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Cumulative dietary exposure to a selected group of pesticides of the triazole group in different European countries according to the EFSA guidance on Probabilistic modelling.

(paper ready for submission)

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Contents

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Abstract

The practicality was examined of performing a cumulative dietary exposure assessment according to the requirements of the EFSA guidance on probabilistic modelling within the assessment context of periodic reviews of monitoring data on actual exposures (EFSA, 2012). For this the cumulative exposure to triazole pesticides from acute and chronic Cumulative Assessment Groups (CAGs) was estimated using national food consumption and monitoring data of eight European countries. Both the acute (eight countries) and chronic (two countries) cumulative dietary exposure were calculated according to the two model runs (optimistic and pessimistic) as recommended in the EFSA guidance. The exposures obtained with the two model runs differed substantially for all countries, with the highest exposures obtained with the pessimistic model run. In this model run, animal commodities including cattle milk and different meat types, entered in the exposure calculations at the level of the MRL, contributed most to the exposure. We conclude that application of the optimistic model run on a routine basis for cumulative assessments is feasible. The pessimistic model run is laborious and the exposure results could be too far from reality. More experience with this approach is needed to stimulate the discussion of the feasibility of all the requirements, especially the inclusion of MRLs of animal commodities which seem to result in unrealistic conclusions regarding their contribution to the dietary exposure.

1. Introduction

In October 2012, the European Food Safety Authority (EFSA)'s Plant Protection Products and their Residues (PPR) panel published a guidance on the use of the probabilistic methodology for modelling dietary exposure to pesticide residues (EFSA, 2012). In this guidance, the panel proposes a methodology for performing probabilistic dietary exposure assessment of single and multiple active substances, both acute and chronic, in the assessment contexts of authorisation, enforcement actions and periodic reviews of monitoring data on actual exposures. Two different model runs are proposed to address these different contexts, namely an optimistic and a pessimistic model run. In the optimistic model run the major uncertainties are treated using assumptions that are expected to result in underestimates of exposure, whereas in the pessimistic model run these uncertainties are treated in such a way that it is expected to result in overestimates of exposure. The outcomes of both model runs can be used to determine whether further refinement of the assessment is useful. In this paper we address the feasibility and practicality of this guidance document regarding the performance of a cumulative dietary exposure assessment to pesticide residues within the context of periodic reviews of monitoring data on actual exposures.

For this, the acute cumulative dietary exposure was estimated to a group of pesticides from the triazole group belonging to an acute Cumulative Assessment Group (CAG) (Table 1; acute effect: cranio-facial toxicity) as identified in a scientific opinion of the PPR panel on cumulative exposure (EFSA, 2009). The exposure was estimated following the requirements of both model runs. National food consumption data were combined with national monitoring data, including available information on the effect of processing on pesticide residues if appropriate. Information on unit variability was included in the pessimistic model run. Additionally, for two countries the chronic cumulative exposure was calculated for the group of triazole pesticides of the chronic CAG (Table 1; chronic effect: hepatoxicity) according to both model runs. Calculations were performed with the Monte Carlo Risk Assessment (MCRA) software version 8, developed to facilitate cumulative exposure assessments {van der Voet, 2014 #2928}. This new version of the software includes the assessment components needed to calculate the cumulative exposure according to both the optimistic and pessimistic model run.

2. Materials and Methods

2.1. National food consumption data

All national food consumption databases included in this study refer to the data that are part of the Comprehensive database of EFSA (EFSA, 2011c). The food consumption data used in this paper are described below (see also Table 2). For more detailed descriptions references per food consumption survey are given.

2.1.1. Cyprus (CY)

In CY, a national study evaluating the frequency of eating disorder cases (Cyprus Study on eating disorders among High School students, "Child Health") was conducted in 2003. Food consumption data were collected of 303 children, aged 11 to 15 years using a 3-day estimated dietary record. Most, but not all, dietary records were collected during consecutive days. Amounts consumed were estimated using food package sizes and household measures (e.g. cups and spoons).

2.1.2. Czech Republic (CZ)

In CZ a food consumption survey (SISP04) was conducted between November 2003 and 2004 covering a 1-year period (Ruprich et al., 2006). In this national study 2177 persons aged 10–90 years were asked about their eating habits via two 24-h recalls. The repeated recall was within a period of 1–6 months after the first recall and addressed another day of the week. Amounts consumed were estimated using either photographs of portions for the most frequently consumed meals, or measuring guides, such as spoons and cups.

2.1.3. Denmark (DK)

For DK food consumption levels derived from the National Food Consumption Survey conducted in 2000–2002 were used (Lyhne et al., 2005). In this survey 4120 persons aged 4–75 years were asked to record their food consumption during seven consecutive days using the 7-d dietary record method. Amounts consumed were estimated using photographs of portion sizes or household measures (e.g. cups and spoons).

2.1.4. France (F)

The French food consumption data were derived from the second French Individual National Food Consumption Survey (INCA 2) conducted between December 2005 and May 2007 (AFSSA, 2009; Dubuisson et al., 2010; Lioret et al., 2010). Two independent population groups were included in the study: 2,624 adults aged 18-79 and 1,455 children aged 3-17. Subjects were asked to complete a

seven-day food record diary (consecutive days). Participants estimated portion sizes using photographs or expressed by weight or household measures (spoons, cups, etc.).

2.1.5. Italy (IT)

For IT food consumption data collected by the Italian Agricultural Research Council - Research center for food and nutrition (CRA-NUT), former National Research Institute on Food and Nutrition (INRAN), during the period of 2005-2006 were used. In this survey, named INRAN-SCAI 2005-06 (Leclercq et al., 2009), information on food consumption was collected from 1,329 households randomly selected. The individual food consumption levels were quantified using a consecutive 3-day dietary record. Amounts consumed were estimated using a photographic booklet. Food consumption data were collected from 3,323 individuals aged 0-97 years.

2.1.6. The Netherlands (NL)

The food consumption data from NL were those of the Dutch National Food Consumption Survey of 2003 (Ocké et al., 2005). In this survey 750 persons aged 19–30 years were asked about their eating habits via two independent computerized 24-hour dietary recalls administered by telephone. The repeated recall was within a period of 7-14 days after the first recall and on another day of the week. Amounts consumed were estimated using photographs of portion sizes or household measures.

2.1.7. Sweden (SE)

Food consumption data from SE were those of the 'Riksmaten' study (Becker and Pearson, 2002). This dietary study was performed in 1997–1998 among 1211 respondents aged 18–74 years. Participants were asked to record their food consumption during seven consecutive days using the 7-d dietary record method. Amounts consumed were estimated using pre-printed quantity indications in household measures and photographs of portion sizes or household measures. It was also possible to record food consumption in free text.

2.1.8. United Kingdom (UK)

Food consumption data from the UK were derived from the National Diet and Nutrition Survey (NDNS) of 2000-2001 among 1,724 adults aged 19 to 64 years living in private households in Great Britain (Hoare et al., 2004). Participants completed a weighed dietary record for seven consecutive days.

All the national food consumption databases covered all seasons of the year and days of the week, excluding holidays and festive periods due to divergent food habits during those periods. All surveys obtained non-food characteristics, including sex, age and body weight.

2.2. National monitoring programmes for pesticide residue data

EU Member States perform annually analyses of pesticides mainly on raw agricultural commodities (RACs) intended for human consumption to monitor the occurrence of pesticide residues and to check compliance with the maximum residue limits (MRLs) as set in Regulation (EC) No 396/2005 (EC, 2005). These analyses are performed as part of national monitoring programmes undertaken by the Member States' authorities and as part of an EU-wide programme co-ordinated by the European Commission {EC, 2007 #2660}. In this paper we used national monitoring results of the acute and chronic CAG group of triazole pesticides sampled in the period 2007–2010. All countries in our study had monitoring results for these pesticides. Table 3 gives an overview of the residue concentration data per country. RACs and chemicals analysed were all classified via the same coding system, namely the coding system as used in Annex I to Regulation (EC) 396/2005 (EC, 2005) and the PARAM code as used in the Standard Sample Description (EFSA, 2010), respectively.

The monitoring data obtained as part of the EU coordinated monitoring are untargeted. National monitoring programmes, however, may contain samples that are targeted to particular RACs, regions, etc. suspected to contain higher residue levels. Inclusion of these samples may result in an overestimation of exposure, but may also cause underestimation because certain pesticides and/or RACs are not expected to result in exceedances of the MRL may be neglected. In the databases used in this paper, targeted samples were removed from the assessment if clearly identified, but it cannot be excluded that the databases still contained samples obtained via targeted sampling. The effect of this is considered as part of the evaluation of unquantified uncertainties.

2.3 Linking food consumption and concentration data

The food consumption data used in this study were obtained from the Comprehensive database compiled by EFSA (EFSA, 2011c). Foods recorded in this database are classified with the FoodEx1 coding system (EFSA, 2011b). To link food consumption data to the RACs analysed, consumption data of foods were converted to consumption data of these commodities. For this purpose, a conversion database was used which was developed as part of the EFSA project 'Development of a database of conversion factors to transform foods coded according to FoodEx into Raw Agricultural Commodities (RACs), NP/EFSA/DATEX/2010/02" (Boon et al., 2013). In this conversion database FoodEx1 codes used in the Comprehensive database are linked to their RAC ingredients, including weight percentages, based on information in the Dutch food conversion database (Boon et al., 2009; van Dooren et al., 1995). In this Dutch database, foods classified in different Dutch food consumption

surveys are converted to their edible RAC ingredients based on the composition of the foods (e.g. how much tomato in 100 g of pizza) and conversion factors (e.g. how much raw endive is needed to produce 100 g boiled endive). To convert FoodEx1 codes based on the information in the Dutch database, FoodEx1 codes were first linked to the most appropriate Dutch food code, resembling best the food in question. When a comparable food was not present, additional information was obtained to convert the food into its ingredients based on the name of the food and the national codes linked to them within the Comprehensive database. Since all national food consumption surveys used in the present study were classified using FoodEx1, the developed conversion database could be used to translate the consumption of foods recorded in all food consumption surveys to their RAC ingredient(s). The result was eight national food consumption databases with food intake estimates converted to RAC intake estimates. By using the same classification system for RACs analysed for pesticide residues in monitoring programmes (see Section 2.2), pesticide concentration data can be linked directly to consumption data. As part of the conversion of FoodEx1 codes to their RAC ingredients, processing types were also identified and linked to the RAC. For example, FoodEx1 code Apple juice was converted to RAC Apple linked to processing type “Juicing”. In this way, processing factors could be included in the assessment.

2.4. Dietary exposure modelling according to EFSA Guidance

The EFSA guidance on the use of probabilistic methodology for modelling dietary exposure to pesticide residues includes an overview on how to address the different assessment components of an acute and chronic exposure assessment in an optimistic and pessimistic model run. Table 4 summarises the most important components for both model runs per assessment type. Below we elaborate on some of these components.

2.4.1. Pesticide residue data

Monitoring data from national monitoring programmes were used in the exposure assessments per country. Ideally all samples have been measured for all pesticides belonging to both CAGs. In reality however, samples may have missing values (MVs) because not all pesticides are analysed in a sample, or the number of samples analysed is too low to result in a reliable exposure estimate.

In the optimistic model run, these possible shortcomings of the concentration data are ignored. In this model run, only the available monitoring data from the national monitoring programmes are used in the exposure assessments (Table 3 and 4). In the pessimistic model run MVs or too few monitoring data should be supplemented with concentration data from other sources to avoid possible underestimation of the exposure (EFSA, 2012). This is however only true for pesticide - RAC combinations with an authorised use for which positive results cannot be excluded. Given the

wide range of commodities available on the market as well as the wide range of countries from which these commodities can originate, establishing the pesticide authorisation status per pesticide - RAC combination is potentially a very lengthy and complicated process. In this study, we therefore took a pragmatic approach by using the presence of a maximum residue limit (MRL) in Regulation (EC) No 396/2005 (EC, 2005), made available via the MRL database on the Commission website[1], as an indication of whether the pesticide is allowed for use or not. An MRL set at the lowest practicable limit of quantification (LOQ) (indicated by * in the MRL database) was interpreted as no authorised use for the pesticide on that specific RAC.

For each country, a national pessimistic concentration database was generated by establishing first for which pesticide - RAC combinations with an authorised use, no or too few residue data were present in the different national monitoring databases. Too few residue data were defined as less than eight samples present in the national database; the same criterion used in the case study for a single pesticide assessment published as Appendix 3 to the EFSA guidance (EFSA, 2012). Authorised pesticide - RAC combinations with no or too few residue data were supplemented with residue data of the same combination obtained from the other countries included in the project. Furthermore, MRLs for animal commodities were included in the national pessimistic databases to also consider exposure via this route of exposure. MRLs for animal commodities were obtained from Regulation (EC) No 396/2005 (EC, 2005). For drinking water 0.1 µg/L was used for each of the five most toxic pesticides (defined as the five triazole pesticides of the acute CAG with the highest Relative Potency Factors (RPF): bitertanol, cyproconazole, epoxiconazole, flusilazole, triadimefon) (Table 1). To ensure that all metabolites, degradates or other transformation products are included in a dietary exposure assessment, residues quantified according to the residue definition for monitoring (as used in the monitoring programmes) should be adjusted to the residue definition for risk assessment by applying a conversion factor (EFSA, 2012). For all triazole pesticides this conversion factor equalled 1: the observed concentrations could be used directly in the cumulative dietary exposure assessment.

2.4.2. Processing factors

Changes in pesticide residue levels due to processing are the result of possible disappearance due to for example volatilisation or solubilisation in water or oil of the residue during processing. Information on processing used in the optimistic and pessimistic model runs was obtained from the German database developed by the Federal Institute for Risk Assessment[1]. This database contains information on processing factors from different sources including reports and evaluations by the

[1] www.bfr.bund.de

FAO/WHO Joint Meeting on Pesticide Residues (JMPR), draft assessment reports (DAR) prepared in the European Pesticide Risk Assessment Peer Review programme (PRAPER), from Reasoned Opinions on the modification and/or the review of existing MRLs prepared by EFSA and from residue data which have been submitted within the framework of national authorisation procedures. In the pessimistic model run, the highest individual measured processing factor is to be used if higher than 1 (EFSA, 2012). Since the German database contains only the deterministic values as to be used in the optimistic model run, we examined the original data to establish whether higher values than 1 were reported. This was done for those processing types for which we expected processing factors higher than 1, such as drying and oil extraction. For an overview of the processing factors used in the assessments as well as the source of information, see Appendix I.

Changes in residue concentrations can obviously also arise from weight changes of the RAC itself (e.g. drying or cooking of fruits / vegetables), and are also included in a processing factor. This effect on the residue level is however also included in an exposure assessment via the conversion database (section 2.3). To avoid that this effect is applied twice when estimating the dietary exposure, relevant processing factors were corrected for weight change by using the appropriate conversion factor available from the conversion database. In this way, the processing factor included only the effect of degradation, and could be used in combination with the conversion database to estimate the dietary exposure. Processing was included as a fixed factor in all exposure calculations (Table 4).

2.4.3. Variability in pesticides concentrations between individual units of composite samples

Pesticide residue analyses in monitoring programs are typically performed in composite samples of RACs (e.g. apples are analysed in samples consisting of 12 units each), while people usually consume smaller portions of a fruit or vegetable (e.g. one unit). Because concentrations may vary in individual RAC units, consumers may thus be confronted with higher concentrations in single units (e.g. one apple) than the averaged concentration as analysed in composite samples. To account for this possibility, unit variability factors are used in acute dietary exposure assessment of pesticides.

In the EFSA guidance only limited direction is given on how to implement unit variability in an acute probabilistic exposure assessment (EFSA, 2012). We therefore followed the same approach as taken in the case study for a single substance assessment published as Appendix 3 to the EFSA guidance (EFSA, 2012). In this case study, a random composite-sample residue level was assigned to each randomly selected consumed amount obtained from the consumption databases. If necessary, consumed amounts were divided into portions not larger than the unit weight of the RAC. For each portion, a stochastic variability factor was applied to the composite-sample residue level to derive a

single unit residue level. The stochastic variability factors were drawn from a beta distribution with a variability factor (ratio 97.5th percentile to mean) of 5, which was scaled between 0 and the number of units in a composite sample (Table 4). For example, in this way a single apple residue level could be maximally 12 times the composite-sample level. This is a different variability factor than used in the deterministic approach (3 and 7 depending on unit weight). For the RAC unit weights, we used those of the EFSA PRIMo database, available at the EFSA website[2]. If a unit weight was not available, we selected the most likely unit weight of a similar product. The number of units in a composite sample was derived from EU guidance document 'Guidelines for the generation of data concerning residues as provided in Annex II part A, Section 6 and Annex III, part A, Section 8 of Directive 91/414/EEC concerning placing plant protection products on the market', Appendix B[3]. For an overview of the unit weights and number of units in a composite sample used per RAC, see Appendix II.

The simulation of residues for individual units is only relevant for a pessimistic acute exposure assessment, and only for RACs with a unit weight ≥ 25 g. In all other cases (optimistic model run, chronic assessment, unit weights < 25 g), it was assumed that the composite-residue level represents the level to which people are exposed to when consuming the RAC. This was also the case for processed foods, such as fruit juices and apple sauce.

2.5. Cumulative exposure calculation

Acute and chronic cumulative exposure to the acute and chronic CAG of triazole pesticides was calculated using the 'Monte Carlo Risk Assessment' programme (MCRA 8.0, available for registered users at the RIVM website {van der Voet, 2014 #2928}). The procedures as described in the EFSA guidance for performing an acute or chronic cumulative exposure assessment according to both model runs are implemented in MCRA 8.0. These procedures consist of the conversion of single compound concentration databases to cumulative concentration databases containing cumulative residue levels per sample. For this Relative Potency Factors (RPFs) are used. These factors describe the toxic potency of each individual compound belonging to a CAG relative to a predefined 'index compound' and are used to express the pesticide residue levels per sample in equivalents of this index compound (EFSA, 2008). Subsequently, these adjusted residue levels served as input for the cumulative exposure assessment. For the two CAGs, we used the RPFs as published in the scientific opinion of the PPR panel on cumulative exposure with fluzilazole as index compound for the acute CAG and cyproconazole as index compound for the chronic CAG (EFSA, 2009) (Table 1).

[2] www.efsa.europa.eu/en/mrls/docs/calculationacutechronic_2.xls
[3] ec.europa.eu/food/plant/protection/resources/app-b.pdf.

For the optimistic and pessimistic cumulative model runs, the optimistic and pessimistic national databases (section 2.4.1.) were used as input for the generation of national cumulative databases as described above. In this process, MVs and levels below the LOR were treated differently. In the generation of the optimistic cumulative databases, these values were all treated as real zeros. In the national databases to be used in the chronic pessimistic cumulative assessment, levels below the LOR were assumed to equal to the LOR in case of authorised use and the still remaining MVs for which no residue data from other partners were available (section 2.4.1.), were assumed to be zero. In the pessimistic acute cumulative databases, also these still remaining MVs were imputed following the algorithm as documented by EFSA (EFSA, 2012). In short, after setting all residue levels below the LOR to LOR, the MVs were imputed by sampling residue levels at random from a lognormal distribution of residue levels as fitted on other samples of the same pesticide – RAC combination as present in the pessimistic national databases. MVs of samples with an already high RPF-weighed summed concentration based on the available residue data for this sample were subsequently inputted with the highest sampled residue values.

For the estimation of the acute cumulative exposure per country according to the optimistic model run, 100,000 randomly drawn daily consumption patterns of RACs from the national RAC consumption databases were multiplied with randomly selected cumulative residue levels per RAC derived from the relevant national optimistic cumulative databases. Summing over RACs resulted in an empirical estimate of the acute cumulative exposure distribution to the acute CAG. In the pessimistic model run, the same approach was taken, except that the summed residue data were not selected at random from the samples available in the databases, but were first modelled parametrically. This was done to allow for the possibility that the observed data may not completely represent the residue levels to which people are exposed in practice and that in reality residue levels below, between and above the observed values also may be present. For this, a “NondetectSpike-LogNormal” model was fitted to the residue data per RAC when the number of positive data points was at least two. In this model the residues < LOR are replaced by the LOR, and a lognormal distribution is fitted to the positive values. If the number of positive data points was less than two (e.g. only MRLs), the data were sampled empirically as in the optimistic model run.

For the chronic cumulative exposure assessment, the Observed Individual Mean (OIM) approach was used to assess the dietary exposure in both model runs per country {EFSA, 2012 #2917}. In short, daily RAC consumption patterns were combined with mean summed residue levels derived from either the optimistic or pessimistic cumulative database, and added over RACs consumed per day per individual. These daily exposure levels were averaged over the number of days present in the food consumption database per individual, resulting in a distribution of average cumulative exposure levels.

The acute cumulative exposure following both model runs was estimated for all countries and, if the food consumption data allowed, for the adolescents age class (10-17 years) and adults (18-64 years) as defined by EFSA for the Comprehensive database (EFSA, 2011c). The chronic exposure was performed for two countries, DK and IT. These two countries were selected because their food consumption databases covered a wide range of ages, including children and adults, which were all included in the assessment (Table 2). All estimated exposures were adjusted for the individual's self-reported body weight (bw) and expressed as daily exposure in µg/kg bw/d. Following the EFSA guidance, the exposure results were reported as the number of person-days (acute) or persons (chronic) per million that exceeded exposure levels of 100% of the acute reference dose (ARfD) or acceptable daily intake (ADI) of the reference compounds. The ARfD for flusilazole was 500 µg/kg bw/d for the common effect of cranio-facial toxicity and the ADI for cyproconalzole equalled 20 µg/kg bw/d for the common effect of hepatotoxicity (EFSA, 2009). We also reported the 99.9th percentile (P99.9) of the cumulative exposure distributions, as well as the top 3 products and compounds contributing most the exposure per model run, exposure type, country and age class. All cumulative exposure assessments were made for the whole population (rather than consumers only).

2.6. Uncertainty analyses

To quantify the uncertainties in the exposure estimates due to sampling uncertainty of consumption and residue input data, the bootstrap method was used with the exception of the residue data in the acute pessimistic scenario (Table 4). With the bootstrap method a bootstrap database is generated of the same size as the original database for both the food consumption and residue database by sampling with replacement from the original datasets (Efron, 1979; Efron and Tibshirani, 1993). These two bootstrap databases are then used for the exposure calculations to derive the relevant output parameters. Repeating this process many times results in a bootstrap distribution for each output parameter that allows for the derivation of confidence intervals around it. For this, we generated per model run, exposure type, country and age class 100 food consumption and 100 cumulative residue bootstrap databases and calculated the cumulative exposure with 10,000 iterations each. Of the resulting bootstrap distributions we computed a 95% uncertainty interval by computing the 2.5% and 97.5% points of the empirical distribution for the number of person-days or persons per million that exceeded exposure levels of 100% of the ARfD or ADI and the P99.9 of exposure.

In the acute pessimistic model run, the sampling uncertainty due to the residue input data was modelled parametrically as required by the EFSA guidance (EFSA, 2012). The approach taken and implemented in MCRA is the one described in the guidance. In short, in this approach a binomial

distribution is used to model the fraction of positive samples, and an inverse chi-square distribution is used to model the uncertainty of the estimated fraction due to a limited number of measurements. The positive residues are modelled by a lognormal distribution, and another normal distribution is used to model the uncertainty of the mean log-residue. The uncertainty distributions were estimated and used to sample new parameters for the residue distributions in each uncertainty iteration. In this way residue levels were sampled from modified residue distributions in each iteration.

Apart from sampling uncertainty, cumulative exposure assessments are affected by many other sources of uncertainty which cannot be quantified. Following the requirements described in the EFSA guidance, we evaluated these uncertainties using the tabular approach as recommended by EFSA (2006). This evaluation of unquantified sources of uncertainty was performed for the acute pessimistic cumulative exposure assessment.

3. Results

3.1. Assessment of acute cumulative dietary exposure to triazole pesticides per country and age class: optimistic versus pessimistic model run

3.1.1. Exposure

In the optimistic model run, none of the simulated exposures per country and age class exceeded the ARfD, whereas in the pessimistic model run person-days with simulated exposures exceeding the ARfD were observed for only IT: 10 person-days per million in adults and 20 in adolescents, with a 97.5% upper confidence limit of 200 and 100 per million, respectively. The P99.9 of exposures per country, age class, and model run are listed in Table 5. In the optimistic model run the best estimate of the P99.9 for adults ranged from 1.2 µg/kg bw/d in SE up to 3.2 µg/kg bw/d in CZ. Corresponding numbers for the adolescents were 0.34 µg/kg bw/d in CY and 7.6 µg/kg bw/d in CZ. The P99.9 exposures increased for all countries in the pessimistic model run, up to 137 µg/kg bw/d in adolescents living in IT (Table 5). All estimated P99.9 exposure levels were below the ARfD.

3.1.2. Contribution RACs and pesticides

The top 3 RACs contributing most to the cumulative acute exposure to triazole pesticides per country, age class and model run are listed in Table 6. In the optimistic model run, banana and pineapple contributed most to the exposure in both age classes, followed by apple and tomato. In the pessimistic model run, animal commodities were the most important contributors to the exposure in almost all countries with 'Milk, cattle' as the most predominant contributor. In IT tomato contributed most to the exposure (Table 6).

The triazole pesticides contributing most to the exposure in the optimistic approach were bitertanol and triadimefon in both age classes, summing up to a total contribution of more than 90% in most countries (Table 7). In the pessimistic approach, bitertanol remained one of the compounds contributing most to the exposure but at lower percentages (on average 30%), followed by cyproconazole and triadimefon.

3.2. Assessment of chronic cumulative dietary exposure to triazoles: optimistic vs. pessimistic

3.2.1. Exposure

The chronic cumulative exposure was calculated for the total population of DK and IT. The resulting exposures are listed in Table 8 per country and model run, including the number of persons with an exposure level exceeding the ADI of the index compound cyproconazole (20 µg/kg bw/d), and the

P99.9 of exposure. In the optimistic model run no exposures were simulated exceeding the ADI. However in the pessimistic model run, 64,806 persons per million had a simulated chronic exposure that exceeded the ADI in DK, with a 97.5% upper confidence limit of 71,900. Corresponding figures for IT were 43,635 and 48,900, respectively. The P99.9 of chronic exposure exceeded in both countries the ADI in the pessimistic model run.

3.2.2. Contribution RACs and pesticides

Table 9 lists the top 3 RACs and triazole pesticides contributing most to the chronic exposure in both countries. As in the acute assessment, animal commodities replace the vegetable products in the pessimistic model run compared to the optimistic model run as the main contributors to the exposure (Table 8). The triazole pesticides contributing most to the exposure included bitertanol and difenoconazole in the optimistic model run, and bitertanol and flusilazole in the pessimistic model run (Table 8).

4. Discussion

In this paper, we examined the practicality of performing a cumulative dietary exposure assessment according to the requirements of the EFSA guidance on probabilistic modelling within assessment context periodic reviews of monitoring data on actual exposures (EFSA, 2012). For this the cumulative exposure to triazole pesticides from acute and chronic Cumulative Assessment Groups (CAGs) was estimated using national food consumption and monitoring data of eight European countries. Both the acute (all countries) and chronic (two countries) cumulative dietary exposure were calculated according to the two model runs as recommended in the EFSA guidance (EFSA, 2012). The exposures obtained with the two model runs differed substantially for all countries. The pessimistic model run, as expected, resulted in the highest exposures. In this model run, the animal commodities, entered in the exposure calculations at MRL, contributed most to the exposure, including cattle milk and different meat types. The true exposure to the triazole pesticides will be between the estimates obtained with the two model runs.

4.1. Practicality of the EFSA guidance

Using the Monte Carlo Risk Assessment (MCRA, version 8.0) software, developed within the EU project ACROPOLIS (REF), cumulative assessments according to the requirements of the optimistic and pessimistic model runs can be performed easily. Within the software, the special settings of both model runs are clearly indicated, making it easy to select the right parameters. The most laborious part of performing a cumulative assessment according to the EFSA guidance is the preparation of the monitoring databases for the pessimistic model run. In the optimistic model run, preparation of the monitoring data was straightforward and feasible to perform. The monitoring concentration data used were the same as those sent on a yearly basis to EFSA via the Data Collection Framework (DCF) according to the Standard Description Data (SSD) model for analytical measurements in food and feed (EFSA, 2010). Given this standardised coding system, the data of all countries could be prepared in a standardized manner for the exposure calculations. The preparation of the pessimistic concentration databases was however far more laborious, due to two elaborate steps: 1) determination of the authorised uses (including import tolerances) of the substances, and 2) supplementing or replacing concentrations with residue concentrations for those RACs for which no or insufficient observed values were available in the national monitoring data. Determination of the authorised uses is potentially a lengthy process, given the wide range of RACs available on the market as well as the wide range of countries from which these commodities can originate. In this study, we therefore took a pragmatic approach by using the presence of an MRL in Regulation (EC) No 396/2005 (EC, 2005) as an indication whether the substance is allowed for use or not. An MRL set at the LOQ (indicated by * in the MRL database) was defined as no authorised use for that specific

RAC. This is an assumption that may not always have been correct. MRLs are set at LOQ when no authorisation is requested for a certain pesticide-RAC combination, when the use of the pesticide has not left detectable residues or when its use is not safe at MRLs above LOQ. Because of this, it is possible that some pesticide-RAC combinations were identified as non-authorised uses whereas in reality the use of the pesticide is allowed on the crops. This may also be true for RACs imported from outside Europe, and, furthermore, also within Europe there are differences in authorised uses of pesticides between the northern, central and southern region. Due to all of this, it may be that use of the MRL database to establish authorised uses may have resulted in an erroneous imputation of concentration data in the pessimistic model run. The overall expectation is that due to this the exposure was more likely under- than overestimated, due to more probable erroneous assumptions of non-authorised than authorised uses. The approach taken to establish authorised uses was identical to the approach taken by EFSA when performing an indicative chronic cumulative risk assessment in the framework of the 2010 EU Report on Pesticide Residues (EFSA, 2013). Given the complexity of establishing the authorisation status which may change within one year, more suitable databases should be developed that provide information on authorised uses of pesticides for individual RACs to remove or reduce substantially this source of uncertainty related to this assessment component.

After authorised uses have been established, RACs with no or too few observed values for a certain substance in the national databases are to be supplemented or replaced (step 2 of preparing a pessimistic concentration database (EFSA, 2012)). In this study, we used for this purpose, if available, residue concentrations for the same pesticide-RAC combination present in the national monitoring data of the participating countries. Furthermore, animal commodities and water were included in the assessment at the corresponding MRLs. Via this approach, it was ensured that pesticide residue values were available for all commodities expected to contain the pesticide. To facilitate the process of supplementation an Access database was prepared to standardise this. This database followed the requirements of the EFSA guidance, except that the supplementation of MVs and insufficient residue data for authorised uses was restricted to residue data available in the national monitoring databases of the participating countries. Insufficient monitoring data were not replaced with supervised trial/feeding studies or MRLs or supplemented with monitoring data of commodities for which there are established extrapolations (EFSA, 2012). The different databases covered in total 200 different commodities. This included all major foods with authorised use for at least one of the triazole pesticides including apple, banana, wheat, peaches, tomato, etc. The commodities with authorised use for at least one of the triazole pesticides that were not included in the assessment due to lack of monitoring data in all participating countries, included only some minor crops such as several herbs and spices (e.g. anise, caraway, saffron). Given very low or even

absent consumption figures for these commodities, it is not expected that the exposure was significantly affected by neglecting to include these RACs.

The used criterion for supplementation of the monitoring data was < 8 samples per pesticide – RAC combination. The EFSA guidance recommends supplementation when either the assumed lognormal distribution based on ≥ 2 positive monitoring values results in simulated residues unlikely to occur even rarely, or < 2 positive monitoring values are available (EFSA, 2012). Given the complexity of judging when 'residues unlikely to occur very rarely' are simulated, as well as the laboriousness of repeating the process for all residue values simulated, we applied, for practical reasons, the same criterion as used in the case study for a single substance assessment to supplement insufficient residue data (Appendix 3 of (EFSA, 2012)). In this case study, < 8 samples for a RAC-pesticide combination was deemed insufficient to produce a reliable estimate of the exposure as a consequence of consumption of that RAC. Due to this, pesticide-RAC combinations with > 8 samples but with no positive values were not supplemented, making them unsuitable for parametric modelling, needed for the imputation of residues in the pessimistic cumulative residue vector (Appendix 1 of (EFSA, 2012)) and to model the pessimistic cumulative exposure to the acute CAG of triazole pesticides. The same was true for commodities that also after supplementation contained < 2 positive values. Given this observation, as well as the limited number of residues above LOR detected in the national monitoring programmes (Table 3), the majority of residues imputed in the pessimistic cumulative residue vector, as well as the cumulative residue levels used to calculate the exposure were obtained with empirical modelling. Modelling concentration data using a lognormal distribution will result in the generation of additional residue levels that fall below, between and above the observed values obtained in the monitoring programme. The simulated values above the observed values may result in the simulation of higher residue values than the observed ones and thus in higher exposures. We assess that due to empirical instead of parametric modelling, the exposures reported here may have been slightly less conservative than aimed at in the pessimistic approach (EFSA, 2012).

Apart from the preparation of the monitoring data, another laborious step of both model runs (acute and chronic) is the collection of the processing data, given the many pesticide-RAC-processing type combinations possible within a cumulative dietary exposure assessment. The use of the summary information on processing factors as provided by the German database developed by the Federal Institute for Risk Assessment (BfR)[1] was very useful, but the link with concentration databases containing data of multiple substances and RACs needs to be optimised for use on a routine basis. Furthermore, in the German database only the deterministic values as to be used in the optimistic model run are recorded. In the pessimistic model run, the highest individual measured value should be used if higher than 1 (Table 4). For this, it is necessary to go back to the original data.

Inclusion of this information in the BfR database would be helpful to further optimize the use of this database for exposure assessment purposes.

The overall conclusion is that the optimistic model run can be easily performed on a routine basis, whereas the pessimistic model run is far more laborious. Especially the preparation of the pessimistic concentration database is prone to mistakes. An automated process needs to be developed to make this feasible to be performed on a routine basis. The Access database prepared for this as part of this study may be a first step in this direction, but needs further optimization to make it more universally applicable, for example by inclusion of also other concentration data sources (e.g. from field trial studies). Also the criterion that supplementation should be considered when the assumed lognormal distribution results in simulated residues that are unrealistic may need further discussion on what is to be assumed unrealistic. The development of a database providing information on authorised uses of pesticides for individual RACs is also strongly recommended.

4.2. Optimistic and pessimistic model run

In the EFSA guidance an optimistic and pessimistic model run are proposed to perform probabilistic exposure assessments of pesticide residues via diet (EFSA, 2012). The outcomes of both model runs can be used to determine whether further refinement of the assessment is useful. The two model runs are defined in such a way that they relate to the range of possible exposures that may occur in real life, although given the settings of both model runs, the optimistic run will very likely underestimate and the pessimistic run overestimate the real exposure. In practice, underestimation of the exposure in the optimistic approach is primarily due to an incomplete monitoring database and the use of composite-sample residue levels instead of potential higher residues in individual units. The pessimistic model run, on the other hand, is very conservative, mainly, in our example, due to the use of MRLs for animal commodities.

Only a very limited range of animal commodities are included in national monitoring programmes, because residue levels are expected to be present at such levels that infringements of MRLs are not likely to occur. Because of this, little monitoring data are likely to be available for these commodities and MRL data need to be used. Due to this and because consumptions of some of these food items may be substantial (e.g. milk), the exposure in the pessimistic model run, both acute and chronic, may be driven by animal products, as shown in the present study (Table 7 and 9). In the monitoring data available in this study, three countries reported on observed residue levels of triazole pesticides in animal commodities, namely CY, DK and F. DK had the most extensive dataset with concentrations of all triazole pesticides analysed in bovine meat, honey, milk cattle, poultry meat, sheep meat and swine meat, ranging from 20 honey samples up to 655 swine meat samples. In CY, some of the triazole pesticides were analysed in samples of eggs chicken, honey, milk cattle, milk

sheep and swine meat, ranging from three honey samples up to 60 samples of eggs chicken. In F, one sample of milk cattle was included in the national dataset. These monitoring data were not included in the pessimistic model run (acute and chronic), but, for reasons of comparison and to follow the requirements of the EFSA guidance, were replaced by the MRL. All observed residue levels in these samples were reported to be below the LOR, so either no residue was present or it was present in quantities below LOR. These results indicate that the inclusion of animal commodities at the level of the MRL in the pessimistic database is very likely a very conservative assumption, resulting in unrealistically high levels of exposure. Given these findings, inclusion of animal commodities at levels lower than the MRL (e.g. a (small) fraction of the MRL or at the level of the LOR) may already be a conservative choice resulting in an exposure that may be less dominated by animal commodities and therefore more plausible, since animal commodities are not seen as a major source for pesticide exposure. This will also prevent that these commodities that were not regarded as a problem in the past regarding pesticide exposure, may become an issue without real cause. More experience is needed as to whether the dominance of animal commodities in the pessimistic model run as reported here is reproducible, as well as with other scenarios for including animal commodities in a pessimistic exposure assessment. The pessimistic model run also very likely results in higher exposures compared to the optimistic model run by the inclusion of unit variability and of processing factors at levels of 1 or higher, and by parametrically modelling of the residue data. Probabilistic assessments are seen as higher tier assessments, resulting in more refined and realistic exposure estimates compared to deterministic approaches using simple equations and single (conservative) input values (WHO, 2009). In the pessimistic model run it is questionable whether the input variables and model settings are not chosen in such a way that the outcome is even more worst-case than of a deterministic assessment.

In 2009 a study was published regarding the cumulative exposure to triazole pesticides assigned by EFSA as input for the scientific opinion on the risk assessment of this group of pesticides of the PPR Panel (van Klaveren et al., 2009). The acute exposure results for the countries also included in the present study were in line with those of the optimistic model run (Table 10). The results of the pessimistic model run were much higher. The reason for this is that the settings and input data used in the acute assessment reported by van Klaveren et al (2009) were more similar to those of the optimistic model run. Van Klaveren et al (2009) also used only national monitoring data in the assessments, applied processing factors if available, and assigned a zero concentration to all residues below LOR. Also the RPFs used were the same. However, their calculations also differed from the optimistic model run in that they applied variability factors to simulate concentrations in individual units (as done in the pessimistic approach) and missing pesticide-RAC combinations (authorised use but no analytical results) were supplemented with analytical results in comparable

RACs analysed in the same country. Also the methodology to cumulate the exposure differed. In the study of van Klaveren et al (2009), first the acute and chronic exposure distribution per triazole pesticide was calculated. Using the relevant RPFs, the exposure distributions per pesticide were subsequently added to generate an acute or chronic cumulative dietary exposure distribution expressed in equivalents of the relevant index compound. This approach was used because it did not include assumptions regarding imputation of MVs in the pesticide matrix. In the optimistic model run, MVs were assigned a zero value. When there are many samples in which not all pesticides belonging to a CAG are analysed, which is the case in the present study, the optimistic approach may result in lower estimates of exposure compared to the methodology used by van Klaveren et al (2009). Given these differences the expectation would be that, for the optimistic model run, the acute cumulative exposure reported by van Klaveren et al (2009) would have been higher than the exposure reported here. Comparing the exposures calculated for the two countries, addressing the same target population (Adults, IT and SE), showed that this was true for IT. For SE the estimated exposure by van Klaveren (2009) was however lower than reported here. Since the consumption databases used were similar this may have been due to differences in contamination levels. Van Klaveren et al (2009) used the Swedish monitoring data of 2003-2006. The chronic exposure reported by van Klaveren et al (2009) was much lower compared to the results presented here for both model runs. Also here the same CAG was considered as well as the same RPFs. The most likely explanation for this lower exposure is the use of a statistical model to estimate the chronic exposure by van Klaveren et al (2009) as opposed to calculating the mean exposure over the available days in the food consumption databases as used in both model runs, referred to as the Observed Individual Means approach (OIM) (EFSA, 2012). OIM tends to overestimate upper tail exposures in chronic exposure assessment (Boon et al., 2011; Boon et al., 2012). The use of statistical models for chronic exposure is expected to result in more realistic estimates of chronic exposure. In the EFSA guidance these models may be applied as part of the refined assessment (EFSA, 2012).

For all countries no cumulative exposures (acute and chronic) were simulated higher than the ARfD or ADI of the index compounds in either age classes in the optimistic model run (Table 8). In the pessimistic model run however, for IT (acute and chronic; Table 8) and DK (chronic; Table 8) exposures were simulated that exceeded the relevant reference values. If these exceedances are deemed unacceptable from a health point of view, the assessment needs to be refined to arrive at more realistic exposure estimates (EFSA, 2012). These estimates should be somewhere in between the exposure estimates obtained with the optimistic and pessimistic model run. In the EFSA guidance some indications are given on how to arrive at such a refined assessment, but further discussion is needed to clarify the specific requirements, including the input data (e.g. parametric modelling of food consumption, treatment of residues below LOR, unit variability, processing). To refine a chronic

assessment, the use of a statistical model that corrects the exposure for the within person variation is the most obvious first choice, if feasible {Goedhart, 2012 #2929} Also, guidance is required on when a refined assessment is needed. For this, a decision is required on the number of person-days (acute) or persons (chronic) exceeding the toxicological reference value that is associated with an unacceptable health risk.

4.3 Acute versus chronic cumulative exposure to triazole pesticides

Exposures to pesticide residues present in food is normally related to acute risks. Chronic risks are often negligible (EFSA, 2010, 2011a, 2013). In the cumulative exposure assessments reported here for DK and IT this was true for the optimistic model run (Table 5 and 8): on average the P99.9 of exposure was 7.5 times higher in the acute assessment compared to the chronic assessment. However in the pessimistic model run the chronic exposure assessment resulted in a larger number of exceedances of the relevant toxicological health limit than in an acute exposure assessment (Table 8). A very likely explanation for this result is the use of a high ARfD compared to the ADI. The ARfD for the common critical effect was a factor 25 higher than the ADI (500 vs 20 µg/kg bw/d, respectively). Simulated acute exposures needed therefore to be 25 times higher than chronic exposures to result in an exceedance of the ARfD. The common acute effect was not the most sensitive effect of the index compound, flusalizole. For the most sensitive effect the ARfD is 5 µg/kg bw/d, a factor 4 lower than the ADI. The ADI for the common effect was also the most sensitive effect of cyproconazole. This result shows that the use of common effects with much higher reference values than the most sensitive effect of the index compound may result in conclusions that are contrary to past conclusions based on single compound assessments. Risk assessors and managers should keep this in mind when evaluating the outcomes of cumulative exposure assessments.

Also the actual P99.9 of chronic exposure for DK in the pessimistic approach tended to be somewhat higher than the corresponding acute exposure values in the adult population. This effect could be due to the fact that the chronic exposure assessment included the whole population, including young children. Young children are known to have a higher exposure level than adults due to their higher consumptions per kg body weight. This was also the reason why the acute exposures to the CAG in the age class adolescents was higher than in adult age class of the same country (Table 5).

4.4 Uncertainties

In the exposure assessments reported here the uncertainties due to sampling uncertainty of the food consumption and residue concentration data were quantified in the optimistic and pessimistic model run via central 95% confidence intervals (between the 2.5% and 97.5% percentiles of the uncertainty

distribution) around the number of person-days or persons exceeding a toxicological reference value (Table 8) and around the P99.9 of exposure (Tables 5 and 8). These intervals indicate between which limits the true result will fall with a 95% probability and the width characterises the uncertainty from both the consumption and the residue databases. However, exposure assessments are affected by many other uncertainties that may either result in an over- or underestimation of exposure and are not included in the 95% confidence interval. In the EFSA guidance it is therefore recommended 'that, **in every probabilistic assessment**, assessors should systematically examine all parts of the assessment for unquantified uncertainties and evaluate them using the tabular approach as recommended by EFSA (EFSA, 2006)'. Such an evaluation should at least be performed for the pessimistic model run. For the optimistic model run this exercise is optional. Following Table 5 of the EFSA guidance, we have evaluated the different sources using + (potential to cause overestimation) and – (potential to cause underestimation) symbols to indicate the direction and magnitude of the uncertainty on the exposure result (Table 11). We adjusted the argumentation where appropriate to reflect the details of our study. We have done this for an acute assessment according to the pessimistic model run. The evaluation of the chronic counterpart includes some other assessment components, but the overall conclusion is the same. For an elaboration on all the assessment components see Table 11. Two assessment components we address in more detail below, namely: food conversion factors and monitoring data.

To link the food consumption data of the different countries, coded using FoodEx1, to the national monitoring data we used the food conversion database as developed within the EFSA project 'Development of a database of conversion factors to transform foods coded according to FoodEx into Raw Agricultural Commodities (RACs), NP/EFSA/DATEX/2010/02" (Boon et al., 2013) (section 2.3). In this database, the conversion of many FoodEx1 codes was simple, since the codes related to foods consisting of one ingredient. The conversion of FoodEx1 codes relating to mixed foods was predominantly based on Dutch recipes and conversion factors. This approach is not ideal in view of national differences in food recipes and conversion factors. By using the Dutch database it was assumed that the composition of foods within the countries resembles that of NL, as well as the conversion factors used to convert ingredients to their RAC counterpart (e.g. to convert flour to wheat). Although it may be likely that conversion factors will not vary much between countries, this is not true for recipes. Next to differences in composition and possibly conversion factors between countries, there is also variation within a country. For example, the percentage of apple in apple pie may vary between different recipes. Furthermore, in the EFSA project, FoodEx1 codes were converted to their RAC ingredients in so far these ingredients were vegetable products, including vegetables, fruits, cereals, nuts and seeds. These commodities were identified as the main contributors to the exposure to pesticide residues. Water and animal commodities were not included

in the EFSA project conversion and are therefore only included in the current exposure assessment when consumed as such. Because of this, the exposure via these two sources was potentially underestimated. Due to the low pesticide residue levels in water we estimate that ignoring water as ingredient will have a negligible effect on the estimated exposures. However, for animal commodities this may not be true, and if included could have resulted in even higher exposures in the pessimistic model run than reported. EFSA is presently updating the FoodEx1 conversion database by including also animal commodities and water as ingredients. Availability of this database, expected before the end of 2013 (personal communication EFSA) would remove this uncertainty from the calculations. Inclusion of national differences in recipes, both between and within countries, however remains also after the release of this conversion database a source of uncertainty that can only be addressed by the development of national or general European conversion databases. An approach to achieve this could be by taking the conversion of FoodEx1 as published by EFSA as a starting point and refine the conversion of those FoodEx1 codes where the conversion deviates from that in individual countries. Apart from this variability, there is and always will be uncertainty regarding conversion of foods / ingredients to their RAC counterparts.

Another source of uncertainty that we discuss in somewhat more detail is the uncertainty related to the monitoring data used. We used the data obtained from national monitoring programmes and as submitted to EFSA using the SSD system. Before using the data we checked them for possible outliers, which we defined as 1.5 times the MRL. None of the residue concentrations were removed. Furthermore, the coding of the RACs was checked. This resulted in some changes that were made due to inconsistent coding or the use of wrong codes. A more thorough check on the quality of the data was outside the scope of this project. However, when monitoring data are used to exclude or identify possible health risks related to the exposure to (groups of) pesticides, a thorough check on the residue data used in the assessment is important. Important issues are coverage of all relevant RACs, LORs in relation to positive residue levels, residue levels at LOQ instead of LOR, and identification of samples obtained via targeted sampling.

Taking all sources of unquantified uncertainties into account, we conclude that the pessimistic exposure assessment was indeed conservative and resulted in an overestimation of the real exposure. The main assessment components that contributed to this conclusion were the use of MRL data for animal commodities and disregarding of the reducing effect of processing practices on residue levels.

4.5 Conclusion

The EFSA guidance is very extensive and thorough, addressing all relevant issues related to probabilistic modelling of both single and multiple compound exposure to pesticide residues (EFSA, 2012). Application of the optimistic model run on a routine basis for acute and chronic cumulative

assessments is feasible. The link with processing information may be improved to further optimise the application of this model run. It should however be recognised that the resulting exposure estimates are very likely underestimates of the real exposure. The pessimistic model run, on the other hand, is presently very laborious. More experience with this approach is needed to stimulate the discussion of the feasibility of all the requirements. Especially the inclusion of MRLs of animal commodities seems to result in unrealistic conclusions regarding the contribution of animal commodities to the dietary exposure. Furthermore, given the laboriousness of supplementing the pessimistic residue database with concentration data from others sources, tools are needed to standardise this. The Access database developed in this study may be a first step to achieve this but needs further optimisation to include concentration data from other sources such as field trial studies. Also the generation of a database with authorised uses of pesticides worldwide that will be updated and maintained over the years would be needed to make it feasible to perform cumulative assessment according to the pessimistic model run on a routine basis.

More experience is needed with the EFSA guidance, but a possible conclusion may be that some kind of intermediate 'realistic' scenario is needed that combines the optimistic and pessimistic model run in such a way that it results in more realistic acute and chronix exposures that can still be argued to be conservative (precautionary principle) but not over-conservative as now seems the case with the pessimistic model run.

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Table 1

Relative potency factors (RPF) based on benchmark doses (BMD) for the common effect cranio-facial toxicity for triazole pesticides included in the Cumulative Assessment Group (CAG) for acute effects, and on no-observed adverse effect levels (NOAEL) for the common effect hepatoxicity for triazoles included in the CAG for chronic effects {EFSA, 2009 #2751}.

Acute effect: cranio-facial toxicity		Chonic effect: hepatoxicity	
Compound	BMD based RPF[a]	Compound	NOAEL based RPF[b]
Bitertanol	2.1	Bitertanol	2.0
Cyproconazole	2.2	Cyproconazole[c]	1.0
Diniconazole	1.0	Difenoconazole	2.0
Epoxiconazole	1.5	Diniconazole	0.4
Flusilazole[c]	1.0	Epoxiconazole	2.5
Propiconazole	0.1	Flusilazole	4.0
Triadimefon	1.2	Myclobutanil	0.05
		Propiconazole	0.6
		Tebuconazole	0.1
		Triadimefon	0.1
		Triadimenol	0.4

[a] The RPF was the ratio of the BMD of the index compound flusilazole to that of the compound of interest {EFSA, 2009 #2751}.

[b] The RPF was the ratio of the NOAEL of the index compound cyproconazole to that of the compound of interest {EFSA, 2009 #2751}.

[c] Index compound

Table 2

Characteristics of national consumption data from Cyprus (CY), Czech Republic (CZ), Denmark (DK), France (F), Italy (IT), the Netherlands (NL), Sweden (SE) and United Kingdom (UK).

Country	Year	Method of consumption data collection	Population			
			Adolescents		Adults	
			Age (y)	Number	Age (y)	Number
CY	2003	3-d record	11-17	303	-	-
CZ	2003-2004	2 × 24 h recall	10-17	298	18-64	1,666
DK	2000-2002	7-d record	10-17	479	18-64	2,822
F	2005-2007	7-d record	10-17	973	18-64	2,276
IT	2005-2006	3-d record	10-17	247	18-64	2,313
NL	2003	2 × 24 h recall	-	-	19-30	750
SE	1997-1998	7-d record	-	-	18-64	1,081
UK	2000-2001	7-d record	-	-	19-64	1,724

Table 3

Summary of the national monitoring concentrations for triazole pesticides used in Cyprus (CY), Czech Republic (CZ), Denmark (DK), France (F), Italy (IT), the Netherlands (NL), Sweden (SE) and United Kingdom (UK), analysed in 2007–2010.

Country and compound	Number of RACs[a] analysed	Number of samples analysed	Number of samples ≥ LOR[b]
CY	91 (10)[c]	1631	31 (0.1%)[d]
CZ	75 (22)	3309	101 (3.1%)
DK	128 (13)	8826	58 (0.7%)
F	175 (15)	12033	73 (0.6%)
IT	162 (16)	23797	71 (0.3%)
NL	115 (30)	14480	320 (2.2%)
SE	89 (21)	5359	87 (1.6%)
UK	145 (18)	11960	138 (1.2%)

[a] RAC = raw agricultural commodity.

[b] LOR = limit of reporting.

[c] Between brackets the number of RACs with at least one sample with a residue level ≥ LOR.

[d] Between brackets the percentage of samples with a level ≥ LOR.

Table 4

Basic settings of an acute and chronic cumulative dietary exposure calculation following an optimistic and pessimistic model run as described in the EFSA guidance on probabilistic modelling (EFSA, 2012).

Assessment component	Optimistic scenario		Pessimistic scenario	
	Acute	Chronic	Acute	Chronic
Modelling food consumption data	Empirical	Empirical (OIM[1])	Empirical	Empirical (OIM)
Link food consumption / concentration data	Food conversion model		Food conversion model	
Origin residue data	Monitoring		Monitoring, data other partners, MRL[2] and 0.5 ppb for drinking water	
Treatment samples < LOR	Set to zero		Set to LOR when authorised use[3]	
Modelling concentration data	Empirical		Parametric	Empirical
Percentage crop treated[4]	100%		100%	100%
Variability between units	No unit variability		Beta distribution/ Varfac[5] = 5	No unit variability
Processing factors	Value used in deterministic assessment, fixed		Value used in deterministic assessment, fixed, only included when value ≥ 1[6]	
Uncertainties				
Sampling uncertainty food consumption data	Bootstrap		Bootstrap	
Sampling uncertainty residue data	Bootstrap		Parametric	Bootstrap
Proportion < LOR	Bootstrap	-	Parametric	-

[1] OIM = Observed Individual Mean
[2] Animal commodities
[3] Authorised use was determined by the availability of an MRL in the MRL database on the Commission website.
[4] The percentage crop treated was set at the level of 100% due to lack of information on this input variable.
[5] Varfac = variability factor
[6] Deviates from EFSA guidance for pessimistic, chronic assessment where it is stated that 'Distribution of estimates for mean processing factor, obtained by bootstrapping measured values' should be used.

Table 5

P99.9 level of acute dietary cumulative exposure (µg/kg bw/d) to the triazole pesticides included in the Cumulative Assessment Group for acute effects[a]. Numbers are given per country, age group and model run. Numbers in brackets indicate the 2.5% lower and upper uncertainty limits.

Percentile	P99.9 of exposure (µg/kg bw/d) per age group and model run			
	Adolescents		Adults	
	Optimistic	Pessimistic	Optimistic	Pessimistic
CY	0.34 (0.26 – 0.44)	11.4 (8.2 – 11.05)		
CZ	7.6 (7.2 – 11)	59 (46 – 72)	3.2 (2.6 – 3.6)	30 (23 – 41)
DK	2.0 (1.4 – 2.6)	60 (52 - 83)	1.3 (1.1 – 1.7)	40.3 (32.2 – 44.216)
F	3.3 (2.5 – 4.5)	15 (13 – 16)	2.5 (1.9 – 3.0)	12 (9.9 – 13)
IT	1.3 (0.84 – 2.3)	137 (105 – 174)	1.6 (1.0 – 3.0)	110 (83 – 129)
NL	-		2.8 (1.9 – 3.8)	10 (8.8 – 11)
SE	-		1.2 (1.0 – 1.4)	9.4 (8.7 – 11)
UK	-		2.2 (1.8 – 2.6)	15 (9.9 – 15)

[a] Index compound: flusilazole, ARfD = 500 µg/kg bw/d

Table 6

Top 3 commodities contributing most to the acute exposure to the triazole pesticides included in the Cumulative Assessment Group for acute effects per country and model run {EFSA, 2012 #2917}.

Country	Top 3 commodities					
	Optimistic model run			Pessimistic model run		
	1	2	3	1	2	3
Adolescents						
CY	Tomato 50%	Apple 22%	Strawberry 9%	Milk, cattle 67%	Meat, swine 8.1%	Meat, poultry 8.0%
CZ	Banana 80%	Pineapple 15%	Apple 1%	Milk, cattle 69%	Meat, swine 10%	Meat, poultry 8%
DK	Apple 54%	Tomato 28%	Pear 13%	Milk, cattle 60%	Meat, swine 13%	Meat, bovine 10%
F	Banana 81%	Pineapple 10%	Peach 7%	Milk, cattle 64%	Meat, bovine 10%	Meat, poultry 7%
IT	Pineapple 70%	Banana 10%	Peach 5%	Tomato 21%	Milk, cattle 19%	Wheat 14%
Adults						
CZ	Banana 68%	Pineapple 16%	Barley 8%	Milk, cattle 33%	Wheat 11%	Apple 10%
DK	Apple 60%	Tomato 20%	Pear 16%	Milk, cattle 55%	Meat, swine 14%	Meat, bovine 11%
F	Banana 79%	Peach 9%	Pineapple 8%	Milk, cattle 53%	Meat, bovine 12%	Meat, poultry 9%
IT	Pineapple 66%	Banana 10%	Peach 8%	Tomato 24%	Apple 16%	Milk, cattle 14%
NL	Pineapple 74%	Banana 16%	Tomato 6%	Milk, cattle 59%	Meat, swine 9%	Meat, poultry 6%
SE	Pineapple 83%	Tomato 11%	Apple 2%	Milk, cattle 67%	Meat, swine 6%	Apple 5%
UK	Banana 91%	Tomato 3%	Peach 2%	Milk, cattle 60%	Meat, poultry 9%	Meat, swine 6%

Table 7

Top 3 compounds contributing most to the acute exposure to the triazole pesticides included in the Cumulative Assessment Group for acute effects per country and model run {EFSA, 2012 #2917}.

Country	Top 3 compounds					
	Optimistic model run			Pessimistic model run		
	1	2	3	1	2	3
Adolescents						
CY	Cyproconazole 95%	Flusilazole 4%	Triadimefon 1%	Cyproconazole 32%	Bitertanol 29%	Triadimefon 17%
CZ	Bitertanol 99%	Triadimefon 1%	-	Bitertanol 24%	Cyproconazole 24%	Epoxiconazole 16%
DK	Bitertanol 98%	Triadimefon 1%	Flusilazole 1%	Cyproconazole 30%	Bitertanol 30%	Triadimefon 18%
F	Bitertanol 89%	Triadimefon 10%	Flusilazole 1%	Cyproconazole 25%	Bitertanol 24%	Epoxiconazole 16%
IT	Triadimefon 74%	Bitertanol 21%	Cyproconazole 5%	Bitertanol 44%	Cyproconazole 21%	Triadimefon 18%
Adults						
CZ	Bitertanol 73%	Triadimefon 16%	Epoxiconazole 9%	Bitertanol 34%	Cyproconazole 23%	Triadimefon 15%
DK	Bitertanol 97%	Triadimefon 1%	Flusilazole 1%	Cyproconazole 30%	Bitertanol 30%	Triadimefon 18%
F	Bitertanol 90%	Triadimefon 8%	Flusilazole 1%	Cyproconazole 25%	Bitertanol 25%	Epoxiconazole 15%
IT	Triadimefon 70%	Bitertanol 24%	Cyproconazole 5%	Bitertanol 46%	Cyproconazole 21%	Triadimefon 18%
NL	Triadimefon 74%	Bitertanol 24%	Cyproconazole 1%	Cyproconazole 32%	Bitertanol 28%	Triadimefon 18%
SE	Triadimefon 83%	Bitertanol 15%	Flusilazole 1%	Cyproconazole 30%	Bitertanol 29%	Triadimefon 18%
UK	Bitertanol 97%	Triadimefon 1%	Cyproconazole 1%	Bitertanol 25%	Cyproconazole 25%	Epoxiconazole 16%

Table 8

Number of persons per million with a chronic cumulative exposure level to the triazole pesticides included in the Cumulative Assessment Group for chronic effects that exceeded the acceptable daily intake (ADI) of 20 µg/kg bw/d of the index compound cyproconazole and P99.9 of exposure per country and model run. Numbers in brackets indicate the 2.5% lower and upper uncertainty limits.

Country	Optimistic model run	Pessimistic model run
Number of persons per million exceeding an exposure of 20 µg/kg bw/d		
DK	0 (0-0)	64,806 (56,700 – 71,900)
IT	0 (0-0)	43,635 (34,900–48,900)
P99.9 of exposure		
DK	0.17 (0.14 – 0.26)	54 (47 – 62)
IT	0.27 (0.14 – 0.69)	88 (56 – 169)

Table 9

Top 3 commodities and compounds contributing most to the chronic exposure to triazole pesticides included in the Cumulative Assessment Group for chronic effects per country and model run.

Country	Optimistic model run			Pessimistic model run		
	1	2	3	1	2	3
Top 3 products						
DK	Apple 30%	Tomato 24%	Peppers 12%	Milk, cattle 51%	Meat, swine 13%	Eggs, chicken 11%
IT	Peach 32%	Celery 30%	Pineapple 12%	Milk, cattle 21%	Tomato 13%	Wheat 12%
Top 3 compounds						
DK	Bitertanol 49%	Triadimenol 31%	Difenoconazole 10%	Bitertanol 27%	Flusilazole 25%	Difenoconazole 14%
IT	Difenoconazole 69%	Triadimenol 12%	Bitertanol 11%	Bitertanol 30%	Flusilazole 22%	Difenoconazole 15%

Table 10

The P99.9 of acute exposure (µg/kg bw/d) to triazole pesticides included in the Cumulative Assessment Group for acute effects reported in the present study for the adult population and the study of van Klaveren et al. (2009).

Country	P99 of exposure (µg/kg bw/d)		
	Present study, adult population		van Klaveren et al (2009)[a]
	Optimistic	Pessimistic	
Acute			
CZ adolescents CZ adults	7.6 (7.2-11) 3.2 (2.6 – 3.6)	59 (46-72) 30 (23 – 41)	1.2 (10-90 years)
F adolescents F adults	3.3 (2.5-4.5) 2.5 (1.9 – 3.0)	15 (13-16) 12 (9.9 – 13)	3.0 (7-92 years)
IT adolescents IT adults	1.3 (0.84-2.3) 1.6 (1.0 – 3.0)	137 (105-174) 110 (83 – 129)	4.0 (1-17 years) 2.4 (18-64 years)
NL adults	2.8 (1.9 – 3.8)	10 (8.8 – 11)	1.5 (1-97 years)
SE adults	1.2 (1.0 – 1.4)	9.4 (8.7 – 11)	0.9 (17-79 year)
Chronic			
IT whole population	0.27 (0.14 – 0.69)	88 (56 – 169)	0.0 (1-7 years) 0.0 (18-64 years)

[a] Between brackets the population for which the exposure was reported

Table 11

Evaluation of uncertainties for the acute cumulative pessimistic model run. The assessment components were derived from the EFSA guidance on probabilistic modelling (EFSA, 2012). The numbers of the assessment components are the same as used in the guidance. The assessment components not relevant for this study are not included (nr. 16, 20 and 22).At the end of the table, the combined impact of all the uncertainties is considered. For more details see (EFSA, 2012).

Assessment component	Approach in pessimistic model run	Subject evaluation of impact on the upper tail exposures[a]	Brief explanation of evaluation
1.Modelling food consumption data	Empirical + bootstrap	●	Limited data may result in underestimation of high exposure percentiles if there is limited data for the foods driving the risk. The foods driving the risk in both age groups in the present study are however commonly consumed foods. We therefore do not expect that this assessment component resulted in an underestimation of the upper tail exposure.
2.Use of old food consumption survey data	Not considered	●	This is true for almost all used databases. The most recent database is already 5 years old, and the eldest already even more than 15 years. Changes in consumption of animal commodities (main risk drivers) may have occurred but we estimate that these changes are minor and have not affected the exposure significantly.
3.Measurement/reporting uncertainty in consumption surveys	Not considered	●	Based on a study performed by te Biesebeek et al (te Biesebeek et al., 2012) that showed that inclusion of uncertainty in estimation of portion sizes did not result in broader confidence intervals around the exposure results, we assess that this component is not likely to have resulted in a substantial (> ±20%) under- or overestimation of the exposure.
4.Overreporting of fruit and vegetable consumption	Not considered	●/+	This might have resulted in a slight overestimation of the exposure reported in this paper. The EFSA guidance indicates that people may overestimate intake of these foods by up to 2-fold (EFSA, 2012)
5.Relation of consumption to body weight	Kept together in dietary survey records	●	Kept together in dietary survey records.
6.Water consumption	Included as part of the food consumption survey	●	Water consumption as part of recipes was not included in the assessment. We assess however that the contribution to the exposure will be limited due to low levels.
7.Food conversion factors	Use of Dutch recipe	--/++	Due to differences in recipe data between countries this may have resulted

Assessment component	Approach in pessimistic model run	Subject evaluation of impact on the upper tail exposures[a]	Brief explanation of evaluation
(recipes)	data and conversion factors		in an over- and underestimation of the exposure for individual countries. The exact amount is difficult to quantify.
8.Unit weights	Default values as used in deterministic approach	-/●	The effect of this assessment component on the exposure is expected to be similar as described in the EFSA guidance.
9.Residue definition	Considered	●	Conversion factor for the residue definition for monitoring to that of risk assessment was 1 for all triazole pesticides. We therefore do not expect this assessment component to have resulted in an over- or underestimation of the exposure.
10.Residue measurement uncertainty	Not modelled	+	The effect of this assessment component on the exposure is expected to be similar as described in the EFSA guidance.
11.Unmeasured residues in animal commodities	MRL	+++	The MRLs are very likely far above true residues found in animal commodities. Due to MRLs for milk, a commodity consumed in large amounts, we estimate that the use of MRLs has resulted in a large overestimation of the exposure.
12.Between lot/sample variation of residues	Lognormal for positive values (if n>2)	--/++	The effect of this assessment component on the exposure is expected to be similar as described in the EFSA guidance.
13.Sampling uncertainty for lot/samples residues	Parametric model (if > 2 positive values)	-/+++	The effect of this assessment component on the exposure is expected to be similar as described in the EFSA guidance.
14.Treatment of residue below LOR	Set <LOR to LOR	●/+	Many RACs will not have been treated with the pesticides. However, we estimate that this would have had only a minor effect, since exposure in the right tail of the distribution will be driven by residues > LOR.
15.Sampling uncertainty of proportion of residues below LOR	Parametric model	●/+	The effect of this assessment component on the exposure is expected to be similar as described in the EFSA guidance
17.Percent crop treated	100%	●/+	100% treated means that all non-detect samples of authorised uses are assumed to contain the pesticide at LOR. The true % treated will always <100%, often much lower. We estimate that the effect would have been limited, since exposure in the right tail of the distribution will be driven by residues > LOR

Assessment component	Approach in pessimistic model run	Subject evaluation of impact on the upper tail exposures[a]	Brief explanation of evaluation
18.Changes over time in use patterns (e.g. application rate)	Not considered	●	We judge that for the exposure period under consideration, changes over time in use patterns were included in the concentration databases used (2009-2011).
19.Limited amounts of monitoring data	Use of data from other countries	●	Actual level or frequency of positives may differ between countries resulting in over- or underestimations of national exposure when using data from other counties to supplement insufficient data available in national concentration databases. The effect however on the right tail of the exposure distribution is estimated to be small in view of the international trade of commodities traversing the whole of Europe to reach consumers. Furthermore, no monitoring data were available for all commodities with authorised use. These were however minor crops, and are estimated to have not resulted in an underestimation of the exposure.
21.Residues for non-authorised use	Inclusion in assessment if present in national database, set <LOR to zero	●	These residues are only a minor part of the total concentration database, and therefore not expected to affect the upper tail of the exposure distribution.
23.Between unit variation	Beta, v = 5	+	The variability factor used is higher than reported in an EFSA study on variability factors for monitoring data (EFSA, 2005). Together with the beta distribution the true proportion of high residues may be overestimated (EFSA, 2012).
24.Residues in prepared foods	Assumed that prepared foods contain residues as analysed in raw foods, including variability	+	Foods consumed are a mixture of raw and prepared foods. For raw foods the estimated exposure will very likely be realistic, for purchased prepared foods very likely overestimated, since possible reducing effects of processing have been ignored (EFSA, 2012).
25.Relation monitoring to residue encountered by consumer	Monitoring data assumed to be representative of residue encountered by consumer	●	Monitoring may, to a certain extent, be focussed on commodities that may contain the pesticide. Commodities not to be expected to contain the pesticide are not included resulting in a possible underestimation. However, by borrowing data from different countries to fill possible gaps we estimate that the databases used included all relevant foods.

Assessment component	Approach in pessimistic model run	Subject evaluation of impact on the upper tail exposures[a]	Brief explanation of evaluation
26.Processing factors	Set to 1 or use highest value when > 1.	++	Processing is known to affect residue levels. By ignoring the lowering effect of processing, the exposure will be overestimated.
27.Cumulative assessment – selection of substances to be included in the CAG	Assess by repeating assessment including or excluding substances whose memberschip in the CAG is uncertain	●	The goal of the present paper was to assess the practicality of the EFSA guidance by calculating the cumulative exposure to the triazole pesticides included in the acute and chronic CAG as determined by EFSA (2009). The uncertainty in this assessment component is not relevant in this context.
28.Cumulative assessment – relative potency factors (RPFs)	Assume slopes of dose response curves are parallel for all substances in CAG	●	Not relevant. See Brief explanation to previous assessment component (nr 27).
29.Cumulative assessment - imputation of missing residue data	Simple conservative method for imputation	+	Imputation of residues according to the algorithm described in the EFSA guidance will result in an overestimate of exposure (EFSA, 2012). We assess, however, that the effect of this on the right tail of the exposure distribution will not be significant since the majority of imputed values will be at LOR.
30.Residues in water	Assume legal limit (0.5 ppb)	●	Very low value, of no consequence regarding exposure. The other, more important sources of exposure, will drive the exposure.
31.Residues from rotational/succeeding crops	Is to be estimated by expert judgement	●	The effect of this assessment component on the exposure is expected to be similar as described in the EFSA guidance.
32.Targeted monitoring	Ignored	+	The samples included in the assessment were obtained from monitoring programmes. This may have included, to a small extent, samples obtained from targeted sampling. Targeted sampling focusses on those commodities that may have higher residue levels and therefore result in higher exposures, especially via increased frequency of residue levels > LOR.
32.Overall assessment	+ / +++ Overall we conclude that the pessimistic exposure assessment was indeed conservative and resulted in an overestimation of the real exposure. The main assessment components that contributed to this conclusion were the use of MRL data for		

Assessment component	Approach in pessimistic model run	Subject evaluation of impact on the upper tail exposures[a]	Brief explanation of evaluation
	animal commodities and disregarding of the reducing effect of processing practices on residue levels.		

[a] Explanation: +, ++, +++ = uncertainty resulting in a small (<2x), medium (2-5x), and large (>5x) overestimation of the upper tail exposure; -, --, --- = uncertainty resulting in a small (<2x), medium (2-5x), and large (>5x) underestimation of the upper tail exposure; ● within ± 20% (EFSA, 2012).

Appendix I Processing factors used to assess the acute and chronic exposure according to the optimistic and pessimistic model run.

Compound	Product	Processing type	Processing factor		Source[a]
			Optimistic model run	Pessimistic model run	
Bitertanol	Apple	Juicing	0.1	0.1	EFSA
Bitertanol	Apple	Sauce / puree	0.1	0.1	EFSA
Bitertanol	Banana	peeling	0.5	0.5	UK/EU
Bitertanol	Cherry	Canned / conserved	0.6	0.6	EFSA
Bitertanol	Cherry	Juicing	0.17	0.17	JMPR
Bitertanol	Cherry	Marmalade / Jam	0.5	0.5	EFSA
Bitertanol	Cherry	Washing	0.8	0.8	JMPR
Bitertanol	Plums	Marmalade / Jam	0.61	0.61	EFSA
Bitertanol	Plums	Sauce / puree	0.6	0.6	EFSA
Bitertanol	Tomato	Canned / conserved	0.4	0.4	EFSA
Bitertanol	Tomato	Juicing	0.1	0.1	EFSA
Bitertanol	Tomato	Sauce / puree	2	2	EFSA
Bitertanol	Tomato	Washing	0.8	0.8	JMPR
Cyproconazole	Oilseed rape	Oil extraction	0.08	0.08	EFSA
Cyproconazole	Soya bean	Oil extraction	1.8	2.5	JMPR
Difenoconazole	Apple	Drying	1.8	1.8	BFR
Difenoconazole	Apple	Juicing	0.02	0.02	EFSA
Difenoconazole	Apple	Sauce / puree	0.14	0.14	EFSA
Difenoconazole	Apple	Washing	0.78	0.78	EFSA
Difenoconazole	Carrot	Canned / conserved	0.055	0.055	EFSA
Difenoconazole	Carrot	Cooking in water	0.049	0.049	EFSA
Difenoconazole	Carrot	Cooking in water	0.049	0.049	EFSA
Difenoconazole	Carrot	Juicing	0.063	0.063	EFSA
Difenoconazole	Ginseng	Drying	3.3	3.3	JMPR
Difenoconazole	Grapes	Drying	1.2	1.4	JMPR
Difenoconazole	Grapes	Juicing	0.5	0.5	JMPR
Difenoconazole	Grapes	Wine making	0.18	0.18	JMPR

Compound	Product	Processing type	Processing factor		Source[a]
			Optimistic model run	Pessimistic model run	
Difenoconazole	Olives	Oil extraction	1.4	1.51	JMPR
Difenoconazole	Tomato	Canned / conserved	0.07	0.07	EFSA
Difenoconazole	Tomato	Juicing	0.2	0.2	EFSA
Difenoconazole	Tomato	Sauce / puree	0.66	0.66	JMPR
Difenoconazole	Tomato	Washing	0.7	0.7	UK/EU
Epoxiconazole	Barley	Brewing	0.08	0.08	EFSA
Epoxiconazole	Wheat	Baking of bread	1	1	EFSA
Epoxiconazole	Wheat	Milling	0.6	0.6	EFSA
Epoxiconazole	Wheat	Milling	1.3	2	EFSA
Epoxiconazole	Wheat	Milling	4.2	5.3	EFSA
Epoxiconazole	Wheat	Milling	2.5	4	EFSA
Flusilazole	Apple	Juicing	0.19	0.19	JMPR
Flusilazole	Barley	Milling	0.4	0.4	UK/EU
Flusilazole	Grapes	Drying	2	2	EFSA
Flusilazole	Grapes	Juicing	0.42	0.42	JMPR
Flusilazole	Grapes	Wine making	0.1	0.1	EFSA
Flusilazole	Soya bean	Oil extraction	2.2	2.2	JMPR
Flusilazole	Wheat	Baking of bread	1	1	UK/EU
Flusilazole	Wheat	Milling	0.96	0.96	UK/EU
Myclobutanil	Apple	Cooking in water	0.52	0.52	EFSA
Myclobutanil	Apple	Juicing	0.13	0.13	EFSA
Myclobutanil	Apple	Sauce / puree	0.4	0.4	EFSA
Myclobutanil	Apple	Washing	1	1.02	EFSA
Myclobutanil	Banana	Peeling	0.24	0.24	UK/EU
Myclobutanil	Currants[b]	Canned / conserved	0.2	0.2	BFR
Myclobutanil	Currants[b]	Juicing	0.35	0.35	JMPR
Myclobutanil	Grapes	Juicing	0.21	0.21	EFSA
Myclobutanil	Grapes	Wine making	0.12	0.12	EFSA
Myclobutanil	Hops	Brewing	0.01	0.01	JMPR

Compound	Product	Processing type	Processing factor		Source[a]
			Optimistic model run	Pessimistic model run	
Myclobutanil	Mandarins	Juicing	0.4	0.4	UK/EU
Myclobutanil	Mandarins	Peeling	0.05	0.05	UK/EU
Myclobutanil	Strawberry	Canned / conserved	0.81	0.81	JMPR
Myclobutanil	Strawberry	Marmalade / Jam	0.5	0.5	JMPR
Myclobutanil	Tomato	Canned / conserved	0.75	0.75	UK/EU
Myclobutanil	Tomato	Juicing	0.58	0.58	UK/EU
Myclobutanil	Tomato	Sauce / puree	1.6	3	JMPR
Myclobutanil	Tomato	Washing	1	1	UK/EU
Propiconazole	Apple	Juicing	0.11	0.11	EFSA
Propiconazole	Apple	Sauce / puree	0.44	0.44	EFSA
Propiconazole	Barley	Brewing	1	1	EFSA
Propiconazole	Grapes	Drying	1.9	2.5	JMPR
Propiconazole	Grapes	Juicing	0.05	0.05	JMPR
Propiconazole	Grapes	Wine making	0.33	0.33	EFSA
Propiconazole	Maize	Milling	1	1.6	JMPR
Propiconazole	Maize	Oil extraction	0.6	0.6	JMPR
Propiconazole	Peach	Canned / conserved	0.09	0.09	EFSA
Propiconazole	Peach	Marmalade / jam	0.05	0.05	EFSA
Propiconazole	Peanuts	Oil extraction	0.6	0.6	UK/EU
Propiconazole	Plums	Drying	1.1	1.4	UK/EU
Propiconazole	Rice	Parboiling	0.43	0.43	UK/EU
Propiconazole	Tea	Cooking in water	0.02	0.02	JMPR
Tebuconazole	Apple	Juicing	0.42	0.42	JMPR
Tebuconazole	Apple	Sauce / puree	0.42	0.42	JMPR
Tebuconazole	Banana	Peeling	0.6	0.6	UK/EU
Tebuconazole	Barley	Brewing	0.03	0.03	EFSA
Tebuconazole	Barley	Brewing	0.03	0.03	EFSA
Tebuconazole	Coffee	Roasted	2	2	JMPR
Tebuconazole	Coffee	Roasted and ground	0.8	0.8	JMPR

Compound	Product	Processing type	Processing factor		Source[a]
			Optimistic model run	Pessimistic model run	
Tebuconazole	Grapes	Drying	1.2	1.4	JMPR
Tebuconazole	Grapes	Juicing	0.21	0.21	JMPR
Tebuconazole	Grapes	Wine making	0.26	0.26	EFSA
Tebuconazole	Hops	Brewing	0.01	0.01	JMPR
Tebuconazole	Legume vegetables	Cooking in water	0.2	0.2	JMPR
Tebuconazole	Legume vegetables	Washing	0.28	0.28	JMPR
Tebuconazole	Oilseed rape	Oil extraction	0.8	0.8	JMPR
Tebuconazole	Oranges, Sweet	Juicing	0.02	0.02	EFSA
Tebuconazole	Oranges, Sweet	Marmalade / jam	0.17	0.17	EFSA
Tebuconazole	Oranges, Sweet	Peeling	0.14	0.14	EFSA
Tebuconazole	Passion fruit	Peeling	0.09	0.09	EFSA
Tebuconazole	Peanuts	Oil extraction	0.14	0.14	JMPR
Tebuconazole	Plums	Canned / conserved	0.7	0.7	JMPR
Tebuconazole	Plums	Drying	2.9	4.7	JMPR
Tebuconazole	Plums	Marmalade / Jam	1	1	JMPR
Tebuconazole	Plums	Sauce / puree	1	1	JMPR
Tebuconazole	Plums	Washing	0.7	0.7	JMPR
Tebuconazole	Soya bean	Oil extraction	0.07	0.07	JMPR
Tebuconazole	Tomato	Canned / conserved	0.3	0.3	JMPR
Tebuconazole	Tomato	Juicing	0.55	0.55	JMPR
Tebuconazole	Tomato	Peeling	0.25	0.25	JMPR
Tebuconazole	Tomato	Sauce / puree	0.33	0.33	JMPR
Tebuconazole	Tomato	Washing	0.95	0.95	JMPR
Triadimefon	Apple	Juicing	0.63	0.63	JMPR
Triadimefon	Apple	Sauce / puree	0.63	0.63	JMPR
Triadimefon	Apple	Washing	0.92	0.92	EFSA
Triadimefon	Coffee	Roasted	1.1	1.1	JMPR
Triadimefon	Coffee	Roasted and ground	1.3	1.3	JMPR
Triadimefon	Grapes	Drying	3.1	5.8	JMPR

Compound	Product	Processing type	Processing factor		Source[a]
			Optimistic model run	Pessimistic model run	
Triadimefon	Grapes	Juicing	0.45	0.45	EFSA
Triadimefon	Grapes	Wine making	0.42	0.42	JMPR
Triadimefon	Pineapple	Peeling	0.1	0.1	EFSA
Triadimefon	Tomato	Canned / conserved	0.59	0.59	JMPR
Triadimefon	Tomato	Juicing	0.59	0.59	EFSA
Triadimefon	Tomato	Peeling	0.33	0.33	JMPR
Triadimefon	Tomato	Sauce / puree	0.78	0.78	JMPR
Triadimefon	Tomato	Washing	0.97	0.97	EFSA
Triadimenol	Apple	Juicing	0.63	0.63	JMPR
Triadimenol	Apple	Sauce / puree	0.63	0.63	JMPR
Triadimenol	Apple	Washing	0.92	0.92	JMPR
Triadimenol	Coffee	Roasted	1.1	1.1	JMPR
Triadimenol	Coffee	Roasted and ground	1.3	1.3	JMPR
Triadimenol	Grapes	Drying	5.8	5.8	EFSA
Triadimenol	Grapes	Juicing	1.1	1.1	EFSA
Triadimenol	Grapes	Wine making	0.5	0.5	EFSA
Triadimenol	Pineapple	peeling	0.1	0.1	JMPR
Triadimenol	Tomato	Canned / conserved	0.59	0.59	JMPR
Triadimenol	Tomato	Juicing	0.59	0.59	JMPR
Triadimenol	Tomato	Peeling	0.33	0.33	JMPR
Triadimenol	Tomato	Sauce / puree	0.78	0.78	JMPR
Triadimenol	Tomato	Washing	0.97	0.97	JMPR

[a] EFSA = European Food Safety Authority; JMPR = Joint Meeting on Pesticide Residues; UK/EU = United Kingdom/European Union

Appendix II. Unit weights and number of units in a composite sample as used in the acute cumulative exposure assessment according to the pessimistic model run

Product	Unit weight (g)	Nr of units in composite sample
Apple	131.8	12
Apricots	50	24
Aubergine	272.4	12
Avocados	204	12
Bananas	100	24
Beat leaves (chard)	36.2275	12
Beetroot	96.2	12
Broccoli	256.1	12
Cardoons	100	12
Carrots	80	12
Cauliflower	689.9	12
Celeriac	749	12
Celery	462	12
Cherimoya	50	12
Chinese cabbage	649	12
Courgettes	210.5	12
Cucumbers	411.4	12
Fennel	286.3	12
Figs	55	12
Gherkins	38.3	12
Globe artichokes	129.3	12
Grapefruit	270.5	12
Guava	160	12
Head cabbage	1281.9	12
Horseradish	220	12
Jerusalem artichoke	38	12
Kale	165	12
Kiwi	75	12
Kohlrabi	265.4	12
Leek	168.8	12
Lemon	71.8	12
Lettuce	558	12
Limes	67	12
Mandarins	100	12
Mangoes	361.8	12
Medlar	50	12
Melons (kiwano)	1360	12
Onions	150	12
Oranges	160	12
Papaya	196.5	12
Parsley root	140	12
Parsnips	125	12
Passion fruit	16.9	12
Peaches (nectarines)	127.6	24

Product	Unit weight (g)	Nr of units in composite sample
Pear	206.5	12
Peppers	160	18
Persimmon	136	12
Pineapple	1600	12
Plums	53.3	24
Pomegranate	146.8	12
Potatoes	216	24
Pumpkins	950	12
Purslane	29.5	12
Quinces	56	12
Radishes	180	12
Rhubarb	76	12
Salsify	101	12
Scarole	353.4	12
Swedes	668	12
Sweet corn	215	12
Sweet potatoes	65	12
Tablegrapes	581.6	12
Tomatoes	142.5	18
Turnip	110	12
Vine leaves	25	12
Watermelons	690	12
Wild fungi	50	12
Witloof	94.7	12
Yam	160	12