European Journal of Nutrition & Food Safety
3(4): 146-153, 2013

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Benefit-Risk Analysis for Foods (BRAFO)- Executive Project Summary

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Author's contribution

This study has been carried out with partial financial support by the Commission of the European Communities, and was coordinated by ILSI Europe.

Review Article

Received 20th September 2013
Accepted 20th September 2013
Published 11th November 2013

ABSTRACT

BRAFO, Benefit-Risk Analysis for Foods, was a European Commission project funded within Framework Six as a Specific Support Action and coordinated by ILSI Europe. BRAFO developed a tiered methodology for assessing the benefits and risks of foods and food components, utilising a quantitative, common scale for health assessment in higher tiers. A methodology group reviewed and assembled the methodologies available developing a guidance document that describes a tiered ('stepwise') approach for

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performing a risk and benefit assessment of foods. In parallel, three expert groups on natural foods, dietary interventions and heat processing applied the tiered approach to several case studies. Finally a consensus group reported on the implications of the experience gained during the development of the project for the further improvement.

Keywords: BRAFO; Benefit–risk assessment; tiered approach; natural foods; macronutrient; heat processing; risk management.

ABBREVIATIONS

ADI, Acceptable Daily Intake; DALY, Disability Adjust Life Expectancy; QALIBRA, Quality of life - integrated benefit and risk analysis; QALY, Quality Adjust Life Expectancy; MeHg, Methylmercury; PCB, Polychlorinated Biphenyls; SME, Small Medium-sized Enterprises.

1. INTRODUCTION

As the burden of health costs within society increases due to a longer lifespan, overall balanced nutrition can play an important role in disease prevention. There is considerable disparity in the way benefits and risks are compared for compounds found in food, often relying on subjective judgement. This prevents adequate comparison of alternatives and renders resource prioritisation difficult. In addition, it is extremely difficult to provide comprehensible advice to consumers. It is therefore vital that an effective strategy be developed to enable a holistic analysis of the net health impact of chemicals in food to be assessed and quantified, in a manner analogous to the current assessment of risk.

The risk assessment of compounds in food is a mature process that follows a well-developed scientific approach; the strategy followed is the result of a substantial amount of thought and experience. Such a risk assessment has served society well to the extent that it has protected consumers from the potentially harmful effects of chemicals to which they might otherwise have been exposed through food consumption. For chemicals used to secure the integrity of food that require prior approval, such as pesticides or packaging materials, this works well, although indirect benefits are rarely weighed against residual risk. For chemicals with potential direct health benefits such as vitamins, the situation is more complex. It is then essential to evaluate in an integrated assessment both risks, manifest as negative impacts on health, and benefits that produce a positive impact on health.

The aim of BRAFO, a project funded by the European Commission and coordinated by ILSI Europe, was to develop a framework that allows quantitative comparison of human health risks and benefits of foods and food compounds based on a common scale of measurement. The approach should be based on the evaluation of changes in the quality/duration of life using a system that allows weighting of data quality and severity of effect, with quantification using QALY or DALY-like methodology [1]. The framework should consider how risks and benefits are interrelated. It was intended that the methodology developed should be sufficiently transparent to serve as a reference for the harmonisation of the evaluation methods used within the European Union and more widely in international evaluations.

A European network (BRAFO) was set up in September 2007, which involved expertise in benefit/risk analysis and nutrition, with representatives from academia, regulatory agencies and the food industry. The BRAFO Consortium was made up of the European branch of the

International Life Sciences Institute (ILSI Europe, BE), Imperial College London (ICL, UK), the Rijksinstituut voor Volksgezondheid en Milieu (RIVM, NL), the Max Rubner Institute (MRI, DE) and Procter and Gamble (P&G, BE). Additionally more than 50 “external experts”, mostly from academia, were involved in the different work packages.

2. RESULTS AND DISCUSSION

During the first year of the project, a methodology group brought together methodologies from several disciplines relevant to the evaluation of benefits and risks in food. Much of the primary data required for this evaluation exist in a form that may be only partially useful and these require remodelling so as to derive better estimates of benefits and risks. The reprocessing of available data to achieve a standard representation of inputs and outputs (costs and consequences) was required, which in turn necessitates the formulation of agreed guidelines that were common to all constituent elements of the project. This group reviewed and assembled the methodologies available. They produced a guidance document [1] that describes a tiered (‘stepwise’) approach for performing a benefit and risk assessment of foods. It was presented at the BRAFO Methodology workshop held on 25-26 September 2008, in Rome. The process starts with a pre-assessment and problem formulation step to set the scope of the assessment. This includes defining two scenarios for comparison in the assessment: the reference scenario (e.g. current diet, or a zero intake scenario), and an alternative scenario (e.g. introducing a new food or food policy). The approach consisted of 4 tiers (see Fig. 1). In many cases, a lower tier assessment using simple methods may be sufficient to show a clear difference between the health impacts of the two scenarios. In other cases, increasingly sophisticated methods were used at higher tiers until there is sufficient certainty for decision-making.

The tiered approach assesses the benefits and risks of changing from the reference scenario to an alternative, resulting in a statement about which scenario is preferred in terms of net health effects.

In Tier 1, each benefit and risk are assessed independently. These assessments would often use standard screening methods, but it may be worth using more refined methods if this avoids the need to proceed to Tier 2. Tier 1 comprises a separate, but as comprehensive as needed, benefit assessment, and a separate risk assessment.

In Tier 2, benefits and risks are compared in a qualitative way; no common metric is used yet, although the assessment of each individual benefit or risk can be quantitative or even probabilistic.

In Tier 3, benefits and risks are integrated quantitatively in a common metric, by a deterministic approach.

In Tier 4, benefits and risks are integrated quantitatively in a common metric by a probabilistic approach.

As indicated in Fig. 1, there is in practice a continuum between Tiers 3 and 4. Initially all parts of the assessment are treated deterministically (i.e. as fixed values), after which progressively more parameters are treated probabilistically (i.e. using probability distributions), until the net health impact is sufficiently well characterised for decision-making.

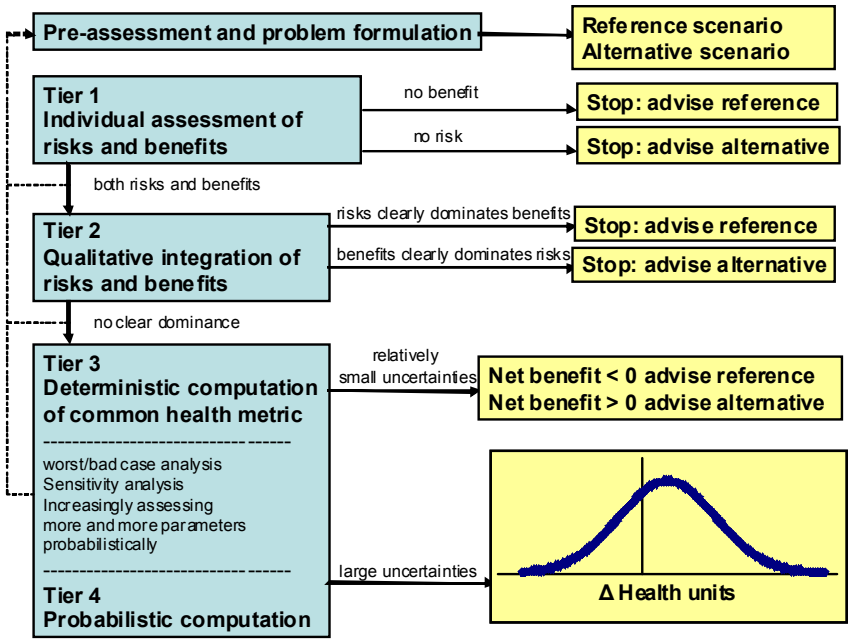

Fig. 1. A flow chart of the BRAFO tiered approach for health benefit-risk assessment of different dietary scenarios (reference and alternative). The formulation of the benefit-risk question may be iteratively refined in consultation with the risk manager/policymaker as the assessment progresses, as indicated by the dashed arrows at the left side of the figure

The steps needed to reach a conclusion in each tier follow largely the same steps as in the risk assessment paradigm. But after the first tier, comparison (tier 2) and integration (tier 3 and 4) of the risks and benefits follow. This is shown in Fig. 2.

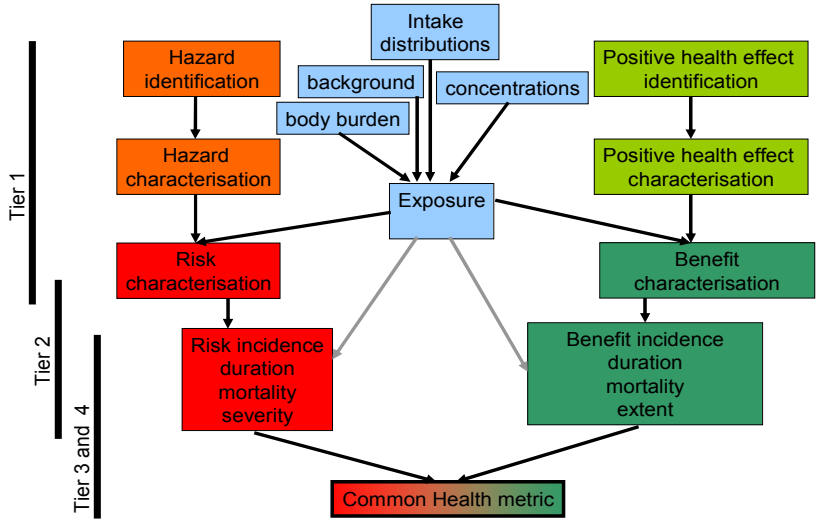

Fig. 2. A schematic description of the steps within each tier

3. CASE STUDIES

The development of the benefit-risk framework was expedited by its use on a number of selected examples of foodstuffs and food components. During the second year of the project, the three case study groups have worked on applying and adapting the methodological approach developed to undertake a benefit assessment, a risk assessment, and quantitative net health impact assessment on the selected cases. The results on the applicability of the BRAFO methodology on the case studies were presented and discussed at a second workshop in October 2009 in order to adapt the methodology according to the findings of the case studies.

The three case studies were:

3.1 Case Study "Natural Foods"

There is evidence that consumption of fish, particularly oily fish, has substantial beneficial effects on health. As a result the public is advised to increase its fish consumption as in many countries people consume considerably less than optimal. On the other hand it should be noted that some fish contain hazardous substances like dioxins, PCBs or methyl-mercury (meHg). The negative effects of these substances include the possible development of cancer or effects on the developing foetus.

As a consequence oily fish is an exceptionally good example of consumer confusion and therefore has been selected as a case study. Both qualitative and quantitative review of benefits and risks within BRAFO link to the work developed in the EU funded project QALIBRA, in which fish in general is one of the case studies.

Therefore, based on the present benefit calculations it is concluded that the consumption of 200 g/week of oily fish (farmed salmon) is more beneficial than no consumption at all as it would result in a significant reduction of incidence of cardiovascular disease. Although this scenario increased the intake of contaminants, for methyl-mercury as well as for dioxins the intake will still not exceed the provisional total weekly intake level.

Soy was selected as a second example of a natural food because it is recognised as a healthy, food delivering various essential nutrients. In addition, soy intake is associated with a reduced risk for cardiovascular disease. However, phytochemicals occurring naturally in soy, such as isoflavones, can have both beneficial and adverse effects, as demonstrated in a number of animal studies. For this case study [2], it was not necessary to go to tier 3. It could be concluded at tier 2 that soy protein consumption would result in an overall benefit for the general adult population.

3.2 Case Study "Dietary Interventions"

This topic consisted of an assessment of benefits and risks associated with dietary interventions. The work comprised as an example folic acid fortification of flour. The folic acid case described in detail the beneficial effects of intake of folic acid across dose levels in qualitative and quantitative aspects up to tier 3, taking into account sub-groups who would experience the greatest benefits or risks, i.e. pregnant women and the elderly. Although it would be necessary to accept both health risks and health benefits, it was possible to identify a scenario in which the benefits substantially outweighed the risks.

The work of this group also comprised examples of macronutrient replacement/food substitution [3]: the isocaloric replacement of saturated fatty acids with carbohydrates, the replacement of saturated fatty acids with monounsaturated fatty acids, and the replacement of sugar-sweetened beverages containing mono- and disaccharides with low calorie sweeteners. The isocaloric replacement of saturated fatty acids resulted in an overall health benefit in relation to cardiovascular disease, in the absence of health risks but did not constitute a genuine benefit-risk question.

The focus of the exchange of mono- and disaccharides for low calorie sweeteners was on the quantification of any residual risks associated with the toxicity of these substances at intakes above the ADI or similar accepted levels, the potential for nutritional interferences, and the nutritional benefits associated with typical ranges of intake. This case study stopped after tier 2 when it was apparent that there was essentially no risk associated with low calorie sweeteners.

Finally, an example of addition of specific ingredients to food, chlorination of drinking water, was addressed. In this case there are clear benefits and risks. However, the quantitative comparison of these falls short because of a lack of suitable scenarios and underlying data.

The respective examples illustrated how the BRAFO-tiered approach provided for various results, ranging from a quick stop as the result of an early, clear conclusion that benefit outweighs risk or non-genuine benefit-risk questions to continuation through the tiers into deterministic/probabilistic calculations.

3.3 Case Study “Heat Processing”

There is evidence that the traditional ways of cooking or heat-processing of foods besides the desired effects (like preservation, increased digestibility and flavour formation) lead also to the formation of heat-formed contaminants that could be damaging to our health.

Due to the individual reactivity of food components (e.g. amino acids, sugars, fatty acids) substantial interactions and changes occur during heat processing. Benefit-risk assessment can be used to give a clearer picture of quality profiles of food systems and their optimisation via positive balancing of the benefit-risk ratio for suitable nutrition.

Building on existing information related to the benefits and risks associated with changes known to occur during such heat treatment processes, this work package focused on three different examples of heat treatment of foods. Two examples involved individual undesired process contaminants (acrylamide and benzo(a)pyrene) as well as health benefits or risks associated with alternative processing methods minimizing these compounds [4]. The work package also addressed changes occurring during the heat treatment of milk and milk products which is commonly seen as beneficial, but also leads to changes in availability of relevant components/nutrients in this natural foodstuff (milk treatment case study).

4. CONSENSUS ON THE FINAL FRAMEWORK

Following the second workshop on case studies, the BRAFO Consensus work package started its work. The aim of this group was to knit together the work performed by the different expert groups. It established the extent to which the BRAFO methodology applied to the three case studies [2,3,4] was broadly applicable across various benefit/risk

categories, based on the experience obtained from the case studies. Priority was given to the harmonisation of the approaches identified by applying the framework to the specific case studies. This group finalised a manuscript [5] addressing a number of outstanding issues related to benefit risk assessment of foods, such as exposure assessment, level of evidence, which biomarkers to use and when, how to deal with animal data or uncertainty factors, particularly when using QALY or DALY methodology, and finally how to extrapolate data to different populations. This group also provided advice on how best to communicate BRAFO's findings to stakeholders and risk managers.

The first draft of the manuscript was presented at the third BRAFO workshop on 16-17 November 2010 in Barcelona. This included representatives of each project work package, and representatives from academia, industry (including SMEs), consumer interest groups and regulators. The main aims were to:

- Review the draft framework produced by the Consensus Group (previously circulated in the working documents) and discuss proposed amendments to this, as necessary, in order to achieve consensus,
- Consider recommendations of the participants for publication of the final document and dissemination of the contents,
- Ensure an as wide as possible dissemination by presenting the consensus framework/methodology.

5. CONCLUSIONS

This manuscript reported on the implications of the experience gained during the development of the project for the further improvement of benefit–risk assessment methodology. It was concluded that the methodology proposed is applicable to a range of situations and that it does help in optimising resource utilisation through early identification of those benefit–risk questions where benefit clearly outweighs risk or vice versa. However, higher tier assessments are complex and demanding of time and resources, emphasising the need for prioritisation. Areas identified as requiring further development to improve the utility of benefit–risk assessment include health weights for different populations and endpoints where they do not currently exist, extrapolation of effects from studies in animals to humans, use of in vitro data in benefit–risk assessments, and biomarkers of early effect and how these would be used in a quantitative assessment.

ACKNOWLEDGEMENTS

This study has been carried out with partial financial support by the Commission of the European Communities, Priority 5 Food Quality and Safety, within the Sixth Framework Programme (Contract No: 031731 BRAFO: Benefit Risk Analysis of Foods). The preparation of this manuscript was coordinated by ILSI Europe. ILSI Europe would like to thank all of the contributors to the BRAFO Scientific Supported Action. Overall, we would like to thank the ILSI Europe Risk Assessment of Chemicals in Food Task Force members and the BRAFO Steering Committee members for their support and guidance. Industry members of the task force are listed on the ILSI Europe website at www.ilsi.eu. For further information about ILSI Europe, please email info@ilsieurope.be or call +32 2 771 00 14. The opinions expressed herein and the conclusions of this publication are those of the authors and do not necessarily represent the views of ILSI Europe nor those of its member companies. This manuscript

does not necessarily reflect the views of the Commission and in no way anticipates the future policy in this area.

COMPETING INTERESTS

Dr Stéphane Vidry and Dr Alessandro Chiodini are employed by ILSI Europe.

REFERENCES

1. Hoekstra J, Hart A, Boobis A, Claupein E, Cockburn A, Hunt A, et al. BRAFO tiered approach for benefit-risk assessment of foods. Food Chem Toxicol. 2012;50(4):S684-98.
2. Watzl B, Gelencsér E, Hoekstra J, Kulling S, Lydeking-Olsen E, Rowland I, et al. Application of the BRAFO tiered approach for benefit-risk assessment to case studies on natural foods. Food Chem Toxicol. 2012;50(4):S699-709.
3. Verhagen H, Andersen R, Antoine JM, Finglas P, Hoekstra J, Kardinaal A, et al. Application of the BRAFO tiered approach for benefit-risk assessment to case studies on dietary interventions. Food Chem Toxicol. 2012;50(4):S710-23.
4. Schütte K, Boeing H, Hart A, Heeschen W, Reimerdes E, Santare D, et al. Application of the BRAFO tiered approach for benefit-risk assessment to case studies on heat processing contaminants. Food Chem Toxicol. 2012;50(4):S724-35.
5. Boobis A, Lagiou P, Hoekstra J,Przyrembel H, Schlatter J, Schütte K, et al. Critical appraisal of the assessment of benefits and risks for foods, 'BRAFO Consensus Working Group'. Food Chem Toxicol. 2013;5(55):659-75.

Peer-review history:
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