STATEMENT

Comparison of cumulative dietary exposure to pesticide residues for the reference periods 2014–2016 and 2016–2018

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Abstract

Retrospective dietary exposure assessments were conducted for pesticides that have chronic effects on the thyroid and pesticides that have acute effects on the nervous system. Exposure assessments were performed using monitoring data collected by Member States under their official pesticide monitoring programmes in 2016, 2017 and 2018. Exposure estimates were obtained for 10 populations of consumers (i.e. from different countries and from different age groups) by means of a two-dimensional probabilistic model. Results were compared to those previously obtained for the years 2014, 2015 and 2016, and exposure did not change significantly over time. However, an increase of the sampling uncertainty was identified for one pesticide in a specific food commodity. Strategies are therefore recommended to reduce the sampling uncertainty and to anticipate potential problems before initiating a cumulative risk assessment.

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Summary

As part of a pilot programme on the cumulative risk assessment of pesticides, EFSA published in April 2020 two reports on the cumulative dietary risk characterisation of pesticides that have chronic effects on the thyroid and pesticides that have acute effects on the nervous system. These assessments relied on retrospective exposure calculations for 10 populations of consumers (i.e. from different countries and from different age groups), using monitoring data collected by Member States under their official monitoring programmes in 2014, 2015 and 2016. Although it was concluded, with varying degrees of certainty, that cumulative exposure to these pesticides did not exceed the threshold for regulatory consideration, exposure to these pesticides may change over time, which would require a new risk characterisation. To identify possible changes in the exposure patterns, EFSA repeated the exposure calculations, using the most recent three-year cycle of monitoring data currently available at EFSA (i.e. for the years 2016, 2017 and 2018), and compared these results to those obtained for the previous reference period.

In analogy with the previous assessments, both chronic and acute exposure estimates were obtained with SAS® software using a two-dimensional Monte Carlo simulation, which is composed of an inner loop execution and an outer loop execution. Variability within the population is modelled through the inner loop execution and is expressed as a percentile of the exposure distribution. The outer loop execution is used to derive 95% confidence intervals around those percentiles (reflecting the sampling uncertainty of the input data).

Exposure estimates were obtained for different percentiles of the exposure distribution and the total margin of exposure (MOET, i.e. the ratio of the toxicological reference dose to the estimated exposure) was calculated at each percentile. Only the estimates obtained at the 99.9th percentile of the exposure distribution were considered for comparison, because this percentile was used as the starting point for the risk characterisation of the previous reference period.

The comparison of the chronic exposure estimates revealed that both, confidence intervals of MOETs and main contributors, did not change substantially compared to the previous period, i.e. 2014–2016. The comparison of the acute exposure estimates, however, revealed that confidence intervals became much wider and bimodal when compared with the previous exposure estimates for 2014–2016. The analysis of the main contributors also indicated a six- to ninefold increase of the contribution of omethoate in olives for oil production, which was caused by one measurement for omethoate in olives for oil production in the occurrence data from 2016 to 2018. Therefore, the acute exposure calculations were executed a second time excluding this specific measurement. The results of the second calculation show narrower confidence intervals and, compared to the exposure estimates for 2014–2016, a shift towards slightly higher margins of exposure.

Overall, compared to the previous reference period (i.e. 2014–2016), exposure to pesticides that have chronic effects on the thyroid and exposure to pesticides that have acute effects on the nervous system did not change significantly. These findings suggest that repeating cumulative risk assessments on a yearly basis is not necessary, and possible changes in exposure will be adequately addressed when cumulative risk assessments are repeated every three years, as intended by EFSA.

Calculations also confirmed previous findings that the outcome of a cumulative exposure assessment at the 99.9th percentile of the exposure distribution is very much influenced by single measurements in specific samples. When sampling uncertainty is high, such measurement will produce unstable exposure estimates, characterised by a wide confidence interval. Commodities that are almost exclusively consumed as a processed product (e.g. olives for oil production and wine grapes) are more susceptible to sampling uncertainty because the number of monitoring samples for the unprocessed commodities is low.

It is therefore recommended to adjust the probabilistic model to include occurrence data for the processed foods (i.e. olive oil and wine) because, in accordance with the EU multi-annual control programme currently in place, the number of monitoring samples for these processed foods is higher than for the unprocessed commodities. Furthermore, it is recommended to implement probabilistic modelling for the assessment of dietary exposure in the annual report on pesticide residues. This would allow EFSA to identify possible concerns for specific active substances and food commodities on a yearly basis, and to initiate an ad hoc cumulative risk assessment when such concerns are expected to impact on the cumulative risks.

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1. Introduction

1.1. Background

Cumulative risk assessment (CRA) has been defined as the analysis, characterisation and possible quantification of the combined risks to health or the environment from multiple agents or stressors (US EPA, 2003). It differs from most current assessments which consider the effects of one agent or stressor in isolation.

Regulation (EC) No 396/2005[1] on maximum residue levels (MRLs) of pesticides in or on food and feed requires cumulative and synergistic effects of pesticide residues to be taken into account for dietary risk assessment, when appropriate methodologies are available. Regulation (EC) No 1107/2009[2] concerning the placing of plant protection products on the market also requires that the residues of plant protection products shall not have any harmful effects on human health, taking into account known cumulative and synergistic effects where the scientific methods accepted by EFSA to assess such effects are available. For this reason, EFSA and the Panel on plant protection products and their residues (PPR Panel) started in 2007 the development of the necessary methodologies to carry out CRA of pesticide residues. This methodological development included a tiered approach for the assessment of cumulative risks of pesticides residues (EFSA PPR Panel, 2008), a guidance on the use of probabilistic methodology for modelling dietary exposure to pesticide residues (EFSA PPR Panel, 2012) and a procedure to establish cumulative assessment groups (CAGs) of pesticides based on their toxicological profile (EFSA PPR Panel, 2013).

After development of the methodologies by the PPR Panel, EFSA initiated in 2014 a pilot programme aiming at implementing the CRA of pesticides. The objectives of this pilot programme were to evaluate the cumulative effects of pesticide residues on two organs which are known to be sensitive to pesticides (the nervous system and the thyroid), and to test the methodologies over the entire risk assessment process (hazard identification and characterisation, exposure assessment and risk characterisation) for acute and chronic effects. During this pilot phase, EFSA worked in close cooperation with the Dutch National Institute for Public Health and the Environment (RIVM), who had previously released the Monte Carlo Risk Assessment (MCRA) software, a web-based software that allows higher tier exposure assessment to multiple pesticides to be performed.

As a result of the pilot programme, EFSA issued two CRAs for the dietary exposure to pesticides that have chronic effects on the thyroid and pesticides that have acute effects on the nervous system. These CRAs relied on retrospective exposure assessments (i.e. using monitoring data collected by Member States under their official pesticide monitoring programmes) conducted for 10 population groups from different countries and different age classes in the reference period 2014–2016 (EFSA, 2019a,b; van Klaveren et al., 2019a,b). These probabilistic calculations followed a tiered approach where the first-tier calculations (Tier I) use very conservative assumptions, and the second-tier assessments (Tier II) use assumptions that are more refined but still intended to be conservative. All exposure estimates are expressed as combined (total) margin of exposure (MOET), which represents the ratio of a toxicological reference point to the estimated exposure.[3] Hence, an MOET estimate below 1 implies that the estimated exposure exceeds the toxicological reference point. An MOET of 100 or above is generally considered to be protective of humans, as it means that the estimated exposure is at least 100 times lower than the toxicological reference point.

The final risk characterisation, accounting for all uncertainties, was based on the Tier II exposure estimates. Risk estimates were assessed against the threshold for regulatory consideration agreed among Member States (i.e. an MOET of 100 at the 99.9th percentile of the exposure distribution) and it was concluded, with varying degrees of certainty, that cumulative exposure to pesticides that have chronic effects on the thyroid and pesticides that have acute effects on the nervous system did not exceed the threshold for regulatory consideration (EFSA, 2020b,c).

Although immediate action by the European Commission and Member States was not triggered, since the previous CRAs, authorisations for some pesticides have been withdrawn while new authorisations may have been issued for other pesticides. Hence, CRAs need to be repeated on a regular basis to capture possible changes in use patterns and exposure. Considering that CRAs rely on

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[1] OJ L 70, 16.3.2005, p. 1–16.
[2] OJ L 309, 24.11.2009, p. 1–50.
[3] The MOET is the reciprocal of the harmonic sum of the individual substances' MOEs. The MOE for each individual substance is the ratio of the toxicological reference point of that substance (i.e. NOAEL) to the estimated exposure (EFSA, 2019a,b).

a 3-year cycle of monitoring data (i.e. in accordance with the European multi-annual control programme), EFSA intends to repeat these assessments every 3 years.

Some concerns were raised as to whether exposure patterns may change on a yearly basis and more regular assessments would be required. To address these concerns, EFSA decided to repeat the exposure assessments for the most recent 3-year cycle of monitoring data currently available at EFSA (i.e. 2016–2018). Comparison with the results obtained for the previous reference period (i.e. 2014–2016) will allow EFSA not only to identify possible changes in exposure patterns but also to develop more efficient strategies for identifying such changes.

1.2. Terms of Reference

Cumulative exposure to pesticides associated with chronic effects on the thyroid and to pesticides associated with acute effects on the nervous system is calculated for the reference period 2016–2018. These calculations are carried out for 10 population groups and four CAGs, which include the following pesticides:

- 18 pesticides associated with hypertrophy, hyperplasia and neoplasia of C-cells, i.e. affecting the parafollicular cells or the calcitonin system of the thyroid (CAG-TCP);
- 124 pesticides associated with hypothyroidism, i.e. affecting the follicular cells and/or the hormone system of the thyroid (CAG-TCF);
- 47 pesticides associated with brain and/or erythrocyte acetylcholinesterase inhibition (CAG–NAN);
- 100 pesticides associated with functional alterations of the motor division (CAG-NAM).

Results are compared with the cumulative exposure estimates previously obtained for the reference period 2014–2016 (EFSA, 2019a,b). The comparison of results concentrates on the exposure estimates that were used for risk characterisation, i.e. MOET estimates obtained at the 99.9th percentile of the exposure distribution for the Tier II scenario.

The current assessment aims to investigate how changes in occurrence data may influence the outcome of the exposure assessment and does not include a detailed assessment of the uncertainties that should be accounted for in a separate risk characterisation.

2. Data and methodologies

2.1. General principles

All cumulative exposure calculations were performed in accordance with the guidance on probabilistic modelling of dietary exposure to pesticide residues (EFSA PPR Panel, 2012). Exposure estimates were obtained using a two-dimensional method where variability is modelled by means of an inner loop execution, and uncertainty is modelled through an outer loop execution (Figure 1).

The ***primary input data*** required for modelling cumulative exposure to pesticide residues are occurrence data (i.e. the amounts of pesticide residue that are present in foods) and food consumption data (i.e. the types and amounts of those food consumed in a person's diet). These data are stored in the EFSA Scientific Data Warehouse. When the exposure calculations are initiated, the data for the relevant food commodities, active substances and dietary surveys are extracted.

Within the ***inner loop execution***, occurrence data are subject to several simulations and imputations. These adjustments are intended to account for inaccuracies and missing information in the occurrence data set (e.g. unspecific measurements, measurements below the analytical limit of quantification etc.). The consumption data and adjusted occurrence data are then combined to generate empirical exposure distributions that represent the variability of chronic or acute exposures within the population.

The different simulations performed during the inner loop execution require the use of additional data, referred to as ***secondary input data***. This includes various types of data which can be used either for the adjustment of the occurrence data (e.g. authorisation status of the active substance) or for improvement of the exposure estimates (e.g. processing factors).

In order to quantify the uncertainties, the model uses an ***outer loop execution*** where the inner loop execution is repeated several times. Prior to each execution, the original consumption and occurrence data sets are modified by means of bootstrapping, a random resampling technique for quantifying sampling uncertainty. By repeating the inner loop execution multiple times, the model

produces multiple distributions of exposure. The differences between those distributions reflect the uncertainty around the true distribution of exposures.

During the **output preparation**, summary statistics (i.e. percentiles of exposure) are generated for the multiple distributions, resulting in multiple estimates for each percentile of exposure. From these multiple estimates, confidence intervals around each percentile are produced. Subsequently, in order to identify main contributors, details on the highly exposed consumers are extracted (i.e. consumers with exposure exceeding the 99th percentile) and average contributions per food commodity and active substance are calculated.

According to the risk management principles agreed among Member States, the methodology described above is normally applied in a tiered approach (EFSA, 2019a,b). While the first-tier calculations (Tier I) use very conservative assumptions, the second-tier assessment (Tier II) includes assumptions that are more refined but still intended to be conservative. For this statement, however, which aims at comparing the outcome of the exposure assessment for the reference period 2016–2018 with a previous assessment for the reference period 2014–2016, only the more refined Tier II calculations were carried out.

All extractions, simulations, imputations and calculations for the current assessment were programmed with SAS$^®$ Studio 3.8 (Enterprise Edition). The figures for this statement were compiled in the programming environment R 4.0.1 with the ggplot package 3.3.2.
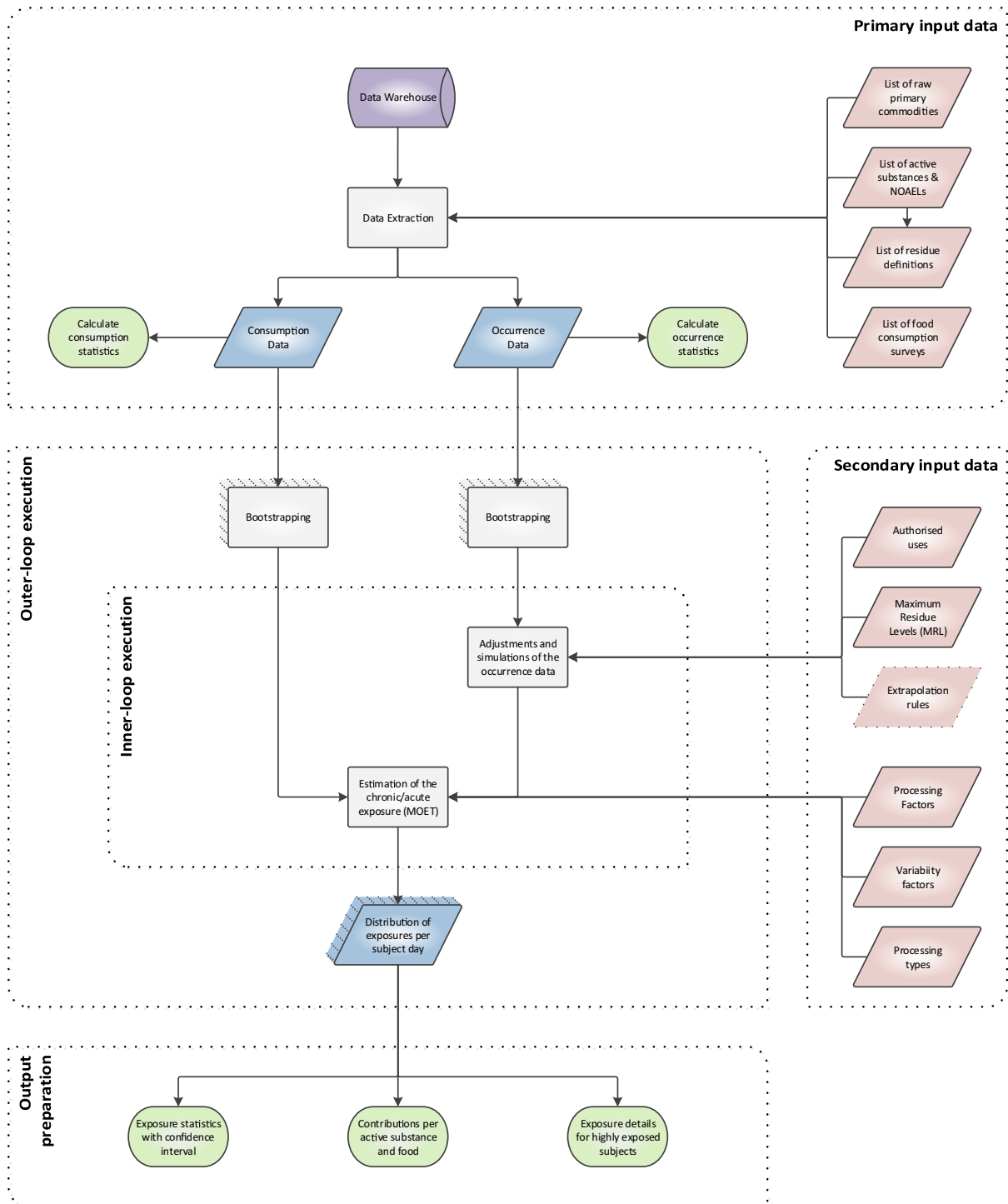
Figure 1: General process for calculating cumulative dietary exposure to pesticides

2.2. Data

This section provides a short summary of the input data used for calculating cumulative dietary exposure to four CAGs in 10 different population groups for the reference period 2016–2018, highlighting the main differences with the previous reference period of 2014–2016. A more extensive description of the data sources and data formats can be obtained from previous reports (EFSA, 2019a,b), whereas the input data tables used for the reference period 2016–2018 are provided in the following annexes.

- Annex A.1 presents the input data for the cumulative exposure calculation to CAG-TCP.
- Annex A.2 presents the input data for the cumulative exposure calculation to CAG-TCF.

- Annex A.3 presents the input data for the cumulative exposure calculation to CAG-NAN.
- Annex A.4 presents the input data for the cumulative exposure calculation to CAG-NAM.

2.2.1. Primary input data

The primary input data consist of chemical occurrence data obtained from the official control activities carried out in the EU Member States, Iceland, Norway and EU pre-accession countries, and food consumption data obtained from national dietary surveys collected at individual level. Both chemical occurrence data and food consumption data are stored in EFSA's Data Warehouse. This data extraction is determined by four primary entities: a list of food commodities, a list of active substances, a list of residue definitions and a list of dietary surveys.

2.2.1.1. Raw primary commodities

The list of food commodities includes 35 raw primary commodities (RPCs) of plant origin that are widely consumed in Europe, water and foods specifically intended for infants and young children (see Annex A.1, Table A.1.02; Annex A.2, Table A.2.02; Annex A.3, Table A.3.02; and Annex A.4, Table A.4.02).

Compared to the previous reference period, the list includes five new RPCs to account for new food commodities that were added to the multi-annual control programme for the years 2017 and 2018 (i.e. grapefruits, kiwi fruits, onions, cultivated fungi and dry beans). The remaining 30 RPCs remained unchanged over both periods.

2.2.1.2. Active substances

The list of active substances refers to the pesticides included in each CAG, where the toxicological potency within each CAG is defined by means of the no observed adverse effect level (NOAEL) (see Annex A.1, Table A.1.01; Annex A.2, Table A.2.01; Annex A.3, Table A.3.01; and Annex A.4, Table A.4.01).

The list of active substances and NOAELs remained unchanged compared to the previous reference period.

2.2.1.3. Residue definitions

The list of residue definitions provides an overview of the residue definitions that were applicable to the selected food commodities and active substances during the reference period 2016–2018 (see Annex A.1, Table A.1.03; Annex A.2 Table A.2.03; Annex A.3, Table A.3.03; and Annex A.4, Table A.4.03). Enforcement residue definitions are defined under Regulation (EC) No 396/2005 and may change over time.

Compared to the previous reference period, the list of residue definitions was updated to account for changes in residue definition that occurred in 2017 and 2018.

2.2.1.4. Dietary surveys

The list of dietary surveys defined the population classes and countries considered for the assessment (see Annex A.1, Table A.1.04; Annex A.2, Table A.2.04; Annex A.3, Table A.3.04; and Annex A.4, Table A.4.04).

The population classes and countries selected for the reference period 2016–2018 remained unchanged compared to the previous reference period.

2.2.1.5. Occurrence data

Chemical occurrence data collected under Article 31 of Regulation (EC) No 396/2005 and validated under the 2016, 2017 and 2018 EU reports on pesticide residues in food (EFSA, 2018, 2019c, 2020a) were extracted for the food commodities and residue definitions reported above. Data from all EU Member States, Iceland, Norway and EU pre-accession countries were pooled into one single data set for each CAG. Occurrence data included in the assessment were submitted to EFSA when the UK was a member of the EU. Summary statistics per residue definition and food commodity are reported for the period 2016–2018 in Annex A.1, Table A.1.09; Annex A.2, Table A.2.09; Annex A.3, Table A.3.10; and Annex A.4, Table A.4.10.

The data considered for the previous reference period referred to those validated under the 2014, 2015 and 2016 EU reports on pesticide residues in food (EFSA, 2016, 2017, 2018). Some residue

definitions and food commodities considered were different for both reference periods (see Sections 2.2.1.1 and 2.2.1.3).

2.2.1.6. Consumption data

Food consumption data were collected at national level, compiled in the EFSA Comprehensive European Food Consumption Database (Comprehensive Database)[4] and subsequently converted to equivalent amounts of RPC (EFSA, 2019d). Relevant data were extracted for the food commodities and dietary surveys reported above but, for chronic exposure assessment (CAG-TCP and CAG-TCF), individuals who participated for only 1 day of the dietary survey were excluded because at least two survey days per individual are normally required to assess repeated exposure (EFSA, 2011). Dietary data included in the assessment were submitted to EFSA when the UK was a member of the EU. Summary statistics on the quantities of RPC consumed per country, survey and population class are reported for the period 2016–2018 in the Annex A.1, Table A.1.10; Annex A.2, Table A.2.10; Annex A.3, Table A.3.11; and Annex A.4, Table A.4.11.

Compared to the previous reference period, summary statistics are now also reported for the five new RPCs. Food consumption data for the other food commodities remained unchanged.

2.2.2. Secondary input data

The secondary input data include various types of data that can be used for different sorts of simulations during the inner loop executions of the calculations (see also Section 2.3).

2.2.2.1. Maximum Residue Levels

Certain assumptions on the extrapolation of occurrence data require information on the MRLs. An MRL is the upper legal level of a concentration for a pesticide residue in or on food or feed set in accordance with Regulation (EC) No 396/2005. For the reference period 2016–2018, EFSA decided to use the MRLs as of 31 December 2018 (i.e. the end of the reference period) for the food commodities and residue definitions reported above (Annex A.1, Table A.1.05; Annex A.2, Table A.2.05; Annex A.3, Table A.3.05; and Annex A.4, Table A.4.05).

Considering that MRLs are regularly modified, this list of MRLs is different from the one used for the previous reference period.

2.2.2.2. Authorised Uses

There are several simulations and imputations of the occurrence data that rely on the authorisations for use of the active substance(s). This includes the extrapolation of occurrence data, the imputation of left-censored data and the imputation of active substances when the enforcement residue definition may refer to more than one active substance (see also Section 2.3). The authorised uses considered for the reference period 2016–2018 are presented in Annex A.1, Table A.1.06; Annex A.2, Table A.2.06; Annex A.3, Table A.3.06; and Annex A.4; Table A.4.06.

Considering that the authorisation status of pesticides may change regularly, this list of authorised uses is different from the one used for the previous reference period.

2.2.2.3. Extrapolation Rules

The extrapolation of occurrence data is carried out in compliance with the guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (European Commission, 2017). The extrapolation rules considered for this assessment are presented in Annex A.1, Table A.1.07; Annex A.2, Table A.2.07; Annex A.3, Table A.3.07; and Annex A.4, Table A.4.07.

These extrapolation rules remained unchanged compared to the previous reference period.

2.2.2.4. Processing Factors

Occurrence data for pesticide residues are collected at the level of RPC while, in reality, these residues will most likely be altered through processing, such as peeling, cooking etc. In the current assessment, the effect of processing is addressed by means of processing factors. The processing factors considered for the reference period of 2016–2018 are listed in Annex A.1, Table A.1.08; Annex A.2, Table A.2.08; Annex A.3, Table A.3.08; and Annex A.4, Table A.4.08.

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[4] https://www.efsa.europa.eu/en/food-consumption/comprehensive-database

For the previous reference period, EFSA considered only processing factors reported in the European database on processing factors which was the most recent and the most comprehensive compilation of processing factors available at that time (Scholz et al., 2018). Meanwhile, additional processing factors were assessed by EFSA in the framework of Regulation (EC) No 396/2005 and Regulation (EC) No 1107/2009. All additional processing factors evaluated and reported by EFSA until 31 December 2019 were therefore also considered in the current assessment.

2.2.2.5. Variability factors

Acute exposure assessments for pesticide residues should account for variability among the single commodity units of the composite laboratory samples. To account for this variability, several parameters are required for each food commodity.

- Unit weight: estimated weight for a single commodity unit.
- Units per sample: estimated number of units within a composite laboratory sample.
- Variability factor (VF): expected variability among the single unit concentrations, which is defined as the ratio between the 97.5th percentile and mean of the distribution of unit concentrations.

These parameters are only relevant for the acute exposure assessment and are reported in Annex A.3, Table A.3.02 and Annex A.4, Table A.4.02.

Compared to the previous reference period, relevant parameters were added for the five new RPCs. Parameters for the other RPCs remained unchanged.

2.2.2.6. Processing types

When performing the acute exposure assessments, variability among the single commodity units of the composite laboratory samples is only relevant when the food consumed is not subject to processing techniques that involve bulking and blending. An overview of the different processing types, including an indication on whether they involve bulking or blending, is provided in Annex A.3, Table A.3.09 and Annex A.4, Table A.4.09.

Compared to the previous reference period, one processing type associated with one of the new RPCs (i.e. grinding/milling/crushing of dry beans) was added. Other processing types remained unchanged.

2.3. Methodologies

The cumulative exposure calculations rely on a two-dimensional probabilistic method. The first dimension consists of an inner loop execution where consumption data and occurrence data are combined to obtain an empirical distribution of exposure estimates. The different percentiles of these distributions represent the variability of exposures within each population group.

The second dimension is an outer loop execution where the inner loop execution is repeated 100 times, each time replacing the consumption and occurrence data sets with bootstrap data sets. Bootstrap data sets are obtained by resampling, with replacement, the same number of observations from the original data sets. The outer loop execution produces 100 exposure distributions and, as a result, 100 MOET estimates are obtained for each percentile of the exposure distribution. These 100 estimates reflect the sampling uncertainty distribution around the true value of those percentiles. From these uncertainty distributions, a 95% confidence interval is calculated for each percentile. The median of the uncertainty distribution is selected as the central estimate for the confidence interval.

Within the inner loop execution, prior to combining consumption and occurrence data, the occurrence data are subject to several simulations and imputations to account for inaccuracies and missing information in the occurrence data sets. These include the following:

- Allocation of active substances to the occurrence data: occurrence data are collected for residues definitions while CAGs are established for active substances; when a residue definition is associated with multiple active substances, imputation of one or more active substances is required.
- Extrapolation of occurrence data: when measurements for an active substance in a given food commodity are too limited or missing, measurements are extrapolated from another closely related food commodity.
- Imputation of left-censored occurrence data (i.e. below the limit of quantification): considering that over 95% of the occurrence data used for the exposure assessments are left-censored,

assumptions are made on whether these data may be low-positive residues or true zeroes (i.e. no-residue situation).

- Imputation of missing occurrence data: in acute cumulative exposure assessments, it is necessary to take account of any correlations that may exist between the concentrations of the different active substances within a given food sample, but available samples were not necessarily analysed for every active substance of the CAG; in order to avoid underestimation, missing measurements are imputed.
- Imputation of occurrence data for water: occurrence data for water are not available to EFSA and are therefore imputed according to agreed principles (EFSA, 2019a,b).

For chronic exposure assessment, the inner loop execution is based on the observed individual means (OIM) method. This method combines the mean consumption with the mean occurrence values for all pesticides (adjusted for their toxicological potency) to calculate chronic exposures for all individuals within the population.

For acute exposure assessment, the inner loop execution relies on a Monte Carlo simulation with 100,000 iterations. This means that, for each population group, 100,000 individual days are selected at random from the consumption data set and, for each food commodity consumed within an individual day, random samples of the occurrence data set are assigned. Using the concentration of the different active substances measured in the different samples (adjusted for their toxicological potency), acute exposures are calculated for each of the 100,000 individual days. Because residue concentrations may vary within a composite laboratory sample, acute exposure calculations, as opposed to chronic exposure calculations, also consider unit-to-unit variability.

The methodological approaches used for the current assessment are all in accordance with the methods used for previous assessments and a more detailed description can be retrieved from those reports (EFSA, 2019a,b).

An overview of the main assumptions and methodological approaches used for this assessment, both chronic and acute, is provided in Table 1.

Table 1: Overview of the main assumptions and methodological approaches used for assessing chronic and acute cumulative exposure to pesticide residues under the Tier II scenario

	Description	
Consumption data		
Number of surveys	10	
Population classes	Adults (Belgium, Czech Republic, Germany and Italy)[(a)] Toddlers (Denmark, Netherlands and United Kingdom)[(b)] Other children (Bulgaria, France and Netherlands)[(c)]	
Food commodities	35 raw primary commodities (includes conversion from foods as eaten) + 4 categories of foods for infants and young children + water	
Other criteria	Chronic: Individuals who participated only 1 day in the dietary survey were excluded	Acute: Not applicable
Occurrence data (extraction)		
Reference period	2016–2018 (latest available 3-year cycle)	
Food commodities	35 raw primary commodities (unprocessed or frozen) + 4 categories of foods for infants and young children	
Residue definitions	All residue definitions associated with CAG-TCP, CAG-TCF, CAG-NAN and CAG-NAM during the reference period	
Sampling framework	EU-coordinated or national control programmes	
Sampling type	Objective or selective sampling only	
Occurrence data (simulations and imputations)		
Unspecific residue definitions	Random allocation of authorised active substances to each sample	
Extrapolations	Extrapolation of measurements per active substance and commodity in accordance with guidance document SANCO 7525/VI/95 (Commission, 2017), when MRL is equal and substance is authorised in both source ($N \geq 10$) and target ($N < 10$) commodities	
Left-censored data	Imputed at 1/2 LOQ based on estimated use frequencies (assuming 100% crop treatment)	
Missing measurements	Chronic: Not applicable	Acute: Random assignment of missing measurements to available samples
Drinking water	Imputed at 0.05 μg/L for the five most potent active substances	
Exposure calculations		
Exposure model	Chronic: Observed individual means approach (inner loop execution)	Acute: Empirical Monte Carlo simulation (inner loop execution, n = 100,000)
Uncertainty model	Empirical bootstrapping (outer loop execution, n = 100)	
Processed foods	Processing factors obtained or extrapolated from the European database on processing factors for pesticides in food (Scholz et al., 2018)and additional processing factors evaluated by EFSA between July 2016 and December 2019	
Unit-to-unit variability	Chronic: Not applicable	Acute: Unit concentration sampled from beta distribution with a variability factor of 3.6

(a): The population class 'adults' refers to participants from $\geq$ 18 years to < 65 years old.
(b): The population class 'toddlers' refers to participants from $\geq$ 12 months to < 36 months old.
(c): The population class 'other children' refers to participants from $\geq$ 36 months to < 10 years old.

3. Assessment

This section summarises the cumulative exposure estimates for two CAGs associated with chronic effects on the thyroid (CAG-TCP and CAG-TCF), and two CAGs associated with acute effects on the nervous system (CAG-NAN and CAG-NAM). Exposure estimates were obtained in 10 different population groups for the reference period 2016–2018, and compared to the exposure estimates previously obtained for the reference period 2014–2016 (EFSA, 2019a,b). Detailed results for the reference period 2016–2018 (including graphs and charts) are provided in the annexes.

- Annex B.1 presents the results of the chronic Tier II exposure calculations to CAG-TCP
- Annex B.2 presents the results of the chronic Tier II exposure calculations to CAG-TCF

- Annex B.3 presents the results of the acute Tier II exposure calculations to CAG-NAN
- Annex B.4 presents the results of the acute Tier II exposure calculations to CAG-NAM

All exposure estimates are expressed in MOET, which represents the ratio of a toxicological reference point to the estimated exposure.[5] Hence, an MOET below 1 implies that the estimated exposure exceeds the NOAEL. Likewise, an MOET of 100 means that the estimated exposure is 100 times lower than the NOAEL. The threshold for regulatory consideration agreed among Member States is an MOET of 100 at the 99.9th percentile of the exposure distribution. MOETs below this threshold may therefore trigger a risk management decision by the European Commission and Member States.

It is emphasised that results presented only refer to the outcome of the exposure assessment and do not include a risk characterisation with a detailed analysis of all uncertainties. The present statement is only intended to make a comparative analysis with previous calculations and to identify possible changes in exposure over time.

3.1. Cumulative exposure estimates for the reference period 2016–2018

3.1.1. Chronic exposure estimates for CAG-TCP

The results from the chronic Tier II calculations for CAG-TCP in the period 2016–2018 are presented in Table 2. The largest margins of exposure at the 99.9th percentile were observed for adults, which ranged from 2,640 (Germany) to 3,770 (Belgium). Lower MOETs at the 99.9th percentile are observed for all children and toddlers, with the Dutch population groups showing the lowest median values of 1,900 and 1,830, respectively.

The main contributors were identified for the upper percentile of the exposure distribution, i.e. for individuals exceeding the 99th percentile of the distribution. The main contributors for CAG-TCP were thiram (78.3–87.2%), ziram (8.9–15.3%) and amitrole (4.2–5%) (see Annex B.1, Table B.1.02 and Figure B.1.03). In adults, most of the exposure to thiram and ziram came from wine grapes (27–52.2% and 6–13.3%, respectively). Other important contributors to the thiram exposure are strawberries (up to 54.8%), pears (up to 30.9%), lettuce (up to 29.7%), peaches (up to 20.9%), apples (up to 19.9%) and table grapes (up to 12.5%), while for ziram important contributors are pears (up to 7.6%) and apples (up to 5.5%). Exposure to amitrole, however, came from peaches (up to 3.9%) and drinking water (up to 2.5%). Other substances and commodities contributed less than 5% to the 99th percentile exposure estimates.

Table 2: Estimates of the total margin of exposure (MOET) and their corresponding 95% confidence intervals at the 50th, 95th, 99th and 99.9th percentiles of the exposure distribution for the Tier II scenario of CAG-TCP

Country	Population class	50th Percentile	95th Percentile	99th Percentile	99.9th Percentile
Belgium	Adults	25,100 [20,100–30,100]	7,700 [3,540–10,900]	5,430 [2,350–8,010]	3,770 [1,400–5,710]
Czechia	Adults	42,300 [33,900–48,600]	9,700 [4,620–13,200]	5,930 [2,440–7,850]	3,340 [1,610–5,310]
Germany	Adults	19,000 [15,900–22,500]	6,030 [3,710–7,710]	4,020 [2,270–5,280]	2,640 [1,450–3,500]
Italy	Adults	19,400 [14,600–24,000]	7,630 [4,110–9,840]	5,470 [2,880–6,990]	3,690 [2,070–4,890]
Bulgaria	Other children	14,700 [12,100–16,800]	4,000 [3,090–4,750]	2,610 [2,180–3,440]	2,100 [1,560–2,770]
France	Other children	16,200 [13,200–19,100]	6,470 [4,830–7,590]	4,640 [3,460–5,690]	3,690 [2,610–4,690]
Netherlands	Other children	11,800 [9,500–14,000]	4,820 [3,770–5,610]	3,060 [2,440–3,830]	1,900 [1,360–2,580]
Denmark	Toddlers	10,000 [8,600–11,400]	4,100 [3,390–4,920]	2,930 [2,410–3,490]	2,310 [1,890–2,840]

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[5] The MOET is the reciprocal of the harmonic sum of the individual substances' MOEs. The MOE of each individual substance is the ratio of the toxicological reference point (i.e. NOAEL) to the estimated exposure (EFSA, 2019a,b).

Country	Population class	50th Percentile	95th Percentile	99th Percentile	99.9th Percentile
Netherlands	Toddlers	8,800 [6,590–10,390]	3,400 [2,730–4,190]	2,230 [1,720–3,350]	1,830 [1,470–2,310]
United Kingdom	Toddlers	13,800 [11,900–15,500]	5,000 [4,210–5,730]	3,500 [2,810–4,230]	2,730 [2,060–3,260]

3.1.2. Chronic exposure estimates for CAG-TCF

The results from the chronic Tier II calculations for CAG-TCF in the period 2016–2018 are presented in Table 3. The median MOET estimates at the 99.9th percentile for adults ranged from 276 (Germany) to 324 (Belgium). Lower MOETs at the 99.9th percentile are observed for all children and toddlers, with Denmark toddlers (133), Bulgarian children (132) and Dutch toddlers (101) being the lowest.

Major contributors to the 99th percentile exposure estimates were bromide ion (35–62.8%), ziram (8–18.1%), thiabendazole (6.4–16.8%), probineb (2.6%–11.6%), pyrimethanil (2.1–10.9%), mancozeb (4–10%) and cyprodinil (0.93–8.9%) (see Annex B.2, Table B.2.02 and Figure B.2.03). Most bromide came from wheat (up to 34.5%), tomatoes (up to 13.6%), oat (up to 12.7%) and rice (up to 10.5%). For ziram, the contribution was mainly driven by wine grapes (up to 14.6%, adults only) and apples (up to 10%). Likewise, for propineb and cyprodinil in adults, wine grapes was the major contributor (up to 10.2% and 8.1%, respectively). Most of the exposure to mancozeb, thiabendazole and pyrimethanil, however, came from oranges (up to 8.3%, 19.7% and 9.5%, respectively). Other substances and commodities contributed less than 5% to the 99th percentile exposure estimates.

Table 3: Estimates of the total margin of exposure (MOET) and their corresponding 95% confidence intervals at the 50th, 95th, 99th and 99.9th percentiles of the exposure distribution for the Tier II scenario of CAG-TCF

Country	Population class	50th Percentile	95th Percentile	99th Percentile	99.9th Percentile
Belgium	Adults	983 [910–1,043]	520 [444–572]	421 [333–463]	324 [189–397]
Czechia	Adults	1,030 [970–1,080]	536 [469–583]	393 [319–448]	285 [195–353]
Germany	Adults	1,020 [960–1,080]	503 [451–550]	377 [325–424]	276 [230–316]
Italy	Adults	770 [725–820]	451 [397–494]	363 [324–410]	296 [265–335]
Bulgaria	Other children	332 [313–358]	198 [184–212]	154 [131–173]	132 [119–153]
France	Other children	519 [484–552]	286 [267–317]	225 [205–268]	205 [191–220]
Netherlands	Other children	473 [441–506]	270 [245–297]	213 [193–236]	179 [161–203]
Denmark	Toddlers	332 [311–360]	219 [206–238]	189 [159–202]	133 [103–176]
Netherlands	Toddlers	360 [330–401]	205 [179–238]	160 [132–188]	101 [86.2–162]
United Kingdom	Toddlers	409 [384–437]	235 [221–249]	191 [172–205]	143 [102–174]

3.1.3. Acute exposure estimates for CAG-NAN

The results from the acute Tier II calculations for CAG-NAN in the period 2016–2018 are presented in Table 4. Although margins of exposure were generally found to be higher for adults compared to children and toddlers, the lowest margin of exposure at the 99.9th percentile of the exposure distribution was observed for Italian adults (19.3). Median MOET estimates at the 99.9th percentile for children and toddlers ranged from 36.9 (French children) to 70.1 (Danish toddlers).

The most important contributor to the exposure was omethoate, accounting for 19.3–83% of the 99th percentile exposure estimates (see Annex B.3, Table B.3.02 and Figure B.3.03). These high

contributions were very much driven by olives for oil production (up to 82.8%), but important contributions from mandarins (up to 6.8%), tomatoes (up to 6.6%) and oranges (up to 5.4%) were also noted. The contribution of dimethoate, which ranged from 0.9% to 12.9%, was also entirely driven by its presence in olives for oil production.

Other substances like triazophos, chlorpyrifos and dichlorvos contributed for 0.8–27.5%, 0.5–27.7% and 2.9–8.1%, respectively. The driving commodities for triazophos were green beans with pods (up to 21.2%) and rice (up to 7.8%), whereas contribution of chlorpyrifos was driven by apples (up to 11.8%), tomatoes (up to 6.8%) and oranges (up to 5.2%) and contribution of dichlorvos was driven by wheat (up to 7.4%). Other substances and commodities contributed less than 5% to the 99th percentile exposure estimates.

Table 4: Estimates of the total margin of exposure (MOET) and their corresponding confidence intervals at the 50th, 95th, 99th and 99.9th percentiles of the exposure distribution for the Tier II scenario of CAG-NAN

Country	Population class	50th Percentile	95th Percentile	99th Percentile	99.9th Percentile
Belgium	Adults	2,890 [2,810–2,960]	1,290 [1,220–1,340]	645 [518–724]	124 [48–187]
Czechia	Adults	2,770 [2,690–2,830]	1,250 [1,190–1,310]	657 [349–754]	75.9 [30.1–225]
Germany	Adults	2,290 [2,250–2,340]	1,050 [840–1,110]	461 [122–669]	71.6 [30.5–191]
Italy	Adults	3,770 [3,380–4,430]	1,190 [739–1,630]	212 [18.3–708]	19.3 [10–167]
Bulgaria	Other children	1,840 [1,750–1,920]	619 [600–657]	281 [253–315]	61.6 [42.4–81.2]
France	Other children	2,400 [2,310–2,460]	827 [772–888]	342 [220–409]	36.9 [13.3–94.2]
Netherlands	Other children	2,090 [2,040–2,150]	766 [729–807]	360 [325–391]	81 [57.8–110]
Denmark	Toddlers	1,620 [1,590–1,660]	592 [507–625]	267 [143–333]	70.1 [43.2–112]
Netherlands	Toddlers	1,640 [1,550–1,740]	581 [545–612]	269 [242–300]	63.4 [50.5–84]
United Kingdom	Toddlers	1,550 [1,510–1,590]	613 [577–637]	306 [198–358]	53.6 [21.5–101]

3.1.4. Acute exposure estimates for CAG-NAM

The results from the acute Tier II calculations for CAG-NAM in the period 2016–2018 are presented in Table 5. Similar to the CAG-NAN, the lowest MOETs at the 99th percentile were observed for Italian adults (33.4) and median MOET estimates for children and toddlers ranged from 52.2 (French children) to 86 (Dutch children).

As for CAG-NAN, omethoate is also the predominant contributor for CAG-NAM, accounting for 6.9–93.6 % of the highest exposure estimates (see Annex B.4, Table B.4.02 and Figure B.4.03). In this case, exposure to omethoate was almost entirely driven by olives for oil production (up to 93.4%). Other substances driving the exposure were deltamethrin (0.7–42.1%), triazophos (2.2–31.6%) and lambda-cyhalothrin (0.4–7.5%). For triazophos, the exposure was mainly resulting from its occurrence in beans with pods (up to 32.8%) and rice (up to 6.9%) and the contribution of deltamethrin was driven by wheat (up to 40.1%). A further contributor of exposure was lambda-cyhalothrin, driven by mainly oranges (up to 5.1%). Other substances and commodities contributed less than 5% to the 99th percentile exposure estimates.

Table 5: Estimates of the total margin of exposure (MOET) and their corresponding 95% confidence intervals at the 50th, 95th, 99th and 99.9th percentiles of the exposure distribution for the Tier II scenario of CAG-NAM

Country	Population class	50th Percentile	95th Percentile	99th Percentile	99.9th Percentile
Belgium	Adults	3,490 [3,390–3,560]	1,420 [1,320–1,500]	706 [579–789]	150 [67.6–258]
Czechia	Adults	3,280 [3,220–3,350]	1,390 [1,310–1,450]	651 [384–782]	109 [44.1–263]
Germany	Adults	2,710 [2,670–2,760]	1,170 [1,050–1,250]	544 [287–715]	114 [50.5–232]
Italy	Adults	4,630 [4,230–5,220]	1,280 [987–1,610]	212 [31.4–673]	33.4 [14.7–201]
Bulgaria	Other children	2,230 [2,110–2,330]	668 [635–704]	273 [240–304]	64.9 [37.2–93.4]
France	Other children	2,890 [2,830–2,980]	854 [793–909]	325 [251–386]	52.2 [20.1–110]
Netherlands	Other children	2,480 [2,410–2,560]	807 [746–861]	352 [312–392]	86 [54–123]
Denmark	Toddlers	1,830 [1,760–1,890]	577 [483–641]	259 [198–308]	81.5 [55.1–114]
Netherlands	Toddlers	1,930 [1,840–2,040]	642 [597–680]	277 [240–308]	68 [47.5–89.3]
United Kingdom	Toddlers	1,900 [1,860–1,940]	658 [606–698]	280 [210–336]	63.8 [36.2–106]

3.2. Comparison with the previous reference period 2014–2016

Cumulative exposure estimates obtained for the reference period 2016–2018 were compared to those obtained for the previous reference period 2014–2016 (EFSA, 2019a,b). This comparison was limited to the estimates obtained at the 99.9th percentile of the exposure distribution, because the threshold for regulatory consideration agreed among Member States was defined for the same percentile. This percentile of the exposure distribution was therefore also used as the starting point for a complete characterisation of risks (EFSA, 2020b,c).

For this comparison, a distinction was made between pesticides associated with chronic effects on the thyroid and pesticides associated with acute effects on the nervous system.
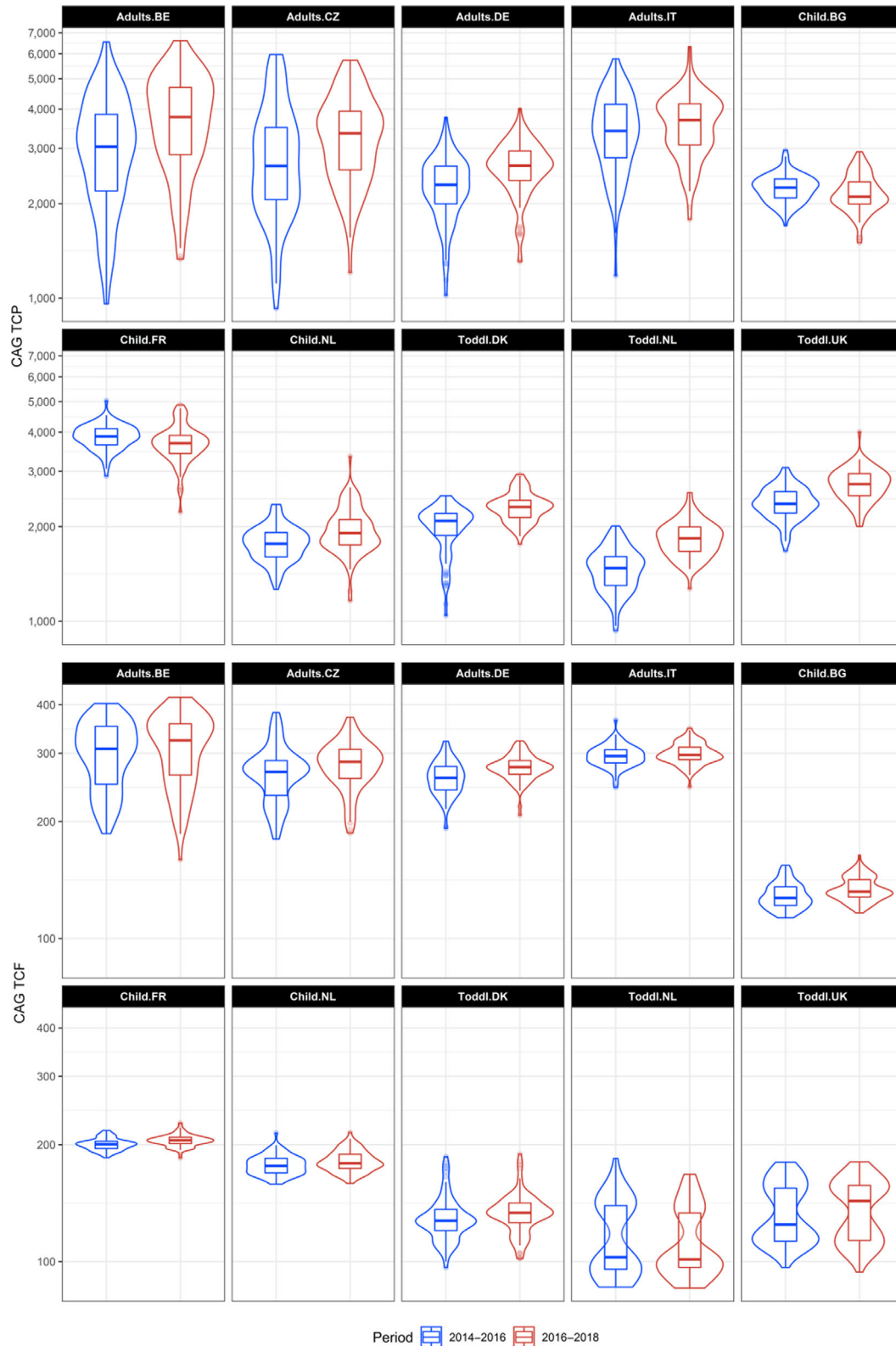
3.2.1. Pesticides associated with chronic effects on the thyroid

The comparison of Tier II confidence intervals obtained for CAG-TCP and CAG-TCF at the 99.9th percentile of the exposure distribution is visualised in Figure 2 by means of box plots and violin plots. A comparison of results in tabular form is also reported in Appendix A, Table A.1.

In comparison to the period of 2014–2016, cumulative exposure estimates for both CAG-TCP and CAG-TCF did not change substantially. For some populations, a slight shift towards higher margins of exposure was observed (e.g. CAG-TCP in toddlers) but, overall, the confidence intervals overlap largely.

This observation is also confirmed by a comparison of main contributors. The contributors described in Sections 3.1.1 and 3.1.2 are the same as those described for the reference period 2014–2016 (EFSA, 2019a,b). Only for CAG-TCP a new contribution of amitrole in peaches was observed (up to 3.8%). This new contribution is mainly attributed to a positive finding of amitrole in peaches reported at 0.5 mg/kg (see Annex A.1, Table A.1.09), while for the reference period 2014–2016 all findings for amitrole in peaches were reported below the limit of quantification. Despite this new finding, a decrease of the total margin of exposure was not observed.

It is important to highlight that the calculations for 2016–2018 included additional RPCs (see Section 2.2.1.1) and processing factors (see Section 2.2.2.4). However, none of the new RPCs were identified as major contributors and, although some processing factors referred to the major contributors (e.g. thiram and propineb), these additional data did not affect the outcome of the calculations.

Legend: The box represents the interquartile range and the vertical line inside the box is the median, the two lines outside the box (whiskers) range from the 97.5th percentile to the 2.5th percentile (i.e. 95% confidence). The width of the violin plot represents the density of observations within the confidence interval.

Figure 2: Confidence intervals for estimates of the total margin of exposure (MOET) at the 99.9th percentile of the exposure distribution for CAG-TCP and CAG-TCF in the reference periods 2014–2016 and 2016–2018, presented as a combination of box plots and violin plots on logarithmic scale

3.2.2. Pesticides associated with acute effects on the nervous system

The comparison of Tier II confidence intervals obtained for CAG-NAN and CAG-NAM at the 99.9th percentile of the exposure distribution is visualised in Figure 3 by means of box plots and violin plots. A comparison of results in tabular form is also reported in Appendix A, Table A.2.

Median MOET estimates for most children and toddler populations were equal or slightly higher compared to the period 2014–2016. For adult populations and French children, the median MOET estimates decreased but, more importantly, the confidence intervals have become much wider and bimodal, i.e. when observations of the confidence intervals are clustered at the upper end and lower end of the confidence intervals. This shows that sampling uncertainty increased for the period 2016–2018 and that the median estimate of the confidence interval is less reliable (i.e. the median estimate will fluctuate when additional bootstrapping is performed).

Furthermore, the comparison of main contributors (see Sections 3.1.3 and 3.1.4) revealed a six- to ninefold increase of the contribution of omethoate in olives for oil production compared to period 2014–2016. EFSA therefore investigated the occurrence data that were used as input (see Annex A.3, Table A.3.10 and Annex A.4, Table A.4.10). From the 79 samples of olives for oil production, 67 samples were analysed for either omethoate or the sum of dimethoate and omethoate, and only three positive results were measured up to 4.9 mg/kg. All other measurements were below the limit of quantification. For the period 2014–2016, 81 out of 94 samples were analysed for the sum of dimethoate and omethoate and 10 positive measurements up to 0.34 mg/kg were identified.

This demonstrates that the outcome of a cumulative exposure assessment at the 99.9th percentile of the exposure distribution can be very much influenced by a single finding in a specific sample, in this case a measurement of 4.9 mg/kg for the sum of omethoate and dimethoate in olives for oil production. The impact of such a single measurement would normally be captured by the confidence interval that accounts for sampling uncertainty. In this case, however, due to the relatively low number of samples (79 samples vs. 400–10,000 for the other commodities), average concentration in each bootstrap data set will be strongly influenced by the extreme measurement of 4.9 mg/kg. Furthermore, this measurement will not be part of around 36% of the bootstrap data sets, whereas it may be sampled twice or thrice in about 26% of the data sets. Under such circumstances, the bootstrapping method does not perform well and the reliability of the estimates can only be improved by increasing the number of samples in the original data set (not by increasing the number of bootstraps).

To further demonstrate the impact of this specific measurement, EFSA repeated the acute exposure calculations for the reference period 2016–2018 after exclusion of this olive sample (see Figure 4 and Appendix A, Table A.3). In this case, confidence intervals become narrower and a shift towards higher margins of exposure is noted. This second calculation does not necessarily demonstrate that the cumulative exposure patterns moved towards a more favourable situation for the reference period 2016–2018, just like the first calculation does not demonstrate that cumulative exposure patterns moved towards a less favourable situation.

Overall, there is no evidence that exposure to these pesticides has changed significantly because confidence intervals for both reverence periods overlapped. The differences observed between both periods mainly demonstrate that sampling uncertainty for omethoate in olives is high and that the evidence in this food commodity should be further improved to provide a more reliable cumulative exposure assessment.

Exposure estimates from olives for oil production may in a first instance be improved by using occurrence data measured in the olive oil, rather than the unprocessed olives. The probabilistic model currently used for cumulative exposure assessment relies on occurrence data for the RPCs only. However, for RPCs that are almost exclusively consumed as a processed product (e.g. olives for oil production and wine grapes), the coordinated multiannual control programme of the Union (MACP),[7] already requires official laboratories to collect samples for the processed food (e.g. olive oil and wine). The number of monitoring samples for the processed food is therefore higher than for the unprocessed RPC (EFSA, 2018, 2020a). Hence, if the probabilistic model would be adjusted to include occurrence data for the processed foods, this would not only increase the evidence base for olives in general, it would also reduce uncertainties related to the effect of processing.

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[6] OJ L 99 16.4.2015 p. 7-20.
[7] OJ L 94, 7.4.2017, p. 12–24.

Furthermore, identification of active substances and food commodities with a limited evidence base may also be improved by implementing probabilistic exposure assessment in the annual report on pesticide residues. Currently, such cases are difficult to identify since deterministic models are used. Integration of probabilistic models in the annual report would facilitate the identification of active substances and food commodities where sampling uncertainty is high.

As for the chronic exposure calculations (see Section 3.2.1), additional input data on RPCs and processing factors did not affect the outcome of the calculations.
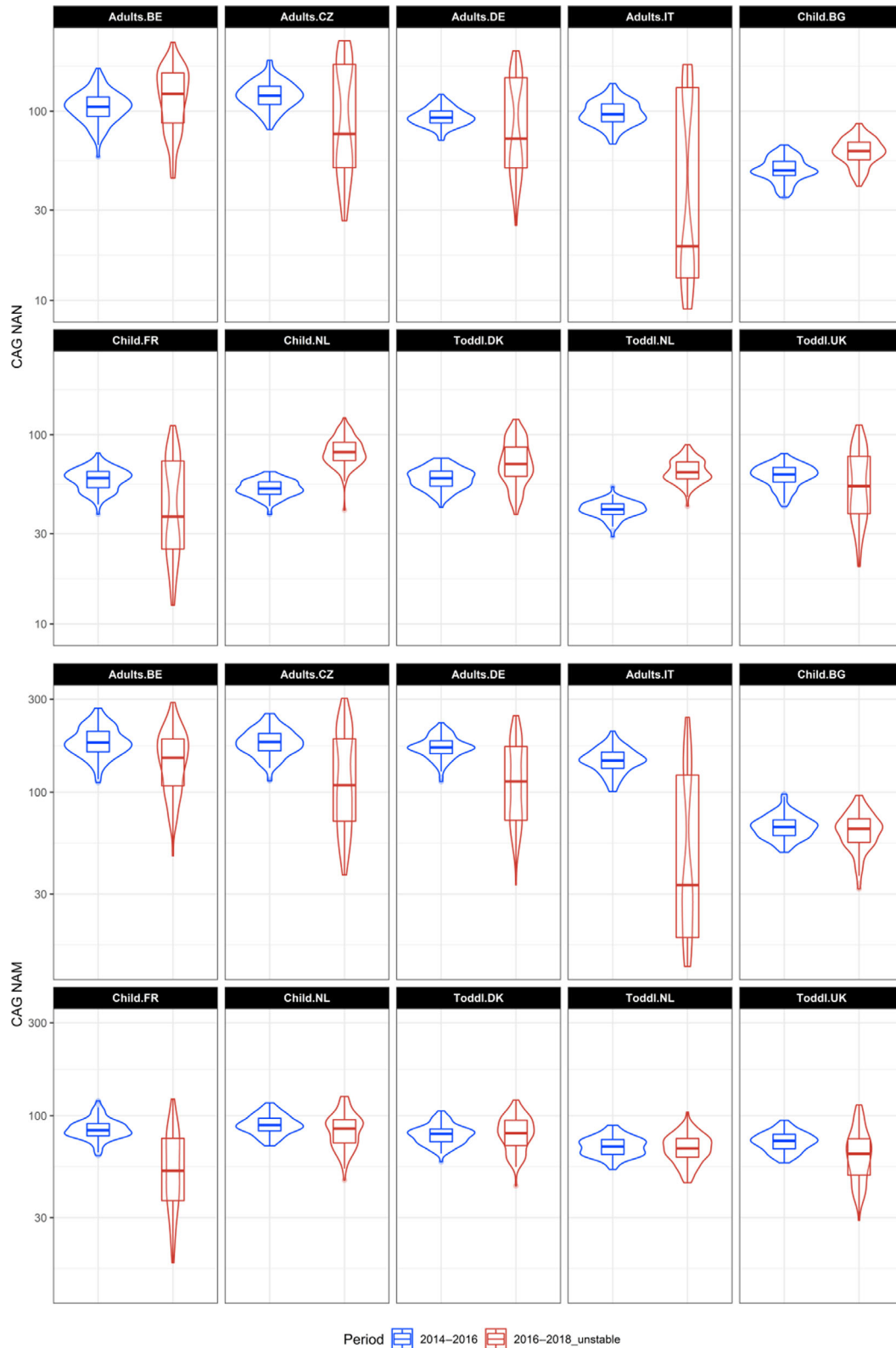
Legend: The box represents the interquartile range and the vertical line inside the box is the median, the two lines outside the box (whiskers) range from the 97.5th percentile to the 2.5th percentile (i.e. 95% confidence). The width of the violin plot represents the density of observations within the confidence interval.

Figure 3: Confidence intervals for the total margin of exposure (MOET) at the 99.9th percentile of the exposure distribution for CAG-NAN and CAG-NAM in the reference periods 2014–2016 and 2016–2018, presented in a combination of box plots and violin plots on logarithmic scale
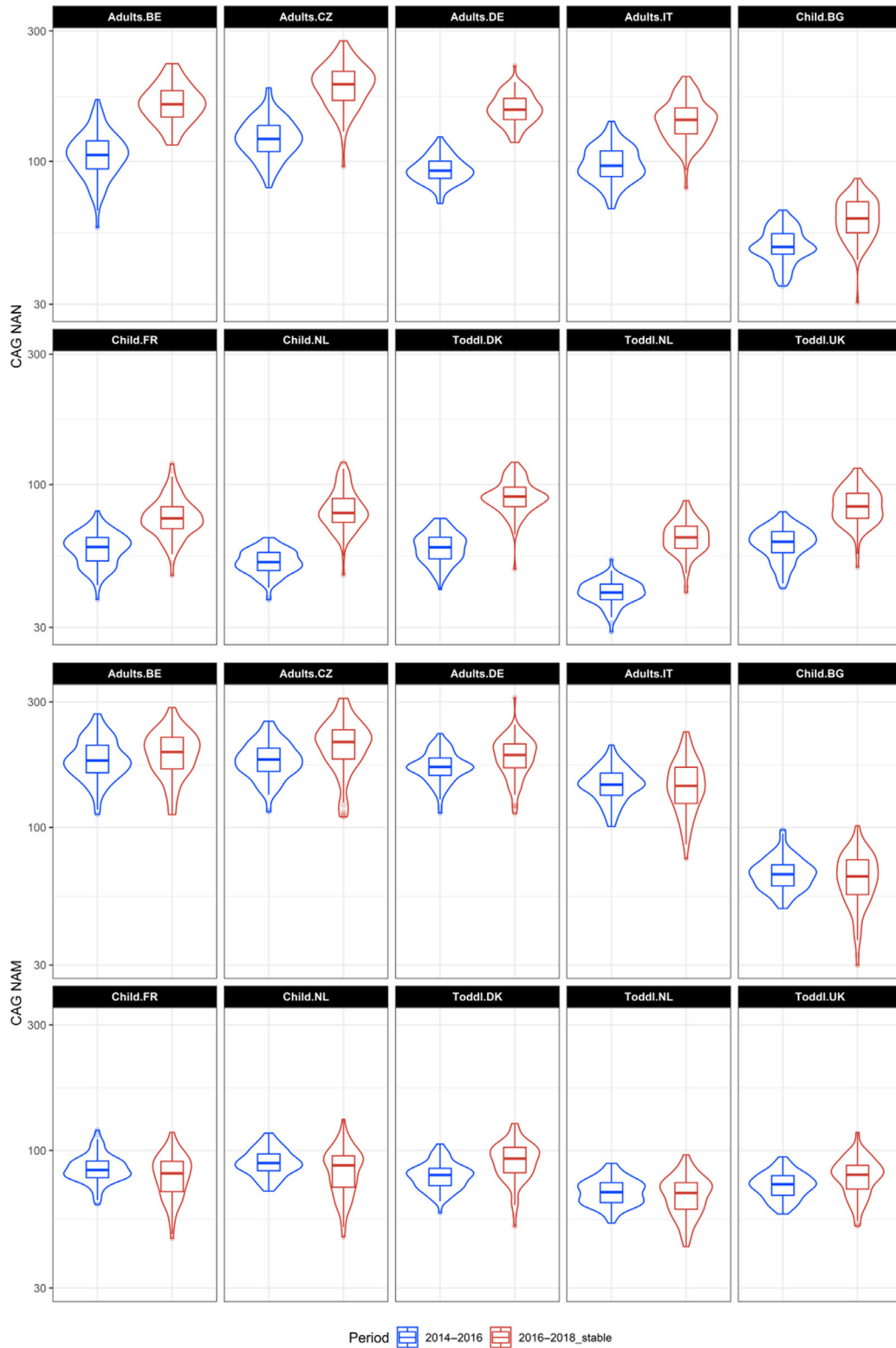
Legend: The box represents the interquartile range and the vertical line inside the box is the median, the two lines outside the box (whiskers) range from the 97.5th percentile to the 2.5th percentile (i.e. 95% confidence). The width of the violin plot represents the density of observations within the confidence interval.

Figure 4: Confidence intervals for the total margin of exposure (MOET) at the 99.9th percentile of the exposure distribution for CAG-NAN and CAG-NAM in the reference periods 2014–2016 and 2016–2018 (after exclusion of one sample in olives for oil production), presented in a combination of box plots and violin plots on logarithmic scale

4.   Conclusions and recommendations

Cumulative dietary exposure was estimated for pesticides that have chronic effects on the thyroid and for pesticides that have acute effects on the nervous system, in the reference period 2016–2018. Compared to the previous reference period (i.e. 2014–2016), exposure to these pesticides did not change significantly. These findings suggest that repeating cumulative risk assessments on a yearly basis is not necessary, and possible changes in exposure will be adequately addressed when cumulative risk assessments are repeated every 3 years, as intended by EFSA.

Calculations also confirmed previous findings that the outcome of a cumulative exposure assessment at the 99.9th percentile of the exposure distribution is very much influenced by single measurements in specific samples. When sampling uncertainty is high, such measurements will produce unstable exposure estimates, characterised by a wide confidence interval. Commodities that are almost exclusively consumed as a processed product (e.g. olives for oil production and wine grapes), are more susceptible to sampling uncertainty because the number of monitoring samples for the unprocessed commodities is low.

It is therefore recommended to adjust the probabilistic model to include occurrence data for the processed foods (i.e. olive oil and wine) because, in accordance with the MACP currently in place, the number of monitoring samples for these processed foods is higher than for the unprocessed commodities. Furthermore, it is recommended to implement probabilistic modelling for the assessment of dietary exposure in the annual report on pesticide residues. This would allow EFSA to identify possible concerns for specific active substances and food commodities on a yearly basis, and to initiate an ad hoc cumulative risk assessment when such concerns are expected to impact on the cumulative risks.

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Abbreviations

CAG	cumulative assessment group
CAG-NAM	cumulative assessment group of pesticides associated with functional alterations of the motor division
CAG-NAN	cumulative assessment group of pesticides associated with brain and/or erythrocyte acetylcholinesterase inhibition
CAG-TCF	cumulative assessment group of pesticides associated with hypothyroidism, i.e. affecting the follicular cells and/or the hormone system of the thyroid
CAG-TCP	cumulative assessment group of pesticides associated with hypertrophy, hyperplasia and neoplasia of C-cells, i.e. affecting the parafollicular cells or the calcitonin system of the thyroid
LOQ	limit of quantification
MOET	total margin of exposure resulting from multiple chemicals and food commodities
MRL	maximum residue level
MACP	coordinated multiannual control programme
NOAEL	no observed adverse effect level
OIM approach	observed individual means approach, i.e. an approach for estimating longer term exposures by taking each individual's observed mean consumption over the duration of a dietary survey
PPR Panel	EFSA Panel on Plant Protection Products and their Residues
RPC	raw primary commodity, i.e. a single-component food which is unprocessed or whose nature has not been changed by processing (e.g. apples)
VF	variability factor, i.e. the ratio between the 97.5th percentile and mean of the distribution

Appendix A – Comparison of results

Table A.1: Comparison of estimates of the total margin of exposure (MOET) and their corresponding 95% confidence intervals at the 99.9th percentiles of the exposure distribution for the chronic Tier II scenario of CAG-TCP and CAG-TCF, between reference periods 2014–2016 and 2016–2018

Country	Population class	CAG-TCP		CAG-TCF	
		2014–2016	2016–2018	2014–2016	2016–2018
Belgium	Adults	3,030 [1,150–5,040]	3,770 [1,400–5,710]	307 [198–387]	324 [189–397]
Czechia	Adults	2,620 [1,130–5,600]	3,340 [1,610–5,310]	269 [186–366]	285 [195–353]
Germany	Adults	2,290 [1,210–3,250]	2,640 [1,450–3,500]	259 [205–313]	276 [230–316]
Italy	Adults	3,400 [1,780–5,030]	3,690 [2,070–4,890]	295 [252–330]	296 [265–335]
Bulgaria	Other children	2,250 [1,840–2,760]	2,100 [1,560–2,770]	127 [114–151]	132 [119–153]
France	Other children	3,870 [3,100–4,460]	3,690 [2,610–4,690]	201 [187–216]	205 [191–220]
Netherlands	Other children	1,760 [1,340–2,300]	1,900 [1,360–2,580]	176 [159–197]	179 [161–203]
Denmark	Toddlers	2,080 [1,210–2,460]	2,310 [1,890–2,840]	127 [102–175]	133 [103–176]
Netherlands	Toddlers	1,480 [990–1,900]	1,830 [1,470–2,310]	103 [86.3–165]	101 [86.2–162]
United Kingdom	Toddlers	2,360 [1,810–2,940]	2,730 [2,060–3,260]	124 [104–176]	143 [102–174]

Table A.2: Comparison of estimates of the total margin of exposure (MOET) and their corresponding 95% confidence intervals at the 99.9th percentiles of the exposure distribution for the acute Tier II scenario of CAG-NAN and CAG-NAM, between reference periods 2014–2016 and 2016–2018

Country	Population class	CAG-NAN		CAG-NAM	
		2014–2016	2016–2018	2014–2016	2016–2018
Belgium	Adults	106 [72.1–153]	124 [48–187]	180 [122–259]	150 [67.6–258]
Czechia	Adults	121 [85.7–166]	75.9 [30.1–225]	181 [133–243]	109 [44.1–263]
Germany	Adults	92.4 [72.9–116]	71.6 [30.5–191]	170 [128–216]	114 [50.5–232]
Italy	Adults	96.5 [70.9–131]	19.3 [10–167]	145 [102–190]	33.4 [14.7–201]
Bulgaria	Other children	48.6 [36.5–63.4]	61.6 [42.4–81.2]	66.3 [51.4–93.5]	64.9 [37.2–93.4]
France	Other children	59.1 [43–72.7]	36.9 [13.3–94.2]	84.3 [65.6–111]	52.2 [20.1–110]
Netherlands	Other children	52 [41.9–62]	81 [57.8–110]	89.5 [71.7–113]	86 [54–123]
Denmark	Toddlers	58.9 [45.3–72.8]	70.1 [43.2–112]	80.7 [64.1–101]	81.5 [55.1–114]
Netherlands	Toddlers	40.2 [32.7–47]	63.4 [50.5–84]	69.5 [56–88.4]	68 [47.5–89.3]

Country	Population class	CAG-NAN		CAG-NAM	
		2014–2016	2016–2018	2014–2016	2016–2018
United Kingdom	Toddlers	61.7 [44.7–74]	53.6 [21.5–101]	74.4 [59.4–90.9]	63.8 [36.2–106]

Table A.3: Comparison of estimates of the total margin of exposure (MOET) and their corresponding 95% confidence intervals at the 99.9th percentiles of the exposure distribution for the acute Tier II scenario of CAG-NAN and CAG-NAM, between reference periods 2014–2016 and 2016–2018 (after exclusion of one sample in olives for oil production)

Country	Population class	CAG-NAN		CAG-NAM	
		2014–2016	2016–2018	2014–2016	2016–2018
Belgium	Adults	106 [72.1–153]	162 [117–224]	180 [122–259]	193 [113–274]
Czech Republic	Adults	121 [85.7–166]	192 [128–256]	181 [133–243]	211 [112–302]
Germany	Adults	92.4 [72.9–116]	155 [122–193]	170 [128–216]	188 [121–234]
Italy	Adults	96.5 [70.9–131]	142 [102–192]	145 [102–190]	144 [86.8–216]
Bulgaria	Other children	48.6 [36.5–63.4]	61.8 [45.8–79.8]	66.3 [51.4–93.5]	65.1 [37.3–91.5]
France	Other children	59.1 [43–72.7]	75.2 [55.5–107]	84.3 [65.6–111]	81.9 [53.3–107]
Netherlands	Other children	52 [41.9–62]	78.7 [59.9–112]	89.5 [71.7–113]	87.8 [51.2–113]
Denmark	Toddlers	58.9 [45.3–72.8]	90.3 [68.3–116]	80.7 [64.1–101]	93.2 [62.1–123]
Netherlands	Toddlers	40.2 [32.7–47]	64 [47.2–84]	69.5 [56–88.4]	69 [46–91.6]
United Kingdom	Toddlers	61.7 [44.7–74]	83.1 [60–109]	74.4 [59.4–90.9]	80.9 [53.8–102]

Annex A.1. − Input data for the chronic exposure assessment of CAG-TCP

Annex A.1 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765

Annex A.2. − Input data for the chronic exposure assessment of CAG-TCF

Annex A.2 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765

Annex A.3. − Input data for the acute exposure assessment of CAG-NAN

Annex A.3 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765

Annex A.4. − Input data for the acute exposure assessment of CAG-NAM

Annex A.4 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765

Annex B.1. – Output data from the chronic Tier II exposure assessment of CAG-TCP

Annex B.1 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765

Annex B.2. – Output data from the chronic Tier II exposure assessment of CAG-TCF

Annex B.2 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765

Annex B.3. – Output data from the acute Tier II exposure assessment of CAG-NAN

Annex B.3 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765

Annex B.4. – Output data from the acute Tier II exposure assessment of CAG-NAM

Annex B.4 is available online on EFSA's knowledge junction: https://doi.org/10.5281/zenodo.4457765