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Commentary

Recommendations for successful substantiation of new health claims in the European Union

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ABSTRACT

Background: While functional foods offer promise for public health and innovation in the food industry, the efficiency of such foods should be assured to protect consumers from misleading claims. Globally, many countries regulate the communication of the health effects of such foods to final consumers.

Scope and approach: In the European Union (EU), the use of health claims was harmonized in 2006. All claims need to be scientifically assessed by the European Food Safety Authority (EFSA) and pre-approved. Implementing the regulation has involved a steep learning curve for stakeholders, resulting in many health claims being rejected. The EU-funded REDICLAIM project used existing guidance documents, analyses of Scientific Opinions on new health claim applications, and a series of interviews with experts involved in such applications to identify key points in the process of authorizing new health claims.

Key findings and conclusions: Recommendations for the successful substantiation of new health claims in the EU were prepared. The substantiation of health claims is primarily based on human efficacy studies, and greater resources are required to authorize more innovative claims. The reported recommendations should be seen as a starting point for researchers in the area of nutrition and food technology, and for those dealing with functional foods, including the food industry.

1. Introduction

Nutrition is recognized as an important modifiable factor influencing human health. While overconsumption of energy-dense foods results in high energy intakes and growing incidence of obesity and a series of non-communicable diseases, specific populations are still at risk of nutrient deficiencies. Foods are a source of nutrients for the human body, but can also support body functions beyond adequate nutritional effects – providing health benefits. Discussions regarding functional food as a regulatory concept originated in Japan in late 1980s (Kwak & Jukes, 2001; Weststrate, van Poppel, & Verschuren, 2007). The development of functional foods was later particularly affected by regulations related to the use of health claims on foods (Ashwell, 2002; Weststrate et al., 2007). In the USA, evidence-based health or disease prevention claims have been allowed since 1990, when the Nutrition Labelling and Education Act was adopted

(Arvanitoyannis & Houwelingen-Koukaliaroglou, 2005). In the European Union (EU), harmonization was achieved in 2006 with Regulation (EC) No 1924/2006 on nutrition and health claims made on foods (NHCR) (EC, 2006), which requires health claims to be authorized before market entry (Verhagen & van Loveren, 2016). There is evidence of substantive use of health claims in EU countries, particularly in certain food categories (Hieke et al., 2016; Kaur et al., 2016; Kaur et al., 2015; Lalor, Kennedy, Flynn, & Wall, 2010; Lopéz-Galán & De-Magistris, 2017; Pravst & Kušar, 2015; Storcksdieck genannt Bonsmann et al., 2010). In a 2013 study, about 7–14% of pre-packed foods in selected EU countries were found to carry health claims (Hieke et al., 2016).

While functional foods with health claims provide opportunity for fostering innovation in the food sector and improving public health, there are also potential risks associated with their use, for example the lack of beneficial health effects or even health concerns which may

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arise from the regular consumption of these foods. Therefore many countries carefully regulate the use of health claims (de Boer & Bast, 2015).

The rationale behind the requirement for pre-approval of all specific health claims is ensuring fair competition and effective functioning of the internal EU market, as well as protection of consumers from misleading claims (EC, 2006). The latter is particularly important because health benefits are credence attributes, that is qualities that cannot be observed by a consumer. After a scientific assessment by the European Food Safety Authority (EFSA), the NHCR requires all health claims to be authorized by the European Commission (EC) through the comitology procedure (EC, 2017c). The Commission must act in line with the principles of good administration, and this imposes a duty of care on the Commission to act in good faith (“Demo-Studio Schmidt v Commission,” 1983), to give due consideration to all the arguments presented (“Nolle v HZA Bremen-Freihafen,” 1991), and to the task in hand (“Commission v Estonia,” 2012). In particular, Recital 16 of the NHCR requires the Commission to ensure that the claim can be well understood by consumers.

A key aspect of any health claim application is the provision of evidence regarding the cause-effect relationship between consumption of the food (constituent) and the claimed health outcome (Martínez & Siani, 2017; Navas-Carretero & Martínez, 2015). Implementing the NHCR has involved a steep learning curve for different stakeholders, including policy makers and authorities in the EU member states, the EFSA, and the food industry (Martin, 2015; Vero & Gasbarrini, 2012), with several suggestions having been made to improve it (Cappuccio & Pravst, 2011; de Boer, Urlings, & Bast, 2016; Kaur et al., 2016; Pravst, 2011). In many cases, health claim applications were evaluated with a negative outcome by the EFSA – often because they were not supported by sufficient scientific evidence (Verhagen & van Loveren, 2016). While an important objective of the NHCR was to foster innovation in the food sector, some evidence suggests that the opposite might be the case (Bröring, Khedkar, & Ciliberti, 2017; Khedkar, Ciliberti, & Bröring, 2016).

The challenges associated with the use and substantiation of health claims have been recognized by the European Commission (EC), resulting in the funding of specific projects in the EC's Seventh Framework Programme on topics including the role of health claims in consumer behaviour [CLYMBOL project (Hieke et al., 2015)] and food constituents that show potential [FIBEBIOTICS project (Mes, 2013), BACCHUS project (Buttriss, 2015)]. The REDICLAIM project was funded, with the aim to assess the NHCR, where a particular emphasis was on “reduction of disease risk” (RDR) claims (so called Art 14.1.a claims), and also new function claims (so called Art 13.5 claims). The project's focuses are: (1) understanding the main issues and hurdles concerning the substantiation and use of health claims on foodstuffs, and the level of awareness about legal obligations regarding the use of claims among the relevant stakeholders; and (2) to produce a three-fold study of the NHCR's impact on the claim substantiation process, health research and/or innovation in the food chain, and nutrition economic models – to determine the health impact (Raats et al., 2015). Another

key project objective was to support the food business in the enhanced development of innovative and competitive products, and their better compliance with the regulation.

2. Methodology and approaches

One of the REDICLAIM's work streams ascertained the interaction between legislation and the claim substantiation process, and on prepared key recommendations for the successful substantiation of new health claims in the EU – covering new function claims, as well as and RDR claims.

The health claims legislation in selected developed countries/regions (EU, USA, Canada and Australia/New Zealand) was compared, focusing on the advantages and disadvantages of different solutions from a research and development perspective (Raats et al., 2016). In all selected jurisdictions, RDR claims must be pre-approved before being used in the market. Applicants are usually food companies or producers of food ingredients and the application procedures are well defined. The strength of scientific evidence needed to substantiate such health claims is typically described as “generally accepted scientific evidence of beneficial physiological effect in humans” (EU), “significant scientific agreement” (USA and Canada), and an “established food-health relationship based on the totality and weight of evidence” (Australia and New Zealand) (Raats et al., 2016).

Health claim applications receiving an unfavourable evaluation from EFSA are either a result of poor quality available scientific data, or poor presentation of such data (i.e. the quality of the application) (Martínez & Siani, 2017; Pravst, 2010). In order to understand this in more detail, existing EFSA Opinions on new health claim applications were analysed, and interviews were conducted with experts experienced in preparing health claim dossiers, mostly from the food industry and research consultancy service providers specialized in the health claim authorization process. Analysis of the EFSA's Opinions focused on all, favorable and unfavorable, applications for RDR claims after the NHCR was introduced in 2007. Critical issues were identified and coded. Interviews were conducted with successful and unsuccessful RDR claim and new function health claim applicants. In practice, these claims can result in the authorization of company-specific, proprietary health claims, and may therefore represent a driving force for innovation in the food industry. Interviewees found the health claim application process to be either easy or challenging, depending on the novelty of the claimed health benefit and/or underlying science. The process was perceived as straightforward for food constituents for which existing knowledge can be exploited (e.g. for various well investigated types of dietary fibre in relationship to cholesterol lowering), while the process was regarded as much more challenging for health claims based on emerging scientific findings (i.e. less investigated types of fibre, plant extracts and their specific constituents, probiotics).

Based on the results of the above mentioned literature review of EFSA Opinions and interviews, key recommendations for the successful substantiation of new health claims in the EU (Fig. 1) were identified and a draft document containing the recommendations was prepared

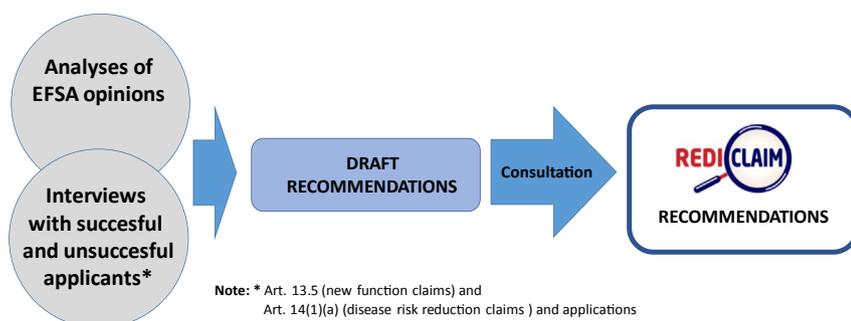


Fig. 1. Schematic approach to identifying key recommendations for the successful substantiation of new health claims in the European Union.

for consultation with experts from the food industry, research consultancy providers specialized in the health claim authorization process, academics, the EC and the EFSA. Experts were invited to provide comments and suggestions on the draft recommendations, which were next discussed at a workshop in Brussels in February 2017. All comments were discussed at a post-workshop consortium meeting, resulting in a revised version of the recommendations, which was sent for a final review to the consortium members and selected key external experts; resulting in a final list of key recommendations, as set out below.

3. Recommendations for the successful substantiation of new health claims in the European Union

The decision to start the application process for the authorization of a new health claim should be taken with care. While a new health claim can benefit food business operations, the application process requires time and effort. Companies can apply for new health claims for a variety of reasons, not just the communication of health benefits to the consumer. Reasons include the opening of new business-to-business channels, increasing a company's reputation, and in some cases also influencing decisions in countries outside the EU. A key question at the outset of the application process is whether the particularly claim in fact falls within the scope of the NHCR. In the EU, medicinal claims are not allowed on foodstuffs (EC, 2011). Moreover, some claims that are only considered to be indirectly related to health are not considered to fall within the scope of the regulation. An example of this are claims referring to the improved bioavailability of food constituents to which the general food labelling regulation applies (EC, 2011), requiring that information provided on foods is correct and not misleading for consumers.

The REDICLAIM project identified the following recommendations to support the preparation of applications for new function claims and RDR health claims in the EU:

- **Consider the EFSA's extensive guidance documents on the submission and substantiation of health claims.** These documents are considerably revised from time to time as a result of the experience gained in previous evaluations, and therefore the EFSA's webpage¹ is an excellent starting point for anyone interested in new health claims. A second revision of the *Scientific and technical guidance for the preparation and presentation of a health claim application* was published in 2017 (EFSA, 2017c), with more details of the requirements associated with presenting unpublished data. While this guidance provides all the details of how a health claim application should be compiled, including the requisite forms, the general scientific principles used by the EFSA in the evaluation of health claims are provided in the *General scientific guidance for stakeholders on health claim applications* (EFSA, 2016a). In addition, a series of documents provides specific guidance on the scientific requirements for health claims related to specific health relationships (Table 1). These documents are also occasionally revised. The guidance for health claims related to the immune system, the gastrointestinal tract and defence against pathogenic microorganisms was revised in 2016 (EFSA, 2016b), while the guidance targeting antioxidants, oxidative damage and cardiovascular health is currently undergoing revision (EFSA, 2017b).
- **Consider the EFSA's previous Opinions, particularly those published since the last revision of specific guidance concerning the health outcome in question.** All health claim applications are publicly listed in the EFSA's Register of Questions (EFSA, 2017a) and the Opinions are published in the open-access EFSA Journal. These Opinions provide important comments on study

designs and (in) appropriate biomarkers for certain health outcomes. Opinions related to the health outcome in question can be particularly valuable, even if they refer to other food constituents. It is also important to note both Opinions with favorable and unfavorable outcomes.

- **Consider the novelty of the food (constituent) and the science providing the evidence.** In the case of novelty, the claim application process will require considerable resources and a careful consideration of the strength of the evidence linking consumption of the food constituent and the health outcome. When the application is based on a new health effect, no previous evaluations are available for use as a reference point.
- **Consider the results of key EU-funded research projects dealing with health claims.** All funded projects are listed at the CORDIS portal (EC, 2017b) and have resulted in useful guidance documents, for example the Guidance for the design and implementation of human dietary intervention studies for health claim submissions (Lucey, Heneghan, & Kiely, 2016) produced within the BACCHUS project (the toolkit is available at the EuroFIR website: www.eurofir.org).
- **Evaluation time can be cut considerably if the health claim application (dossier) contains details of all pertinent data.** For unpublished data, full study reports are needed; the submission of abstracts or incomplete data will result in a delay – either before the evaluation process, or by way of a 'stop-the-clock' procedure during the evaluation. In the case of new function claims, applicants only have 15 days to provide clarifications or additional data, while in the case of RDR claims the clock-stop time can be negotiated with the EFSA depending on the type and amount of additional information requested (EFSA, 2014).
- **Data protection is possible when the scientific substantiation is primarily based on companies' own data.** When the substantiation of a health claim is based on (unpublished) proprietary data and the health claim cannot be substantiated without such data, the applicant can request five years of data protection. Such a request needs to be included in the health claim application. If data protection is not granted, all food business operators will be allowed to use the health claim in the EU immediately after the health claim has been authorized (on foods complying with the defined conditions of use).
- **In the process of scientifically evaluating a health claim, the safety of a food (constituent) is not systematically assessed.** If a food (constituent) is not authorized for sale in the EU market, its safety needs to be cleared in a separate process for authorizing a novel food (ingredient) (EC, 2017a). The submission of a new health claim application for a non-authorized (novel) food (constituent) could result in a scenario where the officially authorized health claim cannot be used in practice because the product cannot be put on the market. In the EU, the regulation of novel foods has been harmonised since 1997 (EU, 1997), however the new regulation (EU) 2015/2283 on novel foods will come into force in January 2018 (EC, 2015). When data protection is requested (Art. 28), the new regulation provides the possibility for a parallel authorisation procedures for novel foods (ingredients) and health claims (EC, 2015).
- **Assure that the food (constituent) can be sufficiently characterized.** A precondition of any health claim is that the evidence should be provided for a well-characterized food (constituent), and that food authorities will be able to control use of the authorized claim in practice (where applicable, appropriate laboratory methods should be provided). When the proposed health claim refers to a combination of food constituents, all active constituents should be sufficiently characterized. The EFSA has published recommendations for characterizing plant products and microorganisms in guidance documents (EFSA, 2016a).
- **A health claim's wording must reflect the scientific evidence and should be (where applicable) comparable with already**

¹ <https://www.efsa.europa.eu/en/applications/nutrition/regulationsandguidance>.

Table 1
EFSA's scientific guidance documents related to health claim applications.

Title	Reference
General scientific guidance for stakeholders on health claim applications	(EFSA, 2016a)
Guidance on the scientific requirements for health claims related to functions of the nervous system, including psychological functions	(EFSA, 2012c)
Guidance on the scientific requirements for health claims related to physical performance	(EFSA, 2012d)
Guidance on the scientific requirements for health claims related to bone, joints, skin and oral health	(EFSA, 2012b)
Guidance on the scientific requirements for health claims related to appetite ratings, weight management, and blood glucose concentrations	(EFSA, 2012a)
Guidance for health claims related to the immune system, the gastrointestinal tract and defence against pathogenic microorganisms	(EFSA, 2016b)
Guidance on health claims related to antioxidants, oxidative damage and cardiovascular health	(EFSA, 2011)
	Draft revision: (EFSA, 2017b)

authorized claims. If the proposed wording of a health claim is not comparable with a similar authorized claim (e.g. where a similar claim has already been authorized for another food constituent) it is quite likely the wording will be changed during the authorization process. All authorized health claims are listed in the EU Register of nutrition and health claims made on foods (EC, 2017d). Unless a propriety claim is being sought, the use of brand names should be avoided. As seen from the EU Register, the wording of authorized health claims mostly refers to the generic name of the food (constituent) for which the evidence was provided in the authorization process.

- **The claimed effect should be clearly defined and relevant for human health.** A number of effects have to date not considered to have been relevant (e.g., an increase in the number of bifidobacteria in the gut, a reduction of the waist circumference) (Pravst, 2010).
- **For all claims other than those based on the essentiality of nutrients, the substantiation of a health claim should primarily be based on good quality human efficacy studies.** Randomized controlled trials (RCT) are considered as a gold standard. Non-blinded RCTs are acceptable in cases where blinding is not possible. In weighing up the evidence, all aspects of the design and quality of the studies are considered (including the risk of bias). Tools for assessing study quality are available (EFSA, 2015).
- **The proposed conditions of use should reflect the conditions in which the studies used for substantiating the claim were conducted.** If not otherwise specified, health claims should be directed to the general population. The population used for claim substantiation should reflect the target population. Alternatively, the specific study group in which the evidence was obtained should enable the results to be extrapolated to the proposed target population. Particular attention is needed when studies are not conducted with a healthy population. It is also important to ensure that the consumer can reasonably consume enough of the food (constituent) as part of a balanced diet to obtain the claimed effect.
- **The application should provide the totality of the available scientific data.** Applications must also include unpublished results and studies that show no or the opposite effects. Results of unpublished studies should be delivered with full study reports. Reporting should be in line with the International Conference on Harmonization (ICH) guideline E3 on the structure and content of clinical study reports (ICH, 1995), adapted for the purpose of health claim substantiation. Appropriate standards should also be used in proprietary studies. Consider Good Clinical Practice and take care of all safety and ethical aspects, including appropriate informed consents. Studies should be registered in an on-line clinical trials registry using one of the registers included in the WHO International Clinical Trials Registry Platform (ICTRP) (WHO, 2017) before the first subject is recruited.
- **Successful scientific substantiation of a health claim does not ensure that it will be authorized.** Based on the Scientific Opinion, the EC prepares a draft decision for submission to the Standing Committee on Plants, Animals, Food and Feed (PAFF). After this

Committee votes in its favor, the European Parliament and the Council have the right of scrutiny over the proposed decision. If there is no objection, the EC adopts the decision. There are examples of scientifically substantiated health claims which have not been authorized due to public health concerns (i.e. safety issues; classification of the food constituent as a medicine in most member states; claims not in line with current dietary recommendations). A typical example of such a scenario is a health claim related to hydroxyanthracene derivatives and improvement of bowel function (EFSA, 2013), which was not authorized due to safety concerns expressed by the EU member states.

In conclusion, the key recommendations outlined above were identified to support applicants in preparing successful applications for new function claims and RDR health claims in the European Union. The outcome of this process provides key references and highlights the issues to be addressed in all phases of the authorization of new claims – from deciding whether to apply for a new health claim and the formulation of its wording, establishing and collecting the supporting evidence through to the post-evaluation process, and the final specification of the health claim for formal incorporation into the Annex of the regulation. The recommendations should be seen as a starting point for researchers in the area of nutrition and food technology, and for those dealing with functional foods, including the food industry.

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