



## Risk Benefit Assessment of foods: Key findings from an international workshop

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1 **Risk Benefit Assessment of foods: key findings from an international workshop**

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19 policy

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## 21 **Abstract**

22 Whilst risk management measures, including food policy, are developed for the protection of public health and  
23 the environment, they may also lead to a reduction in health benefits. Policy decisions require then  
24 consideration of these necessary trade-offs, which leads to an increasing need to apply formal risk-benefit  
25 assessment (RBA) of foods. In this context, the European Food Safety Authority sponsored a Risk-Benefit  
26 Assessment Workshop on “past, current and future developments within the risk-benefit assessment of foods  
27 (RBA)” held in May 2017. The overall aims of the RBA Workshop were to discuss existing methods, challenges  
28 and needs within RBA, and to draft a roadmap for future development of RBA. The specific objectives were to i)  
29 identify RBA activities in Europe and globally; ii) discuss how to further develop and optimize RBA  
30 methodology; iii) identify challenges and opportunities within RBA; and iv) increase collaboration  
31 internationally. The two-day workshop gathered 28 participants from 16 institutions in 11 countries. It included  
32 technical presentations of RBA methods and case studies, and two break-out sessions for group discussions. All  
33 participants agreed that RBA has substantial potential to inform risk-management decisions in the areas of  
34 food safety, nutrition and public health. Several activities to optimize further developments within RBA were  
35 suggested. This paper provides a summary of workshop presentations, a discussion of challenges that limit  
36 progress in this area, and suggestions of next steps for this promising approach supporting a science-based  
37 decision process in the area of risk-benefit management of foods.

38

## 39 **1. Introduction**

### 40 1.1. History of RBA of foods

41 Risk-benefit assessment (RBA) of foods is a relatively new decision-support tool that assesses the combined  
42 beneficial and adverse health effects of consumption of foods in one integrated methodology. It integrates

43 knowledge on nutrition, toxicology, microbiology, chemistry and human epidemiology for comprehensive  
44 health impact assessments. RBA is part of the Risk-Benefit Analysis paradigm that combines RBA, risk-benefit  
45 management and risk-benefit communication, similar to the risk analysis paradigm (FAO, 2007). RBA is thus  
46 useful to inform food safety policies or to provide dietary advice based on an integration of the available  
47 scientific knowledge, with the ultimate aim of preventing food-associated diseases and promoting health and  
48 wellbeing of consumers.

49

50 Research to inform public health policies in the area of food and diets has been traditionally focused either on  
51 food safety, i.e. assessing risks and implementing strategies to limit the presence of microbiological or chemical  
52 hazards, or on nutritional assessments, i.e. assessing both risks or benefits of a lack or surplus of foods and  
53 nutrients. RBA is a conceptual and practical shift from the separate assessment of risks or benefits, typically  
54 within toxicology, microbiology and nutrition, to an integrated and multidisciplinary assessment of both risks  
55 and benefits. International organizations such as the World Health Organization (WHO) and Food and  
56 Agriculture Organization (FAO) have conducted RBA of foods to address risk-benefit questions (FAO/WHO,  
57 2008, 2010). In the USA, several RBA studies have been performed on health risks and benefits of seafood  
58 consumption (FDA, 2014; Gochfeld & Burger, 2005; Malden C. Nesheim and Ann L. Yaktine, 2007; Rheinberger  
59 & Hammitt, 2012) Furthermore, the European Food Safety Authority (EFSA) started a discussion on RBA  
60 methodology in 2006, and in 2010 launched a scientific opinion on Guidance on human health risk-benefit  
61 assessment of foods (EFSA, 2006, 2010). Following these initial developments and discussions, important  
62 research and progress within RBA has been performed, for example within European research projects like  
63 BRAFO (Hoekstra et al., 2012), Qalibra (Hart et al., 2013), Beneris (Leino, Karjalainen, & Tuomisto, 2013), and  
64 BEPRARIBEAN (H. Verhagen et al., 2012). In these projects, important steps have been taken to develop RBA  
65 methodology, and first generation software tools were developed to facilitate RBA while taking relevant

66 uncertainties into account. In addition, a series of initial case studies was conducted (see e.g. Boobis et al.,  
67 2013; Hart et al., 2013; Hoekstra et al., 2012; Hoekstra, Fransen, et al., 2013). These projects were also  
68 important to identify main challenges and limitations of the implementation of RBA at that time. After the  
69 termination of these EU projects, progress in RBA has been made by individual research groups, which have  
70 addressed RBA questions in *ad-hoc* case studies in response to questions of food safety managers (Anonymous,  
71 2017a; Eneroth, Wallin, Leander, Nilsson Sommar, & Åkesson, 2017; Steffensen et al., 2018) or to make further  
72 progress in RBA method development (Berjia et al., 2014; Boué, 2017).

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74 Several of the challenges identified as a result of the European RBA projects (Boobis et al., 2013) still remain, and  
75 include data and knowledge gaps; methodological limitations; difficulties in aggregating/comparing risks and  
76 benefits and in combining human data with data extrapolated from animal studies; lack of harmonization of  
77 concepts; and complexities in communicating RBA results. Furthermore, new research questions and agendas  
78 emphasize a need for assessments that include other societal impacts such as environmental, sustainability and  
79 economic concerns, in addition to public health effects. Tackling these challenges and paving the way for further  
80 development and implementation of RBA requires commitment and contribution of international experts in all  
81 aspects of risk assessment, food safety and nutrition. International collaboration will be crucial for the  
82 establishment and consolidation of RBA as a tool to evaluate scientific evidence to inform decision makers in  
83 public health and food safety at national and international levels. Several research groups in different countries  
84 are committed to further advance the field of RBA of foods, develop methodologies and provide evidence to  
85 support risk-benefit management in food safety and nutrition at national and global level. Leveraging on these  
86 research activities, EFSA sponsored a two-day workshop to gathered international RBA experts to pave the way  
87 forward within the RBA area. This paper describes the structure, contents and overall conclusions of the  
88 workshop. It starts by providing a brief overview of the RBA process and methodology (section 2), describes  
89 examples of current developments of RBA that were presented at the workshop (section 3), as well as the most  
90 important challenges within the field (section 4), and presents the opportunities and suggestions for next steps  
91 within RBA discussed by the experts (section 5).

### 1.2. Workshop objectives and structure

92 The overall aims of the RBA Workshop were to discuss methods, challenges and needs within RBA and to draft  
93 a roadmap for its future development. The specific objectives were to i) identify RBA activities in Europe and  
94 worldwide; ii) discuss how to further develop and optimize RBA methodology; iii) identify challenges and  
95 opportunities within RBA; and iv) increase collaboration internationally. The two-day workshop gathered 28  
96 participants from 16 institutions in 11 countries in Copenhagen, Denmark, May 2017. Participants and their

97 affiliations are presented in the appendix 1. The workshop included scientific presentations sharing past and  
98 current achievements in the area of RBA; break-out discussion sessions to identify challenges and to discuss  
99 opportunities for further developments in terms of data collection; methodologies and expansion of the scope  
100 of RBA to include other measures of impact; and an overall discussion to plan the future of RBA.

## 101 **2. Risk-benefit assessment process and methodology**

102 The process of an RBA is similar to the process of a traditional risk assessment. First, the risk-benefit question is  
103 defined by the risk manager, describing the purpose, scope and boundaries of the assessment including at  
104 what level (component, food or diet) the assessment is performed. As part of the problem formulation, the  
105 scenarios to be investigated are defined and the relevant subpopulations are identified. A reference scenario,  
106 which is usually current exposure or consumption, is compared to one or more alternative scenarios. The  
107 alternative scenarios serve to investigate the health impacts of a change in intake, and may be defined based  
108 on for example a worst-case exposure scenario or a recommended intake. Next, the RBA process can be  
109 divided into five steps, where the first four are common to the ones of traditional risk assessments but applied  
110 to risks and benefits separately (Boobis et al., 2013) (Figure 1). Lastly, risks and benefits are integrated to  
111 answer the risk-benefit question. Hence, the RBA process includes i) the identification of adverse and beneficial  
112 health effects associated with the consumption of food(s) and the exposure to food components considered; ii)  
113 the assessment of food consumption or exposure to food components; iii) the characterisation of the relevant  
114 health effects by determining the dose-response relationships for the food components or foods, describing  
115 the association between exposure and likelihood of an effect; and iv) the characterization of risks and benefits  
116 by integrating the information on dose-response relationships and the outcome of the exposure assessment.  
117 The conclusion of the risk-benefit characterization (i.e. step v) can be that a change in intake scenario is  
118 expected to lead to an increase or decrease in the incidence of the studied health effects. This conclusion may



119 be based on a qualitative assessment, stating that the health impact of one scenario is beneficial as compared  
120 to another without giving an estimate of the size of the health impact, but it can also be a quantitative  
121 estimate, expressing the health impact in terms of a common health metric such as incidence, mortality,  
122 disability adjusted life years (DALY) or quality adjusted life years (QALY) (Gold, Stevenson, & Fryback, 2002;  
123 Tijhuis et al., 2012). A quantitative assessment may be necessary if one scenario does not clearly stand out  
124 more beneficial or adverse compared to another in the qualitative assessment (Tijhuis et al., 2012);  
125 alternatively the aim of the RBA may be a quantitative outcome from the beginning.

126 RBA methods have evolved substantially over the years, allowing for improved evaluations of the health impact  
127 of foods. These developments have been equally evident in terms of data collection and analysis, and of  
128 method development and modelling (see 3.). As examples, while the first RBA studies focused on one single  
129 food (e.g. fish) (e.g. Hoekstra et al., 2013; Skåre et al., 2015) or one single food component (e.g. folic acid  
130 (Hoekstra et al., 2008)) and investigated risks and benefits in the population as a whole, recent work has taken  
131 into account the health effects of substitution of foods in overall dietary patterns, or variation in the population  
132 in terms of susceptibility or dietary preferences (see 3.2. and 3.3.). The technical session of the workshop  
133 included presentations of past and present RBA case studies illustrating different approaches, some of which  
134 are summarized below.

135

### 136 **3. Current developments in quantitative RBA of foods**

#### 137 **3.1. RBA of single foods**

138 The majority of published RBA in the area of food safety and nutrition focused on single foods (Berjia et al.,  
139 2014; Eneroth et al., 2017; Hoekstra, Fransen, et al., 2013; Hoekstra, Hart, et al., 2013), with fish being most

140 frequently evaluated (Boué, Guillou, Antignac, Bizec, & Membré, 2015). These RBA studies aimed to assess the  
141 overall impact of a food consumed while considering different levels of exposure and different factors affecting  
142 human health related to the fields of nutrition and/or microbiology and/or toxicology. Although many RBA  
143 performed recognize the broad impact of chemical hazards, nutrients and pathogens, most of them limited the  
144 analysis to only a few. For instance, the first RBA studies addressing fish consumption balanced potential  
145 nutritional benefits with chemical risks without considering potential microbiological effects, whereas another  
146 study on cold smoked salmon considered microbiological risks and nutritional benefits (Berjia et al., 2012). Only  
147 three out of more than 70 RBA studies included microbiological, chemical and nutritional concerns (ANSES,  
148 2013; NAP, 2007; VKM, 2013), but these covered microbiology only with regard to hygiene practices  
149 recommendations.

150 Until recently, several studies have made efforts to address the challenges of including all potential types of  
151 risks and benefits of foods (Büchner, Hoekstra, & van Rossum, 2007; FAO/WHO, 2006; VKM, 2013), but none of  
152 them were comprehensive by including the three fields of research, nor were they quantitative to enable  
153 estimation of an overall health impact. A recent study that aimed to progress on RBA method development  
154 focused on infant milk consumption during the first months of life, considering breast milk and powdered  
155 infant formula (Boué et al., 2017). Methodological developments were investigated by taking into account a  
156 limited selection of five agents relevant to the case study (Boué et al., 2017). The model was built to quantify  
157 the risk of microbiological and chemical hazards (*Cronobacter sakazakii*, *Cryptosporidium*, dioxin like  
158 polychlorinated biphenyls (dl-PCBs) and arsenic), and the benefit of nutrients (docosahexaenoic acid (DHA)) by  
159 taking into account the variability in the population and data and model uncertainty (Boué et al., 2017). In  
160 addition, to progress further on RBA methodological development, variability and uncertainty were studied  
161 separately, using second-order Monte Carlo simulation.

162 This study's individual risk and benefit assessments components (microbiological, nutritional, and chemical)  
163 involved the use of different methods, highlighting the difficulty of using a single harmonized approach.  
164 Likewise, it was not possible to apply one common health metric for all health effects considered. Therefore,  
165 the assessment ended with different output measures (e.g. exposure or DALYs), which hampered the  
166 comparison of all health impacts in a single metric and thus restrained scenarios comparison. To overcome this  
167 limitation, a scoreboard table was suggested, which also facilitated communication of RBA results while  
168 providing a transparent and comprehensive overview. The RBA model developed was the first fully three-  
169 disciplinary and quantitative RBA performed for a single food and highlighted that the integration of different  
170 methods and the assessment and communication of variability and uncertainties are still some of the  
171 challenges that have to be tackled.

### 172 3.2. Health impact of substitution of foods

173 Changes in the intake of one food will lead to changes in the consumption of other foods, which will indirectly  
174 affect the overall health impact of the food under study. If the intake of a food product is increased or  
175 decreased, it either leads to a change in overall food intake, or it is compensated by a change of the rest of the  
176 diet. Hence, to obtain a more integrated and realistic assessment of the overall health impact of our diet, it is  
177 essential to consider the whole diet and the potential substitution of foods. Thus far, few studies have  
178 addressed food substitutions in RBA. Van der Voet et al. applied a probabilistic model to assess the health  
179 impact of substituting 10-100% of red meat (beef/pork) with fish in the Dutch diet (van der Voet, de Mul, & van  
180 Klaveren, 2007). The health impact was assessed in terms of probability of exposure being below the tolerable  
181 daily intake (TDI) of hazardous substances (dioxin) and above the adequate intake of beneficial components (n-  
182 3 long-chain polyunsaturated fatty acids, DHA and eicosapentaenoic acid (EPA)). By estimating individual  
183 probabilities, this approach allowed the authors to include variability of food consumption between consumers  
184 into the RBA. Hollander et al. 2018 (Hollander, De Jonge, Biesbroek, Hoekstra, & Zijp, 2018) assessed

185 qualitatively the health effects of a gram for gram substitution of meat by fish, and Temme et al. 2013  
186 investigated the effects of replacing dairy and meat by plant based products (Temme et al., 2013).  
187 Substitutions on a nutrient level were also assessed as part of the BRAFO project, which included substitution  
188 of saturated fatty acids with mono-unsaturated fatty acids, substitution of saturated fatty acids with  
189 carbohydrates, and substitution of mono- and di-saccharides with low-calorie sweeteners (Hans Verhagen et  
190 al., 2012). However, none of the RBAs reached a quantitative health impact estimate, either due to the lack of  
191 a true risk-benefit question or inconclusive evidence. Others investigated the risk-benefit balance of  
192 substituting added sugar in beverages with artificial sweeteners, in terms of either risk of exceeding established  
193 reference doses (Husøy et al., 2008) or body mass index (BMI) (Hendriksen, Tijhuis, Franssen, Verhagen, &  
194 Hoekstra, 2011).

195 Current work at DTU Food investigates the health impact of changing from the current Danish diet to a diet  
196 that follows the Danish National Dietary Guidelines (Thomsen et al., 2018). The approach weighs nutritional  
197 benefits against nutritional and toxicological risks, and accounts for the substitution of foods. The model is  
198 based on a case study on substitution of red and processed meat with fish in the Danish adult diet. In this case  
199 study, the observed individual mean daily fish intakes for all adult individuals (> 15 years) in the Danish  
200 National Survey of Diet and Physical Activity are increased to 50 g/day as recommended in the guidelines (350  
201 g/week). Using pre-defined substitution factors that take portion sizes and meal-specific differences into  
202 account, a corresponding decrease in the intake of red and processed meat was modelled. Four substitution  
203 scenarios addressing the impact of varying chemical and nutrient exposures on the final health impact were  
204 investigated and the net health gain or loss of the substitutions was measured in DALYs. Other foods could  
205 potentially be added to the model to reflect a more realistic substitution and the whole diet. The approach may  
206 account for changes in energy intake associated with substitutions, as well as the health impact of these

207 changes. To our knowledge, this is the first quantitative RBA that uses DALYs as health metric whilst taking  
208 substitution of foods into account.

### 209 3.3. Optimization of personalized dietary recommendations

210 Even though official dietary guidelines are developed to motivate the population to follow healthy food  
211 consumption patterns, repeated national surveys have shown that most individuals do not meet the intakes  
212 recommended by the food and health authorities (Pedersen et al., 2010; Tetens et al., 2013). To investigate  
213 how to inform dietary advice that has a higher adherence by individuals, recent studies have applied  
214 mathematical optimization techniques to propose personalized intake recommendations (Maillot et al., 2009;  
215 Maillot, Vieux, Amiot, & Darmon, 2010; Persson et al., 2018). Personalized recommendations may be perceived  
216 as more relevant, because they can account for individual preference, needs, and beliefs (Brug, Campbell, &  
217 van Assema, 1999).

218 In a case-study on consumption of fish in the Danish adult population, quadratic programming models were  
219 applied to generate personalized fish intake recommendations fulfilling pre-defined criteria in terms of intake  
220 recommendations for EPA, DHA, and vitamin D and tolerable intake levels for methyl mercury, dioxins, and dl-  
221 PCBs, while simultaneously deviating as little as possible from observed individual intakes (Persson et al.,  
222 2018). Such an approach has the potential to increase compliance with dietary guidelines by targeting the  
223 individual consumers and minimizing the need for large and potentially unrealistic changes in consumption  
224 patterns. The output is a range of intakes for different fish species that can be proposed as a personalized  
225 recommendation for each individual in the population.

226 The approach of optimization of a single food recommendation can be improved by taking into account  
227 individual exposures to nutrients and contaminants from other sources than the food of interest, which enable  
228 refined minimum and maximum exposure criteria. The approach can also be used to optimize whole diets

229 (Barre et al., 2016; Maillot et al., 2009, 2010). Environmental or other specific individual background exposures  
230 may still require consideration in both cases. Current research at DTU Food analyses the impact of individual  
231 exposures due to foods other than fish, dietary supplements and the environment, by expanding the case study  
232 of fish intake in Denmark (Persson et al., 2018) with individual data on this background exposure. Lastly, the  
233 optimization approach can be expanded to include other food-related issues beyond public health, such as  
234 sustainability (Horgan, Perrin, Whybrow, & Macdiarmid, 2016; Kramer, Tyszler, Veer, & Blonk, 2017), economic  
235 impact (Darmon, Ferguson, & Briend, 2002; Maillot, Vieux, Delaere, Lluch, & Darmon, 2017) or both (Van  
236 Dooren, Tyszler, Kramer, & Aiking, 2015)

#### 237 **4. Current challenges within RBA**

238 Although significant progress has been made in the development of RBA, several challenges remain (Maarten J.  
239 Nauta et al., 2018). RBA has to face challenges of traditional risk assessment in the different disciplines, which  
240 are not specific for RBA, i.e. challenges related to data availability, variability between groups of consumers and  
241 individuals, strength of evidence and uncertainty in the dose response. In addition, there are challenges in  
242 defining how uncertainties should be presented to policymakers and the general public, and what guidance can  
243 be given to help policymakers make decisions based on uncertain evidence. Because of the parallel streams  
244 assessing adverse and beneficial impacts of foods or components, RBA faces additional challenges, including  
245 the integration of diverse data sources (e.g. from experimental animal studies and human epidemiological  
246 studies); heterogeneity of information between risks and benefits, classification of approaches for different  
247 types of risk-benefit questions (i.e. focusing on foods, food components or diets); scenario development  
248 including relevant policy options; and selection of metrics to evaluate and compare risks and benefits. Lastly,  
249 there are also challenges related to the current need to incorporate more than just health risks and benefits  
250 (e.g.: sustainability and economic consequences) to allow policymakers to make better informed decisions, and

251 the consequent requirement to further develop methodologies and approaches to perform those “expanded  
252 RBA”. During the workshop, two categories of challenges were discussed in working groups, those related to  
253 “health RBA” and those specific to “expanded RBA”.

#### 254 4.1. Challenges related to RBA of health impact of foods

##### 255 *Aligning the Risk-Benefit question and the methodological approaches*

256 The formulation of a risk-benefit question precedes the RBA and is of crucial importance to ensure that the  
257 RBA is focused, *fit for purpose*, and well-structured (Boobis et al., 2013; Hoekstra et al., 2012). The risk-benefit  
258 question will guide the choice of the RBA methodology and also the choice of risk-benefit metric. It is usually  
259 the risk-benefit manager that asks the RBA question, refined as necessary in dialogue with the risk-benefit  
260 assessors. Risk-benefit managers may be regulatory agencies such as national governments. However, policy  
261 makers with focus in the various aspects of food are often scattered in different regulatory bodies, with distinct  
262 interests, areas of action and potentially RBA questions. In addition, food companies and consumers may also  
263 have the “risk-benefit manager role” and will have different interests for such assessments. As an example,  
264 regulatory bodies may be primarily interested in defining safety criteria, priority setting and public health,  
265 whereas consumers may have more interest in their personal dietary choices and the anticipated health  
266 impacts of these choices. Hence, a broad range of risk-benefit questions and objectives are possible. For  
267 example, RBA may want to consider different levels of aggregation (e.g. a food component, food product or the  
268 whole diet), or the objective may be to compare specific scenarios and/or sub-populations to assess if the risk  
269 exceeds the benefit or vice versa (Hans Verhagen et al., 2012). The goal may also be to identify the most  
270 advantageous intake scenario (Berjia et al., 2014), or to provide a quantitative estimate of the overall health  
271 impact. RBA can include only health effects or be “expanded” to include non-health factors such as economy,  
272 sustainability and consumer preference (Ocké MC, Toxopeus IB, Geurts M, Mengelers MJB, Temme EHM, 2017;

273 Juliana M. Ruzante, Grieger, Woodward, Lambertini, & Kowalczyk, 2017; Seves et al., 2016; Temme et al., 2013;  
274 van de Kamp, Seves, & Temme, 2018).

275 Development of guidance on the approaches that can be adopted for different types of risk-benefit questions  
276 would facilitate the framing and the performance of RBA, and would support methodological harmonization in  
277 the future. Depending on the type of question, such guidance could for example assist in the selection of food  
278 components and foods as well as the health effects to be included in the RBA, and point out when quantitative  
279 approaches are needed. In general, clear and continuous communication between risk-benefit assessors and  
280 risk-benefit managers about the risk-benefit question and the methodological approach of choice is of crucial  
281 importance to ensure *fit for purpose* RBA.

#### 282 *Variability between groups of consumers and individuals*

283 The inherent differences between individuals may lead to the risks and benefits differing between individuals  
284 and certain subpopulations (e.g. children, pregnant women, elderly). If this variability is ignored in RBA, certain  
285 (groups of) vulnerable individuals suffering from higher health risks may be ignored in its conclusions, even if  
286 an intake scenario, on average, is beneficial for the population. However, inclusion of variability demands  
287 knowledge on potential differences in health effects between groups of consumers and individuals, and this  
288 knowledge may not be available. Also, it increases the complexity of the RBA.

289 Variability is for example a concern for decisions on fortification, such as folic acid fortification of bread and  
290 iodine fortification of salt. This fortification may be considered beneficial for the majority of the population, or  
291 beneficial as expressed by overall population health gain, but may have negative health effects for subgroups  
292 (Hoekstra et al., 2008). Food policies such as fortification may lead to (health) winners and losers and it is an  
293 ethical political question whether such a policy should be implemented. However, it is the responsibility of the  
294 risk-benefit assessor to inform the policy maker of the effects on different subpopulations. Due to this different



295 susceptibility among the population groups, the application of folic acid fortification is still debated (Eckner,  
296 Bjørn, Lunestad, & Rosnes, 2014). Taking the variability into account is crucial in RBA and can reveal population  
297 groups that are at high risk or that will gain large benefit. It enables evaluation of the effect of specific  
298 interventions (i.e. assessing which groups gain the largest benefit and which population group might  
299 experience a health loss due to the intervention), thus enabling better informed policy decisions (Hart et al.,  
300 2013; Hoekstra, Hart, et al., 2013).

301 There are different levels at which the variability can be assessed in RBA. First, the entire distribution of  
302 exposures within the population can be used instead of a mean exposure estimate (Hart et al., 2013). This has  
303 been addressed by different methods in previous RBAs (Hart et al., 2013; Hoekstra, Hart, et al., 2013; van der  
304 Voet et al., 2007). Second, if detailed population statistics are available, variability between sub-population  
305 groups can also be taken into account explicitly. In such cases, RBAs are performed for each sub-population  
306 group and results are compared.

#### 307 *Risk-Benefit comparison metrics*

308 There are several health metrics that can be used in RBA. Fransen et al (2010) divided risk-benefit comparison  
309 metrics into three categories: single outcome (e.g.: disease incidence, mortality); integrated (or summary)  
310 health (e.g.: DALY and QALY); and economically oriented measures such as WTP (willingness to pay). The choice  
311 of metric will depend on the type of question being asked by the risk-benefit manager and the complexity of  
312 the evaluation being done. For instance, in a situation where different components affect the same endpoint in  
313 an individual both positively and negatively, a net effect for the health outcome can be calculated, and  
314 integrated measures might not be needed (Fransen et al., 2010; Zeilmaker et al., 2013b). However, it is often  
315 the case that risk-benefit questions are more complex and involve multiple health effects, including different  
316 health effects for hazards and benefits, and therefore summary population measures such as disability

317 adjusted life year (DALY) can be helpful. For this reason, we focused our discussions during the workshop on  
318 the use and challenges associated with integrated measures, more specifically DALY.

319 In recent years, the DALY has been frequently used in quantitative RBA as it is able to aggregate both mortality  
320 and morbidity measures associated with several health outcomes (Murray, 1994). It is the metric of choice for  
321 the Global Burden of Disease studies (Anonymous, 2017b), and has been shown to be a valuable instrument for  
322 risk ranking of foodborne hazards (Havelaar et al., 2012, 2015). It has also been applied in RBA studies to  
323 summarize the overall health impacts of foods (Berjia et al., 2014; Eneroth et al., 2017; Hoekstra, Fransen, et  
324 al., 2013; Hoekstra, Hart, et al., 2013). While a single DALY estimate is usually the final estimate in burden of  
325 disease studies, the difference in DALYs between a reference and an alternative scenario ( $\Delta$ DALY) has been  
326 used as the final estimate of RBA studies (Eneroth et al., 2017; Firew Berjia, Andersen, Hoekstra, Poulsen, &  
327 Nauta, 2012).

328 Several limitations of the DALY have been identified, both in terms of how the metric is communicated and  
329 perceived, and in the assumptions behind the method. Underlying the DALY metric is the idea that many  
330 people suffering from a mild disease is as bad as few people suffering from a severe disease. The DALY provides  
331 an expected value for the population and does not clearly reflect the two dimensions used for its calculation:  
332 the probability of effect for individuals in the population and the severity of these effects. As an illustration,  
333 consider a population of 100,000 people with a remaining life expectancy of 20 years, where all individuals get  
334 infected by a pathogen. If the single effect of this infection is a probability of immediate death of one in a  
335 million (0.0001%), this yields a loss of  $100,000 * 0.000001 * 20 = 2$  DALYs. If the single effect is that 10% of the  
336 people get 1 day of mild diarrhea, with severity weight 0.074 (Salomon et al 2015), this also yields a loss of  
337  $100,000 * 1/365 * 0.074 * 0.1 = 2$  DALYs. Despite the same DALY estimation, the two scenarios are clearly  
338 different: in the first case, it is most likely that none of the 100,000 people involved will suffer from anything; in  
339 the second case, 10% of the people get ill, so around 10,000 people will be affected. If risk managers are only

340 informed about the 2 DALY and not about this difference (about 10,000 ill people versus maybe one death),  
341 they may base their decisions on incomplete information. Hence, the advantage of an integrated metric, i.e.  
342 that it summarizes complex issues into one figure allowing direct comparison of multiple risks and benefits,  
343 may also be a disadvantage if improperly used or misinterpreted. Care should therefore always be given to  
344 presenting all of the relevant underlying information (such as the basic assumptions and estimates of  
345 incidence, mortality and attending uncertainty) to the decision makers. Likewise, because multiple health  
346 outcomes may be considered in the total DALY estimate, the impact on the net health of one subgroup may be  
347 clearly greater than for another subgroup in the population. Again, an example would be folic acid fortification  
348 in which one group benefits whereas another group experiences the risks (Hoekstra et al. 2008).

349 Quality adjusted life years (QALY) were not the focus of the discussions, but have also been used as integrated  
350 measures in RBA (EFSA, 2006; Ponce et al., 2000). QALY has similar advantages and disadvantages as the DALY  
351 and is also part of the Qalibra software tool (Hart et al., 2013).

#### 352 *The strength of evidence and uncertainty*

353 Weighing and integrating evidence represents a substantial challenge because RBA involves various individual  
354 risks and benefits assessments, for which the current scientific strength of evidence might be different (Dorne  
355 et al., 2016). Consequently, evidence for each health is collected from different types of studies (e.g.  
356 epidemiological and toxicological studies). To date, all lines of evidence considered in RBA are reported only  
357 qualitatively, as advised by the EFSA guidance on RBA and the BRAFO approach (EFSA, 2010; Hoekstra et al.,  
358 2012). This qualitative integration does not allow for integrating the strength of evidence in the final output of  
359 quantitative RBA (e.g. DALY), which introduces an additional source of uncertainty.

360 The criteria for minimum weight of evidence are different in toxicology and nutrition. In general, the evidence  
361 accepted to refer to a toxicological hazard as “hazard” may be much weaker than the evidence needed to refer

362 to a benefit as “benefit”. In risk assessment, it is likely that a precautionary approach will be applied if there are  
363 indications of a potential risk, even if the evidence is weak (Boobis et al., 2013; Hoekstra, Hart, et al., 2013; M.J.  
364 Nauta et al., 2018; Tijhuis et al., 2012). In contrast, claims for beneficial or adverse health effects of a food or  
365 nutrient need to be supported by convincing scientific evidence before they are acknowledged (Boobis et al.,  
366 2013). If the established criteria for inclusion of adverse and beneficial health effects are used, toxicological  
367 risks with a low level of evidence may be more likely to be included than nutritional benefits with the same low  
368 level of evidence., This may lead to a skewed RBA. For example, the relative risk of colorectal cancer from  
369 folate supplements is around 1, with an upper 95% confidence interval of around 1.2, but as high as 1.7 is some  
370 studies (see (SACN, 2017)). The relative risk of a neural tube affected pregnancy is 0.29 after folic acid  
371 supplements, with 95% CI of 0.12-0.71 (MRC Vitamine Study Research Group, 1991), An approach to assess an  
372 upper bound risk of up to 77% increased incidence from a non-significant risk against a significant benefit of a  
373 70% reduction, on average, in NTDs is still not available. This is clearly an area of RBA that needs further  
374 development, such that risks and benefits can be weighted in some way for the respective levels of evidence  
375

376 The characterization of the risks and benefits (i.e. the estimated health impact) is not necessarily affected by  
377 this discrepancy, unless uncertainty factors that address the high uncertainty for low level evidence effects are  
378 included in the dose response. However, if effects with a low level of evidence i.e. high uncertainty of  
379 occurring, but potentially high health impact are ignored, the assessment could give a misleading suggestion.  
380 Therefore, in communication with policymakers or risk managers, it is important to clearly address the  
381 intentions of the RBA, and carefully demonstrate the assumptions in the inclusion and exclusion criteria of  
382 adverse and positive health effects and their level of evidence. RBA should not be misused to play down health  
383 risks associated with foods, nor should it overemphasize or ignore potential health benefits. This implies again  
384 that transparency is of crucial importance for RBA, and that communication is an essential component of the

385 RBA process. Ultimately, it is the RBA manager that is responsible for the policy decision, and to support this  
386 decision, it is the role of the RBA assessor to provide all relevant information, including an assessment of the  
387 uncertainties, in as clear and transparent manner as possible, to support this.

388 Within RBA, strength of evidence is closely connected to the uncertainty assessment, which expresses the  
389 belief in the obtained results. Uncertainties are propagated for example via the derived dose-response models  
390 to the final DALY estimate and may, if not quantified, lead to misleading conclusions (Benford et al., 2018). This  
391 stresses the need for quantification, or at least a qualitative assessment, of uncertainties in RBA (Hart et al.,  
392 2013). For RBA, the EU project Qalibra has developed a tool to include uncertainty in stochastic quantitative  
393 models (Hart et al., 2013). The methodology of uncertainty assessment is still in development, it is not specific  
394 to RBA but inherent to any science-based decision: the lack of knowledge generates imprecision in the results.  
395 The impact of this imprecision has to be assessed before making decision. Sensitivity analysis is a powerful  
396 technique to assess this impact (Saltelli, 2002). In particular, it helps prioritizing additional data collection or  
397 research. However, when quantification is not possible, reporting a qualitative expression of uncertainty is still  
398 important as advised in the BRAFO tiered approach (Hoekstra et al., 2012) and illustrated in (Hoekstra, Hart, et  
399 al., 2013) and (Boué, 2017).

#### 400 *Uncertainty in the dose response*

401 One of the major sources of uncertainty in RBA is the relationship between intake of a food or food component  
402 and a health effect. The ideal scientific studies to establish causality between exposure to a component and a  
403 health effect are randomized control trials with human participants. However, these are often not feasible for  
404 ethical and/or economic reasons. Other types of studies, such as (human or animal) observational studies that  
405 may reveal associations between intake of food components, contaminants, foods and diets and the likelihood  
406 of a health effect, may be used alternatively. Systematic reviews and meta-analyses of all available  
407 epidemiological evidence (e.g. derived by longitudinal cohort studies), which are suitable for ensuring a higher

408 level of evidence compared to using single studies available, are commonly used to describe the change in risk  
409 of health effects associated with dietary patterns and chronic exposure to chemicals (e.g. (Aune et al., 2015;  
410 Aune, Ursin, & Veierød, 2009; Hoekstra, Hart, et al., 2013)). Data from animal studies may be used to establish  
411 dose-response relations for chemical hazards, preferably supported by epidemiological studies.

412 For establishing the dose response relation, different types of evidence may be used in toxicology,  
413 microbiology and nutrition. Specifically in microbiological risk assessment, animal experiments are often not  
414 informative to establish a dose response relation, because the response to exposure to human pathogens is  
415 not comparable between humans and animals. The evidence often originates from either experimental studies  
416 with human volunteers, usually healthy young people that are not representative for the whole population  
417 (Teunis, Nagelkerke, & Haas, 1999), or outbreak studies that typically involve the more virulent strains or more  
418 vulnerable people (Teunis et al., 2010). In nutrition, whilst some data may be available from controlled clinical  
419 studies, more often reliance is on observational human epidemiological studies, which demand advanced  
420 statistical analysis, and interaction and confounding plays an important role: as only association can be studied,  
421 the evidence for causal relations may be weak (Tijhuis et al., 2012). In toxicological risk assessment,  
422 extrapolation/uncertainty factors are used to account for intra-species differences, and interspecies differences  
423 when translating observations from animal experiments into anticipated human health effects (van der Voet &  
424 Slob, 2007). . Another challenge is that adverse effects observed in animal studies may not be easily translated  
425 into human disease. Similarly, extracting the time of onset of a disease can be difficult, often requiring  
426 debatable assumptions. Examples of how in some cases exposure to chemicals is converted in DALYs can be  
427 found in (Gibb et al., 2015; Hoekstra, Hart, et al., 2013; Zeilmaker et al., 2013a).

428 The difference in methods for deriving dose response relations in RBA may be associated with different biases  
429 and systematic errors, and the attending uncertainties are of a different nature. Within a research discipline,  
430 these biases and errors may be relatively unimportant when risks or benefits that are derived by the same

431 methods are compared. But in RBA these differences may have a large impact on the output of the RBA.  
432 Currently, no established methods are available to overcome these differences. Performing a sensitivity  
433 analysis to highlight which sources contribute more to the overall uncertainty is recommended.

434

#### 435 *Data availability*

436 The availability and quality of data is a common challenge in RBA, just as it is in traditional nutrition and risk  
437 assessments. Previous reviews have identified a number of data needs and general challenges, and most of  
438 these still remain (Boobis et al., 2013; EFSA, 2010; Maarten J. Nauta et al., 2018). There are different types of  
439 data to consider: data on food consumption, levels of nutrients and contaminants in foods, microbial  
440 contamination of food, background data on human disease (e.g. incidence, disability weights, pattern of  
441 disease progression), and dose-responses relationships. Food consumption data may be available from national  
442 dietary food surveys, which have been expanded and improved continuously (e.g. (ANSES, 2017; Pedersen et  
443 al., 2010)), but it may be difficult to compare them between countries, due to differences in their design.  
444 Regional databases such as the EFSA Comprehensive Food Consumption Database and harmonization guidance  
445 (e.g. the EFSA's general principles for the collection of national food consumption data in the view of a pan-  
446 European dietary survey, known as the EU Menu) are a valuable resource to overcome these limitations and  
447 ensure comparability (EFSA, 2011, 2014b). National food databases usually include information on nutrient  
448 content of foods, but national monitoring data on the concentration of contaminants in foods may not be  
449 available. Data from which dose-response relationships can be constructed are crucial to enable risks and  
450 benefits to be estimated quantitatively. The type of data and source of information greatly differ between  
451 microbiology, toxicology, nutrition, and epidemiology; and between foods, food components, and  
452 contaminants. If using an integrated metric such as the DALY to compare risks and benefits, data on life  
453 expectancy, disability weights and duration associated with the different health effects are needed

454 (Develesschauwer et al., 2014; Hart et al., 2013). These data are specific to the sub-population of interest but  
455 rarely available at the national level. In addition, even though substantial amounts of data were published,  
456 these may be available in different formats or not directly suitable for use in RBA. Increased efforts to establish  
457 available, transparent and easily accessible database(s), with suitable contextual information i.e. the metadata,  
458 are needed to fill these data gaps for RBA. If observational or experimental data are lacking, another option is  
459 to gather information through expert elicitation (Cooke, 1991; EFSA, 2014a; EPA, 2009). This technique is  
460 already used in microbial risk assessment (Albert et al., 2012; Pujol, Johnson, Magras, Albert, & Membré, 2015;  
461 Van der Fels-Klerx, Cooke, Nauta, Goossens, & Havelaar, 2005) and more generally in food safety (Hald et al.,  
462 2016).

463

#### 464 **4.2. Challenges related to RBA including non-health related impact**

465 RBA research has so far built on the principles of risk analysis for food safety, where the end-point is the human  
466 health impact of food intake scenarios. However, decision makers must take into consideration factors other  
467 than human health when making policy decisions (FAO/WHO, 2011; FAO, 2017). Thus, what the risk benefit  
468 manager needs is a comprehensive understanding and a way to consider and balance the health impacts of  
469 changes in food intake with effects on other factors such as sustainability, consumer preferences, the  
470 economy, and societal values. For clarity, the question whether other disciplines should be included in the RBA  
471 must be included in the risk-benefit question. Often, this question is in line with the general interests of  
472 society, e.g. discuss how risk and benefits are balanced in other disciplines, including pharmaceutical drugs (H.  
473 Verhagen et al., 2012) . There is consensus that, in the longer-term, RBA based only on health will not be  
474 sufficient to address risk management and societal questions, and including non-health factors is inevitable and  
475 necessary. This need is not unique to RBA and has been thoroughly discussed in different food-related policy  
476 areas such as food safety, agriculture, the environment and nutrition (Anonymous, 2018; FAO, 2017). Clear



477 priorities need to be identified at national and international levels in order to make best use of finite resources,  
478 and to ensure that decisions to ensure food safety do not negatively impact on other dimensions essential for  
479 development, e.g. trade, economics, food security, tourism, social well-being (FAO, 2017). An integrated  
480 approach requires an interdisciplinary procedure as well as exchange of data from the different disciplines  
481 involved. Bringing together data on safety (e.g. contamination), health aspects (e.g. nutrient composition),  
482 sustainability indicators (e.g. land use) and other characteristics (such as price) concerning the same products is  
483 important in order to facilitate interdisciplinary research. However, adding such factors makes the analysis  
484 more complex, potentially less transparent and harder to be updated as new data becomes available. Also, it  
485 increases the number of stakeholders involved, and requires a methodology in which those effects can be  
486 transparently weighted and compared. Multi-criteria decision analysis (MCDA) has been designed to address  
487 such complex decision problems, while making the analysis transparent and systematic. MCDA has been used  
488 in innumerable fields from emerging technologies (Bates et al., 2016) to establishing priorities for foodborne  
489 illness (Juliana Martins Ruzante et al., 2010). It is a robust decision analysis tool that integrates different factors  
490 (i.e. criteria), while considering the preference and values of policy makers as well as stakeholders (FAO, 2017).  
491 MCDA has been used to balance risk and benefits of pharmaceutical drugs (Hsu, Tang, & Lu, 2015; Tervonen,  
492 van Valkenhoef, Buskens, Hillege, & Postmus, 2011), emerging technologies (Tsang, Bates, Madison, & Linkov,  
493 2014), and just recently a framework was proposed describing how it could be applied to foods (Juliana M.  
494 Ruzante et al., 2017). The challenges associated with incorporating other factors relevant to policy decision  
495 besides the typical RBA will not be related directly to the application of MCDA, but rather with the different  
496 magnitudes of uncertainty and the data availability to characterize those other factors. The field of medical  
497 products and drug development is more advanced in this area than food and nutrition, and has guidelines to  
498 gather and incorporate patient's perspective into their RBA analysis of future drugs (FDA, 2013; Nixon et al.,  
499 2016), which can be used as an example for RBA of foods.

500 At the workshop, sustainability was mentioned as being on the shortlist of aspects to include in the RBA.  
501 However, sustainability is not easily quantified by a single indicator. Several indicators in the area of food exist,  
502 such as greenhouse gas emission, water use, biodiversity, and others (Agovino, Cerciello, & Gatto, 2018;  
503 Chaudhary, Gustafson, & Mathys, 2018; Dora et al., 2015; Hallström, Carlsson-Kanyama, & Börjesson, 2015;  
504 Horgan, Perrin, Whybrow, & Macdiarmid, 2016; van Wagenberg et al., 2017). The choice for the most suitable  
505 indicator and/or weighing between them must be made depending on the assessment. Economic factors and  
506 consumer preferences were mentioned as other aspects that are important in a food policy assessment.  
507 Sustainability factors have been incorporated in some studies (e.g. (Donati et al., 2016; Masset, Soler, Vieux, &  
508 Darmon, 2014)). In another example, Temme et al. 2013 investigated the health and sustainability effects if  
509 meat and dairy were to be replaced by plant derived foods. Health effects were expressed as saturated fatty  
510 acid (SFA) and iron (Fe) intake in women, and sustainability was expressed as land use. An integrative metric  
511 was not necessary as all indicators pointed in the same direction: replacement of meat and dairy foods by  
512 plant-based foods reduced land use for food consumption, and SFA intake of young females and did not  
513 compromise total Fe intake. Seves et al. 2015 examined the health and sustainability effects of the  
514 consumption of different fish species. Sustainability was measured by land use (by fish farms) and greenhouse  
515 gas emission, and having a sustainability label which was partly a measure for overfishing. The health benefits  
516 were expressed by the EPA and DHA (fish oil) content of the fish species. The study concluded that herring and  
517 salmon (cultivate and wild-caught with ASC/MSC logo) are species favorable in terms of beneficial for health  
518 and the environment. In 2017, RIVM published a large study involving the current and future Dutch diet (Ocké  
519 MC, Toxopeus IB, Geurts M, Mengelers MJB, Temme EHM, 2017) that attempted to disentangle and analyze  
520 the integrated complexity of safe, healthy and sustainable diets. It analyzes the population's diet according to  
521 microbial and chemical safety, nutritious value, cost, consumer preference, future trends in production, and  
522 sustainability factors. Ocké et al. (2017) discovered that the trio of safety, health and sustainability is not

523 enough when it comes to the actual behavioral motives related to food. Consumer motives like convenience,  
524 enjoyment and cost, as well as prosperity motives like employment and export and ethical issues like animal  
525 welfare are also involved. These are all issues that carry weight individually and in society. The report is  
526 concentrated on safe, healthy and sustainable diets without disregarding these other motives. Three extreme  
527 scenarios were developed qualitatively, focusing on safety, health or sustainability. The scenarios were  
528 analyzed and scored by experts with a systematic group decision-support method. An attempt was made to use  
529 an MCDA method to weigh different scenarios (Ocké MC, Toxopeus IB, Geurts M, Mengelers MJB, Temme  
530 EHM, 2017; Saaty, 1994). Although the method proved promising, due to the uncertainties in quantifying  
531 underlying sub-criteria of indicators for sustainability, food safety and health, it was not possible to make the  
532 (subjective) weighing of the different aspects transparent and the final outcome was not used. Nevertheless,  
533 using expert-judgement and semi-quantification, the report concludes that opportunities to combine safety,  
534 health and ecological sustainability in an integrated food policy exist.

535

#### 536 4.3. Communication of RBA results

537 The area of risk communication has been growing and has made great progress in better understanding  
538 consumer behavior, and how risk is perceived (Frewer et al., 2016). Despite remaining challenges and  
539 limitations, stakeholders are now better equipped to communicate risks to consumers. Under the risk-analysis  
540 paradigm, risk assessors have also made progress in communicating with risk managers and other stakeholders  
541 before, during and after a risk assessment is conducted and results are published. In most areas there is a  
542 demand for decisions to be transparent, and engaging with stakeholders early-on is key.

543 Communicating RBA messages is more complex than communicating risks or benefits separately. On one hand,  
544 the way risk is perceived is very different of how benefit is perceived by consumers. On the other hand,

545 because the overall process incorporates (at least) those two components' analyses, and their integration, the  
546 data, the uncertainty around it and the assumptions are more difficult to be described, which could potentially  
547 add confusion. It is important to understand the target population and establish trust by working in close  
548 collaboration with stakeholders and social scientists specialized in risk communication. More research is  
549 needed to understand consumer's trade-offs and values when it comes to risk and benefits of foods. Rideout  
550 and Kosatsky (2017) argue that also other factors than risks and benefits associated with physical health should  
551 be assessed when developing advice for specific populations (Rideout & Kosatsky, 2017). They suggest other  
552 factors to weigh in addition to health risks and benefits, such as socioeconomic and sociocultural factors, and  
553 to apply e.g. health impact assessment to evaluate external impacts of a consumption advice or policy (such as  
554 substitution of foods), and other qualitative tools for development of more comprehensive and effective  
555 advice.

556 In addition, it is crucial that the results and methods of RBA studies are transparent and that uncertainty, when  
557 possible, is taken into account and reported with the results. Likewise, it is important that the level of evidence  
558 for all effects is considered, and that the limitations in available data and assumptions made are communicated  
559 with the results. Especially when RBA studies are made for methodology development purposes, particular  
560 care should be taken in how any preliminary results are communicated, if they do not reflect a definitive RBA.

561 Moving towards an optimal communication of RBA results to all stakeholders requires a closer collaboration  
562 with social scientists. While these needs were considered and emphasized at the workshop, communication  
563 tools were not the scope of the discussions.

## 564 **5. Opportunities and way forward**

565 As a last step, the participants of the workshop discussed the practical way forward to take RBA to the next  
566 stage. Building on the challenges and opportunities identified, a number of needs and practical suggestions

567 were presented. In addition, activities that promote collaboration and integration of research efforts were put  
568 on the agenda for a RBA Network formally launched at the event.

569 It was generally agreed that the discussions on needs, methods and challenges should now be followed by the  
570 development of case studies, in which the identified challenges are addressed. Two options were identified: to  
571 develop new cases using the tools and frameworks that are now available; to re-open cases that have been  
572 performed previously, and apply new data and new methods to test the improvements that can be made and  
573 to evaluate their robustness. Examples include probabilistic approaches that allow for the assessment of  
574 variability and uncertainty and models that take substitution of foods into account. These case studies can also  
575 be applied to compare different health metrics (in parallel to the DALY). The latter should preferably be  
576 followed by research on the perception and communication of these different metrics to different  
577 stakeholders.

578 A categorization of RBA studies will be advantageous, for example by comparing the level of aggregation of the  
579 RBA (on food components, foods or diet), the risk-benefit question (which scenarios are to be compared, which  
580 consumer groups are included, what food components and contaminants associated with potential health  
581 effects are included), whether there is a need for a quantitative and/or stochastic approach, etc. (see section  
582 *Aligning Risk-Benefit question and methodological approaches*, section 4.1.). Ideally, these case studies would  
583 be performed by different research groups, and a platform to share and discuss their assessments should be  
584 created.

585 Another generally recognized challenge within RBA is the availability of data (section 4.1). To harmonize RBA  
586 internationally and to facilitate the application of RBA by national and international risk and benefit managers,  
587 it is important to establish and maintain shared databases with dietary intake data, concentration data on  
588 nutrients and contaminants, dose response data, data from observational studies and health data. These

589 databases should be transparent and easily accessible, and setting up and maintaining such a database(s)  
590 would be a community effort that requires broad international support.

591 In Europe, EFSA might expand its role as curator of such databases. RBA research groups should provide input  
592 to EFSA and other data providers on data needs. Furthermore, EFSA is already taking initiative to lead  
593 discussions on current challenges of the integration of evidence with very diverse and not readily comparable  
594 underlying evidence bases, and motivate stakeholders to address them (EFSA, 2018). Again, this should be a  
595 collaborative effort with broad international support.

596 As the challenges associated to RBA are complex, expertise required are numerous and the data needs are  
597 large, the workshop participants concluded that intensive international collaboration is a prerequisite for the  
598 development of this novel discipline. Formalizing an RBA international network will facilitate all future activities  
599 discussed and proposed in the workshop, and will help partners in consolidating and further developing current  
600 activities. Ideally, such a platform should be formed within a European or global international project, to  
601 ensure that harmonized approaches can be developed, and that these build on consensus in the international  
602 scientific community and can serve as a basis for global decision making. Due to the unique multidisciplinary  
603 character of RBA, it may be challenging to identify scientific associations and funding bodies that cover all its  
604 scientific and societal aspects. Still, networking initiatives can be established, for example via research  
605 applications and, at international level, with symposia organized at scientific conferences. With this in mind,  
606 participants have decided to launch the International Network for Risk-Benefit Assessment of Foods. The  
607 network is to be chaired by DTU Food and will be open to any group or individual with an active interest in the  
608 area. Among other overall goals, this network will serve as a forum for continuation of the discussions here  
609 described.

610 Overall, the workshop participants agreed that RBA is a promising and highly relevant research area that  
611 deserves increased attention worldwide. Because the broad range of public-health activities associated with

612 foods and diets brings a high degree of complexity to policy development and a need to involve various  
613 stakeholders to ensure synergy, international bodies such as the FAO have stressed that ‘policy coherence’  
614 across ministries is key (FAO, 2017). RBA approaches, particularly when expanded to include non-health related  
615 impacts, can be a powerful tool to assist risk-managers defining policy that achieves the best societal  
616 outcomes.

617 RBA ultimately may show how integration of a variety of scientific disciplines and approaches can be used to  
618 address specific and general policy questions, and serve governmental regulatory bodies, food industry and  
619 individual consumers alike.

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621 We would like to acknowledge all participants of the workshop for their dedicated contributions to the  
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955 **Appendix 1: List of participants and affiliations**

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