Project title: Understanding the impact of legislation on "reduction of disease risk" claims on food and drinks (rediclaim)
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Summary description of project context and objectives

REDICLAIM seeks to understand the way in which the European Regulation (EC) No. 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods and associated legislation has had and continues to have an impact on the substantiation and use of "reduction of disease risk" claims on food and drinks. To achieve this REDICLAIM will: (1) Seek to understand the (a) main issues and hurdles concerning substantiation and use of "reduction of disease risk" claims on food and drinks; (b) level of awareness about legal obligations with regard to "reduction of disease risk" claims on food and drinks among the relevant stakeholders; and (2) Produce a three-fold study of the impact of nutrition and health claims legislation specific to "reduction of disease risk" claims on food and drinks on: (a) The claim substantiation process, (b) Health research and/or innovation in the food chain, and (c) Nutrition economic models to determine health impact.

The programme of work is being conducted through six Work Packages (WPs):

WP1: Stakeholder engagement and dissemination brings together a community of interested stakeholders (e.g. industry, regulatory bodies, clinical trial specialists, scientists, health professionals and civil society) to reflect on project findings at key stages of the project.

WP2: Establishing the regulatory frameworks is:

- mapping the regulatory framework and decision-making process for health and nutrition claims at EU level;
- mapping and analysing the implementation of the regulatory framework for 'reduction of disease risk' claims at Member State level; and
- mapping and analysing the evidence of compliance to enable research into impacts of legislation on innovation.

WP3: Exploring the interaction between legislation and health research and/or innovation in the food chain is:

- identifying research carried out on beneficial interactions between the presence or absence of a food component and cardio-vascular function(s) in the body
- exploring food manufacturers' willingness/capability to exploit new research findings in cardio-vascular health related innovation processes; and
- exploring the role of health claim regulation as a facilitator or barrier to research-based innovation aimed at developing products based on new findings and risk reduction of diseases.

WP4: Ascertaining the interaction between legislation and the claim substantiation process is conducting:

- a comparison of legislation of EU with that in other developed countries;
- an investigation of known assessments of health claim applications and reasons for rejections and
- case studies on applicants' experiences of the health claim application process with focus on positively and negatively assessed applications.

WP5: Nutrition economic models for food constituents associated with 'reduction of disease risk' claims is using nutrition economic modelling methods to calculate the potential health and economic impact of 'reduction in disease risk' claims on the general population by establishing the proportion of the population with suboptimal consumption of the food (constituent) of interest and the impact of optimal consumption levels on disease burden and health care costs.

WP6: Project management ensures effective technical coordination and project management is implemented and sustained to successfully complete all aspects of the proposal.

REDICLAIM results will contribute to:

- the development of an evidence base of the process by which health and nutrition claims are made and controlled by regulatory frameworks;
- the effectiveness of their control by regulation; and
- the establishment of recommendations for government, industry and the scientific community with a view to conducting the necessary research and development of such products. The aim of this will be to achieve both effective compliance with better regulation and, to contribute to the enhancement of innovative and competitive products.

Description of work performed and main results

WP2: Establishing the regulatory frameworks

Work Package 2 involved four tasks:

- Task 2.1. Mapping regulatory frameworks and decision-making process at EU level;
- Task 2.2. Mapping the implementation framework across Member States;
- Task 2.3. Mapping the case-study countries;
- Task 2.4: Guidance and recommendations on the impact of the legislation on reduction of disease risk legislation.

Task 2.1 involved a desk based exercise coupled with interviews at government level, mapped the regulatory framework and decision-making process for health and nutrition claims at EU level; and mapped and analysed the implementation of the regulatory framework for 'reduction of disease risk' (RDR) claims at Member State (MS) level. It is clear that there are significant problems relating to the operation of the Nutrition and Health Clams Regulation (EC) No 1924/2006 (hereafter NHCR). These arise from a variety of factors including:

- the clash between the twin aims of consumer protection and trade;
- the inevitable centring of the NHCR on Article 114 TFEU;
- the lack of a clear legal basis in the Treaty for public health and nutrition matters;
- the uneasy fit of NHCR into the food safety context when it is in fact based on the medicines evaluation model whereby proof of efficacy rests upon the link between active ingredient and health and the health outcome which is likely to be achieved;
- the role of EFSA in the evaluation of claims under the NHCR where EFSA's primary function is in assessing risk rather than in the evaluation and analysis of the benefit of an ingredient;
- the lack of a clear mandate and basis for EFSA to act in NHCR claims; the lengthy delays in processing claims; and
- legal aspects of the regulation, particularly the 'comitology' procedures which pertained at the time of implementation of NHCR.

Task 2.2 mapped the top-level implementation of RDR claims at MS level. The purpose was to identify and illustrate the role of the MSs in the authorisation and enforcement process, as well as potential differences between the approaches of each MS regarding the use of RDR claims on food. We found that, usually the national framework was concerned with the implementation of Directive 2000/13 EC (now replaced by Regulation 1169/2011) on food labelling. All MSs had national legislation supplementing NHCR but in varying degrees.

As part of Tasks 2.1 and 2.2, we analysed Regulation 1924/2006 (NHCR) from a doctrinal point of view and identified the main aspects of the Regulation's implementation, as well as the process stipulated in the Regulation for the authorisation and enforcement of 'reduction of disease risk' health claims on food. This process of

research allowed us to cascade down from EU level with an analytical understanding into the institutional framework behind the process set against the policy perspective at EU level to a closer examination of the way in which NHCR was bedded down in the 28 Member States where we were able to counterpoint some differences between the authorisation and enforcement processes focusing on the national frameworks, the available guidance, the procedure and enforcement. The final stage of the empirical work enabled us to focus at a deeper level in respect of seven member States where we interviewed key individuals from seven Member States: Austria, Croatia, Finland, Germany, Poland, Slovenia, and the UK.

Our original plan had been to focus on three Member States for the in-depth interviews and empirical analysis but our earlier research suggested that a broader sweep of national authorities should be undertaken and, following advice from the Advisory Board, we extended coverage to as many national authorities that were willing to be interviewed. Eight agreed to be interviewed; two declined (Cyprus and Italy); and there were no responses from the remaining 18. One of the eight interviews was interrupted by the interviewee who had to attend another meeting at the last minute and it proved impossible to rearrange this interview due to the workload of the interviewee.

The first three tasks revealed clearly that there are significant problems relating to the operation of the NHCR. We identified a variety of factors at work. These cascaded down from issues at EU level due to legal competencies of the European Union and comitology procedures to problems in the authorisation process at national authority and EFSA level to enforcement issues. Deliverables 2.1; 2.2 and 2.3 document these issues in detail.

The Conclusions and recommendations of WP2 are:

The provision of better guidelines and Codes of Practice at national level which give clearer information on i) scientific evidence necessary for a successful claim, and ii) appropriate wording of claims was recommended. This arose from consideration of the way the national authorities were operating. At EU level and amongst commentators we noted that there was a view that, as the legislation was in the form of a Regulation, there was little room for manoeuvre at national level. However, we found that the national authorities were very active and engaged extensively with one another especially through the Working Group. They also responded to applicants and gave advice (often consulting the national medicines approval authority). As was noted by the General Court in the case of Hagenmeyer and Hahn v Commission, national authorities are not merely functioning as "mailboxes" for the applications but are expected to facilitate the process of claims' authorisation (see 13.3). It seemed, therefore, that much benefit would be gained for FBOs going through the authorisation process if there were national level guidelines (based on the EU guidelines but produced locally for the regionally-based industrial sector) which were focussed on them and which national authorities could promote and use as the medium for training and awareness building.

Retaining the role of national authorities is recommended as they appear to be providing a useful service in checking the validity of the dossier. It follows from the previous recommendation that, given the good communication at national authority level which should be exploited to provide more information to industry on the process and what is needed for the dossier and on the wording of claims, the role of national authorities should be retained. The process whereby FBOs first submit the claim to a national authority should be retained.

The authorisation process needs to be controlled and expedited. It is recommended that with better and more focussed guidelines (on which see Deliverable 4.4) delivered through the medium of national authorities, the process would be significantly improved. Most interviewees who commented on this considered that there should be an ad hoc process for food. But co-training undertaken alongside those responsible for the medicines evaluation framework where the process bears such similarities in terms of the approach which demands an evaluation of a derived and causally linked benefit rather than a food safety risk would potentially be profitable.

Differentials in enforcement are potentially an issue to be addressed in the future. The wide variety of penalties is a cause for concern but is one which is problematic given the competence for determining penalties and offences which lies with the Member States. A secondary question is the extent to which enforcement activity will vary across the Member States as (/if) health claims become more common.

The role of the EU in the promotion of public health policies. The European Commission's role in health is mainly to support Member States in their efforts to protect and improve the health of their citizens. Thus, the purposes of most 'health-related' legislation, which includes NHCR, relate to the promotion of trade, fair competition between food business operators and protection of consumers from misleading claims. NHCR is not concerned primarily with the promotion of health. This is because 'health-related' regulations are nevertheless normally based on Article 114 TFEU which is concerned with the establishment and functioning of the internal market. This creates a tension between the demands of industry in respect of competition and the desire for a health policy at EU level which would support health claims legislation in promoting good health as a primary objective. One commentator stated that such a change which would involve a Treaty change is 'politically unthinkable'. While that may be correct, nevertheless, it remains a recommendation that, if the EU is to develop a stronger health policy, then the legal basis for 'health-related' regulations needs to be reconsidered.

WP3: Exploring the interaction between legislation and health research and/or innovation in the food chain

The overall objective of Work Package 3 "Explore the interaction between health claim legislation and health research and/or innovation in the food chain" is to identify whether the EU Nutrition and Health Claims legislation acts as a stimulator/facilitator/promoter or a barrier of research-based innovation in the European food and drink industry. Task 3.1 identified the kind of research used to support health claim applications based on new knowledge (13.5 claims) and RDR claims (14.1a claims). Claim substantiation is mainly based on relatively new but not the most recent peer-reviewed and published research. Companies have a role in partly funding the research an in co-operating with the academic researchers, but the use of unpublished data is limited in claim applications. EU's role as a funding body is very limited in the cardiovascular health claim applications submitted by the end of 2013.

The second task (i.e. WP3.2) focused on food manufacturers' willingness and capability to exploit new research findings in their innovation processes and whether this legislation has promoted food industry's interest in developing more innovative, science-based food products and/or products carrying health claims. The findings of this study suggest that from the food industry's point of view, revising the process and criteria associated with health claim substantiation in Regulation (EC) 1924/2006 on nutrition and health claims would be regarded as an act that promotes innovation in the European food and drink industry. As stated in the interviews, the authorisation process was perceived as lengthy, bureaucratic, and not transparent, which made it difficult for companies to navigate. Cutting the time used by EFSA in the evaluation process of health claims applications would facilitate faster introduction of products with new health claims on the market. Findings from the interviews also highlighted that criteria coming from the EFSA for the assessment of the health claim substantiation applications were not deemed as clear and well documented; in particular clarification was requested in terms of study design, definition and selection of healthy population, and selection of biomarkers that are regarded as suitable to provide the evidence. It should be mentioned that EFSA has recently started a process of updating scientific guidance on substantiation of new health claims. Revised general scientific guidance, which applies to health claims across the board, and specific guidance for claims related to the immune system and the gastro-intestinal tract were published in January 2016 . Currently EFSA is working on the revision of other specific guidance targeting other health areas, nevertheless the above mentioned issues related with new biomarkers and study population groups are unlikely to be resolved without considerable investments into basic research.

Second, establishing a pre-submission consultation between EFSA and an individual company was seen as beneficial for the food industry. An open dialogue would increase transparency about the process and enable companies to clarify specific requirements for the clinical research and thereby reduce the uncertainty and associated risks. Pre-process consultation was deemed as a valuable step for the both parties – the applicant and EFSA alike: in addition to lowering the uncertainty and risk in the food industry, it would also reduce EFSA's work load having to make evaluations on claim dossiers that are not complete in the information required.

The task WP3.3 reported here explored the role and impact of the Regulation (EC) No 1924/2006 on nutrition and health claims made on foods (NHCR) (EC 2006) in stimulating research-based innovation is perceived among different actors in food innovation and value chain in general. The study concluded the following:

Health as a drive in innovation and interest in health claims. Healthiness was regarded as an important product attribute in foods, but only a third of respondents thought it as the main driver in new food product development. The research in food and health domain should be a co-responsibility of private and public sectors. Food and ingredient companies were rated as the major contributors together with universities and research institutes in research that supports the development of new and innovative food products. Although food and nutrition is a major contributor in non-communicable diseases, the development of new product-based solutions is mainly seen as the interest of private companies. The results suggest that in food and health domain, the public funding should support food and food ingredient industry in their aims to develop products that support health and healthy eating.

Due to the importance of healthiness as a product attribute, health claims were highly interesting to companies with a majority of those respondents for whose organisation it was relevant reporting that they have already applied the option to use the generic 13.1 claims. Furthermore, all except one of those respondents whose organisation could apply for 13.5 and 14.1a health claims were interested in doing so, and majority in the near future as well. The result partly reflects the recruitment process and respondents who have selected to take part in the survey, but it also shows that there is a great interest in the food sector to utilise the claims. Health claims were perceived as the way to communicate health-related benefits to consumers in the interviews reported in Deliverable 3.2. Although the health claims were acknowledged a cost-efficient tool to communicate about the health benefits to the consumers in this survey as well, the open answers also expressed worries about how the claims can be worded. Highly technical wording of the claims that EU has approved were deemed as difficult to understand by consumers and thereby their usefulness in consumer communication may be limited, especially if the aim is to promote the product.

There is also a difference in the way the different types of health claims are perceived. The generic function claims (so called 13.1 claims) were rated mildly positively as cost-efficient and easy options for companies' marketing activities, whereas claims that are based on new knowledge (13.5 claims) or risk reduction claims (14.1a) were seen as more challenging for companies, because they require an application process (EC 2008). A large part of the open comments at the end of the survey related to this process and problems in building a dossier for the application.

Perception of the application process for claims based on new knowledge or disease risk reduction. The application process required for 13.5 and 14.1a claims (EC 2008) was regarded as resource demanding, slow and bureaucratic with an uncertain outcome by those who had taken part in the process. Their ratings suggest that applicants felt great uncertainty about what kind of information was required in the application dossiers and how the required information and study results should be reported. EFSA has already responded to many of these uncertainties by improving their guidance documents with specific guidance on types of evidence, certain substance areas, and general guidance on how unpublished studies should be reported in order to qualify as evidence in the dossier. Building of the dossiers was a major challenge demanding both heavy financial investment and multidisciplinary expertise, which only large companies are likely to have in-house.

The comments mainly reflect the negative ratings given to the closed items, but some respondents pointed out the need for the legislation. They trusted that the legislation, in long term, proves to be beneficial to all actors. Even the negative comments are not so much about the regulation as such, but about the manner in which it has been implemented, especially in relation to the evidence required to substantiate the claims. The strongest agreement in the survey when asked about the claim application was with the item related to needing a multidisciplinary team to fulfil the requirements of an application dossier.

Impact of Nutrition and Health Claim Regulation. Findings from this survey support the earlier qualitative findings from interviews with industry experts both on the role of NHCR in making decisions about new product development and interest in taking part in research projects (see Deliverable report 3.2 and 4.3). In this study, the responses to NHCR were negative or neutral at the best when respondents assessed whether the claim regulation

has achieved its objectives or has had an impact on interest in multidisciplinary research on food and health area. In general, NHCR was mainly seen as a barrier to innovation and development of new food products that are science-based and have high novelty value, which is in accordance with earlier findings on studies that have explored the impact of generic health claims. However, in our study we can elaborate this picture and see that perceptions differ between different types of claims and most concerns related to claim application process required for 13.5 and 14.1a claims. In comparison to these 13.5 and 14.1a claims generic 13.1 claims were regarded as the easy options for marketing. Furthermore, the responses differed between respondents based on what is their relationship to NHCR, both in relation to how well they report to know the NHCR and whether they work in food and/or ingredient companies or in research, especially in relation to innovation-related impacts.

The interesting point is that those who claimed to know the regulation well were more negative about its impact on innovation and participation in collaborative research projects. Similarly, food industry or ingredient industry saw the impact on innovation and research in much more negative manner than those working on research institutes or in universities. Equal difference could be found between those who worked with major novelty and those who did not with the latter being more positive about the impact on research funding coming from public or private sources. These results are concerning since the better knowledge or higher stake in the claims seems to result in more negative responses: those who are not using the claims seem to be more positive which suggests that experience with the claim regulation does not create enthusiasm. Surprisingly, there were no significant differences between respondents from large organisations and SMEs in these ratings, although the high investment was regarded one of the main barriers in the claim applications and being especially hard for the SMEs to tackle. Respondents from large organisations did not perceive the legislation more positively, although they agreed that the NHCR requirements favour large organisations.

The best-achieved objective of the regulation was consumer protection, which received neutral responses as a mean. Unlike the responses on innovation promotion, there were no differences between respondent groups based on the knowledge on NHCR or type of background organisation. Furthermore, the claims were rated rather positively as marketing tools, and giving credibility and higher profit margins to the companies. Thus, the claims were regarded valuable from the company's point of view, even if the NHCR legislation does not encourage innovation. The perceived high marketing value and innovation barrier creates an incongruity in relation to the objectives of the legislation. Whereas marketing value encourages company to use health claims in their products, attaining health claims based on new knowledge was assessed to demand heavy investments and large resources, while achieving a positive result being unsure. In order to solve this conflict, the generic health claims (Article 13.1 claims) become very tempting: claims can be used without separate application and heavy investment. Thus, industry's worry about legislation becoming a barrier rather than a facilitator for the research-based innovation is the likely outcome.

This study reveals the dilemma industry in facing in relation to the NHCR. Health claims offer an opportunity to differentiate products and create positive marketing messages, but the processes related to applying for claims that would allow companies to create the innovative products based on new knowledge are resource demanding and take a long time with no certainty of outcome. The perceived benefit of claims as marketing tools and the demands set for 13.5 and 14.1a claims push companies to using 13.1 claims that are freely available and require only minor investments in product development. From the new product development point of view these products are likely to be vitamin and other nutrient enriched products, which have two major advantages compared to products based on new knowledge or risk reduction claims: in addition to low investment costs, they are familiar to the consumers and thereby claims are likely to be more appealing to consumers. Whether these products offer real benefits to consumers can be questioned, as most European citizens have adequate intake of most nutrients. Alternatively, companies can devalue the importance of health in their products and put their marketing efforts into other consumer benefits, e.g. hedonic attributes, sustainability, or use cues that imply healthiness to consumers without needing a substantiation such as naturalness.

NHCR does not necessarily discourage companies to use health claims, but it may direct the use of health claims more to the direction of generic health claims that do not require special acceptance process, whereas the claims based on new knowledge remain rare. Those food and ingredient companies who have good research networks, strong internal expertise on food and health within innovation teams, and long-term research focus in their

innovation activities have an advantage in utilising the claims based on new knowledge or disease risk reduction claims (Article 13.5 or 14.1a claims). For these companies, NHCR can offer special opportunities, but for the majority of food and food ingredient industry the more likely road to take is to apply the existing claims that offer an easier access to the market.

WP4: Ascertaining the interaction between legislation and the claim substantiation process

Task 4.1 compared NHCR with that in other developed countries (USA, Canada, Australia, New Zealand (NZ)), focusing on advantages and disadvantages of different solutions from an RandD perspective. In all selected jurisdictions, RDR claims need to be pre-approved before being used on the market. Food businesses have the possibility to apply for authorization of new RDR claims and procedures are well defined. Applicants are fully responsible for preparation of application dossiers. The process of evaluation of the submitted proposals and authorization of new health claims is not subject to fees, however it is likely that fees will be implemented in Australia and NZ. Typical description of the strength of scientific evidence needed for approval of such health claims is "generally accepted scientific evidence of beneficial physiological effect in humans" in the EU, "significant scientific agreement" in the US and Canada, and "established food-health relationship based on the totality and weight of evidence" in Australia and NZ.

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

Consider the EFSA's extensive guidance documents on the submission and substantiation of health claims. The guidance documents can be occasionally considerably revised, taking the experience gained in previous evaluations into account, and therefore the EFSA's webpage[1] 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, with many more detail of what is required when presenting unpublished data. While this guidance provides all the details on 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*. In addition, a series of documents provides specific guidance on the scientific requirements for health claims related to antioxidants, oxidative damage and cardiovascular health, appetite ratings, weight management, and blood glucose concentrations, bone, joints, skin, and oral health, physical performance functions of the nervous system, including psychological functions, and the immune system, the gastrointestinal tract and defense against pathogenic microorganisms. The latter guidance was revised in 2016, and others will be revised in the future.

Consider previous EFSA's Opinions, particularly those published since the last revision of a specific guidance concerning the health outcome in question. All health claim applications are publicly listed in the EFSA's Register of Questions (EFSA, 2017a), while 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. It is necessary to focus on Opinions with a favourable outcome and on Opinions with an unfavourable outcome, as well as on those referring to other food constituents.

Consider the novelty of the food (constituent) and the novelty of the science providing the evidence. With novelty, the claim application process will require considerable resources and careful consideration of the strength of the evidence linking the consumption of the food constituent and the health outcome. When the application is based on new claimed health effect, no previous evaluations are available for use as a reference point.

[1] https://www.efsa.europa.eu/en/applications/nutrition/regulationsandguidance

Consider the results of key EU-funded research projects dealing with health claims. All funded projects are listed at the CORDIS portal. Very useful guidance documents are available, for example the Guidance for the design and implementation of human dietary intervention studies for health claim submissions, produced within the BACCHUS project (the toolkit is available at the EuroFIR website: www.eurofir.org).

Evaluation time can be shortened 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 as '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 with disease risk reduction claims the clock-stop time can be negotiated with the EFSA depending on the type and amount of the additional information requested.

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 5 years of protection for the data. Such a request needs to be included in the health claim application.

In the process of scientific evaluation of 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). The submission of a new health claim application for a non-authorized (novel) food (constituent) could result in a scenario where the officially authorized heath claim cannot be used in practice because the product cannot be put on the market.

Assure that the food (constituent) can be sufficiently characterized. A precondition for 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 the 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.

A health claim's wording must reflect the scientific evidence and should be comparable with already authorized claims (where applicable). If the proposed wording of a health claim is not comparable with a similar authorized claim (if applicable, for example in case where a similar claim has already been authorized for another food constituent) it is very likely that the wording will be changed during the process of the authorization process. All authorized health claims are listed in the EU Register of nutrition and health claims made on foods (EC, 2017b). Unless one is seeking a propriety claim, the use of brand names should be avoided. As seen in 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 already been considered as not relevant (e.g., an increase in the number of bifidobacteria in the gut, a reduction of the waist circumference).

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 of the evidence, all aspects of the design and quality of the studies are considered (including in relation to the risk of bias). Tools for assessing study quality are available.

The proposed conditions of use should reflect the conditions in which the studies used for substantiating the claim were conducted. The target population should reflect the population used for the claim's substantiation. Alternatively, the specific study group in which the evidence was obtained should enable the results to be extrapolated to the proposed target population. Attention is called for studies not conducted on a healthy population. It is also important to ensure that the consumer can reasonably consume enough food (constituent) to obtain the claimed effect as part of a balanced diet.

The application should provide the totality of the available scientific data. Applications must also include unpublished results and studies that show no or opposing 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, 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. A study should be registered in an on-line clinical trials registry before the first subject is recruited. Use one of the registers included in the WHO International Clinical Trials Registry Platform (ICTRP).

The successful scientific substantiation of a health claim does not ensure its authorization. Based on the Scientific Opinion, the EC prepares a draft decision for submission to the Standing Committee on the Food Chain and Animal Health (SCFCAH). After this Committee votes in its favour, 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 authorised 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 in most countries).

In conclusion, the key recommendations outlined above were identified to support applicants in preparing successful applications for new health claims in the European Union. The outcome of this process provides key references and highlights the issues needing to be properly addressed in all phases of the authorization of new claims – from deciding whether to apply at all for a new heath claim and the formulation of its wording, establishing and collecting the supporting evidence, through to the post-evaluation process, when the final specification of the health claim is formally incorporated 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 256 functional foods, including the food industry.

WP5: Nutrition economic models for food constituents associated with 'reduction of disease risk' claims

In Task 5.1, based on a review of the relevant literature, a decision making model has been built and parameters assembled to appraise the cost-effectiveness of the plant sterol/stanols for the management of people with hypercholesterolemia at increased risk of coronary heart diseases. We are using the model to produce estimates that will enable an evaluation of the cost-effectiveness of plant sterols/stanols incorporated in dairy products/margarine spreads when compared to a normal diet.

Raised total or low-density-lipoprotein cholesterol (LDL-c) is a major risk factor predisposing an individual to cardiovascular disease (CVD) which can be modified by various prevention programmes, such as changes in diet. Plant sterols and stanols (a saturated subgroup of sterols), hereafter referred to collectively as plant sterols, are plant equivalents of cholesterol with a very similar molecular structure. They are found naturally in fruit, vegetables, nuts, seeds, grains and legumes and prevent the absorption of cholesterol into the bloodstream, but are unlikely to be consumed in sufficient quantities to reduce cholesterol levels.

Research has shown that adding plant sterols into the daily diet can substantially enhance the cholesterol-lowering effects of diet change, and that functional foods enriched with plant sterols, (including margarine-type spreads, mayonnaise and salad dressing, and dairy products - milk, yogurt, cheese) have a beneficial effect on the serum lipid profile of the consumer. Hence, an increasing number of experts and health organisations recommend consuming plant sterols to reduce CVD risks, including the American and British Heart Associations. Moreover, the European Commission has acknowledged the value of sterol-enriched foods for cholesterol lowering through approval of health claims on some products.

Although the effectiveness of plant sterols in reducing LDL-c has been verified in a number of studies, evidence on whether use of plant sterols is a cost-effective preventive strategy for reducing CVD risks is limited. In Task 5.2 we used a modelling approach to explore the effectiveness and cost-effectiveness of the 'reduction in disease risk'

claim related to plant sterols. This modelling used the consumption of plant sterol-enriched margarine-type spreads for the prevention of CVD in people hypercholesterolemia in England, when compared to a normal diet, as the case study (Yang et al, accepted for publication).

A nested Markov model was employed using the perspective of the British NHS. Effectiveness outcomes were the 10-year CVD risk for individuals with mild (4 to 6 mmol/l) and high (above 6mmol/l) cholesterol (NHS Choices, 2016) by gender and age groups (45-54, 55-64, 65-74, 75-85 years); CVD events avoided; quality-adjusted life year (QALY) gains over 20 years. Cost effectiveness was evaluated against the NICE threshold of £20,000 - £30,000 per QALY gained.

Using a deterministic approach, the results showed that daily consumption of enriched spread reduces CVD risks more for men than women, and for older age groups more than younger ones. Assuming 50% compliance, 69 CVD events (59 non-fatal, 10 fatal) per 10,000 men and 40 CVD events (33 non-fatal, 7 fatal) per 10,000 women would be saved over 20 years; at 100% compliance level, the figures are 141 CVD events per 10,000 men and 80 CVD events for women.

QALY gains rise with compliance level and age, and are also higher for men than women. The ICERs (costs per QALY gained) are higher for mildly elevated cholesterol than for the high cholesterol group. Hence subsidising sterol-enriched spread is more cost effective at higher cholesterol levels. In both the 50% and 100% compliance models, the cost per QALY gained is below the £20,000 NICE threshold for cost-effectiveness for men over 64 years and women over 74 years; it is below the £30,000 threshold for men over 54 and women over 64. If consumers bear the full cost of enriched spread, NHS savings arise from reduced CVD events, although ultimately the impact depends on compliance levels.

To date, only three other studies have evaluated the cost-effectiveness of plant sterols, but these have not used a decision economic modelling approach. A cost-benefit analysis of plant sterol-enriched low-fat margarine for cholesterol reduction based on the German population found that the 10-year CVD risk and associated costs were significantly lower for the plant sterol group compared with the normal diet group. A projection at the level of the German population led to a reduction of 117,000 CVD cases over 10 years for the whole German population and a cost saving of €1.3 billion. Similar results were demonstrated in Canada, where it was estimated that significant savings could be made annually for the publicly funded healthcare system if plant sterol-enriched food was approved for sale. It has also been suggested that plant sterol-enriched spreads are potentially cost-effective in the prevention of CVD risks in adult men and in older women in Finland.

A guidance document providing an overview of the principles and application of decision economic modelling in the health care arena has been produced. It seeks to illustrate some of the additional challenges that arise when nutritional interventions are considered. The challenges of nutrition economic modelling are described.

Strategic impact

The European Regulation on Nutrition and Health Claims of 2006 provides a common regulation, allowing health claims to be made on foods in a uniform manner throughout the member states of the European Union. When introduced, the European Commission stated that the main objectives of the proposal were to:

- achieve a high level of consumer protection by providing further voluntary information, beyond the mandatory information foreseen by EU legislation;
- improve the free movement of goods within the internal market;
- increase legal security for economic operators;
- ensure fair competition in the area of foods; and
- promote and protect innovation in the area of foods.

This action aimed to analyse whether these set goals have been achieved or whether they are regarded as achievable by stakeholders based on their opinions on how the legislation has been implemented. The action concentrated mainly in risk reduction claims which represent a type of claim that can give well-specified benefits

to the consumers and provide a possibility to food industry to create products that can be differentiated from competitors.

High level of consumer protection has been one of the central aims in health claim legislation by requiring that all health claims are based on scientific substantiation and approved beforehand, thereby creating a positive list on claims that can be used in the European market. However, the impact of the legislation depends on how the legislation is implemented and regulated in different EU member states. REDICLAIM identified regulatory gaps and developed guidelines for the effective regulation of health claims which enable and enhance innovation while meeting the consumer and ethical perspectives.

Differences in legislation related to providing health-related information have varied widely before the common EU legislation on claims. For food industry this has acted not only as barrier against free movement of goods and fair competition, but also as a lower interest in investing in health-related research to produce products that have specific health outcomes, including those with contributing to risk reduction. In REDICLAIM we explored whether the legislation has promoted food industry's interest in producing more innovative, science-based products that would respond to the needs of European citizens. REDICLAIM identified regulatory factors that encourage and hamper innovation in European food industry and come out with propositions that can promote more radical innovations in European food industry which in the long run will contribute to the competitiveness of the food industry.

Further details

For more information, please refer to the project website at: www.rediclaim.eu

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