

# Prioritisation of pesticides and target organ systems for dietary cumulative risk assessment based on the 2019–2021 monitoring cycle

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## Abstract

Aiming at accelerating the implementation of cumulative risk assessment to pesticide residues, this report describes a two-step prioritisation analysis, on individual pesticides and on target organ systems, that allows to identify (i) low-priority substances expected to have a marginal contribution to cumulative risk, and (ii) high priority organ systems to be addressed in future cumulative risk assessments. The analysis encompassed 350 substances and 36 raw primary commodities of plant origin surveyed in the monitoring cycle 2019–2021, carried out in 30 population groups, covering 3 age classes, and 17 EU countries. Probabilistic exposure calculations, for chronic and acute effects, were executed on the occurrence and consumption data by a two-dimensional procedure, modelling variability and uncertainty. In the first step, the prioritisation method adopted allowed to reduce the number of substances by about 80%. These substances were in turn grouped based on their capacity to cause toxicological effects on common organ systems and, as second step, probabilistic combined exposure calculations were carried out for 16 target organ systems. This step allowed to identify the organ systems that need further assessment, reducing their initial number by about 70%. The organ systems would need to be prioritised as follows: reproductive and developmental toxicity, liver, kidney, male reproductive system, and haematopoietic system and haematology. The sources of uncertainty stemming from the modelling procedure and from methodological assumptions were discussed and their impact qualitatively assessed. Overall, it was concluded that the risk estimates for the different organ systems were more likely to be overestimated than underestimated.

## KEYWORDS

acute effects, chronic effects, cumulative exposure assessment, pesticide residues, probabilistic risk assessment

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## CONTENTS

Abstract.....	1
Summary .....	3
1. Introduction .....	4
2. Data and Methodologies .....	5
2.1. Prioritisation of pesticides .....	5
2.1.1. Individual exposure assessment and associated risk metrics .....	5
2.1.2. Priority list of pesticides .....	6
2.2. Prioritisation of target organ systems .....	7
2.2.1. Grouping of pesticides .....	7
2.2.2. Combined exposure assessment and associated risk metrics .....	7
2.2.3. Priority list of target organ systems .....	8
3. Results and Discussion .....	8
3.1. Prioritisation of pesticides .....	8
3.1.1. Individual exposure assessment results .....	8
3.1.2. Proposed priority list of pesticides .....	9
3.2. Prioritisation of target organ systems .....	9
3.2.1. Combined organ exposure assessment results .....	9
3.2.2. Proposed priority list of target organ systems .....	11
4. Conclusions.....	13
5. Recommendation.....	14
Abbreviations .....	15
Acknowledgements .....	15
Conflict of Interest .....	15
Requestor .....	15
Question Number .....	16
Copyright for non-EFSA content.....	16
References.....	16
Appendix A.....	18
Appendix B .....	23
Appendix C .....	27
Appendix D.....	32
Appendix E .....	44
Appendix F .....	47
ANNEXES .....	77

## SUMMARY

In the context of cumulative risk assessment (CRA) of dietary exposure to pesticide residues, a prioritisation methodology has been developed and applied. This method aims at identifying (i) low-priority pesticides expected to have a marginal contribution to the cumulative risk and (ii) organ, or organ systems, having a high priority and requiring further refined CRA. This report describes the impact of this prioritisation method on the risk assessment of 350 substances affecting 16 organ systems.

As first step, hazard quotients (HQs) have been assessed for each of the 350 substances by means of probabilistic exposure assessment calculations (HQ is defined as the ratio of exposure of a substance to its health-based guidance value). To calculate HQs, exposure has been assessed per substance, for 36 raw primary commodities of plant origin surveyed in the monitoring cycle 2019–2021, and for 30 population groups, covering 3 age classes, and 17 EU countries. The probabilistic calculations have allowed to estimate the variability of the combined occurrence-consumption data and the uncertainty of the resulting exposure distribution. HQ values  $\geq 0.1$  at the 99.9th percentile of the exposure distribution has been the criterion adopted for the prioritisation; substances whose HQ was below 0.1 have been considered having a marginal contribution to cumulative exposure and thus not retained for further analysis.

In the second step, cumulative exposure has been assessed at the target organ system level. The substances identified in the previous step have been grouped based on their ability to cause toxicological effects on common target organ systems, and for each organ system, CRA was performed using a probabilistic methodology, similar to the one adopted for exposure to single substance, but with less conservative (more realistic) assumptions. The hazard index (HI) was used to establish a priority list of organ systems (HI can be interpreted as an extension at the mixture/group level of the HQ approach adopted for prioritising single substances). A cut-off value of 1 at the 99.9th percentile of the combined exposure distribution was used to screen out organ systems requiring further assessment, in the sense that only those organ systems for which  $HI \geq 1$  at the 99.9th percentile of the combined exposure distribution have been prioritised.

The final priority list of substances is composed by 67 substances (out of the initial 350), obtained by applying the criteria  $HQ \geq 0.1$  and the availability of information to map each substance to a specific organ system. Fifteen of these substances were associated with chronic effects, 21 with acute effects and 31 with both effects. Then, by applying the cut-off value of one to the HI at the 99.9th percentile of combined exposure distribution, 11 organ systems have been identified for prioritisation, 4 common to chronic and acute effects, and 7 only to acute effect. Further analysis revealed that, for at least six of these latter seven organ systems, the risk was driven by two substances only, therefore suggesting that further refinement to the exposure to these two substances would be recommended, rather than prioritising the 6 organ systems for CRA. Hence, together with the organ systems that exceeded the cut-off value under the chronic exposure scenario, it has been concluded that the organ systems would need to be prioritised as follows: reproductive and developmental toxicity (RDT), liver (LIV), kidney (KID), male reproductive system (MRS), and haematopoietic system and haematology.

It is further acknowledged how the estimated exposure values have been subject to several uncertainties that need to be taken into consideration for the correct interpretation of the results. In addition to the modelling uncertainty tackled by the modelling methodology by means of statistical methods, other methodological uncertainties have been introduced to account for inaccuracies and missing information in the data (e.g. measurements below the limit of quantification, lack of processing factors for processed foods, among others). Conservative assumptions (i.e. assumptions that have been formulated to protect end consumers and that likely contribute to overestimation of the exposure) have been adopted in these instances. These uncertainties were qualitatively identified, and their impact taken into consideration in the interpretation of the exposure assessment and of the prioritisation results. Overall, it is concluded that the risk estimates for the different organ systems are more likely to be overestimated than underestimated.

## 1 | INTRODUCTION

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 (U.S. EPA, 2003). It differs from most assessments which consider the effects of one agent or stressor solely.

In order to comply with provisions of Regulation (EC) No 396/2005 on maximum residue levels (MRLs) of pesticides in or on food and feed regarding cumulative and synergistic effects of pesticides, 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 to 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 on the basis of their toxicological profile (EFSA PPR Panel, 2013).

EFSA subsequently initiated a pilot assessment, which started with the establishment of different CAGs for (a) acute effects on the acetylcholinesterase (AChE) inhibition and the possible functional alteration of the motor division of the nervous system and for (b) chronic effects on the thyroid for hypothyroidism and of hypertrophy, hyperplasia and neoplasia of C cells. More than 400 active substances were screened for potential inclusion in these CAGs. Any active substance possessing a chemical structure associated with a mode of action (MoA) of direct relevance for the effects or exhibiting selected indicators (toxicological endpoints) reflecting the specific effect in regulatory toxicological studies was included in the respective CAG (EFSA, 2019a, 2019b).

In the second phase of the pilot assessment, short- and long-term cumulative exposure assessments were conducted for the above-mentioned CAGs. These exposure calculations were carried out by EFSA and the Dutch National Institute for Public Health and Environment (RIVM) using the same probabilistic modelling but different software tools. The results were reported in the EFSA scientific reports on cumulative dietary exposure assessment of pesticides using SAS® software (EFSA, 2019c) and in the external scientific reports on cumulative dietary exposure assessment of pesticides using MCRA software (van Klaveren, Kruisselbrink, et al., 2019; van Klaveren, van der Voet, et al., 2019). The two tools produced nearly identical results and any observed differences were mainly attributed to the random effect of probabilistic modelling. These minor differences did not impact the outcome of the exposure assessment.

As final step of the CRA pilot, risk characterisation was assessed based on the outcome of the first two steps including an uncertainty analysis, performed following the guidance of the EFSA Scientific Committee in order to take account of the limitations in scientific knowledge and data, and of the assumptions used in all steps of the assessment (EFSA, 2020a, 2020b). The combined impact of the uncertainties, and their dependencies, on the assessment, was then quantified in a sequential approach using Expert Knowledge Elicitation (EKE) techniques and 1-D Monte Carlo simulations.

The pilot assessments concluded, with varying degrees of certainty, that cumulative exposure to residues of pesticides in these CAGs did not exceed the threshold for regulatory consideration. Nevertheless, developing the methodology for CRA of pesticides turned out to be much more complex than initially expected thus, only two organ systems were addressed at that time. CAGs still needed to be established for the remaining key organ systems. EFSA and the European Commission (DG SANTE) therefore agreed on an action plan<sup>1</sup> to speed up the implementation of CRA. As part of the action plan and in accordance with EFSA's guidance on grouping of chemicals (EFSA Scientific Committee, 2021), EFSA elaborated a prioritisation method, composed of two phases:

1. In a first phase, a probabilistic screening is carried for each individual pesticide, and only pesticides exceeding a pre-defined cut-off value are retained for further grouping. The underlying assumption is that the substance below the cut-off value can be considered to have a marginal contribution to the cumulative risk and therefore excluded from further assessments.
2. In a second phase, the prioritised substances are grouped for common target organ systems and combined assessments are carried out for each relevant organ system. This second step allows to identify target organ systems requiring an accurate CRA based on specific toxicological effects.

To identify the most appropriate cut-off value to be applied in the first phase of the prioritisation, RIVM assessed the potential impact of this prioritisation method by applying different cut-off values to the CAGs for the nervous system and the thyroid, previously established by EFSA in the framework of the pilot assessments. It was concluded that at the selected cut-off value, depending on the CAG, the number of substances could be reduced by 50%–70% without having a substantial impact on the outcome of the CRA (te Biesebeek et al., 2021).

Based on the above, EFSA proceeded with the first implementation of the prioritisation method for the pesticide residue monitoring cycle 2019–2021, which is now presented in this report.

<sup>1</sup>[https://food.ec.europa.eu/system/files/2021-03/pesticides\\_mrl\\_cum-risk-ass\\_action-plan.pdf](https://food.ec.europa.eu/system/files/2021-03/pesticides_mrl_cum-risk-ass_action-plan.pdf)

## 2 | DATA AND METHODOLOGIES

### 2.1 | Prioritisation of pesticides

#### 2.1.1 | Individual exposure assessment and associated risk metrics

The first step of the prioritisation method relies on the calculations of a risk metric for each active substance or, where applicable, its relevant metabolite. To this end, a probabilistic exposure assessment for each chemical is conducted and the resulting exposure estimates are compared to the relevant health-based guidance value (HBGV). Full details of the data and methods are provided in the Appendices A and B, respectively, while a brief outline of the procedure is given hereafter.

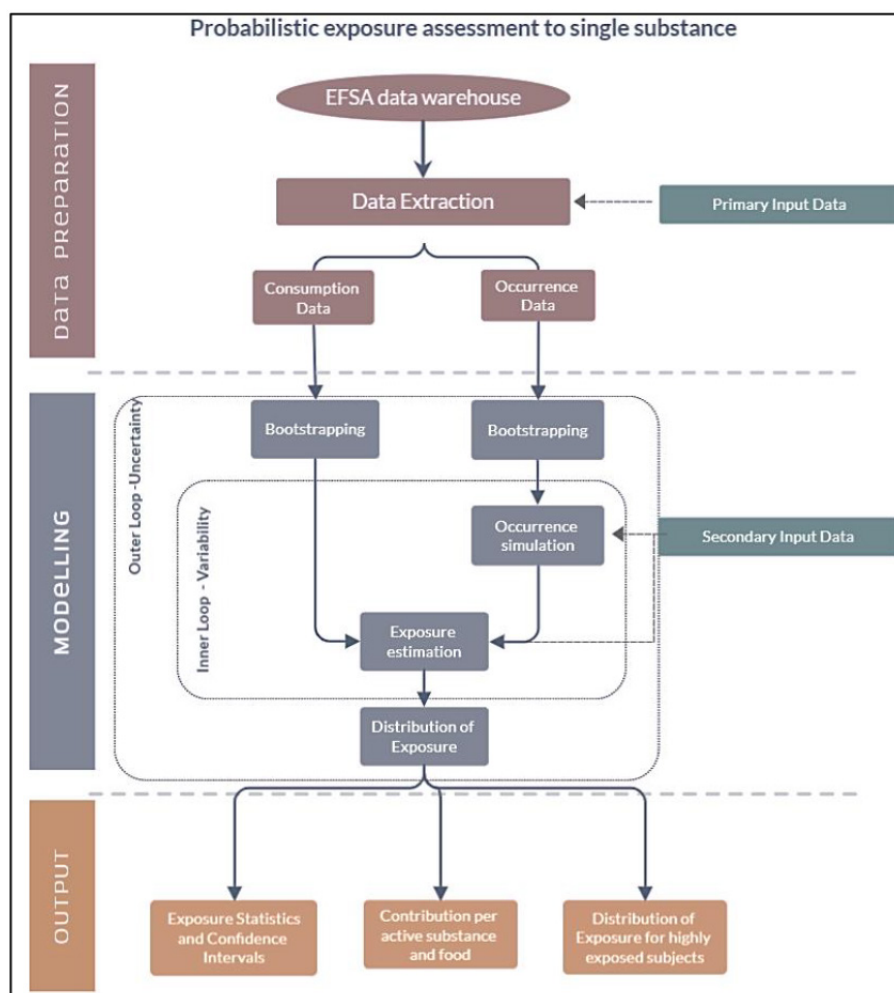
The primary input data required for modelling exposure to pesticide residues are occurrence data (i.e. the amounts of pesticide residue that are present in foods) and food consumption data (i.e. the types and amounts of foods consumed in a person's diet). These data are stored in EFSA's Scientific Data Warehouse (sDWH). The occurrence data used for the analysis are the pesticide residue monitoring data for the 3-year cycle 2019–2021. These data were sampled and analysed by reporting countries, in compliance with Regulation (EU) 2018/555, Regulation (EU) 2019/533 and Regulation (EU) 2020/585, and subsequently collected by EFSA. The analysis was limited to 35 raw primary commodities (RPCs) of plant origin that were considered in the EU multiannual control programme (EU MACP). In addition, courgettes were also included because, according to EFSA's design assessment of the pesticide monitoring programme (EFSA, 2015), courgettes are consumed in higher amounts than other commodities previously included in the EU MACP (e.g. spinaches and broccoli). All the active substances (or, where applicable, their relevant metabolites) with at least one positive finding (i.e. at or above the limit of quantification [LOQ]) were identified and all measurements for those active substances extracted from the sDWH. In total, 371 substances were selected for the analysis. The occurrence data extracted primarily referred to RPCs (e.g. apples) but, depending on the availability of data, monitoring data for the processed foods (e.g. apple juice) were also extracted. Consumption data used for the probabilistic exposure assessment were extracted from the RPC Consumption Database (EFSA, 2019d). To cover as many population groups as possible without compromising the reliability of estimates at the higher percentiles of the exposure distribution, only dietary surveys with more than 300 survey participants per relevant age class were retained. This resulted in the selection of 30 population groups, covering 3 different age classes (i.e. adults, other children and toddlers) and 17 different countries. The limit of 300 survey participants for performing probabilistic exposure assessment is based on the expertise gained from previous assessments.

Probabilistic exposure calculations were executed on the selected occurrence and consumption data, in accordance with the guidance on probabilistic modelling of dietary exposure to pesticide residues (EFSA PPR Panel, 2012). When the exposure calculations are initiated, the data for the relevant food commodities, active substances and dietary surveys are extracted. Exposure estimates are then 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 (see Figure 1). Within the inner loop execution, occurrence data were subject to several simulations and imputations. These adjustments were intended to account for inaccuracies and missing information in the occurrence data set (e.g. unspecific measurements, measurements below the analytical LOQ, etc.). The consumption data and adjusted occurrence data were then used to estimate dietary exposures. The variability distributions of chronic (long-term) and acute (short-term) exposure was calculated using different methodologies. Chronic exposure to single substances was estimated using the Observed Individual Means (OIM) approach. OIM uses the average consumption of each food item by each individual and multiplies it with the mean occurrence of the substance in those respective food items to calculate the individuals' chronic exposure resulting from each food commodity. Acute exposure to each substance was calculated within a large Monte Carlo loop of 100,000 iterations where the consumption data (per individual, day and food commodity) were multiplied with the occurrence data (per sample and per food commodity). For both chronic and acute exposure, the sum of individual exposures over each food commodity consumed produced the individuals' total exposure, then normalised to the individual body weight (bw). The outcome of this inner loop is an empirical exposure distribution representing the variability of chronic and acute exposures within each 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. authorised uses of active substances on specific crops) or for improvement of the exposure estimates (e.g. processing factors [PFs]).

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 100 times the model produces multiple distributions of exposure. The first execution, also referred to as 'the nominal run', is performed with the original data sets, while the remaining executions are performed with bootstrap data sets. The differences between those distributions reflect the sampling 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. All extractions, simulations, imputations and calculations described in the subsequent sections were programmed with SAS® Studio 3.8 (Enterprise Edition).





**FIGURE 1** Process implemented for the probabilistic estimation of exposure. The variability of the exposure estimation relies on the Observed Individual Means (OIM) approach for chronic exposure and on Monte Carlo simulations for acute exposure.

The risk metrics adopted to express the exposure to individual substances is the hazard quotient (HQ), defined as the ratio of exposure to a substance to its HBGV. Therefore, HQ larger than one implies that the estimated exposure exceeds the HBGV. For chronic assessment, the selected HBGV is the substance's acceptable daily intake (ADI, expressed in mg of residue/kg bw per day). In some cases, and due to the absence of derived ADI, the tolerable daily intake (TDI, in mg of residue/kg bw per day) was used. For acute risk assessment, the selected HBGV is the substance's acute reference dose (ARfD, expressed in mg of residue/kg bw). In this analysis, the 99.9th percentiles (P99.9) of the individual substance's exposure distributions obtained from the chronic and acute calculations outlined above were combined with the HBGVs to obtain HQs, setting out the basis for the prioritisation of substances.

ADI and ARfD values established under Regulation (EC) No 1107/2009 were selected, when available. When EFSA's most recent assessment for a given active substance could not conclude on the establishment of HBGVs, a tentative chronic/acute assessment was conducted using ADI/ARfD from previous assessments conducted by EFSA or from assessments conducted by other organisations (e.g. EPA, JMPR), where available. If a tentative HBGV could not be identified for a given substance, the HQ could not be calculated and the exposure assessment was therefore not carried out. The list of the 21 active substances for which no exposure assessment was carried out, is provided in Annex A.1, Table A.1.04 and in Annex A.2, Table A.2.04 for the chronic and acute assessments, respectively.

## 2.1.2 | Priority list of pesticides

The probabilistic HQ estimate at P99.9 is the basis for defining the priority list of substances. This value was set based on the findings of the impact assessment (te Biesebeek et al., 2021) that explored the feasibility of the prioritisation methodology on four CAGs, covering two different organ systems. It concluded that the prioritisation cut-off of HQ larger than 0.1 at P99.9 sensibly reduced the number of substances in both CAGs analysed, without having a substantial impact on the assessment outcome. The underlying assumption is that chemicals whose exposure is below 10% of the relevant HBGV can be considered low risk and excluded from further assessments. While it is acknowledged that the impact of the proposed cut-off criteria was evaluated with four CAGs only, this uncertainty is intrinsically associated to the application of such a prioritisation method.

For chronic effects, the P99.9 HQ estimate of the nominal run was used for comparison with the cut-off value, because it provides a stable estimate that is not affected by probability. For acute effects, a further criterion was used to account for the random nature of the Monte Carlo approach used for the probabilistic acute exposure calculations. It was therefore decided to consider for exclusion substances whose HQ at the P99.9 exceeded the 0.1 threshold only by the upper bound (the lower bound being below the threshold) and only for one survey. It could happen that the exceedance of the threshold in these instances is, in fact, driven by numerical randomness rather than actual risk. Under such circumstances, the substance was excluded from the final acute priority list only if it was not yet part of the priority list for chronic effects. Therefore, 10 substances were excluded from the priority list for acute effects fulfilling the above criteria.

Further considerations on the substances, their toxicological effects and the final list of prioritised substances are presented in Section 3.1.2.

## 2.2 | Prioritisation of target organ systems

### 2.2.1 | Grouping of pesticides

The active substances (or, where applicable, their relevant metabolites) included in the priority list were grouped based on their ability to cause toxicological effects on common target organs or organ systems. To this end, an updated version of the 'database of toxicological effects of pesticides' (Nielsen et al., 2012) currently being developed by DTU (under publication, Contract/Grant number: GP/EFSA/PREV/2020/01), was used.

This updated database contains information on active substances that are either approved in EU as of 2 February 2021, or not approved but still present in products placed in the EU market as indicated by the result of the annual monitoring system of pesticide residues 2019–2021 (see also Section 2.1.1). For each active substance, the target organ systems and the effects that are observed in toxicological studies and considered potentially relevant for the establishment of CAGs, are reported.

For the present exercise, information on the active substances in the priority list and related affected organ system were extracted from the DTU database. Substances were then grouped based on common target organ systems. For each target organ system, assessment groups were defined for chronic and acute assessment separately. The information whether the effect of a given substance was chronic, acute, or both, was directly derived from the priority analysis of single substance obtained as described in Section 2.1.2 and further detailed in Section 3.1.2.

### 2.2.2 | Combined exposure assessment and associated risk metrics

The grouping of the prioritised substances described in Section 2.2.1 constitutes the first step for the combined exposure assessment, executed for each target organ independently, both chronic and acute. The methodology adopted for the combined exposure assessment at organ level is primarily based on the one followed for the retrospective cumulative risk assessments (EFSA, 2020a, 2020b, 2021, 2022), the main difference being that, in the present work, substances were grouped at the level of the target organ systems instead of a toxicological effect (see also Section 2.2.1). Furthermore, risk metrics were expressed as the hazard index (HI), as opposed to the total margin of exposure (MOET) used in the retrospective cumulative risk assessment. The HI assumes a dose-addition model and uses the HBGVs to normalise the exposure to the toxic potency of the different substances. The HI approach was applied in the combined risk calculations for the purpose of this prioritisation work, instead of the MOET approach, because the HI approach requires less resources, i.e. HBGVs (per substance) are more readily available than no observed adverse effect levels (NOAELs) for effects specific to each of the target organs. The HI approach implies a conservative estimation of the combined risk per target organ (see Appendix C, Section C.1.2.1).

Hence, the HI can be seen as an extension at group level of the HQ approach described in Section 2.1.1, where the HI is the sum of the HQ estimates of the substances within the group of interest:

$$HI = \sum_i HQ_i = \sum_i \frac{Exp_i}{HBGV_i},$$

where  $HQ_i$  is the hazard quotient of substance  $i$ ,

$Exp_i$  is the exposure to substance  $i$ ,

$HBGV_i$  is the health based guidance value of substance  $i$ .

As for the probabilistic exposure assessment of single substances outlined in Figure 1, the combined exposure assessment for organ systems is composed of an inner loop to estimate the variability of the exposure, resulting in an exposure distribution for each target organ and population group, and an outer loop to estimate the uncertainty around those distributions, expressed as confidence interval. The combined exposure assessments are also based on the same dietary surveys and food commodities, with the addition of drinking water for which specific simulations are implemented in this case. A comprehensive description of the methodology used for combined exposure assessment is provided in Appendix C.

## 2.2.3 | Priority list of target organ systems

The 99.9th percentile of the HI distributions obtained at the previous step is the basis for the prioritisation of the organ systems. The scope is to identify and prioritise organ systems for which the development of dedicated CAGs and cumulative risk assessment need to be carried out. The cut-off value for the prioritisation of organ systems was set to 1, because the combined assessment per organ system relies on two conservative principles:

1. Substances were grouped based on their potential to affect a certain organ or organ system, without consideration of their capacity to cause a common toxicological effect. Organs exert different functions and chemicals may selectively affect one of these functions. Combined assessments at the level of organs and organ systems are therefore likely to overestimate combined toxicity (EFSA Scientific Committee, 2021).
2. The HI approach relies on the use of HBGVs which are typically based on the most critical toxic effect observed for a given substance. Hence, the toxicological effect used to derive the HBGV may refer to another organ or organ system, hereby overestimating the potency of the substance for the organ system under assessment.

Organs and organ systems with a HI below 1 are therefore not considered to be of concern. A second criterion for ranking the organs was the concurrent risk derived by chronic and acute exposure in at least one population group. Hence, organ systems with  $HI \geq 1$  for both chronic and acute effects were ranked higher than organ systems associated with either acute or chronic. Finally, the higher the HI per target organ and the more population groups with  $HI \geq 1$ , the higher the priority of that target organ.

For the acute assessments, additional sensitivity tests were undertaken to investigate the relative effect of the main contributing substances. Focus was given to organ systems for which the  $HI \geq 1$  for a large proportion of surveyed groups. The tests consisted in removing the main contributing substances from the occurrence data and re-executing the probabilistic combined exposure assessment for the organ systems identified. Then, the new HI values were analysed and benchmarked against the condition  $HI \geq 1$ . If the  $HI \geq 1$  was mainly driven by a limited number of substances, then the target organ was not retained in the priority list.

The final ranked list of organ systems is presented and discussed in Section 3.2.2.

## 3 | RESULTS AND DISCUSSION

### 3.1 | Prioritisation of pesticides

#### 3.1.1 | Individual exposure assessment results

Exposure calculations were carried out for a total of 350 distinct substances (excluding the 21 substances for which HBGV could not be identified, see end of Section 2.1.1). The results of the chronic and acute probabilistic exposure assessments are summarised for the individual active substances in Appendix D. For chronic exposure, this included 262 substances that had an EU-agreed HBGV (see Annex B.1 for details) and 88 substances where only a tentative HBGV could be identified (see Annex B.2 for details). Acute exposure calculations were carried out for 276 substances, which comprises 200 substances with an EU agreed HBGV (see Annex B.3 for details) and 76 substances where only a tentative HBGV could be identified (see Annex B.4 for details). For 74 substances, an acute exposure assessment was not considered necessary.

For the majority of substances (i.e. ~75%), all HQ estimates at the 99.9th percentile of the exposure distributions remained below 0.1, meaning that exposure estimates were 10 times lower compared to the HBGV. Only for a small number of substances (i.e. less than 5%), the estimated exposures were found to be equal or higher than the HBGV (i.e.  $HQ \geq 1$ ). Such estimates, however, should be carefully interpreted and should not be considered as an accurate characterisation of the risks to consumers, but rather an indicator for potential concerns. These estimates are in fact subject to several uncertainties that need to be taken into consideration when interpreting these results.

Most of the substances with a HQ greater than 1 are no longer approved within the EU and for non-approved substances an HBGV agreed at EU level is often not available, making the HQ estimate very uncertain. Furthermore, some of these substances were found to have a high proportion of left-censored data (i.e. measurements below the LOQ). In the current assessment, left-censored data for a substance/commodity combination were all replaced by  $\frac{1}{2}$  LOQ when for this combination one sample was found to contain residues above the LOQ, whereas, in reality, a proportion of these left-censored data might not contain any residue at all, a so-called no-residue situation. This assumption introduces an important bias in the exposure assessments, especially for substances where a very low/tentative HBGV was selected. It is therefore recommended that for future probabilistic assessments of individual substances the assumption used for left-censored data is replaced with an approach that reflects a more realistic proportion of samples with a no-residue situation.

In addition, the main contributors to the exposure estimates were often found to be processed foods for which specific occurrence data or PFs were missing. In the absence of such data, the exposure model assumes that all residues present in the RPC will reach the end consumer. This assumption is conservative because residue concentrations will most likely change due to processing. This overestimation is further intensified when the dietary survey contains a few high consumers of processed foods with a low yield factor (i.e. commodities that, after processing, lose a high proportion of their initial



weight, like dried tomatoes, juice concentrate, wheat germ, for which the ratio between raw and processed weight is very high). Such consumers were shown to have a strong impact on the upper-bound estimates of exposure.

Another important and recurring uncertainty is related to the unspecific residue definitions. The occurrence data reported to EFSA refer to residue definitions for enforcement purposes (see Appendix A, Section A.1.4) and some of these residue definitions are not specific, meaning that they may be associated with multiple active substances. For this prioritisation of substances, the concentrations of measured substances in an unspecified residue definition are assigned to all active substances associated to the residue definition, which results in a worst-case estimation of exposure for each of these active substances, generating a bias for substance/commodity combinations that are not authorised. An example is the residue definition for the dithiocarbamates, which may be associated to six different active substances. For one of these substances, thiram, HQs exceeding 1 are resulting from a high number of positive measurements in a variety of fruits and vegetables. Considering that thiram is no longer approved, it is very likely that these positive measurements are referring to other dithiocarbamate substances that are still approved in the EU, e.g. ziram or metiram. HQ estimates for these two substances were significantly lower. Hence, also for this uncertainty, more realistic assumptions should be explored for future probabilistic assessments of individual substances.

Although these uncertainties would need to be considered more carefully in case of a proper risk assessment, they are more likely to overestimate than to underestimate the HQs and are therefore considered acceptable in the framework of this prioritisation exercise. Nevertheless, it is important that such prioritisation screening is repeated on a regular basis (e.g. every 3 years) and methodologies will need to be further refined to minimise the impact of those uncertainties.

### 3.1.2 | Proposed priority list of pesticides

After applying the criteria outlined in Section 2.1.2 to the P99.9 HQ estimates obtained from the probabilistic chronic and acute calculations carried out for the total number of 350 substances, EFSA identified 90 priority substances, of which, 20 associated with only chronic effects, 27 with only acute effects and 43 associated with both effects.

This list, however, contained 21 substances that were not covered by the data collection performed by DTU, and could therefore not be mapped to any specific organ system (see Appendix E, Table E.2). These substances are no longer approved in the EU and the vast majority (17 organophosphates and 3 *N*-methyl carbamates) are known to affect the nervous system primarily through AChE inhibition. Although most of these substances do not have EU-agreed HBGVs, HBGVs have been defined for the effects on the nervous system. It was therefore considered that including these substances in the combined exposure assessment of other organ systems, using HBGVs derived for the nervous system, would anyhow introduce a very important bias in the prioritisation of organ systems. Also considering that the CAGs have already been established for acetylcholinesterase inhibition (EFSA, 2019a, 2019b), it was concluded that removing these substances from the priority list would have a limited impact on the outcome of future CRA for organ systems other than the nervous system.

After applying the above considerations to the initial priority list, the final list of prioritised substances is composed by 67 substances, 15 associated with chronic effects, 21 with acute effects and 31 with both effects (see Table E.1 in Appendix E).

It is also noted that calculations of HQs could not be performed for a group of 21 active substances (see Section 2.1.1 and Annex A.1, Table A.1.04) and thus the exposure assessment was not carried out. Although most of these substances are no longer approved in the EU, positive findings have been reported by Member States as part of the annual monitoring activities. When establishing new CAGs in the future, special consideration on a case-by-case basis might still be required.

## 3.2 | Prioritisation of target organ systems

### 3.2.1 | Combined organ exposure assessment results

Relevant target organ systems were identified for each of the prioritised substances according to principles laid down in Section 2.2.1 (see Appendix E, Table E.1). In total, 16 target organ systems were considered in the present analysis, while three were excluded for the reasons explained hereafter:

- **Lungs.** Although one active substance (chlordecone) may cause effects on the lungs, these effects are either secondary, non-adverse or age-related. Overall, the lungs do not seem to be a primary target organ for the active substances included in the database. Therefore this organ system was excluded from further analysis and chlordecone is also not included in Appendix E, Table E.1.
- **Nervous system and thyroid gland.** For the nervous system and the thyroid, CRAs have already been conducted (EFSA, 2020a, 2020b) and, for some of the CAGs, estimated exposures were rather close to the threshold for regulatory consideration. Therefore, a regular repetition of the CRAs performed for these organ systems is in any case recommended.

The ranges of median HI values calculated at the 99.9th percentile of the exposure distribution across the different surveys, for each population group and each organ system, and the number of surveys with a HI  $\geq 1$ , are presented in Tables F.1 and F.2 (Appendix E), and in Figures 2 and 3. More detailed results are reported in Appendix F.

When considering chronic combined exposure (see Table F.1 and Figure 2), median HIs are below 1 for the majority of organ systems. The threshold is exceeded in only four target organ systems, namely the KID, the LIV, the MRS and the RDT. Median HIs above 1 were observed in at least one survey for all three population groups for LIV and RDT, only in toddlers for KID, and in both children and toddlers for MRS.

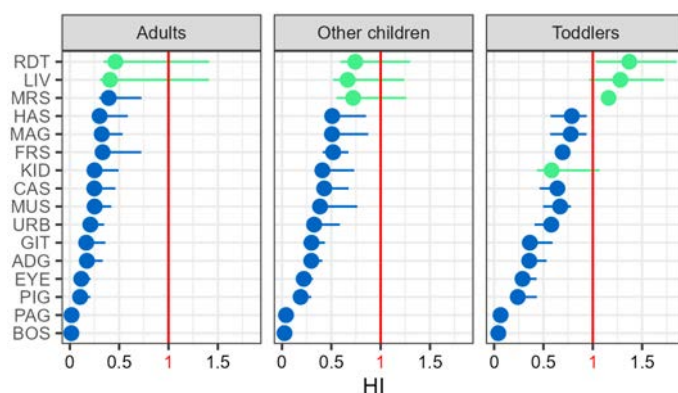
The results of the acute combined risk metrics calculations (see Table F.2 and Figure 3) are higher compared to those for the chronic scenario. For most organ systems, the HI estimate exceeds the cut-off value for all population groups in almost all dietary surveys. The only organ systems for which the median HIs are below 1 across all population groups are the bones/skeleton (BOS), muscular system (MUS), parathyroid gland (PAG), pituitary gland (PIG) and urinary bladder (URB).

As for the individual risk metrics calculations (see Section 3.1.1), the outcome of the combined calculations is strongly affected by the uncertainties around left-censored data, unspecific residue definitions and processed foods. Regarding the left-censored data and the unspecific residue definitions, more realistic assumptions were integrated in the combined exposure assessments that consider the authorisations of the different substances. Therefore, the uncertainties on left-censored data and unspecific residue definitions are reduced compared to the individual exposure assessments. Assumption applied to the processed foods, however, is the same. This means that when specific occurrence data or PFs are missing for the processed foods, the exposure model assumes that all residues present in the RPC will reach the end consumer. The commodities contributing most to the combined exposures were often identified as food commodities that are usually peeled (e.g. citrus fruits) or frequently processed prior to consumption (i.e. potatoes, green beans, tomatoes and peaches). Should information be available on the occurrence of pesticides in the processed foods thereof, HI estimates are expected to decrease significantly. For future prioritisation exercises, it is recommended to integrate an additional sensitivity analysis to better estimate the impact of this uncertainty. Meanwhile, previous cumulative risk assessments have demonstrated that, depending on the CAG assessed, this uncertainty may overestimate the exposure estimates by a multiplicative factor between 1 and 10 (EFSA, 2020a, 2020b, 2021, 2022).

Another important uncertainty is related to the use of the HI approach, which relies on HBGVs for the different active substances. They are derived for the most critical toxic effect observed for a given substance, which may refer to another organ or organ system. Applying the HI index approach is therefore likely to overestimate the potency of the substance for the organ system under assessment. It is acknowledged that in some cases the HBGVs might not rely on the most recent data or knowledge, which may also result in underestimation. Considering however that pesticides are periodically peer reviewed at EU level and that this prioritisation will also be repeated on a regular basis, mitigation measures are currently in place to capture this potential underestimation.

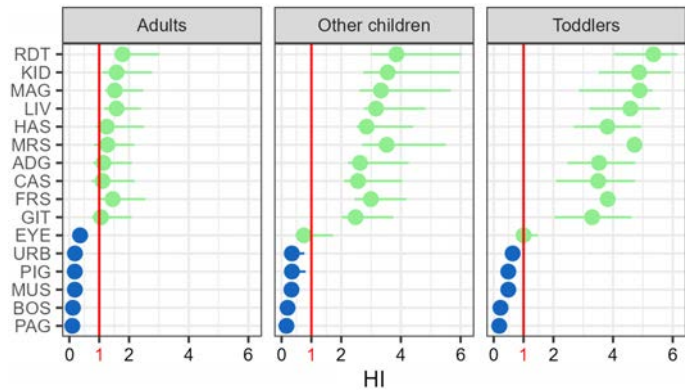
The above-reported uncertainties do not exclude the possibility, however, that combined exposure for a given organ system has been underestimated. The current analysis relies on a priority list of substances and some of the substances that were excluded will most likely affect the organ systems that were assessed. RIVM conducted an impact assessment for the thyroid and the nervous system where HIs were calculated for both organ systems in 10 dietary surveys, and applying different scenarios (te Biesebeek et al., 2021). When excluding substances with HQ estimates below 0.1 at the P99.9 of the exposure distribution, the decline of HI estimates for the thyroid ranged from 28% to 7%, with an average decline of 17%. The average decline in the most critical population groups (i.e. 13% in children and toddlers) was also found to be smaller compared to the adults (23%). For the nervous system, however, a slight increase of the HI estimates was even observed (3%–11%) which was unexpected when removing substances from the assessment. This increase was concluded to be due to the numerical randomness of the probabilistic modelling and the simulations applied. Although this impact assessment was limited to two organ systems only, they provide some indications on the possible impact of this uncertainty.

Overall, it is concluded that the HI estimates for the different organ systems are more likely to be overestimated than underestimated. This means that the HI estimates should not be considered as accurate estimations of risk, but it does make the proposed method fit-for-purpose in terms of prioritisation.



**FIGURE 2** Chronic organ exposure assessment. Distribution of median HI values at the 99.9th percentile of exposure in each population group.

**Keys:** The horizontal lines represent the range of median hazard index values at the 99.9th percentile of the exposure distributions, the dots represent the median value across all surveys for the relevant population group. The vertical red lines indicate the threshold HI value of 1. The green horizontal lines identify organs for which the  $HI \geq 1$  in at least one survey. **Legend:** ADG: adrenal gland; BOS: bones/skeleton; CAS: cardiovascular system; EYE: eye; FRS: female reproductive system; GIT: gastrointestinal system; HAS: haematopoietic system and haematology; KID: kidney LIV: liver; MAG: mammary gland; MRS: male reproductive system; MUS: muscular system; PAG: parathyroid gland; PIG: Pituitary gland; RDT: reproductive and developmental toxicity; URB: urinary bladder.



**FIGURE 3** Acute organ exposure assessment. Distribution of median HI values at the 99.9th percentile of exposure in each population group. **Keys:** The horizontal lines represent the range of median hazard index values at the 99.9th percentile of the exposure distributions, the dots represent the median value across all surveys for the relevant population group. The vertical red lines indicate the threshold HI value of 1. The green horizontal lines identify organs for which the HI  $\geq 1$  in at least one survey. **Legend:** ADG: adrenal gland; BOS: bones/skeleton; CAS: cardiovascular system; EYE: eye; FRS: female reproductive system; GIT: gastrointestinal system; HAS: haematopoietic system and haematology; KID: kidney LIV: liver; MAG: mammary gland; MRS: male reproductive system; MUS: muscular system; PAG: parathyroid gland; PIG: Pituitary gland; RDT: reproductive and developmental toxicity; URB: urinary bladder.

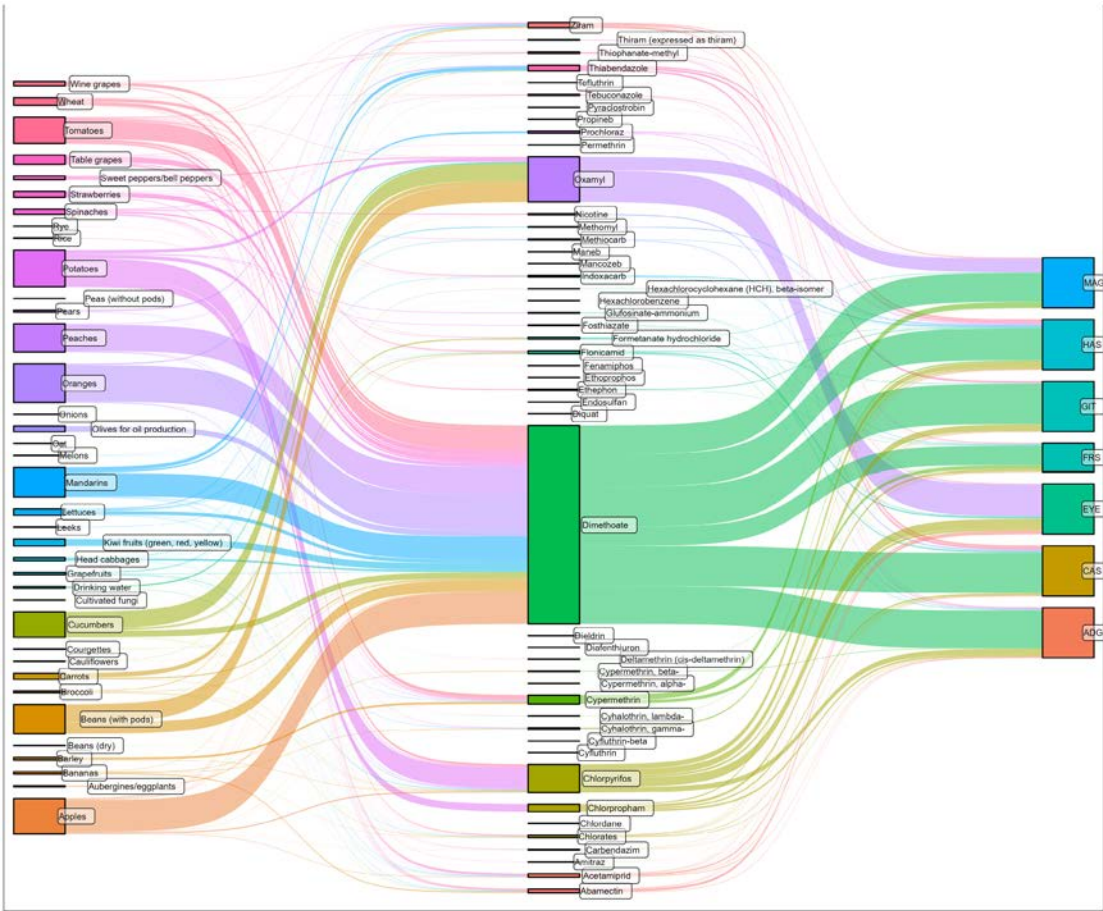
3.2.2 | Proposed priority list of target organ systems

As explained in the previous section, from the initial list of 19 organ systems, three were not considered for the prioritisation: the lungs (observed effects either secondary, non-adverse or age-related), the nervous system and the thyroid (previously assessed already). Considering the results of the exposure assessment, out of the remaining 16 organ systems, 11 were found to have a P99.9 HI exceeding the cut-off value of 1. Four of these are common to the chronic and acute scenarios (i.e. RDT, LIV, KID and MRS), whereas seven are based on the acute scenario only (i.e. MAG, HAS, ADG, CAS, FRS, GIT and EYE).

Results also demonstrated that for the seven organ systems prioritised for acute effects only, the HI was mainly driven by three substances, as illustrated by the Sankey diagram in Figure 4. Among these, dimethoate is the main contributor, playing a major role in the identified organs, together with oxamyl and chlorpyrifos. Dimethoate is the main contributing substance in all the organ systems reported in the flow diagram, except for the eye (EYE). For the latter, oxamyl is a major contributor, as well as for the mammary gland (MAG).

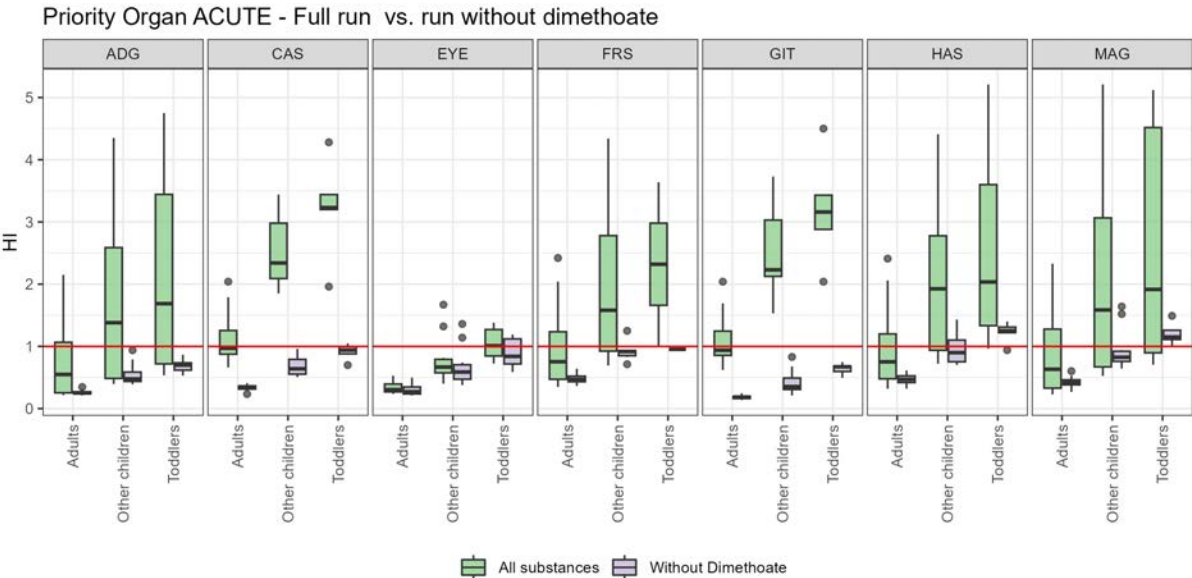
The exposure to dimethoate in the acute scenario is driven by different commodities, the main ones being oranges, apples, peaches and mandarins, followed by beans (with pods), cucumbers, kiwi fruits and olives for oil production. Cucumbers and beans (with pods) are also among the main contributing commodities to the exposure to oxamyl. As for chlorpyrifos, potatoes are the main contributor.

Further details on the contributors to the exposure for each organ system are provided in Appendix F.



**FIGURE 4** Flow diagram of the acute exposure summarising the contributions of RPCs and active substances to the exposures of the prioritised organ systems exceeding the 99th percentile. Stages from left to right: Raw primary commodities, Substances, Organ systems. The dimension of the nodes of the substances reflects the contribution to the exposure of each substance.

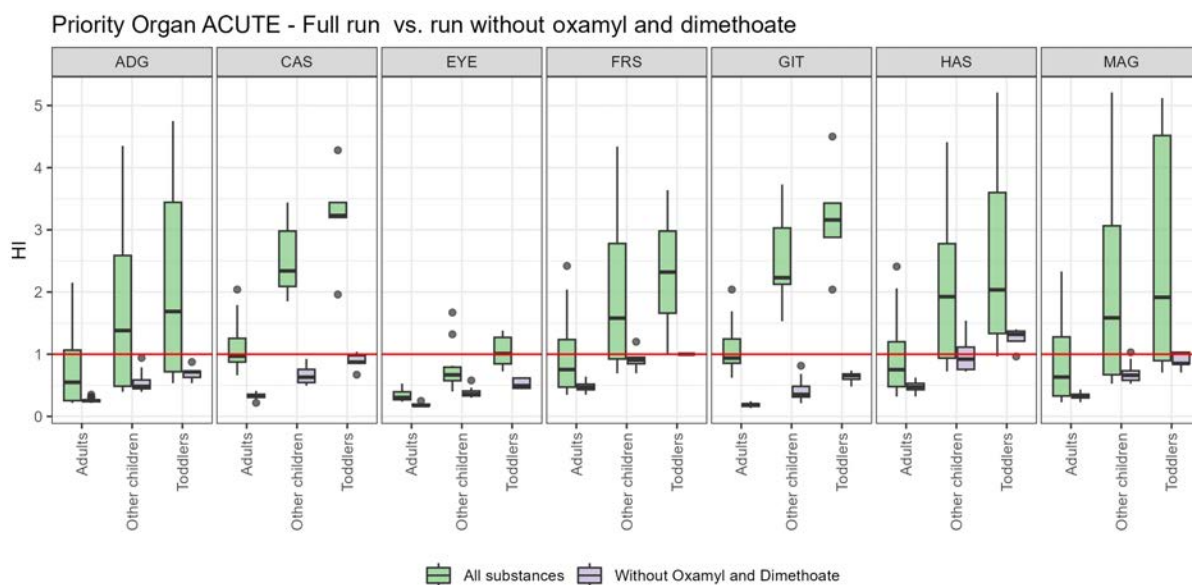
The contribution of these substances is further quantified through dedicated sensitivity analyses, where the occurrences relative to them were screened out from the probabilistic acute exposure calculations, first by removing the occurrences of dimethoate, then by removing that of dimethoate and oxamyl, and finally by removing the occurrences of dimethoate, oxamyl and chlorpyrifos. The comparison of the base run (i.e. with all substances) vs. the sensitivity run without dimethoate is shown in **Figure 5** for the seven organ systems identified.



**FIGURE 5** Comparison between the range of median HI values at the 99.9th percentile of the exposure distributions for the base scenario (all substances) vs the sensitivity run (without dimethoate) per age class and for the organ systems where median HI  $\geq 1$  for acute effect only.



The HI distribution of Figure 5 clearly shows that, by removing dimethoate, exposure is drastically reduced across all organ systems. Dimethoate is the main substance driving the acute exposure above  $HI=1$  for all adult population groups and for all the identified organs. For children and toddlers, exposure is also drastically reduced across all organ systems, but remains above the cut-off value for CAS, EYE, FRS, HAS and MAG. The main reason for this reduction is the combination of the low HBGV, high occurrences of dimethoate in fruit commodities and the high consumption of these commodities (mainly apples and oranges) in their processed form (juice) by children and toddlers.



**FIGURE 6** Comparison between the median HI values at the 99.9th percentile of the exposure distributions for the base scenario (all substances) vs the sensitivity run (without dimethoate and oxamyl) per age class and for the organ systems where median  $HI \geq 1$  for acute effect only.

By screening out also oxamyl from the occurrences (Figure 6), HI decreases below one for EYE (all age classes) and reduces sensibly for MAG (children and toddler). The removal of occurrences of chlorpyrifos did not affect further the assessment and is not shown.

On the basis of the sensitivity analysis and the results obtained, it is concluded that the risk for the organ systems ADG, CAS, EYE, FRS, GIT and MAG is driven by two substances only. It is therefore recommended to further investigate (and possibly refine) exposure to these two substances (i.e. oxamyl and dimethoate), rather than prioritising these seven organ systems for cumulative risk assessment. Regarding the organ system HAS, considering that even after removal of dimethoate and oxamyl, acute exposure estimates for toddlers and children remain above the cut-off value of 1; this organ system is still considered relevant for prioritisation.

Hence, together with the organ systems that exceeded the cut-off value under the chronic exposure scenario, it is concluded that the organ systems would need to be prioritised as follows: RDT, LIV, KID, MRS and HAS. Considering however that activities on the cumulative risk assessment of KID and LIV have already been initiated, RDT will be postponed accordingly. This prioritisation will be repeated on a regular basis (e.g. every 3 years) and the priority list may be adjusted accordingly in the future.

## 4 | CONCLUSIONS

In view of accelerating the implementation of cumulative risk assessment to pesticide residues, EFSA has performed a two-step prioritisation analysis – both on individual pesticides and on target organ systems – based on the monitoring cycle 2019–2021. The analysis encompassed the consumption of 36 raw primary commodities of plant origin surveyed in 30 population groups, covering 3 different age classes (adults, other children and toddlers) and 17 EU countries. All the pesticides, with at least one positive finding on these commodities, were extracted for a total of 371 substances, of which 350 used for the analysis (after excluding 21 substances for which HBGV could not be identified). Probabilistic exposure calculations, for chronic and acute effects, have been executed on the selected occurrence and consumption data by adopting a two-dimensional method where variability is modelled by means of an inner loop execution, and uncertainty through an outer loop execution.

The metrics adopted to express the exposure to individual substances is the HQ, defined as the ratio of exposure to a substance to its HBGV. HQ larger than 0.1 at the 99.9th percentile of the exposure distribution has been used as cut-off value for the prioritisation of substances. The substances included in the priority list were then grouped based on their ability to cause toxicological effects on common organ systems and combined exposure calculations were carried out for each target organ. The combined exposure estimates of an organ system have been expressed as HI, the sum of the HQ



estimates of the substances affecting that organ system. Organ systems with  $HI \geq 1$  at the 99.9th percentile of the exposure distribution have been prioritised, with higher priority given to organ systems for which the cut-off value was exceeded in both chronic and acute scenarios.

After having filtered out substances not associated with any organ system and substances for which no HBGV was established, the final list of prioritised substances is composed of 67 substances: 15 associated with chronic effects, 21 with acute effects and 31 with both effects. Moreover, 11 organ systems were found to have a HI exceeding the cut-off value of 1 at the 99.9th percentile of the exposure distribution, 4 of which were common to the chronic and acute scenarios (RDT, LIV, KID and MRS), and 7 associated to the acute scenario only (MAG, HAS, ADG, CAS, FRS, GIT and EYE). For these latter organ systems, ad hoc sensitivity analyses have shown that the risk is driven by two substances only: oxamyl and dimethoate. It is therefore recommended to further investigate (and possibly refine) exposure to these two substances, rather than prioritising these seven organ systems for cumulative risk assessment. Regarding the organ system HAS, considering that even after removal of dimethoate and oxamyl, acute exposure estimates for toddlers and children remain above the cut-off value of 1; this organ system is still considered relevant for prioritisation. Hence, it is concluded that the organ systems to be prioritised are RDT, LIV, KID, MRS and HAS.

The estimated exposure values are subject to several uncertainties that need to be taken into consideration when interpreting these results. In addition to the modelling uncertainty tackled by the outer loop of the model by means of statistical methods, other methodological uncertainties have been introduced to account for inaccuracies and missing information in the data, following conservative assumptions (i.e. assumptions that were formulated to protect end consumers and that likely contribute to overestimation of the exposure). These uncertainties have been qualitatively identified and their impact taken into consideration in the interpretation of the results. For instance, most of the substances with a HQ greater than 1 are no longer approved within the EU and for non-approved substances an EU-agreed HBGV is often not available, making the HQ estimate very uncertain. Furthermore, some of these substances have a high proportion of left-censored data (measurements below the LOQ). In the current individual exposure assessment, such left-censored data have been replaced by  $\frac{1}{2}$  LOQ whereas, in reality, a proportion of these left-censored data are unlikely to contain any residue. This assumption introduces an important positive bias (overestimation) in the exposure assessments, especially for substances with a very low HBGV. Although more realistic assumptions have been used for the combined exposure of organ systems, the high proportion of left-censored data remains a main source of uncertainty of this assessment. In addition, the main contributors to the exposure estimates have been often found to be processed foods for which specific occurrence data or PFs were missing. In these instances, the exposure model assumes that all residues present in the raw food will reach the end consumer. This assumption is conservative because residue concentrations will most likely decrease due to processing. Further uncertainty stems from the unspecific residue definitions, in that occurrence data reported to EFSA refer to residue definitions for enforcement purposes and some of these residue definitions are not sufficiently specific, meaning that they may be associated with multiple active substances. For this prioritisation of substances, the concentrations of measured substances in a residue definition are assigned to all active substances associated to the residue definition, which results in a worst-case estimation of exposure for each of these active substances, which is not entirely realistic. For the combined exposure assessment, further uncertainty is related to the use of the HI approach, which relies on HBGVs for the different active substances. They are derived the most critical toxic effect observed for a given substance, which may refer to another organ or organ system. Even though it cannot be excluded that the HBGV may rely on outdated knowledge or data, applying the HI index approach is generally more likely to overestimate the potency of the substance for the organ system under assessment. Finally, the exclusion of substances due to missing HBGV or incomplete mapping to organ systems, may also impact the estimation of the HI. Overall, it is concluded that the risk estimates for the different organ systems are more likely to be overestimated than underestimated.

## 5 | RECOMMENDATION

Based on the outcome of this prioritisation, it is recommended to proceed with the implementation of dietary cumulative risk assessment to pesticide residues as follows:

- Identify toxicological effects of relevance, develop associated cumulative assessment groups, and perform retrospective cumulative risk assessment for the following target organ systems: RDT, LIV, KIDS, MRS and haematopoietic system.
- When establishing new cumulative assessment groups, the 67 priority substances identified in this analysis should be examined and considerations on a case-by-case basis may be required for 21 substances where an individual exposure assessment was not carried out due to lack of health-based guidance values.
- In accordance with the EU multiannual control programme, which relies on a 3-year monitoring cycle, repeat this prioritisation analysis every 3 years to account for changes in exposure patterns and possible updates of HBGVs.
- Further investigate (and possibly refine) exposure to oxamyl and dimethoate in the framework of the annual report on pesticide residues.

Furthermore, to reduce the impact of the uncertainties identified in this assessment, it is also recommended to:

- Replace the assumptions applied to left-censored data and unspecific residue definitions with more realistic approaches for individual exposure assessment.

- Consolidate the list of validated PFs available and strengthen the monitoring of pesticide residues in processed food commodities.

## ABBREVIATIONS

ADI	acceptable daily intake
ADG	adrenal gland
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARfD	acute reference dose
AUP	agricultural use pattern
BOS	bones/skeleton
bw	body weight
CAG	cumulative assessment group
CAS	cardiovascular system
CCPR	Codex Committee on Pesticide Residues
CRA	cumulative risk assessment
DTU	Danish Technical University
EKE	Expert Knowledge Elicitation
EPA	Environmental Protection Agency of the US
EU MACP	EU-coordinated multiannual control programme
EYE	eye
FAO	Food and Agriculture Organization of the United Nations
FRS	female reproductive system
GIT	gastrointestinal system
HAS	haematopoietic system and haematology
HBGV	health-based guidance value
HI	hazard index
HQ	hazard quotient
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
KID	kidney
LIV	liver
LOQ	limit of quantification
MAG	mammary Gland
MNCP	Multiannual National Control Programme
MOET	total margin of exposure
MRL	maximum residue level
MRS	male reproductive system
MUS	muscular system
OIM	Observed Individual Means
PAG	parathyroid gland
PIG	pituitary gland
PF	processing Factor
RDT	reproductive and developmental toxicity
RPC	raw primary commodity
sDWH	Scientific Data Warehouse
SSD	standard sample description
TDI	tolerable daily intake
URB	urinary bladder
WHO	World Health Organization

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## CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact [interestmanagement@efsa.europa.eu](mailto:interestmanagement@efsa.europa.eu).

## REQUESTOR

European Food Safety Authority

## QUESTION NUMBER

EFSA-Q-2020-00761

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## APPENDIX A

### Description of the input data

The probabilistic exposure calculations to single substances and to groups of substances share the same primary and secondary input data, which are described in this Appendix. The primary input data refer to the occurrence of a given substance in foods, and to the consumption of those foods in a person's diet. These data are stored in the EFSA Data Warehouse. When the exposure calculations are initiated, the data for the relevant food commodities, active substances and dietary surveys are extracted. The execution of the probabilistic calculations requires the use of additional data, referred to as secondary input data. These include various types of information which are used either for the adjustment of the occurrence data (e.g. authorised uses of active substances on specific crops) or for improvement of the exposure estimates (e.g. processing factors). Full details are given hereafter.

### A.1 | PRIMARY INPUT DATA

#### A.1.1 | Raw primary commodities

To calculate the probabilistic exposure to pesticide residues, EFSA has selected the same 35 raw primary commodities (RPCs) of plant origin that were considered in the EU MACP over the years. In addition, courgettes were also included because, according to EFSA's design assessment of the pesticide monitoring programme (EFSA, 2015), courgettes are consumed in higher amounts than other commodities previously included in the EU MACP (e.g. spinach and broccoli).

The full list of RPCs considered for this assessment is provided in Annex A.1, Table A.1.01

#### A.1.2 | Active substances and health-based guidance values

The active substances under analysis are those selected from the occurrence data (see Section A.1.4) from which at least one positive measurement was found. For each active substance, health-based guidance values (HBGVs) are used to express the results of both individual exposure assessment (see Appendix B) and combined exposure assessment (see Appendix C). In particular, the acute reference dose (ARfD) is used for acute calculations, while the acceptable daily intake (ADI) or tolerable daily intake (TDI) is used in chronic calculations. In cases where the ARfD is not available for a substance (either because it is considered not necessary, or the assessment of an acute HBGV was not performed), the ADI is tentatively used as a conservative surrogate.

HBGVs established in the framework of Regulation (EC) No 1107/2009 before 31 December 2022 were selected. Where applicable, the most recent HBGV adopted by EFSA was preferred over the HBGV previously endorsed by the European Commission. In the absence of such HBGVs, tentative HBGVs were retrieved from the additional sources of information listed below (in order of priority):

- Previous EFSA Peer Review Conclusions: when HBGVs were not confirmed by EFSA in its latest review but they are available in a previous evaluation, the latter were tentatively used for the calculations. This was not applied in cases where demonstrated genotoxic properties were established for the substance under consideration. In this latter case, exposure estimates were not compared to a HBGV.
- EFSA outputs other than Peer Review Conclusions: i.e. Scientific Opinions, Reasoned Opinions, Scientific support for preparing an EU position for the Sessions of the Codex Committee on Pesticide Residues (CCPR). HBGVs that were reported in these outputs, either proposed by EFSA or proposed/established by other national or international bodies, were tentatively used for the calculations.
- The Joint FAO/WHO Meeting on Pesticide Residues (JMPR) evaluations reports: HBGVs reported in these outputs were tentatively used for the calculations.
- Assessments from other national or international bodies, such as French Agency for Food, Environmental and Occupational Health & Safety (ANSES), Dutch National Institute for Public Health and the Environment (RIVM), U.S. Environmental Protection Agency (US EPA), Australian Pesticides and Veterinary Medicines Authority (APVMA) database, etc. HBGVs reported in these outputs were tentatively used for the calculations.

The active substances and HBGVs considered for chronic exposure assessment, which incorporates the key input data for the prioritisation exercise, are reported in Annex A.1. The substances were listed in two different tables when an EU-agreed HBGV is available and in force on 31 December 2022 (Table A.1.02) or when another HBGV is considered for tentative assessment (Table A.1.03). Active substances where an HBGV could not be retrieved for chronic assessment are listed Table A.1.04.

Similarly, the active substances and HBGVs considered for acute exposure assessment are reported in Annex A.2. These substances were also listed in two different tables when an EU-agreed HBGV is available and in force on 31 December 2022 (Table A.2.02) or when another HBGV is considered for tentative assessment (Table A.2.03). Active substances where an HBGV could not be retrieved for acute assessment are listed Table A.2.04.



### A.1.3 | Residue definitions

While the probabilistic exposure calculations are executed at the level of the active substances, the occurrence data reported to EFSA refer to the residue definition for enforcement (see also Section A.1.4). As the residue definitions defined in Regulation (EC) No 396/2005 may change over time, single active substances may be associated to multiple residue definitions throughout the reference period 2019–2021. EFSA, therefore, collected all the residue definitions that were applicable to the selected food commodities and active substances during the reference period. The residue definitions collected for chronic and acute exposure assessment are, respectively, reported in Annex A.1, Table A.1.05, and Annex A.2, Table A.2.05.

Depending on the metabolism and availability of analytical methods, the residue definitions may either be equal to the active substance, may include additional metabolites, or even incorporate multiple active substances. When the residue definition includes additional metabolites that are specific to the active substance (i.e. *complex* residue definition), the residue definition is assigned to the active substance assuming that all metabolites will have the same toxicological properties as the parent compound (e.g. sum of tebuconazole, hydroxy-tebuconazole and their conjugates, expressed as tebuconazole). When the residue definition includes or applies to multiple active substances, however, the active substances may have different toxicological properties (e.g. dithiocarbamates). The latter are referred to as *unspecific* residue definitions. When active substances are associated with an unspecific residue definition (e.g. sum of carbendazim and thiophanate-methyl, expressed as carbendazim), further distinction is made between exclusive and non-exclusive associations:

- Supposing that carbendazim would be applied to the field, carbendazim cannot be metabolised into thiophanate-methyl and the measured residue would be attributed to carbendazim only. In this case, the association is considered exclusive.
- Supposing that thiophanate-methyl would be applied to the field, thiophanate-methyl would partially metabolise into carbendazim. In this case, only a proportion of the measured residue would be attributed to thiophanate-methyl and the remaining part would be attributed to carbendazim. Hence, the association is not exclusive.

Data on the proportions, however, were not readily available to EFSA. Therefore, a default proportion of 0.5 ( $\approx 50\%$ ) was assumed for all associations that are not exclusive. To allow for the correct allocation of active substances to the measured residues for combined exposure assessment (see Section C.1.1.1), this information was also integrated in the list of residue definitions.

### A.1.4 | Occurrence data

The occurrence data collected under Article 31 of Regulation (EC) No 396/2005 are the most appropriate data available to EFSA for performing a retrospective probabilistic exposure assessment. These data are obtained from the official control activities carried out in the EU Member States,<sup>2</sup> Iceland and Norway. These data are reported to EFSA using the Standard Sample Description ver. 2.0 (SSD2) (EFSA, 2013). Although the occurrence data are collected at the level of individual measurements, the SSD2 allows identification of measurements associated to a single food sample (e.g. samples analysed for multiple pesticide residues). After validation by EFSA, the collected data are integrated in the EFSA's Scientific Data Warehouse (sDWH).

All occurrence data referring to the relevant food commodities (see Section A.1.1) and residue definitions (see Section A.1.3) were extracted from the sDWH. Only measurements validated under 2019, 2020 and 2021 EU reports on pesticide residues in food were included (EFSA, 2023).

The following criteria were applied to the extracted data:

- Only samples resulting from the EU-coordinated control programme (EU MACP), national control programmes (MANCP) or a combination of those were selected (SSD2 programme type codes K005A, K009A and K018A). Samples associated to increased control programmes or any other type of programme were excluded as they were not considered to be representative of the market.
- Only samples obtained through selective or objective sampling were retained (SSD2 sampling strategy codes ST10A and ST20A). Samples obtained through suspect sampling (SSD2 sampling strategy codes ST30A), or any other type of sampling were not considered to be representative of the market and therefore excluded.
- When the occurrence data were primarily reported for the RPC, samples for processed commodities were excluded and the assessment was based on the RPCs. However, when a sufficient number of samples were found, the occurrence data for the processed foods (i.e. raw primary commodity derivatives, RPCDs) were also retained.
- Only measurements reported as a numerical (i.e. quantifiable) value or as a non-quantified value were considered useful for the assessment (SSD2 resType codes VAL and LOQ). Other result types were not considered valid and therefore excluded.
- Only measurements reported for the enforcement residue definition that was applicable at the time of sampling, or for the most complete subset of that enforcement residue definition, were used (SSD2 paramType codes P004A and P005A). Measurements referring to parts of the residue definition were excluded from the assessment.
- When the LOQ value for a measurement could not be reported by the Member States (i.e. for residue definitions composed of multiple components), the median LOQ of all measurements referring to the same residue definition/commodity combination was assumed.

<sup>2</sup>Pursuant to Article 5(4) and Section 24 of Annex 2 of the Protocol on Ireland/Northern Ireland, which is an integral part of the Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community, the EU requirements on data sampling are also applicable to Northern Ireland and, for the purpose of this report, references to Member States are read as including the United Kingdom in respect of Northern Ireland.

- When the LOQ value for a measurement was found to be more than 100 times higher compared to the median LOQ of all measurements referring to the same combination of commodity and residue definition, the measurement was no longer considered valid and excluded from the assessment.
- When several measurements with overlapping residue definitions were reported for the same sample, only the measurement referring to the most recent enforcement residue definition was retained for assessment.

Occurrence data from all EU Member States, Iceland and Norway were pooled into one single data set for the purpose of this assessment. Considering the size of the occurrence data set, only the summary statistics per residue definition and food commodity are reported (see Annex A.1, Table A.1.06 and Annex A.2, Table A.2.06).

### A.1.5 | Consumption data

The EFSA Comprehensive European Food Consumption Database (Comprehensive Database) provides a compilation of existing national information on food consumption at individual level. Details on how the Comprehensive Database is used are published in the Guidance of EFSA (EFSA, 2011). Data reported in the Comprehensive Database may either refer to RPCs, RPCDs (i.e. single-component foods altered by processing) or composite foods (i.e. multicomponent). Consumption data for RPCDs and composite foods, however, cannot be used in exposure assessments when the occurrence data are reported for the RPCs.

To address the above issue, EFSA transformed the Comprehensive Database into a new RPC Consumption Database by means of the RPC model (EFSA, 2019a). This model converts the consumption data for composite foods or RPC derivatives into their equivalent quantities of RPCs. The RPC model was applied to the Comprehensive Database as of 31 March 2018, when it contained results from 51 different dietary surveys carried out in 23 different Member States covering 94,523 individuals.

Furthermore, to cover as many populations as possible without compromising the reliability of intake estimates at the 99.9th percentile of the exposure distribution, only the dietary surveys with more than 300 survey subjects were retained, covering 17 different countries.

- Toddlers:<sup>3</sup> Bulgaria, Denmark, Finland, Germany, the Netherlands.
- Other children:<sup>4</sup> Belgium, Bulgaria, Czechia, Finland, France, Germany, Greece, the Netherlands, Spain, Sweden.
- Adults:<sup>5</sup> Austria, Belgium, Czechia, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, the Netherlands, Romania, Spain, Sweden.

For chronic exposure assessment, 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).

An overview of the selected dietary surveys is provided in Annex A1, Table A.1.07 and Annex A.2, Table A.2.07. Summary statistics on the amounts consumed per country, survey, age class and food commodity are also reported (see Annex A.1, Table A.1.08 and Annex A.2, Table A.2.08).

## A.2 | SECONDARY INPUT DATA

### A.2.1 | Maximum residue level

Certain assumptions on the authorised uses (see Section A.2.2) require information on the maximum residue levels (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. This regulation also defines a procedure for the setting and modification of MRLs. MRLs may therefore have been modified throughout the 2019–2021 reference period. To obtain a single list of MRLs, EFSA decided to use the MRLs as of 31 December 2021 (i.e. the end of the current reference period) and it was assumed that those MRLs were applicable during the entire reference period, regardless of whether the MRL or residue definition may have changed during that period.

MRLs for the relevant food commodities (see Section A.1.1) and enforcement residue definitions (see Section A.1.3) were extracted from the EU Pesticides Database and organised in a data format that can be used directly for exposure assessment.

### A.2.2 | Authorised uses

In some cases, the imputations and simulations performed on the occurrence data rely on the authorisations for use of the active substance(s) (see Sections C.1.1.1 and C.1.1.2). While the approval status of an active substance under Regulation (EC) No 1107/2009 is regulated at EU level, the authorisations for plant protection products (PPPs, i.e. formulated products containing the active substances) are delivered at national level within the EU Member States. A centralised database compiling these national authorisations is not yet available at EU level.

National authorisations can be reported to EFSA under Regulation (EC) No 396/2005, either for an MRL application under Article 10, or for an MRL review under Article 12. There is, however, no legal obligation to systematically report all national

<sup>3</sup>The population class 'toddlers' refers to participants from ≥ 12 months to < 36 months old.

<sup>4</sup>The population class 'other children' refers to participants from ≥ 36 months to < 10 years old.

<sup>5</sup>The population class 'adults' refers to participants from ≥ 18 years to < 65 years old.

authorisations and the MRL review programme is still in progress. A comprehensive overview of all pesticides authorisations within the EU is therefore also not available to EFSA. Meanwhile, a tentative list of authorised uses was elaborated according to the following principles.

- When the MRL for a given combination of active substance and RPC was not set at the LOQ (see Section A.2.1), the active substance was assumed to be authorised for use on that specific commodity. This assumption also accounts for uses authorised outside the EU and for which treated products may be placed on the EU market. Furthermore, this assumption concerns non-approved substances, including persistent organic pollutants, which are assumed to be authorised on crops for which MRLs are above the LOQ.
- When non-LOQ MRLs referred to unspecific residue definitions (i.e. including or applying to multiple active substances, see also Section A.1.3), only the substances approved under Regulation 1107/2009 were assumed to be authorised for use on that crop. If none of the active substances was approved, it was assumed that any substance may be authorised for use outside the EU.
- When non-LOQ MRLs refer to an active substance that is phased out under Regulation 1107/2009 (e.g. carbendazim) but may still occur as a metabolite from another active substance (thiophanate-methyl), the MRL was not considered to represent an authorised use of the active substance that was phased out.
- For the remaining combinations of active substance and RPC (i.e. where the MRL was set at LOQ), EFSA screened the relevant reasoned opinions issued under Article 12 of Regulation (EC) No 396/2005 and the subsequent reasoned opinions issued under Article 10. Any authorised use reported in those reasoned opinions was recorded. When a review under Article 12 of Regulation (EC) No 396/2005 had not been issued, it was assumed that the use was not authorised.

The authorised uses considered for chronic and acute exposure assessment are listed in Annex A.1, Table A.1.09, and Annex A.2, Table A.2.09.

### A.2.3 | Processing factors

Occurrence data for pesticide residues are collected at the level of the RPC (see Section A.1.4). Food consumption data may be collected at the level of RPC, RPCD or composite food, but for the purpose of this assessment all consumption data for composite foods and RPCDs were converted into their equivalent quantities of RPCs (see Section A.1.5). Combining occurrence and consumption data at RPC level implies that all residues present in the RPC will reach the end consumer. This assumption, however, is conservative as residue concentrations will most likely change due to processing, such as peeling, washing, cooking, etc.

The effect of processing is usually addressed by means of processing factors. A processing factor accounts for the change in residue concentrations and is specific to each RPC, processing type and active substance. Processing factors are quantified by dividing the residue concentration in the processed commodity by the residue concentration in the raw commodity.

The European database on processing factors is the most recent and the most comprehensive compilation of processing factors currently available at EU level (Zincke et al., 2022). Processing factors for the active substances and RPCs under assessment were extracted from the database according to the following criteria:

- For each active substance, RPC and processing technique, only the median processing factor was extracted.
- Only the processing factors indicated as reliable, or indicative were extracted. Processing factors indicated as unreliable were excluded from the assessment.

Processing techniques reported in the processing factor database were then compared to the processing techniques reported in the RPC consumption data set. The processing techniques from both databases were matched according to the following principles:

- When a generic processing technique was reported in the RPC consumption database (e.g. juice) while more specific processing techniques were reported in the processing factor database (e.g. pasteurised juice and unpasteurised juice), the specific processing technique with the highest processing factor was selected.
- When a specific processing technique was reported in the RPC consumption database (e.g. mashed potato) while a more generic processing technique was reported in the processing factor database (e.g. boiled potato), the generic processing factor was applied to the specific processing techniques.
- Processing factors were extrapolated between raw primary commodities with similar properties (i.e. oranges and mandarins, apples and pears, table and wine grapes, wheat and rye grain).
- Processing factors for peeling were applied to the corresponding fruit with inedible peel, even when the processing technique was not specified in the RPC consumption database (i.e. oranges, mandarins, bananas and melons).

Based on the above principles, lists of PFs were obtained for both chronic and acute exposure assessment (see Annex A.1, Table A.1.10 and Annex A.2, Table A.2.10, respectively).

## A.2.4 | Variability factors

The occurrence data used for probabilistic exposure assessment refer to the average concentrations in composite laboratory samples (see Section A.1.4). Consumers, on the other hand, are exposed to individual units of the commodity. Residue concentrations may vary among the individual units, referred to as unit-to-unit variability. To account for this unit-to-unit 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.

Unit weights for each commodity were retrieved from the Pesticide Residues Intake Model (EFSA, 2018). For RPCs that have a unit weight inferior to 25 g and for processed foods that were subject to blending or bulking, the unit-to-unit variability is not considered relevant since the residue concentration in the composite laboratory sample is expected to reflect the residue concentration in the portion that would be consumed (FAO, 2003).

The number of units per sample was obtained from Commission Directive 2002/63/EEC, establishing community methods of sampling for the official control of pesticide residues in and on products of plant and animal origin. This directive defines a minimum weight and a minimum number of units for composite laboratory samples of each food category. Hence, the minimum number of units (as defined by Directive 2002/63/EEC) was used, unless the minimum sample weight divided by the corresponding unit weight was higher. In that case, the latter calculated value (rounded up to the next integer) was retained.

For the individual exposure assessments, VFs were from the Pesticide Residues Intake Model (EFSA, 2018) were used (see also Section B.1.2.2), whereas a default VF of 3.6 was considered for the combined exposure assessments (see also Section C.1.2.2).

While a fixed VF is usually applied for acute deterministic calculations, for probabilistic exposure assessment the use of a distribution of unit concentrations is considered more adequate than using a fixed VF. Therefore, unit-to-unit variability is modelled using a beta distribution, which can be bounded between 0 and an upper limit. Indeed, if the average concentration in a composite sample is 1, the concentration in a single unit can never be higher than the number of units within the composite sample (assuming all other units have a concentration of zero). Hence, for each RPC with a unit weight exceeding 25 g, the beta distribution was parametrized with the following restrictions:

- Lower bound = 0;
- Mean = 1;
- 97.5th percentile = VF;
- Upper bound = number of units per sample.

The corresponding alpha and beta parameters of the beta distribution were obtained for each commodity through an iterative what-if analysis. An overview of the different parameters used for acute individual exposure assessment and acute combined exposure assessment are provided in Annex A.2 (Table A.2.11 and Table A.2.12, respectively).

## A.2.5 | Processing types

Variability among the single commodity units of the composite laboratory samples is not relevant when the food consumed is subject to processing techniques that involve bulking and blending.

EFSA therefore extracted all processing techniques reported in the RPC consumption data (see Section A.1.5) and identified the processes that normally involve blending or bulking. Typically, these are processing techniques performed at industrial level (e.g. milling, oil production, etc.). Household processes, however, were assumed not to involve any bulking or blending (e.g. boiling, stewing, etc.). Although juicing may also be carried out at household level, EFSA assumed that most fruit juices are produced at industrial level.

The list of processing types was used for acute exposure assessment only (see Annex A.2, Table A.2.13).



## APPENDIX B

### Methodology for individual exposure assessment

The individual exposure calculations were performed for each pesticide active substance independently, addressing chronic and, where relevant, acute effects separately. The primary and secondary input data used for executing the exposure assessment to single substance were those described in the Appendix A. The probabilistic approach used for this assessment relies on a two-dimensional method where variability is modelled by means of an inner loop execution, and (sampling) uncertainty is modelled through an outer loop execution (EFSA, 2021, 2022). Considering that the individual exposure assessment is intended for prioritisation of substances, several conservative assumptions have been integrated in the calculation methods which are expected to overestimate the exposure (see also Sections B.1.1.1, B.1.1.2 and B.1.2). As opposed to the combined exposure assessment, an adjustment for drinking water was not included in the individual exposure assessment. For substances with low occurrence values in food, theoretical assumptions on drinking water were found to mask the exposure from other sources which introduced an important bias in the prioritisation of substances.

The metrics adopted to express the exposure to individual substances is the hazard quotient (HQ), defined as the ratio of the substance's exposure to its HBGV. Therefore, HQ lower than one is general considered safe, whereas an HQ larger than one implies that the estimated exposure outweighs the HBGV, indicating that further attention is needed considering the potential overestimation in the exposure estimates.

### B.1 | INNER LOOP EXECUTION

#### B.1.1 | Adjustments and simulations on the occurrence data

##### B.1.1.1 | Allocation of active substances to occurrence data

While the probabilistic exposure assessment is executed at the level of the active substances, the occurrence data reported to EFSA refer to residue definitions for enforcement purposes (see Section A.1.4). Hence, the original occurrence data set obtained from the EFSA Data Warehouse is converted into a new intermediate data set where measurements are assigned to active substances instead of residue definitions. Some of these residue definitions, however, referred to as unspecific residue definitions, may be associated with multiple active substances.

For the prioritisation of substances in this report, the concentrations of measured substances in a residue definition were assigned to all active substances associated to the residue definition, allowing for a worst-case estimation of exposure for each of these active substances.

##### B.1.1.2 | Imputation of left-censored occurrence data

The imputation of left-censored occurrence data takes place after completion of the allocation of active substances to occurrence data. Over 97% of the occurrence data used for the current exposure assessment are left-censored (see Appendix A). Left-censored data are measurements reported below the LOQ and for which an accurate value is not available. Some of these results may be low positive residues while others will be true zeroes (no-residue situation). To address the uncertainties resulting from the high proportion of left-censored data, when a measurement was reported below LOQ, the concentration used for the assessment was set at  $\frac{1}{2}$  LOQ for food–substance combinations with at least one quantifiable finding. In all other cases, the measurements below LOQ were substituted with zero.

This assumption implies that all samples of a food commodity were treated with a pesticide as soon as one positive measurement was found for that commodity, which is generally considered to be a conservative assumption.

##### B.1.1.3 | Calculation of mean occurrence values for chronic exposure

Mean occurrence values are only calculated for chronic exposure assessment. Although individual residue measurements are required to enable bootstrapping and quantify the impact of sampling uncertainty, short-term variability of residues between samples is not relevant when modelling chronic exposure (EFSA PPR Panel, 2012). Chronic exposure is therefore estimated using the average concentration for each commodity. Hence, the occurrence data set obtained after imputation of left-censored occurrence data (see Section B.1.1.2) is used to calculate the average concentrations per food commodity.

#### B.1.2 | Exposure distributions

##### B.1.2.1 | Chronic exposure distribution

Chronic dietary exposure is modelled by means of an empirical approach, referred to as the OIM approach (EFSA PPR Panel, 2012). This method uses the mean consumption over the survey days of each individual to estimate the individuals' long-term consumption. Using the individuals' bodyweight and the mean occurrence values obtained as described in Section B.1.1.3, the individuals' chronic exposures resulting from each food commodity are calculated. The exposure is expressed as the Hazard Quotient (HQ), defined as the ratio of the substance's exposure to its HBGV. It should be noted, however that, due to the limited duration of the dietary surveys, the OIM approach tends to overestimate upper tail exposures in chronic assessments.



Furthermore, when combining occurrence and consumption data, attention must be given to the possible effect of processing. Ideally, occurrence data should be available for the RPCD. Under such circumstances, the occurrence data can be combined directly with the amount of RPCD consumed. When occurrence data are only available for the RPC but a processing factor is available (see Section A.2.3), the processing factor will be integrated in the calculation to obtain an estimate of the substance's concentration in the RPCD. However, if occurrence data are only available for the RPC and a processing factor is not available, the occurrence value for the RPC will be combined with the corresponding amount of RPC consumed. The latter option implies that all residues present in the RPC will reach the end consumer, while alteration of residues is expected to occur when the RPCs are processed prior to consumption. This uncertainty is generally expected to overestimate exposure. As the consumed amounts are expressed in grams and occurrence data are expressed in mg/kg, a correction factor of 1000 needs to be considered. Based on the considerations above, the HQ is calculated for each individual according to the following formula:

$$HQ_i = \sum_c^{\text{commodities}} \sum_p^{\text{processes}} \left\{ \begin{array}{l} \frac{RPCD_{idcp} \cdot \bar{X}_{cp}}{BW_i \cdot Days_i \cdot HBGV \cdot 10^3}, \exists \bar{X}_{cp} \\ \frac{RPCD_{idcp} \cdot \bar{X}_c \cdot PF_{cp}}{BW_i \cdot Days_i \cdot HBGV \cdot 10^3}, \nexists \bar{X}_{cp} \wedge \exists PF_{cp} \\ \frac{RPC_{idcp} \cdot \bar{X}_c}{BW_i \cdot Days_i \cdot HBGV \cdot 10^3}, \nexists \bar{X}_{cp} \wedge \nexists PF_{cp} \end{array} \right.$$

where  $HQ_i$  is the hazard quotient (HQ) of individual  $i$ ;

$RPCD_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in g of raw primary commodity derivative (RPCD);

$RPC_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in g of raw primary commodity (RPC);

$\bar{X}_{cp}$  is the average concentration in commodity  $c$  with processing type  $p$ , expressed in mg/kg;

$\bar{X}_c$  is the average concentration in unprocessed commodity  $c$ , expressed in mg/kg;

$PF_{cp}$  is the processing factor (PF) in commodity  $c$  with processing type  $p$ ;

$BW_i$  is the bodyweight (BW) of individual  $i$ , expressed in kg;

$Days_i$  is the number of survey days of individual  $i$ ;

$HBGV$  is the health-based guidance value, expressed in mg/kg bodyweight per day.

After having calculated the HQ for each individual, empirical distributions of individual HQs were obtained. The distributions represent the variability of exposure within the different population groups.

#### B.1.2.2 | Acute exposure distribution

Acute dietary exposure is modelled at the level of individual consumption days by means of an empirical Monte Carlo simulation (EFSA PPR Panel, 2012), where individual days are selected at random from the consumption data set. For each food commodity consumed within the individual days, random samples of the occurrence data set are assigned. The acute exposures resulting from each food commodity within each individual day are calculated using the individuals' body weights and the concentration of the active substance measured in the different samples. The occurrence data used for the assessment, however, represent the average concentrations of composite laboratory samples (see Section A.1.4). Consumers, on the other hand, are exposed to individual units of the commodity. Residue concentrations may vary among the individual units, referred to as unit-to-unit variability. For RPCs having a unit weight below 25 g and for processed foods subject to blending or bulking, the unit-to-unit variability is not considered relevant (FAO, 2003). For the remaining food commodities, a fixed VF is usually applied for acute deterministic calculations while for probabilistic exposure assessment, a beta probability distribution is considered independent of the average concentration observed in the specific sample. Assuming an average concentration of 1 in the composite sample, the concentration in a single unit can never be higher than the number of units within the composite sample (assuming all other units have a concentration of zero) and the beta distribution is bounded between 0 as lower bound and the number of units per sample as upper bound (see Section A.2.4). Furthermore, 97.5th percentile of the beta distribution is assumed to be equal to the fixed VF usually applied in deterministic assessment. For the prioritisation of individual substance, very conservative VF (i.e. 5 or 7) for all commodities with a unit weight exceeding 25 g, as defined in the Pesticide Residues Intake Model (EFSA, 2018) were considered most appropriate to define the 97.5th percentile of the beta distribution.

Stochastic VFs can then be drawn from the beta distribution and multiplied with the composite sample concentration to obtain a plausible estimate of the unit concentration. When the portion consumed by an individual is smaller than a single unit, the stochastic VF is directly applicable to the consumed portion. When the consumed portion is composed of multiple units however, multiple stochastic VFs will be drawn from the same beta distribution to estimate concentration

in the whole portion consumed. Therefore, the concentration in the whole portion is estimated by multiplying the sample concentration with a weighted VF, which is calculated as:

$$WVF = SVF_n \text{ if } n = 1,$$

$$WVF = \frac{\sum_{i=1}^{n-1} SVF_i + SVF_n(n_0 - n + 1)}{n_0} \text{ if } n > 1,$$

where  $WVF$  is the weighted VF;

$SVF_i$  is the stochastic VF drawn for unit  $i$ ;

$n_0$  is the estimated number of units within the consumed portion (unrounded), assuming the unit weights reported in Appendix A;

$n$  is the number of stochastic VFs to be drawn (i.e. ceiling of  $n_0$ ).

Apart from the unit-to-unit variability, the exposure modelling also needs to account for the effect of processing prior to consumption and for the potency of the different substances. These two aspects are addressed similarly to the chronic exposure assessment (see Section B.1.2.1). Based on these considerations, the HQ is calculated for each individual day according to the equations reported below.

$$HQ_{id} = \sum_c^{\text{commodities}} \sum_p^{\text{processes}} \left\{ \begin{array}{l} \frac{RPCD_{idcp} \cdot X_{idcp}}{BW_i \cdot HBGV \cdot 10^3}, \exists X_{idcp} \\ \frac{RPCD_{idcp} \cdot X_{idc} \cdot WVF_{idcp} \cdot PF_{cp}}{BW_i \cdot HBGV \cdot 10^3}, \nexists X_{idcp} \wedge \exists PF_{cp} \\ \frac{RPC_{idcp} \cdot X_{idc} \cdot WVF_{idcp}}{BW_i \cdot HBGV \cdot 10^3}, \nexists X_{idcp} \wedge \nexists PF_{cp} \end{array} \right.$$

where  $HQ_{id}$  is the hazard quotient (HQ) of individual  $i$  on day  $d$ ;

$RPC_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in g of raw primary commodity (RPC);

$RPCD_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in g of raw primary commodity derivative (RPCD);

$BW_i$  is the body weight (BW) of individual  $i$ , expressed in kg;

$X_{idcp}$  is the average concentration in a sample of commodity  $c$  with processing type  $p$  that was randomly assigned to individual  $i$  on day  $d$ , expressed in mg/kg;

$X_{idc}$  is the average concentration in a sample of unprocessed commodity  $c$  that was randomly assigned to individual  $i$  on day  $d$ , expressed in mg/kg;

$WVF_{idcp}$  is the weighted variability factor (WVF) that was randomly assigned to individual  $i$  on day  $d$  in commodity  $c$  with processing type  $p$ ;

$PF_{cp}$  is the processing factor in commodity  $c$  with processing type  $p$ ;

$HBGV$  is the HBGV of the substance, expressed in mg/kg body weight.

The Monte Carlo simulation described above is executed 100,000 times, implying that, for each dietary survey, 100,000 individual days are randomly selected with replacement and HQs are calculated for each individual day. This results in empirical distributions of HQs, representing the variability of single day exposures within the different population groups. A more detailed description of the methodology used to estimate acute dietary exposure is provided in Appendix E of EFSA (2022).

## B.2 | Outer loop execution

The consumption data used for this assessment are subject to sampling uncertainty and will not perfectly represent the true diets within the population. Likewise, the occurrence data will not perfectly reflect the true distribution of residue concentrations in food. These sampling uncertainties are addressed by repeating the inner loop execution multiple times, each time replacing the consumption and occurrence data sets with bootstrap data sets (EFSA PPR Panel, 2012). Bootstrap data sets are obtained by resampling, with replacement, the same number of observations from the original data sets. Each time the inner loop is executed with bootstrap data sets, a bootstrap distribution of hazard quotients (HQs) is obtained. This shows how the distribution of HQs may have looked like if random sampling from the population would have generated different samples compared to the initial data set (Efron & Tibshirani, 1993).

It should be noted, however, that the consumption data considered for individual exposure assessment incorporate multivariate patterns (e.g. association of foods and individuals' characteristics). These patterns need to be preserved in the bootstrap data sets. Consumption data are, therefore, resampled at the individual day level by selecting all consumption events of the resampled individual day. Hence, for each dietary survey, the bootstrap data sets contain the same number of individual days as the initial data set.

In the current exposure model, the inner loop execution is repeated 100 times. The first execution, also referred to as the nominal run, is performed with the original data sets. The remaining executions are performed with bootstrap data sets. Although the outer loop execution is primarily intended to address the sampling uncertainty of the consumption and occurrence data, it also addresses uncertainty resulting from several simulations and imputations that rely on the random selection of measurements (see Sections B.1.1.1 and B.1.1.2).

### B.3 | Output preparation

Through the inner and outer loop executions, multiple HQ distributions are generated (i.e. 100 bootstrap distributions per dietary survey and active substance). To describe each bootstrap distribution, the following parameters are derived:

- mean of the HQ;
- standard deviation of the HQ;
- percentiles of the HQ (P2.5, P5, P10, P25, P50, P75, P90, P95, P97.5, P99, P99.9 and P99.99).

As a result, 100 estimates are obtained for each parameter of the HQ distributions. These 100 estimates reflect the uncertainty distribution around the true value of those parameters. From these uncertainty distributions, a 95% confidence interval is calculated for each parameter. The median of the uncertainty distribution is selected as the central estimate for the confidence interval.

For chronic exposure assessment, to better understand the factors that influence the highest HQs, individuals with an HQ higher than the HQ calculated at the 99th percentile of the HQ distribution are extracted for each dietary survey and all bootstrap distributions. The relevant information associated with those individuals is also retrieved (i.e. amounts of foods consumed and concentrations of active substances). Based on the individuals' information, average contributions are calculated per dietary survey and food commodity. For acute exposure assessment, a similar extraction is applied at the level of individual days. Due to limitations in terms of computational capacity, this extraction for acute assessment is limited to the nominal run only.

Additional information is gathered throughout the calculation process to support the identification of missing information. These intermediate outputs mainly refer to the food–substance combinations with limited occurrence data (possibly underestimating the HQ).

The above-reported percentiles were calculated using SAS® software, which provides five validated options for the definition of percentiles. In this assessment, the following percentile definition was selected:

Let  $n$  be the number of non-missing values for a variable, and let  $x_1, x_2, \dots, x_n$  represent the ordered values of the variable, and set  $p = t/100$ . Then, the  $t$ -th percentile is calculated as:

$$y = (1 - g)x_j + gx_{j+1},$$

where  $y$  is the  $t$ -th percentile;

$np$  is the product of  $n$  and  $p$ ;

$j$  is the integer part of  $np$ ;

$g$  is the fractional part of  $np$ .

The percentile definition is not expected to have a substantial impact for the acute exposure estimates because 100,000 individual days are simulated for each exposure distribution. With such a high number of observations, calculated percentiles are expected to be stable regardless of the percentile definition used. For chronic exposure, on the other hand, this relationship was the most appropriate because it allows for the differentiation of percentiles, even when  $p > (n - 1)/n$ . This is particularly useful for the dietary surveys with toddlers and children where a 99.9th percentile needs to be calculated even though the number of individuals is lower than 1000. This method still contains an important bias because the calculated percentile will always be lower than, or equal to, the highest observation. For dietary surveys with a low number of individuals, it is not unlikely that the true percentile will be higher than the highest observation in the empirical distribution. However, estimation of percentiles beyond the highest observation would require parametric modelling of the exposure distribution which needs to be further investigated before being implemented in cumulative exposure assessment.

## APPENDIX C

### Methodology for combined exposure assessment

The combined exposure calculations were performed for each target organ independently, addressing both chronic and acute effects separately. The primary and secondary input data used for executing the combined exposure assessment per target organ system are described in the Appendix A. An additional table containing the target organ for each substance and the relative effect (acute and/or chronic), similar to Table E.1, was produced and provided as input.

The probabilistic approach used for these assessments is primarily based on the approaches used for the cumulative exposure assessment of pesticide residues Tier II, which relies on a two-dimensional method where variability is modelled by means of an inner loop execution, and (sampling) uncertainty is modelled through an outer loop execution (EFSA, 2021, 2022). The main difference compared to the cumulative exposure assessment of pesticide residues refers to the expression of results. The cumulative exposure assessment of pesticide residues refers to specific effects where the potency of the different substances is defined by means of a specific point of departure (i.e. no observed adverse effect level, NOAEL), and the outcome of the exposure calculations is expressed as total margin of exposure (MOET). In this case, however, only health-based guidance values are available to characterise the potency of the different substances. Therefore, in accordance with EFSA's guidance on harmonised methodologies for risk assessment of combined exposure to multiple chemicals (EFSA Scientific Committee, 2019), expression of results as the hazard index (HI) was considered more appropriate.

A detailed description of the methodology applied is provided below.

### C.1 | INNER LOOP EXECUTION

#### C.1.1 | Adjustments and simulations on the occurrence data

##### C.1.1.1 | Allocation of active substances to occurrence data

While the organ assessment groups are defined at the level of the pesticide active substances, the occurrence data reported to EFSA refer to residue definitions for enforcement purposes (see Section A.1.4). Hence, the original occurrence data set obtained from the EFSA Data Warehouse is converted into a new intermediate data set where measurements are assigned to active substances instead of residue definitions. Some of these residue definitions, however, referred to as unspecific residue definitions, may be associated with multiple active substances.

To address this uncertainty, in accordance with the Tier II assumptions used in cumulative risk assessment of pesticides, each measurement for unspecific residue definitions is randomly assigned to one of the active substances authorised on that commodity, regardless of whether the active substance belongs to the group for the target organ being analysed or not. If none of the active substances associated with the unspecific residue definition is authorised for use on the commodity, any other active substance is selected at random. Furthermore, special consideration is given to the active substances that may metabolise into another active substance, referred to as non-exclusive substances. If the measurement is assigned to a non-exclusive substance, the model assumes that the measurement is partially composed of the assigned active substance while the remaining fraction is attributed to the exclusive active substance into which it is metabolised. Data on the proportions however were not readily available to EFSA. Therefore, a default proportion of 0.5 ( $\approx 50\%$ ) was assumed for all associations that are not exclusive (see Section A.1.3).

##### C.1.1.2 | Imputation of left-censored occurrence data

The imputation of left-censored occurrence data takes place after completion of the allocation of active substances to occurrence data. Over 97% of the occurrence data used for the current exposure assessment are left-censored (see Appendix A). Left-censored data are measurements reported below the LOQ and for which an accurate value is not available. Some of these results may be low positive residues while others will be true zeroes (no-residue situation). To address the uncertainties resulting from the high proportion of left-censored data, measurements below the LOQ were imputed in compliance with Tier II assumptions used in cumulative risk assessment of pesticides. Hence, use frequencies are estimated for each pesticide and each commodity, assuming that all samples were treated according to at least one agricultural use pattern (AUP). An AUP is one pesticide, or a combination of several pesticides applied to a single commodity or crop. Information about the exact AUPs occurring in practice is not available. The AUPs and their frequencies are therefore subject to an assumption, which relies on the observed combination of pesticides with measurable findings (i.e. above the LOQ) in the occurrences, affecting the target organ under consideration. The estimated use frequencies are then recalibrated to ensure that the total AUP frequency reaches 100% and the adjusted frequencies are used to calculate a proportion of true zeroes. The corresponding number of left-censored measurements is selected at random from the data set. While the selected measurements are imputed with zero, the remaining left-censored measurements are imputed with 1/2 LOQ. A more detailed description of the methodology is provided in Appendix C of EFSA (2022).

### C.1.1.3 | Imputation of missing occurrence data for acute exposure

The imputation of missing occurrence data is only performed for acute exposure assessment and executed after completion of the imputation of left-censored occurrence data.

In an acute combined exposure assessment, 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 (EFSA PPR Panel, 2012). Under the current assessment, the co-occurrence of chemicals within a single sample are accounted for because in the inner loop execution the model assigns to the amount of commodity consumed a random sample which includes measured concentrations for the different active substances (see Section C.1.2.2). The samples, however, were not necessarily analysed for every substance in the group of pesticides affecting the target organ. Measurements within a sample may therefore be missing for some substances. To avoid underestimation of the acute cumulative exposure, missing measurements are imputed according to the Tier II assumptions used in cumulative risk assessment of pesticides. For each substance/commodity combination, the number of missing values is counted, and the same number of measurements is randomly selected from the available data set. The missing values are then randomly replaced with the selected measurements. A more detailed description of the methodology is provided in Appendix D of EFSA (2022).

### C.1.1.4 | Imputation of occurrence data for water

Occurrence data for water are not available to EFSA (see Appendix A). In accordance with Tier II assumptions used in cumulative risk assessment of pesticides, occurrence data for water are imputed with a concentration of 0.00005 mg/kg (i.e. 0.05 µg/L) for the five most potent active substances within the group of pesticides affecting the target organ. Considering that non-approved substances are less likely to occur in drinking water, the five approved substances with the lowest HBGV are extracted from the list of active substances and a measurement of 0.00005 mg/kg in water is added to the occurrence data set for each of these substances. These measurements are associated with a single fictitious sample code.

### C.1.1.5 | Calculation of mean occurrence values for chronic exposure

Mean occurrence values are only calculated for chronic exposure assessment. Although individual residue measurements are required to enable bootstrapping and quantify the impact of sampling uncertainty, short-term variability of residues between samples is not relevant when modelling chronic exposure (EFSA PPR Panel, 2012). Chronic exposure is therefore estimated using the average concentration for each active substance and commodity. Hence, the occurrence data set obtained after imputation of the occurrence data for water (see Section C.1.1.4) is used to calculate the average concentrations per active substance and food commodity.

## C.1.2 | Exposure distributions

### C.1.2.1 | Chronic exposure distribution

Chronic dietary exposure is modelled by means of an empirical approach, referred to as the OIM approach (EFSA PPR Panel, 2012). This method uses the mean consumption over the survey days of each individual to estimate the individuals' long-term consumption. Using the individuals' bodyweight and the mean occurrence values obtained as described in Section C.1.1.5, the individuals' chronic exposures resulting from each food commodity and active substance are calculated. It should be noted, however that, due to the limited duration of the dietary surveys, the OIM approach tends to overestimate upper tail exposures in chronic assessments. Aiming to combine the different substances in a total chronic exposure estimate, the toxicological potency of each substance also needs to be taken into consideration. Considering that the toxicological potency is not yet known for all the different pesticides and target organ systems, it was decided to rely on the health-based guidance value (HBGV) of each pesticide active substance as a worst-case assumption. Since the HBGV relies on the most critical toxicological effect observed, which may be associated to one target organ system only, the use of the HBGV will overestimate the potency of the pesticide for all other target organ systems. Hence, the combined exposure for each individual was expressed as their hazard index (HI), which is the sum of the hazard quotients calculated for each substance (see also Section B.1.2.1).

Furthermore, when combining occurrence and consumption data, attention must be given to the possible effect of processing. Ideally, occurrence data should be available for the RPCD. Under such circumstances, the occurrence data can be combined directly with the amount of RPCD consumed. When occurrence data are only available for the RPC but a processing factor is available (see Section A.2.3), the processing factor will be integrated in the calculation to obtain an estimate of the substance's concentration in the RPCD. However, if occurrence data are only available for the RPC and a processing factor is not available, the occurrence value for the RPC will be combined with the corresponding amount of RPC consumed. The latter option implies that all residues present in the RPC will reach the end consumer, while alteration of residues is expected to occur when the RPCs are processed prior to consumption. This uncertainty is generally expected to overestimate exposure. As the consumed amounts are expressed in grams and occurrence data are expressed in mg/kg, a correction factor of 1000 needs to be considered. Based on the considerations above, the HI is calculated for each individual according to the following formula:



$$HI_i = \sum_c^{\text{commodities}} \sum_p^{\text{processes}} \sum_s^{\text{substances}} \left\{ \begin{array}{l} \frac{RPCD_{idcp} \cdot \bar{X}_{cps}}{BW_i \cdot Days_i \cdot HBGV_s \cdot 10^3}, \exists \bar{X}_{cps} \\ \frac{RPCD_{idcp} \cdot \bar{X}_{cs} \cdot PF_{cps}}{BW_i \cdot Days_i \cdot HBGV_s \cdot 10^3}, \nexists \bar{X}_{cps} \wedge \exists PF_{cps} \\ \frac{RPC_{idcp} \cdot \bar{X}_{cs}}{BW_i \cdot Days_i \cdot HBGV_s \cdot 10^3}, \nexists \bar{X}_{cps} \wedge \nexists PF_{cps} \end{array} \right. ,$$

where  $HI_i$  is the hazard index (HI) of individual  $i$ ;

$RPCD_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in  $g$  of raw primary commodity derivative (RPCD);

$RPC_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in  $g$  of raw primary commodity (RPC);

$\bar{X}_{cps}$  is the average concentration of substance  $s$  in commodity  $c$  with processing type  $p$ , expressed in  $mg/kg$ ;

$\bar{X}_{cs}$  is the average concentration of substance  $s$  in unprocessed commodity  $c$ , expressed in  $mg/kg$ ;

$PF_{cps}$  is the processing factor (PF) for substance  $s$  in commodity  $c$  with processing type  $p$ ;

$BW_i$  is the bodyweight (BW) of individual  $i$ , expressed in  $kg$ ;

$Days_i$  is the number of survey days of individual  $i$ ;

$HBGV_s$  is the health-based guidance value (HBGV) for substance  $s$ , expressed in  $mg/kg$  bodyweight per day.

After having calculated the HI for each individual, empirical distributions of individual HIs were obtained. The distributions represent the variability of exposure within the different population groups.

#### C.1.2.2 | Acute exposure distribution

Acute dietary exposure is modelled at the level of individual consumption days by means of an empirical Monte Carlo simulation (EFSA PPR Panel, 2012), where individual days are selected at random from the consumption data set. For each food commodity consumed within the individual days, random samples of the occurrence data set are assigned. The acute exposures resulting from each food commodity and active substance within each individual day are calculated using the individuals' body weights and the concentration of the different active substances measured in the different samples. The occurrence data used for the assessment, however, represent the average concentrations of composite laboratory samples (see Section A.1.4). Consumers, on the other hand, are exposed to individual units of the commodity. Residue concentrations may vary among the individual units, referred to as unit-to-unit variability. For RPCs having a unit weight below 25 g and for processed foods subject to blending or bulking, the unit-to-unit variability is not considered relevant (FAO, 2003). For the remaining food commodities, a fixed VF is usually applied for acute deterministic calculations while for probabilistic exposure assessment, a beta probability distribution is considered independent of the average concentration observed in the specific sample. Assuming an average concentration 1 in the composite sample, the concentration in a single unit can never be higher than the number of units within the composite sample (assuming all other units have a concentration of zero) and the beta distribution can be bounded between 0 as lower bound and the number of units per sample as upper bound. Furthermore, 97.5th percentile of the beta distribution is assumed to be equal to the VF. For the combined exposure assessment, in analogy to the Tier II assumption of the cumulative risk assessment of pesticides, a default VF of 3.6 was considered for all commodities with a unit weight exceeding 25 g.

Stochastic VFs can then be drawn from the beta distribution and multiplied with the composite sample concentration to obtain a plausible estimate of the unit concentration. When the portion consumed by an individual is smaller than a single unit, the stochastic VF is directly applicable to the consumed portion. When the consumed portion is composed of multiple units, however, multiple stochastic VFs will be drawn from the same beta distribution to estimate concentration in the whole portion consumed. Therefore, the concentration in the whole portion is estimated by multiplying the sample concentration with a weighted VF, which is calculated as:

$$WVF = SVF_n \text{ if } n = 1,$$

$$WVF = \frac{\sum_{i=1}^{n-1} SVF_i + SVF_n(n_0 - n + 1)}{n_0} \text{ if } n > 1,$$

where  $WVF$  is the weighted VF;

$SVF_i$  is the stochastic VF drawn for unit  $i$ ;

$n_0$  is the estimated number of units within the consumed portion (unrounded), assuming the unit weights reported in Appendix A;

$n$  is the number of stochastic VFs to be drawn (i.e. ceiling of  $n_0$ ).

Apart from the unit-to-unit variability, the exposure modelling also needs to account for the effect of processing prior to consumption and for the potency of the potency of the different substances. These two aspects are addressed like for the chronic exposure assessment (see Section C.1.2.1). Based on these considerations, the HI is calculated for each individual day according to the equations reported below.

$$HI_{id} = \sum_c^{commodities} \sum_p^{processes} \sum_s^{substances} \left\{ \begin{array}{l} \frac{RPCD_{idcp} \cdot X_{idcps}}{BW_i \cdot HBGV_s \cdot 10^3}, \exists X_{idcps} \\ \frac{RPCD_{idcp} \cdot X_{idcs} \cdot WVF_{idcps} \cdot PF_{cps}}{BW_i \cdot HBGV_s \cdot 10^3}, \nexists X_{idcps} \wedge \exists PF_{cps} \\ \frac{RPC_{idcp} \cdot X_{idcs} \cdot WVF_{idcps}}{BW_i \cdot HBGV_s \cdot 10^3}, \nexists X_{idcps} \wedge \nexists PF_{cps} \end{array} \right.$$

where  $HI_{id}$  is the hazard index (HI) of individual  $i$  on day  $d$ ;

$RPC_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in  $g$  of raw primary commodity (RPC);

$RPCD_{idcp}$  is the amount of commodity  $c$  with processing type  $p$  consumed by individual  $i$  on day  $d$ , expressed in  $g$  of raw primary commodity derivative (RPCD);

$BW_i$  is the body weight (BW) of individual  $i$ , expressed in kg;

$X_{idcps}$  is the average concentration of substance  $s$  in a sample of commodity  $c$  with processing type  $p$  that was randomly assigned to individual  $i$  on day  $d$ , expressed in mg/kg;

$X_{idcs}$  is the average concentration of substance  $s$  in a sample of unprocessed commodity  $c$  that was randomly assigned to individual  $i$  on day  $d$ , expressed in mg/kg;

$WVF_{idcps}$  is the weighted variability factor (WVF) that was randomly assigned to individual  $i$  on day  $d$  for substance  $s$  in commodity  $c$  with processing type  $p$ ;

$PF_{cps}$  is the processing factor (PF) for substance  $s$  in commodity  $c$  with processing type  $p$ ;

$HBGV_s$  is the health-based guidance value (HBGV) for substance  $s$ , expressed in mg/kg body weight.

The Monte Carlo simulation described above is executed 100,000 times, implying that, for each dietary survey, 100,000 individual days are randomly selected with replacement and HIs are calculated for each individual day. This results in empirical distributions of HIs, representing the variability of single day exposures within the different population groups. A more detailed description of the methodology used to estimate acute dietary exposure is provided in Appendix E of EFSA (2022).

## C.2 | Outer loop execution

The consumption data used for this assessment are subject to sampling uncertainty and will not perfectly represent the true diets within the population. Likewise, the occurrence data will not perfectly reflect the true distribution of residue concentrations in food. These sampling uncertainties are addressed by repeating the inner loop execution multiple times, each time replacing the consumption and occurrence data sets with bootstrap data sets (EFSA PPR Panel, 2012). Bootstrap data sets are obtained by resampling, with replacement, the same number of observations from the original data sets. Each time the inner loop is executed with bootstrap data sets, a bootstrap distribution of hazard indexes (HIs) is obtained. This shows how the distribution of HIs may have looked like if random sampling from the population would have generated different samples compared to the initial data set (Efron & Tibshirani, 1993).

It should be noted, however, that both the consumption and occurrence data incorporate several multivariate patterns (e.g. association of foods and individuals' characteristics, co-occurrence of residues, etc.). These patterns need to be preserved in the bootstrap data sets. Consumption data are, therefore, resampled at the individual day level by selecting all consumption events of the resampled individual day. Hence, for each dietary survey, the bootstrap data sets contain the same number of individual days as the initial data set. Occurrence data, on the other hand, are resampled at the level of the laboratory sample, that is, by selecting all measurements obtained in the resampled laboratory sample. Consequently, the bootstrap data sets contain for each food commodity the same number of laboratory samples as the initial data set.

In the current exposure model, the inner loop execution is repeated 100 times. The first execution, also referred to as *the nominal run*, is performed with the original data sets. The remaining executions are performed with bootstrap data sets. Although the outer loop execution is primarily intended to address the sampling uncertainty of the consumption and occurrence data, it also addresses uncertainty resulting from several simulations and imputations that rely on the random selection of measurements (see Sections C.1.1.1, C.1.1.2 and C.1.1.3).

### C.3 | Output preparation

Through the inner and outer loop executions, multiple HI distributions are generated (i.e. 100 bootstrap distributions per dietary survey). To describe each bootstrap distribution, the following parameters are derived:

- mean of the HI;
- standard deviation of the HI;
- percentiles of the HI (P2.5, P5, P10, P25, P50, P75, P90, P95, P97.5, P99, P99.9 and P99.99).

As a result, 100 estimates are obtained for each parameter of the HI distributions. These 100 estimates reflect the uncertainty distribution around the true value of those parameters. From these uncertainty distributions, a 95% confidence interval is calculated for each parameter. The median of the uncertainty distribution is selected as the central estimate for the confidence interval.

For chronic exposure assessment, to better understand the factors that influence the highest HIs, individuals with an HI higher than the HI calculated at the 99th percentile of the HI distribution are extracted for each dietary survey and all bootstrap distributions. The relevant information associated with those individuals is also retrieved (i.e. amounts of foods consumed and concentrations of active substances). Based on the individuals' information, average contributions are calculated per dietary survey, active substance and food commodity. For acute exposure assessment, a similar extraction is applied at the level of individual days. Due to limitations in terms of computational capacity, this extraction for acute assessment is limited to the nominal run only.

Additional information is gathered throughout the calculation process to support the identification of missing information. These intermediate outputs mainly refer to the food–substance combinations with limited occurrence data (possibly underestimating the HI) and the estimated use frequencies (see Section C.1.1.2).

The above-reported percentiles were calculated using SAS<sup>®</sup> software, which provides five validated options for the definition of percentiles.<sup>6</sup> In this assessment, the following percentile definition was selected:

Let  $n$  be the number of non-missing values for a variable, and let  $x_1, x_2, \dots, x_n$  represent the ordered values of the variable, and set  $p = t/100$ . Then, the  $t$ th percentile is calculated as

$$y = (1 - g)x_j + gx_{j+1},$$

where  $y$  is the  $t$ th percentile;

$np$  is the product of  $n$  and  $p$ ;

$j$  is the integer part of  $np$ ;

$g$  is the fractional part of  $np$ .

The percentile definition is not expected to have a substantial impact for the acute exposure estimates because 100,000 individual days are simulated for each exposure distribution. With such a high number of observations, calculated percentiles are expected to be stable regardless of the percentile definition used. For chronic exposure, on the other hand, this relationship was the most appropriate because it allows for the differentiation of percentiles, even when  $p > (n - 1)/n$ . This is particularly useful for the dietary surveys with toddlers and children where a 99.9th percentile needs to be calculated even though the number of individuals is lower than 1000. This method still contains an important bias because the calculated percentile will always be lower than, or equal to, the highest observation. For dietary surveys with a low number of individuals, it is not unlikely that the true percentile will be higher than the highest observation in the empirical distribution. However, estimation of percentiles beyond the highest observation would require parametric modelling of the exposure distribution which needs to be further investigated before being implemented in cumulative exposure assessment.

<sup>6</sup>[https://support.sas.com/documentation/cdl/en/proctat/66703/HTML/default/viewer.htm#procstat\\_univariate\\_details13.htm](https://support.sas.com/documentation/cdl/en/proctat/66703/HTML/default/viewer.htm#procstat_univariate_details13.htm)

## APPENDIX D

### Individual exposure assessment results for all pesticides

This section details the chronic and acute exposure to individual substances, distinguishing between substances for which (i) the HBGV is agreed at EU level (i.e. primary substances), and (ii) for which the HBGV is tentatively established based on best knowledge (i.e. tentative substances). The findings are summarised in plots showing, over population and substances, the range of the HQ estimates,<sup>7</sup> the minimum lower-bound values<sup>8</sup> and the maximum upper-bound values<sup>9</sup> across dietary surveys. For clarity of display and interpretation, the plots only show the substances for which the maximum upper-bound estimate exceeds 0.05 and the follow-up discussion focuses on those peculiar substances for which HQ exhibits large values. Considerations for the other substances can be derived from the results in Annexes B.

Generally, the HQ values are larger for 'tentative' substances than for 'primary' substances, reflecting the higher uncertainty introduced by the lack of specific HBGV for the former (easily seen by comparing the range of HQ of Figures D.1 and D.2, and that of Figure D.3 with Figure D.4). Another general comment relates to the skewness of the P99.9 distribution for most substances, where the median value is closer to the left tail of the distribution. This indicates that the distribution is unbalanced due to a limited number of consumer/commodity occurrences in some dietary surveys, as it is detailed in the discussion of the results for single substances. Similar reasoning applies to the maximum upper-bound values.

#### D.1 | CHRONIC

The full list of substances of this group, including those for which all the values for all populations are close to zero, are listed in the Annex B.1.

##### *Abamectin*

The HQ distribution for abamectin is markedly skewed across the three age groups. The minimum of the HQ estimates remains below 0.1 for adults, 0.15 for other children and 0.27 for toddlers, very close to their respective minimum lower bound, while the maximum of the HQ range estimates (maximum upper bound) are of 0.21 (0.43), 0.42 (0.59) and 0.67 (0.96) for adults, other children and toddlers, respectively. This might suggest that the maximum upper values are due to specific surveys and products, and possibly to high exposure of a specific consumer. For instance, for the adult population, the maximum upper bound HQ value is driven by a single Hungarian consumer who consumed 80 g of wheat's germ, which the model translates into over 4 kg of raw wheat. Similarly for the toddler's population, the maximum upper value is due to consumption of 30 g of wheat's germ by a Bulgarian toddler, corresponding to 1.5 kg of raw wheat. Since neither specific monitoring data and nor processing factors for wheat germ are available, it is assumed that the processed form (germs) conserves the same pesticide amount of the raw commodity (the wheat), which likely overestimates the exposure. Furthermore, the percentage of left-censored occurrence data is rather high for wheat and orange (two of the commodities mostly contributing to the exposure), with only ~2% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment, contributing to increased uncertainty.

##### *Carbofuran*

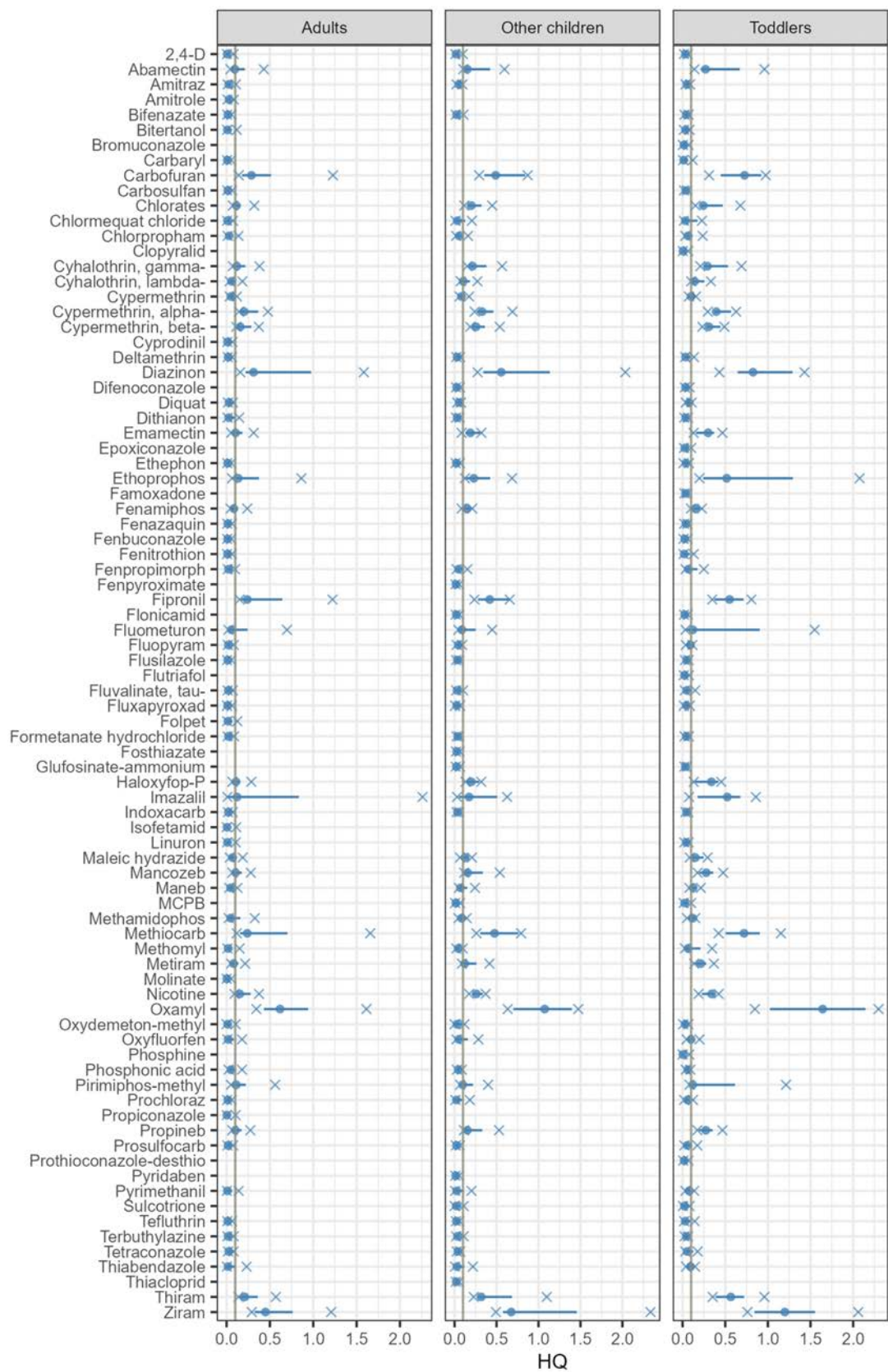
The top two commodities contributing to exposure for each population class are dried tomatoes and table grapes for adults, strawberry and processed tomatoes for other children, and grape juice and strawberry for toddlers. The median HQ estimates are 0.29 for adults, 0.49 for other children and of 0.73 for toddlers. The outlying value for adults (maximum upper bound of HQ equal to 1.23) is due to the consumption of 100 g of dried tomatoes by a consumer from Finland (equivalent to the consumption 2 kg of raw tomatoes). Due to the lack of specific monitoring data and processing factors, it is conservatively assumed that the residues present in the raw commodity (tomatoes) will concentrate in the processed commodity (dried tomatoes) without any decline of residues. This introduces a high uncertainty in the HQ estimate. A further source of uncertainty is introduced by the mode of imputation of left-censored occurrence data that, for tomatoes and grapefruit (two of the commodities mostly contributing to the exposure), has a quantification rate of ~3%. Carbofuran is also one of the substances for which the residue definition is not univocally specified, possibly contributing to enhance the overall uncertainty, as highlighted in Section 3.1.1. In this specific case, however, none of the four active substances associated to this residue definition are approved. In such a case, it is likely that the imputation of left-censored data introduces a more significant overestimation of the exposure, as probably a large proportion of the measurements were true zeros (no-residue situation).

<sup>7</sup>The range of HQ estimates refers to the range of median value of the confidence intervals calculated at the P99.9 of the HQ distributions across dietary surveys.

<sup>8</sup>The minimum lower-bound values refer to the lowest lower-bound estimate of the confidence intervals calculated at the P99.9 of the HQ distributions across dietary surveys.

<sup>9</sup>The maximum upper-bound values refer to the highest upper-bound estimate of the confidence intervals calculated at the P99.9 of the HQ distributions across dietary surveys.





**FIGURE D.1** Summary of chronic probabilistic exposure results for primary substances that have an EU-agreed HBGV. The lines represent the range of median value of the confidence intervals calculated at the P99.9 of the HQ distributions across dietary surveys, the dots represent the median of the range (for ease and clarity of display, the graph shows only the substances for which the maximum upper bound HQ value for at least one population is larger than 0.05). The 'x' indicates the minimum lower and maximum upper estimates of the P99.9 exposure distribution. The continuous vertical line at HQ = 0.1 identifies the exposure threshold for prioritisation.

### *Diazinon*

The range of HQ estimates for diazinon exhibits a skewed pattern (more markedly for adults) with the median HQ estimates remaining below 0.22, 0.34 and 0.65 for adults, other children and toddlers, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.97 (1.58), 1.13 (2.04) and 1.29 (1.43) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are apples and orange juice for adults, mandarins' juice and processed (cooked) apples for other children, and again mandarins' juice for toddlers. The HQ value of 2.04 for other children is due to a large consumption of mandarin juice in Belgium (460 g, corresponding to over 1 kg of mandarins), whereas the HQ of 1.58 for adults is due to the consumption of ~620 g of orange juice concentrate in Finland which, in absence of processing factors or specific monitoring data, corresponds to the consumption of over 6 kg of oranges. Furthermore, the percentage of left-censored occurrence data is high for apples and oranges (two of the commodities mostly contributing to the exposure), with less than 4% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Ethoprophos*

The HQ distribution for ethoprophos is markedly skewed for adults and other children, and less for toddlers. The range of HQ estimates remains below 0.08 for adults, 0.14 for other children and 0.24 for toddlers, very close to their respective minimum lower bound (0.06, 0.12 and 0.2, respectively). The maximum of the HQ range estimates (maximum upper bound) are of 0.37 (0.86), 0.42 (0.68) and 1.3 (2.1) for adults, other children and toddlers, respectively. This might suggest that the maximum upper values reflect specific surveys and products, and possibly the high exposure of a specific consumer. For instance, for the adult population, the maximum upper bound exposure is due to a Hungarian consumer who consumed ~83 g of wheat's germ that translate into over 4 kg of raw wheat due to the absence of detail monitoring data and of processing factors. Similarly for the toddler's population, the maximum upper HQ value is due to consumption of 30 g of wheat's germ by a Bulgarian toddler that are converted to 1.5 kg of raw wheat. Since neither specific monitoring data and nor processing factors for wheat germ are available, it is assumed that the processed form (germs) conserves the same pesticide amount of the raw commodity (the wheat), which likely overestimates the exposure. The percentage of left-censored occurrence data is rather high for oranges and wheat (two of the commodities mostly contributing to the exposure), with only 1% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Fipronil*

The HQ distribution for fipronil is noticeably skewed for adult population, while it is centred for other children and toddlers. The range of HQ estimates remains below 0.17 for adults, 0.28 for other children and 0.37 for toddlers, while their respective minimum lower bounds are of 0.15, 0.24 and 0.81, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.64 (1.22), 0.65 (0.66) and 0.71 (0.81) for adults, other children and toddlers, respectively. For adults, the maximum upper values reflect specific surveys and products, and possibly the high exposure of a specific consumer. Indeed, it is driven by the consumption of ~620 g of orange juice concentrate, which are equivalent to the consumption of over 6.2 kg of oranges, by a Finnish consumer. The top two commodities contributing to exposure for other children are bananas and potatoes, potato and oranges for toddlers. The percentage of left-censored occurrence data is rather high for oranges and tomatoes (two of the commodities mostly contributing to the exposure), with only 3.5% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Fluometuron*

The HQ distribution for fluometuron is markedly skewed across the three age groups. The range of HQ estimates remains below 0.027 for adults, 0.063 for other children and 0.041 for toddlers, very close to their respective minimum lower bound (0.021, 0.045 and 0.033, respectively). The maximum of the HQ range estimates (maximum upper bound) are of 0.24 (0.70), 0.25 (0.45) and 0.90 (1.55) for adults, other children and toddlers, respectively. This might suggest that the maximum upper values are due to specific surveys and products, and possibly to high exposure of a specific consumer. For instance, for the adult population, the maximum upper bound HQ value is driven by a single Hungarian consumer who consumed ~80 g of wheat's germ, which the model translates into over 4 kg of raw wheat. For the other children's population, the maximum upper value is due to consumption of 8 g of wheat's germ by a Belgian consumer, corresponding to 0.4 kg of raw wheat, and similarly for toddlers, the maximum upper value is due to a Bulgarian toddler consuming 30 g of wheat's germ, corresponding to 1.5 kg of raw wheat. Since neither specific monitoring data and nor processing factors for wheat germ are available, it is assumed that the processed form (germs) conserves the same pesticide amount of the raw commodity (wheat), which introduces a large uncertainty and likely overestimates the exposure. The percentage of left-censored occurrence data is rather high wheat, with only 1.09% quantification rate, indicating that the assumption of imputing left-censored data (see Section C.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Imazalil*

The HQ distribution for imazalil is noticeably skewed towards the left tail for adult and other children's populations, while it is slightly skewed towards the right tail for toddlers. The range of HQ estimates is below 0.017 for adults, 0.053 for other children and 0.18 for toddlers, while their respective minimum lower bounds are of 0.01, 0.029 and 0.076, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.83 (2.26), 0.51 (0.63) and 0.68 (0.76) for adults, other children and toddlers, respectively. For adults, the maximum upper value is among the highest found for primary substances and is driven by the consumption of orange juice concentrate by a Finnish consumer (~620 g of orange juice, which is equivalent to the consumption of over 6.2 kg of oranges). The top two commodities mostly contributing to exposure across the three population classes are orange and grapefruit juice.

### *Methiocarb*

The HQ distribution for methiocarb is noticeably skewed for adult population, while it is centred for other children and toddlers. The range of HQ estimates is below 0.15 for adults, 0.31 for other children and 0.50 for toddlers, while their respective minimum lower bounds are of 0.12, 0.26 and 0.42, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.70 (1.66), 0.76 (0.79) and 0.91 (1.15) for adults, other children and toddlers, respectively. For adults, the maximum upper values reflect specific surveys and products, and possibly the high exposure of a specific consumer. Indeed, it is driven by the consumption of ~620 g of orange juice concentrate, which are equivalent to the consumption of over 6.2 kg of oranges, by a Finnish consumer. The maximum upper value for toddlers is driven by the consumption of ~620 g of peaches by a Bulgarian toddler. The top two commodities contributing to exposure for other children are peach juice and table grape juice, while for toddlers are table grape juice and pears. Furthermore, the percentage of left-censored occurrence data is rather high for peach, oranges and table grape (three of the commodities mostly contributing to the exposure), with only 2% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Oxamyl*

All three population groups show high exposure to oxamyl, more markedly toddlers. The top two commodities contributing to exposure for each population class are tomatoes and potatoes for adults, potatoes and cucumbers for other children, and carrots and potatoes for toddlers. The median HQ estimates are 0.61 for adults, 1.07 for other children and 1.64 for toddlers. The maximum upper bound of HQ for adults (1.61) is due to the consumption of 100 g of dried tomatoes by a consumer from Finland (equivalent to 2 kg of raw tomatoes). Due to the lack of specific monitoring data and processing factors, it is conservatively assumed that the residues present in the raw commodity (tomatoes) will concentrate in the processed commodity (dried tomatoes) without any decline of residues. This introduces a high uncertainty in the HQ estimate.

### *Pirimiphos-methyl*

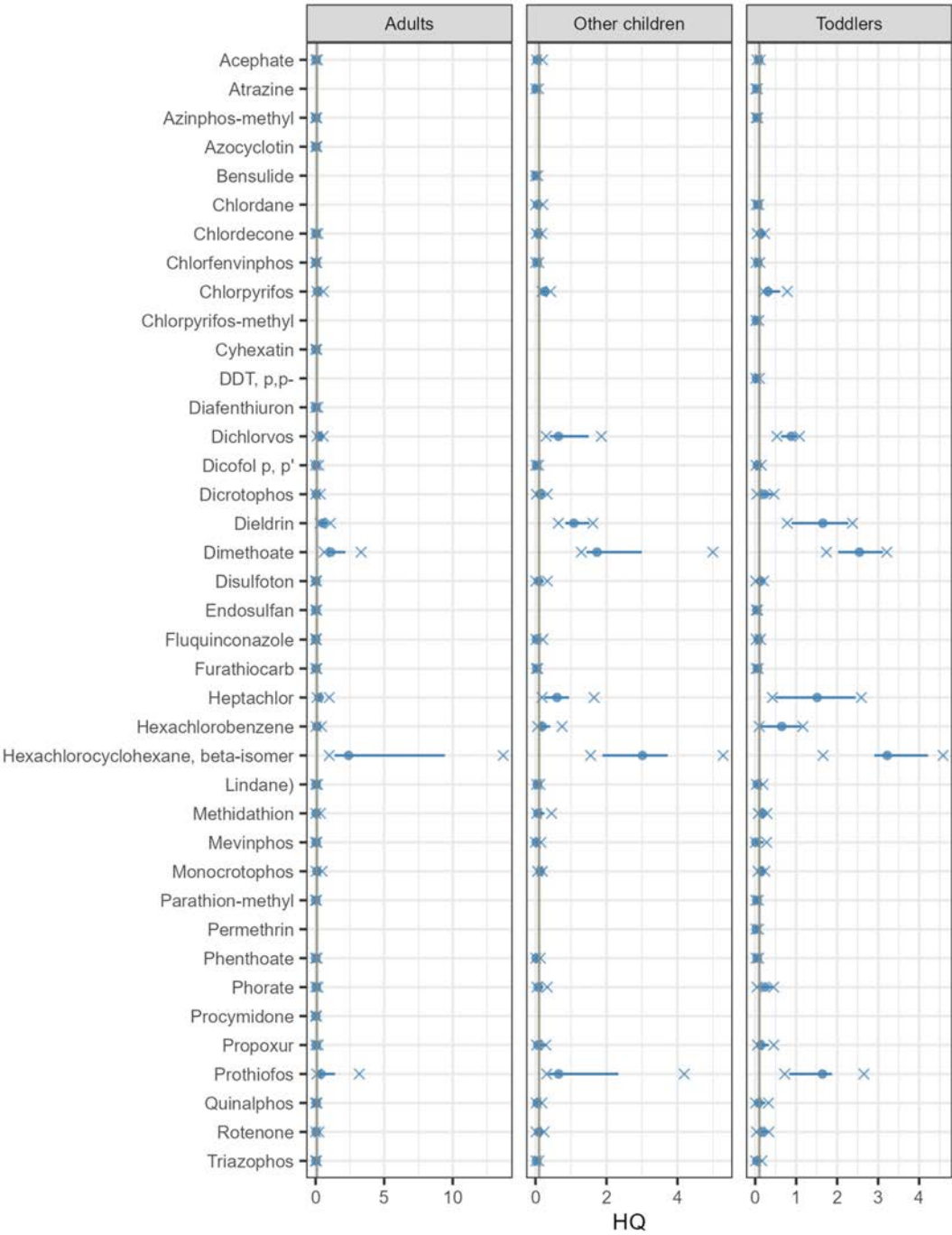
The HQ distribution for pirimiphos-methyl is markedly skewed across the three age groups. The median HQ estimates remains below 0.07 for adults, 0.089 for other children and 0.092 for toddlers, very close to their respective minimum lower bounds (0.050, 0.066 and 0.081, respectively). The maximum of the HQ range estimates (maximum upper bound) are of 0.22 (0.56), 0.22 (0.40) and 0.61 (1.21) for adults, other children and toddlers, respectively. This might suggest that the maximum upper values are due to specific surveys and products, and possibly to high exposure of a specific consumer. For instance, for the adult population, the maximum upper bound HQ value is driven by a single Hungarian consumer who consumed ~83 g of wheat's germ, which the model translates into over 4 kg of raw wheat. Similarly for the toddler's population, the maximum upper value is due to consumption of 30 g of wheat's germ by a Bulgarian toddler, corresponding to 1.5 kg of raw wheat. Since neither specific monitoring data and nor processing factors for wheat germ are available, it is assumed that the processed form (germs) conserves the same pesticide amount of the raw commodity (the wheat), which likely overestimates the exposure.

### *Ziram*

The HQ distribution for ziram is skewed for adult and other children populations, and more centred for toddlers. The range of HQ estimates remain below 0.32 for adults, 0.57 for other children and 0.84 for toddlers, while their respective minimum lower bounds are of 0.29, 0.49 and 0.76, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.76 (1.21), 1.46 (2.34) and 1.55 (2.06) for adults, other children and toddlers, respectively. The maximum upper values reflect specific surveys and products, and possibly the high exposure of a specific consumer. For adults, it is due to the consumption of orange juice by a Finnish adult (622 g of juice equivalent to the consumption of 6.2 kg of raw oranges). For other children the maximum upper bound of HQ is driven by the consumption of 460 g of mandarin juice by a Belgian child (equivalent to over 1 kg of raw mandarins). Similarly, for toddler the value is due to the consumption of 30 g of wheat germ (equivalent to the consumption of 1.5 kg of raw wheat). Since neither specific monitoring data and nor processing factors for these commodities are available, it is assumed that the processed form (juice, germs) conserves the same pesticide amount of the raw commodity, which likely



overestimates the exposure. Ziram is also one of the substances for which the residue definition is not univocally specified, possibly contributing to enhance the overall uncertainty, as highlighted in Section 3.1.1. In this specific case, only two (metiram and ziram) of the six active substances associated to this residue definition are approved. It is correct that the HQ of ziram is higher than that of other residues of the same group of dithiocarbamates which are not approved (e.g. thiram), as likely most of the positive findings of the dithiocarbamates groups are relative to the two approved substances. However, part of these residues are possibly attributed to the other approved substance metiram, and the true HQ for ziram is likely lower than the one estimated.



**FIGURE D.2** Summary of chronic probabilistic exposure results for substances for which the HBGV is tentatively established based on current knowledge. The lines represent the range of median value of the confidence intervals calculated at the P99.9 of the HQ distributions across dietary surveys, the dots represent the median of the range (for ease and clarity of display, the graph shows only the substances for which the maximum upper bound HQ value for at least one population is larger than 0.05). The 'x' indicates the minimum lower and maximum upper estimates of the P99.9 exposure distribution. The continuous vertical line at HQ = 0.1 identifies the exposure threshold for prioritisation.

The full list of substances of this group, including those for which all the values for all populations are close to zero, are listed in the Annex B2.



### *Chlorpyrifos*

The HQ distribution of chlorpyrifos for toddlers is skewed and exhibits a maximum upper bound of 0.78, compared to a median value of 0.31. The maximum upper values reflect specific surveys and product and is due to the consumption of 30 g of wheat germ (equivalent to 1.5 kg of raw wheat) by a Bulgarian toddler. Other commodities most contributing to exposure in the toddler population group are orange and grapefruit juices. Since neither specific monitoring data and nor processing factors for these commodities are available for the selected surveys, it is assumed that the processed form (juice, germs) conserves the same pesticide amount of the raw commodity, which likely overestimates the exposure. Furthermore, the percentage of left-censored occurrence data is rather high for wheat with only 1.4% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Dichlorvos*

The minimum HQ estimates for dichlorvos is below 0.13 for adults, 0.40 for other children and 0.63 for toddlers, while their respective minimum lower bounds are of 0.10, 0.30 and 0.53, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.53 (0.55), 1.50 (1.85) and 1.03 (1.08) for adults, other children and toddlers, respectively. The HQ distribution is thus markedly skewed for other children. The top commodities contributing to exposure in this population group are strawberries and cucumbers, the maximum upper bound is due to the consumption of these two commodities by a Bulgarian consumer. For toddlers, the top commodities contributing to exposure are again strawberries and cucumbers, followed by rice. Furthermore, the percentage of left-censored occurrence data is rather high for cucumbers and strawberries with 7.9% and 1.05% quantification rate, respectively, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Dieldrin*

The minimum HQ estimates for dieldrin is below 0.39 for adults, 0.84 for other children and 0.89 for toddlers, while their respective minimum lower bounds are of 0.33, 0.64 and 0.78, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.92 (1.08), 1.52 (1.62) and 2.27 (2.38) for adults, other children and toddlers, respectively. The top commodities contributing to exposure for other children and toddlers are carrots (juice), peaches (raw and juice) and potatoes, for which the quantification rate is of 5.3%, 3.5% and 3.7% for peaches, potatoes and carrots, respectively, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Dimethoate*

The minimum HQ estimates for dimethoate is below 0.84 for adults, 1.44 for other children and 2.02 for toddlers, while their respective minimum lower bounds are of 0.63, 1.29 and 1.74, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 2.18 (3.32), 3.0 (5.0) and 3.12 (3.21) for adults, other children and toddlers, respectively. The HQ distribution is thus highly skewed for other children and, less prominently, also for adult population. Commodities highest contribution to exposure in the three age classes are: processed forms of oranges, potatoes, wine grapes, apples for adults, mandarin and peach juices for other children, and peaches, carrots, mandarin and grapefruit juices for toddlers. The maximum upper HQ values is driven by the consumption of an average amount of 461 g of mandarin juice by other children from Belgium, corresponding to over 1 kg of mandarins, while for adults it is due to the consumption by a Finnish consumer of an average amount of 620 g of orange juice concentrate (corresponding to over 6 kg of oranges). Since neither specific monitoring data nor processing factors for orange juice concentrate and mandarin juice are available, it is assumed that the processed form (juice) conserves the same pesticide amount of the raw commodity (orange/mandarin), which likely overestimates the exposure. Furthermore, the percentage of left-censored occurrence data is rather high for orange, mandarins and apples (three of the commodities mostly contributing to exposure), with a quantification rate of about 1.6%, 0.6% and 2.1% respectively, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment, contributing to increase its uncertainty.

### *Heptachlor*

The minimum HQ estimates for heptachlor is below 0.16 for adults, 0.25 for other children and 0.49 for toddlers, while their respective minimum lower bounds are of 0.10, 0.18 and 0.42, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.47 (1.0), 0.95 (1.65) and 2.4 (2.6) for adults, other children and toddlers, respectively. Commodities most contributing to exposure in the three age classes are carrots (raw and juice) and cucumbers. The maximum upper HQ values for other children is detected in the Finnish population and is due to the consumption of 475 g of cucumbers. Furthermore, the percentage of left-censored occurrence data is rather high for carrots and cucumbers, (two commodities mostly contributing to the exposure), with a quantification rate of about 2.6% and 7.9%, respectively, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment, contributing to increase its uncertainty.

### Hexachlorobenzene

The minimum HQ estimates for hexachlorobenzene is of 0.053 for adults, 0.093 for other children and 0.12 for toddlers, while their respective minimum lower bounds are of 0.036, 0.059 and 0.098, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.19 (0.43), 0.41 (0.74) and 1.12 (1.16) for adults, other children and toddlers, respectively. The only commodity with measurable findings of this substance is carrot (processed and unprocessed) across all surveys. The percentage of left-censored occurrence data is rather high for carrots, with only 2.9% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### Hexachlorocyclohexane (beta isomer)

The minimum HQ estimates for hexachlorocyclohexane (beta isomer) is of 1.4 for adults, 1.9 for other children and 2.9 for toddlers, while their respective minimum lower bounds are of 1.0, 1.5 and 1.7, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 9.4 (13.7), 3.7 (5.3) and 4.2 (4.6) for adults, other children and toddlers, respectively. The maximum upper HQ values are the highest among all substances analysed, for all age groups. For adults, the maximum upper HQ value is due to the consumption of 4.6 kg of apple cider, which correspond to over 6.6 kg of raw apples by an Irish adult. For other children, the maximum corresponds to a German consumer of an average amount of apples of over 450 g. The maximum upper HQ values for toddlers is recorded in the Netherlands due to the equivalent consumption of 230 g of apples (raw and juice combined). In general, the high exposure for adults is driven by the consumption of apples, raw and cider. Furthermore, the percentage of left-censored occurrence data is rather high for apples, with a quantification rate of 6%, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment, contributing to increase its uncertainty.

### Prothiofos

The minimum HQ estimates for prothiofos is of 0.19 for adults, 0.36 for other children and 0.83 for toddlers, while their respective minimum lower bounds are of 0.090, 0.32 and 0.72, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 1.42 (3.19), 2.33 (4.19) and 1.87 (2.65) for adults, other children and toddlers, respectively. Commodities with highest contribution to exposure are grapefruit and oranges (adults), mandarin juice (other children and toddlers). The maximum upper HQ value for adults is found in Finland (orange juice concentrate), for other children in Belgium (mandarin juice), and for toddler in Finland (mandarin juice). Since neither specific monitoring data and nor processing factors for orange juice concentrate and mandarin juice are available, it is assumed that the processed form (juice) conserves the same pesticide amount of the raw commodity (orange/mandarin), which likely overestimates the exposure. Furthermore, the percentage of left-censored occurrence data is rather high for orange and mandarins, with a quantification rate of only 1.26% and 1.02%, respectively, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment, contributing to increase its uncertainty.

## D.2 | ACUTE

The full list of substances of this group, including those for which all the values for all populations are close to zero, are listed in the Annex B.3.

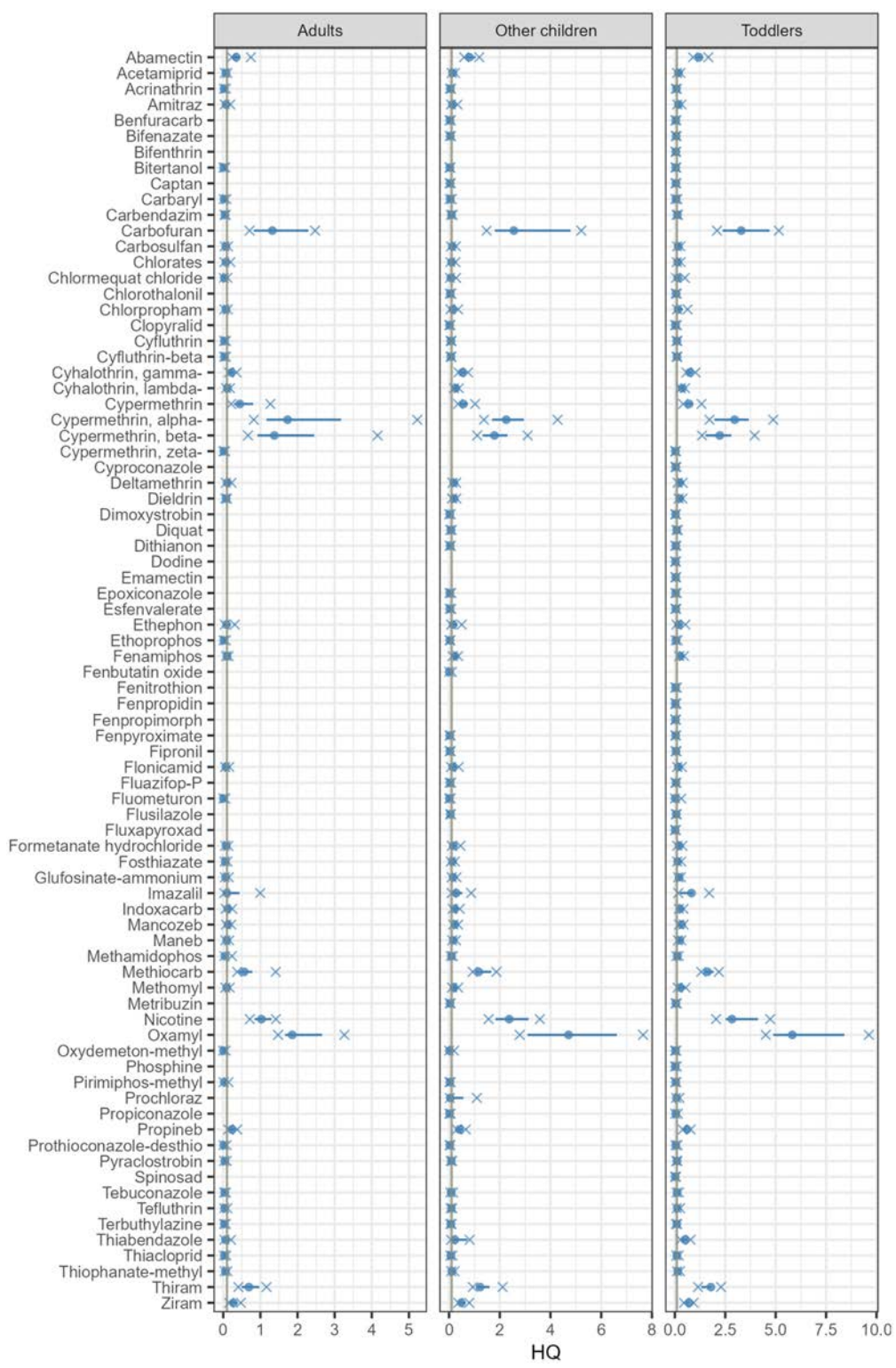
### Abamectin

The minimum of the HQ estimates for abamectin is below 0.25 for adults, 0.65 for other children and 1.03 for toddlers, while their respective minimum lower bounds are of 0.24, 0.59 and 0.90, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.45 (0.74), 1.05 (1.19) and 1.34 (1.66) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are tomatoes and orange for adults, mandarins' juice and bananas for other children, and bananas and pears for toddlers. The maximum upper bound HQ for adults is mainly driven by the consumption of 250 g of wheat germ (which, in absence of processing factors or specific monitoring data is equivalent to 12.5 kg of wheat) by a Hungarian consumer. Furthermore, the percentage of left-censored occurrence data is high for wheat and mandarins (two of the commodities mostly contributing to the exposure), with less than 1.7% and 1.2% quantification rate, respectively, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### Carbofuran

The minimum of the HQ estimates for carbofuran is below 0.82 for adults, 1.81 for other children and 2.37 for toddlers, while their respective minimum lower bounds are of 0.71, 1.48 and 2.09, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 2.29 (2.47), 4.79 (5.21) and 4.70 (5.16) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are tomatoes for all the age groups and, to a lesser extent, table grapes (juice and raw). The consumption of this latter is the responsible for the maximum upper bound HQ for adults and other children, while for toddlers is the consumptions of tomatoes. The quantification rate for these two commodities is of 3.4% and 2.7% and the assumption

of imputing missing occurrence data to half of the LOQ value (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty. As per the chronic case described in Section D.1, carbofuran is one of the substances for which the residue definition is not univocally specified, possibly contributing to enhance the overall uncertainty, as highlighted in Section 3.1.1. In this specific case, however, none of the four active substances associated to this residue definition are approved. In such a case, it is likely that the imputation of left-censored data introduces a more significant overestimation of the exposure, as probably a large proportion of the measurements were true zeros (no-residue situation).



**FIGURE D.3** Summary of acute probabilistic exposure results for primary substances that have an EU-agreed HBGV. The lines represent the range of median value of the confidence intervals calculated at the P99.9 of the HQ distributions across dietary surveys, the dots represent the median of the range (for ease and clarity of display, the graph shows only the substances for which the maximum upper bound HQ value for at least one population is larger than 0.05). The 'x' indicates the minimum lower and maximum upper estimates of the P99.9 exposure distribution. The continuous vertical line at HQ = 0.1 identifies the exposure threshold for prioritisation.

### *Cypermethrin*

The minimum of the HQ estimates for cypermethrin is below 0.29 for adults, 0.42 for other children and 0.50 for toddlers, while their respective minimum lower bounds are of 0.21, 0.36 and 0.41, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 0.81 (1.27), 0.74 (1.03) and 0.91 (1.32) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are tomatoes and malted barley, apples and potatoes for adults, and potatoes and wheat (processed as semolina and flour) for other children and toddlers, for which no processing factors nor observations are available. Furthermore, cypermethrin is one of the substances for which the residue definition is not univocally specified, possibly contributing to enhance the overall uncertainty, as highlighted in Section 3.1.1. In this specific case, however, only cypermethrin is approved of the four active substances associated to this residue definition. This uncertainty is therefore expected to have a limited impact on the assessment of cypermethrin.

### *Cypermethrin, Alpha*

The minimum of the HQ estimates for alpha-cypermethrin is of 1.17 for adults, 1.70 for other children and 1.97 for toddlers, while their respective minimum lower bounds are of 0.82, 1.38 and 1.72, respectively. The maximum of the HQ range estimates (maximum upper bound) are of 3.17 (5.22), 2.95 (4.28) and 3.66 (4.88) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are tomatoes and malted barley and processed wheat for adults, and potatoes and wheat (processed as semolina and flour) for other children and toddlers, for which no processing factors nor observations are available. The maximum upper bound value of HQ for adults is due to the consumption of malted barley in the Czech Republic (~540 g, corresponding to ~740 g of raw barley). Cypermethrin-alpha is one of the substances for which the residue definition is not univocally specified, possibly contributing to enhance the overall uncertainty, as highlighted in Section 3.1.1. Of the four active substances associated to this residue definition, only cypermethrin is approved (discussed previously). Nonetheless, the HQ of cypermethrin-alpha is markedly larger than that of cypermethrin across the three age groups (Figure C.3). The assessment in this case is therefore expected to significantly overestimate the exposure.

### *Cypermethrin, Beta*

The minimum of the HQ estimates for beta-cypermethrin is below 0.92 for adults, 1.32 for other children and 1.52 for toddlers, while their respective minimum lower bounds are of 0.67, 1.11 and 1.34, respectively. The medians of the HQ range estimate are of 1.73, 2.25 and 2.97. The maximum of the HQ range estimates (maximum upper bound) are of 2.45 (4.15), 2.31 (3.10) and 2.80 (3.96) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are tomatoes and malted barley and processed wheat for adults, and potatoes and wheat (processed as semolina and flour) for other children and toddlers, for which no processing factors nor observations are available. As for the case of cypermethrin-alpha discussed above, also cypermethrin-beta is one of the substances for which the residue definition is not univocally specified, possibly contributing to enhance the overall uncertainty, as highlighted in Section 3.1.1. Of the four active substances associated to this residue definition, only cypermethrin is approved. Nonetheless, the HQ of cypermethrin-beta is markedly larger than that of cypermethrin across the three age groups (Figure C3). The assessment in this case is therefore expected to significantly overestimate the exposure.

### *Methiocarb*

The minimum of the HQ estimates for methiocarb is below 0.41 for adults, 1.04 for other children and 1.46 for toddlers, while their respective minimum lower bounds are of 0.37, 0.93 and 1.31, respectively. The medians of the HQ range estimate (0.56, 1.17, 1.62) are very close to their respective minimum of the range, indicating skewed distributions. The maximum of the HQ range estimates (maximum upper bound) are of 0.78 (1.41), 1.67 (1.87) and 1.92 (2.18) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are oranges and pears for adults and for other children, pears and peaches for toddlers. The maximum upper bound value for adult is due to the consumption of orange juice concentrate by a consumer from Finland (no processing factor, nor monitoring data available). For oranges, the percentage of left-censored occurrence data is high with less than 1.6% quantification rate, pointing out that the assumption of imputing left-censored data (see Section B.1.1.2) has a high impact on the exposure assessment and increases its uncertainty.

### *Nicotine*

The minimum of the HQ estimates for nicotine is below 0.84 for adults, 1.83 for other children and 2.52 for toddlers, while their respective minimum lower bounds are of 0.72, 1.56 and 2.05, respectively. The medians of the HQ range estimate are 1.03, 2.37 and 2.83 for the three age classes, which is positioned towards the minimum of the range for toddlers, indicating a skewed distribution. The maximum of the HQ range estimates (maximum upper bound) are of 1.30 (1.42), 1.83 (3.58) and 2.52 (4.73) for adults, other children and toddlers, respectively. The commodity most contributing to exposure is potato across the three age groups, followed by tomatoes and pears. The skewed distribution of HQ for toddlers is due the large consumption of potatoes by Finnish toddlers, who recorded a percentage of ARfD per day and subject exceeding 400%



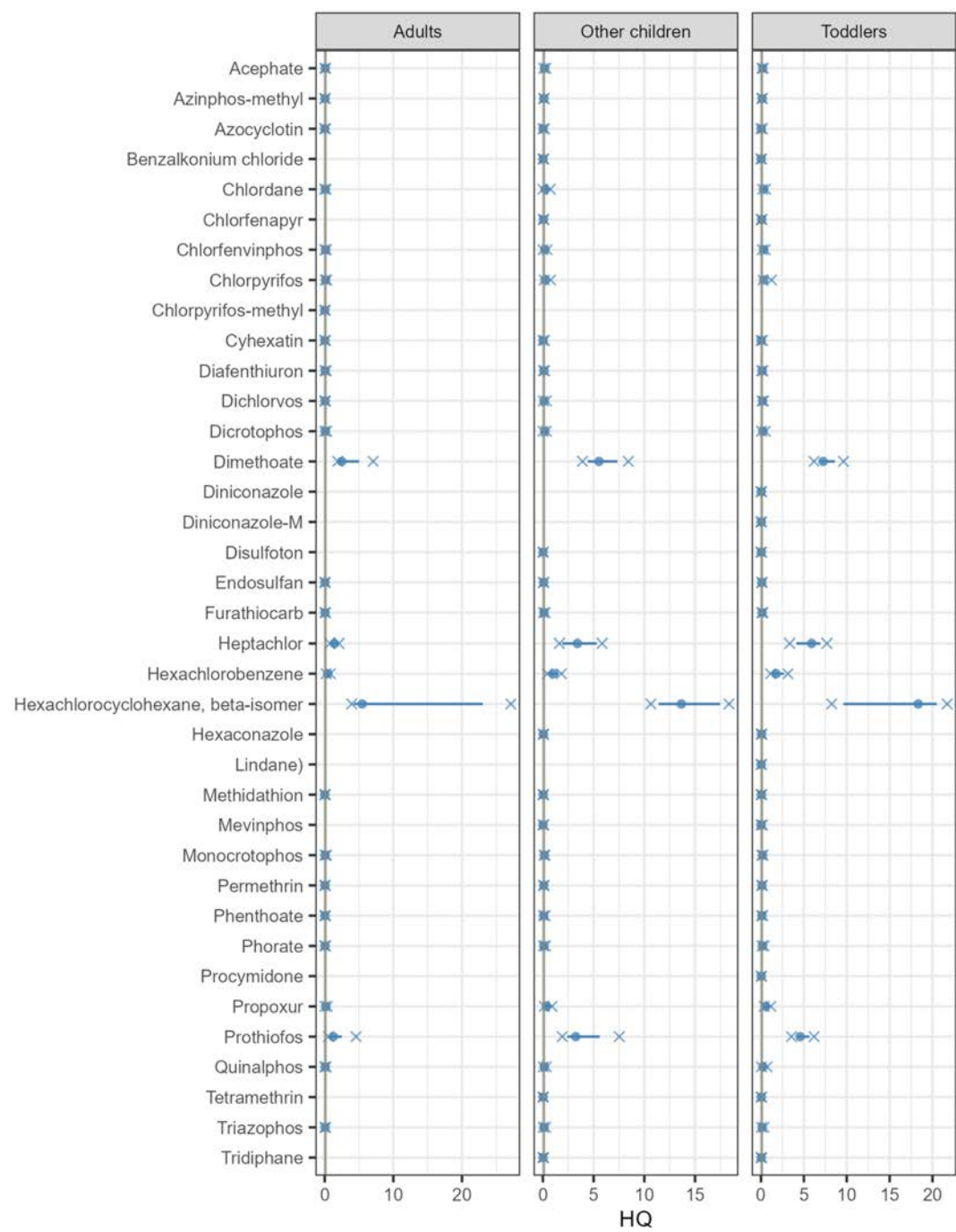
(amount consumed between 61 g and 233 g). Furthermore, the percentage of left-censored occurrence data is rather high for potatoes, with only 0.25% quantification rate, indicating that the assumption of imputing left-censored data (see Section B.1.1.2) has high impact on the exposure assessment and increases its uncertainty.

### *Oxamyl*

The minimum of the HQ estimates for oxamyl is below 1.66 for adults, 3.09 for other children and 4.88 for toddlers, while their respective minimum lower bounds are of 1.48, 2.79 and 4.51, respectively. The medians of the HQ range estimate are 1.85, 4.71 and 5.82 for the three age classes, which for adults is positioned towards the minimum of the range, indicating a skewed distribution. The maximum of the HQ range estimates (maximum upper bound) are of 2.66 (3.26), 6.62 (7.65) and 8.41 (9.62) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are potatoes across the three age groups, followed by beans (with pods) and cucumbers. The maximum upper bound for adult is recorded in Romania due to consumption of sweet pepper (sample with high concentration of 0.2 mg/kg) and potatoes. For potatoes, the exposure is significantly driven by samples with concentration sets at the limit of quantification due to the low quantifiable measurements of this commodity (3.14%).

### *Thiram*

The minimum of the HQ estimates for thiram is below 0.49 for adults, 1.07 for other children and 1.31 for toddlers, while their respective minimum lower bounds are of 0.41, 0.94 and 1.15, respectively. The medians of the HQ range estimate are 0.69, 1.22 and 1.78 for the three age classes, which for other children is positioned towards the minimum of the range, indicating a skewed distribution. The maximum of the HQ range estimates (maximum upper bound) are of 0.97 (1.16), 1.60 (2.11) and 1.81 (2.29) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are head cabbage, pears and lettuce for adults and for other children, and head cabbage and pears for toddlers. The skewed distribution for other children is due to Belgian consumers of fruits (apples, pears) in excess of 170% of the ARfD per day and subject. For pears, a sample with high concentration (5.056 mg/kg) has a contribution to the exposure of 97.2% and 99.6% in two surveys (other children, the Czech Republic and Belgium). Thiram is also one of the substances for which the residue definition is not univocally specified, possibly contributing to enhance the overall uncertainty, as highlighted in Section 3.1.1. In this specific case, however, only two (metiram and ziram) of the six active substances associated to this residue definition are approved. Nonetheless, the HQ of thiram is higher than that of ziram, suggesting that the assessment in this case is very likely to overestimate the exposure, indicating that more realistic assumptions should be explored for future assessments.



**FIGURE D.4** Summary of acute probabilistic exposure results for substances for which the HBGV is tentatively established based on current knowledge. The lines represent the range of median value of the confidence intervals calculated at the P99.9 of the HQ distributions across dietary surveys, the dots represent the median of the range (for ease and clarity of display, the graph shows only the substances for which the maximum upper bound HQ value for at least one population is larger than 0.05). The 'x' indicates the minimum lower and maximum upper estimates of the P99.9 exposure distribution. The continuous vertical line at HQ=0.1 identifies the exposure threshold for prioritisation.

The full list of substances of this group, including those for which all the values for all populations are close to zero, are listed in the Annex B4.

*Dimethoate*

The minimum of the HQ estimates for dimethoate is below 1.98 for adults, 4.41 for other children and 6.79 for toddlers, while their respective minimum lower bounds are of 1.90, 3.90 and 6.18, respectively. The medians of the HQ range estimate are 2.47, 5.53 and 7.25 for the three age classes, which for adults is positioned towards the minimum of the range, indicating a skewed distribution. The maximum of the HQ range estimates (maximum upper bound) are of 5.03 (7.07), 7.36 (8.42) and 8.62 (9.63) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are apples for winemaking and potatoes for adults, and for other children, potatoes and apples for other children and toddlers. The maximum upper bound value for adult is recorded in the Finnish population, due to the consumption of ~400 g of orange juice concentrate which, in the absence of monitoring data or processing factors, is equivalent to the consumption of 4 kg

of oranges. A further source of uncertainty for the exposure to oranges is due to the method of imputation of left-censored data (residues of dimethoate on oranges have a level of quantification of 1.6%).

### *Heptachlor*

The minimum of the HQ estimates for heptachlor is below 0.87 for adults, 1.91 for other children and 4.14 for toddlers, while their respective minimum lower bounds are of 0.77, 1.63 and 3.35, respectively. The medians of the HQ range estimate are 1.40, 3.40 and 5.90 for the three age classes. The maximum of the HQ range estimates (maximum upper bound) are of 1.91 (2.07), 5.31 (5.84) and 6.93 (7.69) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are carrots (raw and processed) and cucumbers for the three age groups. No monitoring data or processing factors are available for carrots, contributing to increase the uncertainty of the exposure estimate to this commodity. A further source of uncertainty for the exposure to carrots is due to the method of imputation of left-censored data (residues of heptachlor on carrots have a level of quantification of 2.6%).

### *Hexachlorocyclohexane beta-isomer*

The minimum of the HQ estimates for hexachlorocyclohexane beta-isomer is below 4.26 for adults, 11.4 for other children and 9.6 for toddlers, while their respective minimum lower bounds are of 3.94, 10.6 and 8.24, respectively. The medians of the HQ range estimate are 5.46, 13.6, 18.3 for the three age classes. The maximum of the HQ range estimates (maximum upper bound) are of 23 (27.1), 17.5 (18.3) and 20.5 (21.7) for adults, other children and toddlers, respectively. Residue of hexachlorocyclohexane beta-isomer is only detected on apples. For adults, the skewed HQ distribution is due to the large consumption of apples for winemaking in Ireland, for which no processing factor nor monitoring data are available. A further source of uncertainty for the exposure to apple is due to the method of imputation of left-censored data (residues of hexachlorocyclohexane beta-isomer on raw apples have a level of quantification of ~6%).

### *Prothiofos*

The minimum of the HQ estimates for prothiofos is below 0.71 for adults, 2.39 for other children and 4.25 for toddlers, while their respective minimum lower bounds are of 0.54, 1.92 and 3.55, respectively. The medians of the HQ range estimate are 1.25, 3.24 and 4.56 for the three age classes. The maximum of the HQ range estimates (maximum upper bound) are of 2.48 (4.57), 5.61 (7.54) and 5.66 (6.20) for adults, other children and toddlers, respectively. Commodities most contributing to exposure are pears and oranges for adults, mandarin juice, oranges and pears for other children, pears and mandarin juice for toddlers. The maximum upper bound value of HQ for other children is recorded in Finland due to the consumption of pears (for which the percentage ARfD per day exceeds 500% for all subjects). The exposure is strongly influenced by sample concentration set at the limit of quantification as the share of quantifiable measurements for residues of prothiofos on pears is of 2.6% only.

## APPENDIX E

## Proposed priority list of pesticides

The list of substances prioritised according to the criteria discussed in Sections 2.1.2 and 3.1.2 is presented in the following Table.

**TABLE E.1** List of priority substances in alphabetic order with target organs and type of effect.

Substance code	Substance name	Target organs <sup>a</sup>	Type of effect <sup>b</sup>
RF-0000011-VET	Abamectin	ADG, EYE, GIT, HAS, KID, LIV, FRS, PIG, MRS, RDT	C/A
RF-0014-001-PPP	Acetamiprid	ADG, CAS, MRS, EYE, HAS, KID, LIV, MAG, FRS, PAG, PIG, RDT	A
RF-0024-002-PPP	Amitraz	ADG, HAS, LIV, MRS, RDT, GIT	A
RF-0041-002-PPP	Carbendazim	CAS, MRS, HAS, KID, LIV, FRS, PIG, RDT	A
RF-0000015-CHE	Chlorates	ADG, HAS, CAS, KID, LIV, FRS, GIT, PIG, RDT, MRS	C/A
RF-0075-002-PPP	Chlordane	LIV, MAG, RDT	C/A
RF-00005769-PAR	Chlormequat chloride	RDT	C/A
RF-0086-003-PPP	Chlorpropham	RDT, HAS, EYE, KID, LIV, ADG, CAS, MRS, MUS, PIG	C/A
RF-0087-001-PPP	Chlorpyrifos	ADG, HAS, EYE, GIT, KID, LIV, RDT, FRS	C/A
RF-0108-003-PPP	Cyfluthrin	LIV, FRS, RDT	A
RF-0108-002-PPP	Cyfluthrin, beta-	HAS, KID, LIV, MRS, RDT	A
RF-0585-001-PPP	Cyhalothrin, gamma-	HAS, KID, LIV, RDT	C/A
RF-0261-001-PPP	Cyhalothrin, lambda-	LIV, MAG, RDT	C/A
RF-0112-004-PPP	Cypermethrin	LIV, MAG, RDT, FRS	C/A
RF-00000161-VET	Cypermethrin, alpha-	MRS, KID, LIV, MAG, RDT, FRS	C/A
RF-0112-003-PPP	Cypermethrin, beta-	ADG, CAS, MRS, HAS, KID, LIV, RDT, FRS	C/A
RF-0120-001-PPP	Deltamethrin (cis-deltamethrin)	MRS, LIV, FRS, RDT	A
RF-0596-001-PPP	Diafenthiuron	ADG, CAS, EYE, KID, LIV, HAS, FRS, GIT, MRS	A
RF-0130-002-PPP	Dicofol	ADG, HAS, CAS, MRS, KID, LIV, FRS, RDT, URB	C
RF-0021-003-PPP	Dieldrin	HAS, KID, LIV, RDT	C/A
RF-0139-003-PPP	Dimethoate	ADG, CAS, MRS, HAS, KID, LIV, MAG, FRS, GIT, RDT	C/A
RF-0148-001-PPP	Diquat	ADG, MRS, EYE, HAS, KID, LIV, MAG, MUS, PIG, RDT, FRS	A
RF-0000016-VET	Emamectin	ADG, HAS, BOS, CAS, EYE, KID, LIV, MUS, MRS, RDT, URB	C
RF-00004821-PAR	Endosulfan	MRS, HAS, KID, LIV, MAG, FRS, PAG, PIG, RDT, URB, ADG	A
RF-0160-001-PPP	Ethephon	BOS, HAS, KID, LIV, FRS, RDT, MRS	A
RF-0164-001-PPP	Ethoprophos	ADG, CAS, EYE, GIT, HAS, KID, LIV, PIG, RDT, MRS, FRS	C/A
RF-0173-004-PPP	Fenamiphos	ADG, CAS, HAS, KID, LIV, FRS, GIT, RDT	C/A
RF-00012326-PAR	Fenpropimorph	HAS, LIV, RDT, MRS	C
RF-0192-003-PPP	Fipronil	MRS, HAS, KID, LIV, MAG, FRS, RDT	C
RF-0194-002-PPP	Flonicamid	ADG, HAS, MRS, EYE, GIT, KID, LIV, MUS, FRS, PIG, RDT	A
RF-0207-001-PPP	Fluometuron	ADG, CAS, MRS, EYE, HAS, KID, LIV, FRS, PIG, RDT, GIT	C/A
RF-0213-001-PPP	Fluquinconazole	ADG, GIT, HAS, KID, LIV, MAG, RDT, MRS, FRS	C
RF-0402-001-PPP	Fluvalinate, tau-	ADG, CAS, EYE, HAS, KID, LIV, MAG, FRS, RDT	C
RF-00001688-PAR	Formetanate hydrochloride	CAS, LIV, MAG, FRS, RDT, MRS	A
RF-0226-001-PPP	Fosthiazate	ADG, EYE, KID, MUS, FRS, RDT	A
RF-0231-001-PPP	Glufosinate-ammonium	CAS, EYE, HAS, KID, MRS, RDT	A
RF-0235-006-PPP	Haloxypop-P	KID, FRS, MRS	C
RF-0236-004-PPP	Heptachlor	LIV, RDT	C/A
RF-0237-001-PPP	Hexachlorobenzene	ADG, BOS, CAS, KID, LIV, HAS, PAG, RDT	C/A
RF-0239-002-PPP	Hexachlorocyclohexane (HCH), beta-isomer	KID, LIV, RDT, MRS, HAS	C/A
RF-0246-001-PPP	Imazalil	LIV, RDT, MRS	C/A

TABLE E.1 (Continued)

Substance code	Substance name	Target organs <sup>a</sup>	Type of effect <sup>b</sup>
RF-00004822-PAR	Indoxacarb	MRS, HAS, FRS, RDT	A
RF-0263-001-PPP	Lindane (Gamma-isomer of hexachlorocyclohexane (HCH))	ADG, HAS, KID, LIV, PIG, RDT, MRS	C
RF-0267-001-PPP	Maleic hydrazide	LIV, MRS, RDT, URB	C
RF-0151-004-PPP	Mancozeb	ADG, HAS, BOS, MRS, EYE, KID, LIV, MAG, MUS, FRS, GIT, PIG, RDT	C/A
RF-0151-003-PPP	Maneb	HAS, LIV, MAG, MUS, RDT	C/A
RF-0291-002-PPP	Methiocarb	ADG, HAS, KID, LIV, RDT, MRS	C/A
RF-0293-003-PPP	Methomyl	HAS, KID	C/A
RF-0151-002-PPP	Metiram	HAS, LIV, MAG, MUS, FRS, RDT, MRS	C
RF-0809-001-PPP	Nicotine	CAS, RDT	C/A
RF-0320-001-PPP	Oxamyl	EYE, KID, MAG, RDT, MRS	C/A
RF-0324-001-PPP	Oxyfluorfen	ADG, HAS, CAS, MRS, EYE, KID, LIV, MAG, FRS, GIT, PAG, PIG, RDT, URB	C
RF-00012330-PAR	Permethrin	ADG, HAS, KID, LIV, RDT	A
RF-00004675-PAR	Phosphonic acid	CAS, HAS, KID, LIV	C
RF-0348-001-PPP	Pirimiphos-methyl	MRS, KID, RDT	C/A
RF-0349-002-PPP	Prochloraz	ADG, HAS, KID, LIV, MAG, FRS, PIG, MRS, RDT	A
RF-0359-002-PPP	Propineb	HAS, LIV, MAG, MUS, FRS, MRS, RDT	C/A
RF-0366-001-PPP	Prosulfocarb	EYE, HAS, KID, LIV, FRS, MRS, RDT	C
RF-0370-001-PPP	Pyraclostrobin	HAS, KID, LIV, RDT, MRS	A
RF-0377-001-PPP	Pyrimethanil	KID, LIV, MRS, RDT, URB	C
RF-0403-001-PPP	Tebuconazole	ADG, MRS, EYE, HAS, KID, LIV, MUS, FRS, PIG, RDT	A
RF-0408-001-PPP	Tefluthrin	CAS, EYE, HAS, KID, LIV, MAG, FRS, PIG, RDT, MRS	A
RF-0414-001-PPP	Tetraconazole	BOS, MRS, KID, LIV, MAG, FRS, RDT	C
RF-0416-001-PPP	Thiabendazole	CAS, GIT, HAS, KID, LIV, RDT, MRS, URB	C/A
RF-0422-001-PPP	Thiophanate-methyl	ADG, BOS, CAS, HAS, KID, LIV, FRS, PAG, MRS, RDT	A
RF-0423-001-PPP	Thiram	ADG, HAS, CAS, MRS, EYE, KID, LIV, MAG, MUS, FRS, GIT, PIG, RDT, URB	C/A
RF-0451-001-PPP	Ziram	CAS, MRS, HAS, LIV, MAG, MUS, FRS, RDT, URB	C/A

<sup>a</sup>ADG, adrenal gland; BOS, bones/skeleton; CAS, cardiovascular system; EYE, eye; FRS, female reproductive system; GIT, gastrointestinal tract; HAS, haematopoietic system and haematology; KID, kidney; LIV, liver; MAG, mammary gland; MRS, male reproductive system; MUS, muscles; PAG, parathyroid gland; PIG, pituitary gland; RDT, reproductive and developmental toxicity; URB, urinary bladder.

<sup>b</sup>C, chronic; A, acute.

TABLE E.2 Substances that were not covered by the data collection performed by DTU, and could therefore not be mapped to any specific organ system.

Substance code	Substance name	Type of effect <sup>a</sup>
RF-0012-001-PPP	Acephate	C/A
RF-0033-001-PPP	Azinphos-methyl	A
RF-0062-001-PPP	Carbaryl	A
RF-0065-003-PPP	Carbofuran	C/A
RF-0068-001-PPP	Carbosulfan	A
RF-0079-001-PPP	Chlorfenvinphos	A
RF-0123-001-PPP	Diazinon	C
RF-0127-001-PPP	Dichlorvos	C/A
RF-0612-001-PPP	Dicrotophos	C/A
RF-0228-001-PPP	Furathiocarb	A
RF-0289-001-PPP	Methamidophos	C/A
RF-0290-001-PPP	Methidathion	C
RF-00012328-PAR	Mevinphos	C/A

(Continues)



TABLE E.2 (Continued)

Substance code	Substance name	Type of effect <sup>a</sup>
RF-0305-001-PPP	Monocrotophos	C/A
RF-0323-004-PPP	Oxydemeton-methyl	A
RF-0846-001-PPP	Phenthoate	A
RF-0336-003-PPP	Phorate	C/A
RF-0361-001-PPP	Propoxur	C/A
RF-0869-001-PPP	Prothiofos	C/A
RF-0380-001-PPP	Quinalphos	C/A
RF-0432-001-PPP	Triazophos	C/A

<sup>a</sup>C, chronic; A, acute.

APPENDIX F

Combined exposure assessment results for the target organ systems

This section reports more detailed information on the food commodities and active substances that contributed to the chronic and acute exposure in the analysed organ systems. Summary of the range of median HI at the P99.9 of the organ systems exposure distributions for chronic and acute combined exposure assessment is reported in Tables F.1 and F.2.

TABLE F.1 Chronic combined exposure assessment.

Organ system	Range of median HI values by population class and N survey above HI = 1					
	Adults	N surveys	Other children	N surveys	Toddlers	N surveys
ADG	0.15–0.33	[0/15]	0.23–0.41	[0/10]	0.32–0.53	[0/5]
BOS	0.01–0.03	[0/15]	0.02–0.04	[0/10]	0.03–0.06	[0/5]
CAS	0.2–0.46	[0/15]	0.37–0.68	[0/10]	0.46–0.72	[0/5]
EYE	0.09–0.21	[0/15]	0.18–0.31	[0/10]	0.22–0.43	[0/5]
FRS	0.26–0.73	[0/14]	0.41–0.67	[0/6]	0.69	[0/1]
GIT	0.14–0.36	[0/15]	0.22–0.44	[0/10]	0.3–0.59	[0/5]
HAS	0.26–0.59	[0/15]	0.44–0.85	[0/10]	0.57–0.94	[0/5]
KID	0.22–0.49	[0/15]	0.33–0.73	[0/10]	0.43–1.07	[1/5]
LIV	0.31–1.41	[1/15]	0.52–1.24	[3/10]	0.96–1.72	[4/5]
MAG	0.25–0.54	[0/15]	0.43–0.87	[0/10]	0.57–0.94	[0/5]
MRS	0.3–0.73	[0/14]	0.55–1.26	[2/6]	1.16	[1/1]
MUS	0.19–0.42	[0/15]	0.33–0.76	[0/10]	0.5–0.78	[0/5]
PAG	0.01–0.06	[0/15]	0.02–0.12	[0/10]	0.04–0.09	[0/5]
PIG	0.09–0.21	[0/15]	0.13–0.3	[0/10]	0.23–0.43	[0/5]
RDT	0.34–1.41	[1/15]	0.59–1.3	[3/10]	1.03–1.85	[5/5]
URB	0.17–0.35	[0/15]	0.29–0.59	[0/10]	0.41–0.62	[0/5]

Note: Range of median HI values at the 99.9th percentile of the exposure distribution across the different surveys, for each population group. The number of surveys where the HI > 1, compared to the total number of surveys (N survey with exceedance/N total surveys), is also reported by population group and organ system. The cells where the HI > 1 in at least one survey are highlighted in grey.

Organ system: ADG: adrenal gland; BOS: bones/skeleton; CAS: cardiovascular system; EYE: eye; FRS: female reproductive system; GIT: gastrointestinal system; HAS: haematopoietic system and haematology; KID: kidney; LIV: liver; MAG: mammary gland; MRS: male reproductive system; MUS: muscular system; PAG: parathyroid gland; RDT: reproductive and developmental toxicity; URB: urinary bladder.

N surveys: number of surveys with HI>1/total number of surveys.

TABLE F.2 Acute combined exposure assessment.

Organ system	Range of median HI values by population class and N survey above HI = 1					
	Adults	N surveys	Other children	N surveys	Toddlers	N surveys
ADG	0.8–2.1	[11/15]	2.24–4.26	[10/10]	2.47–4.74	[5/5]
BOS	0.09–0.21	[0/15]	0.15–0.35	[0/10]	0.16–0.39	[0/5]
CAS	0.75–2.19	[11/15]	2.09–4.05	[10/10]	2.09–4.73	[5/5]
EYE	0.26–0.56	[0/15]	0.46–1.73	[2/10]	0.78–1.48	[2/5]
FRS	1–2.55	[13/14]	2.45–4.18	[6/6]	3.82	[1/1]
GIT	0.75–2.09	[10/15]	2.02–3.75	[10/10]	2.03–4.62	[5/5]
HAS	0.91–2.5	[12/15]	2.51–4.42	[10/10]	2.68–4.96	[5/5]
KID	1.1–2.77	[15/15]	2.73–5.97	[10/10]	3.52–5.93	[5/5]
LIV	1.15–2.39	[15/15]	2.76–4.83	[10/10]	3.21–5.58	[5/5]
MAG	1.2–2.47	[15/15]	2.61–5.67	[10/10]	2.85–5.32	[5/5]
MRS	0.83–2.18	[12/14]	2.7–5.51	[6/6]	4.72	[1/1]
MUS	0.14–0.24	[0/15]	0.31–0.49	[0/10]	0.37–0.54	[0/5]
PAG	0.06–0.14	[0/15]	0.14–0.26	[0/10]	0.14–0.29	[0/5]
PIG	0.14–0.22	[0/15]	0.25–0.8	[0/10]	0.4–0.65	[0/5]
RDT	1.51–3.01	[15/15]	2.99–6.03	[10/10]	4.03–6.15	[5/5]
URB	0.11–0.24	[0/15]	0.25–0.76	[0/10]	0.42–0.73	[0/5]

Note: Range of median HI values at the 99.9th percentile of the exposure distribution across the different surveys, for each population group. The number of surveys where the HI > 1, compared to the total number of surveys (N survey with exceedance/N total surveys), is also reported by population and organ system. The cells where the HI > 1 in at least one survey are highlighted in grey.

Organ system: ADG: adrenal gland; BOS: bones/skeleton; CAS: cardiovascular system; EYE: eye; FRS: female reproductive system; GIT: gastrointestinal system; HAS: haematopoietic system and haematology; KID: kidney; LIV: liver; MAG: mammary gland; MRS: male reproductive system; MUS: muscular system; PAG: parathyroid gland; RDT: reproductive and developmental toxicity; URB: urinary bladder.

N surveys: number of surveys with HI>1 / total number of surveys.

Some extreme consumption records are observed across the organ systems, as in the case of Finnish adults for the chronic exposure results, leading to higher exposure estimates compared to the rest of the subjects within the same survey. For this specific survey, these mostly refer to high consumptions of concentrated orange juice, corresponding up to more than 6000 gr of raw oranges (Annex C1, Table C.1.04). For this processed commodity, no processing factor is available and, as mentioned in Section 3.2.1, the consumed amount of the RPC is then combined with the concentration of the substance in the raw food. It should be noted that the exposure distributions could vary depending on the sampling of high consumers in the bootstrapping, as their inclusion in the data set could result in higher exposure estimates.

F.1 | ADRENAL GLAND (ADG)

F.1.1 | Chronic

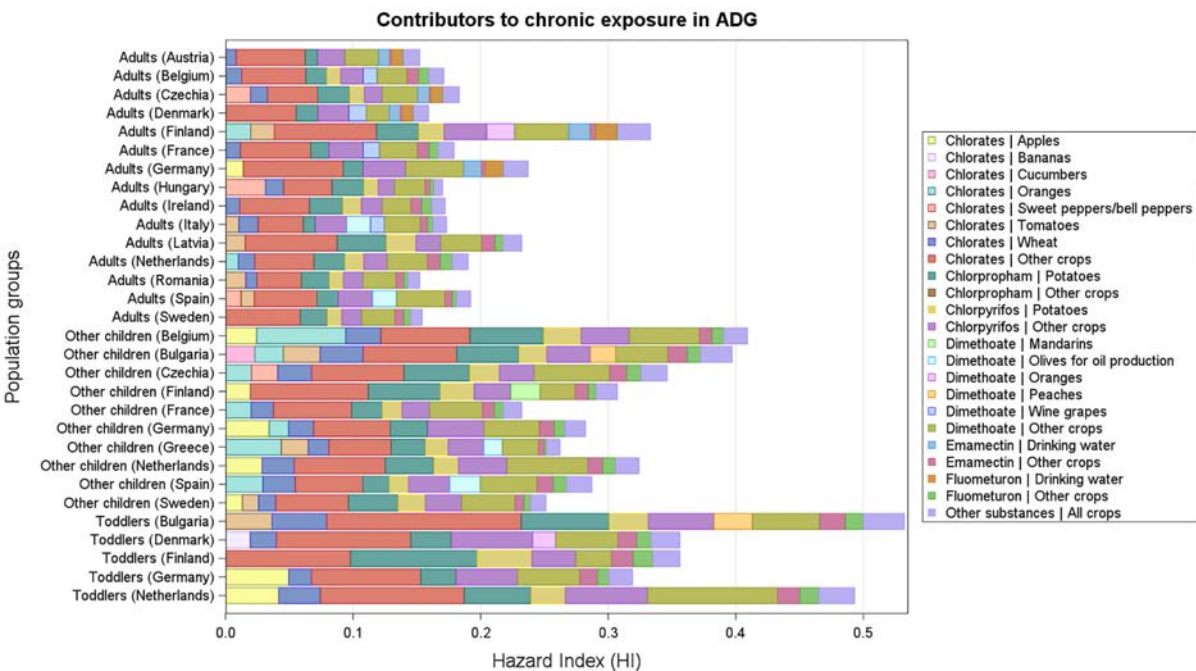
The HI estimates at the 99.9th percentile of the combined chronic exposure distributions in ADG do not exceed 1 in any of the analysed surveys. Median HI estimates range from 0.152 in adults from Austria and Romania to 0.532 in Bulgarian toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.1.

The substance group contributing the most at survey level are chlorates (28%–50%), followed by dimethoate (8%–33%), chlorpropham (5%–28%), chlorpyrifos (14%–22%), emamectin (2%–7%) and fluometuron (1%–6%). All the other substances have an overall contribution by survey below 5%.

The contribution of chlorates is mainly driven by their occurrence in wheat (up to 9%), being equal or above 5% in 22 surveys, oranges (mostly juices, up to 17%), tomatoes (up to 10%) and apples (up to 16%), mostly through the consumption of juices (Annex C1, Table C.1.03). Other RPC contributors are sweet peppers/bell peppers, cucumbers and bananas. Dimethoate is another major contributor, mainly via the consumption of olives for oil production (oil), wine grapes (red wine), oranges, peaches and mandarins. Drinking water is the main RPC contributor for both emamectin and fluometuron (both up to 6%). For this specific RPC, it should be clarified that estimates on contribution are based on imputed occurrence data and should be then considered with caution (see Appendix C, Section C.1.1.4).

The contribution of chlorpyrifos through the consumption of potatoes is equal or above 5% in 21 of the 30 assessed surveys (up to 12%), while that of chlorpropham in all of them (5%–28%).

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.1** Median hazard index (HI) calculated for the adrenal gland (ADG) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

F.1.2 | Acute

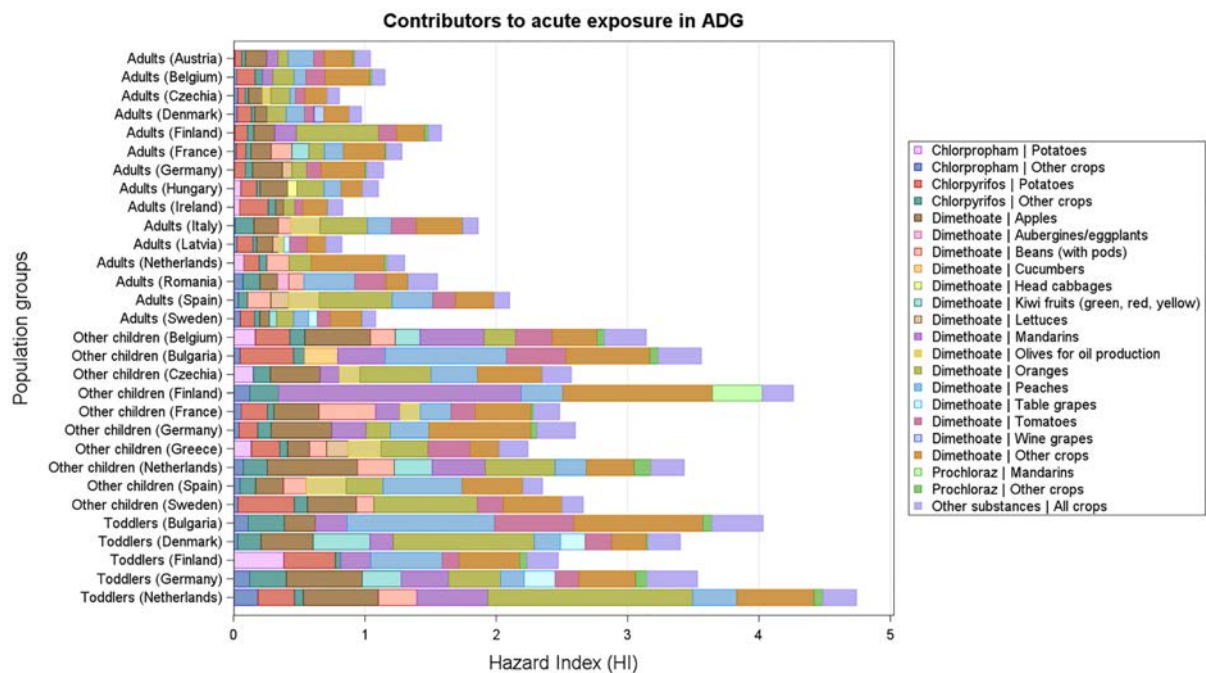
The HI estimates of the cumulative acute exposure in ADG exceed the HI threshold in 26 out of the 30 analysed surveys. Median estimates at the 99.9th percentile range from 0.804 in Czech adults to 4.74 in Dutch toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.2.

Dimethoate is the main driver of the acute exposure in ADG (47%–89%), followed by chlorpyrifos (3%–33%), chlorpropham (up to 1%–16%) and prochloraz (up to 9%). All the other substances have an overall contribution by survey below 5%.

Apples are the main contributing food commodity for dimethoate (up to 20%), followed by oranges (up to 40%), peaches (up to 28%) and tomatoes (up to 16%), all equal or above 5% in at least 20 surveys. Other contributors are mandarins (up to 43%), beans (with pods) (up to 17%), olives for oil production (mainly oil, up to 13%) and kiwi fruits (up to 13%), followed by lettuces, table and wine grapes, cucumbers, head cabbages and aubergines/eggplants.

For both chlorpyrifos and chlorpropham, potatoes are the main contributing food commodity, reaching up to 26% for the first and 16% for the second, and respectively, exceeding 5% in 20 and 7 surveys. Mandarins are the main contributor to the exposure to prochloraz.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.2** Median hazard index (HI) calculated for the adrenal gland (ADG) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

## F.2 | BONES/SKELETON (BOS)

### F.2.1 | Chronic

The HI estimates at the 99.9th percentile of the combined chronic exposure distributions in BOS do not exceed 1 in any of the analysed surveys. Median estimates range from 0.0112 in Italian adults to 0.0633 in German toddlers. The substance/ commodity combinations contributing for at least 5% to the exposure are reported in Figure F.3.

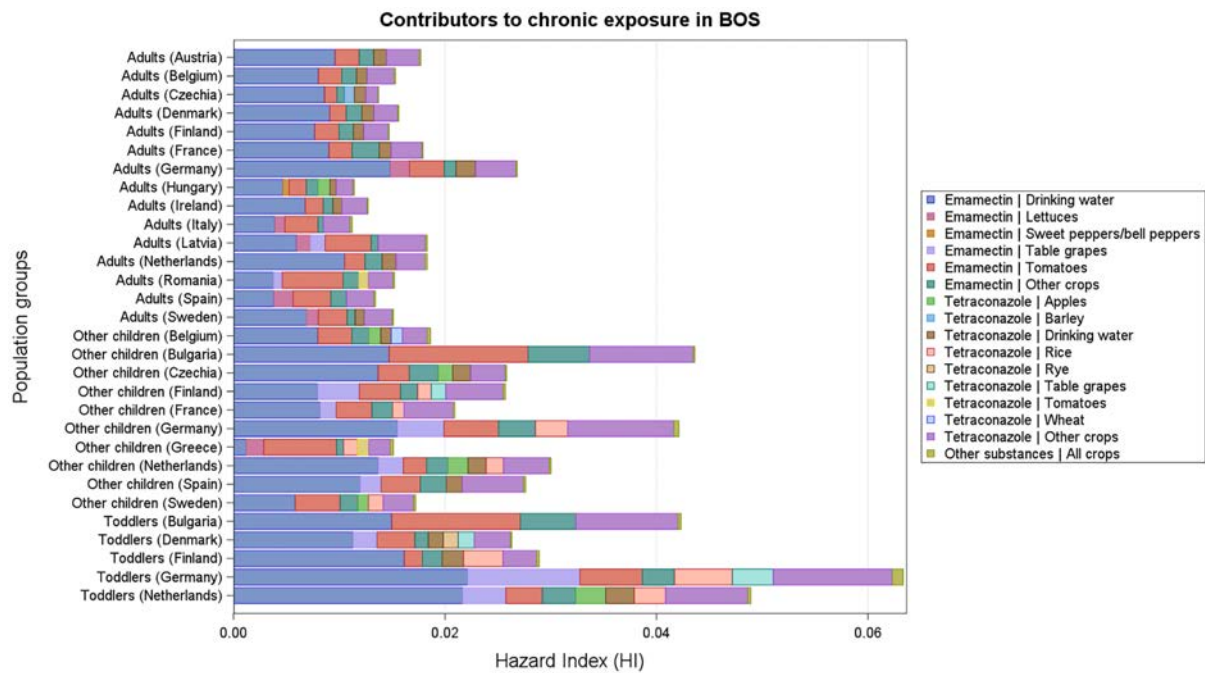
Emamectin (66%–80%) and tetraconazole (19%–33%) are the main contributing substances, mostly through the consumption of drinking water. All the other substances have an overall contribution by survey below 5%.

For emamectin, other major RPC contributors are tomatoes, table grapes (up to 17%) and lettuces (up to 14%), with a minor contribution from sweet peppers/bell peppers, whereas for tetraconazole, rice (up to 13%) and apples (up to 10%) are among the main contributors, followed by tables grapes, tomatoes, barley, wheat and rye.

The exposure to emamectin through the consumption of drinking water (8%–63%) and tomatoes (6%–46%) is equal or above 5% in all the assessed surveys, while for tetraconazole the number of surveys where this value is met or exceeded for drinking water is 18 (up to 8%). However, it should be noted that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4).

For further details, see also Annex C1, Table C.1.03.





**FIGURE F.3** Median hazard index (HI) calculated for the bones/skeleton (BOS) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

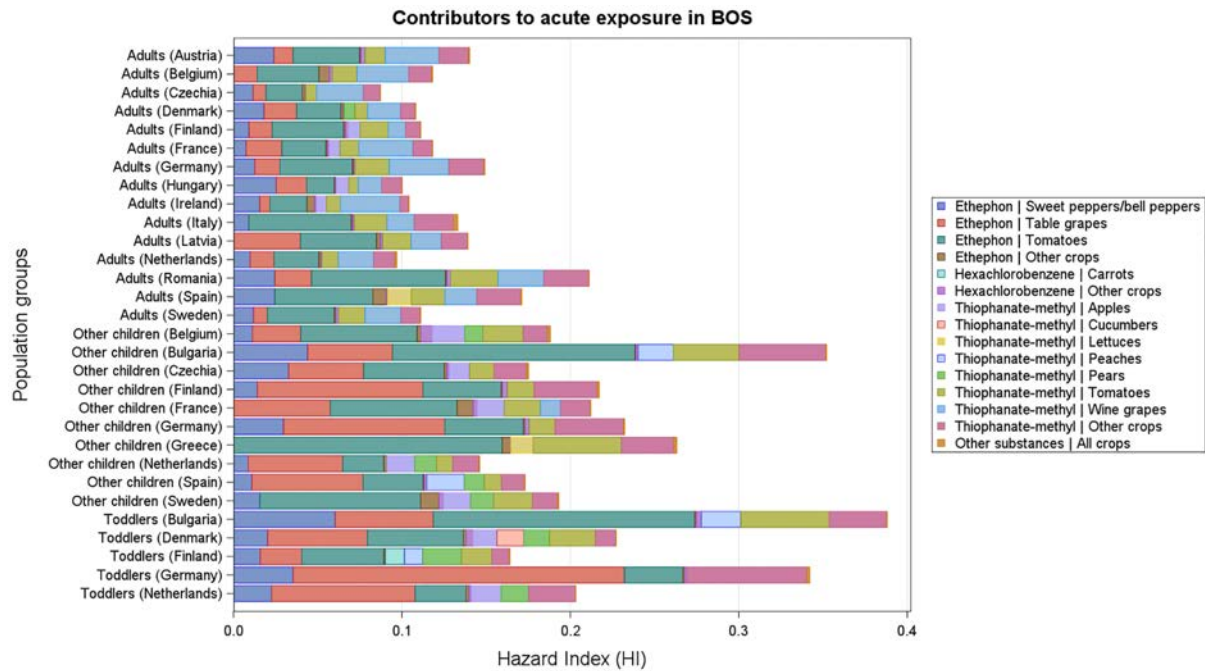
F.2.2 | Acute

The HI estimates at the 99.9th percentile of the combined acute exposure distributions in BOS do not exceed 1 in any of the analysed surveys. Median HI estimates range from 0.087 in adults from Czechia to 0.388 in Bulgarian toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.4.

The main contributors to the exposure are ethephon (46%–78%) and thiophanate-methyl (21%–53%), followed by hexachlorobenzene (up to 7%). All the other substances have an overall contribution below 5% in the analysed surveys.

Tomatoes are the main contributing food commodity in both ethephon and thiophanate-methyl, being equal or above 5% in all 30 surveys for the first and in 28 for the second. Other major contributors for ethephon are table grapes (up to 58%) and sweet peppers/bell peppers (up to 25%), both contributing for more than 5% in 26 surveys. As for thiophanate-methyl, the contribution of wine grapes (up to 34%) and apples (up to 11%) is equal or above 5% in more than 10 surveys, followed by pears (up to 14%). Other contributors are peaches, lettuces and cucumbers. Carrots are the main RPC contributor for hexachlorobenzene.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.4** Median hazard index (HI) calculated for the bones/skeleton (BOS) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

F.3 | CARDIOVASCULAR SYSTEM (CAS)

F.3.1 | Chronic

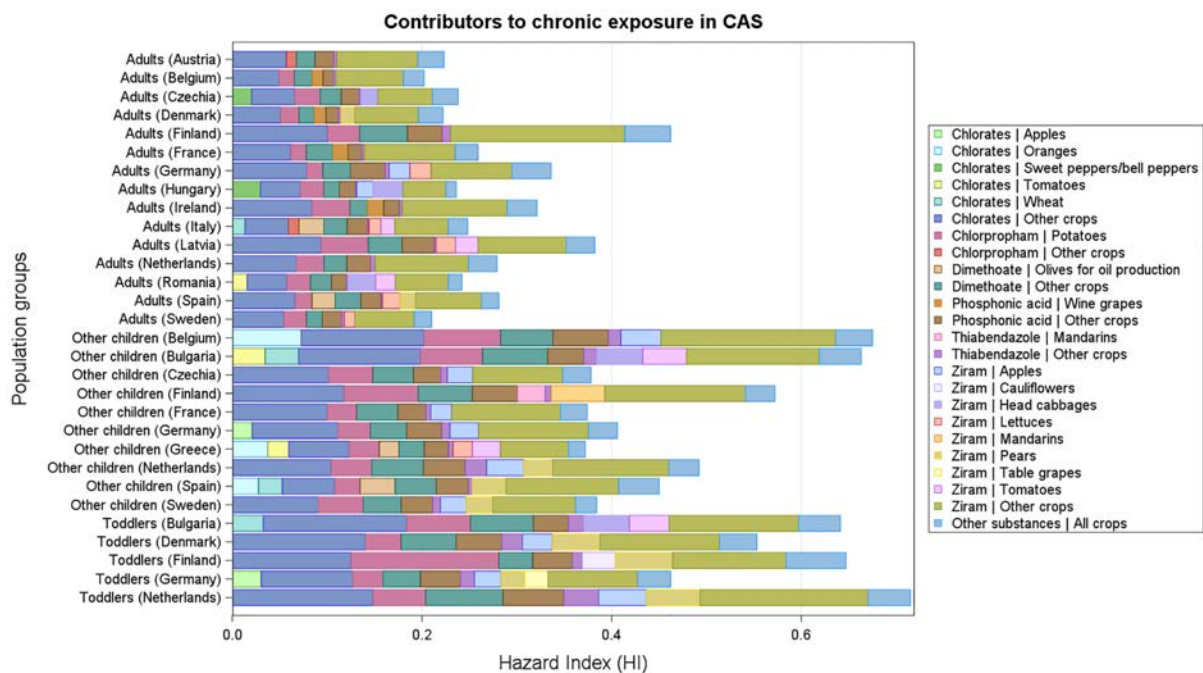
The HI estimates of the combined chronic exposure in CAS do not exceed 1 in any of the analysed surveys. Median HI values at the 99.9th percentile vary between 0.202 in Belgian adults and 0.715 in Dutch toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.5.

The main contributing substances are ziram (32%–44%), chlorates (19%–33%), chlorpropham (4%–24%), dimethoate (6%–21%), phosphonic acid (6%–12%), thiabendazole (up to 6%), emamectin (1%–5%). All the other substances have an overall contribution by survey below 5%.

The food commodities contributing the most to the exposure to ziram are apples (up to 8%) and pears (up to 9%), tomatoes (up to 9%), lettuces (up to 7%) and head cabbages (up to 13%), with other contributors being mandarins, cauliflowers and table grapes. For chlorates, the major contributors are wheat, oranges (mostly orange juice), tomatoes, sweet peppers/bell peppers and apples (mostly juices), whereas for dimethoate these are olives for oil production (mainly oil). Mandarins are the main contributor for thiabendazole, as for phosphonic acid, wine grapes (mainly wine) are the only RPC with a contribution equal or above 5%.

The contribution of potatoes to the exposure to chlorpropham is above 5% in 28 surveys (up to 24%).

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.5** Median hazard index (HI) calculated for the cardiovascular system (CAS) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

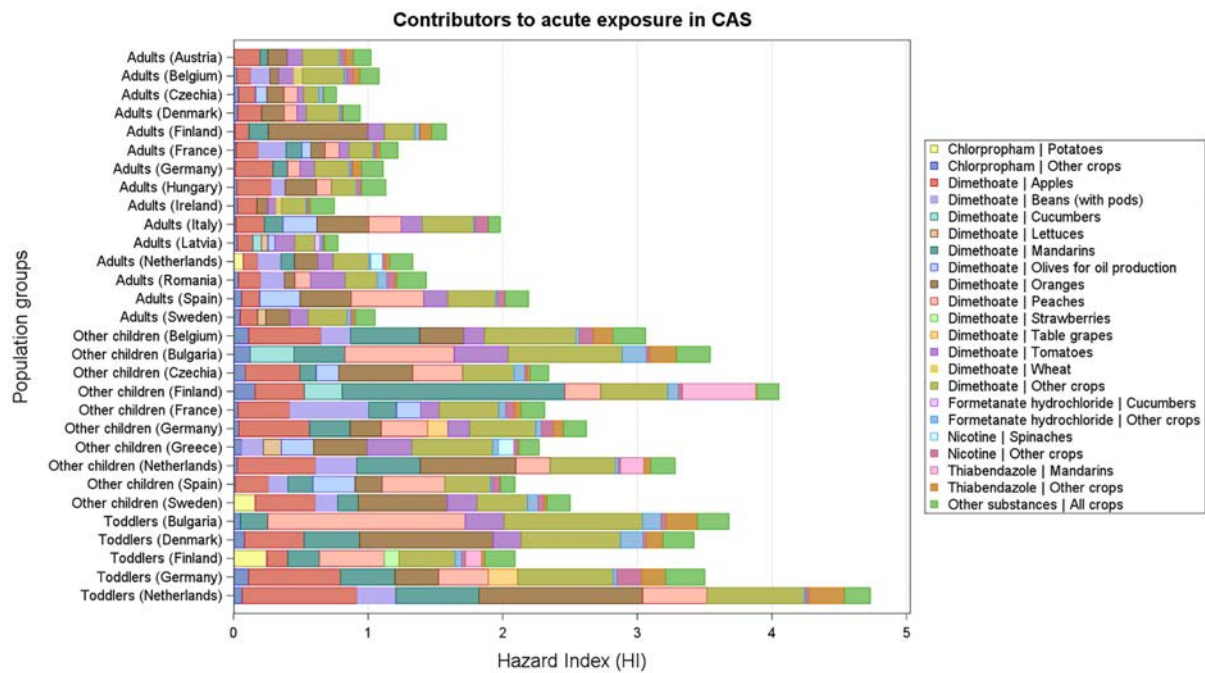
F.3.2 | Acute

The HI estimates of the combined acute exposure at the 99.9th percentile in CAS exceed 1 in 26 surveys, with median estimates ranging from 0.748 in Irish adults to 4.73 in Dutch toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.6.

Dimethoate is the main driver of the acute exposure in CAS (67%–91%), followed by contributors as thiabendazole (up to 14%), chlorpropham (up to 12%), ziram (2%–8%), nicotine (up to 8%) and formetanate hydrochloride (up to 7%). All the other substances have an overall contribution by survey below 5%.

The main drivers of the exposure to dimethoate are apples (up to 25%), contributing more than 5% in 27 surveys, followed by oranges (up to 47%), tomatoes (up to 19%) and mandarins (up to 41%), all equal or above 5% in at least 20 surveys. Other contributors are peaches (up to 40%), beans (with pods) (up to 25%), olives for oil production (mainly oil) (up to 15%). These are followed by cucumbers, lettuces, table grapes, wheat and strawberries. The main contributing RPCs for thiabendazole and chlorpropham are mandarins and potatoes, respectively. Other contributors are spinaches for nicotine and cucumbers for formetanate hydrochloride.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.6** Median hazard index (HI) calculated for the cardiovascular system (CAS) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

**F.4 | EYE (EYE)**

**F.4.1 | Chronic**

The HI estimates of the combined chronic exposure in EYE do not exceed 1 in any of the analysed surveys. Median HI values at the 99.9th percentile vary between 0.0904 in Hungarian adults and 0.43 in Dutch toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.7.

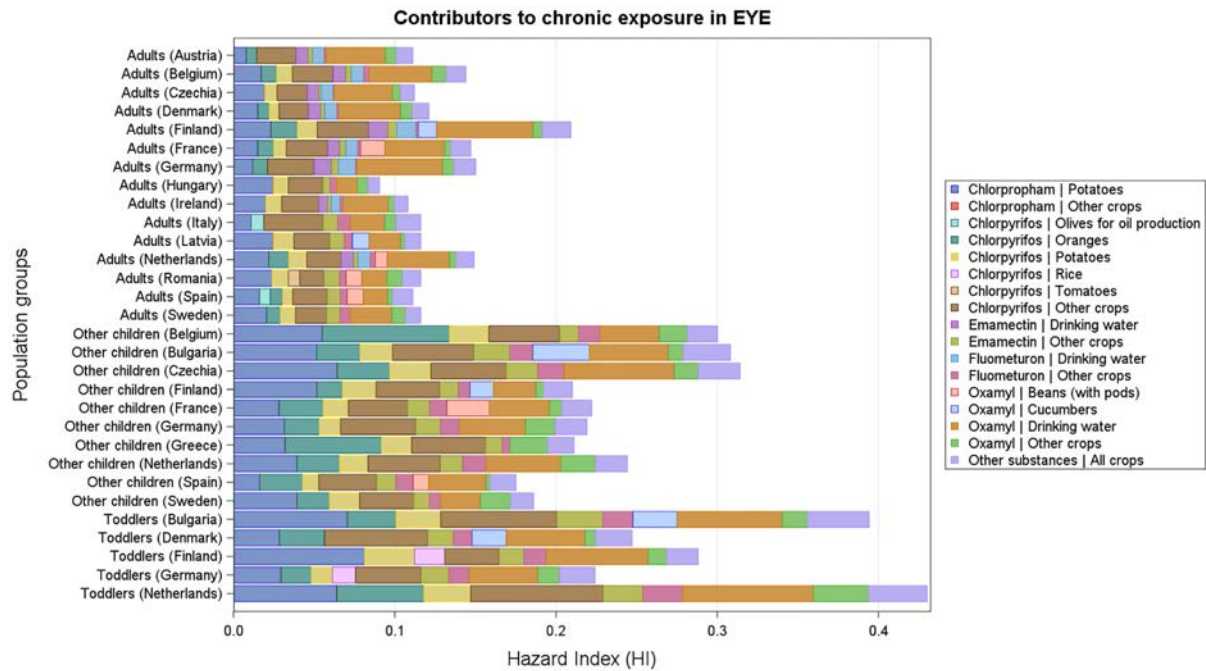
The main contributing substances are chlorpyrifos (24%–59%), oxamyl (11%–40%), chlorpropham (7%–28%), emamectin (4%–10%), fluometuron (2%–8%) and abamectin (3%–6%). All the other substances have an overall contribution by survey below 5%.

The main drivers of the exposure to chlorpyrifos are potatoes (up to 11%) and oranges (up to 28%), with a contribution equal or above 5% in 26 and 23 surveys, respectively. Other contributors are olives for oil production (mainly oil), rice and tomatoes. Drinking water is the main contributor for oxamyl (up to 35%), emamectin and fluometuron (up to 7%). It should be clarified that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4). Beans (with pods) (up to 12%) and cucumbers (up to 11%) are other contributors to the exposure to oxamyl.

The contribution of potatoes for chlorpropham is equal or above 5% in all assessed surveys (7%–28%), while the contribution of drinking water in oxamyl meets or exceeds 5% in 29 surveys.

For further details, see also Annex C1, Table C.1.03.





**FIGURE F.7** Median hazard index (HI) calculated for the eyes (EYE) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

#### F.4.2 | Acute

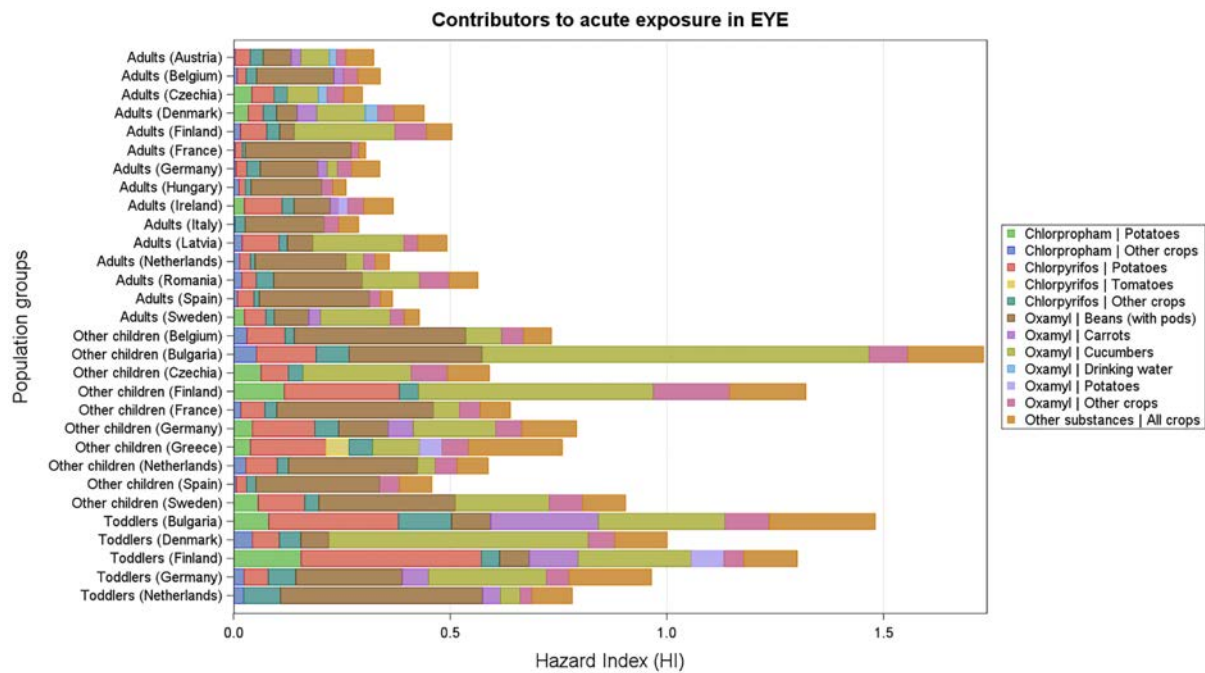
The HI estimates of the combined acute exposure in EYE exceed 1 in four surveys. Median HI values at the 99.9th percentile range between 0.259 in Hungarian adults and 1.73 in children from Bulgaria. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.8.

The main substances contributing to the exposure are oxamyl (29%–86%), chlorpyrifos (8%–37%) and chlorpropham (1%–14%), followed by abamectin (1%–9%), flonicamid and acetamiprid (1%–6%). All the other substances have an overall contribution by survey below 5%.

Beans (with pods) (up to 81%) and cucumbers (up to 60%) are the main contributing food commodities for oxamyl, both with a contribution equal or above 5% in more than 20 surveys, along with carrots (up to 17%), drinking water and potatoes. However, it should be noted that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4). Potatoes are the main driver of the exposure to chlorpyrifos (up to 32%) and chlorpropham (up to 14%), meeting or exceeding 5% in 28 and 11 surveys, respectively. A lower contribution is given by tomatoes for chlorpyrifos.

For further details, see also Annex C2, Table C.2.03.





**FIGURE F.8** Median hazard index (HI) calculated for the eyes (EYE) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

**F.5 | FEMALE REPRODUCTIVE SYSTEM (FRS)**

To assess the combined exposure in FRS, only female participants were considered in the assessment. In cases where the number of subjects in a survey was below 300 after the exclusion of male individuals, the survey was not considered in the calculations. Overall, 21 surveys were considered for the FRS combined exposure calculations.

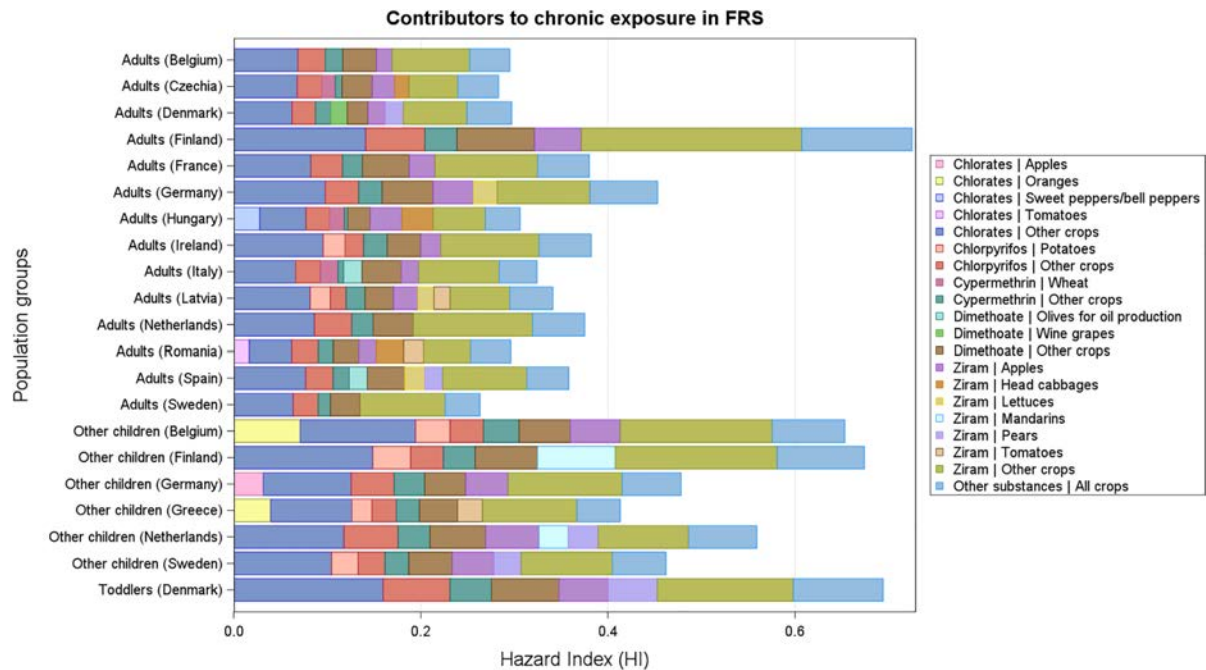
**F.5.1 | Chronic**

The HI estimates of the combined chronic exposure in FRS do not exceed 1 in any survey. Median HI values at the 99.9th percentile range between 0.263 in Swedish adults and 0.725 in Finnish adults. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.9.

The main drivers of the exposure are ziram (31%–40%), chlorates (19%–31%), dimethoate (8%–19%), chlorpyrifos (8%–12%), cypermethrin (5%–8%) and metiram (6%–7%). All the other substances have an overall contribution by survey below 5%.

With respect to ziram, the main contributing food commodities are apples (up to 11%), exceeding 5% in 16 surveys, and pears (up to 8%). Other contributors are head cabbages, tomatoes, lettuces and mandarins. Exposure to chlorates occurs mainly through oranges, sweet peppers/bell peppers, apples and tomatoes, while the main contributors for dimethoate are olives for oil production (mainly oil) and wine grapes (mainly red wine). Main food contributors for chlorpyrifos and cypermethrin are potatoes (up to 6%) and wheat, respectively.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.9** Median hazard index (HI) calculated for the female reproductive system (FRS) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

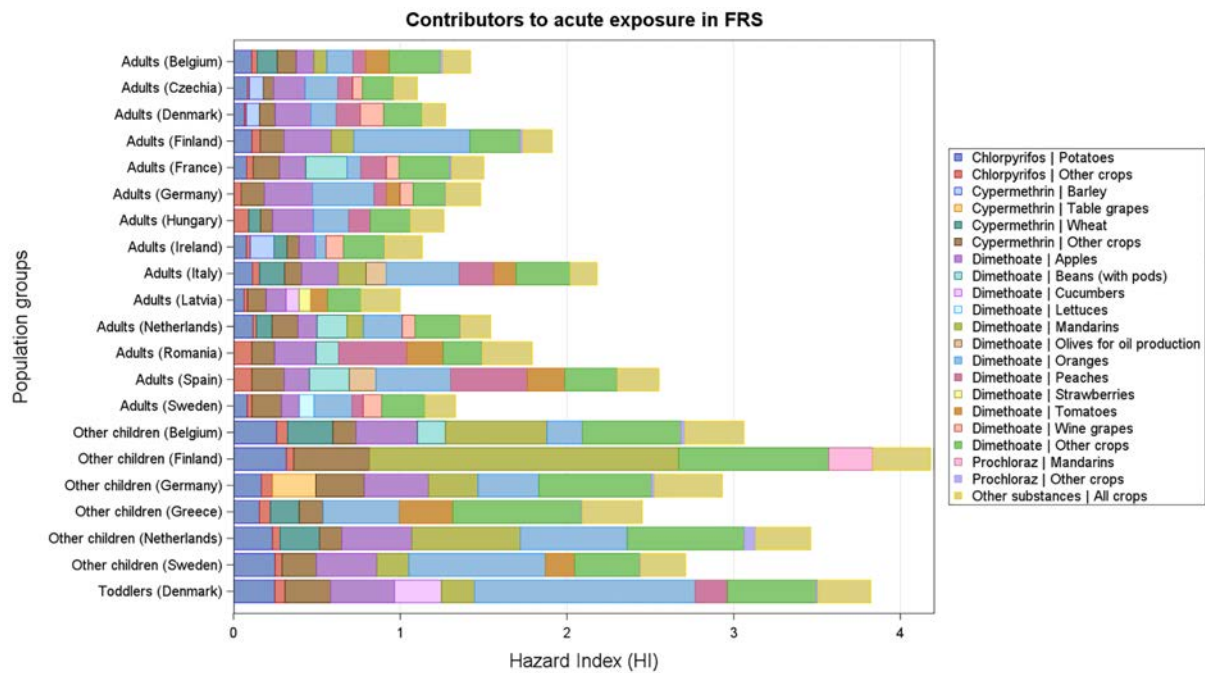
**F.5.2 | Acute**

The HI estimates of the combined acute exposure in FRS exceed 1 in 20 surveys. Median HI values at the 99.9th percentile range between 0.996 in adults from Latvia and 4.18 in Finnish children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.10.

The major contributor to the exposure is dimethoate (45%–78%), followed by cypermethrin (7%–26%), chlorpyrifos (3%–11%), prochloraz (up to 6%) and formetanate hydrochloride (up to 5%). All the other substances have an overall contribution by survey below 5%.

Apples are the main contributing food commodity for dimethoate (up to 19%), together with oranges (up to 36%), above 5% in 19 and 18 surveys, and directly followed by peaches (up to 23%), mandarins (up to 44%), tomatoes (up to 13%), wine grapes (mainly red wine, up to 11%) and beans (with pods) (up to 17%). A lower contribution is given by cucumbers, olives for oil production (mainly oil), strawberries and lettuces. Wheat is the main contributor for cypermethrin (up to 9%), together with barley and table grapes. As for chlorpyrifos, potatoes are the main contributor (up to 9%), exceeding 5% in 17 surveys. Mandarins are the only contributor equal or above 5% for prochloraz.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.10** Median hazard index (HI) calculated for the female reproductive system (FRS) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

F.6 | GASTROINTESTINAL TRACT (GIT)

F.6.1 | Chronic

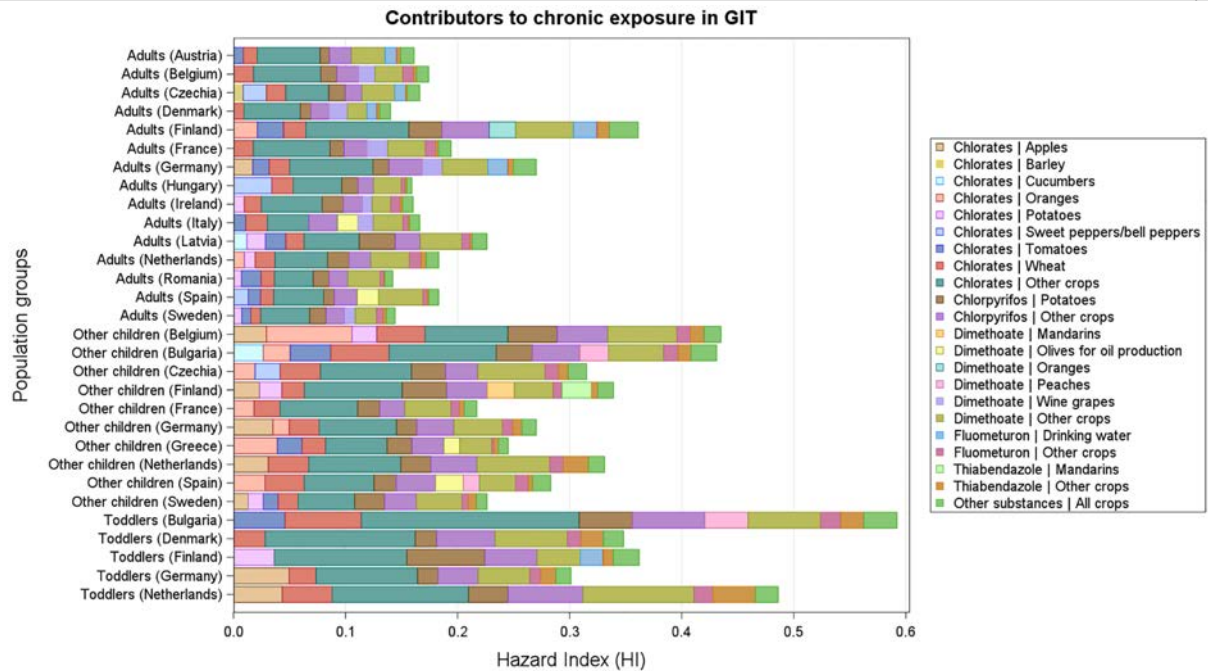
The HI estimates of the combined chronic exposure in GIT do not exceed 1 in any survey. Median HI values at the 99.9th percentile vary between 0.14 in Danish adults and 0.592 in Bulgarian toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.11.

Chlorates (41%–61%), dimethoate (11%–35%), chlorpyrifos (15%–32%) are the main contributors to the exposure, followed by thiabendazole (1%–9%) and fluometuron (1%–7%). All the other substances have an overall contribution by survey below 5%.

For chlorates, the main contributing food commodities are wheat and tomatoes (both up to 12%), oranges (up to 18%), potatoes (up to 10%) and apples (up to 16%), with a minor contribution given by sweet peppers/bell peppers, cucumbers and barley. Wine grapes are the main contributor for dimethoate (red wine, up to 12%), with others being olives for oil production (mainly oil), peaches, mandarins and oranges. Mandarins are also the main contributor for thiabendazole, as is drinking water for fluometuron (up to 7%). It should be highlighted that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4).

The contribution given by potatoes to the exposure to chlorpyrifos is equal or above 5% in 29 surveys, reaching up to 19%.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.11** Median hazard index (HI) calculated for the gastrointestinal tract (GIT) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

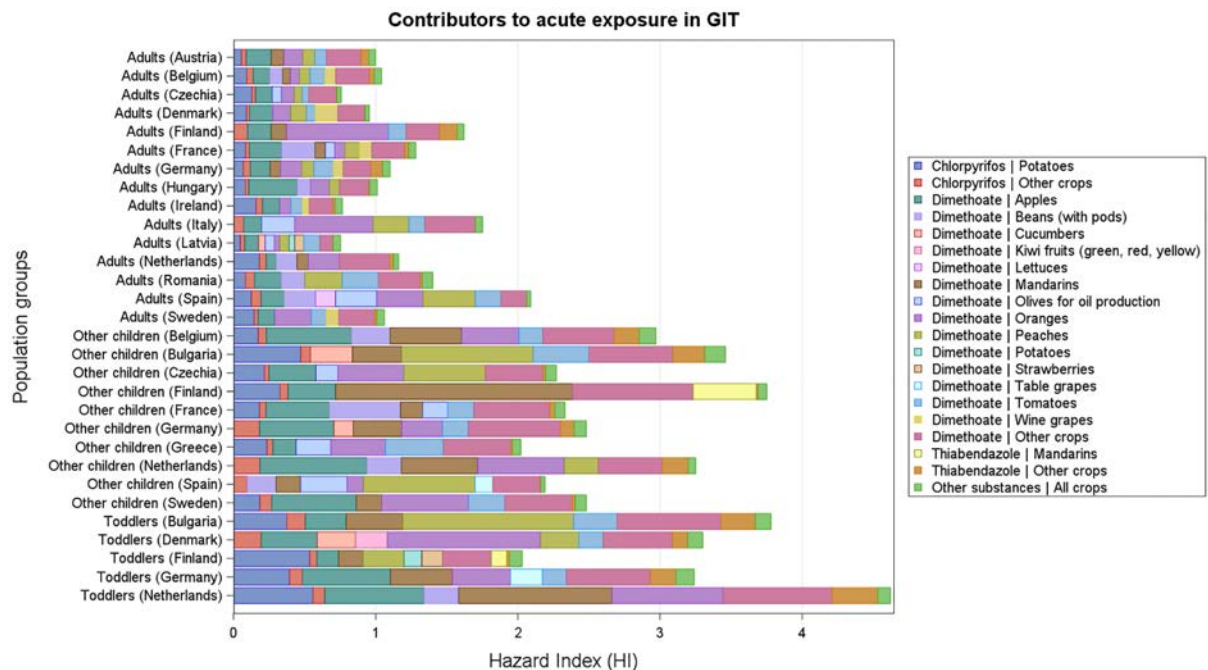
F.6.2 | Acute

The HI estimates of the combined acute exposure in GIT exceed 1 in 25 surveys. Median HI values at the 99.9th percentile vary between 0.752 in adults from Latvia and 4.62 in Dutch toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.12.

Dimethoate is the major contributor to the exposure, ranging from 60% to 94%, followed by chlorpyrifos (4%–29%) and thiabendazole (up to 12%). All the other substances have an overall contribution by survey below 5%.

With respect to dimethoate, apples (up to 34%), oranges (up to 44%) and tomatoes (up to 20%) have a contribution equal or above 5% in more than 20 surveys, with apples exceeding this value in 28 of them. Other main contributing food commodities are mandarins (up to 44%), peaches (up to 36%), beans (with pods) (up to 21%), olives for oil production (mainly oil, up to 15%) and wine grapes (mainly red wine, up to 17%). Cucumbers, strawberries, table grapes, potatoes, kiwi fruits and lettuces are other contributors. Potatoes are the main contributing commodity for chlorpyrifos, exceeding 5% in 24 surveys and reaching up to 26%. As for thiabendazole, the exposure is mainly driven by mandarins.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.12** Median hazard index (HI) calculated for the gastrointestinal tract (GIT) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.



F.7 | HAEMATOPOIETIC SYSTEM AND HAEMATOLOGY (HAS)

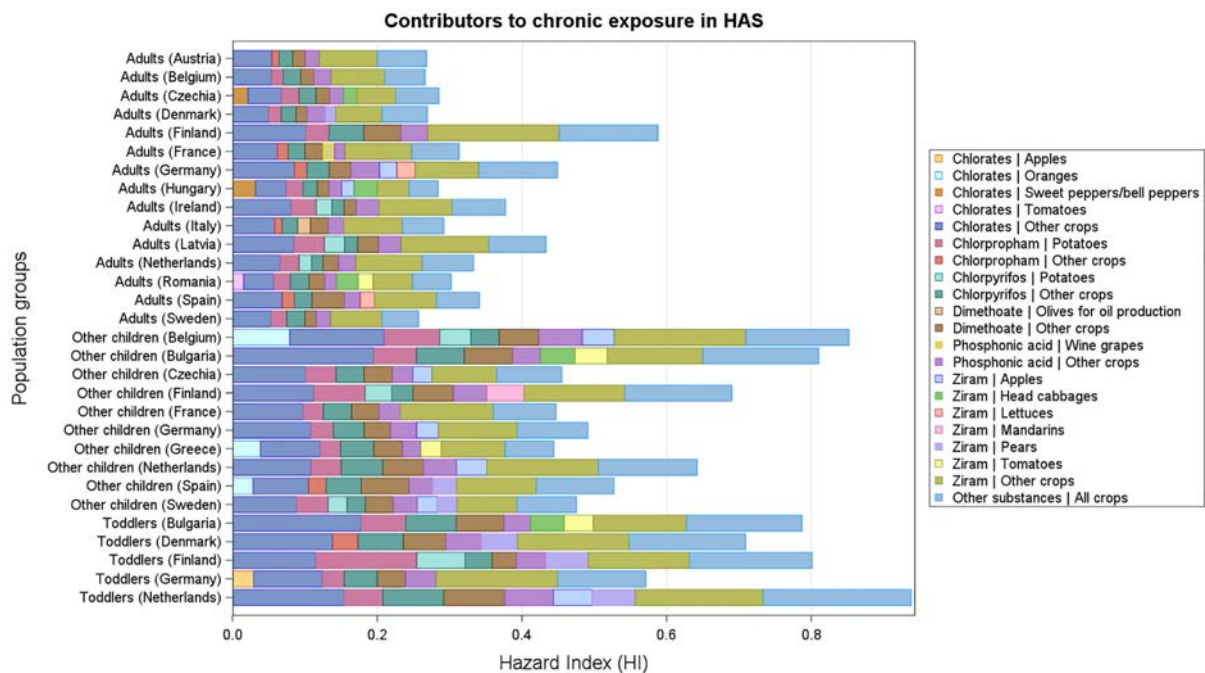
F.7.1 | Chronic

The HI estimates of the combined chronic exposure in HAS do not exceed 1 in any survey. Median HI values at the 99.9th percentile range between 0.257 in Swedish adults and 0.938 in Dutch toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.13.

The main contributing substances are ziram (25%–35%), chlorates (14%–27%), chlorpropham (3%–17%), dimethoate (4%–15%), chlorpyrifos (7%–13%), phosphonic acid (5%–10%) and metiram (4%–6%). All the other substances have an overall contribution by survey below 5%.

Apples and pears are the main contributors to the exposure to ziram, both up to 7%, followed by head cabbages (up to 11%). Tomatoes, lettuces and mandarins are other contributors. For chlorates, the contribution is mainly given by oranges, sweet peppers/bell peppers, tomatoes and apples. The contribution given by potatoes to the exposure to chlorpropham and chlorpyrifos is above 5% in 23 and 7 surveys, respectively, reaching up to 17% and 8%. As for dimethoate and phosphonic acid, the only food commodities with a contribution equal or above 5% are olives for oil production (mainly oil) and wine grapes, respectively.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.13** Median hazard index (HI) calculated for haematopoietic system and haematology (HAS) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

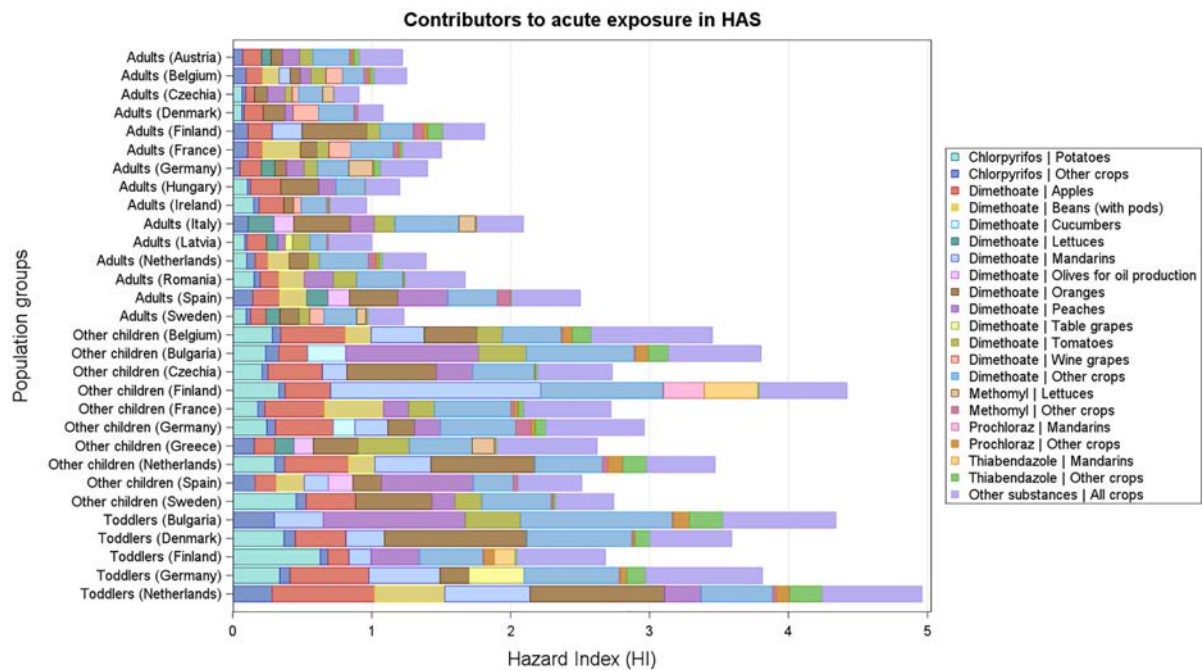
F.7.2 | Acute

The HI estimates of the combined acute exposure in HAS exceed 1 in 27 surveys. Median HI values at the 99.9th percentile range between 0.906 in adults from Czechia and 4.96 in Dutch toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.14.

Dimethoate is the main driver of the exposure, with a contribution ranging from 42% to 74%, followed by chlorpyrifos (4%–26%), methomyl (up to 12%), thiabendazole (up to 9%), prochloraz (up to 7%), ziram and indoxacarb (both 1%–6%). All the other substances have an overall contribution by survey below 5%.

Apples (up to 19%) and oranges (up to 29%) are the two major contributors to the exposure to dimethoate, being above 5% in 28 and 23 surveys, respectively. Other contributors are peaches (up to 26%), tomatoes (up to 14%), mandarins (up to 34%), beans (with pods) (up to 18%), lettuces (up to 9%), wine grapes (mainly red wine, up to 17%), followed by olives for oil production (mainly oil), table grapes and cucumbers. Potatoes are the only food giving a contribution equal or above 5% in chlorpyrifos (up to 24%), exceeding this value in 19 surveys. Lettuces are the main contributor for methomyl (up to 12%), as are mandarins for thiabendazole and prochloraz.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.14** Median hazard index (HI) calculated for haematopoietic system and haematology (HAS) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

F.8 | KIDNEY (KID)

F.8.1 | Chronic

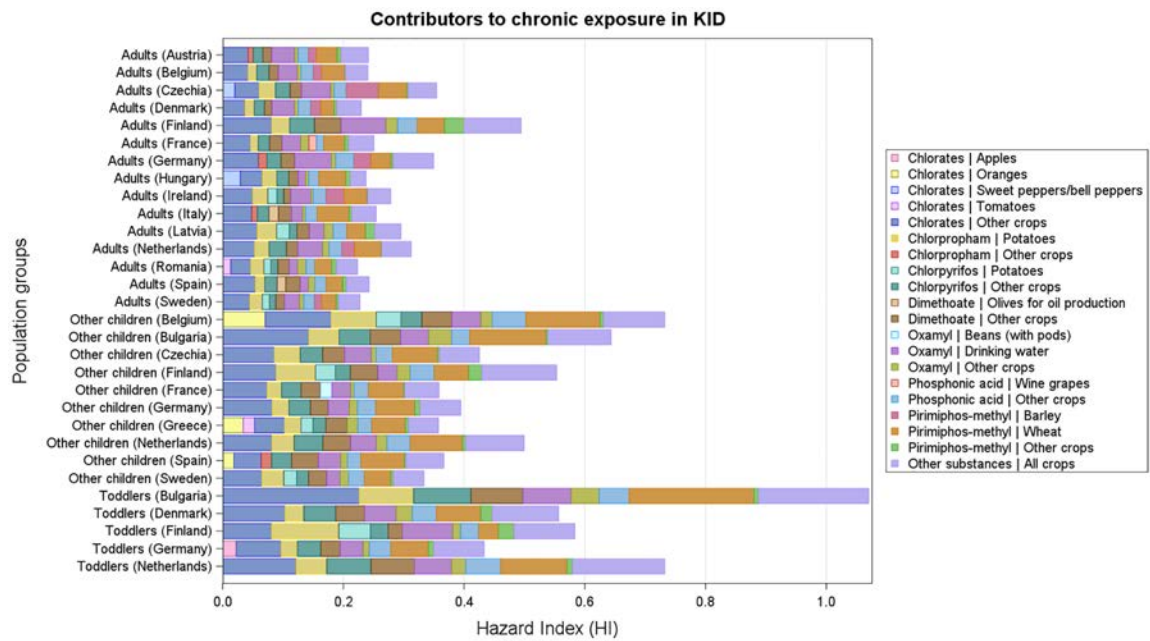
The HI estimates of the combined chronic exposure in KID exceed 1 in only one survey. Median HI values at the 99.9th percentile range from 0.223 in adults from Romania to 1.07 in Bulgarian toddlers. This exceedance seems associated to a high consumption of wheat germ by a single subject in the survey, commodity for which no processing factor was available (Annex C1, Table C.1.04). Therefore, the occurrence in, and consumed amount of, the corresponding RPC are used to calculate the exposure in a more conservative way, which can lead to higher estimations as explained in Section 3.2.1. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.15.

The main contributing substances are chlorates (14%–29%), pirimiphos-methyl (10%–29%), oxamyl (5%–19%), chlorpropham (4%–19%), dimethoate (4%–16%), chlorpyrifos (7%–14%), phosphonic acid (5%–10%), thiabendazole and pyrimethanil (up to 5%). All the other substances have an overall contribution by survey below 5%.

Wheat and barley (up to 15%) are the main contributing commodity for pirimiphos-methyl, while for chlorates the exposure is mainly driven by the consumption of oranges, sweet peppers/bell peppers, tomatoes and apples. The contribution of drinking water to the exposure to oxamyl is equal or above 5% in 29 surveys, reaching up to 17%. However, it should be highlighted that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4). For the same substance, beans (with pods) are also another main contributor. For dimethoate, the main contributors are olives for oil production (mainly oil), while for phosphonic acid the contribution is mostly given by wine grapes. Potatoes are the main contributing food commodity for both chlorpyrifos (up to 9%) and chlorpropham (up to 19%), being equal or above 5% in 9 and 26 in surveys, respectively.

Wheat is the main driver to the exposure to pirimiphos-methyl, contributing above 5% in all 30 surveys and ranging from 6% to 21%.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.15** Median hazard index (HI) calculated for the kidney (KID) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

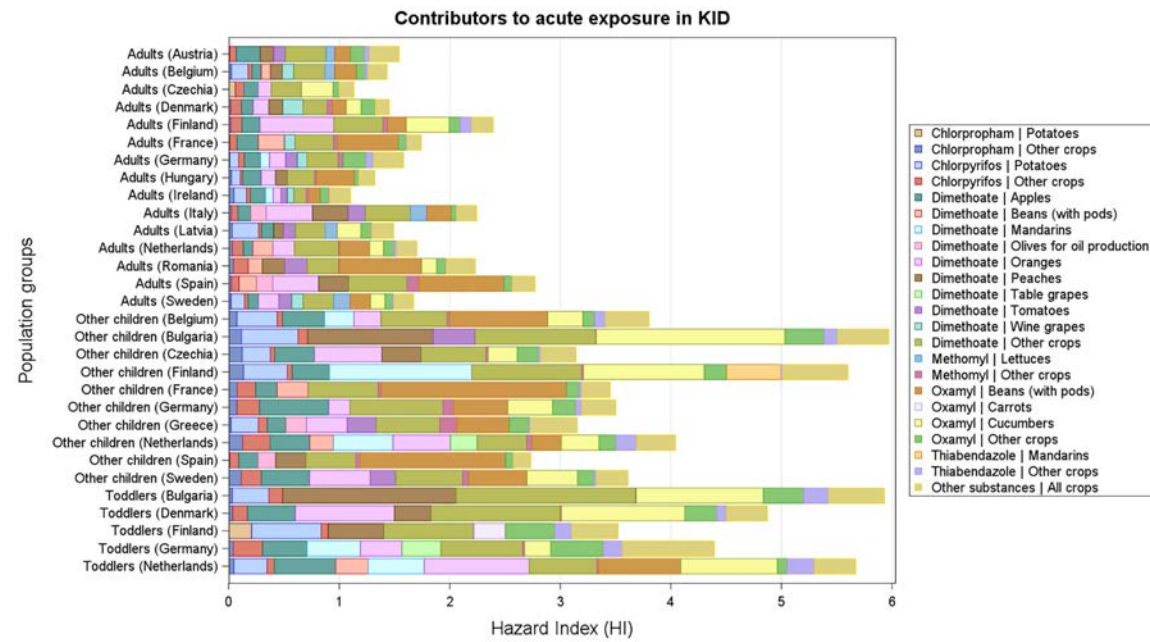
F.8.2 | Acute

The HI estimates of the combined acute exposure in KID exceed 1 in all 30 surveys. Median HI values at the 99.9th percentile range from 1.1 in adults from Ireland to 5.97 in Bulgarian children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.16.

Two substances are the main drivers of the exposure, namely dimethoate (32%–70%) and oxamyl (12%–52%), followed by chlorpyrifos (3%–20%), methomyl and thiabendazole (up to 9%), chlorpropham (up to 6%) and prochloraz (up to 5%). All the other substances have an overall contribution by survey below 5%.

For dimethoate, apples and oranges have a contribution above 5% in 25 and 19 surveys, with a contribution reaching up to 18% and 28%, respectively. Other contributors are peaches (up to 26%), tomatoes (up to 9%), beans (with pods) (up to 14%), mandarins (up to 23%) and wine grapes (mainly red wine, up to 13%). A lower contribution is also given by olives for oil production (mainly oil) and table grapes. Beans (with pods) (up to 49%) and cucumbers (up to 29%) are the main contributors for oxamyl, followed by carrots. For both chlorpyrifos (up to 18%) and chlorpropham, potatoes are the main contributing food commodity, exceeding 5% in 14 surveys for the first. As for methomyl and thiabendazole, lettuces (up to 9%) and mandarins are, respectively, the main contributors.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.16** Median hazard index (HI) calculated for the kidney (KID) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.



F.9 | LIVER (LIV)

F.9.1 | Chronic

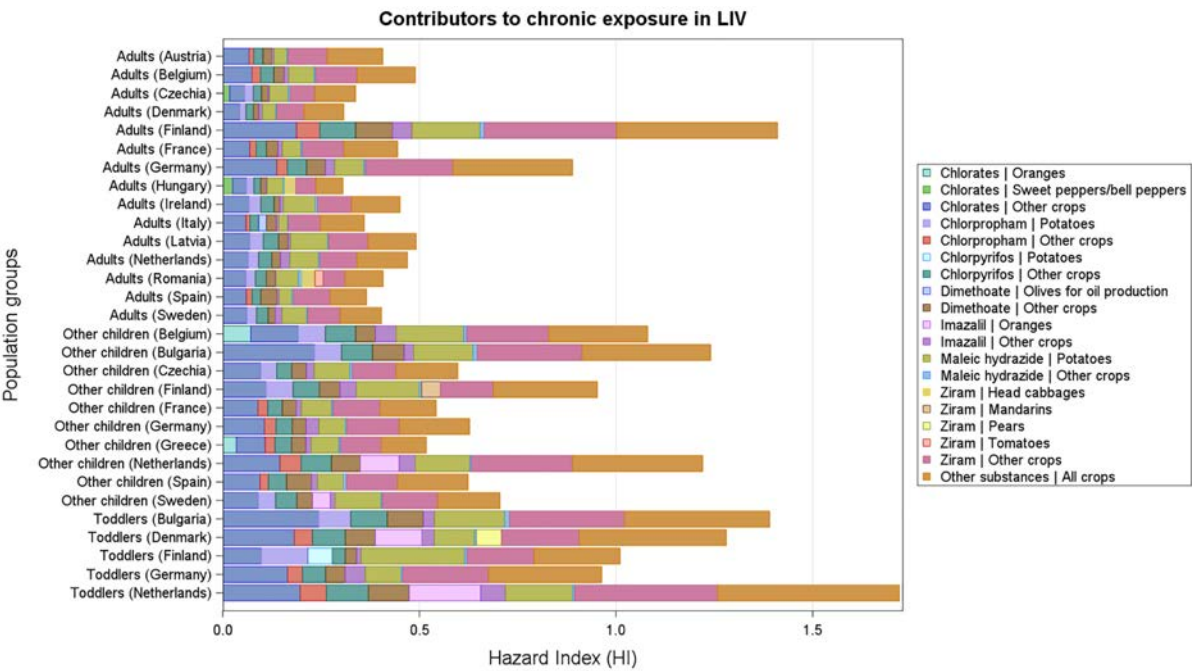
The HI estimates of the combined chronic exposure in LIV exceed 1 in eight surveys. Median HI values at the 99.9th percentile range from 0.305 in Hungarian adults to 1.72 in Dutch toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.17.

The main contributors to the exposure are ziram (17%–27%), maleic hydrazide (7%–27%), chlorates (10%–21%), imazalil (up to 14%), dimethoate (3%–13%), chlorpropham (3%–12%), chlorpyrifos (6%–9%), cypermethrin (2%–9%) and phosphonic acid (4%–8%). All the other substances have an overall contribution by survey below 5%.

Head cabbages, tomatoes, mandarins and pears are the main contributors for ziram, as are sweet peppers/bell peppers and oranges for chlorates. Oranges are also the main contributor to the exposure to imazalil, and olives for oil production (mainly oil) to dimethoate.

Potatoes are the main contributing food commodity to the exposure to chlorpyrifos, chlorpropham (up to 12%) and maleic hydrazide (6%–26%), being above 5% in all 30 surveys for the last one.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.17** Median hazard index (HI) calculated for the liver (LIV) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

F.9.2 | Acute

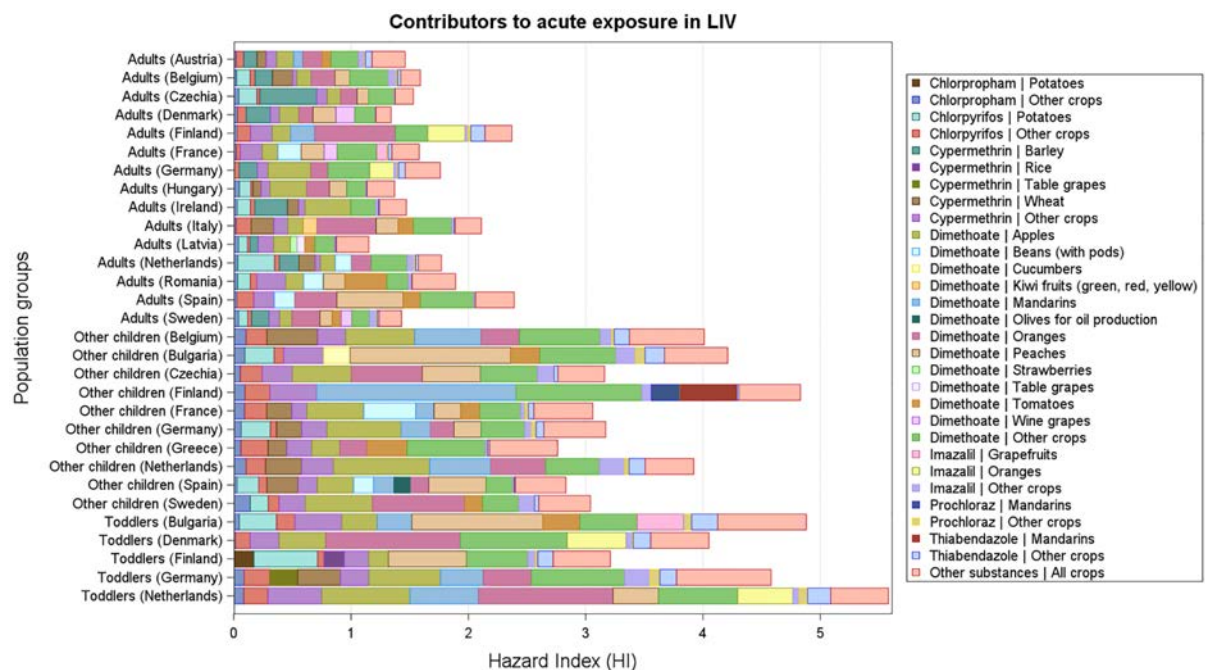
The HI estimates of the combined acute exposure in LIV exceed 1 in all 30 surveys. Median HI values at the 99.9th percentile vary between 1.15 in adults from Latvia and 5.58 in Dutch toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.18.

Dimethoate is the main driver of the exposure, with a contribution varying from 37% to 71%. Other contributing substances are cypermethrin (6%–38%), chlorpyrifos (2%–20%), imazalil (up to 14%), thiabendazole (up to 10%), chlorpropham and prochloraz (both up to 5%). All the other substances have an overall contribution for survey below 5%.

With respect to dimethoate, apples (up to 26%) exceed 5% in 27 surveys and are the main contributor along with oranges (up to 29%) and peaches (up to 33%), followed by mandarins (up to 35%), tomatoes (up to 19%) and beans (with pods) (up to 14%). Other contributors are wine grapes (mainly red wine), table grapes and kiwi fruits, cucumbers, olives for oil production (mainly oil) and strawberries. Wheat is the main contributor for cypermethrin (up to 11%), together with barley (up to 32%), and followed by rice and tables grapes. The contribution to the exposure to imazalil is mainly given by oranges (mostly juices) and grapefruits, while that of thiabendazole and prochloraz by mandarins. Potatoes are the main contributing food commodity for both chlorpyrifos (up to 18%) and chlorpropham, with values above 5% in 14 surveys for the first.

For further details, see also Annex C2, Table C.2.03.





**FIGURE F.18** Median hazard index (HI) calculated for the liver (LIV) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

**F.10 | MAMMARY GLAND (MAG)**

**F.10.1 | Chronic**

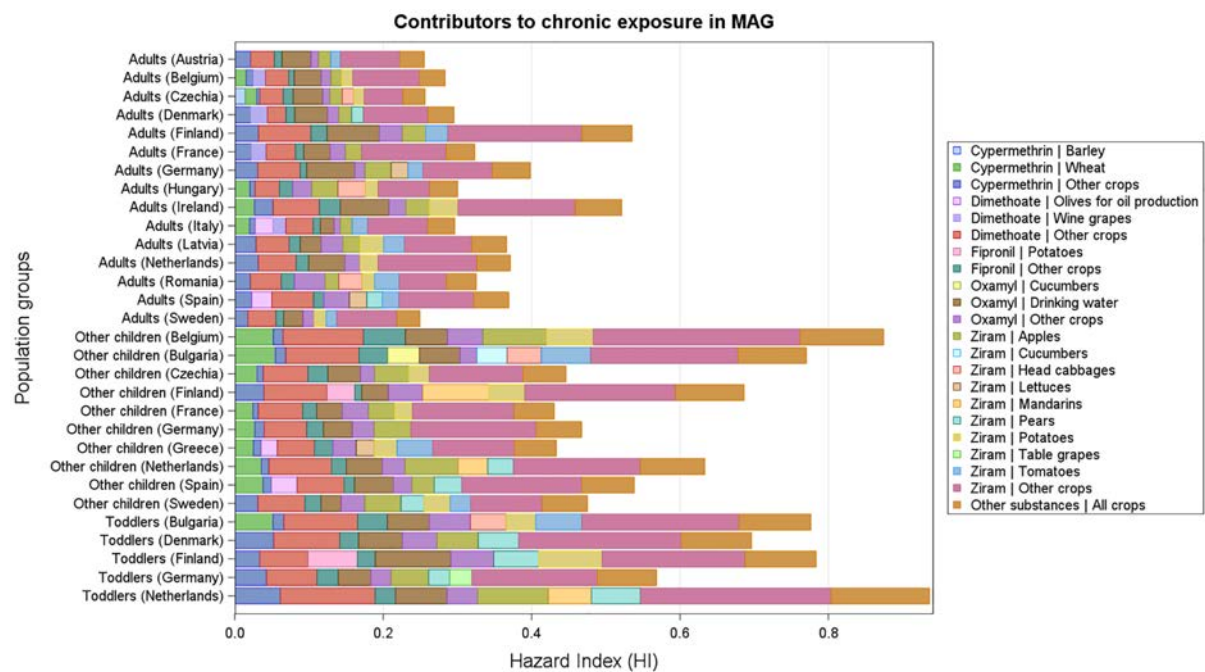
The HI estimates of the combined chronic exposure in MAG do not exceed 1 in any survey. Median HI values at the 99.9th percentile range from 0.249 in Swedish adults to 0.936 in Dutch toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.19.

The major contributors to the exposure are ziram (38%–53%), dimethoate (8%–26%), oxamyl (7%–20%), cypermethrin (4%–13%), fipronil (2%–12%), metiram (7%–10%). All the other substances have an overall contribution by survey below 5%.

For ziram, the food commodities that mostly contribute to the exposure are apples (up to 12%), being equal or above 5% in 22 surveys, followed by potatoes and tomatoes (up to 11%), pears (up to 8%) and head cabbages (up to 12%). Mandarins, lettuces, cucumbers and table grapes are other contributors. Olives for oil production (mainly oil) and wine grapes (mainly red wine) are the main contributing commodities for dimethoate. The exposure to cypermethrin is mainly driven by the consumption of wheat (up to 7%) and barley, while potatoes are the main contributing food commodity for fipronil.

The contribution of drinking water to the exposure to oxamyl exceeds 5% in 26 surveys, reaching up to 16%. However, it should be noted that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4). Another contributor are cucumbers.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.19** Median hazard index (HI) calculated for the mammary gland (MAG) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

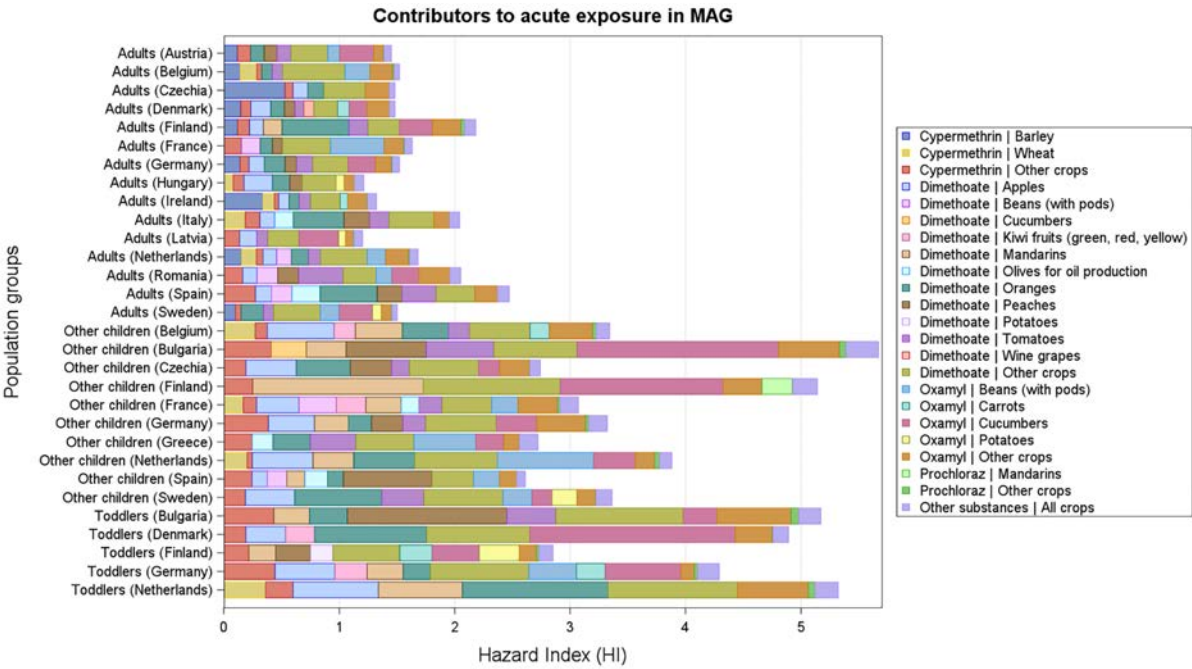
F.10.2 | Acute

The HI estimates of the combined acute exposure in MAG exceed 1 in all 30 surveys. Median HI values at the 99.9th percentile range from 1.2 in adults from Latvia to 5.67 in Bulgarian children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.20.

Dimethoate and oxamyl are the main drivers of the exposure, the first ranging from 40% to 77% and the second from 7% to 43%. Other contributing substances are cypermethrin (4%–40%) and prochloraz (up to 5%). All the other substances have an overall contribution by survey below 5%.

The food commodities mostly contributing to the exposure to dimethoate are oranges (up to 27%), apples (up to 21%) and tomatoes (up to 19%), all being equal or above 5% in at least 20 surveys, together with peaches and mandarins (both up to 29%) and followed by beans (with pods) (up to 11%) and olives for oil production (mainly oil, up to 10%). Other contributors are kiwi fruits, potatoes, wine grapes (mainly red wine) and cucumbers. For oxamyl, major contributors are cucumbers (up to 36%), beans (with pods) (up to 28%), potatoes (up to 12%) and carrots (up to 10%). Barley and wheat are the main contributing commodities to the exposure to cypermethrin, respectively, up to 36% and 10%, as mandarins are for prochloraz.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.20** Median hazard index (HI) calculated for the mammary gland (MAG) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

F.11 | MALE REPRODUCTIVE SYSTEM (MRS)

To assess the cumulative exposure in MRS, only male participants were considered in the assessment. In cases where the number of subjects in the dietary survey was below 300 after the exclusion of female individuals, the survey was not considered in the calculations. Overall, 21 surveys were considered for the MRS combined exposure calculations.

F.11.1 | Chronic

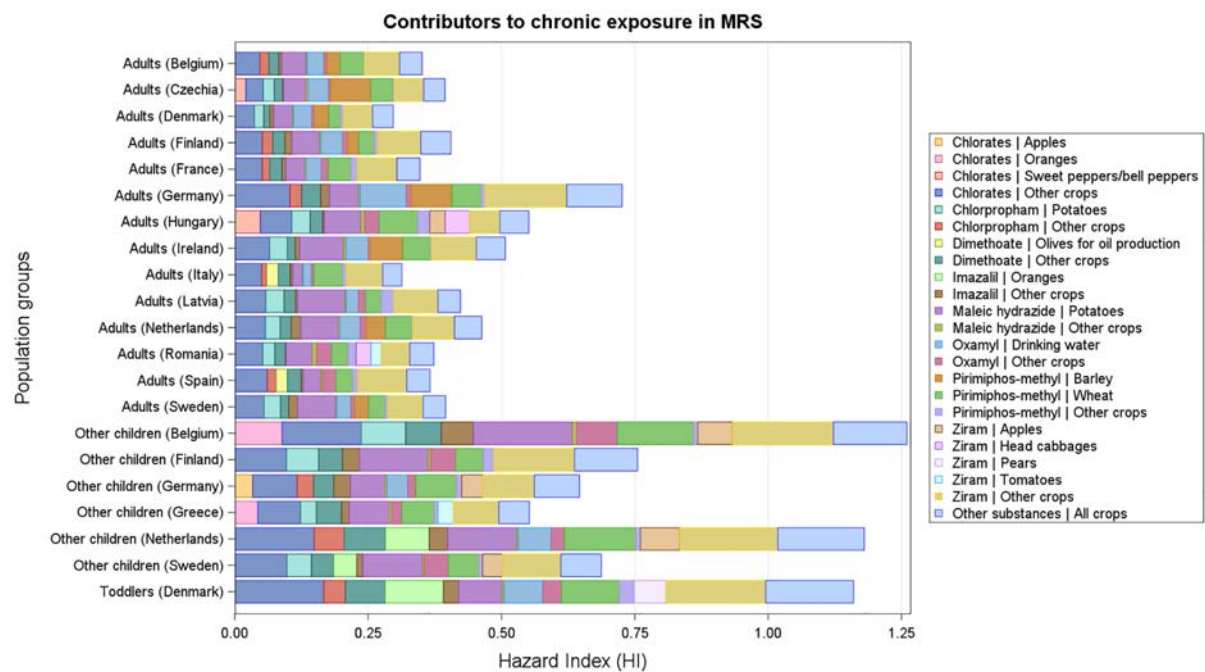
The HI estimates of the combined chronic exposure in MRS exceed 1 in three surveys. Median HI values at the 99.9th percentile range from 0.297 in Danish adults to 1.26 in Belgian children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.21.

The substances that mainly contribute to the exposure are pirimiphos-methyl (9%–30%), ziram (14%–27%), chlorates (12%–22%), maleic hydrazide (6%–21%), dimethoate (3%–14%), oxamyl (3%–13%), imazalil (up to 12%) and chlorpropham (3%–8%). All the other substances have an overall contribution by survey below 5%.

For pirimiphos-methyl, wheat and barley (up to 19%) are the main contributors, as are apples for ziram (up to 6%), followed by head cabbages, tomatoes and pears. Apples are also among the main contributing commodities for chlorates, along with sweet peppers/bell peppers and oranges (mostly juices). Olives for oil production (mainly oil), drinking water and oranges are the main contributors for dimethoate, oxamyl (up to 12%) and imazalil, respectively. It should be clarified that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4).

Potatoes are also the main contributing food commodity to the exposure to chlorpropham (up to 8%) and maleic hydrazide (6%–21%), with a contribution above 5% in all 21 surveys for the latter, as in the case of wheat for pirimiphos-methyl (7%–17%).

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.21** Median hazard index (HI) calculated for the male reproductive system (MRS) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

F.11.2 | Acute

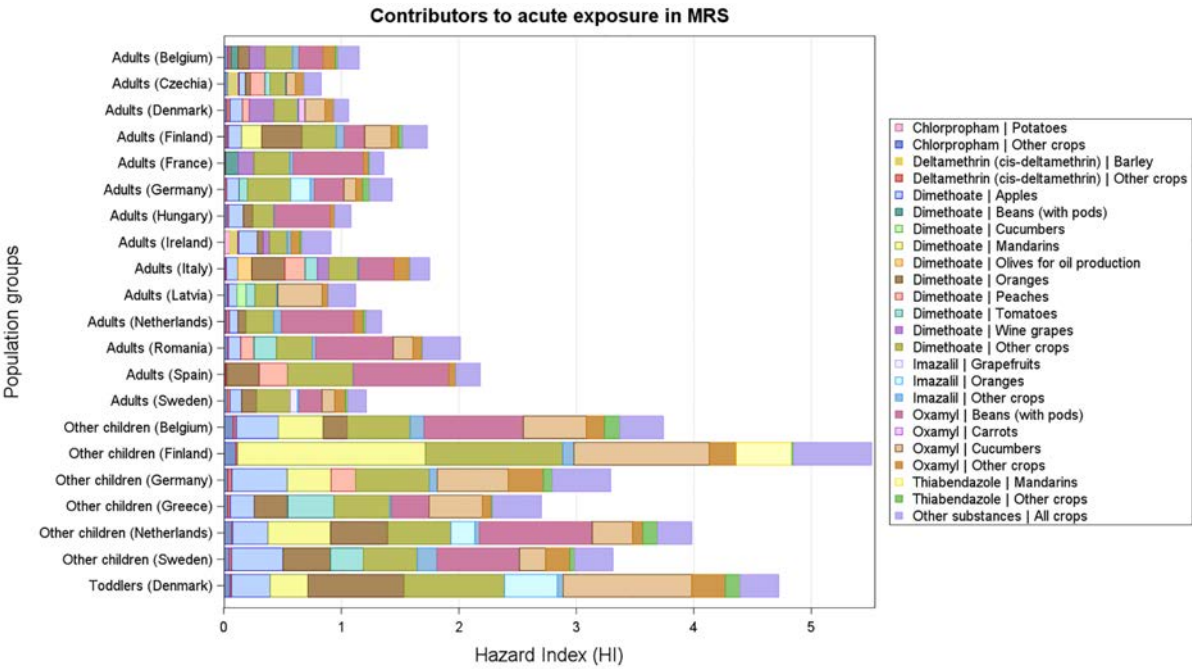
The HI estimates of the combined acute exposure in MRS exceed 1 in 19 surveys. Median HI values at the 99.9th percentile range from 0.827 in adults from Czechia to 5.51 in Finnish children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.22.

The main drivers of the exposure are dimethoate (28%–64%) and oxamyl (9%–52%), with other contributors being imazalil (up to 14%), deltamethrin (cis-deltamethrin) (up to 11%), thiabendazole (up to 9%) and chlorpropham (up to 6%). All the other substances have an overall contribution by survey below 5%.

The main contributing food commodities for dimethoate are apples (up to 17%) and oranges (up to 20%), being equal or above 5% in 17 and 14 surveys, respectively; other important contributors are tomatoes (up to 15%), followed by mandarins (up to 29%), peaches (up to 15%) and wine grapes (mainly red wine, up to 20%). Beans (with pods), cucumbers and olives for oil production (mainly oil), are other contributors. As for oxamyl, beans (with pods) (up to 46%) and cucumbers (up to 34%) are the main contributors, meeting or exceeding 5% in 14 surveys, followed by carrots. The exposure to imazalil, deltamethrin (cis-deltamethrin), thiabendazole and chlorpropham is mainly driven by oranges and grapefruits, barley, mandarins and potatoes, respectively.

For further details, see also Annex C2, Table C.2.03.





**FIGURE F.22** Median hazard index (HI) calculated for the male reproductive system (MRS) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

F.12 | MUSCULAR SYSTEM (MUS)

F.12.1 | Chronic

The HI estimates of the combined chronic exposure in MUS do not exceed 1 in any survey. Median HI values at the 99.9th percentile range from 0.188 in adults from Czechia to 0.778 in Bulgarian toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.23.

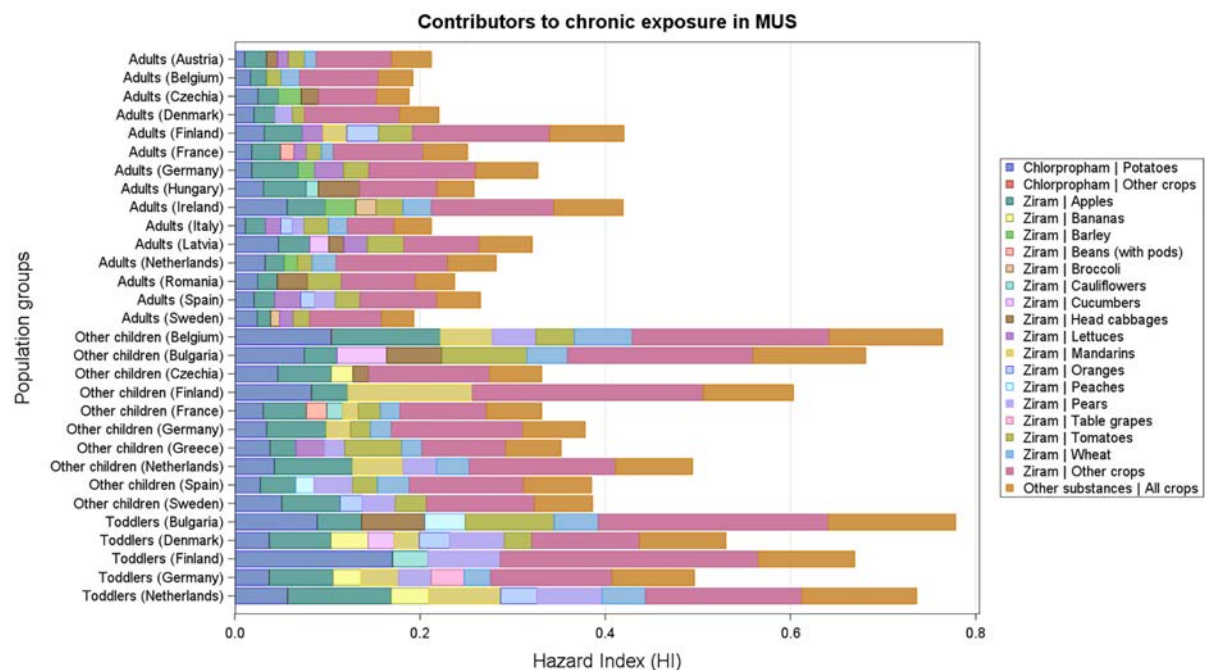
Ziram is the main driver of the chronic exposure in MUS, with a contribution ranging from 59% to 76%. Other contributors are chlorpropham (5%–25%), metiram (11%–14%) and emamectin (2%–7%). All the other substances have an overall contribution by survey below 5%.

With respect to ziram, the exposure is mainly driven by apples (up to 18%), contributing for more than 5% in 29 surveys, followed by tomatoes (up to 17%), wheat (up to 10%), pears (up to 12%), mandarins (up to 22%), lettuces (up to 11%), head cabbages (up to 17%) and oranges (up to 8%). Barley is another contributor, along with bananas, cucumbers, cauliflowers, beans (with pods), peaches, broccoli and table grapes.

Potatoes are the main contributing food commodity for chlorpropham (5%–25%), with a contribution exceeding 5% in all 30 surveys.

For further details, see also Annex C1, Table C.1.03.





**FIGURE F.23** Median hazard index (HI) calculated for the muscular system (MUS) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

**F.12.2 | Acute**

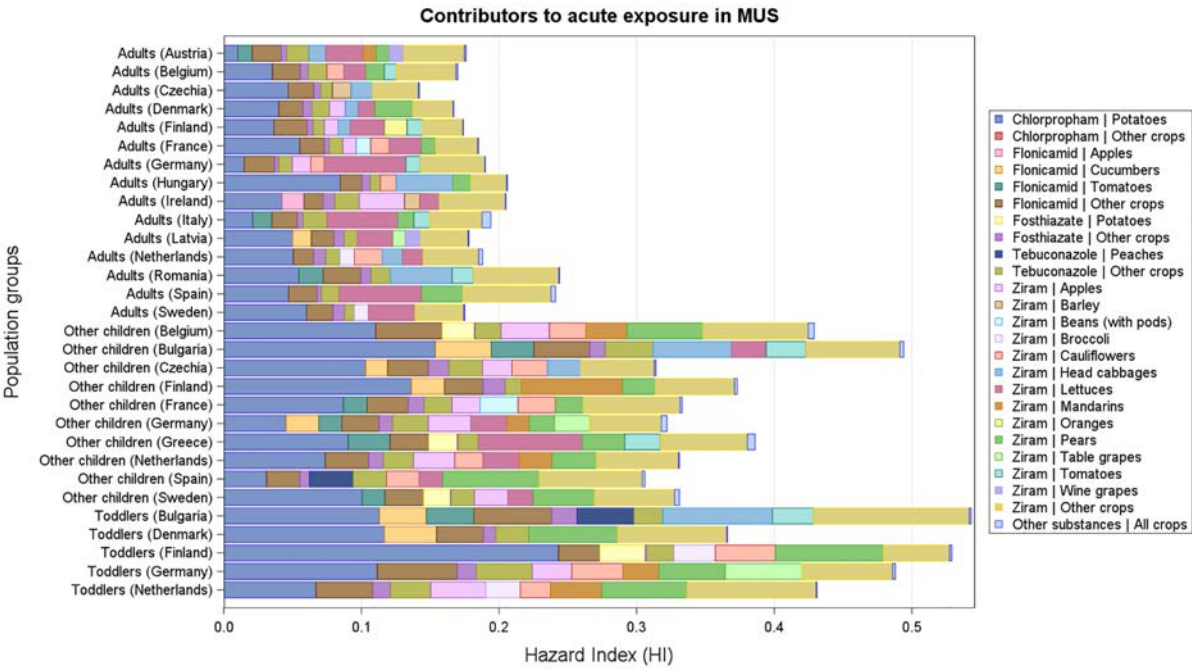
The HI estimates of the combined acute exposure in MUS do not exceed 1 in any survey. Median HI values at the 99.9th percentile range from 0.142 in adults from Czechia to 0.543 in Bulgarian toddlers. The substance/commodity combinations contributing for at least 5% to the exposure in any survey are reported in Figure F.24.

The main contributors to the exposure are ziram (36%–74%) and chlorpropham (6%–46%), followed by flonicamid (6%–23%), tebuconazole (3%–18%) and fosthiazate (1%–6%). All the other substances have an overall contribution by survey below 5%.

The main contributors to the exposure to ziram are pears (up to 23% and above 5% in 19 surveys), lettuces (up to 31%), apples (up to 16%), cauliflowers (up to 11%), head cabbages and mandarins (up to 20%) and tomatoes (up to 7%). Other contributors are broccoli, table grapes, barley, beans (with pods), wine grapes and oranges. As for flonicamid, tomatoes and cucumbers are the main contributors, respectively, up to 8% and 10%, followed by apples. The main contributor for tebuconazole are peaches, as are potatoes for fosthiazate.

The exposure to chlorpropham is mainly driven by the consumption of potatoes (6%–46%), with values above 5% in all 30 surveys.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.24** Median hazard index (HI) calculated for the muscular system (MUS) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

**F.13 | PARATHYROID GLAND (PAG)**

**F.13.1 | Chronic**

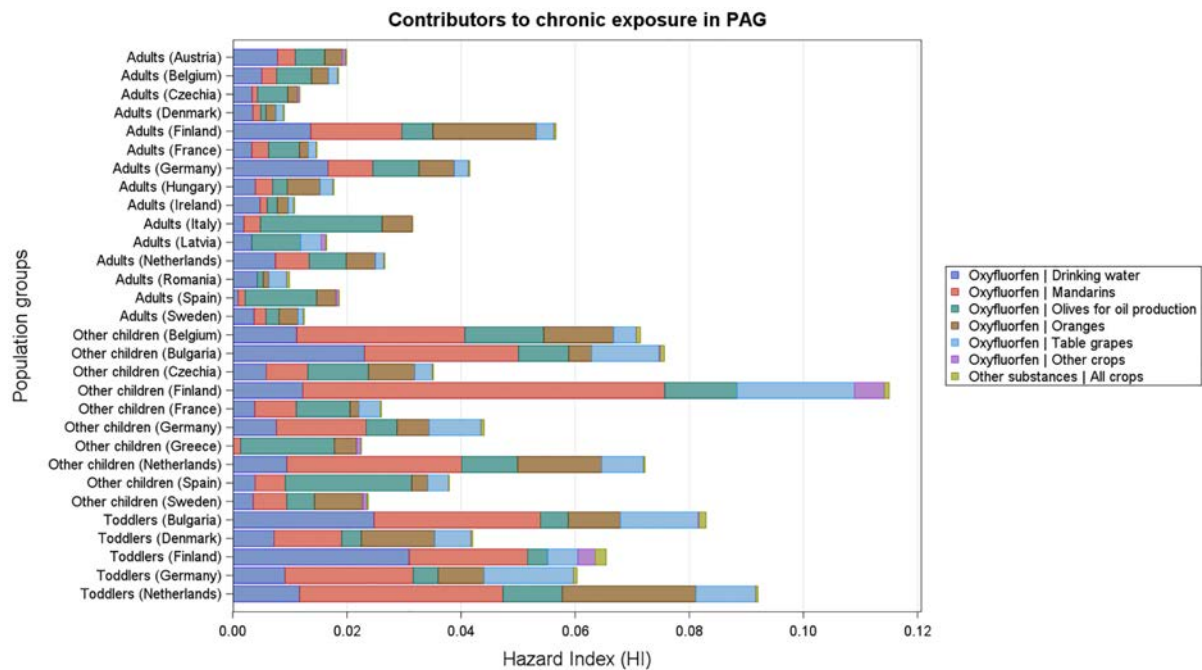
The HI estimates of the combined chronic exposure in PAG do not exceed 1 in any survey. Median HI values at the 99.9th percentile vary from 0.00898 in Danish adults to 0.115 in Finnish children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.25.

The exposure is mainly driven by one substance, namely oxyfluorfen (96%–100%). All the other substances have an overall contribution by survey below 5%.

The main contributing food commodities are olives for oil production (mainly oil, 5%–73%), drinking water (up to 47%), mandarins (up to 55%) and oranges (up to 36%), all equal or above 5% in more than 25 surveys and olives in all 30 of them. It should be highlighted that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4). Another major contributor are table grapes (up to 31%).

For this organ, it was noticed that for olives calculations are based on a relatively smaller occurrence data set compared to other contributors. For this reason, a certain degree of uncertainty in the results cannot be excluded but does not represent an issue as the exposure is anyways much below the HI threshold of 1. This applies to all the three population classes.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.25** Median hazard index (HI) calculated for the parathyroid gland (PAG) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

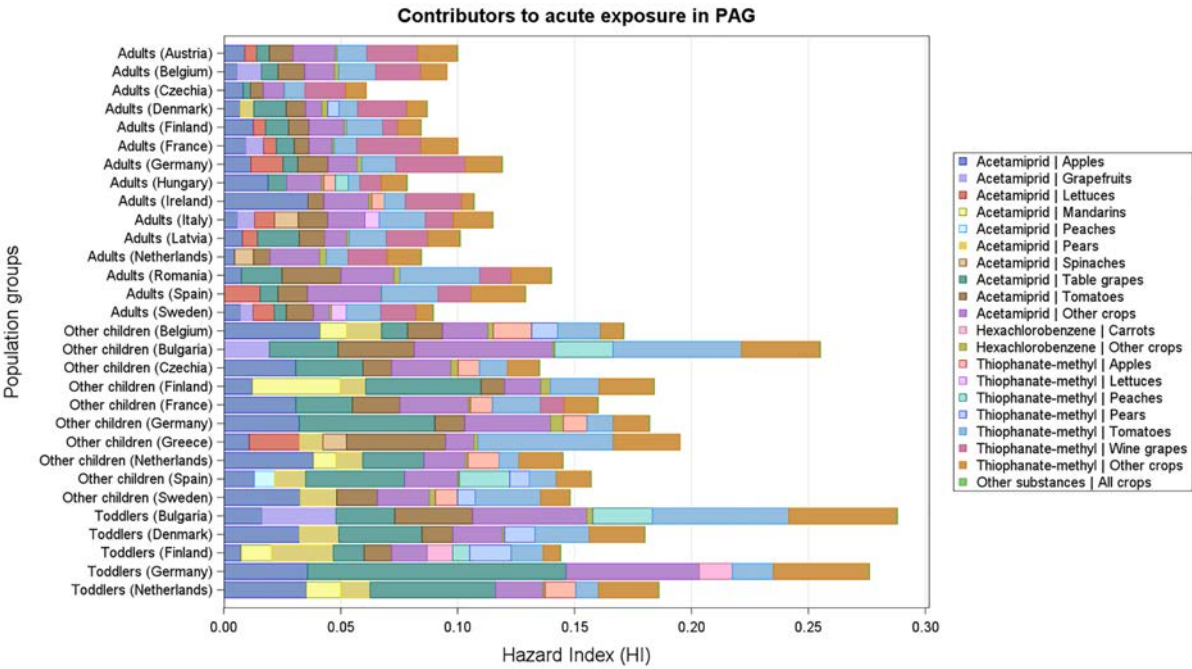
F.13.2 | Acute

The HI estimates of the combined acute exposure in PAG do not exceed 1 in any survey. Median HI values at the 99.9th percentile vary from 0.0608 in adults from Czechia to 0.288 in Bulgarian toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.26.

The main contributors to the acute exposure in PAG are acetamiprid (42%–77%) and thiophanate-methyl (20%–57%), with a minor contribution also given by hexachlorobenzene (up to 8%). All the other substances have an overall contribution by survey below 5%.

The contribution of apples to the exposure to acetamiprid is equal or above 5% in 28 surveys, thus representing the main contributing food commodity for this substance (up to 34%), followed by table grapes (up to 40%), tomatoes (up to 22%), pears and lettuces (respectively, up to 18% and 12%), grapefruits (up to 11%) and mandarins (up to 20%). Spinaches and peaches are other minor contributors. As for thiophanate-methyl, wine grapes are among the main contributors (up to 29%), together with apples (up to 10%), pears (up to 12%) and peaches (up to 14%). Lettuces are minor contributors. Carrots are the main contributing commodity to the exposure to hexachlorobenzene.

Tomatoes have a contribution to the exposure to thiophanate-methyl equal or above 5% in all 30 surveys (5%–30%). For further details, see also Annex C2, Table C.2.03.



**FIGURE F.26** Median hazard index (HI) calculated for the parathyroid gland (PAG) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

**F.14 | Pituitary gland (PIG)**

**F.14.1 | Chronic**

The HI estimates of the combined chronic exposure in PIG do not exceed 1 in any survey. Median HI values at the 99.9th percentile range from 0.0879 in Austrian adults to 0.433 in Bulgarian toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.27.

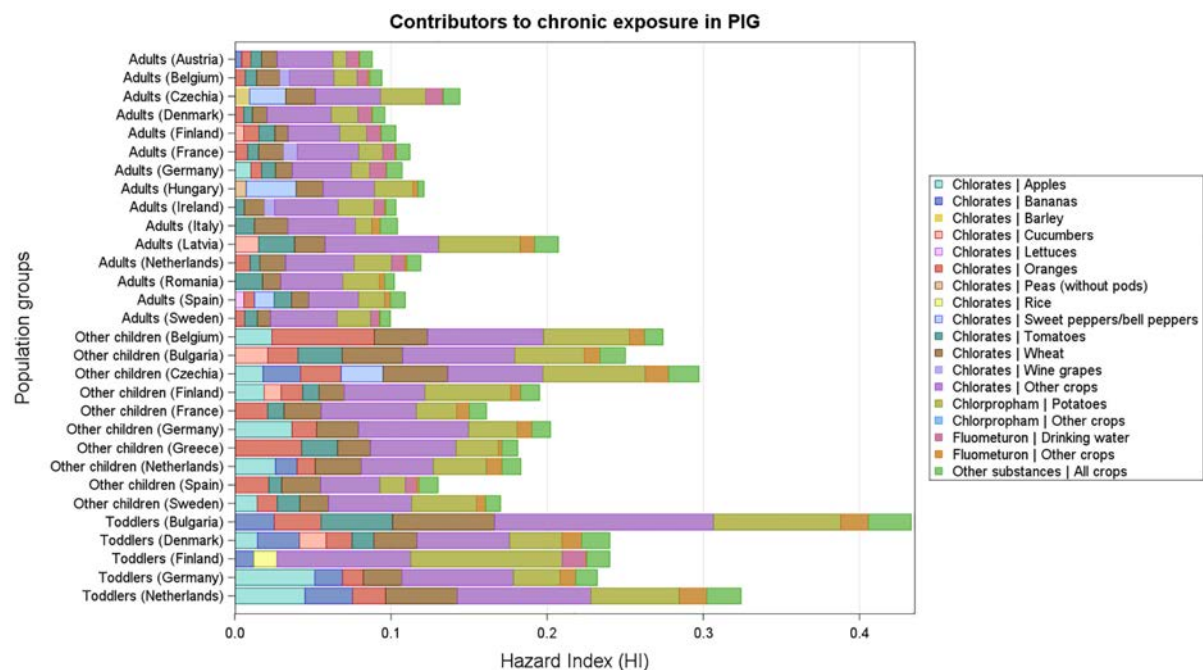
The chronic exposure in PIG is mainly driven by chlorates (47%–78%), followed by chlorpropham (10%–40%), fluometuron (1%–10%), abamectin (2%–7%) and oxyfluorfen (1%–5%). All the other substances have an overall contribution by survey below 5%.

Wheat (up to 21%), oranges (mostly juices, up to 24%) and tomatoes (up to 17%) are the main contributing food commodities for chlorates, all meeting or exceeding 5% in 29, 23 and 21 surveys, respectively. Apples (mostly juices, up to 22%), bananas (up to 11%) and cucumbers (up to 9%) are also contributors, followed by sweet peppers/bell peppers, wine grapes, barley, rice, peas (without pods) and lettuces. Drinking water is the main contributor to the exposure to fluometuron (up to 10%). For this specific RPC, it should be highlighted that estimates on contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4).

The consumption of potatoes is the main driver of the exposure to chlorpropham (10%–40%), being equal or above 5% in all 30 surveys.

For further details, see also Annex C1, Table C.1.03.





**FIGURE F.27** Median hazard index (HI) calculated for the pituitary gland (PIG) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

**F.14.2 | Acute**

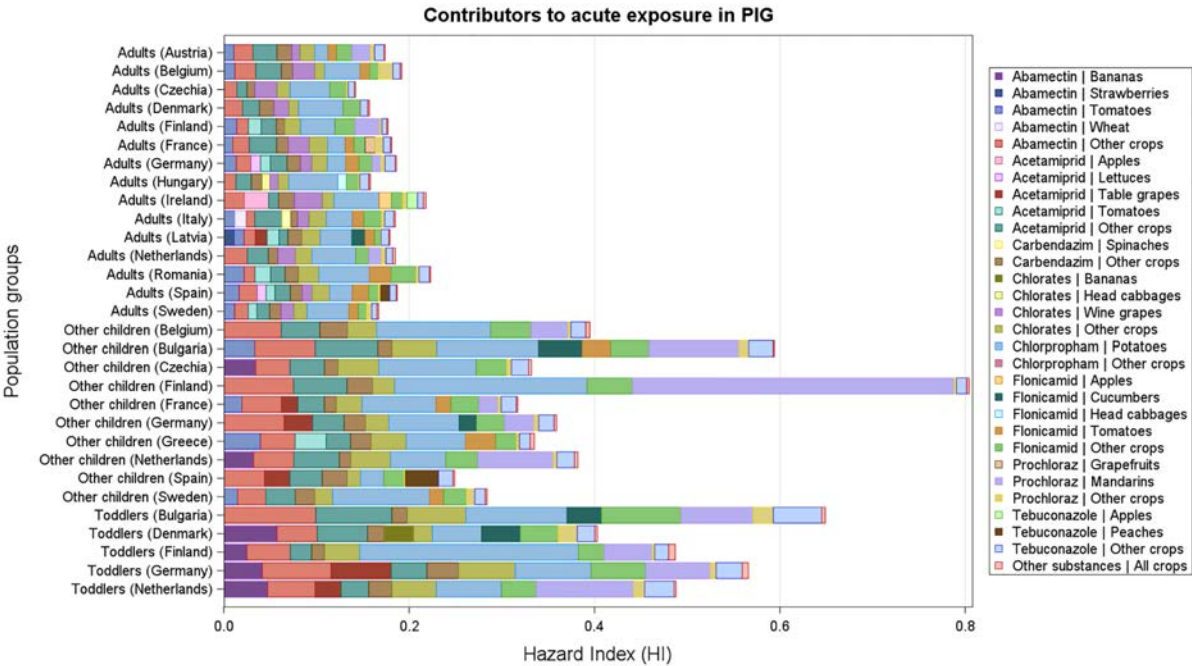
The HI estimates of the combined acute exposure in PIG do not exceed 1 in any survey. Median HI values at the 99.9th percentile range from 0.142 in adults from Czechia to 0.804 in Finnish children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.28.

The main drivers of the acute exposure in PIG are chlorpropham (8%–48%), prochloraz (up to 43%), chlorates (3%–27%), abamectin (8%–25%), acetamiprid (5%–25%), flonicamid (6%–22%), tebuconazole (1%–21%) and carbendazim (3%–11%). All the other substances have an overall contribution by survey below 5%.

Mandarins are then the main contributing food commodity for prochloraz (up to 43%) followed by grapefruits, while for chlorates the main contributors are wine grapes (mostly white wine, up to 17%), followed by bananas and head cabbages. Bananas also contribute to the exposure to abamectin (up to 14%), together with tomatoes (up to 12%), wheat and strawberries. As for acetamiprid, tomatoes and table grapes are major contributors (respectively, up to 10% and 11%), followed by lettuces and apples. Tomatoes, along with cucumbers, are also the main contributing commodity for flonicamid, both contributing up to 10%, with apples and head cabbages. As for tebuconazole, the exposure is mainly driven by the consumption of peaches and apples, while that to carbendazim by spinaches.

Potatoes are a major contributor to the exposure to chlorpropham (8%–48%), exceeding 5% in all 30 surveys.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.28** Median hazard index (HI) calculated for the pituitary gland (PIG) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

**F.15 | REPRODUCTIVE AND DEVELOPMENTAL TOXICITY (RDT)**

**F.15.1 | Chronic**

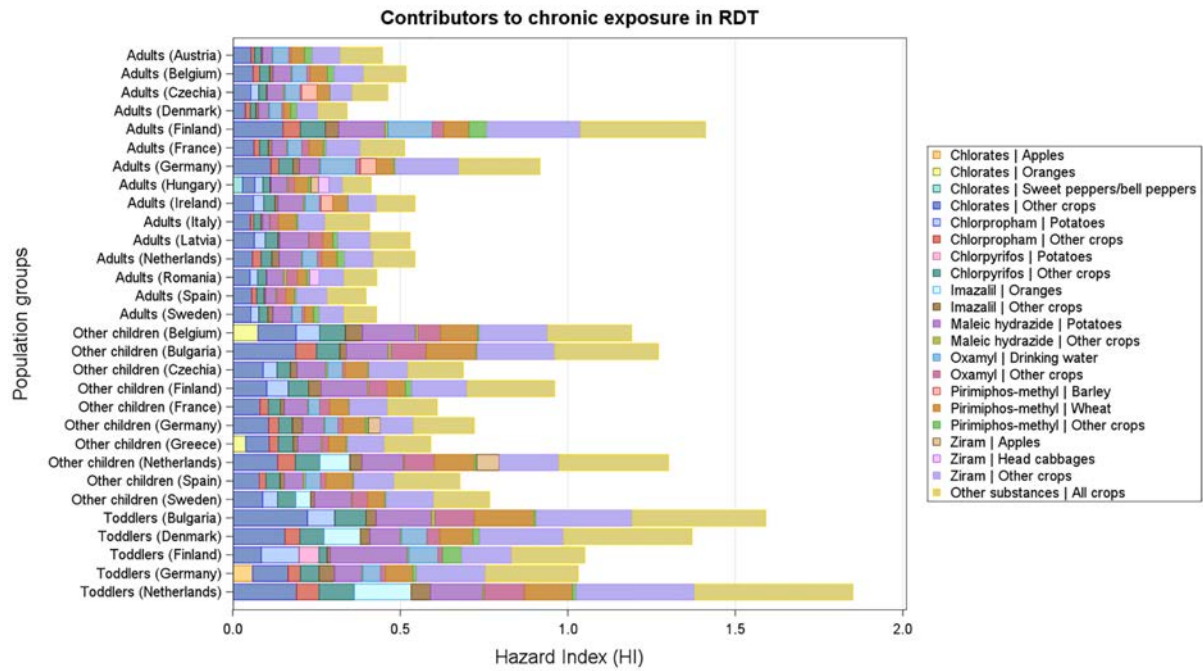
The HI estimates of the combined chronic exposure related to RDT exceed 1 in nine surveys. Median HI values at the 99.9th percentile range from 0.34 in Danish adults to 1.85 in Dutch. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.29.

Ziram (14%–24%), maleic hydrazide (5%–22%), pirimiphos-methyl (6%–19%), chlorates (8%–18%), oxamyl (3%–13%), imazalil (up to 12%), dimethoate (3%–11%), chlorpropham (2%–11%) and chlorpyrifos (4%–8%) are the main drivers of the chronic exposure. All the other substances have an overall contribution by survey below 5%.

Apples are among the main contributing food commodities for both ziram and chlorates. Another contributor to the exposure to ziram are head cabbages, while oranges (mostly juices) and sweet peppers/bell peppers are other ones for chlorates. Oranges are also the main contributing commodity for imazalil. Potatoes are the main driver of the exposure to maleic hydrazide, chlorpropham (up to 11%) and chlorpyrifos. Wheat is a major contributor for pirimiphos-methyl (up to 13%), being above 5% in 29 surveys, followed by barley. Drinking water is the main contributor to the exposure to oxamyl (up to 12%). However, it should be clarified that the occurrence data on drinking water result from imputation and these estimates should then be considered with caution (see Appendix C, Section C.1.1.4).

For maleic hydrazide, the contribution given by the consumption of potatoes is above 5% in all 30 surveys and varies between 5% and 22%.

For further details, see also Annex C1, Table C.1.03.



**FIGURE F.29** Median hazard index (HI) calculated for reproductive and developmental toxicity (RDT) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

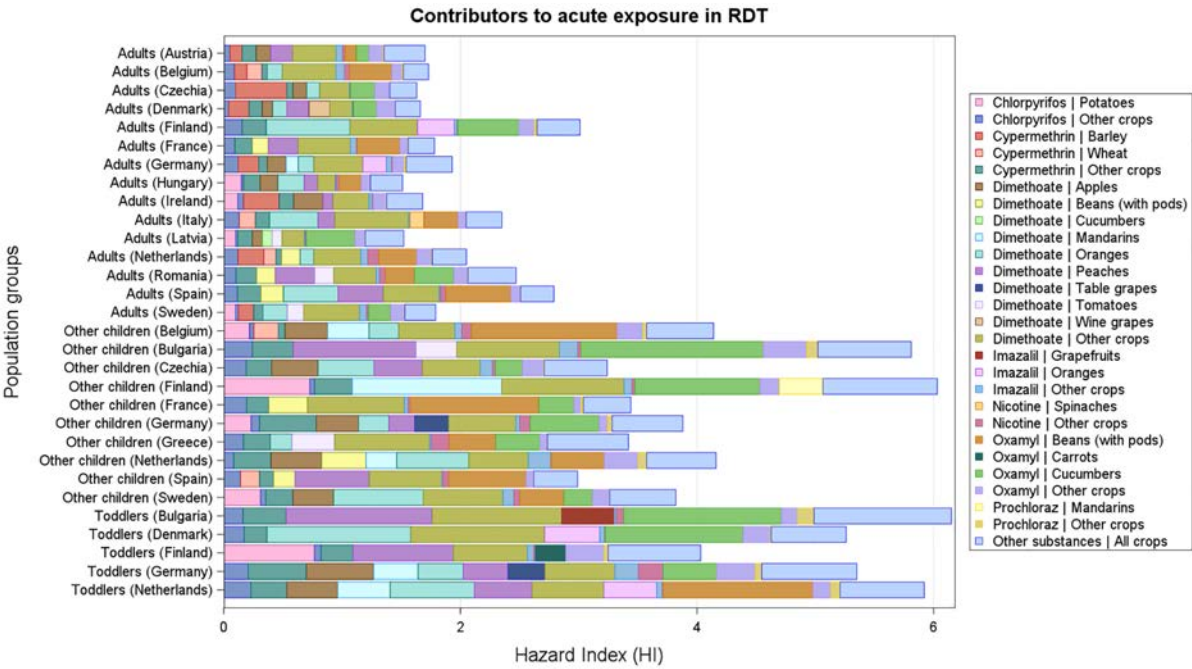
### F.15.2 | Acute

The HI estimates of the combined acute exposure related to RDT exceed 1 in all 30 surveys. Median HI values at the 99.9th percentile range from 1.51 in Hungarian adults to 6.15 in toddlers from Bulgaria. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.30.

The main contributors to the acute exposure in RDT are dimethoate (29%–54%), oxamyl (5%–42%), cypermethrin (4%–30%), chlorpyrifos (2%–20%), imazalil (up to 13%), prochloraz (up to 6%) and nicotine (up to 5%). All the other substances have an overall contribution by survey below 5%.

For dimethoate, oranges are the main contributing commodity (up to 24%) with a contribution equal or above 5% in 19 surveys, followed by peaches (up to 21%), apples (up to 15%), beans (with pods) (up to 10%), mandarins (up to 21%) and tomatoes (up to 11%). Minor, but still important contributors are table grapes, wine grapes and cucumbers. As for oxamyl, the exposure is mainly driven by the consumption of cucumbers (up to 27%) and beans (with pods) (up to 32%), followed by carrots. Barley (up to 27%) and wheat (up to 7%) are the main contributors to the exposure to cypermethrin, and potatoes to chlorpyrifos (up to 19%). Oranges and grapefruits are the main contributors for imazalil, mandarins for prochloraz and spinaches for nicotine.

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.30** Median hazard index (HI) calculated for reproductive and developmental toxicity (RDT) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

F.16 | URINARY BLADDER (URB)

F.16.1 | Chronic

The HI estimates of the combined chronic exposure in URB do not exceed 1 in any survey. Median HI values at the 99.9th percentile range from 0.166 in Italian adults to 0.617 in Bulgarian toddlers. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.31.

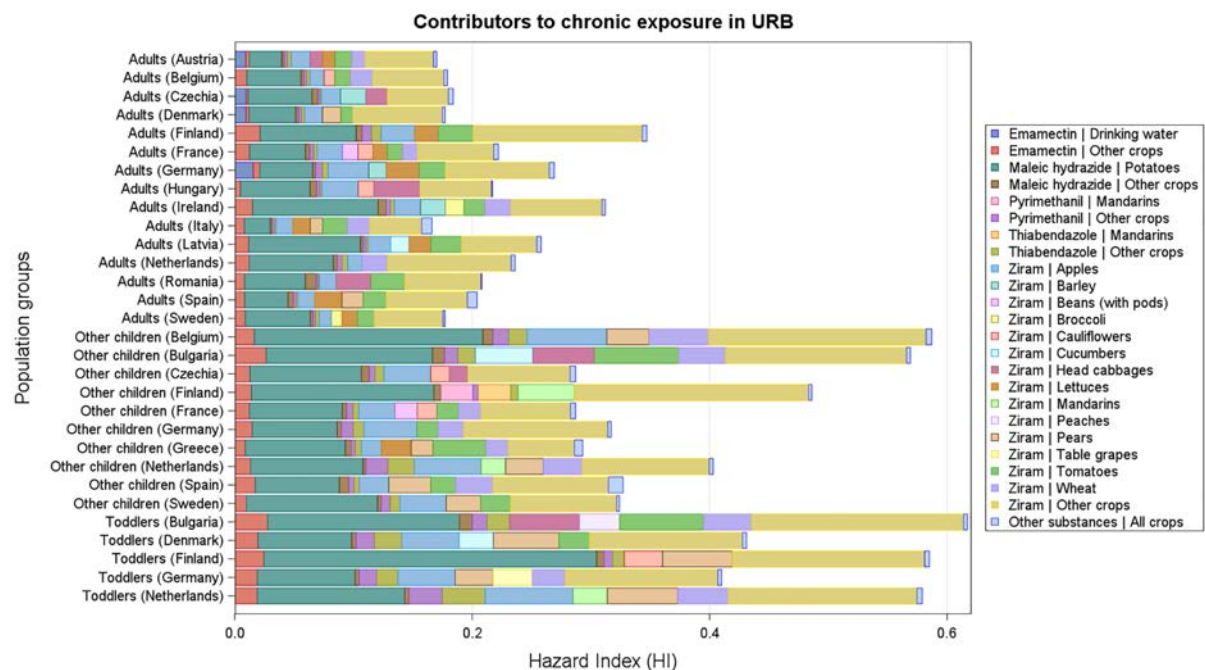
The main drivers of the chronic exposure in URB are ziram (43%–74%) and maleic hydrazide (14%–49%), with other contributors being emamectin (2%–8%), thiabendazole (up to 7%), pyrimethanil (1%–6%). All the other substances have an overall contribution by survey below 5%.

The food commodities that mainly contribute to the exposure to ziram are apples (up to 14%), with a contribution above 5% in 26 surveys, tomatoes (up to 15%), wheat (up to 11%), pears (up to 13%), lettuces (up to 11%), head cabbages (up to 18%) and cauliflowers (up to 6%). Other contributors are barley, mandarins and cucumbers, beans (with pods) and broccoli, table grapes and peaches. The main contributor for emamectin is drinking water. It should be noted that estimates on drinking water contribution are based on imputed occurrence data and should be thus considered with caution (see Appendix C, Section C.1.1.4). For both thiabendazole and pyrimethanil, mandarins (mostly juices) are main drivers.

Potatoes are the main contributing commodity to the exposure to maleic hydrazide, giving a contribution above 5% in all 30 surveys and ranging from 13% to 48%.

For further details, see also Annex C1, Table C.1.03.





**FIGURE F.31** Median hazard index (HI) calculated for the urinary bladder (URB) at the 99.9th percentile of the chronic exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the chronic exposure.

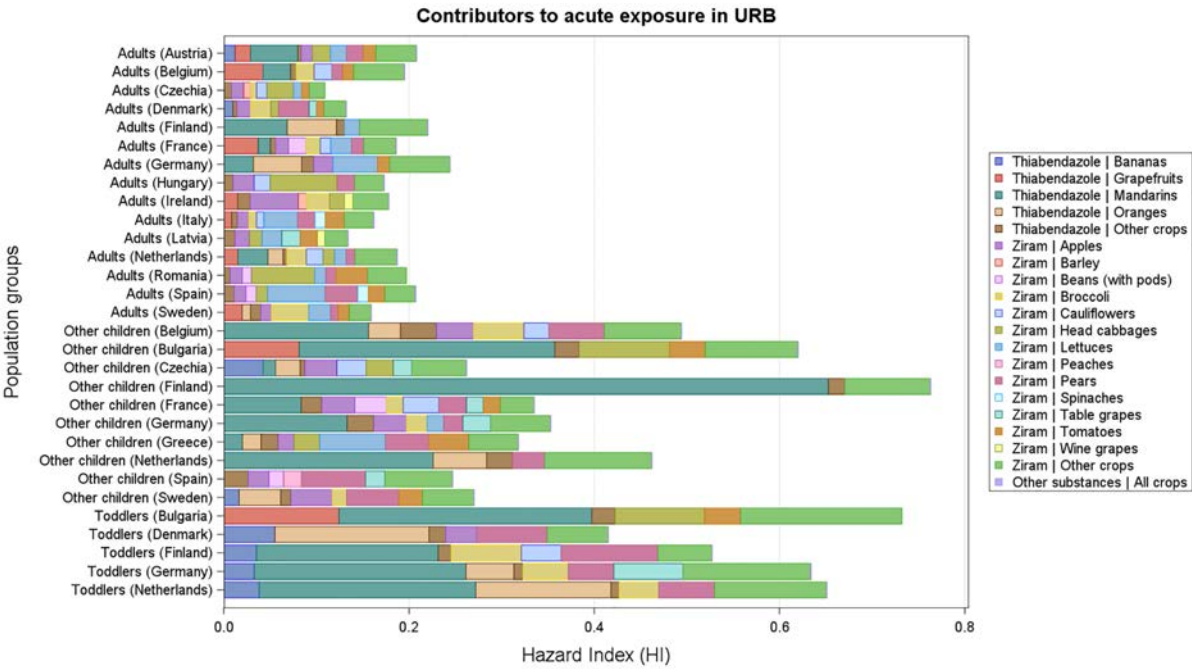
F.16.2 | Acute

The HI estimates of the combined acute exposure in URB do not exceed 1 in any survey. Median HI values at the 99.9th percentile range from 0.109 in adults from Czechia to 0.763 in Finnish children. The combinations of substances and food commodities contributing for at least 5% to the exposure in any survey are reported in Figure F.32.

Two substances are the main drivers of the acute exposure in URB, namely ziram (12%–97%) and thiabendazole (3%–88%). All the other substances have an overall contribution by survey below 5%.

The main contributing food commodity for ziram are pears (up to 28%), followed by apples (up to 29%), exceeding 5% in 21 and 20 surveys, respectively, broccoli (up to 26%) and tomatoes (up to 17%), head cabbages (up to 42%) and lettuces (up to 30%). Other contributors are cauliflowers (up to 12%), table grapes (up to 15%) and beans (with pods) (up to 10%), followed by spinaches, barley, wine grapes and peaches. As for thiabendazole, the exposure is largely driven by mandarins (up to 86%) and oranges (up to 40%), mostly via the consumption of juices, followed by grapefruits (up to 22%) and bananas (up to 16%).

For further details, see also Annex C2, Table C.2.03.



**FIGURE F.32** Median hazard index (HI) calculated for the urinary bladder (URB) at the 99.9th percentile of the acute exposure distribution in the different population groups and countries, highlighting the active substance and food commodity combinations contributing for at least 5% to the acute exposure.

## ANNEXES

The following annexes can be found online on EFSA's Knowledge Junction: <https://doi.org/10.5281/zenodo.10495630>

- Annex A.1 – Input data for the prioritisation of chronic cumulative risk assessment to pesticide residues;
- Annex A.2 – Input data for the prioritisation of acute cumulative risk assessment to pesticide residues;
- Annex B.1 – Output data from the chronic exposure assessment of pesticides that have an EU-agreed health-based guidance value;
- Annex B.2 – Output data from the chronic exposure assessment of pesticides that have a tentative health-based guidance value;
- Annex B.3 – Output data from the acute exposure assessment of pesticides that have an EU-agreed health-based guidance value;
- Annex B.4 – Output data from the acute exposure assessment of pesticides that have a tentative health-based guidance value;
- Annex C.1 – Output data from the combined exposure assessment of pesticides that may have chronic effects on the investigated target organ systems;
- Annex C.2 – Output data from the combined exposure assessment of pesticides that may have acute effects on the investigated target organ systems.