



December 2010



## Research Gaps and Priorities Related to Health Claim Validation

The agri-food sector in Canada is interested in using health claims to promote the value-added health benefits of products. A health claim is any representation in labelling or advertising that states, suggests, or implies that a relationship exists between consumption of a food or food constituent and a person's health. Health claims must be substantiated in a systematic, comprehensive and transparent manner before they appear on food product labels and in advertising. The validity of a prospective health claim is assessed using a systematic scientific literature review process detailed in Health Canada's *Guidance Document for Preparing a Submission for Food Health Claims*.<sup>1</sup>

The evidence obtained from a literature review will more clearly identify the strength of a food-health relationship as well as identify gaps in scientific knowledge and indicate where future research investments should be focused. The level of scientific substantiation revealed by a literature review is also essential in defining the scope of commitment (e.g. time, money and effort) required to prepare a regulatory submission seeking approval for a new food health claim in Canada.

The Food Regulatory Issues Division (FRID) of Agriculture and Agri-Food Canada works with stakeholders along the agri-food value chain to enhance their ability to fulfill the regulatory requirements, including the scientific substantiation of health claims. Accordingly, FRID has commissioned literature reviews<sup>2</sup> that followed the process outlined in the Guidance Document to assess the weight of scientific evidence available for seven food-health relationships.

In keeping with Guidance Document requirements, the reviews focused on intervention and/or prospective observational studies in humans. The available literature was filtered and rated (based on design criteria as well as a quality appraisal tool provided in the Guidance Document) to identify the studies that could provide evidence to evaluate the health claims.

The scope of the commissioned reviews was to:

- Conduct a comprehensive literature review of scientific articles that could be used to substantiate a food health claim;
- Calculate the consistency rate of the data and strength of association using the Guidance Document tool; and
- Identify any research gaps that affect a possible health claim.

The process also served to build sector capacity in conducting, managing and analyzing the information retrieved from a literature review.

<sup>1</sup> Particular attention was given to the requirements identified in Section 5.0 Evaluation of Claim Validity (steps 1 to 9) [www.hc-sc.gc.ca/fn-an/legislation/guide-ld/health-claims\\_guidance-orientation\\_allegations-sante-eng.php](http://www.hc-sc.gc.ca/fn-an/legislation/guide-ld/health-claims_guidance-orientation_allegations-sante-eng.php)

<sup>2</sup> The reviews were conducted by Nutrasource Diagnostics Inc. and by the Richardson Centre for Functional Foods and Nutraceuticals.

The priority ingredients and health claims on which to focus were chosen based on an analysis of marketplace and consumer trends, Canadian sector capacity, and level of scientific evidence for the food-health relationship.<sup>3</sup>

## Pulses and Cardiovascular Disease

From a literature search that identified 5,774 articles that may be relevant to this claim, 12 articles met inclusion and exclusion screening criteria.

### Consistency of Effect and Strength of Association

- The effects of consumption of pulses (whole pulses or as a food constituent) on blood LDL-cholesterol and total cholesterol were found to have **high consistency** ratings; all other parameters had a low consistency of effect.
- Pulse consumption had a **moderate strength of association** with changes in blood total cholesterol, but all other parameters had low strengths of association.

### Research Gaps Related to Health Claim Substantiation

In the area of pulses and cardiovascular disease, research gaps include:

- patterns of pulse consumption including varieties consumed;
- data showing long-term effects;
- data for acute studies; and
- comparison of the effect of different pulses (e.g. pea vs. chickpea) on cardiovascular disease.

## Berries and Other Fruits and Antioxidant Status

From a literature search that identified 7,323 articles that may be relevant to this claim, 26 articles met inclusion and exclusion screening criteria.

### Consistency of Effect and Strength of Association

- Consumption of berries and other fruits (whole, as juice, or as freeze-dried whole fruit) had a **moderately consistent** effect on antioxidant status as measured by changes to blood malondialdehyde (MDA) levels.
- The strength of association between the consumption of berries and other fruits and blood MDA levels was also found to be **moderate**.

### Research Gaps Related to Health Claim Substantiation

The following research gaps for berries/fruit and antioxidant status were identified:

- analysis of the results of combining fruit and vegetable consumption on antioxidant status;
- data that clearly support which biomarker is best to monitor antioxidant status in humans;
- the appropriate duration of a clinical trial to measure the antioxidant effect of a food; and
- experiments with better-defined pre-intervention dietary data.

## Vegetables and Antioxidant Status

From a literature search that identified 12,662 articles that may be relevant to this claim, 27 articles met inclusion and exclusion screening criteria.

### Consistency of Effect and Strength of Association

- The consumption of vegetables was found to have a **moderately consistent** effect on changing blood MDA levels.
- Only a **low** strength of association was found between vegetable consumption and antioxidant status as measured by MDA levels.

<sup>3</sup> *Promising Health Claim Opportunities for Canada's Agri-Food Sector*, August 2010  
[www.agr.gc.ca/food-regulatory-issues](http://www.agr.gc.ca/food-regulatory-issues)

### Research Gaps Related to Health Claim Substantiation

For the relationship between vegetables and antioxidant status, the research gaps include:

- analysis of the results of combining fruit and vegetable consumption on antioxidant status;
- comprehensive compositional analysis of antioxidants in many vegetables;
- effects of individual vegetables on antioxidant status; and
- the minimum dose required to produce an effect.

### Canola Oil and Cardiovascular Disease

From a literature search that identified 1,310 articles that may be relevant to this claim, 12 articles met inclusion and exclusion screening criteria.

#### Consistency of Effect and Strength of Association

- The consumption of canola oil was found to have a **highly consistent** effect on blood LDL-cholesterol and total cholesterol. For blood HDL-cholesterol and triglycerides, the effect had **low consistency**.
- The strength of association calculation was not conducted in this literature review.

### Research Gaps Related to Health Claim Substantiation

The following are research gaps related to canola oil and cardiovascular disease:

- data to set an effective minimum dose;
- dose-response data;
- the effects of different processing procedures (such as baking or frying) on the cardio-protective properties of canola; and
- the effects of canola with different fatty acid patterns on the cardio-protective properties.

### Soy/Issoflavones and Bone Health

From a literature search that identified 2,880 articles that may be relevant to this claim, 14 articles met inclusion and exclusion screening criteria.

#### Consistency of Effect and Strength of Association

- The effects of soy consumption on fracture risk and lumbar spine bone mineral content had **high consistency** ratings; effects on femoral trochanter bone mineral density had a **moderate consistency** rating. Effects on all other measures of bone health had low consistency.
- Strengths of association between soy consumption and all measures of bone health were **low**.

### Research Gaps Related to Health Claim Substantiation

The following research gaps related to soy/issoflavones and bone health were identified:

- patterns of soy consumption in the target population;
- demonstration of a dose-response relationship;
- strong data to identify the optimum time of life for introduction of soy into the diet; and
- knowledge of the impact of other factors on the bioavailability and metabolic activity of soy.

### Soy and Cardiovascular Disease

From a literature search that identified 14,658 articles that may be relevant to this claim, 59 articles met inclusion and exclusion screening criteria.

#### Consistency of Effect and Strength of Association

- The effects of consuming whole soy products on blood total cholesterol and blood LDL-cholesterol had **high consistency** ratings.
- The effects of consuming soy protein on blood total cholesterol and blood LDL-cholesterol had a **high consistency**. There was a **moderate consistency** between soy protein consumption and blood HDL-cholesterol levels.

- Consumption of whole soy products or soy protein had a **low strength of association** with changes in blood total cholesterol, LDL-cholesterol and HDL-cholesterol.

### Research Gaps Related to Health Claim Substantiation

In the area of soy and cardiovascular disease, research gaps include:

- demonstration of a dose-response relationship;
- data on the bioavailability of soy;
- data on the effects of processing on probable bioactives;
- defining the role of soy isoflavones in cardiovascular disease.

### Milled/Ground Flaxseed and Cardiovascular Disease

From a literature search that identified 1,630 articles that may be relevant to this claim, 7 articles met inclusion and exclusion screening criteria.

### Consistency of Effect and Strength of Association

- The consumption of milled/ground flaxseed was found to have a **highly consistent** effect on blood total cholesterol, LDL-cholesterol, lipoprotein A\* and apolipoprotein B\*\*. A **moderately consistent** effect was seen for C-reactive protein\*\*. For blood HDL-cholesterol, triglycerides and apolipoprotein A1\*\*, the effects had **low consistency**.

*\*Note that only 4 of the studies measured lipoprotein A.*

*\*\*Note that only 3 studies measured apolipoprotein A1, apolipoprotein B and C-reactive protein.*

- The strength of association between milled/ground flaxseed consumption and blood total cholesterol and LDL-cholesterol was **weak**. For HDL-cholesterol, **no association** was seen.

### Research Gaps Related to Health Claim Substantiation

For the relationship of milled/ground flaxseed and cardiovascular disease, the following research gaps were identified:

- an effective minimal dose;
- the health impact on male participants and on pre-menopausal women;
- whether partially defatted milled/ground flaxseed provides the same cardio-protective effects as whole milled/ground flaxseed; and
- studies with adequate numbers of participants to demonstrate a statistically significant effect of flax on blood cholesterol.

### Research Considerations

Authorization of a health claim in Canada requires not only satisfactory evidence on causality, but also the characterization of the food including its safety for human consumption. Results from comprehensive research studies conducted on humans are required to evaluate the applicability of the claim to the general population.

The research gaps identified in these commissioned reviews provide direction for additional studies required to substantiate health claims for these priority food-health relationships. The findings are intended to provide insights for the agri-food industry as well as to inform the setting of priorities by the Research Branch of Agriculture and Agri-Food Canada.

Numerous research studies encountered during these reviews were found to be lacking in one or more of the requirements and were thus rejected for consideration. Following the process outlined in the Guidance Document when initiating research would help ensure that studies are acceptable to Health Canada and therefore included in the final analysis of claim validity.

**Contact us** to learn more about regulations for health claims, novel foods and ingredients.

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Cat. No. A72-98/2010E-PDF  
ISBN 978-1-100-17282-8  
AAFC No. 11288E

Electronic version available at [www.agr.gc.ca/food-regulatory-issues](http://www.agr.gc.ca/food-regulatory-issues)

Aussi offert en français sous le titre :

*Lacunes et priorités de la recherche liées à la validation des allégations santé*