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Viale delle Terme di Caracalla, 00153 Rome, Italy - Tel: (+39) 06 57051 - E-mail: codex@fao.org - www.codexalimentarius.org

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The International Estimate of Short-Term Intake (IESTI) Revision and its Consequences

Foreword (Extract)

Árpád Ambrus and Denis Hamilton

Some issues requiring further data analysis or research have been identified but could not be properly examined as part of the impact assessment carried out by the international working group. The main points are recorded hereunder for future reference.

The practices of national regulatory agencies and the JMPR/ Codex for allocating bulked and mixed commodities into case 1 or case 3 are sometimes different leading to different outcomes of IESTI estimates. There is no clear guidance for which products bulking and blending are reasonable. Therefore, information on bulking and blending practices needs to be gathered for refining the methods for case 3 commodities for both MRL setting and dietary risk assessment.

The long-term goal of harmonization of the variability factor was supported by the ISW. The variability factor is intended to account for the variability of residues among crop units. Removal of unit weight from the IESTI equation and using the variability factor to adjust residues in large portion is a different concept and the basis for the value of the factor is yet to be explained. Further on, lists of commodities should be developed for which no variability factor (that is $\nu = 1$) is needed.

On a global level, the desired large portion data are currently not available and consumption surveys need to be re-evaluated or repeated. To establish updated large portion data based on kg food/kg bw/day, consumption surveys need to record individual body weights at the same time as recording the food portions consumed.

Further guidance on how to derive a large portion is also required, and a harmonized list of relevant raw and processed commodities for which large portion data need to be derived, should be prepared.

It was noted that the metabolite to parent ratio changes over time, with the type of crop and with the part of the crop considered. The use of medians of the two residue datasets (defined for enforcement and dietary risk assessment) for calculation of the CF, assumes proportionality between measured residue levels in the whole commodity and measured residue levels in the edible portion. Since the ratio between the two datasets may depend on several external and pesticide-crop specific factors, presently there is not sufficient information to fully support this assumption. Further research would be required, as recommended by EFSA and the ISW to develop additional guidance on the derivation of conversion factors. It should be recognized that 100% certainty and safety can never be reached and therefore consensus on the protection goal is needed, which requires further interaction between scientists and risk managers.

The full paper can be accessed at: https://www.tandfonline.com/eprint/6P72CzB6DupCHnDjG8Up/full

Setting the stage for the review of the international estimate of short-term intake (IESTI) equation

Anke Richter, Christian Sieke, Hermine Reich, Bernadette C. Ossendorp, Nicolas Breysse, Jason Lutze, Karin Mahieu, Sam Margerison, Anton Rietveld, Xavier Sarda, Gaelle Vial, and Trijntje van der Velde-Koerts

ABSTRACT

In the framework of setting Maximum Residue Limits (MRLs) for pesticides, both chronic and acute health risks to consumers arising from the long-term and short-term dietary exposure to pesticide residues have to be assessed. The current internationally harmonized approach for assessing the acute dietary exposure is based on deterministic methods for calculating the IESTI (International Estimate of Short-Term Intake). Recently, it became apparent that the IESTI approach needs a revision in the light of new scientific and political aspects. The main reasons that require this review were the lack of an international harmonization of the methodology which implies trade barriers as well as difficulties in risk communication concerning the public trust in regulatory systems. The most recent milestone in the scientific debate on a possible revision of the IESTI equation was an international scientific workshop held in Geneva in September 2015. The main objectives of this meeting were the re-evaluation, and where possible, the international harmonization of the input parameters for the IESTI equations as well as the equations themselves. The main recommendations from the workshop were (i) to replace the highest residue and supervised trials median residue with the maximum residue limit (MRL), (ii) to use a standard variability factor of three, (iii) to derive the P97.5 large portion value from the distribution of consumption values of dietary surveys expressed as kg food/kg bw/d, and (iv) to remove the commodity unit weight from the equations. In addition, the application of conversion factors and processing factors was addressed. On the initiative of the (World Health Organization) WHO Collaborating Centre on Chemical Food Safety at the National Institute for Public Health and the Environment (RIVM), the Netherlands, an international working group with members from the French Agency for Food, Environmental and Occupational Health and Safety, France (ANSES), Australian Pesticides and Veterinary Medicines Authority, Australia (APVMA), German Federal Institute for Risk Assessment, Germany (BfR), Chemical Regulation Division, the United Kingdom (CRD), European Food Safety Authority (EFSA), and RIVM, the Netherlands was formed after the IESTI workshop to conduct a comprehensive impact assessment of the proposed changes of the IESTI equations.

The abstract can be accessed at: https://www.tandfonline.com/eprint/SqP8ZW8kk8PGTPChWdZZ/full

Impact of a proposed revision of the IESTI equation on the acute risk assessment conducted when setting maximum residue levels (MRLs) in the European Union (EU): A case study

Nicolas Breysse, Gaelle Vial, Lauriane Pattingre, Bernadette C. Ossendorp, Karin Mahieu, Hermine Reich,

Anton Rietveld, Christian Sieke, Trijntje van der Velde-koerts, and Xavier Sarda

ABSTRACT

Proposals to update the methodology for the international estimated short-term intake (IESTI) equations were made during an international workshop held in Geneva in 2015. Changes to several parameters of the current four IESTI equations (cases 1, 2a, 2b, and 3) were proposed. In this study, the overall impact of these proposed changes on estimates of short-term exposure was studied using the large portion data available in the European Food Safety Authority PRIMo model and the residue data submitted in the framework of the European Maximum Residue Levels (MRL) review under Article 12 of Regulation (EC) No 396/2005. Evaluation of consumer exposure using the current and proposed equations resulted in substantial differences in the

exposure estimates; however, there were no significant changes regarding the number of accepted MRLs. For the different IESTI cases, the median ratio of the new versus the current equation is 1.1 for case 1, 1.4 for case 2a, 0.75 for case 2b, and 1 for case 3. The impact, expressed as a shift in the IESTI distribution profile, indicated that the 95th percentile IESTI shifted from 50% of the acute reference dose (ARfD) with the current equations to 65% of the ARfD with the proposed equations. This IESTI increase resulted in the loss of 1.2% of the MRLs (37 out of 3110) tested within this study. At the same time, the proposed equations would have allowed 0.4% of the MRLs (14 out of 3110) that were rejected with the current equations to be accepted. The commodity groups that were most impacted by these modifications are solanacea (e.g., potato, eggplant), lettuces, pulses (dry), leafy brassica (e.g., kale, Chinese cabbage), and pome fruits. The active substances that were most affected were fluazifop-p-butyl, deltamethrin, and lambda-cyhalothrin.

The Full paper can be accessed at: https://www.tandfonline.com/eprint/vRzri53JMxQRtuRuKYvA/full

Impact of proposed changes in IESTI equations for short-term dietary exposure to pesticides from Australian and Codex perspective

Trijntje van der Velde-Koerts, Sam Margerison, Nicolas Breysse, Jason Lutze, Karin Mahieu, Hermine Reich, Anton Rietveld, Xavier Sarda, Christian Sieke, Gaelle Vial, and Bernadette C. Ossendorp

ABSTRACT

In 2015 a scientific workshop was held in Geneva, where updating the four equations for estimating the short-term dietary exposure (International Estimated Short Term Intake, IESTI) to pesticides was suggested. The impact of these proposed changes on the exposure was studied by using residue data and large portion consumption data from Codex and Australia. For the Codex data, the exposure increased by a median factor of 2.5 per commodity when changing to the proposed IESTI equations. The increase in exposure was highest for bulked and blended food commodities (case 3 equations), followed by mediumsized food commodities (case 2a equations) and small- and large-sized food commodities (case 1 and case 2b equations). For the Australian data, out of 184 maximum residue limit (MRL) large portion combinations showing acute exposures below the acute reference dose (ARfD) with the current IESTI equations, 23 exceeded the ARfD with the proposed IESTI equations (12%). The percentage exceeding the ARfD was higher for the Australian MRL large portion combinations (12% of 184) than for those of Codex (1.3% of 8,366). However, the percentage MRL loss in the Australian dataset may not be representative of all pesticide MRLs since it concerns six pesticides only, specifically selected to elucidate the potential effects of the use of the proposed IESTI equations. For the Codex data, the increase in exposure using the proposed equations resulted in a small increased loss of 2.6% of the 1,110 MRLs estimated by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR): 1.4% of the MRLs were already not acceptable with the current equations, 4.0% of the MRLs were not acceptable with the newly proposed equations. Our study revealed that case 3 commodities may be impacted more by the proposed changes than other commodities. This substantiates one of the conclusions of the Geneva workshop to gather information on bulking and blending practices in order to refine MRL setting and dietary risk assessment for case 3 commodities where possible.

The Full paper can be accessed at: https://www.tandfonline.com/eprint/5SFeyaCNMckVETzFZTNB/full

Effect of individual parameter changes on the outcome of the estimated short-term dietary exposure to pesticides

Trijntje van der Velde-Koerts, Nicolas Breysse, Lauriane Pattingre, Paul Y. Hamey, Jason Lutze, Karin Mahieu,

Sam Margerison, Bernadette C. Ossendorp, Hermine Reich, Anton Rietveld, Xavier Sarda, Gaelle Vial,

and Christian Sieke

ABSTRACT

In 2015 a scientific workshop was held in Geneva, where updating the International Estimate of Short-Term Intake (IESTI) equations was suggested. This paper studies the effects of the proposed changes in residue inputs, large portions, variability factors and unit weights on the overall short-term dietary exposure estimate. Depending on the IESTI case equation, a median increase in estimated overall exposure by a factor of 1.0-6.8 was observed when the current IESTI equations are replaced by the proposed IESTI equations. The highest increase in the estimated exposure arises from the replacement of the median residue (STMR) by the maximum residue limit (MRL) for bulked and blended commodities (case 3 equations). The change in large portion parameter does not have a significant impact on the estimated exposure. The use of large portions derived from the general population covering all age groups and bodyweights should be avoided when large portions are not expressed on an individual bodyweight basis. Replacement of the highest residue (HR) by the MRL and removal of the unit weight each increase the estimated exposure for small-, medium- and large-sized commodities (case 1, case 2a or case 2b equations). However, within the EU framework lowering of the variability factor from 7 or 5 to 3 counterbalances the effect of changes in other parameters, resulting in an estimated overall exposure

change for the EU situation of a factor of 0.87-1.7 and 0.6-1.4 for IESTI case 2a and case 2b equations, respectively.

The full paper can be accessed at: https://www.tandfonline.com/eprint/gjP6Ck5uvRyhXq4dYUth/full

Factors affecting the quantitative uncertainty of the estimated short-term intake.

Part I—Calculation methods

Árpád Ambrus, Zsuzsanna Horváth, Júlia Szenczi-Cseh, and István J. Szabó

ABSTRACT

The calculation of the combined uncertainty of the international estimated short-term intake (IESTI) of ethephon residues in apples is shown as an example. The ethephon residues in apples were reported by the Joint FAO (Food and Agriculture Organization of the United Nations)/WHO (World Health Organization) Meeting on Pesticide Residues (JMPR). The apple consumption data were taken from the IESTI (international short-term intake) calculation template used by the JMPR. The IESTI was calculated with the currently used method (case 2a) and a proposed one recommended by the EFSA (European Food Safety Authority)/RIVM (Dutch National Institute for Public Health) Scientific Workshop co-sponsored by FAO and WHO. In this example, the ratio of IESTIproposed/IESTIcurrent and their combined relative uncertainty are about 2.8, and 1.7, respectively. The larger IESTI and uncertainty obtained with the proposed equation are the consequence of calculation only with the large portion (LP) instead of its combination with unit mass, and the MRL instead of the highest residue (HR). The LP is the major contributor to the combined uncertainty. Both the calculated IESTI and its combined uncertainty depend on the actual food – pesticide residue combination and should be calculated for each case.

The full paper can be accessed at: https://www.tandfonline.com/eprint/VCykTV78hJPiBZiSDVQI/full

Factors affecting the quantitative uncertainty of the estimated short-term intake.

Part II—Practical examples

Árpád Ambrus, Zsuzsannna Horváth, and Júlia Szenczi-Cseh

ABSTRACT

The effects of the spread of residue concentrations in the samples derived from the selected supervised trials and the number of trials were studied on the magnitude and uncertainty of the short-term dietary intakes calculated with the proposed new procedure (IESTIp) and that one used currently by the FAO (Food and Agriculture Organization) and WHO (World Health Organization) Joint meeting on Pesticide Residues (JMPR) (IESTIc). The residue data of 10 pesticides were obtained from supervised trials conducted on apples and pears. The methods described in Part I were used for the calculations of the uncertainty. The results indicate that the ratio of IESTIP to IESTIc (fIESTI) is directly proportional to the ratio of the estimated maximum residue level (MRL), recommended by the JMPR; to the highest residue (HR) observed in supervised trials, and it may have a wide range depending on the particular conditions. The fIESTI becomes greater with the increase of the difference between the mrl or maximum residue limit (MRL, established by the Codex Alimentarius Commission, CAC) and HR, and becomes smaller if the difference between the large portion (LP) and unit mass (U) decreases. The fIESTI ranged between 2 and 5.1 in the 16 cases examined indicating that the IESTIp calculation method leads to higher intake estimates. The ratio of CVIESTIp and CVIESTIc ranged typically between 0.62 and 1.71. It rapidly increased up to 12 trials. For a larger number of trials, the ratio remained practically constant (1.69–1.71). The processing factor (PF) equally affects the MRL and HR values, therefore, it will not practically influence the fIESTI. The uncertainty of the estimated median residues depends on the spread and number of values in the residue datasets, which affects the uncertainty of the conversion factor (CF) and subsequently the uncertainty of the estimated IESTIp. Residue values obtained from minimum nine independent trials are required for the correct calculation of the 95% confidence intervals of the calculated median residues. The uncertainty of the analytical results directly affects the median, HR values and indirectly the calculated mrl and the MRL derived from it. Therefore, it should also be considered for the calculation of the combined uncertainty of the conversion factors. For the correct interpretation of the results of dietary exposure calculations, the upper 95% confidence limit of the short-term intake should also be considered. However, it is not the current practice of regulatory agencies or JMPR.

The full paper can be accessed at: https://www.tandfonline.com/eprint/4c3FE5zd3tzajKDXuNww/full