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Guidance Document for Preparing a Submission for Food Health Claims Using an Existing Systematic Review

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Bureau of Nutritional Sciences
Food Directorate
Health Products and Food Branch

Canada

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Note: The "SR" in the headings throughout this document is intended to distinguish these sections from those in Health Canada's Guidance Document for Preparing a Submission for Food Health Claims.

List of Tables

Overview

Food health claims are statements in labelling or advertising that link the consumption of a food to health. In Canada, false, misleading or deceptive product representations are prohibited. The following document is a guide to help the food industry prepare an application for a new health claim. It explains how to use an existing systematic review of the scientific literature to demonstrate that a proposed health claim is valid.

Summary

The purpose of this document is 1) to help industry petitioners determine whether an existing systematic review is eligible to serve as the basis for a health claim, and 2) to provide specific guidance for preparing the appropriate documentation in order to substantiate a health claim based on an existing systematic review. Health Canada developed this guidance to make the preparation of a health claim submission more efficient while maintaining the standards that ensure the claim is scientifically valid.

In order to be accepted as the scientific basis for a new health claim, an existing systematic review must have been prepared according to the guidelines of a regulatory or scientific organization with standards of evidence that are similar to those of Health Canada. Furthermore, the review should be current and directly address the food/health relationship in the proposed claim. In addition to the systematic review, petitioners are required to submit information about the food that will carry the claim, the proposed health effect, how the food/health relationship relates to the general population (i.e., generalizability), and the feasibility of consuming an effective intake of the food in the context of the Canadian diet.

This document provides guidance on how to meet these requirements is provided in this document and should be used in conjunction with the Guidance Document for Preparing a Submission for Food Health Claims.

1.0(SR) Background

Health Canada's standards for the scientific substantiation of health claims are described in the Guidance Document for Preparing a Submission for Food Health Claims. In response to industry's concerns regarding the resources required to meet health claim substantiation standards, Health Canada developed guidance for a health claim submission process that allows petitioners to use certain existing systematic reviews as the basis for health claim substantiation.

1.1(SR) Purpose of this Guidance Document

The purpose of this document is 1) to help petitioners determine whether an existing systematic review is eligible to serve as the basis for substantiation of a health claim and 2) to provide specific guidance for preparing the appropriate documentation to substantiate a health claim when an existing systematic review is used. The term "systematic review" is used throughout this document to refer to a review of scientific literature that uses explicit, systematic methods intended to minimize bias. This document will frequently refer to, and is intended to be used in conjunction with, the Guidance Document for Preparing a Submission for Food Health Claims.

1.2(SR) Types of Food Health Claims and Scientific Substantiation

A **health claim** is any representation in labelling or advertising that states, suggests or implies that a relationship exists between the consumption of a food[1] and health. All health claims are subject to subsection 5.(1) of the Food and Drugs Act, which prohibits false, misleading or deceptive product representations.

1.2.1(SR) Disease Risk Reduction and Therapeutic Claims

Generally, **disease risk reduction claims** are statements that link a food to a reduced risk of developing a diet-related disease or condition in the context of the total diet. For example, "[Naming the food] may reduce the risk of cardiovascular disease". **Therapeutic claims** refer to the treatment or mitigation of a disease or health-related condition, or about restoring, correcting or modifying body functions. For example, "[Naming the food] lowers blood cholesterol".

1.2.2(SR) Function Claims

Health claims about the specific beneficial effects that the consumption of a food or food constituent has on normal functions or biological activities of the body are referred to as

[1] The term "food" refers to a food category, a food (whole or processed) or a food constituent, added or inherent.

function claims. Such claims relate to a positive contribution to health or performance. For example, "[naming the food] promotes regularity or laxation".

Statements or claims to the effect that a food's energy value or a nutrient[2] contained in the food is generally recognized as an aid in maintaining the functions of the body necessary to the maintenance of good health and normal growth and development are a subset of function claims referred to as **nutrient function claims**.

1.2.3(SR) Scientific Substantiation

Detailed information on the substantiation of health claims can be found in the Guidance Document for Preparing a Submission for Food Health Claims, which is applicable to all food health claims, with the exception for claims about a nutrient. Submissions[3] for health claims made on food sold in Canada can be made to the Food Directorate of Health Canada to ensure that claims are adequately substantiated and are compliant with applicable sections of the Food and Drugs Acts and its associated regulations. Consultation with the Food Directorate is encouraged before preparing a health claim submission. Contact information for the Food Directorate can be found in Section 1.3(SR) below.

An abbreviated process exists for assessing the acceptability of new function claims for nutrients that meet specified criteria. For information on documenting the supporting evidence for new nutrient function claims, please refer to the Canadian Food Inspection Agency website, here.

1.3(SR) Submission Procedures and Health Canada Contact Information

1.3.1(SR) Organization of the Submission

The submission package should meet the following requirements:

- The submission should include all components outlined in the checklist in Section 4.0(SR).
- Pagination must be sequential for the entire submission.
- Paper copies must be bound or organized in a binder.
- The applicant's identification (*e.g.*, company name) should be included on all pages of the submission.
- Submissions must be in English or French. Relevant submission material in other languages must be translated into English or French.

[2]The term "nutrient" is not defined in the Food and Drug Regulations for the purposes of food labelling and advertising. Health Canada considers a substance to be a nutrient if it is recognized as such by the Institute of Medicine of the National Academies, Washington, DC.
[3]The term "submission" usually refers to a stand-alone dossier containing all of the information required to substantiate a health claim.

- Applicants are responsible for clearly indicating parts of the application that contain proprietary or confidential data (*e.g.*, results from an unpublished clinical trial, details on manufacturing, *etc.*).
- Applicants are responsible for the accuracy of all cited references, published or unpublished. An established style for citing references must be used.
- The submission must be signed by the petitioner or by his/her attorney or agent, or, if a corporation, by an authorized official.

All submissions will be screened for completeness and the petitioner will be informed of deficiencies.

1.3.2(SR) Submission to Health Canada

Two hard copies of the submission must be forwarded by mail to the address below.

Submission Management and Information Unit
Food Directorate, Health Products and Food Branch, Health Canada
251 Sir Frederick Banting Driveway
Postal Locator: 2202E
Ottawa, Ontario K1A 0K9

An electronic submission may be forwarded to the following e-mail address in addition to, but not in place of, hard copies: smiu-ugdi@hc-sc.gc.ca.

1.3.3(SR) Health Canada Contact Information for Questions / Pre-submission Consultation

Contacting Health Canada with questions or for a pre-submission consultation is optional, however these steps may reduce the time it takes to review a submission by minimizing the number of deficiencies in the submission. Pre-submission consultations allow petitioners to seek clarification on regulatory requirements and on specific information that should be included in the submission. Health Canada may also be able to identify specific issues that should be addressed in the submission.

Questions or requests for pre-submission meetings may be directed to:

Nutrition Labelling and Claims Section
Food Directorate, Health Products and Food Branch, Health Canada
251 Sir Frederick Banting Driveway
Postal Locator: 2202E
Ottawa, Ontario K1A 0K9

The following email address may also be used: healthclaims-allegationssante@hc-sc.gc.ca.

1.3.4(SR) Review Process Following a Submission

Within 15 days of receipt of the submission, Health Canada will notify the petitioner by letter that the submission has been received.

1.3.5(SR) Re-evaluation of a Health Claim

Health Canada may re-evaluate an approved health claim in response to a petitioner, or on its own initiative, due to new scientific evidence that brings into question the certainty of the claim or the conditions for its use.

2.0(SR) Health Canada's Health Claim Submission Requirements

An overview of Health Canada's requirements for full health claim submissions, described in Health Canada's Guidance Document for Preparing a Submission for Food Health Claims, is provided in Table 1(SR), below. The most resource intensive component is the evaluation of claim validity (Section 5.0); as such the main intent of this guidance is to help to make the preparation of a health claim submission more efficient while maintaining the standards that ensure the claim is scientifically valid.

Table 1(SR): Health Canada's health claim submission requirements	
Relevant Section of the Full Guidance Document	**Description**
Contact information (Section 2.1)	Identifies the organization submitting the health claim and a person that can be contacted for scientific or regulatory questions
Details pertaining to the proposed claim (Section 2.2)	Communicates important aspects related to the health claim (*e.g.*, food of interest, health outcome of interest)
Regulatory status of the health claim in other jurisdictions (Section 2.3)	Describes the regulatory status of the health claim in other jurisdictions
Characterization of the food (Section 3.0)	Describes the composition and manufacturing of the food and ensures it meets quality standards and pre-defined specifications
Characterization of the health effect (Section 4.0)	Characterizes the health effect, the validity of biomarkers used, and the relevance of the health effect to the Canadian population
Evaluation of claim validity (Section 5.0)	Guides the retrieval and evaluation of the totality of relevant evidence on the food/health relationship to allow for an assessment of: 1) causality, 2) generalizability, 3) biological relevance of the health effect, and 4) feasibility of consuming an effective intake of the food

Important Note

If you are preparing a health claim submission using an existing systematic review, you will need to follow the steps described in Sections 2.1, 2.2, 2.3, 3.0, and 4.0 of the Guidance Document for Preparing a Submission for Food Health Claims. You will then need to follow the steps described in Section 3.0(SR) of the present document to fulfill the requirements for evaluating claim validity using an existing systematic review, rather than those described in Section 5.0 of the full Guidance Document. The figure in Appendix A illustrates where the requirements for the systematic review-based submission process diverge from those of the full process.

3.0(SR) Requirements for Submissions that Use an Existing Systematic Review

3.1(SR) Source of Scientific Evidence to Support the Health Claim

Objective: To ensure that health claim submissions that use an existing systematic review are based on an appropriate source of scientific evidence to support claim validity and to provide general information about the source report, including the relevant review question and corresponding conclusion.

Background

In Canada, scientific substantiation of a health claim is guided by standards of evidence (see Appendix B). Based on a comparison between Health Canada's standards and those of other scientific or regulatory organizations who provide guidance for conducting a systematic review, Health Canada made the decision to accept certain existing reviews as evidence of claim validity in a health claim submission[4]. The accepted regulatory or scientific organizations that developed the guidance as well as the guidance documents used to prepare reviews are included in Table 2(SR).

The standards of evidence described in the relevant guidance documents are generally consistent with those of Health Canada; however, Health Canada will nonetheless conduct a detailed evaluation of the evidence included in the report to ensure that the health claim is substantiated.

Table 2(SR): Eligible reviews prepared according to specific guidance from a regulatory or scientific organization

Eligible Review Type	Regulatory or Scientific Organization	Relevant Guidance Document(s)
High-level health claim petitions	Food Standards Australia/New Zealand (FSANZ)	Proposed Amendments to *Applications Handbook* (FSANZ, 2008)
Article 14 and 13(5) health claim petitions	The European Food Safety Authority (EFSA)	Scientific and Technical Guidance for the Preparation and Presentation of the Application for Authorization of a Health Claim (EFSA, 2007)
Cochrane Reviews	The Cochrane Collaboration	Cochrane Collaboration Handbook for Systematic Reviews of Interventions (Higgins and Green, 2009)
Systematic Literature Reviews	The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR)	Systematic Literature Review Specification Manual (WCRF and AICR, 2006)
Evidence-based Practice Center (EPC) Evidence Reports	The Agency for Health Care Research and Quality (AHRQ)	Methods Reference Guide for Effectiveness and Comparative Effectiveness Reviews (AHRQ, 2007a)

[4] Health Canada may be willing to consider reviews other than those listed in Table 2(SR) if the standards of evidence are consistent with those of Health Canada.

Procedure:

- Complete Table 3(SR): *Information about the source for health claim substantiation*
- If the review was an eligible review type prepared according to the guidance of a scientific or regulatory organization involved in the evaluation of health claims (*i.e.,* FSANZ, EFSA), a hard copy of the full health claim application must be included as an appendix to the submission.
- If the review was an eligible review type prepared according to the guidance of a scientific organization, include a hard copy of the full publication as an appendix to the submission.

Table 3(SR): Information about the source for health claim substantiation	
Eligible review	☐ High-level health claim petition *(FSANZ)* ☐ Article 14 and 13(5) health claim petitions *(EFSA)* ☐ Cochrane Review *(Cochrane Collaboration)* ☐ Systematic Literature Review *(WCRF/AICR)* ☐ EPC Evidence Report *(AHRQ)*
Report reference (full citation)	
Review question (*i.e.,* question/objective that describes the food/health relationship being assessed)	
Relevant conclusion of the review (*i.e.,* the conclusion that supports the food/health relationship in the proposed claim)	

3.2(SR) Required Addenda

3.2.1(SR) Updating the Scientific Evidence

3.2.1.1(SR) Information about the Original Search

Objective: To describe the original literature search and selection criteria used to identify relevant evidence and to determine whether an update to the literature search is required.

Background

Systematic reviews used as the basis for health claim substantiation must be up to date in order to ensure that all relevant evidence pertaining to the food/health relationship is considered. In an area where the evidence is evolving rapidly, it is possible that a systematic review may require updating even at the time of publication. Recommendations from an AHRQ technical review on updating systematic reviews suggest that publishers of systematic reviews should consider a policy of requiring authors to update searches performed more than 12 months prior to

submission (AHRQ, 2007b). In order to ensure that the evidence for health claim substantiation is as current as possible, Health Canada requires petitioners to update a literature search performed more than 12 months prior to submission of the application.

Procedure:

- Complete Table 4(SR): *Information about the literature search from the original review*, identifying the date of search (*i.e.*, the date the databases were last searched for studies for the review), the electronic databases searched, the search strategy(ies) employed, the selection criteria (inclusion/exclusion criteria) and whether an update to the literature search is required.

Table 4(SR): Information about the literature search from the systematic review	
Date of search	
Databases searched	
Search strategy(ies)*	
Selection criteria	
Is an update required?	☐ Yes – the date of search is more than 12 months prior to the submission date of this health claim petition ☐ No – the date of search is less than 12 months prior to the submission date of this health claim petition (if "No", please skip to Section 3.2.2 (SR))

*If multiple strategies were used (*e.g.*, for different electronic databases) please include each strategy indicating the relevant database.

3.2.1.2(SR) Update the Original Literature Search

Objective: To search the literature for new studies published since the original review and to maintain a record of the literature search results.

Procedure:

- If the "no" box in Table 4(SR) is checked, please skip to Section 3.2.2(SR) *Generalizability of the Data to the Target Population*.
- If the 'yes' box in Table 4(SR) is checked, it is recommended to seek the assistance of a **qualified reference librarian/information scientist** to re-execute the original literature search. Use the original search strategy(ies) described in Table 4(SR) to re-execute the search in each electronic database. Note, it will be necessary to use search limits to specify the date range for the search. If such limits were used in the original search, they can be modified for this search.
    - Include a copy of the literature search results in an appendix to the submission, either by printing it directly from the databases or by saving it and submitting to Health Canada electronically.
    - Complete Table 5(SR): *Number of references identified in the update to the literature search.*

Table 5(SR): Number of references identified in the update to the literature search	
A. Number of references identified during the literature search update	
B. Number of duplicates	
TOTAL references identified (A-B)	

3.2.1.3(SR) Filter the Literature Search Results

Objective: To apply the selection criteria used in the original review to the literature search results so that non-relevant/non-useful references are excluded.

Procedure:

- Apply the selection (inclusion/exclusion) criteria to the titles of references identified during the literature search update. Note, it is best to err on the side of over-inclusion at the title-filtering stage to minimize the likelihood of excluding relevant/useful literature early on.
- Apply the selection criteria to the abstracts of references that were not excluded during the title-filtering.
- Retrieve full-text versions of references that were not excluded during the abstract filtering. Apply the selection criteria to the full text version of references.
- Count the number of references excluded at each stage and complete Table 6(SR): *Number of references excluded at each stage of the literature selection process*.

Table 6(SR): Number of references excluded at each stage of the literature selection process	
A. References prior to applying selection criteria (this should be the same number as the TOTAL (A-B) in Table 5(SR) above)	
B. References excluded at title filtering stage	
C. References excluded at abstract filtering stage	
D. References excluded at full-text filtering stage	
TOTAL references included (A-B-C-D)	

Important Note

If, after the selection criteria are applied, there are several new relevant studies, the systematic review may be too outdated to serve as the sole basis for claim validity. It may be appropriate to abandon the systematic review-based submission process in favour of the full process. The Guidance Document for Preparing a Submission for Food Health Claims provides step-by-step guidance on the tabulation, appraisal and interpretation of data from a group of studies.

3.2.1.4(SR) Generate Reference Lists

Objective: To list the included studies and the excluded studies from the literature search update, along with reasons for their exclusion in a transparent manner.

Procedure:

- Produce a reference list of studies that met the selection criteria at the full-text filtering stage and include it in Table 7(SR): *List of references that meet the selection criteria.*
- Produce a reference list of all studies that were identified in the literature search update but that did not meet the selection criteria at the full-text filtering stage. Include the reference and the reason(s) for exclusion in Table 8(SR): *List of references excluded and reason(s) for exclusion*.
- Ensure you have the full-text copy of all publications that meet the selection criteria. Copies of the full-text references should be included with the submission in an appendix. If studies in languages other than English or French were included, then translations of the studies in either English or French must be provided.

Table 7(SR): References that meet the selection criteria	
#	Reference (full citation)
1.	
2.	

Table 8(SR): References that do not meet the selection criteria at the full-text filtering stage		
#	Reference (full citation)	Reason(s) for Exclusion*
1.		
2.		

*Reason(s) for exclusion may include: report type, health effect, population health status, etc. Only one reason per reference is required.

3.2.1.5(SR) Consistency of New Evidence

Objective: To determine whether the new evidence identified by the updated search is consistent with the evidence reviewed as a part of the original report.

Procedure:

- Complete Table 9(SR): *Consistency between the new evidence and the systematic review*.
- For each new study identified, discuss how the new data impact the conclusions of the original systematic review (*e.g.*, do the studies increase or decrease the certainty of the pre-existing results? Are the amounts of food and the observed effect sizes consistent with those in the studies originally included? Does the totality of the evidence support the claim?).
- If the findings of the new studies do not support the conclusions of the original review, petitioners must explain why the health claim is still justified based on the totality of the evidence, including both the new data and the data in the original review.

Table 9(SR): Consistency between the new evidence and the systematic review	
Reference	Consistency*
	☐ Yes ☐ No
	☐ Yes ☐ No
	☐ Yes ☐ No

*"Yes" indicates that the new data are consistent with the conclusions of the original review whereas "No" indicates that the new data are <u>not</u> consistent with the conclusions of the original review

3.2.2(SR) Generalizability of the Data to the Target Population

Objective: To demonstrate that the food/health relationship is relevant to the target population identified in Table 2: *Details pertaining to the proposed health claim* (Section 2.2 of the Guidance Document for Preparing a Submission for Food Health Claims).

Procedure:

- Using all of the studies that support a favourable direction of effect, discuss the health status of the sample populations studied and whether the baseline health status of sample populations was a factor in the effect of the food (*e.g.*, suppose a systematic review examined the effect of whole grains on coronary heart disease among participants previously diagnosed with CHD or with existing risk factors for CHD, is the evidence still generalizable to the Canadian population?).

3.2.3(SR) Physiological Meaningfulness of the Effect of the Food Exposure

Objective: To understand the impact of exposure to the food on human health.

Procedure:

- Based on the studies included in the review and those identified during the literature search update, discuss whether the effects (range of effects and/or a specific effect) observed with food exposure (range of exposures and/or a specific exposure) are physiologically meaningful/relevant to human health. Provide reasons to support your response. Include a discussion on the sustainability of the beneficial effect.

3.2.4(SR) Feasibility of Consuming an Effective Amount of the Food

Objective: To demonstrate that the amount of food required for a meaningful beneficial effect can be feasibly consumed as part of a healthy, balanced diet by the target population in Canada.

Procedure:

- Provide information on the feasibility of incorporating the effective amount of food into a healthy diet. Include information on the current intakes of the food (from Table 4 – *Information requirements for the characterization of the food*) in the target population (from Table 2 – *Details pertaining to the proposed health claim*).
- Provide information on the expected* intakes of the food from all sources, if added to one or more foods, in the target population using Canadian intake data where possible.
- Estimate changes* in usual dietary patterns (*i.e.*, substitution or elimination of existing foods) with potential approval of the food for a health claim.
- Identify the subgroups of the population expected to have the greatest exposure to the food and subgroups at risk from exposure to the food.

*Clearly communicate the assumptions (and the evidence on which they were based) and statistical simulations used for these estimations.

3.2.5(SR) Conclusions

Objective: To justify the health claim based on the totality of the evidence.

Procedure:

- Make concluding remarks on the food/health relationship and its relevance to public health.
- Finalize claim wording, making sure that the subject of the claim and the health effect are those for which there is scientific evidence.
- Propose and justify conditions for a food to qualify for the health claim such as:
    - Minimum amount of the food eligible to carry the claim; *e.g.*, minimum 1g beta-glucan per reference amount or minimum 3 servings per day required
    - Maximum levels of food to be consumed, *e.g.*, no more than 3g plant sterols per day
    - Proposed food matrices, *e.g.*, a fermented dairy matrix
    - Minimum, maximum levels of nutrients in the food that are not the subject of the claim, *e.g.*, meets the criterion for low in saturated fat
- Comment on any adverse effects (*i.e.*, adverse direction of effect) observed in the evaluated human studies, and subgroups at risk from excessive intakes of the food.
- Propose risk management strategies (if necessary) to address adverse effects and/or restrictions on use of the food (*e.g.*, indicate wording of recommended warning statements).

4.0(SR) Checklist for Submission

Objective: To ensure that all requested information is included in the submission. Health Canada will use this checklist when evaluating submissions for completeness. If deficiencies exist, petitioners may be asked to address them before the full evaluation can proceed.

Procedure:

- Please complete and submit the checklist in Table 10(SR). Please ensure that all applicable required elements are addressed before submitting to Health Canada.

Table 10(SR): Checklist for a submission based on an existing systematic review

Requirement	Section Details	Yes	No	N/A*
Organization and Presentation of the Submission				
All required sections are properly identified	1.3.1(SR)			
Pagination is sequential throughout the submission	1.3.1(SR)			
Submission is bound or organized in a binder	1.3.1(SR)			
Applicant is identified on every page	1.3.1(SR)			
Language of submission is English or French	1.3.1(SR)			
References are accurate and formatted	1.3.1(SR)			
Submission is signed by the person responsible for it	1.3.1(SR)			
Two hardcopies of the submission are provided	1.3.1(SR)			
All confidential/proprietary data are identified	1.3.1(SR)			
Content of the Submission				
Applicant information is provided	2.1; Table 1			
Details pertaining to proposed health claim are provided	2.2; Table 2			
Regulatory status of health claim in other jurisdictions is described	2.3; Table 3			
Information requirements for characterization of the food are met	3.0; Table 4			
If the food is a bioactive substance (added or inherent), lab-certified specifications are included in an Appendix	3.0			
Requirements for characterization of the health effect and all relevant biomarkers are met	4.0			
A hard copy of the systematic review is included as an appendix to the submission	3.1(SR)			
Source for health claim substantiation is identified	3.1(SR); Table 3(SR)			
Information about the literature search from the original review is provided	3.2.1.1(SR); Table 4(SR)			

Table 10(SR): Checklist for a submission based on an existing systematic review				
Requirement	**Section Details**	**Yes**	**No**	**N/A***
Number of new references selected is provided	3.2.1.2(SR); Table 5(SR)			
Results of literature filtering are described	3.2.1.3(SR); Table 6(SR)			
References that meet the selection criteria are listed	3.2.1.4(SR); Table 7(SR)			
Copies of full-text references of publications that meet the selection criteria are included in an appendix to the submission	3.2.1.4(SR)			
References that do not meet the selection criteria at the full-text filtering stage and reasons for exclusion are listed	3.2.1.4(SR); Table 8(SR)			
Consistency of new evidence with systematic review findings is evaluated	3.2.1.5(SR); Table 9(SR)			
Generalizability of the evidence to the target population is discussed	3.2.2(SR)			
Physiological meaningfulness of the effect of the food is discussed	3.2.3(SR)			
Feasibility of consuming an effective amount of the food is discussed	3.2.4(SR)			
Conclusions are made	3.2.5(SR)			

*N/A=Not applicable

5.0(SR) References

CFIA (Canadian Food Inspection Agency). (2009). *Guide to Food Labelling and Advertising*. Available at: http://www.inspection.gc.ca/english/fssa/labeti/guide/toce.shtml
Accessed on September 15, 2010.

EFSA (European Food Safety Authority). (2007). Opinion of the Scientific Panel on dietetic products, nutrition and allergies (NDA) on a request from the Commission related to scientific and technical guidance for the preparation and presentation of the application for authorisation of a health claim. Available at: http://www.efsa.europa.eu/en/scdocs/scdoc/530.htm.
Accessed on January 7, 2011.

Health Canada. (1985). Food and Drugs Act. Available at: http://laws.justice.gc.ca/en/f-27/.
Accessed on February 14, 2011.

FSANZ (Food Standards Australia New Zealand). (2008). *Proposed Amendments to "Applications Handbook".* Available at:
http://www.foodstandards.gov.au/_srcfiles/Amendments%20to%20Handbook%20-%20Consolidated%20changes%20for%20consultation1.pdf.
Accessed on January 6, 2011.

Health Canada. (2009). *Guidance Document for Preparing a Submission for Food Health Claims*. Available at: http://www.hc-sc.gc.ca/fn-an/legislation/guide-ld/health-claims_guidance-orientation_allegations-sante-eng.php.
Accessed on January 6, 2011.

Higgins J, Green S (2009). *Cochrane Handbook for Systematic Reviews of Interventions.* Available at: http://www.cochrane.org/resources/handbook/.
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AHRQ (Agency for Healthcare Research and Quality). (2007a). *Methods Reference Guide for Effectiveness and Comparative Effectiveness Reviews*. Available at:
http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=318.
Accessed on September 15, 2010.

AHRQ (Agency for Healthcare Research and Quality). (2007b). *Updating Systematic Reviews* (Technical Review no. 16, AHRQ Publication no. 07-0087). Available at:
http://www.ahrq.gov/clinic/tp/sysrevtp.htm.
Accessed on October 4, 2010.

WCRF and AICR (World Cancer Research Fund & American Institute for Cancer Research). (2006). *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective: 2nd Expert Report: Systematic Literature Review Specification Manual Version 1.5*. Available at: http://www.dietandcancerreport.org/downloads/SLR_Manual.pdf. Accessed on January 7, 2011.

Appendix A

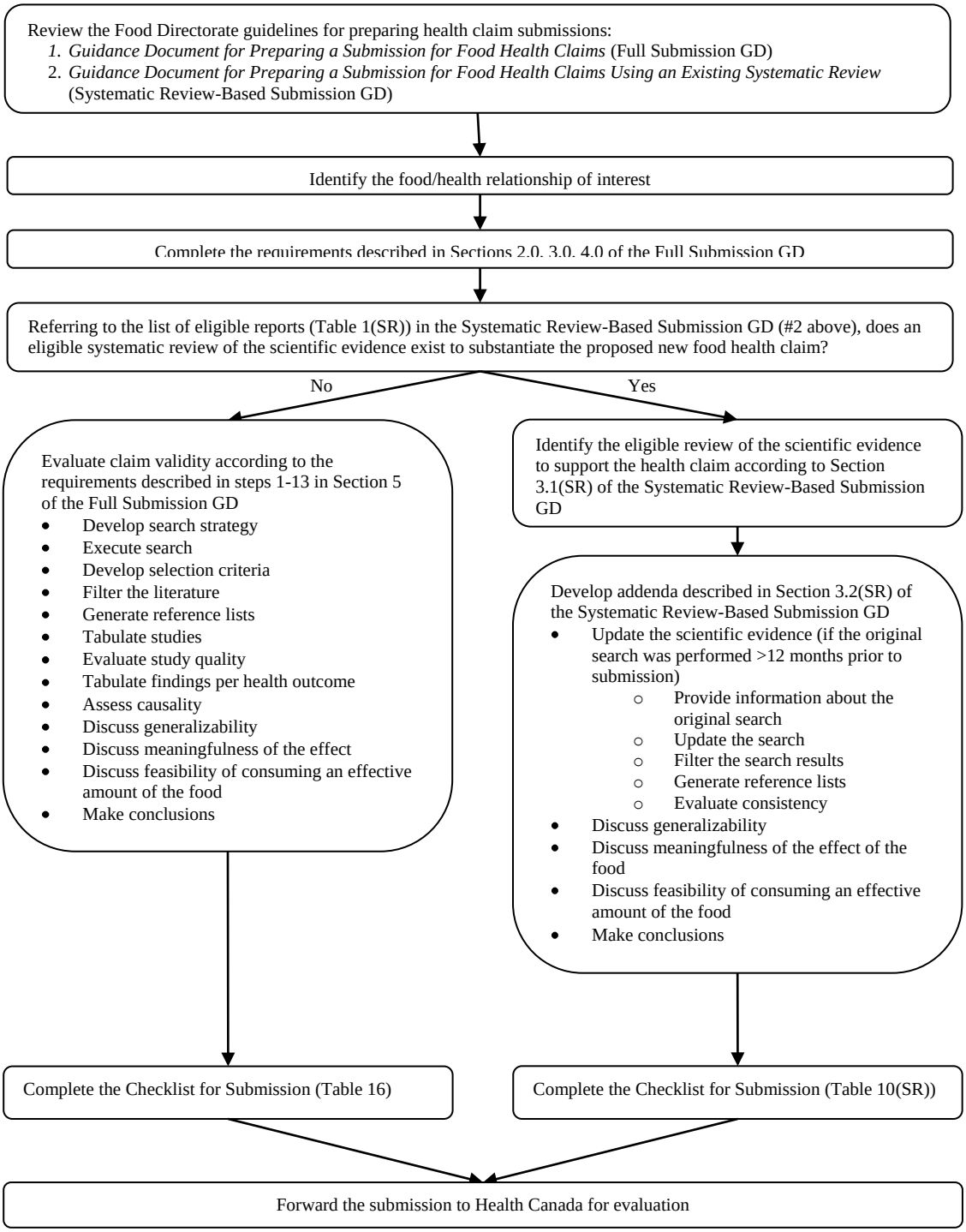

Figure: Overview of the two processes to develop a health claim submission in Canada[5]

[5]It is not necessary to complete the requirements described in this diagram in order; it might be easier to leave certain steps until others have been completed first.

Appendix B

Guiding Principles / Standards of Evidence for the Substantiation of a Food Health Claim[6]

a. **Systematic Approach**: A methodical, consistent approach is applied to substantiate a health claim.

b. **Transparency:** Search strategies, literature selection and evaluation, as guided by the document, are fully disclosed, to increase the credibility of the submission and to permit reproducibility.

c. **Comprehensiveness:** All original research in humans, pertaining to the health claim, is captured, including evidence in favour and not in favour of the health claim.

d. **Human Evidence:** The focus is on original research in humans that measures the food and health effect of interest.

e. **High level of Certainty**: The health claim is supported by a high level of certainty. This means that the majority of high quality human studies support a statistically significant favourable effect. Consideration will be given to statistical significance achieved at $p \leq 0.05$.

f. **Demonstration of Causality:** Demonstration of causality will consider the quality and quantity of original research in humans that support a beneficial effect of the food (*i.e.*, direction of effect); the strength of the association between the food and health effect (*i.e.*, statistical significance of the favourable effect) and the relationship between the amount of the food and the health effect (*i.e.*, dose-response).

g. **Biological Relevance of the Claimed Effect:** The claimed effect of the food is biologically/physiologically relevant and expected to benefit the health of the target population.

h. **Feasibility of Consumption of Effective Dose:** The amount of food to be consumed to achieve a beneficial effect can be incorporated into a healthy, balanced diet by the target population.

i. **Health Claim Wording:** The health claim wording communicates the health outcome that is substantiated in the submission, *i.e.*, it is specific to the substantiated health outcome. If, for example, the submission supports a reduced risk of infectious diarrhea, this does not mean that the product "supports healthy immune function". The correct claim wording would more directly make a statement to the effect that the product "reduces risk of infectious diarrhea".

[6] These principles are also described in Section 1.4 of the Guidance Document for Preparing a Submission for Food Health Claims.

j. **Substantiation of one food-health relationship in a submission:** One food/health relationship is to be addressed per submission. Multiple formulations/matrices of a food can be proposed by the petitioner, provided the scientific evidence is valid for all proposed formulations/matrices, but only a single health effect can be the object of a submission. However, more than one biomarker of a single health effect may be used – *e.g.*, using total cholesterol and LDL cholesterol as biomarkers of one health effect – heart disease.