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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 CCPR in 2003 to prepare a paper considering the adoption of the probabilistic methodology for international acute intake estimations. 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. Within the CCPR / JMPR presently the point estimate methodology is used to assess the acute dietary exposure to pesticide residues. However, gradually the probabilistic approach was recognized as an important tool to address acutely toxic pesticides through the diet.

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 document namely 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; 2) to assess the dietary exposures associated with some specific pesticide residues, as requested by the CCPR; 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 exposure; and 4) to develop a view on how to incorporate probabilistic modelling 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 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 this meeting 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 to perform probabilistic exposure calculations. 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 (consumption, field trial residue levels, processing, variability).
- Harmonisation of terminology was recognised as very important (e.g. residue people use 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. Recipe databases are not available from most countries and the level of detail is not comparable between countries. However, lack of recipe databases at a national level should not hamper the introduction of whole food consumption databases.
- Use of a total population approach in probabilistic modelling, makes risks better comparable. Although the total population approach results in a dilution of risk, the population for which the risk estimates apply is always the same, while for the consumers' only approach, the population is different for each commodity.

In chapter 3 the dietary exposure to some specific pesticide residues and food combinations, as requested by the CCPR, was assessed using food consumption data from the Netherlands. For this six work examples were generated in such a way to facilitate the understanding of results of probabilistic modelling by risk managers and to address certain issues important in probabilistic exposure assessment. Items addressed were point estimate

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), and effect of variability (work example 5), and use of different end points (work examples 1, 2 and 6). These examples showed that

- In general, point estimates result in higher estimates of exposure than the probabilistic approach, when considering the P99.9 of exposure. Sometimes the P99.9 of exposure was higher, especially when considering only consumers of one food.
- The probabilistic approach takes a more holistic approach to risk, by addressing all consumption levels, all residue levels and all foods contributing to the exposure to a compound simultaneously into the exposure assessment.
- Addressing consumers only in a probabilistic simulation when addressing more than one food may result in a lower overall exposure level compared to the exposures per food. This is because risks are incomparable as the population on which they are based are different and as a result may hamper clear risk management decisions. For calculating percentiles of exposure for people eating more than one food a day with the residue of interest, only the total population approach should be applied. Apart from calculating exposures for consuming more than one food item, analysis per food item gives additional relevant information for risk management decisions.
- For foods eaten by only a small part of the population, additional analyses are needed, because of risk dilution in the total population approach.
- In the probabilistic approach different processing types of one food (e.g. apple raw, apple juice, apple peeled) can be addressed simultaneously in one analysis, including (types of) foods 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 well possible with the probabilistic approach, provided data is available on food consumption 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 modeling 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 modeling). In the US the tiered approach, including probabilistic modeling, 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, which define four tiers, the last two 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 EU integrated project Safe Foods 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. The 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” by following already existing guidelines (US, EU) for reasons of comparison and consistency.
- Because of the inability to calculate population-based risks when addressing only the consumers, and to apply a comparable approach as the US, a total population approach is preferable in acute exposure assessment. Also the European Union aims at a comparison of risks between countries in the future, for which a total population based approach is better suitable. Due to probabilistic dilution, for commodities consumed by only a small part of the population, the consumers’ only approach adds additional valuable information. A proposed possible strategy is to always perform calculations using the total population concept, and to perform additional calculations ising the consumer only concept only for those products consumed by a small percentage of consumers. In this strategy we should avoid a discrepancy between the results of both calculations.
- 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 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. 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).
- 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 EU 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 the 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.

1 INTRODUCTION

Risk of 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 probabilistic approach for 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) they discussed this approach, 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).

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 commodity 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 make 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 food and one pesticide at a time.

Probabilistic modelling
Probabilistic modelling takes the above-mentioned issues into account. Furthermore, the result is a distribution of all possible exposure levels that may occur in a population as opposed to just one single exposure level resulting from the point estimate approach. These dietary intake distributions provide insight in both the likelihood and the magnitude of a certain level of dietary intake. Comparison of these intake levels with the ARfD will then give information on the acceptability of consumer risk from these residues. This is a large advantage compared to the point estimate approach, which results in just one level of exposure with no information on the probability that such a level of exposure will occur in a certain population.

Probabilistic modelling (also commonly referred to as Monte Carlo analysis) is particularly useful in acute dietary intake estimates in that the probability of a consumer eating more than one food in one day, each containing pesticide residues can be assessed. This is important, because in acute dietary risk assessment the focus should be on the population risk. In the population risk approach, risk estimates are comparable, the number of people at risk can be estimated and risk management decisions are more transparent. Apart from that, the exposure to a certain (group of) pesticides from eating different commodities on one day can be calculated.
This contrasts with "point estimates" of acute dietary intake 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 total population approach, commodities consumed by a small number of consumers, might not be recognized as of risk. In this case, the consumers' only approach gives valuable additional information. However, 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.

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 there 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 (97.5th 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. (2003), to reduce these variability factors to 3 for all commodities (annex 5). 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 are 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

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

[2] unit weight of whole portion > 250 g, except head cabbage: v = 5; 25 ≤ 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.

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 to 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 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, and (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 (Suhre 2000, US EPA 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 risk assessment for more complete decision-making within the CCPR. Important aims of the project are to explore the technical possibilities in probabilistic risk assessment at the international level, and to study the most appropriate concept in the case of 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 exposure; 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 risk assessment was performed only with consensus data as used by CCPR in the point estimate approach. The only difference was that the Dutch consumption database provided the underlying data on consumption. For reasons of comparison, point estimates are also presented using Dutch large portion sizes.

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 6).

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, annex 5)
  - 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 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.
  - Use of a total population approach in probabilistic modelling, because of the difficulty in comparing risks for different 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 of this year (§ 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 are focussed on five compounds and several foods as identified at the 35th CCPR relevant for further study. For a complete list of relevant compound – food combinations see annex 6.

3.2 Methods

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

Food consumption data

Food consumption data derived from the Dutch National Food Consumption Survey (DNFCS) of 1997/1998 was used in the exposure calculations (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 is 24 h in order to obtain random daily consumption patterns. In this way 12,500 eating 'moments' were available for the total Dutch population and 1,060 moments for young children.

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 to the consumption of raw agricultural commodities (RACs; (Dooren et al. 1995)). In this way the field trial residue concentrations analysed in RACs could be linked directly to consumption.

Field trial residue data

Field trial residue data were derived from different JMPR reports. For levels used and source see annex 7. The residue levels are those selected by 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 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 the point estimate exposure. Default variability factors (*v*) were applied (see footnote 2 on page 7). The newly proposed general default variability factor of 3 was only used in work example 5 (annex 5). In this approach we used the large portion sizes and body weights from the Netherlands for the total Dutch population and for children, 1 – 6 years. Point estimates as calculated by JMPR are presented as well for comparison.

Probabilistic modelling

The 'Monte Carlo Risk Assessment' (MCRA) programme was used for probabilistic modelling (Boer et al. 2003, Voet et al. 2003). This is an Internet based programme (http://www2.rikilt.dlo.nl/mcra/mcra.html) developed at the RIKILT – Institute of Food Safety in co-operation with Biometris (Wageningen UR) to assess the acute exposure to pesticides through the diet using the probabilistic approach. For a detailed overview of the (statistical aspects) model and the practical use of the model we refer to the user manual (http://www2.rikilt.dlo.nl/mcra/Usermanual.pdf) and the reference guide (http://www2.rikilt.dlo.nl/mcra/Referencemanual.pdf) that can 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 program depends on possibilities to maintain and update the software and to support the user at the international level (helpdesk function). This programme operates as follows. First it randomly selects a consumer out of the consumption database. The consumption of every single food (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 food. After each food 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 all possible combinations of consumption and residue level. All estimates of possible intakes are adjusted for the individual's self-reported body weight. Apart from the percentiles of exposure per commodity, the intake of a certain pesticide by the consumption of more than one product was also assessed. For an accurate assessment of the daily intake of a certain pesticide, the list of foods should contain all possible commodities that 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 it 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 are Bernoulli and lognormal distribution. See reference guide (http://www2.rikilt.dlo.nl/mcra/Referencemanual.pdf) for theoretical background. Details can also be found in annex 8. Currently there are no guidelines on how to incorporate variability into the probabilistic approach.

To estimate the different percentiles of the dietary exposure distribution, we performed the Monte Carlo analyses with 100,000 iterations. When addressing one food 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 food 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.

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 eaters of a food, because the point estimate methodology deals also only with consumers of a food. For reasons of comparison, the calculations for the total population are also presented. The percentile of exposure is also calculated for the consumers eating more than one of the foods of interest on one day (e.g. consumption of 150 gram of grapes after lunch and 1 nectarine after dinner).

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. Aldicarb and carbaryl were used in this example. To compare the point estimate outcome with the probabilistic approach, we chose the 99.9th percentile (P99.9) of the exposure distribution, as is 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 foods 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 consumption data than those submitted to the WHO or a change in approach to derive large portion size. 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 97,5 percentile for the raw agricultural product (e.g. apples).

Compared to the Dutch point estimate, most P99.9 exposure levels for consumers only were either lower or the same; some were higher (e.g. 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 for aldicarb and carbaryl with the P99.9 level of exposure for consumers only, aldicarb would have been acceptable for use on banana (also true for total population). Carbaryl may pose a risk when used on grape (general population and children) and peach, nectarine and plum (children). Also when all foods were considered simultaneously, the P99.9 for carbaryl and consumers only exceeded the ARfD in both the general population and children (table 1). With the total population approach carbaryl would have been acceptable on all foods addressed. Considering the P99.99 in consumers only and the total population conclusions about safety of use would have been somewhat different. For example, use of carbaryl on grape would have been a problem with the P99.99 of exposure. 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.

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

compound, population and food	point estimate		probabilistic approach			
	JMPR[2]	NLD[3]	consumers only		total population	
			P99.9	P99.99	P99.9	P99.99
aldicarb (ARfD = 0.003 mg·kg^{-1}·d^{-1})						
general population						
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						
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
foods together			133	303	42	143
children (1- 6 years)						
apricot	127	32	32	46	0.00	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
foods together			588	1224	94	376

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

The obstacles in the consumers' only approach in relation to the total population approach in probabilistic modelling will be addressed in work example 3.

Conclusion
Work example 1 showed that the P99.9 exposure levels for consumers only were generally lower or comparable to the point estimate exposure levels. Considering only consumers in the probabilistic approach resulted in higher exposure levels compared to the total population approach.

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 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 in the point estimate approach is based on consumers' only and only one high food consumption level, the large portion size (LP) is addressed as opposed to all possible consumption levels in the probabilistic approach when addressing the total population (including zero consumption levels). Apart from one high consumption level, the point estimate also addresses only one high (the

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

compound, population and food	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					
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					
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)
foods together			42	143	
children (1- 6 years)					
apricot	127	32	0.00	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)
foods 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

highest) residue level and a high default variability factor. Another factor that may sometimes explain the higher exposure levels calculated with the point estimate approach is that in the point estimate a mean body weight is used which sometimes does not correspond with the person consuming the LP. This may result in the estimation of high exposure levels, because the LP may sometimes 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.

Comparing the ARfD of aldicarb and carbaryl with the P99.9 of exposure, use of aldicarb on banana would be considered safe for both the general population and children. With the point estimate approach, however, this was not true for children. Carbaryl would not have been considered safe for use on grape according to the point estimate approach for both the general population and children. With the probabilistic approach on the other hand, taking into account all foods simultaneously or separately, carbaryl would have been considered safe for use on all six foods when using the P99.9 of exposure as reference point. Using the P99.99 of exposure the conclusions would have resembled those of the point estimate for alidcarb on banana in children and carbaryl on grape for both populations. 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 food were either comparable or higher than those calculated for all foods 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 general population. It is clear that in the exposure distribution intakes via combinations of foods may occur.

Table 2B. Possible sampled field trial residue levels (mg·kg-1) and consumption levels (g) belonging to the ten highest exposure levels simulated in the general population 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	.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

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 over represented 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. The total population approach in the probabilistic risk assessment results in some probabilistic dilution, but on the other hand makes it easier to compare different risks. 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 probabilistic modelling

In work example 3 we demonstrate the differences between the consumers' only approach in probabilistic modelling opposed to the total population approach. The data as presented in work example 1 and 2 are used for explaining the differences. The interpretation of the outcomes when calculating the percentiles of exposure for foods together, the different results between the two methods and the difficulties that arise when risk is assessed commodities that are consumed by only a small portion of the population or food consumed infrequently will be discussed in this work example.

In the total population approach the percentile of exposure is always expressed for the same population. In the consumers' only approach, only the consumers are selected. This means that the underlying food consumption data are different for each compound-commodity combination. On the other hand, in the total population approach, the risk of commodities consumed rarely can be obscured due to probabilistic dilution.
From a conceptual point of view, it is more plausible to address consumption of different food items to assess the risk of being exposed to a certain pesticide via the diet. In the upper tail of the distribution, the exposure to more than one food item can be made visible (see also table 2B). When addressing the total population, the P99.9 and (P99.99) exposure levels were either equal or higher than the highest exposure level from one of the separate food items. A higher exposure level is calculated for one food compared to all foods together in the consumers' only approach, because calculations for one food are based on a subset of the population addressed for the foods together calculation. When addressing all foods simultaneously for consumers only, the P99.9 (and P99.99) of exposure were lower than the highest exposure level of one of the foods (table 1). The 'consumers only' database used when addressing more than one food containing the residue of interest, contains a mixture of persons who are consumers of a certain food (e.g. grape) and non-consumers of other foods in the list (e.g. plums, nectarine). This result in an exposure level, which is neither a population based exposure nor on a consumers' based exposure. By adding more food items to the list, the percentiles of exposure for all foods will decrease and theoretically reach the same value as the foods together estimate in the total population approach. For assessing P99.9 exposure levels for more than one commodity at the same time, the consumers' only approach is not preferable, because it may hamper clear risk management decisions.

Comparability of percentiles of exposure when using the total population approach is demonstrated in the carbaryl case for peach and plums (table 2A). For the 128 plum eaters in the total population, the P99.9 exposure level is 7.2 and for the lower number of peach eaters (n=92), the P99.9 exposure level is 4.7. In the consumers' only approach (table 1), the P99.9 value would on the other hand be larger for peach. So even though more people eat plums, the consumers' only approach would result in a different risk management decision for peach when for example the ARfD would be between these two P99.9 exposure levels. The risk of a person in the total population of eating fruits with high values of carbaryl on it would not effectively decrease.

For foods eaten infrequently, (e.g apricot which is consumed by only 0.1% of the study population), the P99.9 exposure is about 8 times smaller than for grapes in the consumers only approach. In the total population approach, the P99.9 exposure for carbaryl on apricot is 3300 times lower than for grapes, which is consumed by 2.2% of the population. On a population basis, the differences in risk are well understandable in the total population approach. However to protect the consumers when eating apricot, even if it is rarely eaten, a supplementary analysis is needed. A risk estimate based on the consumers only population should be presented, but the risk should be made comparable to the risk in the total population approach.

If such an approach is to be followed, discrepancy should be avoided between the calculations based on total population and the calculations based on the consumer only population. From a statistical point of view it is unreliable to calculate a 99.9 percentile for a very small number of consumers in relation to the number of field trial observations. It is therefore proposed to use a cut-off level for risk evaluation calculations that can be compared the outcome of the total population. This cut-off level can be calculated with the formula 100–(((100-P)/X)*100) percent, where P is the percentile of interest in the total population (e.g. 99.9%), X is the percentage of consumers related to the total population. An example is given in table 3. For four percentiles of exposure (P90, P95, P97.5 and P99), the results are given. The results for the consumers only are all lower than the point estimates, but in most cases higher than the total population approach. For apricot, cherries, nectarine and peach, the results are still not very reliable, because the number of consumers is still small. For grapes and plums, the P94 and P93 respectively should be chosen as cut-off, but even the P95 for consumers' only is below the value for the P99.9 for the total population.

Discussion is still necessary on the percentile the risk manager should use as a cut-off level for foods eaten infrequently. The above presented method is one option, but a higher percentile can also be chosen, even a small numbers of consumers in a consumers only concept. As presented in table 3, the simulated exposure model is sometimes based on only 1 consumer (e.g. apricot). For several reasons it is not recommended to focus on extreme high level in this consumers only concept;

1. It is not statistically correct to perform a large number of iterations with only 1 or a very limited number of consumers. The number of field trial data will then explain all variance in exposure assessment and the way variability is modelled. Using a parametric distrubution (beta-distribution) for variability and a decomposition model (e.g. large portion size will be split up into different edible portions) might overestimate the risk. A possible option is to include more consumers for a particular product by the use of other food consumption databases.
2. Endpoints in risk assessment should be consistent. A cut off point for the percentile of exposure in a consumers' only strategy should be in the same order of magnitude as the 99.9-percentile in the total population approach, covering a large number of consumers, who might eat large quantities or combinations of fruit and vegetables leading to high intakes. Whatever the cut-off level or approach, a risk managemer cannot exclude all the risk for a rarely eaten food item, because of insufficient data. This also accounts for the point estimate approach where the estimation of the large portion size is also based on very small numbers. When the risk manager addresses the very high percentiles in the consumers' only concept for rarely eaten food items, the risk managers has to be aware that such an approach has already been followed in the point estimate (first tier of a tiered approach). There is a need to refine the risk assessment and not to do redo the same type of calculations in a more complicated way.
3. Based on these three arguments it canbe concluded that refinement of risk management decisions should also include a probability of exceedance of the Acute Reference Dose, which is especially visible when rarely eaten food items are considered. Risk managers should aim at minimizing the probability of exceedance rather than ignoring it. This can be justified by the scientific arguments that the calculated risk is overestimating the real measured risk (duplicate diet study [Voet, Boon et al. 2003]) and the fact that monitoring data is usually much lower than field trial data. Even monitoring data can be considered conservative, because it does not include processing of the food (washing, cooking etc). It is also mentioned that a significant safety margin exist between the No Adverse Effect Level (NOEL) and the Acute Reference Dose. This safety margin is usually a factor 100 and the exposure estimates of *extreme* consumers are compared with the Acute Reference Dose.
4. When the percentage of consumers is less the 1 % (e.g. 0.1%) the above mentioned formulae 100–(((100-P)/X)*100) percent will result in a undesirable low percentile for the consumers only concept. It proposed that the P90 (or P 95) should therefore be taken as the lowest limit of risk assessment. The P95 might be considered as being the lowest risk assessment level when there are more then 10 residue levels above the LOD measured in a field trial.

Conclusion

We showed that with probabilistic modelling simulations can be made to assess exposure for all foods of interest, as opposed to only one food at a time in the point estimate. We demonstrated that using the consumers' only concept when addressing more than one food resulted in an overall exposure level that is not clearly 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 simulation of exposure for all foods together resulted in outcomes that were explicable. With the total population approach exposure as a result of eating more than one food item with the pesticide of interest can be assessed. In the total population approach P99.9 exposure levels are comparable, because they account for frequency of consumption. Due to probabilistic dilution, for foods eaten by a small percentage of consumers, an alternative approach might be necessary. Depending on the percentage of consumers, a lower percentile of exposure might be more logical, to allow comparison of risk estimates of the same order of magnitude. For a small number of consumers, the P99.9 level is not reliable either. It is recommended to use a cut-off level for risk evaluation calculations with consumers only of 100 – a/X percent, where X is the percentage of consumers related to the total population. For percentage of consumers below 1% this approach is not applicable. The P90 should therefore be taken as the lowest limit for risk assessment, even if percent of consumers is below 1%. Again, the foods together simulation for the consumers only resulted in exposure levels that were neither based on consumers only, nor on the total population. This results in attenuation of the true risk for the consumers only.

Table 3. Comparison of the point estimate and the probabilistic approach (in % of ARfD[1]) for carbaryl for consumers and the total population (work example 3).

compound, population and food	point estimate JMPR[3]	point estimate NLD[4]	probabilistic approach: Total population P99.9	consumers only P90.0	consumers only P95.0	consumers only P97.5	consumers only P99.0	% consumers[2]
carbaryl (ARfD = 0.2 mg·kg-1·d-1)								
children (1- 6 years)								
apricot	127	32	0.00	3.5	4.0	6.0	7.7	0.1 (1)
cherries	134	38	5.9	14	33	34	34	0.3 (3)
grape	1137	875	84	45	64	100	199	1.7 (18)
nectarine	82	144	2.6	12	20	29	38	0.3 (3)
peach	170	152	12.5	27	40	50	79	0.4 (4)
plum	158	140	27	17	25	33	42	1.4 (15)
foods together			94	31	46	64	108	

[1] ARfD = acute reference dose (= 0.02 mg ·kg-1·d-1)
[2] Number in brackets indicates number of consumers.
[3] JMPR = Joint FAO/WHO Meeting on Pesticide Residues.
[4] NLD = the Netherlands

Table 4A. 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 used (work example 4A)[2].

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

[1] ARfD = acute reference dose
[2] For more details, see text and annex 9.
[3] NLD = the Netherlands

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 raw agricultural commodities (RACs), including peel and (other) non-edible parts. These commodities 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.

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 large portion consumption for this food in the general Dutch population and young children (annex 9). 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 9, 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 large portion consumptions. 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.

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 4A). 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

Table 4B. 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 used (work example 4B).

population and processing type	point estimate	probabilistic approach	
	NLD[2]	total population	consumers only
general population			
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

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 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 large portion consumption. In the point estimate only one processing type at a time can be addressed, resulting often in the choice of the worst-case approach where no processing is addressed. For example in the case of apples, there are people who consume their apples either with or without peel. In the point estimate where only one situation at a time can be addressed, the worst-case assumption will be that nobody consumed peeled apples as opposed to the optimistic situation where everybody consumes peeled apples (table 4B). In food consumption surveys however 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, both consumers and non-consumers, the decision here would have been that methomyl is 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

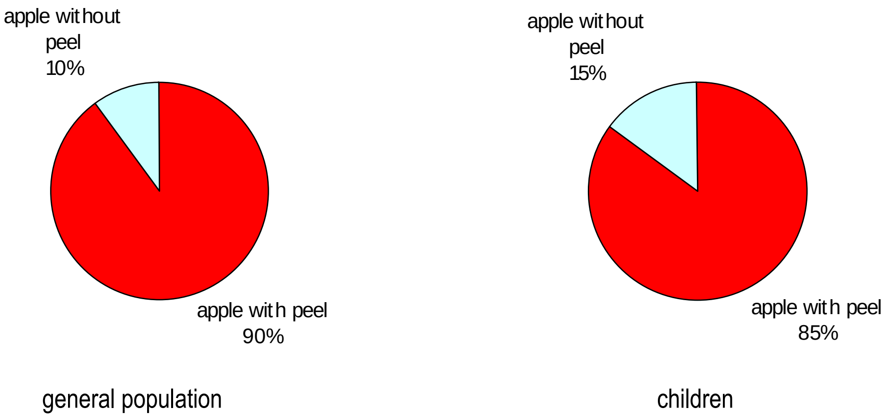

Figure 1. Contribution (%) of apple without and with peel to the total dietary exposure, addressing both consumers and non-consumers (work example 4B).

In work example 4 it was demonstrated that with the probabilistic approach different types of processing per food (peeling, not peeling, juicing) can be addressed in one analysis. When doing this each food type is linked to the correct variability factor (e.g. apples eaten whole are subjected to variability, while those mixed in juices are not). In the point estimate only one processing type 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 last JMPR meeting in 2003 it was decided to reduce the variability factor to 3 for all commodities as recommended by Hamilton et al. (2003; annex 5). The effect of this reduction on the exposure assessment was studied in this fourth work example. More details on how the model addresses variability can be found in the reference guide (http://www2.rikilt.dlo.nl/mcra/Referencemanual.pdf).

The point estimate exposures to aldicarb and carbaryl for the general population were recalculated applying the 'new' variability factor. Table 5A 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, using 'old' variability factors, an edible portion weight of 118 g (France) was used, while in 2003 this was changed to 438 g (Sweden). 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 factors. 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 5B). This resulted also in lower exposure levels, although less distinct compared to the point estimate approach (table 5A). Large decreases were seen for all foods together and for the food with the highest exposure level, grape. For the other foods the influence was minimal, due to the low exposure levels. The decision of allowing aldicarb and carbaryl for use on the foods 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 foods, when using the P99.9 of exposure as reference point and when addressing the general population. For children exposure levels would have been somewhat higher (see work example 2).

Table 5A 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).

compound and food	'old' varfac[2]		'new' varfac[3]	
	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	463[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.
[3] 'new' varfac is the variability factor of 3 as proposed by the 2003 JMPR meeting (personal communication)
[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. In the probabilistic approach the influence of lowering the variability factor was largest when considering all foods together or when dealing with one food that initially had a relatively high exposure level.

Table 5B 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).

compound and food	'old' varfac[2]		'new' varfac[3]	
	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
foods together	42	142	31	98

[1] ARfD = acute reference dose
[2] 'old' varfac are the default variability factors. See footnote 2
[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 foods listed in annex 6 were calculated. Calculations were performed for the general population and for children (1-6 years), considering both the total population and consumers only. For reasons of comparison the point estimates as calculated by the JMPR were included.

In table 6A we listed the exposures estimates for the general population and in table 6B 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, 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 6A and 6B) for both consumers and non-consumers. For an explanation see work example 2 (§ 3.4). The P99.99 of exposure for both consumers and non-consumers 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 foods together was a little lower than the highest exposure level calculated for one food (153% of the ARfD vs. 159% of the ARfD for tomato, respectively; table 6A). 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 all foods may be somewhat lower than to one food. However, the difference will always be very small and statistically not significant. Also the uncertainty in the P99.99 of exposure as discussed in work example 1 may play a role: the P99.9 exposure for all foods was always equal or higher than the exposure levels calculated per food when addressing both consumers and non-consumers as expected.

When addressing only the consumers of a certain food both the P99.9 and P99.99 of exposures increased compared to the situation where the total population was addressed (table 6A and 6B), as was also shown in work example 1. The levels of exposure frequently exceeded the corresponding point estimate exposure levels. Addressing consumers only resulted for the assessment of percentiles of exposure resulted in estimates that are complicated to interpret.
Compared to aldicarb and carbaryl, taking the P99.9 as reference point and using the total population approach (consumers and non-consumers), none of the three compounds would have been considered safe for use on the foods addressed. In other words, the P99.9 of exposure for all foods together exceeded or equalled (fenamiphos for children) the ARfD for all three compounds. In the exposure calculations performed we used however the 'old' variability factors (see work example 5 and footnote 2 of chapter 1) and no effect of processing was taken into account. Refinements of the calculations made are therefore possible by applying the newly proposed general variability factor of 3 (annex 5) and including information on processing effects. This will result in more realistic exposure estimations that will be lower than those presented in table 6A and 6B (see also work example 4 and 5).

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

compound and food	point estimate		probabilistic approach				% consumers[2]
			total population		consumers only		
	JMPR[3]	NLD[4]	P99.9	P99.99	P99.9	P99.99	
disulfoton (ARfD[3] = 0.003 $mg{\cdot}kg^{-1}{\cdot}d^{-1}$)							
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)
foods together			101	262	211	473	
fenamiphos (ARfD = 0.003 $mg{\cdot}kg^{-1}{\cdot}d^{-1}$)							
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)
foods together			74	153	117	213	
methomyl (ARfD = 0.020 $mg{\cdot}kg^{-1}{\cdot}d^{-1}$)							
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)
foods 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 6B. 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 food	point estimate		probabilistic approach				% consumers[2]
			total population		consumers only		
	JMPR[3]	NLD[4]	P99.9	P99.99	P99.9	P99.99	
disulfoton (ARfD[3] = 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)
foods 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)
foods 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)
foods 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

Conclusion
The results demonstrated in this work example are in line with the conclusions formulated in § 3.3 and § 3.4. Disulfoton, fenamiphos and methomyl were not considered safe for use on the foods addressed when all foods were addressed simultaneously in one analysis. Calculations were however performed using a default setting ('old' default variability factors, no processing). Refinements are therefore possible by using the newly proposed general variability factor of 3 and including information on processing effects in the calculations. These refinements will result in more realistic estimations of exposure that will most likely be reduced to those listed in tables 5A and 5B.

3.9 Conclusion and discussion

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

1. Work example 1: The consumers' only approach in probabilistic modelling results in somewhat lower or comparable outcomes as the point estimate approach. The total population approach generally resulted in much lower P99.9 exposure levels. Sometimes the result of a point estimate is overly conservative, because the calculated exposure level is out of the range of all possible exposure levels, when the reported large portion size was actually the portion size of a consumption from a person with a much higher body weight than the average body weight.

2. Work example 2 and 6: In general, point estimates result in higher estimates of exposure than the probabilistic approach, when considering the P99.9 of exposure. Compared to the Dutch point estimate, the P99.9 exposure level was sometimes higher for certain compound – food combinations, especially when considering only consumers of the food. The probabilistic approach takes a more holistic approach to risk, by addressing all consumption levels, all residue levels and all foods contributing to the exposure to a compound simultaneously into the exposure assessment.

   Aldicarb and carbaryl would have been considered safe for use on the foods addressed when the P99.9 had been selected as the reference point to be compared with the ARfD and when addressing the total population (both consumers and non-consumers). 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 (annex 5) and information on processing effects in the exposure assessment.

3. Work example 3: The population definition is not transparent in the consumers' only approach when addressing consumption of more than one food on one day. This approach may result in a lower overall exposure level compared to the exposure from one food. This may hamper a clear risk management decision. For calculating percentiles of exposure for all foods together, the total population approach is preferable. For population based risk assessment, the total population approach is also preferable. Only for foods eaten by a small part of the population, an additional exposure assessment for the comsumers' only is recommended. If both a total population and a consumers' only approach are followed, the result should be in the same order of magnitude. This can be achieved by comparing a lower percentile of the consumers' only calculation with the 99.9 percentile in a total population concept. The percentile to be chosen depends on the number of consumers and the statistical reliability of calculating a percentile based on a small number of observations.

3. Work example 4: In the probabilistic approach different processing types of one food (e.g. apple raw, apple juice, apple peeled) can be addressed simultaneously in one analysis. In the point estimate, each processed food is addressed separately. The use of large portion sizes (LP) that may contain a combination of processing types of one food (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. all people consume apple with skin), which may result in very conservative risk management decisions.

4. Work examples 4 and 5: In the probabilistic approach it is possible to address different (types of) foods simultaneously that should be treated differently with regard to variability (e.g. apple raw and apple juice).

5. In the work examples described in this chapter we used the P99.9 of exposure as cut-off point in risk assessment 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 choice of percentile that should not exceed the ARfD is a difficult issue. The choice 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). The quality of the underlying data is 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 US EPA defends their policy of using the P99.9 of exposure as a reference by stating that
   a. the residue levels used still include levels that are higher than those people actually consume for one or more commodities.
   b. their risk estimation methods incorporate sufficiently conservative approaches to provide sufficient protection for the small percentage of the population with exposure levels above the ARfD.
   c. given the size of the food consumption data used, the occurrence of an exceedance (at the P99.9) would be very infrequent for the typical individual. They state, that at the P99.9, the time between exceedances, on average, would be 2 to 3 years (US EPA 2000c).

   Point a may especially be true when using field trial residue data which are not representative of the levels people will be exposed to in normal life and which may be unrealistically high, resulting in the calculation of high exposure levels. 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.

   It is important that exposure levels at the level of the selected reference point are discussed in relation to the uncertainties in the database, and should also be considered in relation to the ARfD used. This is especially true when the level of the reference point used is close to or exceeds the ARfD.

6. 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 data bank 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 raw agricultural commodities (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 and 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 data bank 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) mustard). 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 raw agricultural commodities. 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 estimates 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 raw agricultural commodities. 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 (see www.barc.usda.gov/bhnrc/foodsurvey/).

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 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 only on those 12 years of age and above). Of approximately 10% of respondents (n=1,489) a second, non-consecutive, 24-hour 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-hour 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 January 2004 the practical possibilities will be viewed to make the food consumption database of Australia and New Zealand compatible with the MCRA-software.

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 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 was 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 are 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 food frequency method. 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 old, from all ethnic groups and provinces in South Africa, with over-sampling of children living in low socio-economic areas. The method used to quantify food consumption were the 24-h recall method and a quantitative food frequency method.
- *The Lebowa Study:* This study was undertaken in rural villages of the Northern Province in 1991. Dietary data (24-h recalls) were collected for 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- hour 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- hour 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 were obtained by means of a quantified food frequency method.

- *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 food frequency questionnaire.
- *Weight and Risk Factor Study:* In the WRFS survey dietary consumption data was obtained by means of a semi-quantitative food frequency questionnaire. 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) and again in 1983.

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

The 99.9 and 99.99 percentile 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 foods listed in annex 6 and using the field trial residue levels as listed in annex 7. 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 7 lists the P99.9 and P99.99 levels of exposure (as % ARfD) for the individual foods and for foods together of all four countries.

Table 7. Results acute dietary exposure assessment to carbaryl (in % of the ARfD[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 food	exposure level (%ARfD)	
	P99.9	P99.99
Denmark		
peach, nectarine, apricot	6	14
plum	1	2
grape	20	64
foods together	20	64
Sweden		
apricot	2	9
peach, nectarine	3	13
plum	4	17
cherries	1	6
grape	23	87
foods together	24	129
US		
apricot	0	8
peach, nectarine	20	65
plum	6	97
cherries	5	11
grape	127	480
foods together	119	467
the Netherlands		
apricot	0	5
peach	5	33
nectarine	4	22
plum	7	37
cherries	6	19
grape	33	143
foods together	42	142

[1] ARfD = acute reference dose

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, while the highest levels were calculated for the US (foods together; table 7). At the time of writing this report, the daily consumption data was not available yet for Denmark. The low Danish exposure levels can be explained by the fact that the consumption levels used were average consumption levels over 7 days. The high levels for the US are an overestimation, because no weighing was used for the difference in age distribution between their study population and 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 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 of chapter 1) 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 (annex 5) 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 foods 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. However, they are there and 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 needs, such as food consumption data. It is however recognised that food consumption data of different countries are not harmonised at all (Verger et al. 2002), making it difficult to compare exposure assessment derived from different 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 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 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. However, 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 raw agricultural commodities
Pesticide residue measurements are mainly performed in raw agricultural commodities (RACs). 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 RACs 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 RACs (Dooren et al. 1995). In this database also the type of processing a RAC has undergone is recorded. E.g. apple juice may be converted to RAC 'apple' with processing type 'juicing', and apple eaten peeled to RAC 'apple' with processing type 'peeling'. In this way the effect of processing on field trial residue levels in RACs 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 RACs is a quite extensive job, but recommended to make a link between residue levels derived from field trial studies 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 RACs. Another option is to link the field trial data to foods as eaten, selecting those foods that 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.

The year round surveys cover for seasonal variation, but it is complicated to get information on products consumed by only a selective part of the population. For example, some tropical fruits are consumed much more by people coming from abroad, but the are likely to be underreported in the study. Over reporting is another problem, because is especially affects the upper percentiles. Over reporting can result from the overestimation of ones own consumption or the overrepresentation of people who are more aware of healthy eating habits.
All uncertainties recognised for food consumption data applies for probabilistic modelling but also for the derivation of a large portion size data from these databases as used in the point estimates.
Advantages of probabilistic modelling are that all data are considered and that uncertainty or sensitivity analyses regarding the effect of these uncertainties can be performed.

5 UNCERTAINTIES IN RISK ASSESSMENT AND PROPOSITION OF A TIERED APPROACH

5.1 Uncertainties in Risk Assessment

Independent of the method used for risk assessment, uncertainties in the underlying assumptions are of influence on risk management decisions. Therefore they should be transparent. In principle, the same uncertainties that exist in risk assessment using point estimates exist in the probabilistic approach. However, some uncertainties have resulted in a precautious approach in the calculation of point estimates, where use of more complete data would have resulted in a more realistic risk assessment. An advantage of probabilistic modelling is the possibility to perform sensitivity analyses; the effect of the uncertainties on the results of the exposure assessment can be measured.

It has been recognised that many uncertainties exist in data that are drawn from food consumption studies. The real intake of fruits and vegetables might be under- or overestimated, due to recall bias, error in reporting etc. In food science and epidemiology it has been well recognised that consumption of fruit and vegetables can be overestimated. Such an overestimation certainly affects the higher percentiles of the exposure distribution. However, the error in the consumption distribution and overall consumption values is usually minor when the study population was large enough, but the extremes could just as well be outliers. The extremes in food intake (large portion size) have a large influence on the outcome of the point estimate, while the extreme consumptions might only occur rarely. In the probabilistic assessment the whole distribution of data is used.

Next to the uncertainties which are inherrent to all food consumption data surveys, there are additional uncertainties in the derivation of the large portion size (the 97.5 percentile). There are as far as known, no clear guidelines on how consumption from food as eaten has to be converted into raw agricultural products as used in the point estimates. It is also not clear which food items were included into the the P97.5-percentile of consumption of raw agricultural products and which were not. E.g some countries might have included apples eaten as such and apple juice when a 97.5 percentile of the raw agricultural product of apples was reported while other countries might have decided to include only apples eaten as such. This might be logical, because apple juice does not have to be included in case 2a of the point estimate.
There is also uncertainty in how well field trial data reflects the real exposure for a certain population. Not all pesticide applications will be done at the critical GAP, some might have longer Post Harvest Intervals or lower dose rates. It is, however, well recognised that monitoring residue levels are on average much lower than field trial residue levels. Only a very small percentage of the monitoring data may exceed the level of the field trial data used in the risk assessment. The overestimation of exposure by use of field trial data is supported by studies in the US (field trial data compared with the PDP data program) and by many other residue-monitoring databases.

5.2 True pesticide intake and validation study

The real exposure to pesticides is usually unknown, but some scientifically based studies are performed to validate the calculated intake of pesticides against the true measured intake. The real intake has been measured by using a duplicate diet study.
A validation study has been performed in an EU project on Monte Carlo Risk Assessment (Voet, Boon et al. 2003, [Lopez A, 2003 #1718]). Dutch monitoring data were compared from duplicate diets from 250 infants were compared with the results from probabilistic exposure assessment and with the point estimate IESTI calculated from the same data. The Monte Carlo model was considered to be validated for the intended application if the predicted 99^{th} percentile (p99) of the exposure distribution was higher than the estimate from the duplicate diet study, but lower than the point estimate. The main conclusion was that the traditional point estimate results in an enormous overestimation of the actual exposure as measured in the duplicate diet study. The Monte Carlo model provides much more realistic estimates, but the estimates were still conservative in the comparison with the duplicate diet results. For the six pesticides (Chlorfenvinphos, Chlorpyriphos, Iprodion, Methamidophos, Pirimicarb, Pirimiphos-mehtyl) studied, there was a gross overestimation of the real exposure to these pesticides. Depending on the percentile or the model assumptions made in the comparison, the overestimation was on average one or two orders of maginitude . This only applies for the six pesticides studied and it is unknown wether this applies for all pesticides.. However, it indicates that even when using monitoring data a serious overestimation of risk occurs and therefore the Monte Carlo results seem to be in accordance with the precautionary principle. A similar study has been performed in Spain and similar conclusions were drawn from this study as well (Lopez A et al. 2003).

5.3 Tiered approach in the US

In chapters 3 and 4 we demonstrated the use of the probabilistic approach when assessing the acute dietary exposure to pesticide residues. Especially in chapter 3 the potential of the probabilistic approach is demonstrated clearly. more information is on the probability of a certain exposure level, more than crop can be addressed, whole range of residue and consumption levels are considered.

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 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 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 employed 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.

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 (Suhre 2000, US EPA 2000b,d). The first two tiers are of a deterministic nature, 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 (Suhre 2000, US EPA 2000d, Wright et al. 2002).

5.4 Tiered approach in the 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 the development of 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 and will be discussed within the EU in the coming months.

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 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.

Another important 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 them in such a way that they 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 already being realised within the EU integrated project Safe Foods. This project starts in 2004 in which 30 research institutes from all over Europe and three from outside Europe (China, Cuba and South Africa) aim at the promotion of food safety through a new integrated risk analysis approach for foods. The EU integrated project 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), FDIR (Institute of Food Safety and Toxicology, 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 was 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.

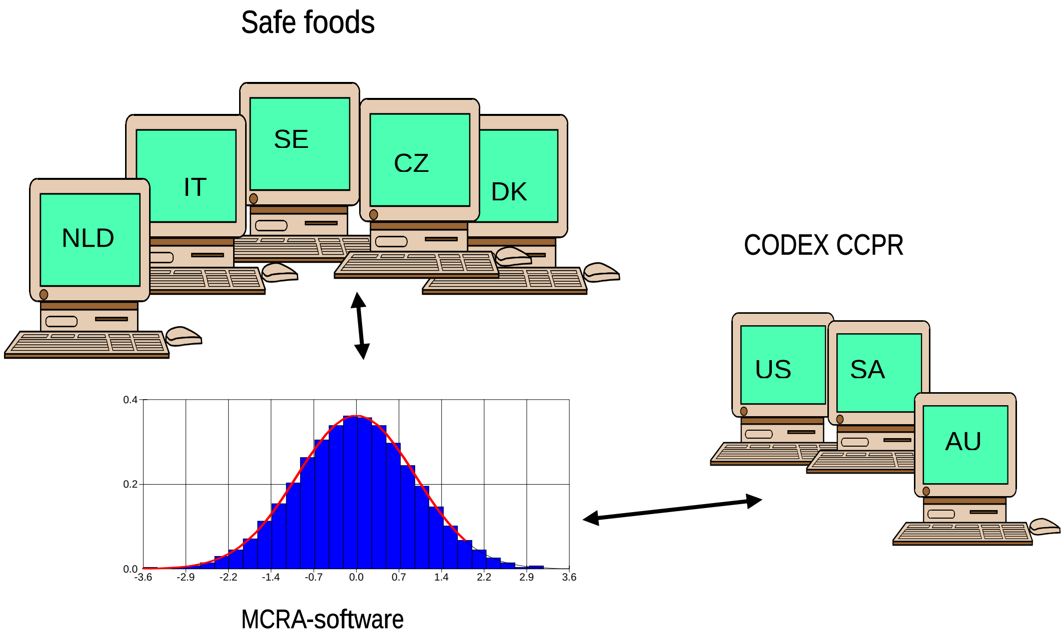

Figure 2. Conceptual network of different national food consumption databases linked to the MCRA (Monte Carlo Risk Assessment) software (NLD = the Netherlands, IT = Italy, SE = Sweden, CZ = Czech Republic, DK = Denmark, US = United States, SA = South Africa and AU = Australia / New Zealand.

This will result in a conceptual framework of different national food consumption databases that can be made compatible with 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 food per country.

7 CONCLUSIONS AND RECOMMENDATIONS

In this document we addressed the probabilistic approach to assess the acute exposure to pesticides via the diet, and compared this methodology with the one presently used worldwide, the point estimate approach.
In general it can be concluded that probabilistic risk assessment results in more complete and transparent data for risk management decisions, there are no computational restrictions, and no lack of models. For the total population approach, the P99.9 exposure levels are in general lower than the point estimates. For accurate and comparable calculations quality requirements are needed for the underlying consumption and residue databases.

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. The probabilistic approach takes a more holistic approach to risk, by addressing all consumption levels, all residue levels and all foods contributing to the exposure to a compound simultaneously into the exposure assessment. Both the single food exposure and the exposure assessed in the case of eating more than one food with the same residue on one day should be taken in consideration for risk management decisions. Also it is well recognised that probabilistic modelling is necessary when addressing cumulative and aggregated risk assessment (chapter 3).
4. In order to assess population based risks and to be able to assess exposure to a compound on more than one commodity eaten on one day, a total population approach may be the way to proceed in probabilistic modelling of acute exposure. This is also consistent with the US approach. Another factor that argues for this approach is that the European Union aims at a comparison of risks between countries in the future (SSC 2003), for which a total population based approach is better suitable. It is recognised that in the total population approach, risk may dilute when addressing the total population, especially when foods are consumed infrequently or by a small number of consumers. The calculation of percentiles of exposure for consumers' only gives valuable additional information for foods that are eaten by a small part of the population. It is also recommended to perform a probabilistic exposure assessment based on a consumers only approach in addition to the total population (both consumers and non-consumers) for rarely eaten food commodities.
5. The working group recognizes that for small numbers of consumers, the P99.9 exposure levels based on a consumers only approach are not reliable. Lower percentiles might be more appropriate for these groups. It is also desirable to make the results of both a total population and a consumers only concept consistent to avoid more strict regulation of rarely eaten products compared to commonly eaten food.
6. The working group recognised that many uncertainties will affect the result of any exposure assessment. Probabilistic exposure assessment makes these uncertainties visible, but the same uncertainties apply for the point estimate approach. Probabilistic exposure assessment, however, enables the risk manager to include sensitivity analyses.
7. Based on scientific research it is recognised that the calculated intake using probabilistic exposure assessment using monitoring data was one to two orders of magnitude higher than the real intake measured by a duplicate diet study. The study was done for six pesticides. It was also recognised that monitoring data is usually much lower than field trial data used in the risk assessment.
8. In order to be consistent with the US and the 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 ArfD and the safety margins (usually a factor 100) between the No Adverse Effect Level and the Acute Reference Dose. This is especially true when the reference point is close to or exceeds the ARfD (chapter 3). It should also be stated that the comparison between intake data and the Acute Reference Dose is based on consumers with extreme consumption patterns and not on consumers with average consumption patterns, as is the case when comparing intakes with the Acceptable Daily Intake.
9. 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 are available, as well as a model to which the data can be connected. We demonstrated that such a model exists (chapter 4).
10. Presently a significant number of international food consumption databases will or can be made compatible with the MCRA-software. Within the EU integrated project 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.

11. 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 is important for the acceptance of this methodology for acute dietary exposure assessments.

The most important recommendations are:

1. The working group recommends incorporating the probabilistic way of examining the exposure to an acutely toxic compound in a risk assessment procedure via a “tiered approach”. In a tiered approach relative 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 guidelines (US, EU) for reasons of comparison and consistency (chapter 5).
2. The working group recommends applying the “more than one food together” concept as a starting point for risk analysis. The rationale is that the risk of total daily intake of a residue is of concern from the consumers’ point of view, not the intake from one commodity. The working group realises that that so far, there is little experience with this approach.
3. The working group recommends always performing calculations using the total population approach when using probabilistic risk assessment in a tiered approach. Firstly because in this concept, the exposure to the pesticide of interest can be calculated when individuals consume more than one food item on one day. Secondly, because with this concept a population based risk estimate is attained, in which risk estimates are comparable and the frequency of consumption is included.
4. The working group recommends addressing the total population concept and calculating the 99.9 percentile of exposure for comparison with the acute reference dose. The working group also recommends that when addressing food items eaten infrequently, to additionally calculate percentiles of exposure using the consumers’ only concept. To make the outcomes of the calculations comparable, a lower percentile of exposure should be chosen for the consumers’ only approach. A cut-off level for risk evaluation calculations with the consumers’ only approach could be calculated as 100–(((100-P)/X)*100) percent, where P is the percentile of interest in the total population (e.g. 99.9%), X is the percentage of consumers related to the total population. (as a simple cipher, e.g. 5 for 5%) and not lower than 90-percentile.
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 methodology. 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), but it should not hamper the progress of probabilistic modelling for the JMPR/CCPR, because incompatible databases are considered to be already an improvement.
6. Guidelines should be developed on how to deal with the results of probabilistic modeling in a tiered approach in a consistent way. These guidelines should also address the contradictory outcomes regarding acceptability of use of a compound when using databases from different countries. For representative results, requirements on the quality and quantity of the input data (e.g. minimal number of consumers, consumption database to select) should be made clear.
7. We propose to form a project team consisting of database managers from databases most likely to be used in probabilistic risk 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.

REFERENCES

Andersen NL, Fagt S, Groth MV, Hartkopp HB, Møller A, Ovesen NL, Warming DL (1996). Dietary intakes for the Danish population 1995 (Publication no. 235). Søborg: The National Food Agency of Denmark.

Becker W (1999). Riksmaten 1997 - 1998. Svenskarna äter nyttigare - allt fler väljer grönt (Riksmaten 1997 - 1998. The Swedes eat more healthy). Voar Föda, 51, 24-7.

Boer WJ d, Voer H vd, Boon PE, Donkersgoed G v, Klaveren JD v (2003). MCRA, a GenStat program for Monte Carlo Risk Assessment, Release 2, User Manual. Wageningen: Biometris and RIKILT - Institute of Food Safety, Wageningen UR

Boon PE, Voet H vd, Klaveren JD v (2003). Validation of a probabilistic model of dietary exposure to selected pesticides in Dutch infants. Food Additives and Contaminants, 20 Suppl 1, 36-49.

CCPR (2000). Report of the thirty-second session of the Codex Committee on Pesticide Residues (ALINORM 01/24). The Hague, The Netherlands: Codex Alimentarius Commission (http://www.codexalimentarius.net/).

CCPR (2001). Report of the thirty-third session of the Codex Committee on Pesticide Residues (ALINORM 01/24A). The Hague, The Netherlands: Codex Aimentarius Commission (http://www.codexalimentarius.net/).

CCPR (2002a). Discussion paper on the methodology of cumulative risk assessment (CX/PR 02/4). The Hague, The Netherlands: Codex Alimentarius Commission (http://www.codexalimentarius.net/).

CCPR (2002b). The probabilistic approach to acute dietary exposure analysis and its applicability at the international level (CX/PR 02/3-Add.1). The Hague, The Netherlands: Codex Alimentarius Commission (http://www.codexalimentarius.net/).

CCPR (2002c). Report of the thirty-fourth session on the Codex Committee on Pesticide Residues (ALINORM 03/24). The Hague, The Netherlands: Codex Alimentarius Commission (http://www.codexalimentarius.net/).

CCPR (2003a). Dietary exposure in relation to MRL setting: discussion paper on proposals for improvement methodology for point estimates of acute intake of pesticide residues (CX/PR 03/3). Rotterdam, The Netherlands: Codex Alimentarius Commission (http://www.codexalimentarius.net/).

CCPR (2003b). Report of the thirty-fifth session of the Codex Committee on Pesticide Residues (Report No: ALINORM 03/24A). Rotterdam, The Netherlands: Codex Alimentarius Commission (http://www.codexalimentarius.net).

Dooren MMH v, Boeijen I, Klaveren JD v, Donkersgoed G v (1995). Conversie van consumeerbare voedingsmiddelen naar primaire agrarische produkten (RIKILT Report 95.17). Wageningen: RIKILT-DLO (*in Dutch*).

FAO/WHO (1997). Food consumption and exposure assessment of chemicals. Report of FAO/WHO Consultation, Geneva, Switzerland, 10-14 February 1997 (WHO/FSF/FOS/97.5). Geneva: World Health Organization.

FAO (2002). Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. FAO Plant Production and Protection Paper 170, Rome.

Gregory JR, Collins DL, Davies PSW, Hughes CL, Clarke PC (1995). National Diet and Nutrition Survey: children aged 1½ and 4½ years. Volume 1: Report of the diet and nutrition survey. London: HMSO.

Gregory JR, Lowe S, Bates CJ, Prentice A, Jackson LV, Smithers G, Wenlock R, Farron M (2000). National Diet and Nutrition Survey: young people aged 4 to 18 years. Volume 1: Report of the diet and nutrition survey. London: TSO.

Hamilton DJ, Ambrus Á, Dieterle RM, Felsot AS, Harris CA, Kuiper HA, Petersen B, Racke KD, Wong S-S, Gonzalez R, Tanaka K, Earl M, Roberts G, Bhula R. Pesticide residues in food – acute dietary exposure. *In press.*

Harris CA (2000). How the variability issue was uncovered: the history of the UK residue variability findings. Food Additives and Contaminants, 17, 491-5.

ILSI (2002). Towards harmonised guidance on applying probabilistic methods to assess operator exposure to plant protection products. Brussels, Washington DC: ILSI Europe and ILSI Risk Science Institute.

Kistemaker C, Hulshof KFAM, Bouman M (1998). De consumptie van groepen voedingsmiddelen naar maaltijdtypering - Voedselconsumptiepeiling 1997-1998. (TNO Report 98.809). Zeist: TNO-Voeding (*in Dutch*).

Nel JH, Steyn NP (2002). Report on South African food consumption studies undertaken amongst different population groups (1983 - 2000): average intakes of foods most commonly consumed. Pretoria: Directorate: Food Control, Department of Health (http://www.health.gov.za).

SCP (1998). Opinion of the Scientific Committee on Plants regarding the inclusion of aldicarb in annex 1 to Directive 91/414/EEC concerning the placing of plant protection products in the market (SCP/ALDIC/041-Final). Brussels: Scientific Committee on Plants, EU.

SSC (2000). First report on the harmonisation of risk assessment procedures - The Report of the Scientific Steering Committee's Working Group on Harmonisation of Risk Assessment Procedures in the Scientific Committees advising the European Commission in the area of human and environmental health. Brussels: Scientific Steering Committee, EU.

SSC (2003). The future of risk assessment in the European Union. Second report on the harmonisation of risk assessment procedures. Brussels: Scientific Steering Committee, EU.

Suhre FB (2000). Pesticide residues and acute risk assessment - the US EPA approach. Food Additives and Contaminants, 17, 569-73.

US EPA (1997). Guiding principles for Monte Carlo analysis (EPA/630/R-97/001). Washington DC: National Center for Environmental Assessment, Office of Research & Development, US Environmental Protection Agency.

US EPA (1998). Guidance for submission of probabilistic human health exposure assessments to the Office of Pesticide Programs (Report No: 6021). Washington DC: US Environmental Protection Agency.

US EPA (2000a). Assigning values to non-detected/non-quantified pesticide residues in human health food exposure assessments (Report No: 6047). Washington DC: US Environmental Protection Agency.

US EPA (2000b). Available information on assessing exposure from pesticides in food. A user's guide. Washington DC: US Environmental Protection Agency.

US EPA (2000c). Choosing a percentile of acute dietary exposure as a threshold of regulatory concern (Report No: 6046). Washington DC: US Environmental Protection Agency.

US EPA (2000d). Guidance for refining anticipated residue estimates for use in acute dietary probabilistic risk assessment (Report No: 6063). Washington DC: Office of Pesticide Programs, Office of Prevention, Pesticides, and Toxic Substances, US Environmental Protection Agency

US EPA (2001). General principles for performing aggregate exposure and risk assessments (Report No: 6043). Washington DC: Office of Pesticide Programs, Office of Prevention, Pesticides, and Toxic substances, US Environmental Protection Agency (http://www.epa.gov/pesticides/trac/science/aggregate.pdf).

US EPA (2002). Guidance on cumulative risk assessment of pesticide chemicals that have a common mechanism of toxicity. Washington DC: Office of Pesticide Programs, Office of Prevention, Pesticides and Toxic Substances, US Environmental Protection Agency.

Verger P, Ireland J, M/oller A, Abravicius JA, De Henauw S, Naska A (2002). Improvement of comparability of dietary intake assessment using currently available individual food consumption surveys. European Journal of Clinical Nutrition, 56 (Suppl 2), S18-S24.

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

WHO (1997). Guidelines for predicting dietary intake of pesticide residues (GEMS/Food Document, WHO/FSF/FOS/97.7). Geneva: World Health Organization

Wright JP, Shaw MC, Keeler LC (2002). Refinements in acute dietary exposure assessments for chlorpyrifos. Journal of agricultural and food chemistry, 50, 235-41.

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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 7out 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 data base 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

DAY 3 (9.00 till 12.30)

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

DAY 1

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

<u>DAY 2</u>

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*

2.9 IMPROVING ESTIMATES OF DIETARY INTAKE

The Meeting considered the areas where the estimations of dietary intake could be improved. It was concluded that the calculations are greatly simplified by the automated spreadsheet applications elaborated by RIVM/SIR[3], The Netherlands, in co-operation with WHO/GEMS/Food. However the calculated values cannot be better than the data-base or estimated factors used. For many Codex commodities for which maximum residue levels, STMR(-P)s and HR(-P)s are estimated, no dietary intake is available. Consequently, immediate refinements could be achieved by:

- improving the accuracy of consumption figures for long-term exposure by introducing the proposed 13 sub-regional diets which have been discussed in recent years by the CCPR and JMPR instead of the currently used five regional diets;
- the increased availability of large portion sizes and unit weights for the calculation of short-term exposure, especially those from developing countries.

Further improvement could be obtained by:

- evaluation of the studies submitted to the JMPR in the last decade representing typical commercial processing to investigate whether it would be possible to derive default processing factors and/or extrapolate processing data;
- refinement of generic and commodity-specific variability factors as used in the short-term intake calculations;
- elaboration of procedures for probabilistic modelling at the international level.

The last two points are discussed further below.

The 35th Session of the CCPR (ALINORM 03/24A, paras 20-31) discussed the paper "Discussion paper on the proposals for improvement methodology for point estimates" [of acute intake of pesticide residues] (CX/PR 03/3). The Report of the Session (para 28) states "The Chair summarized the discussion that: (1) the possibility of accepting limited exceedance should not be considered at present time; (2) the possibility of using a tiered approach could be considered in the future; and (3) JMPR should be asked to mention the probabilistic aspects in the point estimates, when the results exceed the acute RfD."

The Committee also requested the JMPR to consider this paper especially in relation to the use of probabilistic aspects of point estimates.

The Committee also agreed to establish a Working Group to prepare a paper on the possible adoption of probabilistic methodology for the purpose of setting Codex MRLs. This should include worked examples of probabilistic calculations for some compounds, using supervised trials data, where the IESTI exceeds the acute RfD. The Working Group should also discuss and propose parameters to be used in probabilistic calculations at the international level, and the paper should be considered by the next Session of the Committee.

In response, the Meeting agreed in principle to adopt a tiered (i.e. sequential) approach to estimating short-term dietary intake, in which the second tier could be probabilistic modelling. However it also recognized the lack of consumption data and the lack of an available model validated at the international level, which hamper the development of such a second tier. It observed that a possible solution would be to ask the country from which the large portion as used in the JMPR point estimate came, to provide the second tier. However, this would necessitate international consensus on the parameters used in the probabilistic model. The Meeting therefore welcomed the initiative of the CCPR in deciding to establish a Working Group on this subject. The Meeting noted that a probabilistic model useful for JMPR purposes is under development in The Netherlands (RIKILT, Institute of Food Safety) and agreed that it would consider this model when available.

The Meeting took note of the IUPAC report on short-term dietary risk assessment[4] and on the basis of the evidence presented there agreed to use in future a new default variability factor of 3 in the calculation of residue levels in high-residue units used in point estimates of short-term intake. See also Item 2.10.

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[3] National Institute for Public Health and the Environment (RIVM); Centre for Substances and Integrated Risk Assessment (SIR)

[4] Hamilton D, Ambrus A, Dieterle R, Felsot A, Harris C, Petersen B, Racke K, Wong S, Gonzalez R, Tanaka K, Earl M, Roberts G and Bhula, R. 2003. Pesticide residues in food – acute dietary exposure. Submitted for publication.

In the situation that the IESTI exceeds the acute RfD, the Meeting agreed to indicate in the section on Dietary Risk Assessment ways in which those parameters used in the dietary risk assessments which are based on conservative assumptions might be refined.

2.10 IESTI CALCULATIONS: REFINING THE VARIABILITY FACTOR FOR ESTIMATION OF RESIDUE LEVELS IN HIGH RESIDUE UNITS

Current JMPR procedures for estimating the short-term dietary intake of pesticide residues rely on the deterministic procedures proposed by the FAO/WHO Consultation in 1997[5].

The Consultation proposed methods for calculating short-term intake (1) where the residue in a composite sample reflects the residue level in a meal-sized portion of the commodity, and (2) where the meal-sized portion such as a single unit of fruit might have a higher residue than the composite. The concept of the variability factor was introduced to calculate the residue level in that single unit, originally with the conservative assumption that all of the residue might be in one unit of the composite sample. For fruit such as apples the variability factor was 10 because 10 apples were expected in a typical composite sample.

The 1999 JMPR[6] summarized the methods for calculating the short-term intake of residues and reported the results of such calculations for the first time. The 1999 Meeting, taking into account the available data, used a variability factor of 7 for most items (>25 g and <250 g), a value of 5 for large items (>250 g) and a value of 10 for granular soil treatments and leafy vegetables.

The 2002 JMPR, on the basis of new data, concluded that a variability factor of 3 would be suitable for residues in head lettuce and head cabbage.

At the 35th Session of the CCPR (Paras 20-31, ALINORM 03/24A, 2003) the delegation of The Netherlands introduced a discussion paper on improved methodology for point estimates of dietary exposure in relation to setting MRLs. An unpublished IUPAC report on short-term dietary risk assessment had been used in the preparation of the paper. The CCPR agreed to establish a Working Group to prepare a paper considering the adoption of probabilistic methodology for the purpose of setting Codex MRLs. The same Session also requested the JMPR to consider possible improvements in the point estimates.

The IUPAC report[7], now submitted for publication, summarized and analysed the available data on residue level variability from unit to unit for a number of pesticides over a range of crops (apples, carrots, celery, grapes, kiwifruit, lettuce and potatoes).

In cases where the number of unit analyses was large enough to provide 95% assurance that at least one value exceeded the 97.5th percentile, the average variability factor (97.5th percentile value of residue ÷ mean) was 2.7 (range 1.5-7.2) for supervised trials involving approximately 8000 unit analyses. The average variability factor was 3.0 (range 2.4-3.5) for market-place monitoring data involving almost 3000 unit analyses. Most of the estimated variability factors were in the 2.0-3.0 range for the 30 sets of data representing trials and market-place monitoring.

The variability factor did not generally seem to be dependent on the pesticide or the crop. However in one trial with a post-harvest application of a mixture of 3 compounds on apples there appeared to be a separation of the compounds during the post-treatment drainage of the fruit, with one of the compounds producing substantially higher residues in fruit at the bottom of the stack. Variability factors for the three compounds were 7.2, 2.8 and 2.5. In this instance the variability factor was dependent on the pesticide in combination with the method of treatment.

The Meeting agreed to adopt a default variability factor of 3 for the estimation of residue levels in high-residue units in the IESTI calculations where unit weights exceed 25 g. A variability factor is not used in IESTI calculations where unit weights are below 25 g.

The current practice will continue of using specific unit variability factors in preference to the default value where the supporting data are available, valid and sufficient.

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[5] WHO, Food consumption and exposure assessment of chemicals. *Report of a FAO/WHO Consultation, Geneva, Switzerland, 10-14 Feb, 1997*. Document WHO/FSF/FOS/97.5 (1997)

[6] FAO. Dietary risk assessment for pesticide residues in food, in Pesticide residues in food – Report 1999. *FAO Plant Production and Protection Paper* 153:21-25 (1999).

[7] Hamilton D, Ambrus A, Dieterle R, Felsot A, Harris C, Petersen B, Racke K, Wong S, Gonzalez R, Tanaka K, Earl M, Roberts G and Bhula, R. 2003. Pesticide residues in food – acute dietary exposure. Submitted for publication.

ANNEX 6. Compounds and foods to be considered in the work examples

compound	foods 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 in $mg \cdot kg^{-1}$

ANNEX 7. Field trial residue levels used in the calculations of the point estimate and the probabilistic approach

compound and food	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 8. 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 for individual units a measure for the variability between units within a composite sample needs to be specified, namely a coefficient of variation (CV). The CV of the individual units in a composite sample is equal to the standard deviation divided by the mean of these individual units, which is then converted to parameters *a* and *b* of the beta distribution. Following this definition we need residue levels on individual units within a composite sample to calculate the CV. However these were not available. We therefore estimated the CV per food - pesticide combination based on the default variability factor used in the point estimate and the number of units in a composite sample (table 8). 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).

REFERENCES

FAO/WHO (1997). Food consumption and exposure assessment of chemicals. Report of an FAO/WHO Consultation, Geneva, Switzerland, 10-14 February 1997 (WHO/FSF/FOS/97.5). Geneva: World Health Organization.

FAO (2002). Submission and evaluation of pesticide residues data for the estimation of maximum residue levels

Table 8. Coefficient of variation used in the probabilistic approach based on the default variability factor and number of units in a composite sample.

default variability factor[1]	number of units	coefficient of variation
3	4 - 30	0.8
5	6 - 30	1.4
7	8 - 30	1.9
10	11	2.5
	20	2.6
	30	2.8

[1]Based on the default variability factors as listed on the WHO GEMS/food website.

in food and feed. FAO Plant Production and Protection Paper 170, Rome.
Voet H vd, Boer WJ de, Boon PE, Donkersgoed G v, Klaveren JD v (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 9. 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·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·kg^{-1})	1.6	-
STMR (mg·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