factor. Further, the *uncertainty* of the percentile estimates increases due to the uncertainty about the correctness of the correction factor. In order to assess how large this effect is, we compare the standard deviations estimated for the normal distribution of log percentiles to the standard deviation due to the use of the correction factor (see Table 3). The total uncertainty is obtained by summing the squares of the standard deviations:

$$s^2_{\ln(p99_{corr})} = s^2_{\ln(p99)} + s^2_{\ln(f)}$$

Table 3. Influence of recovery correction on percentile p99 of the duplicate diet (DD) intake distribution and its uncertainty interval.

Entries in each cell are mean, lower and upper limit of 95 % confidence interval. The intervals in column 2 and 3 are based on the sd's in columns 4 and 6, respectively.

Pesticide	DD p99 uncorrected	DD p99 corrected	sd for uncertainty in ln(p99)	sd for added uncertainty in ln(concentration) and ln(intake)	sd combined
	$p99$	$p99_{corr}$	$s_{ln(p99)}$	$s_{ln(f)}$	$s_{ln(p99,corr)}$
Chlorfenvinphos	0.042 0.029 0.076	0.068 0.026 0.181	0.26	0.43	0.50
Chlorpyrifos	0.047 0.035 0.068	0.097 0.022 0.427	0.17	0.74	0.76
Iprodione	0.041 0.032 0.056	0.048 0.023 0.101	0.16	0.35	0.38
Methamidophos	0.036 0.032 0.040	0.040 0.013 0.127	0.07	0.58	0.58
Pirimicarb	0.048 0.039 0.058	0.243 0.038 1.552	0.10	0.94	0.95
Pirimiphos-methyl	0.039 0.034 0.045	0.113 0.041 0.311	0.09	0.51	0.52

The uncertainty due to the recovery correction overwhelms the sampling uncertainty. Consequently the uncertainty intervals for the corrected percentiles are much wider than the original intervals. Therefore it may be worthwhile to direct future research to an investigation and possible improvement of the recovery and/or better calibration of the analytical method.