

Developing Health Claims for Probiotics in Canada : a case study

**Nutri-Net Canada 1st
Annual Conference
Québec
February 17 - 19th, 2008**

**Paul Paquin, Ph.D.
Denis Roy, Ph.D.
Renée Michaud, M.Sc.
November 2007**



AISA

Association
pour les ingrédients
santé en alimentation

tonic

Stratégies en innovation agroalimentaire,
nutrition et santé



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

Purposes of the case study



- The intent of this proposal is to build a case study on health claims for probiotics in foods
- The main objective of this case study is to provide at Health Canada practical recommendations on how to integrate function claims, and possibly risk reduction claims for probiotics in foods; based on the existing scientific body of evidence
- Project financed by Nutri-Net Canada and DPAC

Purposes of the case study

First step: Scientific body of evidence
Project leader: Denis Roy, Ph.D.

- **Overview of available scientific evidence to support health claims**
- **Basic criteria to select and identify probiotics**
- **Safety considerations (clinical, observational, anecdotal and history of safe use of probiotics)**
- **Content claims**
- **Function claims (without amendment)**
- **Enhanced function claims**
- **Reduction of disease risk or risk factor claims**
- **Procedures for assessment of specific claims**
- **Identification of the additional evidence required to support a function and risk reduction claim with a regulatory amendment**



Purposes of the case study

Second step: Assemble and assess the amount of scientific information necessary to meet Health Canada's requirements for pre-market evaluation

Project leader: Paul Paquin, Ph.D.

- **Application for function claims**
- **Examine the process for submitting a function claim for foods**
- **Meet with Health Canada for guidance and follow up**
- **Prepare a specimen that will be submitted to HC**
- **Compile modifications required by the authority and assess a time frame**
- **Formulate specific recommendations on the process**
- **Application for product specific claims**
- **Compare the two main types of regulatory processes for specific health claims, i.e. drug regulatory process with amendment or NHP with a specific claim**



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

**First step:
Scientific body
of evidence**

Bioactive ingredients added to food

- Many products at the NHP/food interface contain added bioactive ingredients
- Added substances are not always traditionally associated with the food that contains them

Managing Health Claims for Foods in Canada: Towards a Modernized Framework



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

Issues - Bioactive ingredients added to food

- Food products being marketed without a health claim but with bioactive substances added at levels that would not provide a meaningful health benefit
- The simple declaration of the added bioactive substance in the food, when highlighted and positioned on the front of the package, could be misleading to consumers if it is perceived to provide a health benefit



Front-of-Package Claims

- (1) implied claims used as alternatives to specific disease risk reduction or function claims; and
- (2) claims used to convey simplified nutritional or general health messages.



Issues - Front-of-Package Claims

- In practice, health claims are expressed explicitly, in a statement, or implicitly, through slogans, logos or symbols
- Food regulations require implicit disease risk reduction claims to be accompanied by explicit claims

Managing Health Claims for Foods in Canada: Towards a Modernized Framework



UNIVERSITÉ
LAVAL

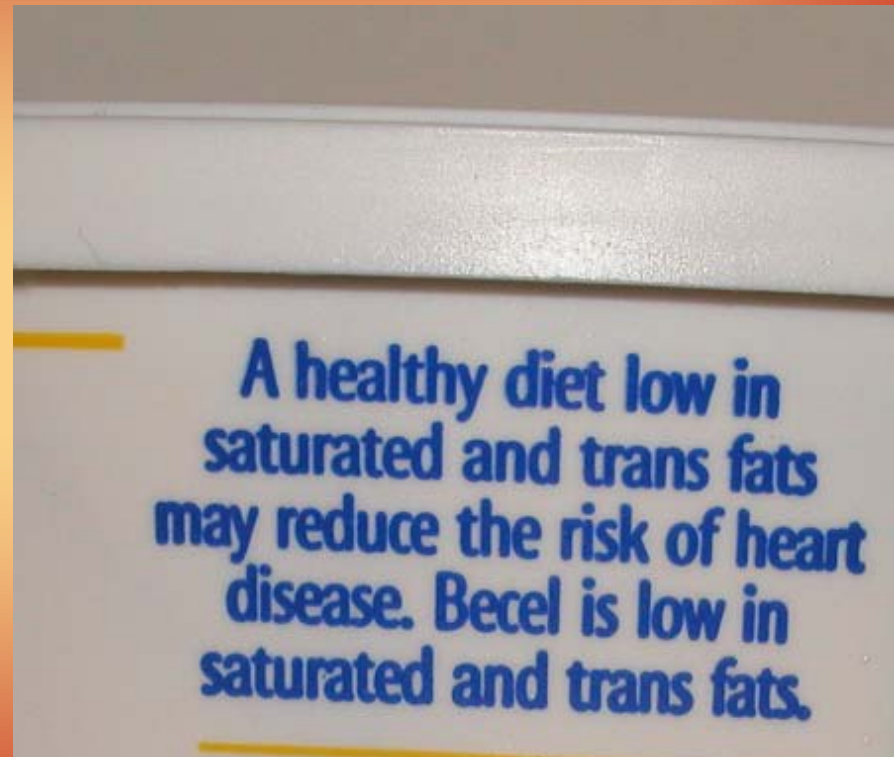
Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

Front-of-Package Claims

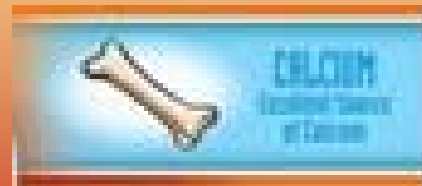
Explicit Claims

**Disease Risk
Reduction**



Front-of-Package Claims

Implicit Claims



Implicit Claims



Probiotics



World Health
Organization

Live microorganisms
which when administered
in **adequate amounts**
confer a **health benefit**
on the host

Requirements

Live Probiotics

For successful delivery in foods, probiotics must survive food processing and storage during product maturation and shelf-life.

Adequate amount

Probiotic culture must be present in the product at minimum numbers of 10^7 CFU ml⁻¹ and even higher numbers have been recommended

Regularly consumed

The probiotic food product should be regularly consumed in sufficient quantities to deliver the relevant 'dose' of live bacteria to the gut, keeping in mind the losses in cell viability typically encountered during gastric transit.

Criteria

- must be shown to exert a beneficial effect on the consumer, preferably with a mechanistic explanation of how this occurred;
- contain an adequate number of viable cells to confer the health benefit;
- are labeled in a truthful and informative manner to the consumer.

CAST Issue Paper 36 2007, Probiotics: Their Potential to Impact Human



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

Probiotic-containing foods

- can be categorized as functional foods
- Probiotic foods may be of benefit to help at-risk individuals avoid disease, including acute conditions such as bacterial vaginosis, necrotizing enterocolitis, and antibiotic-associated diarrhea
- Studies that validate such effects, and communication of these benefits **for foods**, should be facilitated, not suppressed, by regulatory agencies

CAST Issue Paper 36 2007, Probiotics: Their Potential to Impact Human



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

Label

- Ideally, products labeled as probiotics would conform to the guide-lines established by a working group of the FAO (UNFAO/WHO 2002)
- It was recommended that the following information be described on the label:
 - genus, species, and strain designation;
 - minimum viable numbers of each probiotic strain at end of shelf-life;
 - the suggested serving size, which must deliver the effective dose of probiotics related to the health claim;
 - health claim;
 - and proper storage conditions.



Health claims

- Claims currently made can broadly be categorised into five main groups:
 - Content
 - Functional
 - Enhanced function
 - Reduction of disease risk or disease risk factor
 - Medical claims (not permitted on product)

PASSCLAIM - gut health and immunity



Type of Claims

Medical

Protection against colon/bladder cancer

Reduction of disease risk

Counteracts potentially harmful bacteria

Drug

Content

Product X provides all the good bacteria your body needs

Functional

Aids regular transit

Enhanced function

Improves intestinal transit

Food



Indirect claims

- Indirect claims can be made, but these are of limited benefit
- An example of an indirect claim might be "***contains acidophilus and bifidobacteria, which are considered normal inhabitants of a healthy intestinal flora***"
- In the United States, many yogurts contain *Lactobacillus acidophilus*, bifidobacteria, or both, which are mentioned in the list of ingredients, but often no information about the strains is available



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

Content claim

- **Specific mention of the genus, species and strain**
 - **Minimum viable number of each probiotic strain**
 - **Origin and ability to survive transit through the gut**
-
- In Japan a standard was developed by the Fermented Milks and Lactic Acid Bacteria Beverages Association stipulating that a product contain 1×10^7 viable bifidobacteria/g or mL product to be considered a probiotic food
 - The International Standard of Federation Internationale de Laiterie/International Dairy Federation (FIL/IDF) standards ((IDF 1992) requiring a minimum of 10^7 CFU/mL of *L. acidophilus* and 10^6 CFU/g of bifidobacteria in fermented milk products at the time of sale have been introduced by various organizations worldwide
 - The Swiss Food Regulation as well as the MERCOSOR regulations requires a minimum of 10^6 CFU of viable bifidobacteria in similar products

Probiotic concept

- Adding the right live microbes can result in physiological benefits.
- Effects may result from :
 - alteration of the population or activities of colonizing microbes.
 - direct interaction of the probiotic with host cells.
 - The gut remains the most studied site of action for probiotics.



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

Targets

- Gastrointestinal functions
 - control transit time
 - bowel habits,
 - balanced colonic microbiota,
 - that are associated with control of nutrient bioavailability
 - that modify gastrointestinal immune activity,
 - lipid homeostasis that are indirectly influenced by nutrient digestion or fermentation represent promising targets

Functional Health claims for probiotic foods

- **Bowel Transit**

- *Daily consumption of probiotic food to decrease the amount of time it took food to travel from the mouth to the anus for people who had longer-than-desired transit time*

- **Examples:**

- Aids regular transit
- Modulates bowel activity
- Improves intestinal transit



Functional Health claims for probiotic foods

- **Modification of intestinal microbiota**
 - **Activities such as**
 - decrease in fecal enzymes and mutagenicity
 - enhancing the intestinal barrier to prevent unwanted microbes from entering the blood stream,
 - colonization resistance
- **Examples**
 - To help balance the probiotics in your digestive system
 - Promotes natural healthy digestion



Functional Health claims for probiotic foods

- **Improved nutritional value of foods**
 - Probiotics have been shown to improve lactose digestion by reducing the intolerance symptoms as well as by slowing orocecal transit.
 - Assimilation of cholesterol within bacterial cell
 - Increased excretion of bile salts due to conjugation by bile salt hydrolase
 - Antioxidative effect
 - Antihypertensive effect : Peptidase action on milk proteins tripeptides which inhibits angiotensin
- **Examples**
 - Improves digestion
 - Promotes natural healthy digestion



Functional Health claims for probiotic foods

- **Immune enhancement**
 - enhances concentrations of circulating immunoglobulin A (IgA)
 - enhances the nonspecific immune phagocytic activity of circulating blood granulocytes
 - stimulates the production of cytokines by blood mononuclear cells
- **Examples**
 - Supports the body's natural defences
 - Stimulates the immune system
 - Helps your body to protect itself



**Second step: Assemble and
assess the amount of
scientific information
necessary to meet Health
Canada's requirements for
pre-market evaluation**

Health Canada interim guidance document

Preparing a Submission for Foods with
Health Claims: STANDARDS OF
EVIDENCE FOR EVALUATING FOODS
WITH HEALTH CLAIMS

Bureau of Nutritional Sciences
Food Directorate
Health Products and Food Branch
Health Canada



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

Health Canada definitions

- **(1) Health claims:** authorization of health claims for foods, refer to claims that relate primarily to paragraphs (a) or (b) of the definition of “drug” found in section 2 of the *Food and Drugs Act* and include structure/function claims, risk reduction claims, and therapeutic claims.

A claim is a statement or representation in product labelling or advertising regarding the character, value, quantity, composition, merit or safety of the product.

- **(2) Structure/function claims** are claims that relate primarily to paragraph (b) of the definition of “drug” with respect to modifying, restoring, or correcting an organic function or body structure of human beings, beyond normal growth and development or maintenance of good health.¹
- **(3) Risk reduction claims** are claims that relate primarily to paragraph (a) of the definition of “drug” with respect to significantly altering a major risk factor(s) for a disease or adverse health condition



Health Canada definitions

- **Biological role claims** are claims related to “maintaining the functions of the body necessary to the maintenance of good health and normal growth and development”. Under sections B.01.311, D.01.006 and D.02.004 of the *Food and Drug Regulations*, generally recognized “biological role claims” for *known* nutrients listed in the regulations are already permitted on foods and do not require premarket assessment under the existing or proposed regulations, nor are foods carrying such claims subject to drug regulations. “Calcium helps build strong bones” is an example of “biological role claim” that does not trigger the drug definition.
- **Function claims expressly permitted by current food regulations** Function claims about the maintenance of body functions that are necessary to the maintenance of good health and normal growth and development are expressly permitted in B.01.311(3), D.01.006 and D.02.004 of the *FDR*. These sections of the regulations provide only for statements or claims “to the effect that the food's energy value or a nutrient 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.”

II. General Information - Manufacturing, Specifications, Consumption

- The following information is relevant to more than one area of the review with respect to product safety, claim validity and quality assurance. It is important to provide the information requested as fully as possible to facilitate Health Canada in completing the review. Information on quality control aspects of manufacturing and raw material testing is to be provided under segment V.
- Information requested under paragraphs 1-3 below will help assess if the food is subject to the requirements of novel foods under Division 28 of Part B of the *Food and Drug Regulations*.
 - 1-Manufacturing of finish food
 - 2-Manufacturing and properties of added bioactive substance
 - 3- specifications of other raw materials
 - 4- consumption data
 - 5- estimated consumption vs recommandations
 - 6- list of references



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

III. Product Safety

- The information requested below is applicable to an altered food, including a novel food, as defined in Division 28, Part B of the *Food and Drug Regulations*. For the purpose of product safety evaluation, “altered food” means: the addition of a bioactive substance to the food, or other modification in the food, including modifying the level and/or bioavailability of a bioactive substance naturally occurring in the food in order to achieve the claimed effect, that is not already regulated in the *Food and Drug Regulations*.
- 1- indicate which of following product safety categories
- 2- history of use
- 3- susceptible and vulnerable groups
- 4- interactions and nutritional adverse effects
- 5- microbial ecology
- 6- information on to establish that the food is safe for consumption
- 7- references



IV. Claim Validity

- Part A - Background Information
 - Original research conducted on the product
 - Only review of the existing literature
- Part B: Literature review
- Part C*: Primary evidence - information on the product for which a claim is sought (product research)
- * Part C is required for products with health claims to be reviewed under the product-specific authorization process
- Part D: Assessment of the totality of evidence
- Part E: Reference list
- Part F: Detailed description of primary evidence



IV. Claim Validity

Study	Design	Diet component	Subjects	Duration	Diet method	Results	Comments																																																																														
Zino et al., 1997 New Zealand	RCT (B)	Fruit and vegetables	90 healthy volunteers (26 men aged 19-69 yrs, and 64 women aged 18-61 yrs). Subjects had to be consuming 3 or fewer servings of fruit and vegetables daily.	2 week run-in period; 8 week treatment period.	Subjects were randomly assigned to control (habitual diet) or intervention groups; intervention group instructed to increase consumption of fruit and vegetables to 8 servings/day and not to alter intake of nuts, oil, butter or margarine. Four day diet records completed during run in and week 4. Unannounced 24 hr recalls were taken in week 6 as an additional measure of compliance.	<p><i>Reported consumption of fruit, vegetables and other nutrients (means ± SD):</i></p> <table border="1"> <thead> <tr> <th>Intake</th> <th>Baseline Control</th> <th>Baseline Treatment</th> <th>Week 4 Control</th> <th>Week 4 Treatment</th> <th>Adjusted Difference (95% CI)^a</th> </tr> </thead> <tbody> <tr> <td>Fruit (g)</td> <td>37 ± 51</td> <td>93 ± 118</td> <td>55 ± 84</td> <td>256 ± 132</td> <td>177 (125- 228)</td> </tr> <tr> <td>Juice (g)</td> <td>25 ± 68</td> <td>56 ± 96</td> <td>46 ± 104</td> <td>413 ± 283</td> <td>341 (243- 438)</td> </tr> <tr> <td>Vegetable (g)</td> <td>196 ± 87</td> <td>228 ± 127</td> <td>218 ± 104</td> <td>332 ± 149</td> <td>104 (47-162)</td> </tr> <tr> <td>Total (g)</td> <td>258 ± 131</td> <td>377 ± 210</td> <td>319 ± 183</td> <td>1001 ± 313</td> <td>630 (510-751)</td> </tr> <tr> <td>No. of servings/d</td> <td>1.9 ± 0.7</td> <td>2.4 ± 0.9</td> <td>2.1 ± 1.0</td> <td>7.1 ± 1.4</td> <td>4.7 (4.2-5.2)</td> </tr> <tr> <td>Total fat (% MJ)</td> <td>36</td> <td>35</td> <td>36</td> <td>32</td> <td>-3.5 (-6.1 to -1.0)</td> </tr> <tr> <td>Fibre (g)</td> <td>17</td> <td>19</td> <td>19</td> <td>25</td> <td>6.2 (2.4- 10.0)</td> </tr> </tbody> </table> <p>^a Between treatment and control groups at week 4 adjusted for age, sex and baseline value.</p> <p><i>Plasma lipid concentrations (mmol/L) during study period (mean ± SD):</i></p> <table border="1"> <thead> <tr> <th>Lipid</th> <th>Baseline Control</th> <th>Baseline Treatment</th> <th>Week 8 Control</th> <th>Week 8 Treatment</th> <th>Adjusted Difference (95% CI)^a</th> </tr> </thead> <tbody> <tr> <td>TC</td> <td>5.13 ± 0.97</td> <td>4.72 ± 0.98</td> <td>4.94 ± 1.05</td> <td>4.64 ± 0.94</td> <td>-0.02 (-0.29- 0.25)</td> </tr> <tr> <td>LDL</td> <td>3.18 ± 0.85</td> <td>2.96 ± 0.92</td> <td>2.96 ± 0.92</td> <td>2.83 ± 0.85</td> <td>0.02 (-0.23- 0.27)</td> </tr> <tr> <td>HDL</td> <td>1.28 ± 0.38</td> <td>1.19 ± 0.38</td> <td>1.36 ± 0.41</td> <td>1.24 ± 0.41</td> <td>-0.08 (-0.15- 0.001)</td> </tr> <tr> <td>TG</td> <td>1.48 ± 0.55</td> <td>1.26 ± 0.81</td> <td>1.34 ± 0.50</td> <td>1.26 ± 0.68</td> <td>0.06 (-0.12- 0.24)</td> </tr> </tbody> </table>	Intake	Baseline Control	Baseline Treatment	Week 4 Control	Week 4 Treatment	Adjusted Difference (95% CI) ^a	Fruit (g)	37 ± 51	93 ± 118	55 ± 84	256 ± 132	177 (125- 228)	Juice (g)	25 ± 68	56 ± 96	46 ± 104	413 ± 283	341 (243- 438)	Vegetable (g)	196 ± 87	228 ± 127	218 ± 104	332 ± 149	104 (47-162)	Total (g)	258 ± 131	377 ± 210	319 ± 183	1001 ± 313	630 (510-751)	No. of servings/d	1.9 ± 0.7	2.4 ± 0.9	2.1 ± 1.0	7.1 ± 1.4	4.7 (4.2-5.2)	Total fat (% MJ)	36	35	36	32	-3.5 (-6.1 to -1.0)	Fibre (g)	17	19	19	25	6.2 (2.4- 10.0)	Lipid	Baseline Control	Baseline Treatment	Week 8 Control	Week 8 Treatment	Adjusted Difference (95% CI) ^a	TC	5.13 ± 0.97	4.72 ± 0.98	4.94 ± 1.05	4.64 ± 0.94	-0.02 (-0.29- 0.25)	LDL	3.18 ± 0.85	2.96 ± 0.92	2.96 ± 0.92	2.83 ± 0.85	0.02 (-0.23- 0.27)	HDL	1.28 ± 0.38	1.19 ± 0.38	1.36 ± 0.41	1.24 ± 0.41	-0.08 (-0.15- 0.001)	TG	1.48 ± 0.55	1.26 ± 0.81	1.34 ± 0.50	1.26 ± 0.68	0.06 (-0.12- 0.24)	<p>Concentrations of lipids and lipoproteins remained unchanged throughout the study.</p> <p>The percentage of energy from total and saturated fat was lower in the intervention group.</p> <p>- healthy volunteers -good study- does not support</p>
Intake	Baseline Control	Baseline Treatment	Week 4 Control	Week 4 Treatment	Adjusted Difference (95% CI) ^a																																																																																
Fruit (g)	37 ± 51	93 ± 118	55 ± 84	256 ± 132	177 (125- 228)																																																																																
Juice (g)	25 ± 68	56 ± 96	46 ± 104	413 ± 283	341 (243- 438)																																																																																
Vegetable (g)	196 ± 87	228 ± 127	218 ± 104	332 ± 149	104 (47-162)																																																																																
Total (g)	258 ± 131	377 ± 210	319 ± 183	1001 ± 313	630 (510-751)																																																																																
No. of servings/d	1.9 ± 0.7	2.4 ± 0.9	2.1 ± 1.0	7.1 ± 1.4	4.7 (4.2-5.2)																																																																																
Total fat (% MJ)	36	35	36	32	-3.5 (-6.1 to -1.0)																																																																																
Fibre (g)	17	19	19	25	6.2 (2.4- 10.0)																																																																																
Lipid	Baseline Control	Baseline Treatment	Week 8 Control	Week 8 Treatment	Adjusted Difference (95% CI) ^a																																																																																
TC	5.13 ± 0.97	4.72 ± 0.98	4.94 ± 1.05	4.64 ± 0.94	-0.02 (-0.29- 0.25)																																																																																
LDL	3.18 ± 0.85	2.96 ± 0.92	2.96 ± 0.92	2.83 ± 0.85	0.02 (-0.23- 0.27)																																																																																
HDL	1.28 ± 0.38	1.19 ± 0.38	1.36 ± 0.41	1.24 ± 0.41	-0.08 (-0.15- 0.001)																																																																																
TG	1.48 ± 0.55	1.26 ± 0.81	1.34 ± 0.50	1.26 ± 0.68	0.06 (-0.12- 0.24)																																																																																



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca

V. Quality Assurance

- If the product is an “altered food” for the purpose of health claim authorization, i.e., the processing of the product involves the addition to the food or other modification in the food of a bioactive substance to achieve the claimed effect not regulated in the *Food and Drug Regulations*, complete:
- Parts A-F Otherwise, complete:
 - Part A: Bioactive substance added to or otherwise modified in the food - analysis and control
 - Part B: The food bearing the claim - manufacturing and analysis
 - Part C: Stability of finished food
 - Part D: Methods of analysis used in testing bioactive substance and finished food
 - Part E: References
 - Part F: Supporting documents



Conclusions

- Prochaines étapes à venir
- Échéancier



UNIVERSITÉ
LAVAL

Institut des nutraceutiques
et des aliments fonctionnels

www.inaf.ulaval.ca