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Fantke, Peter; Jolliet, Oliver

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1 **Life cycle human health impacts of 875 pesticides**

2 Peter Fantke[a,*], Olivier Jolliet[b,c]

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4 [a] Quantitative Sustainability Assessment Division, Department of Management Engineering,

5 Technical University of Denmark, Produktionstorvet 424, 2800 Kgs. Lyngby, Denmark

6 [b] Environmental Health Sciences, School of Public Health, University of Michigan, Ann

7 Arbor, MI 48109, USA

8 [c] Quantis, EPFL Science Park (PSE-D), CH-1015 Lausanne, Switzerland

9

10 *Corresponding author: Tel.: +45 45254452, fax: +45 45933435. E-mail: pefan@dtu.dk

Abstract

11

12   *Purpose* Residues in field crops grown and harvested for human consumption are the

13 main contributor to overall human exposure toward agricultural pesticides for the general

14 population. However, exposure from crop residues is currently not considered in life cycle

15 assessment practice. We therefore present a consistent framework for characterizing human

16 toxicological impacts associated with pesticides applied to agricultural crops in the frame of

17 life cycle impact assessment based on state-of-the-art data and methods.

18   *Methods* We combine a dynamic multicrop plant uptake model designed for evaluating

19 human exposure to residues for a wide range of pesticide-crop combinations with latest

20 findings of pesticide dissipation kinetics in crops and post-harvest food processing. Outcome

21 is a set of intake fractions and characterization factors for 875 organic pesticides and 6 major

22 food crops along with specific confidence intervals for each factor.

23   *Results and Discussion* Intake fractions aggregating exposure via crop residues and

24 exposure via fractions lost to air and soil for pesticides applied to agricultural crops vary

25 between 10^{-8} and 10^{-1} kg intake per kg applied as a function of pesticide and crop. Intake

26 fractions are typically highest for lettuce and tomato and lowest for potato due to differences

27 in application times before crop harvest and soil as additional barrier for uptake into potato

28 tubers. Uncertainty in intake fractions is mainly associated with dissipation dynamics in

29 crops, where results demonstrate that using pesticide- and crop-specific data is crucial.

30 Combined with the uncertainty in effect modeling, characterization factors per pesticide and

31 crop show squared geometric mean standard deviations ranging from 38 to 15560 over a

32 variability range across pesticide-crop combinations of 10 orders of magnitude.

33   *Conclusions* Our framework is operational for use in current life cycle impact assessment

34 models, is made available for USEtox, and closes an important gap in the assessment of

35 human exposure to pesticides. For ready use in life cycle assessment studies, we present

36 pesticide-crop combination-specific characterization factors normalized to pesticide mass

2

37 applied and provide default data for application times and loss due to post-harvest food

38 processing. When using our data, we emphasize the need to consult current pesticide

39 regulation, since each pesticide is registered for use on certain crops only, which varies

40 between countries.

41

42 **Keywords:** dynamiCROP plant uptake model; human toxicity characterization factors;

43 pesticides; life cycle impact assessment (LCIA); food crop consumption; intake fractions

1   Introduction

Food is an important source of human exposure to toxic chemicals which includes residues of pesticides, perfluorinated chemicals, metals, phthalates, and persistent organic pollutants including dioxins and polychlorinated biphenyls. Common sources of residues in food along food product life cycles are agricultural production and harvesting, food packaging, storage, industrial and domestic food processing, and finally serving (Dickson-Spillmann et al. 2009, Freeman 2011, Lippmann 2009, Muncke 2009, Tittlemier et al. 2007). In this context, pesticides are a special chemical class of interest, because they are intentionally applied to agricultural field crops, they have by design toxic properties, and the general public in various countries is concerned about chronic effects from low-level exposure (European Commission 2006, McKinlay et al. 2008, Pretty 2005, Slovic 2010). For pesticides, food crop consumption is the predominant pathway for human exposure (Caldas & Jardim 2012, Fantke et al. 2011a, Lu et al. 2008). Therefore, assessing pesticide residues in food crops is a key component in current pesticide authorization in Europe (European Commission 2009) and elsewhere and needs to be considered for assessing the environmental performance of food products over their life cycle.

Life cycle assessment (LCA) is a tool that is frequently applied to evaluate the environmental performance of agricultural production systems as well as various food products including crops (Andersson 2000, Perrin et al. 2014, Roy et al. 2009, Schau & Fet 2008). However, although health impacts from environmental emissions associated with the use of pesticides in food crop production are considered in some agrifood-related LCA studies, human exposure to pesticide residues in the treated food crops is still mostly disregarded (Fantke et al. 2011b, Juraske & Sanjuán 2011). This is mainly due to the fact that current tools for estimating pesticide residues in food crops show considerable uncertainties – mostly associated with dissipation kinetics in crops (Fantke et al. 2012a, Juraske et al. 2008). Furthermore, these tools are not implemented in current life cycle impact assessment (LCIA)

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70   models and methods for assessing human health impacts from exposure to potentially toxic

71   chemicals including pesticides. To address this gap, we propose to (a) develop an operational

72   framework for consistently incorporating health impacts from exposure to residues in food

73   crops associated with field applications of agricultural pesticides into LCIA. We further aim

74   at reducing uncertainty of pesticide-related characterization factors by integrating the latest

75   findings from Fantke and Juraske (2013) and Fantke et al. (2014) in estimating dissipation

76   kinetics in crops to (b) calculate harvest fractions, intake fractions and characterization factors

77   for 875 pesticides and to (c) estimate the resulting specific uncertainty for each of these

78   factors.

79

80   **2   Methods**

81   The general framework applied in LCIA for characterizing human toxicological impacts

82   associated with chemical emissions combines factors representing environmental fate, human

83   exposure, and health endpoint-specific dose-response into characterization factors (European

84   Commission 2010, Udo de Haes et al. 2002). At midpoint level, human toxicological

85   characterization factors relate numbers of health incidences to emitted chemical mass. At

86   endpoint level, characterization factors contain an additional term accounting for the (damage

87   or health endpoint-specific) severity and are expressed in terms of disability-adjusted life

88   years (DALY) per emitted chemical mass. Environmental fate and human exposure can be

89   aggregated into the human intake fraction that directly relates the chemical mass taken in by

90   an exposed (or the entire global) human population to the chemical mass emitted (Bennett et

91   al. 2002). This general framework for assessing human toxicity impacts in LCIA under

92   assumed steady-state conditions was originally designed to be applied for environmental

93   emissions, i.e. related characterization factors are normalized to a unit mass continuously

94   released into a specific environmental compartment, such as air, water, or soil (Rosenbaum et

95   al. 2008). However, pesticides are not emitted continuously, but are rather applied as pulses to

96 agricultural crops that are harvested within days to weeks after the (latest) application.

97 Steady-state might, hence, often not be reached, especially when pesticides are applied shortly

98 before crop harvest (Fantke et al. 2013, Rein et al. 2011). In addition, the fraction of the

99 applied pesticide mass that is intercepted by the crop surface and that ends up as residues in

100 crop harvest along with the fractions that are lost during and after the application and that

101 reach target field and off-target soil, air and water including surface and groundwater are not

102 typically reported or available for LCA practitioners (Perrin et al. 2014). Instead, in most

103 cases the applied pesticide mass or mass per area is available, from which fractions reaching

104 the treated crop and fractions reaching the environment as emissions then need to be

105 estimated (Rosenbaum et al. 2015). Consequently, the current framework applied for human

106 toxicity assessment of chemicals in LCIA needs to be extended and modified as detailed in

107 the following to reflect the mass distribution dynamics between pesticide application and food

108 crop harvest.

109

110 2.1 Modeling framework for pesticide exposure

111 *Characterization factors:* Our starting point is the multicrop model for characterizing

112 health impacts from pesticide residues in food crops, dynamiCROP, that describes the mass

113 evolution of pesticides in different crop-environment systems based on solving a set of

114 coupled differential equations. This model is fully described in Fantke et al. (2011a) and

115 Fantke et al. (2011b) and is designed for evaluating human toxicological impacts associated

116 with pesticide residues in wheat, paddy rice, apple, tomato, potato and lettuce, representing

117 the most relevant crop archetypes with respect to human vegetal food consumption.

118 Following this approach, human toxicity characterization factors, $CF_{x,t,e}$ [incidences $kg^{-1}_{applied}$

119 at midpoint level, $DALY\,kg^{-1}_{applied}$ at endpoint level], for pesticides applied to crop x harvested

120 at time t [days after application] associated with health endpoints e are calculated from

121   toxicity effect factors for aggregated cancer and non-cancer health effects, EF_e

122   [incidences kg_{intake}^{-1} at midpoint level, $DALY\,kg_{intake}^{-1}$ at endpoint level] and

123   human intake fractions, $iF_{x,t}$ [$kg_{intake}\,kg_{applied}^{-1}$], as

124    $$CF_{x,t,e} = EF_e \times iF_{x,t} \tag{1}$$

125   *Effect factors:* Effect factors are derived as

126    $$EF_e = \begin{cases} DRF_e & \Rightarrow \text{midpoint level} \\ DRF_e \times SF_e & \Rightarrow \text{endpoint level} \end{cases} \tag{2}$$

127   with DRF_e [incidences kg_{intake}^{-1}] as dose-response slope factor and SF_e [$DALY\,incidence^{-1}$] as

128   damage or severity factor. Dose-response slope factors relate risks of humans to potentially

129   develop a health effect from pesticide exposure to the quantity inhaled or ingested and are

130   mainly taken from Rosenbaum et al. (2008). In case of missing data, DRF_e are extrapolated

131   from chronic lifetime doses affecting 50% of exposed humans or – if chronic data are not

132   available as for most non-cancer effects – from no-observed effect levels of exposed animal

133   species assuming linear dose-response relationships (Huijbregts et al. 2005, Kramer et al.

134   1996). The difference in the units of the effect factors (Eq. 2) and consequently of the

135   characterization factors is related to the fact that at midpoint level, the effect factor is solely

136   derived from (and therefore equal to) the dose-response slope factor, whereas at endpoint

137   level, a severity factor is included accounting for differences in effect severity. Severity

138   factors of 11.5 and 2.7 $DALY\,incidence^{-1}$ are applied for cancer and non-cancer effects,

139   respectively (Huijbregts et al. 2005), to be used for comparative purposes rather than for

140   estimating absolute damages. Disability-adjusted life years are undiscounted and without age-

141   weighting.

142   *Human intake fractions:* To account for both the pesticide mass fraction reaching the crop

143   as residues and the fractions lost as emissions to air and soil during and after application,

144   human intake fractions relate the mass that is ultimately taken in by humans via all exposure

7

145 pathways to the mass of applied pesticide. Hence, the total intake fraction per mass applied

146 combines the specific intake fractions for exposure to crop residues from the applied mass

147 reaching the treated crop with intake fractions for different exposure pathways *p* including

148 inhalation and ingestion of drinking water and different food items from the applied mass

149 reaching air and soil:

150 $$\text{iF}_{x,t} = \text{iF}_{x,t}^{\text{residues}} + fr_x^{\text{air}} \times \sum_p \text{iF}_p^{\text{air}} + fr_x^{\text{soil}} \times \sum_p \text{iF}_p^{\text{soil}} \tag{3}$$

151 where $\text{iF}_{x,t}^{\text{residues}}$ [$kg_{\text{intake}}\ kg_{\text{applied}}^{-1}$] is the intake fraction associated with exposure to residues in

152 the treated crop at harvest time based on a mechanistic plant uptake model accounting for

153 partitioning, transport and dissipation kinetics (see Section 2.2), iF_p^{air} [$kg_{\text{intake}}\ kg_{\text{emitted to air}}^{-1}$] is

154 the exposure pathway-specific intake fraction related to the fraction lost to air via e.g. wind

155 drift, fr_x^{air} [$kg_{\text{emitted to air}}\ kg_{\text{applied}}^{-1}$], and $\text{iF}_p^{\text{soil}}$ [$kg_{\text{intake}}\ kg_{\text{emitted to soil}}^{-1}$] is the exposure pathway-

156 specific intake fraction related to the fraction lost to soil via e.g. deposition, fr_x^{soil}

157 [$kg_{\text{emitted to soil}}\ kg_{\text{applied}}^{-1}$]. Intake fractions referring to mass emitted to air (beyond treated field

158 boundaries) and to soil (considering run-off and leaching to freshwater and disregarding direct

159 crop uptake as already considered in the intake fractions related to crop residues) are

160 calculated with USEtox (Rosenbaum et al. 2008) assuming continuous emissions and steady-

161 state conditions. Related fractions lost (emitted) to air during and after pesticide application

162 are assumed to be pesticide-generic, but crop-specific for a typical foliar application and

163 range from 5% for lettuce, 14.8% for potato, and 16.5% for wheat and paddy rice to 23.7%

164 for tomato and 35.4% for apple (Ganzelmeier et al. 1995, Rautmann et al. 2001, van de Zande

165 et al. 2007). We thereby acknowledge that different application techniques, such as aerial or

166 soil application would yield different fractions lost to air. Fractions lost to soil range from 2.3

167 to 81% assuming foliar application and are a function of pesticide properties (e.g. molecular

168 weight influencing deposition velocities), application time (where we distinguish per crop

8

169   between averages for herbicides and other pesticides), and crop characteristics (e.g. growth

170   stage and interception area influencing intercepted pesticide mass).

171

172   2.2 Exposure to residues in crops

173   Intake fractions for crop residues are calculated from harvest fractions representing the

174   residual mass fraction of applied pesticide found in crop harvest, $hF_{x,t}$ [$kg_{in\,harvest}\,kg_{applied}^{-1}$], and

175   a food processing factor, PF_x [$kg_{intake}\,kg_{in\,harvest}^{-1}$], accounting for post-harvest reduction of crop

176   residues due to subsequent food processing steps:

177      $$iF_{x,t}^{residues} = PF_x \times hF_{x,t} \qquad\qquad (4)$$

178   Since data are only available for a limited number of pesticide-crop combinations, pesticide-

179   generic food processing factors are applied as proxies, i.e. 0.59 $kg_{intake}\,kg_{in\,harvest}^{-1}$ for washing

180   with tap water, 0.31 $kg_{intake}\,kg_{in\,harvest}^{-1}$ for parboiling or cooking, and 0.33 $kg_{intake}\,kg_{in\,harvest}^{-1}$ for

181   bread making (Kaushik et al. 2009, Keikotlhaile et al. 2010, Liang et al. 2014).

182   Harvest fractions are defined as the ratio of residual pesticide mass in all harvested crop

183   components c, $m_{x,c,t}^{residues}$ [$kg_{in\,harvested\,crop\,component}$], and the sum of applied pesticide mass, $m_x^{applied}$

184   [$kg_{applied}$], and background mass, $m_x^{background}$ [$kg_{in\,crop\text{-}environment\,system}$]:

185      $$hF_{x,t} = \frac{\sum_c m_{x,c,t}^{residues}}{m_x^{applied} + m_x^{background}} \approx \frac{\sum_c m_{x,c,t}^{residues}}{m_x^{applied}} \qquad\qquad (5)$$

186   Both the pesticide mass applied directly to the treated crop and the soil residues from

187   deposition or from earlier applications (background mass) that are taken up into the crop via

188   the root system need to be considered according to Eq. 5. However, following the FAO

189   recommendations for good agricultural practices for pesticide application (FAO 2003) as best

190   estimate in LCIA, we assume that the background pesticide input via root uptake from

191   previous applications and/or cross-field wind drift and subsequent deposition onto soil are

192   negligible, i.e. we assume $m_x^{\text{background}} \approx 0$ kg. We justify this assumption with the fact that even

193   when applied in relatively quick succession to the same crop, previous studies have

194   demonstrated that typically only the latest direct application is dominating overall residues in

195   crop harvest (Juraske et al. 2011, Rein et al. 2011). Hence, harvest fractions and all

196   subsequent metrics, i.e. intake fractions and characterization factors, are normalized to the

197   (latest) pesticide mass applied to the respective crop, m_x^{applied}.

198   To obtain harvest fractions, we have solved the dynamics of a mass balance system of

199   environmental compartments including air, soil and paddy water (the latter only for paddy

200   rice) and crop components including root, stem, leaves, leaf surface, fruit and fruit surface

201   (the latter two for all crops but lettuce and potato), which are all coupled by inter-

202   compartment transfers (Fantke et al. 2011a, Rein et al. 2011). Crop residues and resulting

203   harvest fractions were found to be highly dependent on degradation in crops and time to

204   harvest (Fantke et al. 2012b). From comparing modeled crop residues with measured data, we

205   found that predicted residual masses over time were in good agreement with measured

206   residues with R^2 between 0.81 and 0.99 (Fantke et al. 2011a, Fantke et al. 2011b, Itoiz et al.

207   2012, Juraske et al. 2012). Since most input parameters that are required for solving the

208   underlying mass balance system are typically not available to LCA practitioners and to be

209   compatible with the format of assessment models and intake fractions applied in LCIA for

210   human toxicity assessment, the dynamiCROP model was linearized and a parametric

211   regression model was developed for each of the six crops still accounting for the main

212   influences on the dynamics between pesticide application and crop harvest (Fantke et al.

213   2012b, Fantke et al. 2013). Each model combines the contributions of different crop and

214   environmental components $c \in \{$crop interior, crop surface, soil$\}$ at harvest time to the overall

215   residual pesticide mass found in crop harvest:

216   $$\text{hF}_{x,t} = \sum_c \text{hF}_{x,c,t} = \sum_c 10^{(\alpha_{x,c}^* + \beta_{x,c} \times k_{x,c} \times t_x)} \tag{6}$$

217   where $\alpha_{x,c}^*$ and $\beta_{x,c}$ denote dimensionless coefficients, $k_{x,c}$ [kg$_{\text{reaching component}}$day^{-1} per

218   kg$_{\text{in component}}$], represent removal rate coefficients and t_x [day] is the time between pesticide

219   application and crop harvest. Crop- and crop/environmental component-specific coefficients

220    $\alpha_{x,c}^*$ and $\beta_{x,c}$ are detailed in the Supporting Information (SI), Section S-1, and are adapted

221   from Fantke et al. (2012b). Removal rate coefficients for the soil component

222    $k_{x,c\in\{\text{soil}\}} = 1/\text{FF}_{\text{soil}}$ are derived from the inverse of pesticide residence times in soil

223   corresponding to the fate factors for continental agricultural soil, FF$_{\text{soil}}$ [kg$_{\text{in soil}}$ per

224   kg$_{\text{emitted to soil}}$ day^{-1}], in the USEtox matrix of fate factors (Rosenbaum et al. 2008). Removal

225   rate coefficients for crop interior and crop surface are generally obtained as

226    $k_{x,c\in\{\text{crop;crop-surface}\}} = \ln(2)/\text{HL}_{x,c}^{\text{dissipation}}$ from overall removal (dissipation) half-lives $\text{HL}_{x,c}^{\text{dissipation}}$

227   [day] estimated by Fantke et al. (2014) by fitting dissipation kinetics for 1485 distinct

228   pesticide-crop combinations reported in Fantke and Juraske (2013). For tomato, apple and

229   lettuce, additional terms contribute to $k_{x,c\in\{\text{crop;crop-surface}\}}$ accounting for the influence of

230   substance properties (see SI, Section S-1). Finally, crop-specific harvest times are taken from

231   Fantke et al. (2011b), Table S1, separately averaged for herbicides typically applied before or

232   during early crop stages and other pesticides, such as fungicides and insecticides, applied

233   during all crop stages including shortly before harvest and during post-harvest storage. With

234   these assumptions, we yield best estimates for crop residues and typically do not exceed

235   regulatory maximum residue limits (MRL) as demonstrated by Juraske et al. (2011), Juraske

236   et al. (2012), Itoiz et al. (2012), and Fantke et al. (2011a).

237

238   2.3 Uncertainty analysis

239   Uncertainty of harvest fractions, intake fractions and characterization factors (model

240   output) is expressed as 95% confidence interval ranges. Confidence intervals around model

11

241 output y are derived from a combination of uncertainty related to model input variables (input

242 parameter uncertainty) and uncertainty related to modeling of harvest fractions (regression

243 model uncertainty). Input parameter and model uncertainty are expressed as squared

244 geometric standard deviations $\mathrm{GSD}^2_{x_i} := \exp(2 \times \sigma_{x_i})$ with $\sigma_{x_i} > 0$ the standard deviation of

245 the natural logarithm of input variable or regression model x and the probability

246 $\{x_i / \mathrm{GSD}^2_{x_i} < x_i < \mathrm{GSD}^2_{x_i} \times x_i\} = 0.95$ representing the 95% confidence interval around x:

247 $$\mathrm{GSD}^2_y = \exp\left(2 \times \sqrt{\sum_i \mathrm{var}(\ln(x_i))}\right) = \exp\left(\sqrt{\sum_i \left(\ln(\mathrm{GSD}^2_{x_i})\right)^2}\right) \tag{7}$$

248 In Eq. 7, we use the fact that the variance of each input variable is related to the

249 corresponding $\mathrm{GSD}^2_{x_i}$ by $\mathrm{var}(\ln(x_i)) = \left(\ln(\mathrm{GSD}^2_{x_i})\right)^2$. The choice of 2 in the exponent of the

250 geometric standard deviations reflects the rounded critical value from the Student's t-

251 distribution. All input variables are mutually independent – see Fantke et al. (2012b) for

252 details. With that, relative sensitivities S_{x_i} are unity, i.e. $S_{x_i} = 1$, for all input variables and

253 regression models (Slob 1994) and the uncertainty of model output exclusively depends on

254 the variances of input variables and regression models. Considered in this analysis are

255 pesticide-specific uncertainty factors for regression models and data for dissipation half-lives

256 in crops (Fantke et al. 2014) representing the most uncertain variable in determining pesticide

257 mass in crop harvest (Fantke et al. 2012b, Juraske et al. 2008), degradation half-lives in soil as

258 proxy for soil residence times taken from the Pesticide Properties Database (Footprint 2014)

259 or U.S. EPISuite (US-EPA 2012), crop-specific residue regression models for different

260 harvest fraction ranges (Fantke et al. 2012b), post-harvest food processing (Keikotlhaile et al.

261 2010, Liang et al. 2014), fractions of applied pesticides lost to air and soil (DEFRA 2006),

262 cancer and non-cancer dose-response information and severity factors (Huijbregts et al. 2005).

263 $\mathrm{GSD}^2_{x_i}$ for all considered input variables and regression models are summarized in the SI,

264 Section S-2. Since the harvest fraction regression model for each crop c in Eq. 6 involves an

265   exponent of the complex form $hF_{x,c,t} = 10^{(\alpha^*_{x,c} + \beta_{x,c} \times k_{x,c} \times t_x)}$, Eq. 7 was first applied within its

266   domain of application to determine the 95% confidence interval of

267    $\log(hF_{x,c,t}) = \alpha^*_{x,c} + \beta_{x,c} \times k_{x,c} \times t_x$. The two-sided limits forming the confidence interval are

268   then calculated as $hF_{x,t} = \sum_c 10^{\log(hF_{x,c,t})}$, yielding separate upper and lower 95% confidence

269   interval limits at the level of harvest fractions, intake fractions and characterization factors.

270

271   **3   Results**

272   3.1   Intake fractions from pesticides applied to food crops

273   The variability of intake fractions for 875 pesticides applied to six crops is shown in

274   <Figure **1**, contrasting the contributions of the fractions of applied pesticide reaching the

275   agricultural food crops as residues and of the fractions reaching air and soil as emissions

276   during and after application, of which the latter two are summed over all contributing

277   exposure pathways. Intake fractions aggregated over crop residues and fractions lost to air and

278   soil vary between 4 (tomato) and 6 (wheat, paddy rice, lettuce) orders of magnitude across

279   pesticides applied to the same crop, demonstrating the importance of substance properties on

280   crop residue dynamics. Aggregated intake fractions for the same pesticide applied to different

281   crops vary between a factor 2.6 for herbicide florasulam and more than 5 orders of magnitude

282   for 1-naphthol, a metabolite of insecticide carbaryl, demonstrating that the influences of crop

283   characteristics and pesticide application times on crop residue dynamics are as important as

284   the influence of substance properties. Individual intake fractions are provided for each of the

285   875 pesticides and six crops in the SI, Section S-3.

286

287   <Figure 1>

288

289   Highest aggregated intake fractions are found in lettuce and tomato with median values

290   across pesticides of 0.035 and 0.013 $\mathrm{kg_{intake}\,kg_{applied}^{-1}}$, respectively, which is mostly due to very

291   short averaged application times before harvest for insecticides and fungicides. In contrast,

292   lowest aggregated intake fractions are found in potato with a median of 6×10^{-6}

293    $\mathrm{kg_{intake}\,kg_{applied}^{-1}}$. The highest intake fractions for individual pesticide-crop combinations are

294   found for fungicides cyproconazole and fuberidazole on lettuce yielding each 0.27

295    $\mathrm{kg_{intake}\,kg_{applied}^{-1}}$. Exposure from intake of crop residues is the main contributor to aggregated

296   intake fractions for 88 to 97% of all pesticides in wheat, paddy rice, tomato, apple, and

297   lettuce. For these crops, exposure from fractions lost to air and soil is the main contributor to

298   aggregated intake fractions for only 1.3 to 7% of all pesticides (<Figure **1**, grey vs. white

299   boxes). Potato is an exception, where exposure from fractions lost to air and soil is generally

300   exceeding exposure from residues in treated crop and where the fraction lost to soil is the

301   main contributor to aggregated intake fractions for 60% of the pesticides. For 35% of

302   pesticides, the main contribution is from fractions lost to air and only 5% of all pesticides

303   show main contribution from crop residues in potato.

304   The largest variability is shown for intake fractions associated with crop residues, which

305   is mainly due to differences in application times between crops and between herbicides and

306   other pesticides applied to the same crop. As an example, intake fractions associated with

307   pesticides applied to apple trees show a variability of 6 orders of magnitude due to the large

308   difference in average application times of 150 days (herbicides) and 14 days (non-herbicides)

309   before crop harvest. Lower intake fraction ranges for all crops are associated with herbicides

310   that are on average applied much longer before harvest than other pesticides, thereby allowing

311   removal processes to limit crop residues at harvest time. In contrast, fungicides and

312   insecticides are typically applied at later crop stages (sometimes even quickly before harvest)

313   and therefore cover the upper range of crop residue-related intake fractions. Aggregated

314   intake fractions for the individual pesticides and crops per kg applied are given in the SI,

315   Section S-3, along with their 95% confidence intervals.

316

317   3.2   Human toxicological characterization factors for pesticides

318   Combining human intake fractions per mass of pesticide applied to different crops with

319   toxicological effect information yields characterization factors shown in <Figure **2**. Whereas

320   intake fractions could be derived for all 875 pesticides, cancer and non-cancer effect data are

321   only available for a subset of 177 pesticides (20%) and 395 pesticides (45%), respectively.

322   Hence, characterization factors are provided in the SI for a total of 465 pesticides associated

323   with each of the six considered crops representing 53% of all pesticides included in this study.

324

325   <Figure 2>

326

327   Characterization factors for cancer-related effects typically show a lower variability than

328   factors for non-cancer effects, which is linked to the fewer dose-response data available for

329   cancer; hence, we provide carcinogenicity-related characterization factors only for a limited

330   number of pesticides. In contrast, characterization factors for cancer effects seem to be more

331   evenly distributed over the variability range than factors for non-cancer effects, most visible

332   for lettuce and least visible for tomato (white boxes in <Figure **2**). This effect is linked to the

333   influence of the variability of crop residue-related intake fractions (dominating overall human

334   intake for all crops but potato) shown in <Figure **1**, where 50% of the data around the mean

335   value for lettuce spread over more than 2 orders of magnitude, while 50% of data around the

336   mean for tomato only differ by a factor 4.5. In line with this, the variability of characterization

337   factors combining cancer and non-cancer effects (grey boxes in <Figure **2**) is influenced by

338   the crop-specific variability of all contributing intake fractions (related to crop residues, air

339   and soil fractions) and the variability of effect factors weighted by the number of contributing

340   data points (less for cancer, more for non-cancer effects). The highest variability of

341   characterization factors is seen for lettuce with more than 9 orders of magnitude between

342   lowest and highest factors of 4.4×10^{-9} $\text{DALY kg}_{\text{applied}}^{-1}$ for ethanol and 9.3 $\text{DALY kg}_{\text{applied}}^{-1}$

343   (attributable to the population-based cumulative risk of 3.4 non-cancer incidences $\text{kg}_{\text{applied}}^{-1}$) for

344   phenylmercuric acetate, respectively. Tomato shows the lowest variability in characterization

345   factors of about 7 orders of magnitude ranging from 5.3×10^{-8} $\text{DALY kg}_{\text{applied}}^{-1}$ for florasulam

346   and 1.5 $\text{DALY kg}_{\text{applied}}^{-1}$ (attributable to 1.6×10^{-3} cancer incidences and 3.9 non-cancer

347   incidences $\text{kg}_{\text{applied}}^{-1}$) for 2,4/2,6-toluene diisocyanate. Median values of characterization

348   factors in aboveground crops across pesticides vary by less than a factor of 2 in descending

349   order as lettuce > tomato > apple > paddy rice > wheat, whereas the median value for potato

350   is 5 orders of magnitude lower. Characterization factors at midpoint level (cancer and non-

351   cancer incidences $\text{kg}_{\text{applied}}^{-1}$) and endpoint level (DALY $\text{kg}_{\text{applied}}^{-1}$ given separately for cancer and

352   non-cancer effects as well as aggregated over both) are given for all pesticide-crop

353   combinations in the SI, Section S-3, including their 95% confidence intervals.

354   In Fig, we demonstrate along a realistic example how we arrived at characterization

355   factors given in <Figure **2** and given per pesticide in SI (Section S-3), and how to apply

356   human intake fractions and characterization factors in the context of LCA. We used as

357   example pesticides tebuconazole and pyraclostrobin, both currently authorized e.g. in the

358   European Union (European Commission 2011), and registered e.g. in Germany for use

359   against leaf rust (*Puccinia recondita*) on wheat (BVL 2015).

360

361   <Figure 3>

362

16

363   3.3 Uncertainty in characterization modeling of pesticides

364   Uncertainty expressed as 95% confidence interval (CI) ranges is shown in Figure 4 for

365   harvest fractions of 5250 pesticide-crop combinations. Confidence intervals are generally

366   smallest for potato (median ratio of 97.5%-ile and 2.5%-ile CI limits of a factor 20), followed

367   by tomato and apple (median 95% CI limit ratios of a factor 120 and 140, respectively), and

368   are largest for lettuce and wheat (median 95% CI limit ratios of a factor 570 and 2680,

369   respectively). The high end uncertainty for wheat is partly attributable to the long assumed

370   time between application and crop harvest for herbicides (see SI, Section S-1). The much

371   lower harvest fraction uncertainty ranges for pesticides applied to potato compared with

372   applications to other crops is related to lacking uncertainty data for residence times in soil

373   and, hence, does not indicate higher quality of regression models for potato.

374   Accuracy is in general higher in the range of high intake fractions and for the upper 97.5[th]

375   percentile, whereas uncertainty grows with decreasing intake fractions as well as for the 2.5[th]

376   percentile lower uncertainty limit. Accounting for improved estimates of half-lives is crops

377   from Fantke et al. (2014) compared to earlier correlations from e.g. Juraske et al. (2008) has

378   led to substantial changes and improvement in the accuracy of estimated harvest fractions (see

379   SI, Figure S1). The range of pesticide half-lives in crops is now much narrower than the

380   earlier estimates leading to a significant reduction in the variability between harvest fractions.

381

382   <Figure 4>

383

384   In all crops except potato, half-lives in/on crops along with time between pesticide

385   application and crop harvest are the main contributor to crop residue dynamics. In case of

386   potato the overall residence time in soil is the most influential factor that accounts for the

387   various removal processes in the heterogeneous soil layer, before pesticides can enter the

388   tuber via root uptake mechanisms (Juraske et al. 2011). Applying relatively large uncertainty

17

389   to the crop-specific residues regression models compared with a relatively low generic

390   uncertainty to soil degradation as proxy for overall soil residence time (most important for

391   potato) yields generally lower uncertainty ranges of harvest fractions for potato than for all

392   other crops. Harvest fractions for all pesticide-crop combinations are given in the SI, Section

393   S-3, along with their 95% confidence intervals.

394

395   Despite uncertainty related to harvest fractions, uncertainty in subsequent human intake

396   fractions (not shown) is scaled for each crop by the uncertainty associated with food

397   processing factors, which were applied for each crop assuming a specific food processing step

398   (see SI, Section S-1), but which were available as specific factors only for very few of the

399   considered pesticides. Uncertainty from food processing, however, contributes on average

400   only with 5.8% to intake fraction uncertainty across crops.

401   The highest share of characterization factor uncertainty with an average contribution of

402   70% is attributable to dose-response information, especially for extrapolated non-cancer

403   effects. This is inherently limited by the availability of toxicity data for both risk assessment

404   and LCA. Effective doses causing an effect in 50% of the exposed population have therefore

405   mainly been extrapolated from toxicological studies with animals for which the specific

406   health endpoints are mostly unknown, but derived from no-observed effect levels (NOEL).

407   Using NOEL as starting point for estimating no-effect exposures leads to higher uncertainties

408   (e.g. Landis & Chapman 2011) due to the large uncertainty around dose-response

409   information. Since this type of effect information has been used in USEtox, we relied on the

410   same data to ensure comparability across impact pathways and chemicals.

411

412   <Figure 5>

413

18

414   Figure 5 shows human health endpoint characterization factors for 465 pesticides with

415   available effect information applied to 6 crops along with pesticide-specific uncertainty

416   ranges that vary up to 9 orders of magnitude across pesticides applied to the same crop.

417   Regarding the level of uncertainty and since uncertainty in the upper range of characterization

418   factors is lower, Figure 5 is especially useful to provide an upper limit on the human health

419   characterization factors and to identify with a food crop-related LCA study which pesticide(s)

420   may provide a significant contribution compared to other life cycle impacts on human health

421   associated with e.g. respiratory effects from exposure to fine particulate matter.

422

423   **4   Discussion**

424   4.1 Influences on intake fraction variability

425   Our results show that pesticide properties and crop characteristics are both strongly

426   contributing to the variability of crop residues, fractions lost to air and soil, and subsequent

427   human intake fractions of pesticides applied to agricultural food crops. We acknowledge that

428   site characteristics, such as local soil and climate conditions during crop growth, and scenario

429   characteristics, such as food processing and human consumption pattern might additionally

430   contribute to the variability of our results, although to a lesser extent. The importance of crop

431   characteristics, such as water content, growth, and leaf area index evolution, for crop residue

432   dynamics is well in line with other studies demonstrating the strong influence of the choice of

433   crop data on chemical distribution kinetics in crops (Trapp 2015) and on plant uptake

434   dynamics from soil (Sun et al. 2014). Most importantly, the influence of all factors

435   contributing to the variability of intake fractions from exposure to crop residues – the

436   predominant component in the aggregated intake fractions from pesticide application to all

437   considered crops except potato – is mostly associated with uncertainty of pesticide dissipation

438   half-lives in crops. Uncertainty is additionally growing with increasing time between

439   application and harvest. Accordingly, uncertainties around intake fraction values are also

440 increasing with longer time to harvest allowing different uncertain model input variables to

441 develop a significant influence on model output. However, with increasing time to harvest,

442 intake fractions are typically lower, which makes the larger uncertainty less relevant than the

443 (comparatively) lower uncertainty in the main range of interest, i.e. intake fractions $\geq 10^{-5}$

444 $\mathrm{kg_{intake}\,kg_{applied}^{-1}}$. This effect is shown in Figure 4 for harvest fractions as main driver of the

445 magnitude of intake fractions. Uncertainty around fractions lost to air and soil along with

446 associated intake fractions for emissions to air and soil are likely being underestimated in our

447 study, since generic values for fractions lost and generic uncertainty for intake fractions have

448 been used lacking more detailed data. This will not influence the general trends of our results,

449 since these indirect contributions are low for most crops. Incorporating more realistic

450 uncertainty values would nevertheless increase the variability of aggregated intake fractions

451 for potato (with increasing time to harvest), where fractions lost to air and soil are dominating

452 aggregated intake fractions for most pesticides (see <Figure **1**).

453   Overall, we reduced intake fraction variability between 1 and 9 orders of magnitude for

454 pesticides applied to potato and apple, respectively, compared with estimates reported by

455 Fantke et al. (2011b) for 121 pesticides (accounting for only 14% of the number of pesticides

456 included in the present study). This reduction of variability in intake fractions is mainly

457 attributable to improved dissipation data in crops. Overall, the uncertainty around intake

458 fractions that is mainly driven by uncertainty in crop residues (Figure 4), is generally limited

459 compared to uncertainty of characterization factors (Figure 5) that is strongly increased and

460 dominated by uncertainty of (mainly non-cancer) dose-response information.

461

462 4.2 Accounting for realistic pesticide application

463   According to current national and international pesticide legislation we acknowledge that

464 not all pesticides are allowed for use on all crops. In fact, there are many pesticides that are

465 registered in some countries but banned for use in agriculture in other countries. Atrazine for

20

466   example is a herbicide with endocrine disrupting properties (Hayes et al. 2011) that is one of

467   the most widely used agricultural pesticides registered for use in the U.S. primarily on maize

468   and sugarcane (US-EPA 2006), whereas its authorization in EU member states is withdrawn

469   since 2004 (European Commission 2004). Given the heterogeneity in pesticide regulation

470   between countries, we emphasize the need to verify the authorization status of all pesticides

471   when applying our data. This is especially relevant when using our results for purposes of

472   pesticide substitution and similar comparative assessments, where comparing two pesticides

473   of which only one is registered for use on a specific crop could be misleading, if the

474   unregistered pesticide shows lower intake fractions or characterization factors. Furthermore,

475   we acknowledge that application times (days before crop harvest) are pesticide-crop

476   combination-specific as a function of distribution dynamics in each crop-specific

477   environment. In this study, we used application times before harvest that are averaged

478   separately for herbicides and other pesticides to represent "typical" application times as best

479   estimates for LCA that can also be applied to pesticides currently not included in our

480   assessment. However, the uncertainty related to pesticide-specific application times before

481   harvest for each crop (and country) is not included in our study and varies strongly between

482   pesticides.

483

484   4.3 Data limitations and applicability in LCA studies

485   Our study shows several limitations. Experimental data for the most sensitive input

486   variable, that is dissipation half-lives in crops, are only available for 311 out of 875 pesticides

487   (35%). To account for the related uncertainty, we considered the higher uncertainty of the

488   regression model to estimate crop dissipation to all pesticides, where experimental data were

489   missing. The new correlations on half-lives have however substantially improved the

490   accuracy of estimating related crop residues. Residence times in soil are the output of a

491   generic system of mass balance equations accounting for the environmental fate of pesticides

492   solved under the assumption of steady-state conditions with continuous emission input

493   (Rosenbaum et al. 2008). Soil residence times are thereby influenced by a wide range of

494   environmental characteristics including crop-related aspects and pesticide properties, of which

495   degradation in soil plays an important role (Dubus et al. 2003). Lacking uncertainty data for

496   soil residence times we applied uncertainty associated with soil degradation as proxy. We

497   thereby acknowledge that we might underestimate the overall uncertainty specifically for

498   potato, where soil residence time is driving the magnitude of crop residues and subsequent

499   human intake. Whenever possible, soil degradation data are based on measurements

500   aggregated in Footprint (2014) and only complemented by estimated data from the US-EPA

501   (2012) when no experimental data were available. Differences in soil degradation data sources

502   lead to differences in associated uncertainty, which were not considered in our study. We

503   thereby acknowledge that data estimated from pesticide physicochemical properties may

504   exceed measured field soil degradation half-lives by up to more than two orders of magnitude

505   as can be seen when comparing e.g. tralomethrin or 8-quinolinol. These differences are

506   becoming relevant in regulatory contexts, but are not as important in pure comparative

507   assessments like LCA, where we are not bound to absolute thresholds for e.g. persistence in

508   soil. Another limitation in our study is the use of generic fractions lost to air during and after

509   pesticide application and associated uncertainty estimates. Further research is required to

510   estimate these fractions more accurately in the context of LCA (Rosenbaum et al. 2015).

511   However, for the majority of pesticide-crop combinations, this will not substantially influence

512   related intake, since fractions lost to air are mostly not dominating intake fractions. Finally,

513   we apply pesticide-specific data and averaged uncertainty factors for human health dose-

514   response slope factors that are extrapolated from distinct exposed animal populations,

515   exposure durations and routes and that are aggregated over a wide range of health endpoints

516   (particularly for non-cancer effects). The difficulty to extrapolate effect factors from such

517   inherently heterogeneous data leads to a significant contribution of dose-response information

518   to overall uncertainty in characterization factors, which has already been acknowledged in

519   previous studies (Huijbregts et al. 2005, Rosenbaum et al. 2008). While the quality of data

520   underlying human toxicological effect factors needs to be improved accordingly, the

521   variability of characterization factors across all pesticide-crop combinations spanning more

522   than 9 orders of magnitude shows that relative to variability, overall uncertainty is not higher

523   for toxicity-related impacts than for other impact categories.

524   Despite abovementioned limitations, our study contributes to significantly advancing the

525   assessment of human health-related impacts from exposure to pesticides in LCA by including

526   the predominant exposure pathway (i.e. intake of crop residues) and by improving the quality

527   of the most uncertain input data for estimating pesticides in crop harvest (i.e. dissipation data

528   in crops; see SI, Figure S1). Since our characterization factors are based on mass applied,

529   LCA practitioners can and need to directly combine our results with pesticide application data

530   as demonstrated in Fig. Whenever such data are not at hand, recommended application

531   dosages as provided in The Pesticide Manual (Tomlin 2012) or on pesticide product labels

532   can be applied as proxy.

533

534   **5   Conclusions**

535   We provide an operational framework for including human toxicity-related effects from

536   exposure to pesticides via consumption of treated food crops into LCIA and provide for the

537   first time uncertainty ranges around harvest fractions, intake fractions and characterization

538   factors that are specific for each pesticide and crop. Results demonstrate that impacts of

539   pesticides in terms of human toxicity are largely underestimated when ignoring exposure to

540   residues in harvested and subsequently consumed crop components. For ready use in LCA

541   studies, we present pesticide-crop combination-specific characterization factors normalized to

542   pesticide mass applied and provide default data for application times and loss due to post-

543   harvest food processing. Uncertainty needs to be considered when comparing results between

544   different pesticides or with other chemicals to properly interpret ranking and maximum

545   contributions, as it has been shown that pesticides with lower median characterization factors

546   can be as important as pesticides with higher median characterization factors when

547   considering the pesticide-specific uncertainty ranges. Improving dissipation half-lives in crops

548   derived from experimental data has been essential in limiting uncertainties on harvest

549   fractions. Further studies are required to better estimate fractions lost to air and soil during

550   and after pesticide application and to reduce the inherent uncertainty in non-cancer toxicity

551   effect information. When using our data, we emphasize the need to consult current pesticide

552   regulation to allow for realistic scenarios where each pesticide is registered for use on certain

553   crops only, which varies between countries.

554

559

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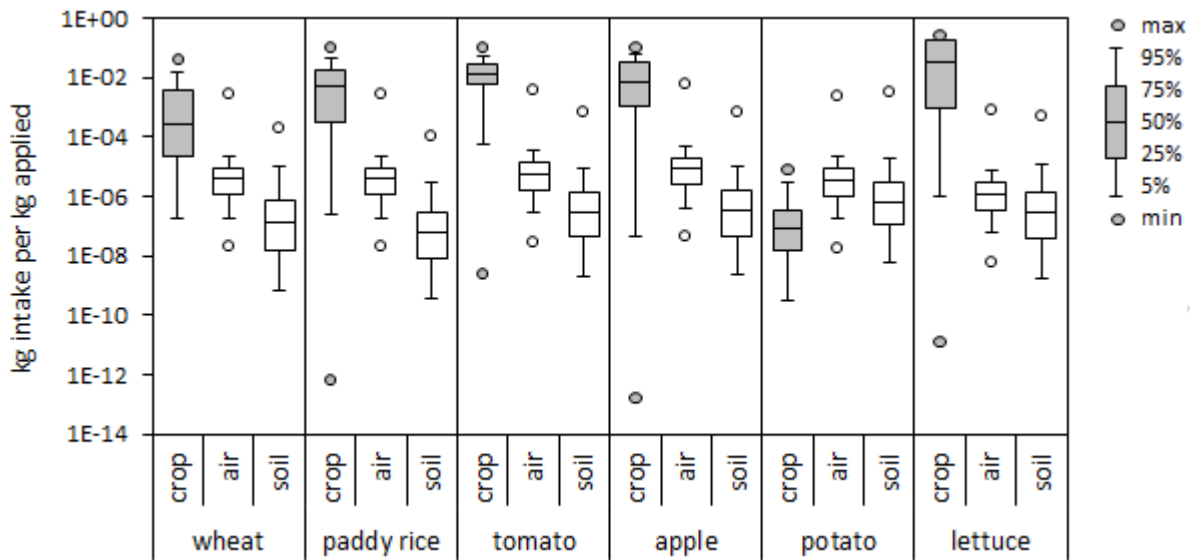
Figures

716

717 Figure 1 Variability of human intake fractions expressed as kg intake per kg applied pesticide

718 grouped for each crop according to fractions reaching the crop as residues (grey boxes) and

719 fractions reaching air and soil as emissions during and after application (white boxes).

720 Minimum values below 10^{-14} are not displayed.

721

722

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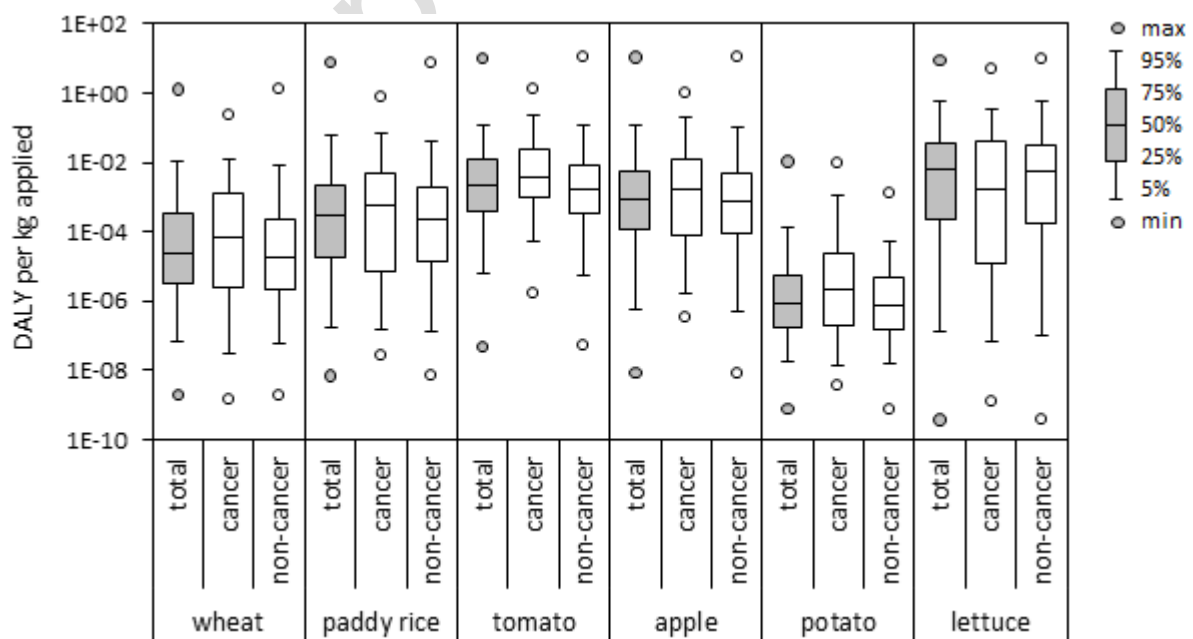
724   Figure 2 Variability of human toxicity endpoint characterization factors expressed as

725   disability-adjusted life years (DALY) per kg applied pesticide grouped for each crop into total

726   aggregated effects (grey boxes), and cancer and non-cancer effects (white boxes).

727

728

(a) human intake = mass applied per functional unit × total intake fraction

human intake (tebuconazole) = 0.25 $kg_{applied}$/ha × 7.1×10^{-4} kg_{intake}/$kg_{applied}$ = 1.8×10^{-4} kg_{intake}/ha

human intake (pyraclostrobin) = 0.125 $kg_{applied}$/ha × 2.0×10^{-5} kg_{intake}/$kg_{applied}$ = 2.2×10^{-6} kg_{intake}/ha

---

(b) characterization factor* = total ingestion intake fraction × non-cancer dose-response for ingestion × non-cancer severity factor

CF (tebuconazole) = 7.1×10^{-4} $kg_{ingested}$/$kg_{applied}$ × 0.015 $incidences_{non-cancer}$/$kg_{ingested}$ × 2.7 DALY/$incidence_{non-cancer}$ = 2.9×10^{-5} DALY/$kg_{applied}$

CF (pyraclostrobin) = 2.0×10^{-5} $kg_{ingested}$/$kg_{applied}$ × 0.042 $incidences_{non-cancer}$/$kg_{ingested}$ × 2.7 DALY/$incidence_{non-cancer}$ = 2.2×10^{-6} DALY/$kg_{applied}$

(c) health impact = mass applied per functional unit × characterization factor

health impact (tebuconazole) = 0.25 $kg_{applied}$/ha × 2.9×10^{-5} DALY/$kg_{applied}$ = 7.3×10^{-6} DALY/ha

health impact (pyraclostrobin) = 0.125 $kg_{applied}$/ha × 2.2×10^{-6} DALY/$kg_{applied}$ = 2.8×10^{-7} DALY/ha

729
730 *In this example, we calculated the characterization factors exclusively from ingestion intake
731 fractions (inhalation intake fractions contribute to overall intake fraction only with 0.02% for
732 tebuconazole and 0.32% for pyraclostrobin) and non-cancer dose-response (cancer effect data
733 were not available). Whenever inhalation intake fractions and/or cancer effects become
734 relevant, they need to be included in the characterization factor calculations.
735
736 Figure 3 Calculation steps for deriving human intake per treated hectare (a), endpoint

737   characterization factors (b), and health impacts per treated hectare (c) for two example

738   fungicides applied to wheat. Tebuconazole is typically applied as 250 g/l emulsion at 1 l/ha
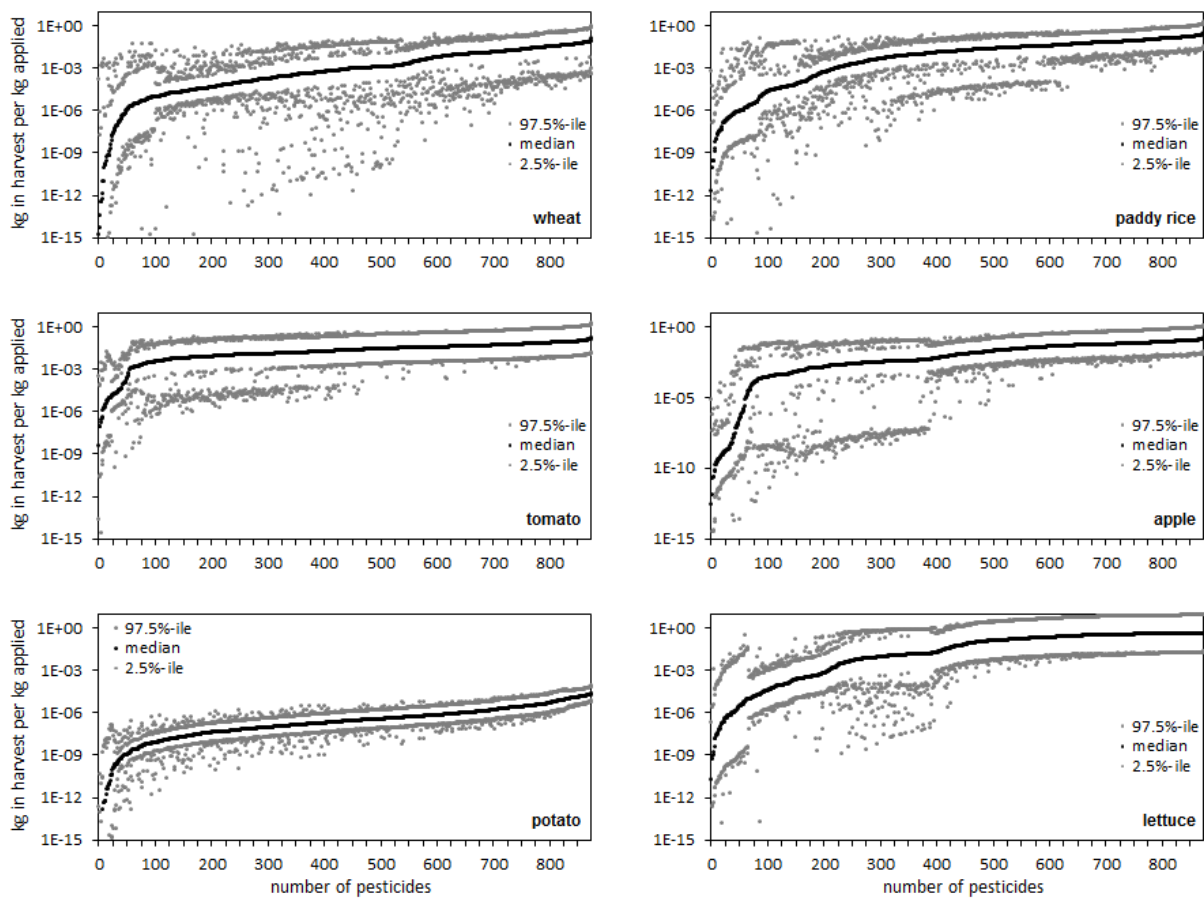
739   (Bayer 2014) and pyraclostrobin is typically applied as 250 g/l emulsion at 0.5 l/ha (BASF

740   2012). Intake fractions, dose-response factors and characterization factors are given in SI
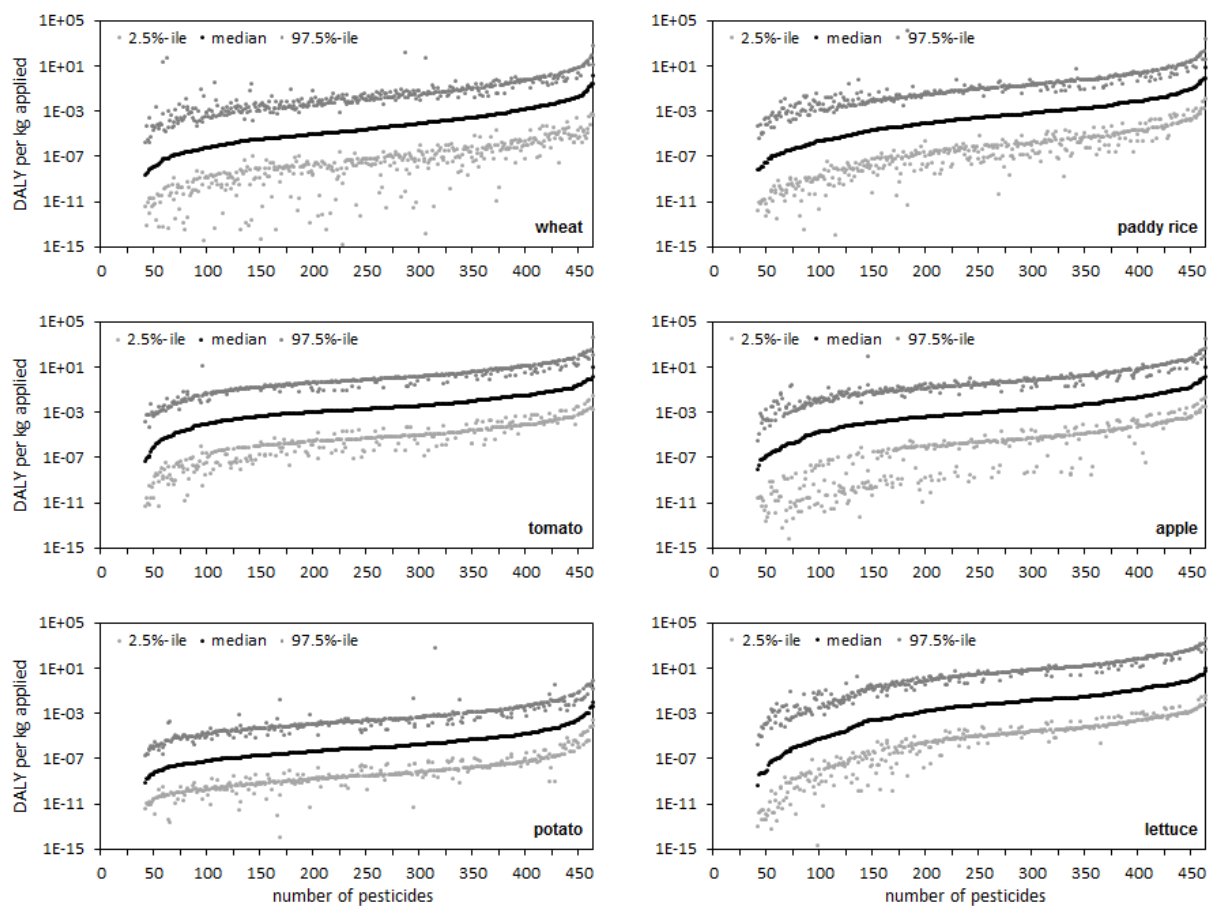
741   (Section S-3).

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744

745   Figure 4 Uncertainty of harvest fractions for 875 pesticides and 6 crops expressed as 95%

746   confidence interval ranges of pesticide mass in crop harvest per kg applied pesticide.

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748

Figure 5 Uncertainty of human toxicological characterization factors at endpoint level for the reduced set of 465 pesticides with available toxicity effect information and 6 crops expressed as 95% confidence interval ranges of disability-adjusted life years (DALY) per kg applied pesticide.