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Probabilistic exposure assessment CCPR

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Probabilistic intake calculations performed for the Codex Committee on Pesticide Residues

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SUMMARY

This report is the result of the instalment of a Working Group at the 35th meeting of the Codex Committee on Pesticide Residues (CCPR) in 2003. The Working Group was asked to prepare a paper considering the adoption of the probabilistic methodology for international acute dietary intake estimations of pesticide residues. The Group consisted of representatives from the Netherlands, Australia, Canada, Denmark, France, Germany, Sweden, the US, WHO, Crop Life International and the International Banana Association.

The project was initiated to explore and show the possibilities of probabilistic modelling of dietary exposure to pesticide residues at national and international levels. For this four objectives were formulated, which are discussed in this report. The objectives were 1) the organisation of a training for Work Group members of the CCPR/JMPR (Joint FAO/WHO Meeting on Pesticide Residues) to familiarise them with probabilistic modelling of acute exposure to pesticide residues; 2) assessment of acute dietary exposure to specific pesticide residues; 3) the development of a view on the parameters used in exposure calculations and how to perform such calculations (e.g. consumers only vs. total population, percentile of exposure); and 4) the development of a view on the way in which probabilistic modelling can be incorporated in the assessment of acute exposure to pesticide residues in the regulatory field. In chapter 2 – 7 these objectives are discussed.

Chapter 2 deals with the two training sessions held in November 2003 in which participants were made familiar with probabilistic modelling. From past experience we had learned that this is a very efficient way to improve the understanding of probabilistic modelling. In both sessions the Monte Carlo Risk Assessment (MCRA) software (an internet based programme) was used. The first session was attended by those who already had (some) experience with probabilistic modelling of acute dietary exposure. This meeting therefore focused on the use of different national food consumption databases at an international level to estimate the acute exposure to pesticide residues. The second training was mainly attended by those not yet familiar with the method and was therefore focused on probabilistic modelling of acute dietary exposure. Both training sessions were very well received by all participating and all were well able to use the MCRA-software. During the first session all participants were able to upload their own food consumption databases onto the software and to run the model for the estimation of the acute exposure to pesticide residues using their own food consumption data. During and after both sessions discussions were held on the use of this approach in the regulatory field and how to treat certain variables. The most important conclusions were:

- A tiered approach is preferable for CCPR/JMPR when addressing the acute dietary exposure to pesticides. This tiered approach should involve both the use of the point estimate methodology and the probabilistic approach
- Probabilistic modelling should start with the same variables as addressed in the point estimate approach (consumption, field trial residue levels, processing, variability).
- Harmonisation of terminology was recognised as very important (e.g. 'residue people' use a different terminology than 'food consumption people')
- Food consumption databases should be organised on national websites and connected with the probabilistic software through internet (maintenance of databases at a national level, avoidance of accessibility problems)

- Conversion of food as eaten in the consumption of raw agricultural commodities (crops) is an important item in acute dietary exposure assessment. Most countries, however, have no recipe databases available. Nevertheless, lack of recipe databases at a national level should not hamper the introduction of whole food consumption databases in exposure calculations.
- Use of a total population approach in probabilistic modelling results in exposure levels that are better comparable between compounds. Although the total population approach results in a dilution of risk, the population for which the risk estimates are calculated is always the same per compound. With the consumers only approach, the population will be different for each commodity - compound combination addressed.

In chapter 3 the acute dietary exposure to specific pesticide residues and crop combinations, as requested by the CCPR, was assessed using Dutch food consumption data. For this six work examples were generated in such a way both to facilitate the understanding of the results of probabilistic modelling by risk managers and to address certain issues important in probabilistic exposure assessment. Items addressed were point estimate approach vs. probabilistic modelling for consumers only (work examples 1 and 5) and the total population, including consumers and non-consumers (work examples 2 and 5), differences in total population approach and consumers only approach in probabilistic modelling (work example 3), effect of processing (work example 4), effect of variability (work example 5) and the use of different end points (work examples 1, 2 and 6). These examples showed that

In general, point estimate exposures resulted in higher estimates of exposure than the probabilistic approach, when considering the P99.9 of exposure. Sometimes the P99.9 of exposure exceeded the corresponding point estimate exposure, especially when considering only consumers of one crop.

The probabilistic approach takes a more holistic approach to risk, by addressing all consumption levels, all residue levels and all crops contributing to the exposure to a compound simultaneously into the exposure assessment.

When addressing consumers only in a probabilistic simulation together with all crops that could contain the compound of interest, the overall exposure was either lower than or equal to the exposure per crop. Exposures are incomparable as the population on which they are based differs per crop, which may hamper clear risk management decisions. For calculating percentiles of exposure for people eating more than one crop a day containing the residue of interest, the total population approach should be used.

For crops eaten infrequently additional analyses may be necessary due to probabilistic dilution when using the total population approach.

In the probabilistic approach different processing types of one crop (e.g. apple raw, apple juice, apple peeled) can be addressed simultaneously in one analysis, including (types of) crops that should be treated differently with regard to variability (e.g. apple raw, orange, apple juice).

In chapter 4 the acute exposure to one pesticide (carbaryl) was calculated using consumption data from Denmark, Sweden and the US, aiming to cover some of the variation in food habits around the world. This chapter demonstrated clearly that assessing the intake of acutely toxic compounds in different countries is possible with the probabilistic approach, provided food consumption data at the level of the individual is available as well as a model for the calculation. When comparing the results between countries it is important to consider the differences in the set-up of the food surveys from which the data is derived (e.g. population addressed, dietary method used).

Chapter 5 deals with the incorporation of probabilistic modelling in the evaluation procedure. In general a tiered approach is used for this where relative simple analyses (e.g. point estimate analyses) are followed by more complex analyses (probabilistic modelling). In the US the tiered approach, including probabilistic modelling, is already applied to assess the safety of acutely toxic compounds. In the EU a draft document has been issued which also proposes the use of a tiered approach within Europe in the safety evaluation of pesticides in the EU-market. In both approaches the upper tiers involve the use of the probabilistic approach.

In chapter 6 a conceptual network is introduced as an important requirement for applying the probabilistic approach at an international level in acute dietary exposure assessment. This conceptual framework consists of different national food consumption databases that are linked to probabilistic software via internet. Within the integrated project SAFE FOODS, subsidised by the European Commission through the 6^{th} framework programme, a start with this is made using the MCRA-software. In this integrated project a multi-database approach will be developed in which national food consumption databases from the Netherlands, Sweden, Denmark, Czech Republic and Italy located on local websites (e.g. of food safety authorities or institutes involved in risk assessments) will be linked to the MCRA-software. Together with databases of other countries, e.g. Australia/New Zealand, South Africa and US, a whole range of food habits across the world can be covered when addressing the safety of pesticides at an international level.

Finally in chapter 7 several recommendations are proposed for the use of probabilistic modelling in the safety evaluation of pesticide residues at an international level. Most important are:

- For a worldwide acceptance of probabilistic modelling in the safety evaluation of pesticides, it is important to make also developing countries familiar with this approach. The organisation of a training on probabilistic modelling for these countries is therefore important.
- Incorporate the probabilistic way of examining the exposure to a toxic compound in a risk assessment procedure following a tiered approach.
- Use a total population approach for the calculation of the acute dietary exposure to pesticide residues. This will allow for consistent comparisons between different crop – residue combinations. Also, when more crops may contain the same residue it is conceptually right to address all these crops in one simulation. This is only possible when using the total population approach.
- Due to probabilistic dilution of crops consumed infrequently when using the total population approach, the consumers only approach may add additional valuable information when dealing with such crops. A possible strategy is to perform calculations using the total population concept and to perform additional calculations with only the consumers of a certain crop when consumed infrequently. However, in those cases it should be avoided that rarely consumed crops receive more strict regulation compared to frequently consumed crops. This may be achieved by accepting a lower percentile of regulatory concern.
- In order to be consistent with the US and a draft guidelines document in the EU the P99.9 percentile of exposure may be chosen as a reference point in the probabilistic approach when dealing with field trial residue data. It is important that exposure levels at the selected reference point are discussed in relation to the uncertainties in the database and that they should also be considered in relation to the derivation of the acute reference dose (ARfD). This is especially true when the reference point is close to or exceeds the ARfD (chapter 3).

- Use food consumption databases that are available world-wide. Despite differences in e.g. set-up of the survey and food coding, using incompatible whole national databases is already a large improvement compared to the present situation of using the point estimate methodology (chapter 6).

To apply probabilistic modelling at an international level a conceptual network should be established which links international food consumption databases to probabilistic software via internet. This will be established within the integrated project SAFE FOODS with databases from the Netherlands, Italy, Sweden, Denmark and the Czech Republic. In the near future also databases from outside Europe (e.g. from Australia/New Zealand, US and South Africa) might be made compatible.

For the adoption of the probabilistic methodology for international acute intake estimations the establishment of a working group that studies compatibility issues concerning the use of different national food consumption databases is very important. Also guidance to be given to the JMPR (e.g. in the form of a helpdesk) when applying the probabilistic approach in practice is important for the acceptance of this methodology at an international level.

This report has also been published in a slightly different form, as an annexed report at the 36th CCPR meeting (CCPR 2004)

1 INTRODUCTION

Acute exposure to pesticides via the diet has been typically addressed using point estimates. However drawbacks and restrictions of this approach have been recognised internationally, resulting in an increased interest in the use of the probabilistic approach when addressing the dietary acute exposure to pesticides. One of the international organisations that recognised the potential of the probabilistic approach for acute dietary intake estimations is the Codex Committee on Pesticide Residues (CCPR). At several meetings (starting in 2000 at the 32nd meeting) this approach was discussed, resulting in 2003 in the instalment of a Working Group to prepare a paper considering the adoption of the probabilistic methodology for international acute intake estimations (ALINORM 03/24A, para 31 (CCPR 2003b)). This Working Group consists of representatives from the Netherlands, Australia, Canada, Denmark, France, Germany, Sweden, the US, WHO, Crop Life International and the International Banana Association (annex 1). This report is the result of this.

In this introduction we shortly address the characteristics of the two methods currently available to perform acute intake calculations (point estimate methodology and the probabilistic approach) and how these calculations are performed worldwide in the regulatory field. We conclude this introduction with the aim of the report.

1.1 Approaches to estimate the acute dietary exposure to pesticides

Point estimate approach

At present, the acute dietary exposure to pesticides is calculated using point estimates. In these estimates a single high residue concentration (the highest residue from a set of field trial data) is multiplied with a single high consumption level for each crop addressed (the 97.5th percentile of the consumption distribution) and divided by a single mean consumer body weight value. In this way a single value for the estimation of the dietary exposure is derived. To determine whether the consumer risk is acceptable, the estimated dietary intake is compared to the short-term toxicological endpoint, the acute reference dose (ARfD). The point estimate approach has proved to be useful since the estimates are simple to calculate and relatively easy to understand.

However, it has been recognised that residue levels are not single values but may be derived from a distribution of possible levels. This also applies for food consumption levels: consumption values may range from consumers never eating the food addressed to those that consume large amounts on a daily basis. Consumers also come in a large range of body weights and people can consume more than one food per day containing the same pesticide or several pesticides with the same mode of action (cumulative exposure). In the point estimate you can only address one crop and one pesticide at a time.

Probabilistic modelling

Probabilistic modelling takes the above-mentioned issues into account. In addition, probabilistic modelling results in a distribution of all possible exposure levels that may occur in a population as opposed to just one single exposure level. These intake distributions provide insight in both the likelihood and the magnitude of a certain level of dietary exposure. Comparison of these intake levels with the ARfD gives information on the acceptability of consumer risk. This is a large advantage compared to the point estimate approach.

Another advantage of probabilistic modelling (also commonly referred to as Monte Carlo analysis) of dietary exposure is that it can address the probability of a consumer eating more than one crop on one day that each may contain the pesticide. Apart from that, also the daily exposure to more than one pesticide present in different commodities can be calculated. This contrasts with point estimates of exposure where it is at present not possible to consider additional residue intake by other food items eaten on the same day. Especially for acute effects this is important.

In the probabilistic approach either the total population can be addressed (both consumers and non-consumers of the product(s) of interest) or only the consumers, as in the point estimate approach. Preferably, the focus of dietary risk assessment should be on the level of the total population. When addressing the total population, estimates of exposure are comparable (e.g. between different compounds), the percentage of the population at risk can be estimated and the risk management decisions will be more transparent. We recognise however that when addressing commodities that are consumed by only a small part of the population, the total population approach may not recognize a potential risk. In those cases, the consumers only approach may give valuable additional information. However, when addressing only a small population of consumers the percentile of acceptable exposure should be in accordance with the smaller size of the consumers population to avoid overprotection relative to products consumed more frequently.

The Monte Carlo approach has been validated by comparing the approach with real pesticide residue intake measured by a duplicate diet study (Boon et al. 2003). From this validation study it was concluded that Monte Carlo simulations are indeed a scientifically justified improvement of the methodology to assess pesticide exposure (for more details see § 5.2).

Reasons why probabilistic modelling has not yet been accepted worldwide as a useful tool to address acute exposure to pesticides via the diet (except in the US) include assumed lower outcomes of acceptable exposure levels, lack of understanding at the side of risk managers (hocus-pocus), lack of guidance on how to use this approach, lack of well-defined international food consumption databases, assumed computational restrictions (long calculation times) and lack of probabilistic models to calculate the exposure.

1.2 Acute intake calculations in the CCPR, European Union and US

Exposure to acutely toxic compounds has received increasing attention since the early nineties of the last century, resulting in the introduction of the acute reference dose (ARfD) as the toxicological parameter for assessing an acute exposure. With the establishment of these ARfDs a need arose for procedures to calculate short-term dietary intakes. Two Consultations were relevant in this respect. Firstly, the FAO/WHO Consultation held in York, UK on the ‘Revision of the Guidelines for Predicting Dietary Intake of Pesticide Residues’ in May 1995, which first discussed this issue of acute intake calculations (WHO 1997). Although the main focus was on chronic intake, the consultation agreed that an assessment of acute dietary intake should be routinely considered at the international level. Subsequently detailed procedures for short-term dietary intake estimates were established at a follow-up consultation “Food Consumption and Risk Assessment of Chemicals” held in Geneva in 1997 (FAO/WHO 1997). The procedure described entailed in short a point estimate of exposure (National or International Estimate of Short-Term Exposure (NESTI or IESTI)) based on a large portion size of consumption (LP) consumed on one single day (97.5^{th} percentile of consumption of consumers only), mean body weight of the population addressed and a high residue level. The main focus was the acute intake of a pesticide via the consumption of single commodities (e.g. one apple or one potato; (FAO/WHO 1997)).

CCPR

In the CCPR (www.codexalimentarius.net/) this point estimate approach is presently used to assess the acute dietary exposure to pesticides (see WHO GEMS/Food website[1]). For the LP the largest LP is used of those provided by Australia, France, the Netherlands, Japan, South Africa, UK and the US. These LPs are listed on the WHO GEMS/Food website (data set 3) and concern the edible portion of the crop (e.g. orange without skin).

The highest residue level observed in relevant field trials is used to represent the high residue level. Effects of processing are taken into account when the LP of the processed food is available, as well as relevant processing factors. Also a variability factor is applied, in recognition of the fact that significant variation in residue levels can occur between individual units within one composite sample (Harris 2000, WHO 1997). This may result in an occasional, random occurrence of high residue levels in individual units. Presently high default variability factors are applied based on the unit weight of the crop addressed[2]. However during the meeting of the 2003 Joint FAO/WHO Meeting on Pesticide Residues (JMPR) it was decided, on the basis of a study performed by Hamilton et al. (2004), to reduce these variability factors to 3 for all commodities (FAO/WHO 2004). The calculations for the CCPR are performed by its scientific advisory body, the JMPR. At the moment no international food consumption data at an individual level is available to the JMPR for probabilistic calculations of exposure.

With the further development of computer technology to perform probabilistic calculations of exposure and that of statistical methods to conduct these analyses, together with the recognised restrictions of the point estimate methodology the potential of probabilistic models to address acute exposure to pesticides became apparent. Also within the CCPR, the potentials of the probabilistic approach compared to the point estimate methodology became a point of discussion, starting at the 32nd CCPR in 2000 when it was observed by some delegations that the use of probabilistic studies would become important in the future (ALINORM 01/24, para 25 (CCPR 2000)). At the 33rd CCPR this issue was discussed further (ALINORM 01/24A, para 246 –247 (CCPR 2001)), resulting in an extensive discussion paper on the use of the probabilistic approach for acute dietary exposure analysis and its applicability at the international level (CX/PR 02/3-Add.1; (CCPR 2002b)). It was concluded that the probabilistic approach deserves to be promoted both nationally and internationally. At the 35th CCPR in 2003 a Working Group (annex 1) was established to prepare a paper considering the adoption of probabilistic methodology for the purpose of Codex MRL (= maximum residue limit) setting, which will be discussed at the next session of the Committee in 2004 (ALINORM 03/24A, para 31 (CCPR 2003b)). This report is the result of this.

Another development within CCPR is the attention given to cumulative exposure, starting at the 33rd CCPR (ALINORM 01/24A, para 74 (CCPR 2001)). Cumulative exposure, i.e. exposure to more than one pesticide residue with the same mode of action during one single day, can only be addressed with

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[1] http://www.who.int/foodsafety/chem/acute_data/en/

[2] unit weight of whole portion > 250 g, except head cabbage: $v = 5$; $25 \leq$ unit weight of whole portion ≤ 250 g: $v = 7$; unit weight of whole portion ≤ 250 g from granular soil treatment: $v = 10$; leafy vegetables, unit weight of whole portion ≤ 250 g, except head lettuce: $v = 10$; head lettuce and head cabbage: $v = 3$.

probabilistic exposure techniques. For discussion at the 34th CCPR the American delegation prepared a paper on that matter (CX/PR 02/4, (CCPR 2002a)), indicating that this issue is very important. To proceed with this it was however recognised that first advancement needs to be made with the probabilistic approach (ALINORM 03/24, para 45 (CCPR 2002c)).

EU

As within the CCPR also in Europe acute exposure assessments are presently performed using the point estimate methodology as described above. However, also here the potential of the probabilistic approach has been recognised. On 18 December 1998 the Scientific Committee in Plants (SCP) expressed an opinion regarding the inclusion of aldicarb in annex 1, in which it stated that use of the probabilistic approach for the assessment of the risk to the consumer is acceptable under certain conditions (SCP 1998). These conditions entailed among others the inclusion of the full input data in the report together with all the assumptions made, an analysis of the stability of the tail end of the distribution and a sensitivity analysis of the major assumptions used in the model.

In 2000 the EU Scientific Steering Committee (SSC) stressed the potential of the probabilistic approach in one report on the harmonisation of risk assessment procedures within the EU (SSC 2000), followed by a second report in 2003 (SSC 2003). In these reports the potential of the probabilistic approach was underlined and the introduction of this approach was stressed with a view that it would become standard practice in the assessment of all kinds of risks in the future.

Also in 2003 the European Commission tendered a study (PACT (Probabilistic Assessment Consumer Training) project; B1-3330/SANCO/2002584) in probabilistic modelling of acute intakes. This study was funded in the recognition that the introduction of probabilistic modelling when addressing acute dietary exposure to pesticides is among others hampered by a lack of understanding and a lack of guidance. The following objectives were formulated: (1) to organise a training for EU regulators to familiarise them with probabilistic modelling of acute dietary exposure to pesticide residues, (2) the generation of work examples (3) the development of draft guidelines on the use of probabilistic exposure assessment. This study was concluded in October 2003 resulting in two documents that will be discussed within the EC in the coming months.

It is clear that both within the EU and the CCPR the probabilistic approach is recognized as an important tool to address acute dietary exposure to pesticides, which very likely will be adopted in the near future within both the EU and the CCPR, most likely as part of a tiered approach (see chapter 5). Important huddles for the implementation of this approach at an international level are at the moment the availability of food consumption databases at an international level and lack of experience with the method.

US

Unlike in Europe and the CCPR, in the US the probabilistic approach is already accepted as an essential part of a tiered approach to assess the acute dietary exposure to pesticide residues (see also chapter 5). The US Environmental Protection Agency (US EPA), responsible for overseeing pesticide registration and tolerance setting for pesticides used in crops within the US, applies this approach in Tiers 3 and 4 to allow for more realistic estimations of exposure as compared to deterministic assessments used in Tier 1 and 2 (US EPA 1998, 2000d). Already in 1997 the US EPA issued a document on 'Guiding Principles for Monte Carlo Analysis' based on recommendations from a workshop on probabilistic methods held in May 1996 (US EPA 1997). This was followed in 1998 by a guidance document for submission and review of probabilistic exposure assessments in the Agency's Office of Pesticide Programs, intended chiefly for those conducting probabilistic exposure assessments for purposes of registration or re-registration of pesticides (US EPA 1998). Since then copious documents have been released regarding different issues related to probabilistic modelling, such as further refinement of the estimations by including information on processing and residue decline studies (US EPA 2000d), how to deal with levels below the limit of reporting within probabilistic modelling (US EPA 2000a) and choice of the percentile to be compared with the ARfD (US EPA 2000c). They also released documents on aggregate exposure (the process of combining exposure to a single pesticide from all sources of exposure (food, drinking water and non-occupational sources such as homes and recreational areas; (US EPA 2001)) and cumulative risk assessment (the process of combining exposures from all pesticides with a common mechanism of toxicity; e.g. (US EPA 2002)).

It is evident that in the US the probabilistic approach is accepted as an important part of the whole procedure of assessing the acute dietary exposure to pesticide residues.

1.3 Aim of the project

This project was initiated to explore and show the possibilities of probabilistic modelling of dietary exposure to pesticide residues at the international level. The general goal was to attain acceptability of probabilistic exposure assessment for more complete decision-making within the CCPR. Important aims of the project were to explore the technical possibilities of probabilistic exposure assessment at the international level and to study the most appropriate concept for probabilistic assessment of acute dietary exposure. For this the following objectives were formulated:

1. to organise a training for Work Group members of the CCPR/JMPR to familiarise them with probabilistic modelling of acute dietary exposure to pesticide residues (chapter 2)
2. to assess the dietary exposures associated with some specific pesticide residues, as requested by the CCPR (chapter 3 and 4)
3. to develop a view on which parameters to use in the exposure calculations and how to perform such calculations (e.g. consumers only vs. total population, percentile of regulatory concern; chapters 3 - 7)
4. to develop a view on how to incorporate probabilistic modelling in the assessment of acute exposure to pesticide residues in the regulatory field (chapter 6)

Probabilistic exposure assessments were performed with consensus data as used by the CCPR in the point estimate approach with the only difference that the Dutch consumption database provided the underlying data on consumption.

2 TRAINING

The introduction of probabilistic modelling when addressing the acute dietary exposure to pesticides is partly hampered by a lack of understanding with this approach by those responsible for the authorisation of pesticides on the market. An efficient way to improve this understanding is the organisation of a training in which those responsible for pesticide authorisation are made familiar with probabilistic modelling.

Two training sessions were therefore organised in November 2003 in Wageningen, the Netherlands for the Working Group and FAO-panel members of JMPR and others involved in the field of pesticide authorisation (annex 2). For the agenda of these sessions see annex 3 and 4. In both sessions the Monte Carlo Risk Assessment (MCRA) programme was used to demonstrate probabilistic modelling of acute dietary exposure. This is an internet based programme to assess the acute exposure to pesticide residues through the diet using the principles of probabilistic modelling (Voet et al. 2003a). Below we address the two sessions separately, due to their different goals.

2.1 First session

During the first meeting (November 10 to 12, 2003) five persons attended who all had (some) experience with probabilistic modelling (annex 2). This meeting focused on the use of different food consumption databases at an international level to calculate the acute dietary exposure to pesticide residues. This training session could thus be considered as a starting point of a feasibility study estimating acute intakes using different national databases, aiming to cover some of the variation in food habits. The participants were asked to bring along their own food consumption databases (except for the participant from the Netherlands, because the Dutch food consumption database is already linked to the MCRA-software). These national databases were linked to the MCRA-software to perform exposure calculations (see chapter 4 for the results).

During this meeting the following subjects were addressed (see also annex 3). First presentations were given of the food consumption databases available in the different countries. Important items were organisation of the food consumption database, number of respondents, number of recording days, how the reporting was done, coding issues, technical structure of database and accessibility to others (e.g. WHO; see chapter 4).

During the second day the food consumption databases of the different countries (except the Dutch food consumption database) were linked to the MCRA-software. For this the data was organised in an MS Access structure, which resulted in the generation of input files for the MCRA-software. These input files contained information on consumption levels of relevant foods, field trial residue levels, processing effects when relevant and information on variability. Participants were instructed on the use of the MS Access database to prepare all input files themselves, including the file with own national food consumption data. With this information they calculated the exposure to carbaryl in their own country during the last day of the meeting (chapter 4). Carbaryl was one of the compounds identified at the 35th CCPR to be addressed in this report (annex 5).

During and after the meeting discussions were held on the use of probabilistic modelling in the regulatory field and how to treat certain variables. The most important conclusions were:

- A tiered approach is preferable for CCPR/JMPR when addressing the acute dietary exposure to pesticides. This tiered approach should involve both the use of the point estimate methodology and the probabilistic approach (JMPR already states this in the general items chapter of their 2003 report provided that there is a validated model (FAO/WHO 2004))
- Probabilistic modelling should start with the same variables as addressed in the point estimate (consumption, field trial residue levels, processing, variability).
- Harmonisation of terminology was recognised as very important (e.g. 'residue people' use a different terminology than 'food consumption people')
- Food consumption databases should be organised on national websites and connected with the probabilistic software through internet (maintenance of databases at a national level, avoidance of accessibility problems)
- Conversion of food as eaten in the consumption of raw agricultural commodities is an important item in acute dietary exposure assessment. However, lack of recipe databases at a national level should not hamper the introduction of whole food consumption databases in exposure assessments of pesticide residues.
- The use of a total population approach in probabilistic modelling, due to the difficulty in comparing exposures for different (sub-)populations when addressing only consumers of certain crops (see chapter 3).

The training was received very well by all participating. All were able to upload their own food consumption databases onto the MCRA-software and to run the model for the estimation of the acute dietary exposure to pesticides using this data.

2.2 Second session

The second session (24 to 26 November, 2003) was mainly attended by those not yet familiar with probabilistic modelling of acute dietary exposure to pesticide residues. In total 13 persons attended the meeting from all over the world (annex 2). This meeting focused on probabilistic modelling of acute dietary exposure with the main objective to make the participants familiar with this approach.

This training consisted of a theoretical (in the form of presentations) and practical part (in the form of exercises to be performed by the participants; annex 4). The training started with simple exercises performed in @RISK, a modelling software package for MS excel. With this programme the basic principles of probabilistic modelling were explained and demonstrated. After that we progressed on to the MCRA-software, a programme that can handle more data and is specially designed to address acute dietary exposure to pesticides. During the training all relevant variables important in acute intake calculations were addressed, including modelling of food consumption data, field trial residue levels, processing and variability. Other important items addressed were conversion of food as eaten into the consumption of raw agricultural commodities, concept consumers only versus total population and selection of which percentile of exposure to choose to be compared with the ARfD. On the third day the participants were asked to calculate the exposure to carbaryl, as in the first session, using Dutch food consumption data.

Discussions were held on the use of the probabilistic approach in the regulatory field and what to do with certain variables. The conclusions formulated at the first meeting were all confirmed at this meeting. Also this training was very well received by all participating and all were well able to use the MCRA-software for probabilistic exposure calculations.

At the end of the second training session an evaluation form was distributed among the participants. The main result was that all those returning the evaluation form (80%) rated the training overall as good to excellent. The same opinion was given to the question whether the training had made the participants more familiar with probabilistic modelling. When asked whether the participants were interested in using the MCRA-software for evaluating pesticides, all answered with yes. So there was a great willingness among the participants to practice further with probabilistic modelling of acute exposure and to apply it in their own working situation. The results of this evaluation were in line with the evaluation given by the EU-regulators who participated in a similar training in June 2003 (§ 1.2).

The training was solely attended by persons from developed countries. People from developing countries were not present, due to lack of funding. It is however recognised that for a world-wide acceptance of the probabilistic approach it is very important that also these people are made familiar with this method. It might therefore be recommendable to organise funding for these countries for a next training session, so that also these countries have the opportunity to receive training in probabilistic dietary exposure assessment to pesticide residues.

3 WORK EXAMPLES USING DUTCH FOOD CONSUMPTION DATA

3.1 Introduction

In this chapter we present several work examples on the use of probabilistic modelling in assessing the acute exposure to pesticides via the diet. These work examples were chosen in such a way to facilitate the understanding of the results of probabilistic exposure assessment by risk managers and to address certain issues important in probabilistic exposure assessment (e.g. consumers only concept, selection of percentile of exposure to be compared with the ARfD). The examples presented focus on five compounds and several crops as identified at the 35th CCPR relevant for further study. For a complete list of relevant compound – crop combinations see annex 5.

3.2 Methods

Calculations were only performed with variables as used in the point estimate approach and on which consensus was reached by CCPR. For example, percentage crop treated and the use of monitoring data were not included in this exercise, although this is optional in the Monte Carlo Risk Assessment (MCRA) programme.

Food consumption data
Food consumption data derived from the Dutch National Food Consumption Survey (DNFCS) of 1997/1998 was used in the exposure calculations ,(Anonymous 1998, Kistemaker et al. 1998). In this survey 6,250 respondents aged 1-97 years (of which 530 young children, aged 1-6 years) recorded their food consumption over two consecutive days. The amount eaten was weighed accurately. The unit of intake for the calculations was 24 h in order to obtain random daily consumption patterns. In this way 12,500 eating 'days' were available for the Dutch population (1 – 97 years) and 1,060 days for young children (1 – 6 years).

With the use of the conversion model Primary Agricultural Products (CPAP), developed at the RIKILT – Institute of Food Safety, the consumption of foods, as recorded in the DNFCS, was translated into the consumption of crops (Dooren et al. 1995)). In this way the field trial residue concentrations analysed in crops could be linked directly to consumption.

Field trial residue data
Field trial residue data was derived from different JMPR reports. For levels used and source see annex 6. The residue levels were those used by the JMPR to estimate an MRL (maximum residue limit), HR (highest residue level in edible portion of a commodity found in the field trials) and STMR (supervised trials median residue).

Calculations of point estimates
Point estimates of exposure were calculated using the equations as defined in the FAO Manual on the Submission and Evaluation of Pesticide Residue Data and used by the JMPR (FAO 2002). For the calculations we applied the unit weights as used by the JMPR when calculating point estimates of exposure. Default variability factors (v) were applied (see footnote 2 on page 9). The newly proposed general default variability factor of 3 was only used in work example 5 (FAO/WHO 2004). In this

approach we used Dutch large portion sizes and body weights for the general population (1 – 97 years) and for young children (1 – 6 years). Point estimates as calculated by the JMPR are presented as well for comparison.

Probabilistic modelling

The MCRA programme was used for probabilistic modelling (Boer et al. 2003, Voet et al. 2003). This is an internet based programme[3] developed by RIKILT – Institute of Food Safety and Biometris (Wageningen UR) to assess the acute (and chronic) exposure to pesticides through the diet using the probabilistic approach. For a detailed overview of the (statistical aspects of the) model and its practical use we refer to the user manual[4] and the reference guide[5], both to be found on the web site. As training is required to perform calculations correctly, only trainees receive a password for access. Future access and use of the programme depend on possibilities to maintain and update the software and to support the user at the international level (helpdesk function).

The MCRA programme operates as follows. First it randomly selects a consumer out of the consumption database. The consumption of every single crop (that could contain the pesticide of interest) for this person on one day is multiplied by a randomly selected residue concentration as present in the residue database for that particular crop. After each crop consumed by the selected person is multiplied with a selected residue concentration, the total residue intake of this consumer is added and stored in the output programme. By repeating this procedure many times a probability distribution for pesticide intake is produced which contains the whole range of possible consumption and residue level combinations. The estimates of possible intakes are adjusted for the individual's self-reported body weight.

Percentiles of exposure to a certain pesticide residue were calculated per crop and for all crops that could contain the pesticide of interest simultaneously. For an accurate assessment of the daily intake of a certain pesticide, the list of crops should contain all possible crops that could contain the pesticide of interest. In the work examples, only a selection of the total list was used.

Variability was accounted for in the probabilistic approach by defining variability as a model parameter. This model parameter describes the variation within one field trial residue level as following a Beta distribution. Other optional assumptions in the model on the shape of the distribution of residue data within a composite sample are the Bernoulli and the lognormal distribution. See reference guide[5] for the theoretical background. Details can also be found in annex 7 of this report. Currently there are no guidelines on how to incorporate variability into the probabilistic approach.

Calculations were performed for both the general population (1 – 97 years) and for young children (1 – 6 years). To estimate the different percentiles of the dietary exposure distribution, probabilistic analyses were performed with 100,000 iterations. When addressing one crop in the group of consumers only in young children we performed the analyses with 10,000 iterations, because of the small number of children (< 150) consuming the crop of interest. We assume that 10,000 iterations using less than 150 consumption days combined with 10 – 30 field trial residue levels and the use of variability was sufficient to cover the whole range of possible exposure levels.

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[3] http://www2.rikilt.dlo.nl/mcra/mcra.html
[4] http://www2.rikilt.dlo.nl/mcra/Usermanual.pdf
[5] http://www2.rikilt.dlo.nl/mcra/Referencemanual.pdf

3.3 Work example 1: point estimates vs. probabilistic modelling, consumers only

In this first work example we compare the point estimate approach with the probabilistic approach for only the consumers of certain crops, because the point estimate methodology deals also only with consumers of certain crops. For reasons of comparison, calculations for the total population (including consumers and non-consumers) are also presented. All pesticides addressed in this work example occur in more than one crop. We therefore also calculated the percentiles of exposure for those respondents that consumed at least one of the crops of interest on a certain day.

For a clear comparison between the two approaches we used the same input data. For this we incorporated in the probabilistic calculations only those consumption levels that also contributed to the derivation of the large portion sizes (LPs). Aldicarb and carbaryl were used in this example. To compare the point estimate outcome with the probabilistic approach, we chose the 99.9^{th} percentile (P99.9) of the exposure distribution, the percentile of regulatory concern as used by the US Environmental Protection Agency (US EPA 2000c). For reasons of comparison we also reported the P99.99 of exposure.

Point estimates calculated by the JMPR were in general higher than the point estimates calculated using Dutch large portion sizes (table 1). The JMPR uses the highest large portion size of those provided by Australia, France, the Netherlands, Japan, South Africa, the United Kingdom and the US. This large portion consumption is rarely the one provided by the Netherlands (data set 1 on the WHO GEMS/Food website). For two crops the Dutch point estimate exposure exceeded the point estimate of the JMPR: nectarine and plums in children. This is either due to our use of more recent Dutch food consumption data than that submitted to the WHO or a change in approach to derive large portion sizes. To our knowledge, there are no guidelines regarding the inclusion of food items (e.g. apples, apple juice, etc.) relevant for the derivation of the P97.5 of consumption for the crop (e.g. apples).

Compared to the Dutch point estimate, P99.9 exposure levels for consumers only per crop were either lower, comparable or higher (e.g. banana, peach and plum in the general population; table 1). Exposure levels calculated with the probabilistic approach for consumers only were always higher than the corresponding levels for the total population (including both consumers and non-consumers).

Comparing the ARfD of aldicarb and carbaryl with the P99.9 level of exposure for consumers only, aldicarb would have been acceptable for use on banana. Carbaryl would have posed a risk when used on grape (general population and children) and peach, nectarine and plum (children). Also when all crops were considered simultaneously, the P99.9 for carbaryl and consumers only exceeded the ARfD in both the general population and children (table 1). Conclusions about the use of aldicarb and carbaryl would have been the same with the point estimate approach. Considering the P99.99 in consumers only conclusions about the safety of use of both compounds would have been somewhat different. However, the P99.99 levels of exposure can be more sensitive to uncertainties in data collection (sample size, reporting mistakes (e.g. over reporting), analytical uncertainties) making these estimations of exposure less reliable.

Children generally had higher exposure levels per kg body weight than the general population (table 1), due to higher consumption levels per kg body weight.

A discussion on the differences between the consumers only approach and the total population approach in probabilistic modelling can be found in work example 3 (§ 3.5).

Table 1. Comparison of the point estimate and the probabilistic approach (in % of ARfD[1]), where probabilistic calculations were performed for the total population (consumers and non-consumers) and consumers only (work example 1).

	point estimate		probabilistic approach			
	JMPR[2]	NLD[3]	consumers only		total population	
compound, population and crop			P99.9	P99.99	P99.9	P99.99
aldicarb (ARfD = 0.003 mg·kg^{-1}·d^{-1})						
general population (1 – 97 years)						
banana	39	24	49	89	20	48
children (1- 6 years)						
banana	108	88	85	153	52	95
carbaryl (ARfD = 0.2 mg·kg^{-1}·d^{-1})						
general population (1 – 97 years)						
apricot	37	27	23	31	0.01	4.6
cherries	48	33	34	34	6.1	19
grape	422	278	191	367	33	143
nectarine	81	66	39	66	4.1	22
peach	84	44	53	91	4.7	33
plum	47	38	47	78	7.2	37
crops together			133	303	42	143
children (1- 6 years)						
apricot	127	32	32	46	0	4.6
cherries	134	38	34	34	5.9	20
grape	1137	875	771	1446	84	376
nectarine	62	144	192	245	2.6	40
peach	170	152	247	437	12.5	93
plum	138	140	153	273	27	87
crops together			588	1224	94	376

[1] ARfD = acute reference dose
[2] JMPR = Joint FAO/WHO Meeting on Pesticide Residues
[3] NLD = the Netherlands

Conclusion

Work example 1 showed that the P99.9 exposure levels for consumers only were either lower, comparable or higher than the point estimate exposure levels. Considering only consumers in the probabilistic approach resulted in higher exposure levels compared to the total population approach. Children had higher exposure levels compared to the general population.

Table 2A. Comparison of the point estimate and the probabilistic approach (in % of ARfD[1]) for aldicarb and carbaryl for the total population (consumers and non-consumers; work example 2).

compound, population and crop	point estimate		probabilistic approach		% consumers[2]
	JMPR[3]	NLD[4]	P99.9	P99.99	
aldicarb (ARfD = 0.003 mg·kg^{-1}·d^{-1})					
general population (1 – 97 years)					
banana	39	24	20	63	12 (1489)
children (1- 6 years)					
banana	108	88	52	95	20 (215)
carbaryl (ARfD = 0.2 mg·kg^{-1}·d^{-1})					
general population (1 – 97 years)					
apricot	37	27	0.01	4.6	0.1 (15)
cherries	48	33	6.1	19	0.4 (49)
grape	422	278	33	143	2.2 (273)
nectarine	81	66	4.1	22	0.5 (62)
peach	84	44	4.7	33	0.7 (92)
plum	47	38	7.2	37	1.0 (128)
crops together			42	143	
children (1- 6 years)					
apricot	127	32	0	4.6	0.1 (1)
cherries	134	38	5.9	20	0.3 (3)
grape	1137	875	84	376	1.7 (18)
nectarine	62	144	2.6	40	0.3 (3)
peach	170	152	12.5	93	0.4 (4)
plum	138	140	27	87	1.4 (15)
crops together			94	372	

[1] ARfD = acute reference dose
[2] Number in brackets indicates number of consumers.
[3] JMPR = Joint FAO/WHO Meeting on Pesticide Residues.
[4] NLD = the Netherlands

3.4 Work example 2: point estimates vs. probabilistic modelling, total population

In work example 2 we compare the point estimate approach with the probabilistic approach for the total population (consumers and non-consumers) using again the same input data to enable a clear comparison between the results. The same data as in work example 1 is presented.

In all cases, the point estimate exposures (either JMPR or NLD) were higher than the corresponding P99.9 of exposures (table 2A). An explanation for this is that the point estimate approach is based on consumers only and uses only one high food consumption level (LP) as opposed to all possible consumption levels in the probabilistic approach (including zero consumption levels when addressing the total population). Apart from one high consumption level, the point estimate also addresses only one high (the highest) residue level and a high default variability factor. Another factor that may explain the higher exposure levels calculated with the point estimate approach is that in the point estimate a mean body weight is used which may not correspond with the person consuming the LP. This will result in the estimation of high exposure levels, because the LP may belong to a consumer with a body weight higher than the mean body weight of the population addressed. In the probabilistic approach every consumption level is matched to its corresponding body weight, as reported by the respondents.

Table 2B. Sampled field trial residue levels (mg·kg^{-1}) and consumption levels (g) belonging to the ten highest exposure levels simulated in the general population (1 – 97 years) for carbaryl (work example 2).

	top 10									
	1	2	3	4	5	6	7	8	9	10
respondent	A	B	C	D	E	F	G	H	I	J
body weight (kg)	20	26	56	14	78	63	74	56	14	78
age (years)	6	5	35	2	39	64	49	40	2	39
total exp.[1] (mg·kg bw^{-1}·d^{-1})	2.22	1.29	0.41	0.38	0.34	0.32	0.32	0.30	0.30	0.29
consumption (g)										
apricot	-	-	-	-	-	-	-	-	-	-
cherries	-	-	-	-	-	-	-	-	-	-
grape	125	184	375	-	400	87.5	138	125	118	900
nectarine	-	-	-	90	-	-	-	-	-	-
peach	-	-	-	-	-	-	-	-	-	-
plum	-	-	-	40	-	-	-	-	-	-
residue level (mg·kg^{-1})										
apricot	-	-	-	-	-	-	-	-	-	-
cherries	-	-	-	-	-	-	-	-	-	-
grape	355	183	60.8	-	66.9	232	171	136	36	25
nectarine	-	-	-	56.4	-	-	-	-	-	-
peach	-	-	-	-	-	-	-	-	-	-
plum	-	-	-	5.2	-	-	-	-	-	-

[1] exp. = exposure

Comparing the ARfD of aldicarb with the P99.9 of exposure, use of aldicarb on banana would have been considered safe for both the general population and children (as in work example 1). Carbaryl would not have been considered safe for use on grape according to the point estimate approach for both age groups. With the probabilistic approach on the other hand, taking into account all crops simultaneously or separately, carbaryl would have been considered safe for use on all six crops when using the P99.9 of exposure for regulatory decisions. Using the P99.99 of exposure the conclusions would have resembled those of the point estimate for carbaryl on grape for both age groups. Point estimate exposure levels above the ARfD for carbaryl in nectarine, plum and peach for children were not confirmed by the probabilistic approach (table 2A).

Exposure levels to carbaryl calculated with the probabilistic approach per crop were either comparable or higher than those calculated for all crops simultaneously. It is clear that grape was the risk driver for carbaryl exposure. This observation is confirmed in table 2B, which lists the ten highest exposure levels to carbaryl with their corresponding consumption and residue levels for the general population. It is clear that in the exposure distribution intakes via combinations of crops may occur.

Again, children generally had higher exposure levels per kg body weight than the general population (table 2A), due to higher consumption levels per kg body weight. This is also evident from table 2B where children were clearly overrepresented when examining the ten highest exposure levels simulated in the general population.

Conclusion

Work example 2 demonstrated that the point estimate approach resulted in higher estimations of exposure compared to the probabilistic approach for the total population (including consumers and non-consumers) when using either the P99.9 or P99.99 as reference point. This was true for both the general population and children. The point estimate approach is based on consumers only and thus addresses only a subset of the population compared to the total population approach. We showed that with the probabilistic approach all residue levels and all possible consumption levels can be addressed in one simulation. Children have higher exposure levels compared to the general population.

3.5 Work example 3: Consumers only approach vs. total population approach

In work example 3 we discuss the differences in exposure outcomes between the consumers only approach and the total population approach in probabilistic modelling. For this, the results of work example 1 and 2 are used (tables 1 and 2A).

It was evident from the examples that the exposure calculations for the total population were generally lower than those for consumers only (table 1 and 2A). This can be explained by a difference in the underlying food consumption data used. In the total population approach both consumers and non-consumers of (a) certain crop(s) are included in the analyses, while in the consumers only approach only consumers of (a) certain crop(s) are addressed. Inclusion of non-consumers of the crop(s) of interest in the analyses will result in lower exposure levels.

In the total population approach the underlying food consumption data used in the analyses is always the same, so that exposures derived from different crop – residue combinations can be compared. In the consumers only concept the food consumption data used differs for each crop - pesticide combination. This will hamper the comparison of exposure results between different crop – residue combinations, but also between crops together and individual crops when addressing the same residue present in more than one crop. As demonstrated in work example 1, in the consumers only approach exposure to carbaryl for all crops together resulted in a lower overall exposure level than when just one crop was addressed, which is conceptually not logical. The reason for this is that the underlying food consumption database used when addressing more than one crop contains persons who are consumers of a certain crop (e.g. grape) but non-consumers of other crops containing the residue (e.g. plum, nectarine). This results in an exposure level that is neither total population based nor consumer based. By including more crops that may contain the residue of interest in the analyses, the percentiles of exposure for all crops together will decrease and will eventually reach the same value as the crops together estimate in the total population approach. Therefore, when assessing P99.9 exposure levels for a residue via the consumption of more than one crop, the consumers only approach is not suitable and the total population approach should be used.

For pesticides occurring in more than one crop, it is, from a conceptual point of view, plausible to address these crops simultaneously in one analysis. This, as discussed above, pleads for a total population approach. However, it should also be kept in mind that by including non-consumers in the exposure calculations the exposure via crops rarely eaten can be obscured (probabilistic dilution). For example, in the total population approach the P99.9 of exposure of carbaryl via the consumption of peach in young children (consumed by only 0.4% (n=4) of the population (table 2A)) was 12.5% of the ARfD, while in the consumers only approach this percentile equalled 247% of the ARfD (table 1). To protect the consumers of apricot a supplementary analysis may therefore be needed. However calculating high percentiles of exposure (e.g. P99.9) using only a small number of consumers is, from a statistical point of view, unreliable. Depending on the number of consumers, the choice for a lower percentile of regulatory concern than used in the total population approach may therefore be preferable. Thus, apart from a discussion on the percentile used in the total population approach, also a discussion is needed on the percentile used as a cut-off level when addressing only consumers of single crops consumed infrequently. Furthermore, it should be avoided that rarely consumed crops receive more strict regulation than frequently consumed crops. Whatever the cut-off level or approach chosen however, all risk for a rarely eaten crop cannot be excluded due to insufficient data. This also applies to the point estimate approach where the estimation of the LPs may be based on a very small number of consumption levels. When high levels of exposure in the consumers only concept for rarely eaten crops are addressed, note that such an approach has already been followed in the point estimate (first tier of a tiered approach).

Conclusion
We showed that with probabilistic modelling exposures can be assessed via the consumption of more than one crop as opposed to only one crop at a time in the point estimate. We demonstrated that the consumers only concept, when addressing more than one crop, resulted in an overall exposure level that was not based on either the total population or the consumers only population. This may hamper a clear risk management decision.

For the total population approach the calculated P99.9 exposure levels were comparable between individual crops and between individual crops and all crops together, because the underlying population on which the calculations were based did not change. Due to probabilistic dilution an alternative approach may be necessary to protect also consumers of infrequently consumed crops. Depending on the number of consumers, the choice of a lower percentile of regulatory concern when addressing rarely consumed crops than the percentile chosen in the total population approach may be more valid.

3.6 Work example 4: effect of processing

Processing is an important variable to be considered when assessing the exposure to a toxic compound via the diet. Most pesticide analyses are performed in crops, including peel and (other) non-edible parts. These crops are however rarely eaten as such, but undergo some form of processing before consumption. In work example 4 we demonstrate the effect of processing on the dietary exposure in both the point estimate and the probabilistic approach for apple in two sub-examples. We used the field trial residue levels of methomyl for apple (annex 8).

In the first example (work example 4A) apple can be consumed as whole apple, apple juice or together. To estimate the point estimate for apple juice we calculated the LP for this food in the general Dutch population and young children (annex 8). When addressing the exposure via the consumption of apple juice (case 3 of the point estimate approach (FAO 2002)) no variability factor was applied in both approaches. Variability was only applied to consumption levels of whole apple when both apple and apple juice were included simultaneously in the probabilistic model. We assumed no effect of juicing on the pesticide level in apple.

For field trial residue levels and other parameters used in this work example see annex 8, as well as for a summary of the consumption levels of apple and apple juice used in the probabilistic approach. For a valid comparison between the point estimate and the probabilistic approach, we incorporated in the probabilistic approach only those apple and apple juice consumption levels that also contributed to the derivation of the LPs. When addressing the exposure to methomyl via the consumption of apple juice we applied in the probabilistic approach only the supervised trials median residue level (STMR) as used in the point estimate approach.

Table 3A. The effect of processing on the acute dietary exposure assessment to methomyl (in % of ARfD[1]) via the consumption of apple and apple juice. For the probabilistic approach the P99.9 was reported (work example 4A)[2].

population and crop	point estimate NLD[3]	probabilistic approach: total population	probabilistic approach: consumers only
general population (1 -97 years)			
apple	130	129	212
apple - juicing	28	76	133
apple + apple - juicing	-	141	222
children (1- 6 years)			
apple	480	319	453
apple - juicing	96	131	133
apple + apple - juicing	-	323	421

[1] ARfD = acute reference dose (= 0.02 $mg \cdot kg^{-1} \cdot d^{-1}$)
[2] For more details, see text and annex 8.
[3] NLD = the Netherlands

Exposure levels calculated with the point estimate for apple were higher or equal to those calculated with the probabilistic approach (using the P99.9 of exposure), except for consumers only of the general population (table 3A). For apple juice the point estimate resulted in lower exposure levels compared to the probabilistic approach. The exposure via the consumption of both apple and apple juice was, for the general population, higher than the two point estimates for each food separately as well as the separate exposure levels calculated with the probabilistic approach. This demonstrates clearly that the exposure via a combination of one food subjected to different forms of processing can be higher than calculated per food – processing type combination. In this particular example the conclusion about the safety of methomyl for use on apple would not have been influenced by this, because the ARfD was already

Table 3B. The influence of processing on the acute dietary exposure to methomyl (in % of ARfD[1]) via apple consumption. For the probabilistic approach the P99.9 was reported (work example 4B).

population and processing type	point estimate NLD[2]	probabilistic approach: total population	probabilistic approach: consumers only
general population (1 -97 years)			
no peeling	130	129	212
all peeling	13	12.9	21
58% peeling /42% not	-	99	167
children (1-6 years)			
no peeling	480	319	453
all peeling	48	32	45
58% peeling /42% not	-	227	340

[1] ARfD = acute reference dose (= 0.02 $mg \cdot kg^{-1} \cdot d^{-1}$)
[2] NLD = the Netherlands

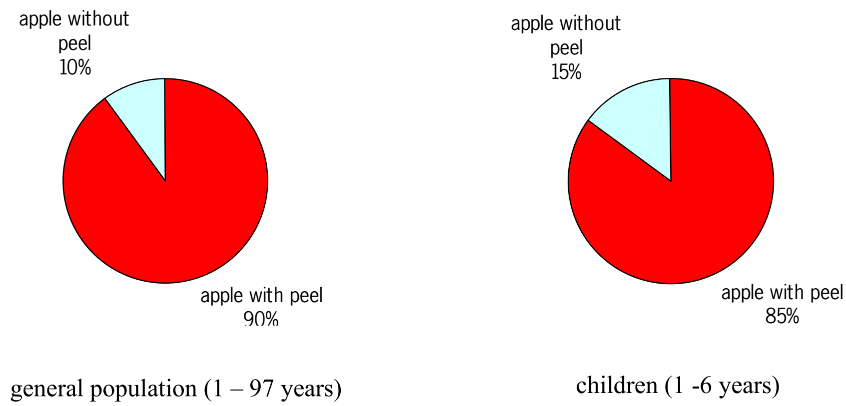

Figure 1. Contribution (%) of apple without and with peel to the total dietary exposure, addressing the total population (both consumers and non-consumers; work example 4B).

exceeded when dealing only with apple raw. However, it is not unlikely that there are situations where exposure to separate foods may not pose a problem, but when addressing them simultaneously in one analysis a problem may emerge. This applies both for considering different foods in one analysis as for one food subjected to different types of processing practices.

Comparing the exposure calculations with the ARfD of methomyl both approaches demonstrated that this compound would not have been considered safe for use on apple.

In another work example (4B) examining the effect of processing, apple could be consumed either without or with peel and peeling reduced the residue level by 90% (processing factor peeling = 0.1). Also here, for a valid comparison between the point estimate and the probabilistic approach, we incorporated in the probabilistic approach only those apple consumption levels that also contributed to the derivation of the LP. In the point estimate only one processing type at a time can be addressed, resulting often in the choice of the worst-case approach (no effect of processing). For example in the case of apples, there are people who consume apples either with or without peel. In the point estimate the worst-case assumption will be that nobody consumed peeled apples as opposed to the optimistic situation where everybody consumes peeled apples (table 3B). In food consumption surveys there may be information on the percentage of people consuming their apple with (in the Dutch survey 42%) or without peel (in the Dutch survey 58%). When no information on processing practices is available from the food consumption survey, general assumptions on processing habits may be derived from other sources (e.g. literature). When information on processing practices is incorporated in the analyses using the probabilistic approach a more realistic estimation of exposure is possible compared to the worst-case assumption that nobody peels their apple or the too optimistic situation that everybody peels their apple (table 4B). For example, in the general population the exposure decreased with about 20% compared to the worst-case assumption. When considering the general population, addressing both consumers and non-consumers, the decision here would have been that methomyl may be safe for use on apple based on the probabilistic approach, while in the point estimate approach, following the worst-case assumption that no one consumes peeled apples, would have resulted in a negative advise for use.

In figure 1 we plotted the contribution (%) of apple with and without peel to the exposure in the general population and in young children. As expected apple with peel contributed most to the exposure (≥ 85%) in both groups, due to the large effect of peeling on the residue level.

Conclusion

Work example 4 demonstrated that with the probabilistic approach different types of processing per crop (peeling, not peeling, juicing) can be addressed in one analysis. When doing this each crop – processing type combination should be linked to the correct variability factor (e.g. apples eaten raw are subjected to variability, while those mixed in juices are not). In the point estimate only one crop - processing type combination can be addressed at a time, which can result in worst-case estimations of exposure as shown above and may thus lead to very conservative risk management decisions.

3.7 Work example 5: effect of variability

To account for variability in residue levels between individual units within a composite sample variability factors were introduced in the point estimate (FAO/WHO 1997). During the 2003 JMPR meeting (FAO/WHO 2004) it was decided to reduce the variability factor to 3 for all crops as recommended by Hamilton et al. (2004). The effect of this reduction on the exposure assessment was studied in this fifth work example. More details on how the model addresses variability can be found in the reference guide (see footnote 5, page 16).

The point estimate exposures to aldicarb and carbaryl for the general population (1 - 97 years) were recalculated applying a variability factor of 3 (‘new’ variability factor). Table 4A demonstrates that a lower variability factor resulted in lower point estimate exposure levels for both the JMPR calculations and those calculated with Dutch data. Only for grape the calculations of the JMPR resulted in an increase of exposure. This was due to the use of a larger edible portion weight for grape compared to the calculations with the ‘old’ variability factor. In the 2002 JMPR report (FAO/WHO 2002) using ‘old’ variability factors, an edible portion weight of 118 g (France) was used, while in 2003 this was changed to 438 g (Sweden; FAO/WHO 2004). Using the same edible portion weight the exposure would have equalled 0.6 $mg \cdot kg^{-1} \cdot d^{-1}$ (306% of the ARfD) with the ‘new’ variability factor, a clear decrease in exposure compared to the ‘old’ variability factor. Replacing the variability factor with a more realistic value resulted in an exposure level below the ARfD of aldicarb on banana for the JMPR calculations. Carbaryl would still pose a problem when used on grape despite a lower variability factor based on both the JMPR and Dutch point estimate.

Dietary exposure to aldicarb and carbaryl for the general population, including both consumers and non-consumers, was also recalculated using the ‘new’ variability factors with the probabilistic approach (table 4B). This resulted also in lower exposure levels, although less distinct compared to the point estimate approach (table 4A). The conclusions about the safe use of aldicarb and carbaryl on the crops addressed was not influenced by the use of a more realistic variability factor. Both with the ‘old’ and ‘new’ variability factor the probabilistic approach resulted in the conclusion that both compounds would have been permitted for use on all crops, when using the P99.9 of exposure as reference point and addressing the general population.

Table 4A Comparison of the point estimate exposure to aldicarb and carbaryl (in % of ARfD[1]) using 'old' and 'new' variability factors for the general population (work example 5).

	'old' varfac[2]		'new' varfac[3]	
compound and crop	JMPR[4]	NLD[5]	JMPR	NLD
aldicarb (ARfD = 0.003 $mg \cdot kg^{-1} \cdot d^{-1}$)				
banana	143	67	40	23
carbaryl (ARfD = 0.2 $mg \cdot kg^{-1} \cdot d^{-1}$)				
apricot	37	27	27	18.5
cherries	48	33	48	33
grape	422	278	460[6]	160
nectarine	81	66	51	36
peach	84	44	60	24
plum	47	38	32	24

[1] ARfD = acute reference dose
[2] 'old' varfac are the default variability factors. See footnote 2, page 9.
[3] 'new' varfac is the variability factor of 3 as proposed by the 2003 JMPR meeting (FAO/WHO 2004)
[4] JMPR = Joint FAO/WHO Meeting on Pesticide Residues
[5] NLD = the Netherlands
[6] using the same edible portion weight as in the calculation with the 'old' variability factor the exposure level equals 0.6 $mg \cdot kg^{-1} \cdot d^{-1}$ (306% of ARfD).

Conclusion

In work example 5 we demonstrated that variability can be included in the probabilistic approach and that the level of variability applied influences the outcome.

Table 4B Comparison of the acute exposure to aldicarb and carbaryl with the probabilistic approach (in % of ARfD[1]) using 'old' and 'new' variability factors for the general population, including both consumers and non consumers (work example 5).

	'old' varfac[2]		'new' varfac[3]	
compound and crop	P99.9	P99.99	P99.9	P99.99
aldicarb (ARfD = 0.003 $mg \cdot kg^{-1} \cdot d^{-1}$)				
banana	23	63	16.7	47
carbaryl (ARfD = 0.2 $mg \cdot kg^{-1} \cdot d^{-1}$)				
apricot	0.01	4.6	0.03	3.7
cherries	6.1	19	6.0	18.5
grape	33	143	29	98
nectarine	4.1	22	4.9	17
peach	4.7	33	5.2	13.5
plum	7.2	37	6.8	23
crops together	42	142	31	98

[1] ARfD = acute reference dose
[2] 'old' varfac are the default variability factors. See footnote 2, page 9.
[3] 'new' varfac is the variability factor of 3 as proposed by the 2003 JMPR meeting (personal communication)

3.8 Work example 6: point estimate vs. probabilistic modelling for disulfoton, fenamiphos and methomyl

In this work example the exposure to the remaining three compounds (disulfoton, fenamiphos and methomyl) for crops listed in annex 5 were calculated. Calculations were performed for the general population (1 - 97 years) and for children (1 - 6 years), considering both the total population and consumers only of the different crops. For reasons of comparison the point estimates as calculated by the JMPR were included.

In table 5A we listed the exposures estimates for the general population and in table 5B those for the children. The results of this work example were in line with those reported in work example 1 and 2 (§ 3.3 and 3.4). Again some Dutch point estimate exposures were higher than those of the JMPR, probably due to the use of more recent Dutch food consumption data than available to the JMPR.

As for carbaryl and aldicarb, also for disulfoton, fenamiphos and methomyl all point estimate exposures were higher than the corresponding P99.9 of exposures (table 5A and 5B) for the total population. For an explanation see work example 2 (§ 3.4). The P99.99 of exposure for the total population exceeded the point estimate calculations in some of the cases in both the general population and in children.

For fenamiphos the P99.99 of exposure for the general population (including both consumers and non-consumers) and for all crops together was a little lower than the highest exposure level calculated for one crop (153% of the ARfD vs. 159% of the ARfD for tomato, respectively; table 5A). Probabilistic modelling deals with probabilities of linking a certain consumption level to a certain residue level and therefore it is possible that with the total population approach the exposure to a certain compound via all crops may be somewhat lower than via one crop. However, the difference will always be very small and statistically not significant. Also the uncertainty in the P99.99 of exposure as mentioned in work example 1 may play a role: the P99.9 exposure via all crops was always equal or higher than the exposure levels calculated per crop when addressing the total population.

When addressing only the consumers of a certain crop both the P99.9 and P99.99 of exposures increased compared to the situation where the total population was addressed (table 5A and 5B), as was discussed in work example 3. The levels of exposure calculated for these subpopulations frequently exceeded the corresponding point estimate exposure levels.

Conclusion

The results demonstrated in this work example were in line with the conclusions formulated in §3.3, § 3.4 and §3.5. Disulfoton, fenamiphos and methomyl were not considered safe for use on the crops addressed when all crops were addressed simultaneously in one analysis. Calculations were however performed using a default setting (‘old’ default variability factors, no processing). Using the newly proposed general variability factor of 3 and including information on processing effects in the calculations will result in more realistic estimations of exposure, which will be lower than those listed in tables 5A and 5B.

Table 5A. Comparison of the point estimate and the probabilistic approach (in % of ARfD[1]) for three compounds for the general population (1 – 97 years; work example 6).

compound and crop	point estimate		probabilistic approach				% consumers[2]
			total population		consumers only		
	JMPR[3]	NLD[4]	P99.9	P99.99	P99.9	P99.99	
disulfoton (ARfD = 0.003 mg·kg^{-1}·d^{-1})							
broccoli	107	90	14	53	73	98	2 (281)
cabbage , head	267	307	32	139	84	214	6 (789)
cauliflower	37	33	16	43	31	70	5 (646)
lettuce, head	700	417	77	250	196	453	6 (795)
lettuce, leaf	933	493	0	23	2	199	0.1 (14)
crops together			101	262	211	473	
fenamiphos (ARfD = 0.003 mg·kg^{-1}·d^{-1})							
carrot	35[5]	34	23	53	67	93	8 (1017)
peppers, sweet	219	143	30	113	94	200	7 (820)
tomato	210	147	61	159	146	257	14 (1789)
(water)melon	99	20	0	6	18	32	2 (209)
grape	77	51	9	35	69	101	2 (273)
pineapple	120	71	0	3	20	65	0.3 (43)
crops together			74	153	117	213	
methomyl (ARfD = 0.020 mg·kg^{-1}·d^{-1})							
apple	260	130	129	310	212	540	26 (3208)
grape	475	440	63	167	230	347	2 (273)
cabbage, head	320	805	153	505	675	1220	6 (789)
broccoli	810	680	123	426	695	720	2 (281)
cauliflower	590	550	259	585	910	1215	5 (646)
Brussels sprouts	200	160	153	555	890	1205	2 (295)
watermelon	52	10	0	2	4	9	0.1 (16)
tomato	57	47	18	44	44	93	14 (1706)
sweet corn	140	100	2	23	39	71	1 (136)
lettuce, head	1225	1215	139	397	495	1040	6 (795)
lettuce, leaf	300	1125	0	42	313	715	0.1 (14)
spinach	2600	2210	540	2210	2770	9600	3 (380)
kale	-	560	188	648	1015	2135	2 (286)
crops together			740	2505	940	2875	

[1] ARfD = acute reference dose
[2] Number in brackets indicates number of consumers.
[3] JMPR = Joint FAO/WHO Meeting on Pesticide Residues
[4] NLD = the Netherlands; [5] edible portion used = 89 g (FR; as for children in 2002 JMPR report and for both populations in 1999 JMPR report)

Table 5B. Comparison of the point estimate and the probabilistic approach (in % of ARfD[1]) for three compounds for the children (1 – 6 years; work example 6).

compound and crop	point estimate		probabilistic approach				% consumers[2]
			total population		consumers only		
	JMPR[3]	NLD[4]	P99.9	P99.99	P99.9	P99.99	
disulfoton (ARfD = 0.003 $mg \cdot kg^{-1} \cdot d^{-1}$)							
broccoli	200	113	3	99	135	208	4 (42)
cabbage , head	477	563	78	278	417	803	6 (59)
cauliflower	103	110	32	79	103	165	5 (51)
lettuce, head	1050	900	74	447	577	777	2 (24)
lettuce, leaf	2300	-	-	-	-	-	0 (0)
crops together			157	463	370	710	
fenamiphos (ARfD = 0.003 $mg \cdot kg^{-1} \cdot d^{-1}$)							
carrot	111	107	59	106	126	174	8 (86)
peppers, sweet	258	143	31	113	157	241	5 (52)
tomato	598	315	76	258	301	510	8 (80)
(water)melon	258	39	-	-	-	-	1 (9)
grape	207	159	23	70	131	242	2 (18)
pineapple	318	125	0	2	13	24	0.2 (2)
crops together			100	263	220	467	
methomyl (ARfD = 0.02 $mg \cdot kg^{-1} \cdot d^{-1}$)							
apple	770	480	319	550	453	770	30 (323)
grape	1620	1380	147	314	347	348	2 (18)
cabbage, head	1250	1475	312	1000	1655	2125	6 (59)
broccoli	1535	870	303	685	1005	1780	4 (42)
cauliflower	1725	1835	580	1270	1605	2525	5 (51)
Brussels sprouts	445	345	143	695	1295	1335	1 (14)
watermelon	135	-	-	-	-	-	0 (0)
tomato	185	115	27	96	113	204	7 (79)
sweet corn	415	155	3	53	109	137	1 (5)
lettuce, head	3075	2595	137	600	1165	2500	2 (24)
lettuce, leaf	3750	-	-	-	-	-	0 (0)
spinach	7180	6800	1310	6300	6700	17500	4 (40)
kale	-	1215	270	1420	2040	2970	2 (21)
crops together			1500	6300	2505	6410	

[1] ARfD = acute reference dose
[2] Number in brackets indicates number of consumers.
[3] JMPR = Joint FAO/WHO Meeting on Pesticide Residues
[4] NLD = the Netherlands

3.9 Conclusion and discussion

Based on the work examples described in this chapter the following conclusions can be drawn:

Work example 1: The consumers only approach in probabilistic modelling resulted in either lower, comparable or higher outcomes as the point estimate approach when using the P99.9 of exposure. The total population approach generally resulted in much lower P99.9 exposure levels.

Work example 2 and 6: In general, point estimates resulted in higher estimates of exposure than the probabilistic approach, when considering the P99.9 of exposure and the total population (including consumers and non-consumers of the crop of interest). Compared to the Dutch point estimate, the P99.9 exposure level was sometimes higher for certain residue – crop combinations when considering only consumers of the crop. The probabilistic approach takes a more holistic approach to risk, by addressing all consumption levels, all residue levels and all crops contributing to the exposure to a residue simultaneously into the exposure assessment.

Aldicarb and carbaryl would have been considered safe for use on the crops addressed when the P99.9 had been selected as the percentile of regulatory concern and when addressing the total population. For the three compounds addressed in work example 6 this was not true. In that case refinements of the calculations may be necessary by including a more realistic variability factor as proposed by the JMPR (FAO/WHO 2004) and information on processing effects in the exposure assessment.

Work example 3: In the consumers only concept, when addressing more than one crop, the exposure to a residue via the consumption of more than one crop on a certain day was not based on either the total population or the consumers only population. This may hamper a clear risk management decision. When calculating percentiles of exposure for all crops together (relevant when dealing with a residue that can be present on more than one crop) the total population approach is preferable. Due to probabilistic dilution an alternative approach may be necessary to protect also consumers of infrequently consumed crops. Depending on the number of consumers, the choice of a lower percentile of regulatory concern when addressing rarely consumed crops than the percentile chosen in the total population approach may be more reliable.

Work example 4: In the probabilistic approach different crop - processing type combinations (e.g. apple - raw, apple - juicing, apple - peeling) can be addressed simultaneously in one analysis. In the point estimate, each crop – processing type combination is addressed separately. The use of large portion sizes (LP) that may contain a combination of processing types per crop (e.g. the LP of apple may contain the consumption of apples with and without skin) may result in worst case assumptions when using the point estimate approach (e.g. assume that all people consume apple with skin), which may result in very conservative risk management decisions.

Work examples 4 and 5: In the probabilistic approach it is possible to address different crop –processing type combinations simultaneously that should be treated differently with regard to variability (e.g. apple - raw and apple - juicing).

In the work examples described in this chapter we used the P99.9 of exposure as the percentile of regulatory concern as applied by the US EPA (US EPA 2000c) and recommended in a draft guidelines document on the use of probabilistic exposure assessment in the safety evaluation of pesticides within the EU. The US EPA defends their policy of using the P99.9 by stating that the field trial residue levels used in the assessments are higher than those people will actually be exposed to for one or more crops. Furthermore, they state that their risk estimation methods incorporate sufficiently conservative approaches (e.g. 100% crop treated in the first two tiers; see also § 5.3) to provide sufficient protection for the small percentage of the population with exposure levels above the ARfD (US EPA 2000c).

The choice of the percentile of regulatory concern is a difficult issue and will depend on the exposure levels considered to be safe and on (un)certainties related to the data used in probabilistic modelling (US EPA 2000c). In the field of pesticide regulation, the quality of the underlying data is mainly related to representativeness and size of the food consumption database. In establishing acceptable exposure levels, risk managers may additionally consider the ARfD's used. Some ARfD's are very conservative, due to lack of sufficient data. This issue was addressed at the 35th meeting on the Codex Committee on Pesticide Residues in 2003 (CCPR 2003a). The eventual choice of the reference point and its inherent acceptance of a certain percentage of the population being at risk is ultimately a risk manager decision.

Overall we conclude that the work examples demonstrate clearly the potential of the probabilistic approach compared to the current methodology used when assessing the acute dietary exposure to pesticides. Different aspects were addressed to help risk managers to better understand and interpret the results of a probabilistic exposure assessment.

4 FOOD CONSUMPTION DATA OF OTHER COUNTRIES

In chapter 3 the acute dietary exposure was calculated to five selected compounds using food consumption data from the Netherlands. In this chapter the acute exposure was recalculated for one compound (carbaryl) using food consumption data from Sweden, Denmark and US. In this chapter we aim at covering some of the variation in food habits around the world.

4.1 Food consumption data from Denmark, Sweden and US

Denmark

Food consumption levels from Denmark were derived from the National Food Consumption Survey conducted in 1995 (Andersen et al. 1996). In this survey 3,098 persons (male and female) were asked to record their food consumption during 7 consecutive days (7-d dietary record). Amounts consumed were estimated using photographs of portion sizes. The age of the respondents ranged from 1 to 80 years.

For the coding of the foods consumed the Danish food composition database was used. Coding was performed at two levels, namely at the level of food consumption (e.g. bread) and at the level of components of the foods (e.g. flour). Food as eaten was not converted into the consumption of crops (a possible third level of disaggregation; e.g. wheat). Data from the Danish food survey is accessible dependent on research agreement. Not all data may be available for external partners due to privacy restrictions.

Sweden

For the Swedish food consumption data we used data derived from the study ‘Riksmaten’ (Becker 1999). This is a dietary study performed in 1997 and 1998 among 1,211 respondents (male and female) in the age of 18 to 74 years. Participants were asked to record their food consumption during 7 consecutive days (7-d dietary record). As in Denmark, amounts consumed were estimated using photographs of portion sizes.

For the coding of the foods consumed the Swedish food composition database was used. Coding was performed at the level of food consumption (food items, e.g. avocado; plum; milk, 0.5% fat; rye bread, 6% fibres and dishes, e.g. creamed spinach; potatoes, cooked; meatballs, beef; salmon, fried; chocolate mousse). For some of the dishes recipes were available to convert the consumption of dishes in the consumption of components. No recipe database was available to convert food as eaten in the consumption of crops. For the accessibility of Swedish consumption data the same arguments apply as for the Danish data.

US

The food consumption data from the US was derived from the Continuing Survey of Food Intakes by Individuals (CSFII) conducted in 1994 – 1996 (all ages, n=15,300) with a supplemental children’s survey in 1998 (0 – 9 years, n=12,000). Data on food consumption was collected via two 24-h recalls separated by 3 or more days. All seasons and all days of the week were included. Amounts consumed were estimated with the help of measuring guides, such as cups and spoons for volume of foods and ruler for length, width and height of foods.

Foods consumed were coded as such, at the food level. A recipe database is available to convert mixed dishes in their ingredients as well as to convert foods as eaten into the consumption of crops. In the exposure calculations performed with American data we used consumption levels of foods eaten as such. Data from the US is publicly available for use[6].

4.2 Description of other sources of food consumption data

EFCOSUM

Most European countries have carried out national dietary surveys. As part of the EFCOSUM project an inventory was made on the availability of food consumption databases in Europe (Verger et al. 2002). In this project 23 European countries (of which 14 EU Member States) participated which had among them 45 nationally representative food consumption surveys on individual level. Between these surveys the population groups, year of conduct, age categories and the dietary methods used differ. Examples of studies are the National Food Consumption Surveys of the Netherlands (2-d record, total population (n=6,250; 1 - 97 years), 1997/98), UK (7-d record, total population (n=2,197; 16 - 64 years, 1986/87) and France (7-d record, total population (n=1,500; 2 - 85 years), 1993/94).

Australia and New Zealand

In Australia the 1995 Australian National Nutrition Survey (NNS) and the 1997 New Zealand NNS are used by the FSANZ (Food Standards Australia New Zealand) to conduct exposure assessments for both Australia and New Zealand. The Australian study, conducted in 1995, consists of food consumption data of 13,858 individuals in the age of 2 years and above. Data on food consumption was collected via a 24-h recall and a food frequency questionnaire (FFQ; FFQ only on those 12 years of age and above). Of approximately 10% of respondents (n=1,489) a second, non-consecutive, 24-h recall was taken. The survey was conducted over a 13-month period to capture seasonal variation in food consumption. Data was collected on all days of the week to account for differences in consumption on weekends.

The New Zealand survey, conducted in 1997, consists of 4,636 respondents in the age of 15 years and above. The methodology used to collect data on food consumption was based on the Australian NNS. So also here a 24 h recall was used, together with an FFQ. Again of approximately 10% of respondents (n=695) a second, non-consecutive, 24-h recall was taken. The survey was conducted over a 12-month period to capture seasonal variation in food consumption and data was collected on all days of the week to account for differences in consumption on weekends. Maori and Pacific Islanders were over-sampled to be able to perform statistically robust assessments on these population groups.

In New Zealand also a Children's NNS (incorporating respondents aged 5-14 years) has recently been released. Data from this study is not yet used by FSANZ for exposure assessments. However the agency will negotiate with the New Zealand Ministry of Health to obtain the data for use in exposure assessments at FSANZ.

In February 2004 the practical possibilities were viewed to make the food consumption database of Australia and New Zealand compatible with the MCRA-software. This was no problem.

[6] www.barc.usda.gov/bhnrc/foodsurvey/

Germany
In Germany a food consumption survey was conducted among young children (6 months – 4 years, n=816) – the VELS-project. The survey was conducted between June 2001 and September 2002 to account for seasonal variation in food consumption. Data on food consumption was collected using a 3-d dietary record method. Amounts consumed were either weighed (scales were provided) or estimated. After 4 to 8 weeks in babies and 3 to 6 months in children the 3-d dietary record was repeated. So for each child 6 days of food consumption are available. Recording of food consumption was performed by the caretakers. During this survey much emphasis was placed on the collection of data on brand names, ingredients, processing practices and cooking recipes. Children drinking solely breast milk were excluded from the survey. Data from the German survey will be made publicly available in the near future.

UK
In the UK three surveys have been conducted as part of the National Diet and Nutrition Survey Programme (NDNS). In 1992 a survey was held among 1,675 pre-school children, in the age of 1½ and 4½ years (Gregory et al. 1995). Data on food consumption was collected using the 4-d dietary record method. In 1997 a second NDNS programme was conducted. This survey studied the food consumption habits of 1,701 young people age 4 to 18 years using the 7-d dietary record method (Gregory et al. 2000). In 2000 – 2001 a third survey was conducted. This time adults aged 19 to 64 years were addressed, again using the 7-d day record method. In this survey 2,000 individuals participated.

All three surveys covered a 12-month period of data collection, to cover any seasonality in eating behaviour and in the nutrient content of foods. Amounts of foods consumed in all three surveys were weighed before recording (scales were provided). When weighing was not possible (e.g. when eating outdoors) the amounts consumed were estimated. Data from the UK food surveys is publicly available.

South Africa
Food consumption data from South Africa is available from different studies conducted between 1983 and 2000 (Nel et al. 2002). Two types of dietary methods were used in these studies, namely the 24-h recall method and the quantified FFQ. The different studies can be summarized as follows:
National Food Consumption Survey: This survey (NFCS), carried out in 1999 (n=2,868), was based on a random representative sample of children aged 1 – 9 years, from all ethnic groups and provinces in South Africa, with over-sampling of children living in low socio-economic areas. The dietary methods used to quantify food consumption were the 24-h recall method and a quantitative FFQ.
The Lebowa Study: This study was undertaken in rural villages of the Northern Province in 1991. Dietary data (24-h recalls) was collected from black preschool children (n=118) and school children aged 6-25 years (n=365).
The Dikgale Study: This study, conducted in 1998, examined the dietary consumption of black adults in rural villages of central Northern Province. Average dietary intakes were calculated for 210 (body weights for only 111 adults available) adults. The repeated 24-h recall method was used to determine dietary consumption levels.
The Black Risk Factor Study: This study (BRISK) was conducted between 1983 and 1990 and examined risk factors for cardiovascular disease in urban black Africans living in Cape Town. The database derived from this study contains data on dietary consumption of 3 – 60+ year-olds (n=1,507), based on the 24-h recall method.

The Transition, Health and Urbanisation Study: The THUSA study, conducted between 1996-1998, examined the effect of urbanisation on the health status and dietary consumption levels of the black population (urban and rural) of the North West Province of South Africa (n=1,854 adults). Data on food consumption was obtained by means of a quantified FFQ.
The Transition, Health and Urbanisation Bana Study: The THUSA Bana study, conducted in 2000 and 2001, examined the prevalence of obesity and associated factors among 10-15 year-old children (n=1,257) in the (rural and urban) North West Province, South Africa. Data on food consumption was obtained by means of a 24-h recall.
First Year Female Students Project: The FYFS project was undertaken in 1994 at the University of the North. The study population consisted of black female students aged 18-34 years (n=431). Dietary consumption data was collected from 136 students by means of a quantified FFQ.
Weight and Risk Factor Study: In the WRFS survey dietary consumption data was obtained by means of a semi-quantitative FFQ. Self-reported height and weight measurements were also collected for black, white, Asian and "coloured" adults aged 18 – 55 years (n=449) from all provinces of South Africa by means of a postal survey.
Coronary Risk Factor Study: The baseline CORIS survey was undertaken in 1979 to establish prevalence and intensity of coronary risk factors in white adult populations in three towns in the Western Cape. Dietary consumption levels (24-h recall) were measured in participants aged 15 to 64 years (n=1,784). The survey was repeated in 1983.

4.3 Acute dietary exposure assessment to carbaryl in Denmark, Sweden and US

The P99.9 and P99.99 of acute exposure to carbaryl was calculated using food consumption data from Denmark, Sweden and the US as described in § 4.1. Exposures were calculated for the crops listed in annex 5 and using the field trial residue levels as listed in annex 6. Calculations were performed using the MCRA-software for the general population, including both consumers and non-consumers. For Denmark the food consumption levels used were the mean consumption levels over 7 days, resulting in one 'consumption day' per respondent. For Sweden and the US consumption levels per day were used, resulting in seven 'consumption days' per respondent for Sweden and two per respondent for the US. Exposure levels calculated with Dutch data are included in this table for reasons of comparison. Table 6 lists the P99.9 and P99.99 levels of exposure (as % ARfD) for the individual crops and for crops together of all four countries. Note that for the calculations no recipe database was used to convert food as eaten into the consumption of corresponding crops. Therefore we linked residue data to food as eaten, selecting only those foods similar to the crop analysed (e.g. grapes eaten as such).

It is clear that in all countries grape is the main risk driver for the exposure to carbaryl. The lowest exposure levels were calculated for Denmark, the highest for the US (crops together; table 6). The low Danish exposure levels can be explained by the use of average consumption levels over 7 days. At the time of writing this report, the daily consumption data was not available for Denmark. The high levels for the US are an overestimation, because no weighing factors were used for the difference in age distribution between their study population and the general population. In the American food consumption database, children (0 - 9 years) are over-represented (see § 4.2). This may have resulted in higher exposure levels due to higher intakes found in children. Weighing factors are available.

The intake of carbaryl in Sweden was lower than the intake in both the US and the Netherlands. The Swedish food consumption database contains only consumption levels of adults (18 - 74 years) Children, known to have higher exposure levels due to a larger food consumption level per kg body

Table 6. Results acute dietary exposure assessment to carbaryl (in % of the ARfD[1]; 0.2 $mg \cdot kg^{-1} \cdot d^{-1}$) using food consumption data from Denmark, Sweden, US and The Netherlands. Calculations were performed for the general population, including consumers and non-consumers.

country and crop	exposure level (%ARfD)	
	P99.9	P99.99
Denmark		
peach, nectarine, apricot	6	14
plum	1	2
grape	20	64
crops together	20	64
Sweden		
apricot	2	9
peach, nectarine	3	13
plum	4	17
cherries	1	6
grape	23	87
crops together	24	129
US		
apricot	0	8
peach, nectarine	20	65
plum	6	97
cherries	5	11
grape	127	480
crops together	119	467
the Netherlands		
apricot	0	5
peach	5	33
nectarine	4	22
plum	7	37
cherries	6	19
grape	33	143
crops together	42	142

[1] ARfD = acute reference dose

weight, were not included in this survey. In both the Netherlands and the US children were part of the study population

In the calculations presented here we applied a high default variability factor (see footnote 2 on page 9) and no effect of processing was included. So also here further refinement of the exposure calculations can be made by incorporating the newly proposed general default variability factor of 3 into the calculations as well as information on processing.

Conclusion

The results of this study show clearly that assessing the intake to acutely toxic compounds in different countries is well possible with the probabilistic approach, provided that data is available on food consumption. When comparing the results between countries it is important to consider the differences in the set-up of the food surveys from which the data is derived (e.g. population addressed, dietary method used).

In the assessment of the acute dietary exposure it is important to have the consumption levels of crops per day. Data used from Denmark (average consumption over 7 days) was therefore not well suitable to assess the acute exposure to carbaryl. The Danish consumption levels per day were not available when writing this report, but will be made available in the near future (see also chapter 6).

4.4 Compatibility issues of using different food consumption databases to calculate the acute dietary exposure to pesticide residues

Internationally there is an overall need to harmonise risk assessment procedures. This need for harmonisation does not only apply to the methodology used but also to the input data used, such as food consumption data. However the way in which food consumption data of different countries has been and is collected is not harmonised at all (Verger et al. 2002). This makes it difficult to compare exposure assessments using different food consumption databases.

Compatibility issues related to the use of food consumption databases in dietary exposure assessment are related to 1) diversity in national food consumption databases and 2) the conversion of food as eaten in that of crops (= raw agricultural commodities).

Diversity in national food consumption databases
Food consumption data collected at national levels can be very diverse. This diversity is related to the population addressed (e.g. children included or not), method of data collection (24-h recall, dietary method), duration of the survey, number of respondents involved, coding of food consumption data and method of quantifying amount consumed (actual weighing vs. estimations on the basis of portion sizes).

Another important item is that most food consumption surveys were (and often still are) set up from a health point of view. This means that the main focus is on the intake of macro - (carbohydrates, protein and fat) and micronutrients (minerals and vitamins). Intake of these nutrients may ask for a different set up of the survey than when the focus is food safety. For example, the distinction between the consumption of individual types of citrus fruits may not be so important and also some processing information, important for a realistic estimation of pesticide exposure, may not be relevant for nutritionists. The extent to which relevant information for pesticide exposure is collected at a national level may differ between countries. For example in Sweden the consumption of fruit juices is not further specified in the consumption of e.g. apple, orange or grape juice. Also no distinction is made between the consumption of apple and pear. In the US however, the level of detail when recording food consumption is very elaborate with much information on processing practices. To what extent food consumption databases set up from a 'health' point of view may be less suitable for food safety issues is not clear and needs to be studied further.

Although much improvement regarding compatibility issues may be needed in the future, we may consider that even the use of incompatible whole national databases in probabilistic modelling is already a large improvement compared to the present situation of using the point estimate methodology where only large portion sizes are used to calculate the acute exposure to pesticides via the diet.

Conversion of food as eaten into the consumption of crops

Pesticide residue measurements are mainly performed in crops. Processed or prepared foods are either not analysed or the number of samples is very small. In food consumption databases however the consumption of food as eaten is registered, including foods prepared by mixing the same or several ingredients. Examples of mixed foods are apple juice, apple sauce, tomato paste and pizza. Before these mixed or processed foods can be included in the assessment a link should be established between the field trial residue levels measured in crops and the consumption of these processed foods. For example, how many raw tomatoes are needed to produce 100 g of tomato juice? In the Netherlands a recipe database has been developed in which all foods coded in the Dutch food composition table are converted to crops (Dooren et al. 1995). In this database also a link was made between the crop and a processing type. For example, food 'apple juice' was converted to the crop – processing type combination apple – juicing and food 'apple without skin' to apple - peeling. In this way the effect of processing on field trial residue levels in crops can be taken into account in exposure assessments. Apart from the Netherlands, also in the US, UK and Germany (VELS-project; see § 4.2) recipe databases have been developed that are connected to food consumption databases.

When developing a recipe database information is needed on ingredients present in a processed food and the amounts present (e.g. from the label, literature, manufacturer, cookbook), processing practices and shrinkage percentage of cooked vegetables. This last item is very important when dealing with pesticides. It is known that vegetables can shrink considerably when being cooked. For example, to produce 100 g of spinach you may need 167 g of raw spinach, depending on the cooking time. Assuming the pesticide is uninfluenced by cooking, ignoring the effect of cooking on the volume of the vegetable will result in an underestimation of exposure.

The conversion of food consumption databases into consumption databases of crops is a quite extensive job, but recommended for making a link between field trial residue levels and food consumption data. Ignoring processed foods in the exposure assessment may result in an underestimation of the exposure. Experience from countries that have already developed recipe databases will be helpful, such as the US, UK and the Netherlands. Lack of a recipe database does however not mean that the food consumption data cannot be used in probabilistic dietary exposure assessment. It may be possible to use a recipe database from another country for converting food as eaten into crops. Another option is to link the field trial data to foods as eaten, selecting those foods that closely resemble the crop analysed (e.g. those foods used in the derivation of the point estimate). Using whole food consumption databases without a recipe database is considered to be an important improvement compared to the point estimate methodology, where large portion consumptions are used to represent consumption levels in different countries.

5 UNCERTAINTIES IN EXPOSURE ASSESSMENT AND PROPOSITION OF A TIERED APPROACH

5.1 Uncertainties in exposure assessment

Independent of the method used for exposure assessment, uncertainties in the underlying assumptions will influence risk management decisions. Preferably these uncertainties should be transparent. When using the point estimate approach however, these uncertainties have resulted in the use of precautionary principles when calculating the exposure (e.g. high consumption level, high residue level, default variability factor). With the probabilistic approach on the other hand, these uncertainties can be quantified by performing sensitivity analyses, making the analysis more transparent. Uncertainties related to food consumption data and residue data used in the exposure assessments are addressed in more detail below.

Food consumption
Food consumption data can be subject to either under- or overestimation due to recall bias, errors in reporting, etc. In food science and epidemiology it has been recognised that consumption of fruits and vegetables are more likely to be over- than underestimated. Such an overestimation may affect the higher percentiles of the exposure distribution, depending on the frequency in which such consumption levels occur in the total population. Mostly extreme consumption levels will occur only rarely.

Next to the uncertainties inherent to all food consumption data surveys, additional uncertainties may arise when deriving LPs (P97.5 of consumption) as used in the point estimate approach. Presently, there are no clear guidelines on how consumption of food as eaten is converted to that of crops (used in the derivation of LPs) and it is unclear which food items are included in the calculations. For example, some countries may have included both apples eaten as such and apple juice when calculating the P97.5 of apple while other countries may have only included apples eaten as such.

Residue data
There is uncertainty in how well field trial data reflects the real residue levels to which people may be exposed in real life. Not all pesticide applications will be performed at the critical GAP (Good Agricultural Practice): sometimes longer post harvest intervals will be used or lower doses will be applied. It is well recognised that monitoring residue levels are, on average, much lower than residue levels found in field trial studies. The overestimation of exposure using field trial residue data is supported by studies in the US and by many other residue-monitoring databases.

5.2 Validation study probabilistic approach

Real exposure to pesticides is usually unknown. However there are studies in which the real intake has been measured using the duplicate diet approach. The results of these studies can be used to validate methods that estimate the intake of pesticides by comparing the estimated intake with the real intake. Such a validation study was performed in the 5th Framework EU project Monte Carlo (Boon et al. 2003). In this study the real intake of 18 pesticides measured in duplicate diets from 250 infants (8 - 12 months) was compared with the calculated intake using both the probabilistic and the point estimate approach. To calculate possible exposure levels, the consumption levels of foods by the infants were combined with Dutch monitoring levels of pesticide residues. The probabilistic approach was supposed to be ‘fit for use’ if the predicted P99 of exposure was higher than the real intake, but lower than the point estimate exposure. The main conclusion of this study was that the traditional point estimate approach resulted in an overestimation of the real exposure, while the probabilistic approach provided more realistic estimates of exposure. However, these exposures still overestimated the real exposure to a large extent, conform the conservative principle. Depending on the percentile addressed or the model assumptions made, the overestimation was on average one or two orders of magnitude. We stress that this only applies for the pesticides studied. It is not known whether it will also apply for all other pesticides. Nevertheless, the studies showed clearly that even when using monitoring data a serious overestimation of exposure can occur and therefore the probabilistic results seem to be in line with the precautionary principle. A comparable study was performed in Spain resulting a similar conclusions (López et al. 2003).

5.3 Tiered approach

In general a probabilistic way of examining the exposure to a toxic compound is incorporated in a risk assessment procedure following a “tiered approach” (CCPR 2002b, ILSI 2002, US EPA 2000d). A tiered approach progresses stepwise from relative simple analyses (point estimate analyses) to more complex analyses (probabilistic modelling). The first Tier(s) generally involve point estimates of exposure or use of simple distributions with conservative input data resulting in conservative estimates of exposure. These conservative estimates tend to overestimate actual pesticide exposure. When these estimates of exposure are below the level of regulatory concern (here the ARfD), there is generally no reason to proceed to higher Tiers, involving probabilistic modelling. If however the conservative estimates of exposure are close to or higher than the ARfD, progression to higher Tiers may be performed, depending on the availability of reliable data.

For a complete review of different tiered approaches used by different organisations in the field of probabilistic modelling, mainly related to occupational exposures, see the guidance document on probabilistic modelling of ILSI (ILSI 2002). We restrict ourselves here to the tiered approach as applied by the US EPA and the one prepared for possible use within the EU, which both deal with dietary exposure to pesticides.

US

The US EPA defines four tiers that proceed from very conservative assumptions about residue levels in food to inclusion of more realistic residue values measured closer to the point of consumption (US EPA 1998, 2000b,d). The first two tiers use simple distributions to assess the exposure, while Tiers 3 and 4 involve probabilistic techniques. In Tier 1 a single residue level (tolerance level or maximum field trial residue) is combined with a distribution of consumption data, resulting in a distribution of possible exposure levels. In Tier 2 the single residue level as used in Tier 1 is replaced by mean field trial residue levels (or 95th percentile residue from monitoring) for processed/blended commodities. In Tier 3 a probabilistic approach is applied, using a distribution of both consumption and residue levels, including processing factors. Also information on percentage crop treated is included when available, together with information on realistic post-harvest intervals (PHI’s) and application rates. In Tiers 1 and 2 these conditions were assumed to be worst-case (100% crop treated, maximum labelled application rates, minimum labelled PHI’s). Tier 4 requires more extensive data on for example single serving market basket surveys, cooking studies, etc and provides thus the most representative exposure picture (US

EPA 1998, 2000d, Wright et al. 2002). Tier 4 can only be performed for pesticides that are already on the market (e.g. when re-evaluated).

EU

As described in §1.2, in the EU the point estimate methodology is used to assess the acute exposure to pesticides. However, also here the potential of the probabilistic approach has been recognised, resulting in the funding of the PACT (Probabilistic Assessment Consumer Training) project. One objective of this project was to develop draft guidelines on the use of probabilistic exposure assessment in the safety evaluation of pesticides in the EU-market. The draft document was finalised in October 2003.

Shortly, in this draft document also four tiers are suggested. The first two tiers deal with the point estimate approach as used at the moment within the EU. In Tier 1 the point estimate, as defined on the WHO GEMS/Food website, is applied per relevant crop (FAO 2002). In Tier 2 the point estimate is again used, but after a critical evaluation which may involve the large portion size used and the variability factor applied. In Tier 3 and 4 the probabilistic approach is used, using both the whole range of field trial residue levels submitted and consumption levels available. When a pesticide is (re)evaluated for more than one crop, all crops are addressed in one probabilistic exposure assessment and not separately as in the point estimate approach.

6 CONCEPTUAL NETWORK

We demonstrated in the previous chapters that the use of the probabilistic approach for assessing the (dietary) exposure to toxic compounds is very well possible and has many advantages compared to the approach presently used, the point estimate approach. To use the probabilistic approach however at an international level three important conditions need to be met.

First a model should be available, preferably accessible via internet, with which the exposure calculations can be performed using the principles of probabilistic modelling. In chapter 3 and 4 we demonstrated that such a model is available at present.

A second condition is the availability of food consumption data at an international level. As we demonstrated in chapter 4 food consumption data at an international level is available and it is technically possible to organise it in such a way that it can be linked to the MCRA-software, resulting in international exposure estimates despite differences between the databases (e.g. due to food description and food coding).

The third condition to be met is the existence of an electronic platform of different food consumption databases all connected to the probabilistic software. This last prerequisite is being realised within the integrated project SAFE FOODS, subsidised by the European Commission through the 6th framework programme (contract no Food-CT-2004506-446). This project has started in 2004 in which more than 30 research institutes from all over Europe and two from outside Europe (China and South Africa) aim at the promotion of food safety through a new integrated risk analysis approach for foods. SAFE FOODS consists of a number of interdependent research projects that aim at a comparative safety evaluation between different production systems (biotechnology, high- and low farming input systems).

In one of these research projects (‘Quantitative Risk Assessment of Combined Exposure to Foods Contaminants and Natural Toxins’) food consumption databases from the Netherlands, Denmark, Sweden and Italy will be linked to the MCRA-software with the aim to perform a Pan-European exposure assessment using different national food consumption databases simultaneously. At the end also food consumption data from the Czech Republic will be incorporated. So in total five food consumption databases will be made compatible with the MCRA-software in this project. The institutes involved in this research project are RIKILT – Institute of Food Safety (the Netherlands), RIVM (National Institute of Public Health and Environment, the Netherlands), BAG (Federal Office of Public Health, Switzerland), NFA (National Food Administration, Sweden), ISS (Institute of Public Health, Italy), DFVF (Danish Institute for Food and Veterinary Research, Denmark) and NIPH (National Institute of Public Health, Czech Republic).

Apart from the five food consumption databases mentioned above, we demonstrated in this report that also data from the US could be made compatible with the MCRA-software for probabilistic calculations of dietary exposure. Further, discussions are held with institutes in Germany and the UK to link data on food consumption levels in these countries to the MCRA-software (see § 4.2 for description of the German and British food consumption data). South Africa has consented to provide the CCPR with their food consumption data and in the near future also food consumption data from Australia/New Zealand may be made compatible with the MCRA-software.

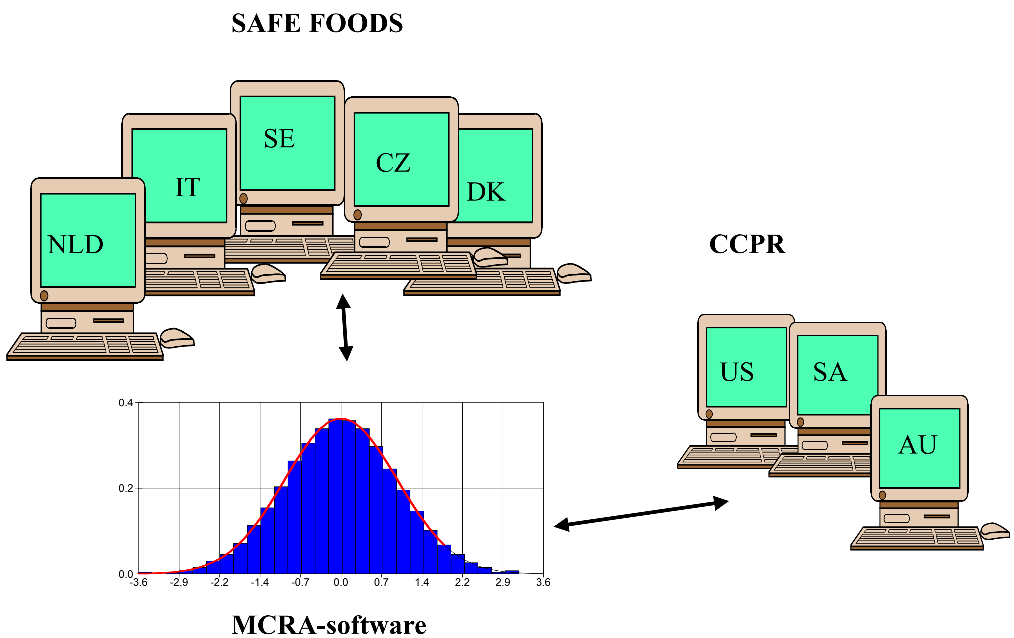

Figure 2. Conceptual network of different national food consumption databases linked to the MCRA (Monte Carlo Risk Assessment) software (NLD = the Netherlands, IT = Italy, SE = Sweden, CZ = Czech Republic, DK = Denmark, US = United States, SA = South Africa and AU = Australia / New Zealand.

This will result in a conceptual framework of different national food consumption databases that can be linked to the MCRA-software. Within the integrated project SAFE FOODS the RIKILT – Institute of Food Safety will develop a multi-database approach in which national food consumption databases located on local websites (e.g. of food safety authorities of institutes involved in risk assessments) will be linked to the MCRA-software (figure 2).

We can thus conclude that at the moment several food consumption databases are available at the international level, which can be or are made compatible with the MCRA-software in the short run for the assessment of dietary exposure to toxic compounds using the principles of probabilistic modelling. This is a significant extension compared to the food consumption databases from which large portion sizes were derived as used in the point estimate approach. We are aware that there are differences between the different national food consumption surveys due to reasons of costs involved, experience with data in the past, food description and food coding. So compatibility issues as discussed in § 4.4 are still to be faced. However, using incompatible whole national databases in probabilistic modelling of exposure is already a large improvement compared to the present situation of using the point estimate methodology with just one consumption level per crop per country.

7 CONCLUSIONS AND RECOMMENDATIONS

In this document we addressed the probabilistic approach to assess the acute dietary exposure to pesticides and compared this methodology with the one presently used worldwide, the point estimate approach. In general it can be concluded that probabilistic exposure assessments result in more complete and transparent information for risk management decisions, that there are no computational restrictions and that there is no lack of models.

The most important conclusions of this report are:

1. Organising trainings on probabilistic modelling and on the use of exposure models is a very efficient way to familiarise people with this approach (chapter 2).
2. For a worldwide acceptance of probabilistic modelling when evaluating the safety of acutely toxic pesticides via the diet, it is important to also make developing countries familiar with this approach. The organisation of a training on probabilistic modelling for these countries is therefore important.
3. In general, point estimates result in higher estimates of exposure than the probabilistic approach when addressing the total population (both consumers and non-consumers) and considering the P99.9 level of exposure (chapter 3).
4. The probabilistic approach takes a more holistic approach to exposure, by addressing all consumption levels, all residue levels and all foods contributing to the exposure to a compound simultaneously into the exposure assessment. Both exposure to a single crop or more crops that all contain the same residue on one day should be taken in consideration. Also it is well recognised that probabilistic modelling is necessary when addressing cumulative and aggregated risk assessment (chapter 3).
5. To allow for consistent comparisons between different crop – residue combinations, the total population approach may be the way to proceed in probabilistic modelling of acute exposure. Also, when more crops may contain the same residue it is conceptually right to address all these crops in one simulation. This is only possible when using the total population approach, which is consistent with the approach used in the US (chapter 3).
6. Due to probabilistic dilution of crops consumed infrequently when using the total population approach, the consumers only approach may add additional valuable information when dealing with such crops. A possible strategy is to perform calculations using the total population concept and to perform additional calculations with only the consumers of a certain crop when consumed infrequently. However, in those cases it should be avoided that rarely consumed crops receive more strict regulation compared to frequently consumed crops. This may be achieved by accepting a lower percentile of regulatory concern (chapter 3).
7. The working group recognised that many uncertainties affect the results of any exposure assessment (using either the probabilistic or point estimate approach). With probabilistic methods however, these uncertainties can be visualised using sensitivity analyses (chapter 5).

8. Scientific research demonstrated that the calculated pesticide intake using the probabilistic approach was one to two orders of magnitude higher than the real intake. The study included 18 pesticides. It was also recognised that pesticide levels measured in monitoring programmes are usually much lower than those measured in field trial data studies (chapter 5).

9. In order to be consistent with the US (and the draft guidelines document in the EU), the P99.9 of exposure may be chosen as a reference point in the probabilistic approach when dealing with field trial residue data. It is important that exposure levels at the selected reference point are discussed in relation to the uncertainties in the database and that they should also be considered in relation to the derivation of the ARfD and the safety margins (usually a factor 100) used. This is especially true when the reference point is close to or exceeds the ARfD (chapter 3).

10. Assessing the exposure to acutely toxic compounds using food consumption data of different countries is very well possible with the probabilistic approach, provided food consumption data is available, as well as a model to which the data can be connected. We demonstrated that such a model exists (chapter 4).

11. Presently a significant number of international food consumption databases will or can be made compatible with the MCRA-software. Within the integrated project SAFE FOODS food consumption databases from the Netherlands, Italy, Sweden, Denmark and the Czech Republic will be made compatible with the MCRA-software. Other consumption databases (e.g. from Australia/New Zealand, US and South Africa) might also be made compatible in the near future (chapter 6).

12. For the adoption of the probabilistic methodology for international acute intake estimations the establishment of a working group that studies the compatibility issues concerning the use of different national food consumption databases is very important. Also guidance needs to be given to the JMPR (e.g. in the form of a helpdesk) when applying the probabilistic approach in practice. This is important for the acceptance of this methodology for acute dietary exposure assessments.

The most important recommendations are:

1. The working group recommends the incorporation of the probabilistic way of examining the exposure to an acutely toxic compound in the risk assessment procedure via a “tiered approach”. In a tiered approach relatively simple analyses (e.g. point estimate analyses) are followed stepwise by more complex analyses (probabilistic modelling). For this the best way to proceed is to follow already existing (draft) guidelines (US, EU) for reasons of comparison and consistency (chapter 5).
2. The working group recommends the application of the “more than one crop together” concept as a starting point for risk analysis. The rationale for this is that the risk of a total daily intake of a residue is of concern from a consumers point of view and not the intake from one crop. The working group realises that there is so far little experience with this approach (chapter 3).
3. The working group recommends to perform exposure calculations for the total population approach when using probabilistic methods in a tiered approach. Firstly because in this concept,

the daily exposure to the pesticide of interest can be calculated when present in more than one crop. Secondly, because with this concept a population based exposure is obtained which allows for consistent comparisons between different crop - residue combinations (chapter 3).

4. The working group recommends the use of the P99.9 of exposure as the level of regulatory concern in the total population approach, when using residue levels from field trials in the assessment. The working group also recommends to perform additional exposure calculations for consumers only when dealing with crops eaten infrequently. To avoid that rarely consumed crops receive more strict regulation compared to frequently consumed crops, accepting a lower percentile of regulatory concern may be chosen for the consumers only approach (chapter 3).
5. The working group recommends the use of food consumption databases that are available worldwide. Despite differences in e.g. set-up of the survey and food coding, using incompatible whole national databases is already a large improvement opposed to the present situation of using exclusively the point estimate approach. Compatibility issues are to be solved in the future, leading to a more efficient use of national food consumption databases for food safety purposes (chapter 6).
6. Guidelines should be developed on how to deal consistently with the results of probabilistic modelling in a tiered approach.
7. We propose the formation of a project team that includes database managers of databases most likely to be used in probabilistic exposure assessment by JMPR and experts to assist the JMPR in future applications of a tiered approach (helpdesk, solve compatibility and technical issues) and to work out further guidelines in line with the current discussions within CCPR and JMPR.

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ANNEX 2. List of participants of both training sessions

Session 1

Stephen Funk (US EPA, US)†
Sanna Lignell (National Food Administration, Sweden)
Anders Møller (Danish Veterinary and Food Administration, Denmark)
Bernadette Ossendorp (RIVM, the Netherlands)†
Annette Petersen (Danish Veterinary and Food Administration, Denmark)

Session 2

Arne Andersson (National Food Administration, Sweden)
Claire Basely (Food Standards Agency, UK)
Nienke Blok (Dutch Food and Consumer Product Safety Authority, the Netherlands)
Eloisa Dutra Caldas (University of Brasilia, Brazil)†
Caroline Harris (International Banana Association, UK)
David Kloet (RIKILT – Institute of Food Safety, the Netherlands)
Gerry Moy (WHO, Switzerland)
Bernadette Ossendorp (RIVM, the Netherlands)†
Christian Sieke (Federal Institute for Risk Assessment, Germany)
Amelia Tejada (FAO Joint Secretary to JMPR, Italy)
Mathilde Touvier (French Food Standards Agency, France)
Claudia Vohman (University of Paderborn, Germany)
Yukiko Yamada (FAO, Japan)†

† FAO-panel members of JMPR. Apart from the four panel members mentioned above, three additional panel members (Sylvie Malezieux, Bernard DeClerq and Ursula Banasiak) participated in a similar training in June in Brussels. So 7 out of 10 FAO panel members were made familiar with probabilistic modelling of dietary exposure to pesticides and the use of the MCRA software.

ANNEX 3. Agenda of the first training in November 2003 (10 – 12 November)

Training 10th of November, RIKILT – Institute of Food Safety, Wageningen

FOOD CONSUMPTION DATA (US, DENMARK, SWEDEN)

<u>DAY 1 (start at 13.00 h)</u>
Food Consumption Database The Netherlands (Polly Boon)
- organisation of the food consumption database
- number of respondents, number of days, how was the reporting done
- coding issues
- technical structure of database and accessibility for others (e.g. WHO)

Food Consumption Database Denmark (Anders Møller)
- organisation of the food consumption database
- number of respondents, number of days, how was the food reporting done
- coding issues
- technical structure of the database and accessibility by others (e.g. WHO)

Food Consumption Database Sweden (Sanna Lignell)
- organisation of the food consumption database
- number of respondents, number of days, how was the food reporting done
- coding issues
- technical structure of the database and accessibility by others (e.g. WHO)

Food Consumption Database US (Stephen Funk)
- organisation of the food consumption database
- number of respondents, number of days, how was the food reporting done
- coding issues
- technical structure of the database and accessibility by others (e.g. WHO)

Presentation LifeLine (Stephen Funk)

Introduction into MCRA (Polly Boon)
- how does it work (what has be dealt with in EU training, structure input files)
- Examples to be worked by participants

Time for discussion

<u>DAY 2 (start at 09:00 h)</u>
Structure of the Dutch Food Consumption Database for compatibility with MCRA (Gerda van Donkersgoed and Evelyn Tjoe Nij)
- MS-Access database: Dutch food consumption data (how does it look)

- MS-Access database: US-consumption data, SE-consumption data, DK-consumption data (as far as possible)
- grouping of consumption data and assigning correct processing and variability factors using NL, US, SE, DK data (as far as possible)
- setting up the consumption files and residue files form Access database to get MCRA running
- Exercises with help of RIKILT

Processing (Polly Boon and Gerda van Donkersgoed)

- different processing factors for different food items
- MS-Access food consumption database and how to assign processing factors
- setting up the processing files (and other files) from Access database to get MCRA running
- exercises with help of RIKILT (influence of processing)

Variability (Polly Boon and Gerda van Donkersgoed)

- different variability factors for different crops and different processing forms
- model options within MCRA regarding variability (lognormal, beta, bernoulli)
- exercise with different model options of MCRA
- MS-Access food consumption database and how to assign variability factors
- exercises with help of RIKILT (influence of variability)

Importance conversion model, an example of how we set it up (Polly Boon)

- how to convert food as eaten into raw agricultural commodities (RACs)
- processing factors for different processing types
- variability for different processing types
- example of how a conversion model may look like (MS-Access)
- availability of conversion models internationally (US? , DK other countries??)

Grouping food items and applying conversion factors (Gerda van Donkersgoed)

- how to assign food items to raw agricultural commodities (RAC's) in MS Access database
- how to apply crop conversion factors for different combinations
- exercises with help of RIKILT

<u>DAY 3 (9.00 till 12.30)</u>

Working out one of the examples as requested by the CCPR using own food consumption databases (Polly Boon, Evelyn Tjoe Nij, Gerda van Donkersgoed)

- group consumption data for carbaryl or methomyl (which foods to include in the analysis belonging to a RAC)
- assign variability factors and possible processing factors as used by the JMPR (variability factor = 3/5/7/10 or according to new insights variability factor = 3 when dealing with Case 2 of the point estimate approach; studying effect of processing)
- calculate exposure using MCRA for all RACs together or separately
- compare the P99.9 with the point estimate calculations as performed by the JMPR
- comparison of exposure levels between the different countries

Time for discussion, how to go on from here, how to apply probabilistic modelling at an international level, possibility of different food consumption databases that can be used for exposure calculations within the same programme

ANNEX 4. Agenda of the second training in November 2003 (24 – 26 November)

AGENDA

CCPR TRAINING ON PROBABILISTIC DIETARY EXPOSURE ASSESSMENT TO PESTICIDES

WAGENINGEN, 24 – 26 November 2003

<u>DAY 1</u>

12.30 Welcome by the Dutch Food and Consumer Product Safety Authority

12.40 Introduction in Probabilistic Approach to Calculate Acute Dietary Exposure to Pesticides
- probabilistic modelling
- tiered approach (EPA, EU)
- need for probabilistic approaches

13.00 @RISK
- explanation of @RISK
- simple examples in @RISK to demonstrate the principle of the probabilistic approach
- exercises performed in @RISK by participants, time for discussion and questions

14.15 Probabilistic Modelling of Food Consumption Data and Field Trial Data
- types of food consumption data
- how do food consumption data look like?
- probabilistic modelling of food consumption data in @Risk
- probabilistic modelling of field trial data in @Risk

15.15 *Coffee / Tea Break*

15:40 Pesticide Present in More Than One Crop
- why important?
- how to model

16.00 Monte Carlo Risk Analysis (MCRA) programme
- drawbacks @RISK
- Monte Carlo Risk Analysis programme
- how does the programme work (getting started, uploading input files, etc)
- exercises in MCRA

18.00 End

DAY 2

9.00 Monte Carl Risk Analysis programme (cont'd)

10.30 *Coffee / Tea Break*

10.45 Refinement Probabilistic Modelling: Processing
- why deal with processing?
- what is a processing factor?
- processing in probabilistic modelling
- examples and exercises in MCRA

12.15 *Lunch*

13.30 Conversion Food As Eaten in Raw Agricultural Commodities
- why is this important?
- examples of how to convert
- data needs

14.00 Refinement Probabilistic Modelling: Variability
- importance of variability in acute dietary exposure
- variability factors and unit weights
- variability in probabilistic modelling
- examples in MCRA

15.30 *Coffee / Tea Break*

15.45 Important Issues To Be Considered in Probabilistic Modelling
- concept consumers only versus total population
- subpopulations
- selection percentile of exposure
- minimum data requirements for P99.9
- is it possible to compare percentile of exposure with IESTI?
- tiered approach / communication

17:30 End

DAY 3

9.00 Working out one of the examples as requested by the CCPR using Dutch food consumption database

- group consumption data for carbaryl (which foods to include in the analysis belonging to a RAC)
- assign variability factors and possible processing factors as used by the JMPR (variability factor = 3/5/7/10 or according to new insights variability factor = 3 when dealing with Case 2 of the point estimate approach; studying effect of processing)
- calculate exposure using MCRA for all RACs together or separately
- compare the P99.9 with the point estimate calculations as performed by the JMPR
- comparison of exposure levels between the different countries

10.30 *Coffee / Tea Break*

10.45 Working out one of the examples as requested by the CCPR using Dutch food consumption database (cont'd)

11.30 Feedback from the food consumption meeting beginning of November

11.50 Time for discussion, how to go on from here, how to apply probabilistic modelling at an international level, possibility of different food consumption databases that can be used for exposure calculations within the same programme

12.30 *End and lunch*

ANNEX 5. Compounds and crops to be considered in the work examples

compound	crops for which the point estimate exceeded the ARfD[1]
carbaryl	apricot, cherries; grapes; peach; plums
disulfoton	broccoli; cabbage, head; cauliflower; lettuce, head; lettuce, leaf
fenamiphos	carrot; grapes; peppers; pineapple; tomato; watermelon
methomyl	apple; broccoli; brussels sprouts; cabbage, head; cauliflower watermelon; grapes; kale; lettuce, head; lettuce, leaf; spinach; sweet corn; tomato
ethephon	cantaloupe; peppers; pineapple; tomato
aldicarb	banana

[1] ARfD = acute reference dose

ANNEX 6. Field trial residue levels used in the calculations of the point estimate and the probabilistic approach

compound and crop	year JMPR report	residue levels (mg·kg^{-1})[1]
aldicarb	2001	
banana		0.01(13), 0.02(3), 0.03, <0.03(5), 0.09, 0.1
carbaryl	2002	
apricot; peach; plum; nectarine		0.37, 0.69, 0.96, 0.99, 1.1(2), 1.4, 1.6, 2, 2.1, 2.3, 2.6, 3, 3.6, 4.8(2), 5.5, 7.8
cherries		2.1, 2.4, 3.4, 3.9, 4.7(2), 6.3, 6.7, 16
grapes		0.42, 2.4(3), 3, 3.3, 3.8, 4.5, 4.9, 5.3, 6.2, 6.5(2), 7.2, 7.5, 7.9, 33
disulfoton	1998	
broccoli		<0.02(6), 0.03(2), 0.05, 0.06, 0.09, 0.11
head cabbage		<0.02(12), 0.02(3), 0.03, 0.06, 0.07 (3), 0.08, 0.09, 0.12, 0.17 (2), 0.23, 0.32
cauliflower		<0.01(6), 0.01(3), 0.02, 0.03, 0.04, 0.05
head lettuce		<0.03, 0.04, <0.05(2), 0.1, 0.44, 0.64
leaf lettuce		<0.03(2), 0.06, 0.11, 0.56, 0.59, 1.15
fenamiphos	1999	
carrot		<0.02(8), 0.02, 0.024, 0.027, 0.05, 0.06(2), 0.07, 0.08
sweet peppers		<0.02, <0.05, 0.05(2), 0.06(2), 0.26, 0.35
tomato		<0.02(4), <0.05(5), <0.1, 0.15, 0.17, 0.27, 0.30
(water)melon		<0.01(4), <0.02(2)
grape		<0.01(11), 0.01(6), 0.02(7), 0.03(5), 0.05(4), 0.07(2), 0.09
pineapple		<0.01(26), 0.01(2), 0.02(2), 0.05, 0.14
methomyl	2001	
apple		0.16, 0.24, 0.25, 0.30, 0.31(2), 0.32, 0.34, 0.39, 0.40, 0.42, 0.43, 0.48(2), 0.61, 0.68(2), 0.77, 0.91(2), 1.5, 1.6
grape		0.15, 0.19, 0.25, 0.26, 0.29, 0.54, 0.58, 0.59, 0.65, 0.7(2), 0.78, 0.93,1(2), 1.2, 1.3, 2.2, 2.3, 2.8, 2.9, 3.5, 4.1, 5.2
head cabbage; broccoli; cauliflower; Brussels sprouts		0.04, 0.08(2), 0.09, 0.12, 0.16, 0.18(2), 0.2,0.24, 0.27, 0.45, 0.51, 0.53, 0.64, 0.71, 0.74, 0.76, 0.97, 1.1, 1.2, 1.3(2), 1.6(2), 1.9, 2, 2.1, 2.3(2), 2.6, 2.7, 2.8, 3, 3.1, 3.5, 3.8(2), 4.3, 4.8, 5(2), 5.3, 5.6(2)
watermelon		<0.02(21), 0.03(2), <0.04(2), 0.07
tomato		0.05, 0.06, 0.08, 0.09, 0.13, 0.16, 0.18, 0.23(2), 0.33, 0.73
sweet corn		<0.02, 0.02, <0.03(6), <0.04, 0.04, 0.06, 0.07(2), 0.08, 0.11, 0.13, 0.22, 0.28, 0.43, 0.54, 0.82, 1.5
head lettuce; lettuce, leaf; spinach; kale		<0.04(3), 0.04(2), <0.05, 0.07(3), 0.09(2), 0.12, 0.14, 0.19, 0.21(2), 0.25, 0.31, 0.34(2), 0.35, 0.36, 0.42, 0.44, 0.48, 0.49, 0.62, 0.71, 0.74, 0.96, 1, 1.1, 1.2, 1.4(2), 1.5(2), 1.7(2), 1.8(2), 1.9, 2.1, 2.2, 2.5, 2.6, 2.9, 3, 3.2(2), 3.5, 3.6, 4.1(2), 4.6(2), 5, 5.5, 5.7, 6.2, 6.3, 6.7, 7.7, 10, 12, 13, 17, 18, 25

[1] Levels below the level of reporting (indicated by <) were considered to be at this level in the probabilistic approach.

ANNEX 7. Variability in residue levels within composite samples

Because hardly any data are available on variability in residue levels between individual units of composite samples, we applied default variability factors, as defined on the WHO GEMS/food website, in the point estimate. In the point estimate one single value for variability is applied. In the probabilistic approach however, one single value for variability cannot be used as such in single simulations of a probabilistic exposure analysis. Due to lack of guidelines on how to apply variability in a probabilistic approach, we incorporated variability in the analyses following the procedure described below.

We simulated new residue levels using the Beta distribution. This means that the simulated residue levels are sampled from a bounded distribution. The lowest residue level sampled is 0 $mg \cdot kg^{-1}$ and the maximum level sampled is equal to the level of the composite sample multiplied with the number of units in the composite sample. So e.g. for orange the number of units in a composite equals 12 (EU-Directive 7029/VI/95 rev.5: Appendix B). For each field trial residue level sampled per unit orange consumed (e.g. 0.01, 0.01, 0.02, etc) a beta distribution is generated bounded by 0 $mg \cdot kg^{-1}$ and 12 times the residue level of the composite sample. Every possible residue level between these two levels can be sampled and used in the exposure calculations. In this way the situation in real life is mimicked using the original definition of the default variability factors as defined in the point estimate (FAO/WHO 1997). To apply the beta distribution for simulating new residue levels 1) information is needed on the variability factor (default value) and the number of units in a composite sample. For more details see (voet et al. 2003).

Variability was applied to each individual unit consumed. It is therefore theoretically possible that a person consuming e.g. two units sampled a high residue level for both units. This is not possible in the point estimate (FAO 2002).

Variability was not applied to foods that were consumed after the raw agricultural commodity had undergone some kind of industrial bulking or blending, e.g. fruit juices or fruit sauces. This is in accordance with the guidelines for the point estimate (FAO 2002).

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Voet H van der, Boer WJ de, Boon PE, Donkersgoed G van, Klaveren JD van (2003). MCRA, a GenStat program for Monte Carlo Risk Assessment, Release 2, Reference Guide. Wageningen, Biometris and RIKILT - Institute of Food Safety, Wageningen UR.

ANNEX 8. Consumption and residue levels used in work example 4

Individual residue levels and other variables used in work example 4A:

characteristics	apple	apple juice
residue level ($mg \cdot kg^{-1}$)	0.16, 0.24, 0.25, 0.30, 0.31(2), 0.32, 0.34, 0.39, 0.40, 0.42, 0.43, 0.48(2), 0.61, 0.68(2), 0.77, 0.91(2), 1.5, 1.6	0.16, 0.24, 0.25, 0.30, 0.31(2), 0.32, 0.34, 0.39, 0.40, 0.42, 0.43, 0.48(2), 0.61, 0.68(2), 0.77, 0.91(2), 1.5, 1.6
HR ($mg \cdot kg^{-1}$)	1.6	-
STMR ($mg \cdot kg^{-1}$)	-	0.41
unit wt (g)	138[1]	-
net edible portion wt (g)	127	-
variability factor	7	7
LP general population (g)	316	896
LP children (1 - 6 years) (g)	260	800
bw general population (kg)	65.8	65.8
bw children (1 - 6 years) (kg)	17.1	17.1

[1] unit weight of the US

Summary statistics of the food consumption levels used in probabilistic modelling in work example 4.

characteristics	apple	apple juice
general population (1-97 years)		
mean level total population (g)	34.7	15.6
mean level cons. only[1] (g)	135	266
minimum level cons. only (g)	1.0	15
maximum level (g)	810	1700
number of consumption days	3208	731
children (1-6 years)		
mean level total population (g)	31.4	45
mean level cons. only (g)	103	239
minimum level cons. only (g)	2.0	40
maximum level (g)	360	1080
number of consumption days	323	201