



NATURAL HEALTH PRODUCT

PROBIOTICS

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredients.

Notes

- ▶ By submitting a PLA referencing this monograph, the applicant is attesting that the product will comply fully with the recommended conditions of use and specifications section outlined in this monograph. These include species identification, strain characterization, quantification in colony forming units (CFU), and a complete assessment of virulence properties (including but not limited to: antibiotic resistance profile, virulence factor production, and toxigenic activity).
- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant.
- ▶ Any non-viable form of the medicinal ingredients found in Appendix I (e.g. heat-killed, thermostabilised) is excluded from this monograph and the compendial application process.

Date

May 26, 2015

Proper name(s) and Common name(s)

Refer to Appendix I for lists of acceptable bacterial (Table 1), bacterial and fungal (Table 2), and fungal (Table 3) proper and common names.

Refer to Appendix I, Table 4 for medicinal ingredients that are excluded from this monograph.

Source material(s)

Whole cell AND Strain Designation

Note

The Product Licence Application (PLA) and label must identify the strain designation as the source material for each microorganism (e.g. *Lactobacillus acidophilus* ABC123 where "ABC123" is the strain designation).

Route(s) of administration

Oral

Dosage form(s)

This monograph is not intended to include foods or food-like dosage forms such as bars, beverages, chewing gums and yogurts.

Dosage forms by age group

- Children 1-2 years:
The acceptable pharmaceutical dosage forms are limited to emulsion/suspension and solution/drops (Giacoaia et al. 2008; EMEA/CHMP 2006).
- Children 3-5 years:
The acceptable pharmaceutical dosage forms are limited to chewables, emulsion/suspension, powders and solution/drops (Giacoaia et al. 2008; EMEA/CHMP 2006).
- Children 6-12 years, Adolescents 13-17 years, and Adults \geq 18 years:
The acceptable pharmaceutical dosage forms include, but are not limited to capsules, chewables (e.g. gummies, tablets), liquids, powders, strips or tablets.

Use(s) or Purpose(s) Statement to the effect of

Medicinal ingredients from Appendix I, Table 1, 2, and 3

Source of probiotics.

Medicinal ingredients from Appendix I, Table 1, 2, and 3 except *Lactobacillus crispatus* and *Lactobacillus gallinarum*

- ▶ Helps support intestinal/gastrointestinal health (Alonso and Guarner 2013; DuPont and DuPont 2011; WGOGG 2011; Rolfe 2000).
- ▶ Could promote a favorable gut flora (Bezkorovainy 2001; Morelli 2000; Collins et al. 1998).

Medicinal ingredients from Appendix I, Table 2 with specific use(s) or purpose(s)

Name(s)	Strain(s)	Use(s) or Purpose(s)	References
<i>Lactobacillus johnsonii</i>	La1/Lj1/ NCC 533	An adjunct to physician-supervised antibiotic therapy in patients with <i>Helicobacter pylori</i> infections	Bergonzelli et al. 2006; Cruchet et al. 2003; Pantoflickova et al. 2003; Felley et al. 2001
<i>Lactobacillus rhamnosus</i>	GG	Helps to manage acute infectious diarrhoea	Canani et al. 2007; Guandalini et al. 2000; Guarino et al. 1997

Name(s)	Strain(s)	Use(s) or Purpose(s)	References
		Helps to manage and/or reduce the risk of antibiotic-associated diarrhoea	Cremonini et al. 2002; Armuzzi et al. 2001; Vanderhoof et al. 1999
<i>Saccharomyces boulardii</i> / <i>Saccharomyces cerevisiae</i>	All	Helps to reduce the risk of antibiotic-associated diarrhoea	Can et al. 2006; Kotowska et al. 2005; Cremonini et al. 2002; McFarland et al. 1995; Surawicz et al. 1989

Dose(s) Statement to the effect of

Subpopulation(s)

- ▶ Adults (≥ 18 y) (Gill and Prasad 2008; Lenoir-Wijnkoop et al. 2007; Hawrelak 2006; Picard et al. 2005; Reid et al. 2003)
- ▶ Adolescents (13-17 y) (Gill and Prasad 2008; Lenoir-Wijnkoop et al. 2007; Hawrelak 2006; Picard et al. 2005; Reid et al. 2003)
- ▶ Children (1-12 y) (Gill and Prasad 2008; Lenoir-Wijnkoop et al. 2007; Hawrelak 2006; Picard et al. 2005; Reid et al. 2003)

Quantity(ies)

Medicinal ingredients from Appendix I, Table 1 and 3

Minimum: 10⁷ Colony Forming Units (CFU) per day (Gill and Prasad 2008; Lenoir-Wijnkoop et al. 2007; Hawrelak 2006; Picard et al. 2005; Reid et al. 2003).

Note

The minimum daily dose is the total CFU count per day provided from all live microorganisms present in the product formulation; it is not to be interpreted as a minimum quantity for individual microorganisms.

Medicinal ingredients from Appendix I, Table 2

Name(s)	Strain(s)	Quantity(ies) Colony Forming Units (CFU) per day	References
<i>Lactobacillus johnsonii</i>	La1/Lj1/ NCC 533	<i>H. pylori</i> infections: 1.25 x 10 ⁸ to 3.6 x 10 ⁹	Bergonzelli et al. 2006; Pantoflickova et al. 2003; Felley et al. 2001
	All	All other uses ¹ : Minimum: 10 ⁷	Gill and Prasad 2008; Lenoir-Wijnkoop et al. 2007; Hawrelak 2006; Picard et al. 2005; Reid et al. 2003
<i>Lactobacillus rhamnosus</i>	GG	Management of acute infectious diarrhoea: 6.0 x 10 ⁹ to 1.2 x 10 ¹⁰	Canani et al. 2007; Guarino et al. 1997
		Management/risk reduction of antibiotic-associated diarrhoea: 1.0 x 10 ¹⁰ to 2.0 x 10 ¹⁰	Cremonini et al. 2002; Armuzzi et al. 2001; Vanderhoof 1999
	All	All other uses ¹ : Minimum: 10 ⁷	Gill and Prasad 2008; Lenoir-Wijnkoop et al. 2007; Hawrelak 2006; Picard et al. 2005; Reid et al. 2003
<i>Saccharomyces boulardii</i> / <i>Saccharomyces cerevisiae</i>	All	Risk reduction of antibiotic- associated diarrhoea: 1.0 x 10 ¹⁰ to 3.0 x 10 ¹⁰	Can et al. 2006; Kotowska et al. 2005; Cremonini et al. 2002; McFarland <i>et al.</i> 1995
		All other uses ¹ : Minimum: 10 ⁷	Gill and Prasad 2008; Lenoir-Wijnkoop et al. 2007; Hawrelak 2006; Picard et al. 2005; Reid et al. 2003

¹ For 'All other uses', the total recommended daily CFU count must meet the minimum of 10⁷ either as a single ingredient or in combination.



Note

- ▶ All individual strain quantities of live microorganisms must be indicated on the PLA form, label and finished product specifications in Colony Forming Units (CFU) per dosage unit.
- ▶ In the case of blends where multiple live microorganisms have been cultured together, only the total microorganism count in CFU per dosage unit must be provided.
- ▶ Volumetric amounts (e.g. g, mL) are not acceptable.

Directions for use

All acceptable medicinal ingredients found in Appendix I, Table 1 and 2 except *Saccharomyces cerevisiae/S. boulardii*

If you are on antibiotic(s), take at least 2-3 hours before or after (NIH 2011; APhA 2006; Biradar et al. 2005).

All acceptable medicinal ingredients found in Appendix I, Table 3 and *Saccharomyces cerevisiae/S. boulardii*

If you are on antifungal(s), take at least 2-3 hours before or after (NIH 2011; APhA 2006; Biradar et al. 2005).

Duration of use

No statement required.

Risk information

Statement to the effect of

Caution(s) and warning(s)

- ▶ If you have fever, vomiting, bloody diarrhoea or severe abdominal pain, consult a health care practitioner prior to use (APhA 2006; WHO 2005; CPhA 2002).
- ▶ If symptoms of digestive upset (e.g. diarrhea) occurs and/or persists beyond 3 days, discontinue use and consult a health care practitioner (APhA 2006; WHO 2005).

Note

If any bacterial/fungal strain in the product has come into contact with a priority allergen or derivative (e.g. soy, gluten, milk, fish via the culture media) (list available at: <http://www.hc-sc.gc.ca/fn-an/securit/allerg/fa-aa/index-eng.php>) that is not listed as a medicinal or non-medicinal ingredient, one of the following risk statements must be included on the product label:

- ▶ If you have a XXX allergy, do not use this product (CG 2011; HC 2009);

OR

- ▶ (May) contain(s) XXX (HC 2012a; HC 2012b; CG 2011; HC2009; HC 2003)



Contraindication(s)

- ▶ If you have an immune-compromised condition (e.g. AIDS, lymphoma, patients undergoing long-term corticosteroid treatment), do not use this product (APhA 2006; Cukovic-Cavka et al. 2006; Ledoux et al. 2006; Riquelme et al. 2003; Lherm et al. 2002).
- ▶ If any bacterial/fungal strain in the product possesses unexplained atypical resistance to any antibiotic/antifungal agent (Mathur and Singh 2005), the name(s) of the antibiotic(s)/antifungal(s) agent(s) must be indicated as a contraindication on the label as follows:
If you are taking XXX, do not use this product (e.g. If you are taking ampicillin, do not use this product).

Known adverse reaction(s)

No statement required.

Non-medicinal ingredients

Must be chosen from the current NHPD Natural Health Products Ingredient Database (NHPID) and must meet the limitations outlined in the database.

Note

Cryoprotectants: All ingredients that are intentionally added during the manufacturing process of a live microorganism to preserve its stability/viability are non-medicinal ingredients.

Storage condition(s) Statement to the effect of

All liquid preparations

Store in refrigerator in a tightly closed, light-resistant container.

Note

This requirement does not apply to shelf-stable liquid preparations such as oil suspensions and emulsions.

All non-liquid preparations (optional)

Store in refrigerator in a tightly closed container (Liu 2009; Juarez Thomas 2004; Shillinger 1999).

Specifications

The following requirements are expected to be met by each live microorganism attesting to this monograph:

- ▶ The species Latin binomial identification must be up to date and validated.
 - ▶ Survivability of the microorganisms in the human gut must be demonstrated. In-vitro gastric acid and bile resistance testing is considered acceptable.
 - ▶ The microorganism must be identified by phenotype and genotype:
 - Phenotyping must be assessed based on characteristics routinely used to distinguish the species from others. This includes a series of testing for sufficient confirmation of observable traits of the species.
 - Genotyping must be assessed as follows:
 - Species identification by comparison of genome sequence homology in percentage, to both “identical” and “closely related” type strains – obtained from an internationally recognized culture collection;
- AND
- Strain characterization through an up to date complete/whole genome sequencing method.
- ▶ Absence of virulence of each live microorganism must be established through the following:
 - Comparison of antibiotic/antifungal resistance profile to typical species resistance – as published by an internationally recognized panel;
- AND
- Explanation of the genetic basis of each atypical antibiotic/antifungal resistance to the species OR demonstration of the absence of all known genetic mechanisms of resistance;
- AND
- Demonstration of lack of horizontal antibiotic/antifungal resistance transfer ability;
- AND
- Demonstration of susceptibility to therapeutic concentrations of at least two commercially available antimicrobial/antifungal agents;
- AND
- Demonstration of the absence of genetic elements responsible for the production of virulence factors characteristic to the genus;
- AND
- Demonstration of lack of toxigenic activity (i.e. production of toxins) known to the genus.

The finished product must meet all quality requirements as detailed in NHPD’s *Quality of Natural Health Products Guide*. In the case of live microorganisms, this includes the following:

- ▶ Stability/viability measures put into place must ensure that a minimum of 80% of the quantity declared on the product label is present at the end of shelf life; this applies to single ingredient counts for live microorganisms cultured separately, or total counts for blends where multiple live microorganisms have been cultured together.
- ▶ In the case where the live microorganism can interfere with microbial impurity testing, a detailed rationale on how the final product complies is required. Such rationale should include measures for live microorganism distinguishing at the finished product stage, along



with a detailed explanation on how quality assurance measures are put into place to ensure microbial purity.

Note

Information on the manufacturing process, including but not limited to the above, must be maintained by the applicant or the manufacturer and provided to Health Canada upon request.

References cited

Abe S, Takayama K, Kinoshita S. Taxonomic studies on glutamic acid-producing bacteria. *Journal of General and Applied Microbiology* 1967;13(3):279-301.

Adiloğlu AK, Gönülateş N, İşler M, Senol A. The effect of kefir consumption on human immune system: a cytokine study. *Mikrobiyoloji Bulteni* 2013;47(2):273-281.

Ahmadova A, Todorov SD, Hadji-Sfaxi I, Choiset Y, Rabesona H, Messaoudi S, Kuliyevev A, Franco BD, Chobert JM, Haertlé T. Antimicrobial and antifungal activities of *Lactobacillus curvatus* strain isolated from homemade Azerbaijani cheese. *Anaerobe*. 2013;20:42-49.

Antonio MA, Hillier SL. DNA Fingerprinting of *Lactobacillus crispatus* Strain CTV-05 by Repetitive Element Sequence-Based PCR Analysis in a Pilot Study of Vaginal Colonization. *Journal of Clinical Microbiology*. 2003; 41(5):1881–1887.

APhA 2006: American Pharmaceutical Association. Berardi RR, Kroon LA, McDermott JH, Newton GD, Oszko MA, Popovich NG, Remington TL, Rollins CJ, Shimp LA, Tietze KJ, editors. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*, 15th edition. Washington (DC): APhA Publications; 2006.

Armuzzi A, Cremonini F, Bartolozzi F, Canducci F, Candelli M, Ojetti V, Cammarota G, Anti M, De Lorenzo A, Pola P, Gasbarrini G, Gasbarrini A. The effect of oral administration of *Lactobacillus GG* on antibiotic-associated gastrointestinal side-effects during *Helicobacter pylori* eradication therapy. *Alimentary Pharmacology & Therapeutics* 2001;15(2):163-169.

Beijerinck MW. Sur les ferments lactiques de l'industrie. *Archives Néerlandaises des Sciences Exactes et Naturelles (Section 2)* 1901;6:212-243.

Bergonzelli GE, Granato D, Pridmore RD, Marvin-Guy LF, Donnicola D, Corthésy-Theulaz IE. GroEL of *Lactobacillus johnsonii* La1 (NCC 533) Is Cell Surface Associated: Potential Role in Interactions with the Host and the Gastric Pathogen *Helicobacter pylori*. *Infection and Immunity* 2006;74(1):425-434.

Bezkorovainy A. Probiotics: determinants of survival and growth in the gut. *American Journal of Clinical Nutrition* 2001;73(2):399S-405S.

Biradar SS, Bahagvati ST, Shegunshi B. Probiotics and antibiotics: a brief overview. *The Internet Journal of Nutrition and Wellness* 2005;2(1):1-7.



Bisby F, Roskov Y, Culham A, Orrell T, Nicolson D, Paglinawan L, Bailly N, Appeltans W, Kirk P, Bourgoin T, Baillargeon G, Ouvrard D, editors. Species 2000 & ITIS Catalogue of Life: 3rd February 2012 [Internet]. Reading (GB): Species 2000. [Source database BIOS: Bacteriology Insight Orienting System, Version Dec 2006; Accessed 2012 March 26]. Available from: <http://www.catalogueoflife.org>

Bohak I, Back W, Richter L, Ehrmann M, Ludwig W, Schleifer KH. *Lactobacillus amylolyticus* sp. nov., isolated from beer malt and beer wort. *Systematic and Applied Microbiology* 1998;21(3):360-364.

Can M, Beşirbelliöglu BA, Avcı İY, Beker CM, Pahsa A. Prophylactic *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhea: a prospective study. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research* 2006;12(4):PI19-122.

Canani RB, Cirillo P, Terrin G, Cesarano L, Spagnuolo MI, De Vincenzo A, Albano F, Passariello A, De Marco G, Manguso F, Guarino A. Probiotics for treatment of acute diarrhoea in children: randomised clinical trial of five different preparations. *British Medical Journal* 2007;335(7615):340.

Casalta E, Montel MC. Safety assessment of dairy microorganisms: the *Lactococcus* genus. *International Journal of Food Microbiology* 2008;126(3):271-273.

CG 2011: Canada Gazette, Part II: Official Regulations 2011-02-16. Vol. 145, No. 4 - February 16, 2011. Registration SOR/2011-28 February 4, 2011 FOOD AND DRUGS ACT Regulations Amending the Food and Drug Regulations (1220 - Enhanced Labelling for Food Allergen and Gluten Sources and Added Sulphites) P.C. 2011-80 February 3, 2011 [Accessed 2011 August 26]. Available from: <http://gazette.gc.ca>

Conway PL, Gorbach SL, Goldin BR. Survival of lactic acid bacteria in the human stomach and adhesion to intestinal cells. *Journal of Dairy Science* 1987;70(1):1-12.

Chiang İY, Worobo RW, Churey JJ, Henick-Kling T. Growth inhibition of foodborne pathogens by *Oenococcus oeni*. *Journal of Food Science* 2012;77(1):M15-M19.

Collins JK, Thornton G, O'Sullivan GO. Selection of probiotic strains for human applications. *International Dairy Journal* 1998;8(5-6):487-490.

Collins MD, Phillips BA and Zannoni P. Deoxyribonucleic acid homology studies of *Lactobacillus casei*, *Lactobacillus paracasei* sp. nov., subsp. *paracasei* and subsp. *tolerans*, and *Lactobacillus rhamnosus* sp. nov., comb. nov. *International Journal of Systematic Bacteriology* 1989;39(2):105-108.

Cousin FJ, Mater DD, Foligné B, Jan G. Dairy propionibacteria as human probiotics: A review of recent evidence. *Dairy Science & Technology* 2011;91(1):1-26.

CPhA 2002: Repchinsky C, editor-in-chief. *Patient Self-Care: Helping Patients Make Therapeutic Choices*. 1st edition. Ottawa (ON): Canadian Pharmacists Association; 2002.



Cremonini F, Di Caro S, Covino M, Armuzzi A, Gabrielli M, Santarelli L, Nista EC, Cammarota G, Gasbarrini G, Gasbarrini A. Effect of different probiotic preparations on anti-*Helicobacter pylori* therapy-related side effects: a parallel group, triple blind, placebo-controlled study. *The American Journal of Gastroenterology* 2002;97(11):2744-2749.

Cruchet S, Obregon MC, Salazar G, Diaz E, Gotteland M. Effect of the ingestion of a dietary product containing *Lactobacillus johnsonii* La1 on *Helicobacter pylori* colonization in children. *Nutrition* 2003;19(9):716-721.

Cukovic-Cavka S, Likic R, Francetic I, Rustemovic N, Opacic M, Vucelic B. *Lactobacillus acidophilus* as a cause of liver abscess in a NOD2/CARD15-positive patient with Crohn's disease. *Digestion* 2006;73(2-3):107-110.

Curk MC, Hubert JC and Bringel F. *Lactobacillus paraplantarum* sp. nov., a new species related to *Lactobacillus plantarum*. *International Journal of Systematic Bacteriology* 1996;46(2): 595-598.

Dalmacio LM, Angeles AK, Larcia LL, Balolong MP, Estacio RC. Assessment of bacterial diversity in selected Philippine fermented food products through PCR-DGGE. *Beneficial Microbes* 2011;2(4):273-281.

Dicks LM, Dellaglio F, Collins MD. Proposal to reclassify *Leuconostoc oenos* as *Oenococcus oeni* [corrig.] gen. nov., comb. nov. *International Journal of Systematic Bacteriology* 1995;45(2):395-397.

Driehuis F, Elferink SJ, and Spoelstra SF. Anaerobic lactic acid degradation during ensilage of whole crop maize inoculated with *Lactobacillus buchneri* inhibits yeast growth and improves aerobic stability. *Journal of Applied Microbiology* 1991;87(4):583-594.

DuPont AW, DuPont HL. The Intestinal microbiota and chronic disorders of the gut. *Nature Reviews Gastroenterology & Hepatology* 2011;8(9):523-531.

EFSA 2012: European Food Safety Authority. Scientific Opinion on the removal of a maximum dose from the authorisation of microbial products assessed using the Qualified Presumption of Safety approach. *EFSA Journal* 2012;10(5):2680. [Accessed 2013 June 29]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/2680.pdf>

Elli M, Callegari ML, Ferrari S, Bessi E, Cattivelli D, Soldi S, Morelli L, Goupil Feuillerat N, Antoine J. Survival of Yogurt Bacteria in the Human Gut. *Applied and Environmental Microbiology* 2006;72(7):5113-5117.

EMA/CHMP 2006: European Medicines Agency: Pre-authorization Evaluation of Medicines for Human Use. Committee for Medicinal Products for Human Use. Reflection Paper: Formulations of choice for the paediatric population. Adopted September 2006. EMA/CHMP/PEG/194810/2005. [Accessed on 2013 June 29]. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003782.pdf



Euzéby JP. 2012. List of Prokaryotic names with standing in nomenclature [Internet] International Journal of Systematic Bacteriology 2011 July 13. [Last full update March 04 2012, Minor changes since the full update March 20 2012; Accessed 2012 March 26]. Available from: <http://www.bacterio.net>

FAO/WHO 2001: Food and Agriculture Organization of the United Nations and World Health Organization. Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria [Internet]. Córdoba (AR): Food and Agriculture Organization of the United Nations and World Health Organization, 2001. [Accessed on 2013 June 29]. Available from: http://www.who.int/foodsafety/publications/fs_management/en/probiotics.pdf

Farrow JAE, Facklam RR, Collins MD. Nucleic acid homologies of some vancomycin-resistant leuconostocs and description of *Leuconostoc citreum* sp. nov. and *Leuconostoc pseudomesenteroides* sp. nov. International Journal of Systematic Bacteriology 1989;39(3):279-283.

Felley CP, Corthésy-Theulaz I, Rivero JL, Sipponen P, Kaufmann M, Bauerfeind P, Wiesel PH, Brassart D, Pfeifer A, Blum AL, Michetti P. Favourable effect of an acidified milk (LC-1) on *Helicobacter pylori* gastritis in man. European Journal of Gastroenterology and Hepatology 2001;13(1):25-29.

Fujisawa T, Adachi S, Toba T, Arihara K, Mitsuoka T. *Lactobacillus kefiranofaciens* sp. nov. isolated from kefir grains. International Journal of Systematic Bacteriology 1988;38(1):12-14.

Fujisawa T, Benno Y, Yaeshima T, Mitsuoka T. Taxonomic study of the *Lactobacillus acidophilus* group, with recognition of *Lactobacillus gallinarum* sp. nov. and *Lactobacillus johnsonii* sp. nov. and synonymy of *Lactobacillus acidophilus* group A3 (Johnson 1980) with the type strain of *Lactobacillus amylovorus* (Nakamura 1981). International Journal of Systematic Bacteriology 1992;42(3):487-491.

Gao W, Weng J, Gao Y, Chen X. Comparison of the vaginal microbiota diversity of women with and without human papillomavirus infection: a cross-sectional study. BMC Infectious Diseases 2013;13(1):271.

Giacoa GP, Taylor-Zapata P, Mattison D. Eunice Kennedy Shriver National Institute of Child Health and Human Development Pediatric Formulation Initiative: selected reports from working groups. Clinical Therapeutics 2008;30(11):2097-2101.

Gill H, Prasad J. Probiotics, immunomodulation, and health benefits. Advances in Experimental Medicine and Biology 2008;606:423-454.

Gilliland SE. 2001. Technological & Commercial Applications of Lactic Acid Bacteria; Health & Nutritional Benefits in Dairy Products [Internet]. Background paper for the Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria. Rome (IT): Food and Agriculture



Organization of the United Nations (FAO). [Accessed 2012 March 26]. Available from: <ftp://ftp.fao.org/es/esn/food/Gilli.pdf>

Golubev WI. Perfect state of *Rhodomyces dendrorhous* (*Phaffia rhodozyma*). *Yeast* 1995;11(2):101-110.

Guandalini S, Pensabene L, Zikri MA, Dias JA, Casali LG, Hoekstra H, Kolacek S, Massar K, Micetic-Turk D, Papadopoulou A, de Sousa JS, Sandhu B, Szajewska H, Weizman Z. *Lactobacillus* GG administered in oral rehydration solution to children with acute diarrhea: a multicenter European trial. *Journal of Pediatric Gastroenterology and Nutrition* 2000;30(1):54-60.

Guarino A, Canani RB, Spagnuolo MI, Albano F, Di Benedetto L. Oral bacterial therapy reduces the duration of symptoms and of viral excretion in children with mild diarrhea. *Journal of Pediatric Gastroenterology and Nutrition* 1997;25(5):516-519.

Hawrelak JA. Probiotics. In: Pizzorno JE, Murray MT, editors. 2006. *Textbook of Natural Medicine*, Third edition, volume 1. St. Louis (MI): Churchill Livingstone Elsevier. p. 1195-1215.

Hawrelak JA, Whitten DL, Myers SP. Is *Lactobacillus rhamnosus* GG effective in preventing the onset of antibiotic-associated diarrhoea: a systematic review. *Digestion* 2005;72(1):51-56.

HC 2003: Health Canada, It's your Health: Severe Allergic Reactions [Internet]. Ottawa (ON): Health Canada [Original: May 2003; Accessed 2013 October 24] Available from: <http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/med/allerg-eng.php>

HC 2009: Health Canada. It's your health. Food Allergies [Internet]. Ottawa (ON): Health Canada. 2009. [Accessed 2013 June 29]. Available from: http://www.hc-sc.gc.ca/hl-vs/alt_formats/pacrb-dgapcr/pdf/iyh-vsv/food-aliment/allerg-eng.pdf

HC 2012a: Health Canada media communication: What to Look For on Food Labels – Allergy Awareness [Internet]. Ottawa (ON): Health Canada [2012; Accessed 2013 October 24] Available from: http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/_2012/2012-130fs-eng.php

HC 2012b: Health Canada: The use of Food Allergen Precautionary Statements on Pre-Packaged Foods [Internet]. Ottawa (ON): Food Directorate, Health Canada [Original: March 2012; Accessed 2013 October 24] Available from: http://www.hc-sc.gc.ca/fn-an/alt_formats/pdf/label-etiquet/allergen/precaution_label-etiquette-eng.pdf

HC 2013: Pathway for Licensing Natural Health Products Making Modern Health Claims. Version 1.0 [Internet]. Ottawa (ON): Natural Health Products Directorate, Health Canada. 2013. [Accessed on June 29 2013]. Available from: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/prodnatur/legislation/docs/modern-eng.pdf

Hjortmo SB, Hellström AM, Andlid TA.. Production of folates by yeasts in Tanzanian fermented togwa. *FEMS Yeast Research* 2008;8(5):781–787.



- Hjortmo S, Patring J, Jastrebova J, Andlid T. Inherent biodiversity of folate content and composition in yeasts. *Trends in Food Science & Technology*. 2005;16(6-7):311–316.
- Hong Y, Yang HS, Li J, Han SK, Chang HC, Kim HY. Identification of lactic acid bacteria in salted Chinese cabbage by SDS-PAGE and PCR-DGGE. *Journal of the Science of Food and Agriculture* 2013;94(2):296-300.
- Howey RT, Lock CM, Moore LVH. Subspecies names automatically created by Rule 46. *International Journal of Systematic Bacteriology* 1990;40(3):317-319.
- Jin HZ, Fan XB, Hang XM, Li KB, Yang H. Analysis of the probiotic Bifidobacterium and Lactobacillus community in child intestinal flora. [Article in Chinese; Abstract in English]. *Wei Sheng Wu Xue Bao*. 2005;45(4):567-70.
- Johnson JL, Phelps CF, Cummins CS, London J and Gasser F. Taxonomy of the Lactobacillus acidophilus group. *International Journal of Systematic Bacteriology* 1980;30(1):53-68.
- Juárez Tomás MS, Ocaña VS, Nader-Macías ME. Viability of vaginal probiotic lactobacilli during refrigerated and frozen storage. *Anaerobe* 2004;10(1):1-5.
- Kalinowski J, Bathe B, Bartels D, Bischoff N, Bott M, Burkovski A, Dusch N, Eggeling L, Eikmanns BJ, Gaigalat L, Goesmann A, Hartmann M, Huthmacher K, Krämer R, Linke B, McHardy AC, Meyer F, Möckel B, Pfefferle W, Pühler A, Rey DA, Rückert C, Rupp O, Sahn H, Wendisch VF, Wiegräbe I, Tauch A. The complete *Corynebacterium glutamicum* ATCC 13032 genome sequence and its impact on the production of l-aspartate-derived amino acids and vitamins. *Journal of Biotechnology* 2003;104(1-3):5-25.
- Karapinar M, Jakobsen M. Identification of lactic acid bacteria isolated from Tarhana, a traditional Turkish fermented food. *International Journal of Food Microbiology* 2009;135(2):105-111.
- Ki MR, Ghim SY, Hong IH, Park JK, Hong KS, Ji AR, Jeong KS. In vitro inhibition of *Helicobacter pylori* growth and of adherence of cagA-positive strains to gastric epithelial cells by *Lactobacillus paraplantarum* KNUC25 isolated from kimchi. *Journal of Medicinal Food*. 2010;13(3):629-634.
- Kinoshita S, Nakayama S, Akita S. Taxonomic study of glutamic acid accumulating bacteria, *Micrococcus glutamicus*, nov. sp. *Bulletin of the Agricultural Chemical Society of Japan* 1958;22:176-185.
- Kotowska M, Albrecht P, Szajewska H. *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhoea in children: a randomized double-blind placebo-controlled trial. *Alimentary Pharmacology & Therapeutics* 2005;21(5):583-590.
- Ledoux D, Labombardi VJ, Karter D. *Lactobacillus acidophilus* bacteraemia after use of a probiotic in a patient with AIDS and Hodgkin's disease. *International Journal of STD & AIDS* 2006;17(4):280-282.



Leite AM, Leite DC, Del Aguila EM, Alvares TS, Peixoto RS, Miguel MA, Silva JT, Paschoalin VM. Microbiological and chemical characteristics of Brazilian kefir during fermentation and storage processes. *Journal of Dairy Science* 2013;96(7):4149-4159.

Lenoir-Wijnkoop I, Sanders ME, Cabana MD, Caglar E, Corthier G, Rayes N, Sherman PM, Timmerman HM, Vaneechoutte M, Van Loo J, Wolvers DA. Probiotic and prebiotic influence beyond the intestinal tract. *Nutrition Reviews* 2007;65(11):469-489.

Lherm T, Monet C, Nougère B, Soulier M, Larbi D, Le Gall C, Caen D, Malbrunot C. Seven cases of fungemia with *Saccharomyces boulardii* in critically ill patients. *Intensive Care Medicine* 2002;28(6):797-801.

Li Y, Raftis E, Canchaya C, Fitzgerald GF, Van Sinderen D and O'toole PW. Polyphasic analysis indicates that *Lactobacillus salivarius* subsp. *salivarius* and *Lactobacillus salivarius* subsp. *salicinii* do not merit separate subspecies status. *International Journal of Systematic and Evolutionary Microbiology* 2006;56(10):2397-2403.

Lindner P. *Schizosaccharomyces pombe* n. sp., ein neuer Gärungserreger, volume 10. 1893. p.1298 (in German).

Liu SQ, Tsao M. Enhancement of survival of probiotic and non-probiotic lactic acid bacteria by yeasts in fermented milk under non-refrigerated conditions. *International Journal of Food Microbiology* 2009;135(1):34-38.

Lodder J. In: Kreger-van Rij NJW, editor. *The Yeasts: A Taxonomic Study*. North-Holland, 1952. p.280.

Lodder J. In: Kreger-van Rij NJW. *The Yeasts: A Taxonomic Study*, Third edition. Elsevier Science, 1984. p.159.

Magnusson J, Schnürer J. *Lactobacillus coryniformis* subsp. *coryniformis* strain Si3 produces a broad-spectrum proteinaceous antifungal compound. *Applied and Environmental Microbiology* 2001;67(1):1-5.

Malgoire JY, Bertout S, Renaud F, Bastide JM, Mallié M. Typing of *Saccharomyces cerevisiae* clinical strains by using Microsatellite Sequence Polymorphism. *Journal of Clinical Microbiology* 2005;43(3):1133-1137.

Masco L, Ventura M, Zink R, Huy G, Swings J. Polyphasic taxonomic analysis of *Bifidobacterium animalis* and *Bifidobacterium lactis* reveals relatedness at the subspecies level: reclassification of *Bifidobacterium animalis* as *Bifidobacterium animalis* subsp. *animalis* subsp. nov. and *Bifidobacterium lactis* as *Bifidobacterium animalis* subsp. *lactis* subsp. nov. *International Journal of Systematic and Evolutionary Microbiology* 2004;54(4):1137-1143.

Mathur S, Singh R. Antibiotic resistance in food lactic acid bacteria - a review. *International Journal of Food Microbiology* 2005;105(3):281-295.



Mattarelli P, Bonaparte C, Pot B, Biavati B. Proposal to reclassify the three biotypes of *Bifidobacterium longum* as three subspecies: *Bifidobacterium longum* subsp. *longum* subsp. nov., *Bifidobacterium longum* subsp. *infantis* comb. nov. and *Bifidobacterium longum* subsp. *suis* comb. nov. *International Journal of Systematic and Evolutionary Microbiology* 2008;58(4):767-772.

McCullough MJ, Clemons KV, McCusker JH, Stevens DA. 1998. Species identification and virulence attributes of *Saccharomyces boulardii* (nom. inval.). *Journal of Clinical Microbiology* 36(9):2613-2617.

Meyen ex E.C. Hansen; 1883. p.29.

McFarland LV, Surawicz CM, Greenberg RN, Elmer GW, Moyer KA, Melcher SA, Bowen KE, Cox JL. Prevention of beta-lactam-associated diarrhea by *Saccharomyces boulardii* compared with placebo. *The American Journal of Gastroenterology* 1995;90(3):439-448.

McFarland LV. Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients. *World Journal of Gastroenterology* 2010;16(18):2202-2222.

Morelli L. In vitro selection of probiotic lactobacilli: a critical appraisal. *Current Issues in Intestinal Microbiology* 2000;1(2):59-67.

Nakamura Y, Fukuhara H, Sano K. Secreted phytase activities of yeasts. *Bioscience Biotechnology and Biochemistry* 2000;64(4):841-844.

Nakamura LK. *Lactobacillus amylovorus*, a new starch-hydrolyzing species from cattle waste-corn fermentations. *International Journal of Systematic Bacteriology* 1981;31(1):56-63.

Nam SH. Genome sequence of *Lactobacillus farciminis* KCTC 3681. *Journal of Bacteriology* 2011;193(7):1790-1791.

NCBI 2009: NCBI taxonomy database [Internet]. Bethesda (MD): National Center for Biotechnology Information, U.S. National Library of Medicine. [Accessed 2012 March 21] Available from: <http://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi>

NIH 2011: National Institute of Health. Medline Plus. U.S. National Library of Medicine Bethesda (MD): U.S. Department of Health and Human Services. [Updated 2011 November; Accessed 2012 March 21].

Pantoflickova D, Corthésy-Theulaz I, Dorta G, Stolte M, Isler P, Rochat F, Enslen M, and Blum AL. Favourable effect of regular intake of fermented milk containing *Lactobacillus johnsonii* on *Helicobacter pylori* associated gastritis. *Alimentary Pharmacology and Therapeutics* 2003;18(8):805-813.

Peinado RA, Moreno JJ, Maestre O, Ortega JM, Medina M, Mauricio JC. Gluconic acid consumption in wines by *Schizosaccharomyces pombe* and its effect on the concentrations of major volatile compounds and polyols. *Journal of Agriculture and Food Chemistry* 2004;52(3):493-497.



Péteri Z, Teren J, Vagvolgyi C, Varga J. Ochratoxin degradation and adsorption caused by astaxanthin-producing yeasts. *Food Microbiology* 2007;24(3):205-210.

Petri A, Pfannebecker J, Fröhlich J, König H. Fast identification of wine related lactic acid bacteria by multiplex PCR. *Food Microbiology* 2013;33(1):48-54.

Picard C, Fioramonti J, Francois A, Robinson T, Neant F, Matuchansky C. Review article: bifidobacteria as probiotic agents -- physiological effects and clinical benefits. *Alimentary Pharmacology & Therapeutics* 2005;22(6):495-512.

Pridmore RD, Berger B, Desiere F, Vilanova D, Barretto C, Pittet AC, Zwahlen MC, Rouvet M, Altermann E, Barrangou R, Mollet B, Mercenier A, Klaenhammer T, Arigoni F, Schell MA. The genome sequence of the probiotic intestinal bacterium *Lactobacillus johnsonii* NCC 533. *Proceedings of the National Academy of Sciences of the United States of America* 2004; 101(8):2512-2517.

Reess M. *Botanische Untersuchungen über die Alkoholgährungspilze*; 1870. p.83. (in German)

Reid G, Jass J, Sebulsky MT, McCormick JK. Potential uses of probiotics in clinical practice. *Clinical Microbiology Reviews* 2003;16(4):658-672.

Reid G. Minireview- The scientific basis for probiotic strains of *Lactobacillus*. *Applied and Environmental Microbiology* 1999;65(9):3763-3766.

Riquelme AJ, Calvo MA, Guzmán AM, Depix MS, García P, Pérez C, Arrese M, Labarca JA. *Saccharomyces cerevisiae* fungemia after *Saccharomyces boulardii* treatment in immunocompromised patients. *Journal of Clinical Gastroenterology* 2003;36(1):41-43.

Robles Alonso V, Guarner F. Linking the gut microiota to human health. *British Journal of Nutrition* 2013;109(Supplement 2):S21-26.

Rolfé RD. The role of probiotic cultures in the control of gastrointestinal health. *Journal of Nutrition* 2000;130(Supplement 2S):396S-402S.

Roos S, Karner F, Axelsson L, Jonsson H. *Lactobacillus mucosae* sp. nov., a new species with in vitro mucus-binding activity isolated from pig intestine. *International Journal of Systematic and Evolutionary Microbiology* 2000;50(Part 1):251-258.

Saccardo PA. *Supplementum Universale, Pars. III*; 11; 1895. p. 457. (in Latin)

Sanders ME. Scientific Status Summary – Probiotics - A Publication of the Institute of Food technologists' Expert Panel on Food Safety and Nutrition. *Food Technology* 1999;53(11):67-77.

Schillinger U. Isolation and identification of lactobacilli from novel-type probiotic and mild yoghurts and their stability during refrigerated storage. *International Journal of Food Microbiology* 1999;47(1-2):79-87.



Schleifer KH, Kilpper-Bälz R. Transfer of streptococcus faecalis and streptococcus faecium to the genus enterococcus nom. rev. as enterococcus faecalis comb. nov. and enterococcus faecium comb. nov. International Journal of Systematic Bacteriology 1984;34(1):31-34.

Sengun IY, Nielsen DS, Karapinar M, Jakobsen M. Identification of lactic acid bacteria isolated from tarhana, a traditional turkish fermented food. International Journal of Food Microbiology 2009;135(2):105-111.

Skerman VBD, McGowan V, Sneath PHA. Approved lists of bacterial names. International Journal of Systematic Bacteriology 1980;30(1):225-420.

Skerman VBD, McGowan V, Sneath PHA, editors. 1989. Approved Lists of Bacterial Names, (Amended) [Internet]. Washington (DC): American Society of Microbiology Press. [Accessed 2012 March 21]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20806452>

Surawicz CM, Elmer GW, Speelman P, McFarland LV, Chinn J, van Belle G. Prevention of antibiotic-associated diarrhea by Saccharomyces boulardii: a prospective study. Gastroenterology 1989;96(4):981-988.

Taverniti V, Guglielmetti S. Health-promoting properties of lactobacillus helveticus. Frontiers in Microbiology 2012;3:392.

Terzic-Vidojevic A, Vukasinovic M, Veljovic K, Ostojic M, Topisirovic L. Characterization of microflora in homemade semi-hard white Zlatar cheese. International Journal of Food Microbiology 2007;114(1):36-42.

Validation of the publication of new names and new combinations previously effectively published outside the IJSB: List No. 4. International Journal of Systematic Bacteriology 1980; 30(3):601.

Validation of the publication of new names and new combinations previously effectively published outside the IJSB: List No. 8. International Journal of Systematic Bacteriology Validation 1982;32(2):266-268.

Validation of the publication of new names and new combinations previously effectively published outside the IJSB: List No. 11. International Journal of Systematic Bacteriology 1983;33(3):672-674.

Validation of the publication of new names and new combinations previously effectively published outside the IJSB: List No. 16. International Journal of Systematic Bacteriology 1984; 34:503-504.

Validation of the publication of new names and new combinations previously effectively published outside the IJSB: List No. 17. International Journal of Systematic Bacteriology 1985;35:223-225.



Validation of the publication of new names and new combinations previously effectively published outside the IJSB: List No. 20. *International Journal of Systematic Bacteriology* 1986; 36:354-356.

Validation of the publication of new names and new combinations previously effectively published outside the IJSB: List No. 68. *International Journal of Systematic Bacteriology* 1999;49:1-3.

van der Aa Kühle A, Jespersen L. The taxonomic position of *Saccharomyces boulardii* as evaluated by sequence analysis of the D1/D2 domain of 26S rDNA, the ITS1-5.8S rDNA-ITS2 region and the mitochondrial cytochrome-c oxidase II gene. *Systematic and Applied Microbiology* 2003;26(4):564-571.

Van der Walt JP. New combinations in the genera *Brettanomyces*, *Kluyveromyces*, *Lodderomyces* and *Wingea*. *Bothalia* 1971;10(3):417-418.

Vanderhoof JA, Whitney DB, Antonson DL, Hanner TL, Lupo JV, Young RJ. *Lactobacillus GG* in the prevention of antibiotic-associated diarrhea in children. *The Journal of Pediatrics* 1999;135(5):564-568.

Vardjan T, Mohar Lorbeg P, Rogelj I, Čanžek Majhenič A. Characterization and stability of lactobacilli and yeast microbiota in kefir grains. *Journal of Dairy Science* 2013;96(5):2729-2736.

Vogel RF, Böcker G, Stolz P, Ehrmann M, Fanta D, Ludwig W, Pot B, Kersters K, Schleifer KH, Hammes WP. Identification of lactobacilli from sourdough and description of *Lactobacillus pontis* sp. nov. *International Journal of Systematic Bacteriology* 1994;44(2):223-229.

Vogel RF, Knorr R, Müller MR, Steudel U, Gänzle MG, Ehrmann MA. Non-dairy lactic fermentations: the cereal world. *Antonie Van Leeuwenhoek* 1999;76(1-4):403-411.

WGO Global Guideline 2011: World Gastroenterology Organisation Global Guidelines. Practice Guideline – Probiotics and Prebiotics. [Accessed 2013 June 29]. Available from: <http://www.worldgastroenterology.org/probiotics-prebiotics.html>

WHO 2005: World Health Organization. The Treatment of Diarrhoea. A manual for physicians and other senior health workers [Internet]. Geneva (CH): Department of Child and Adolescent Health and Development, World Health Organization; 2005. [Accessed 2013 June 29]. Available from: http://www.who.int/entity/child_adolescent_health/documents/9241593180/en/

Wiese BJ, Strohmair W, Rainey FA, Diekmann H. *Lactobacillus panis* sp. nov., from sourdough with a long fermentation period. *International Journal of Systematic Bacteriology* 1996;46(2):449-453.

Witthuhn RC, Schoeman T, Britz TJ. Characterisation of the microbial population at different stages of Kefir production and Kefir grain mass cultivation. *International Dairy Journal* 2005;15(4):383–389.



Zanoni P, Farrow JAE, Phillips BA, Collins MD. *Lactobacillus pentosus* (Fred, Peterson, and Anderson) sp. nov., nom. rev. *International Journal of Systematic Bacteriology* 1987;37(4):339-341.



References reviewed

Alonso RV, Guarner F. Linking the gut microiota to human health. *British Journal of Nutrition* 2013;109(Supplement 2):S21-S26.

Bezkorovainy A. Probiotics: determinants of survival and growth in the gut. *The American Journal of Clinical Nutrition* 2001;73(Supplement):399S-405S.

Collins JK, Thornton G, O'Sullivan GO. Selection of probiotic strains for human applications. *International Dairy Journal* 1998;8(5):487-490.

Dalmacio LM, Angeles AK, Larcia LL, Balolong MP, Estacio RC. Assessment of bacterial diversity in selected Philippine fermented food products through PCR-DGGE. *Benef Microbes* 2011;2(4):273-281.

Dellaglio F, Torriani S, Felis GE. Reclassification of *Lactobacillus cellobiosus* Rogosa et al. 1953 as a later synonym of *Lactobacillus fermentum* Beijerinck 1901. *International Journal of Systematic and Evolutionary Microbiology* 2004;54(Part 3):809-812.

DuPont AW, DuPont HL. The intestinal microbiota and chronic disorders of the gut. *Nature Reviews Gastroenterology and Hepatology* 2011;8(9):523-531.

EFSA 2007: European Food Safety Authority. Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA. Opinion of the Scientific Committee. *EFSA Journal* 2007;587:1-16. [Accessed 2013 June 29]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/587.pdf>

EFSA 2008: European Food Safety Authority. Technical guidance: Update of the criteria used in the assessment of bacterial resistance to antibiotics of human or veterinary importance. Prepared by the Panel on Additives and Products or Substances used in Animal Feed. *EFSA Journal* 2008;732:1-15. [Accessed 2013 June 29]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/732.pdf>

EFSA 2009: European Food Safety Authority. Scientific Opinion on the maintenance of the list of QPS microorganisms intentionally added to food or feed. EFSA Panel on Biological Hazards (BIOHAZ). *EFSA Journal* 2009;7(12):1431. [Accessed 2013 June 29]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/1431.pdf>

EFSA 2010: European Food Safety Authority. Scientific Opinion on the maintenance of the list of QPS microorganisms intentionally added to food or feed. EFSA Panel on Biological Hazards (BIOHAZ). *EFSA Journal* 2010;8(12):1944. [Accessed 2013 June 29]. Available from: <http://www.efsa.europa.eu/fr/efsajournal/doc/1944.pdf>

EFSA 2011: European Food Safety Authority. Scientific Opinion on the maintenance of the list of QPS microorganisms intentionally added to food or feed. EFSA Panel on Biological Hazards (BIOHAZ). *EFSA Journal* 2011;9(12):2497. [Accessed 2013 June 29]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/2497.pdf>



EFSA 2012: European Food Safety Authority. Scientific Opinion on the maintenance of the list of QPS microorganisms intentionally added to food or feed. EFSA Panel on Biological Hazards (BIOHAZ). EFSA Journal 2012;10(12):3020. [Accessed 2013 June 29]. Available from: <http://www.efsa.europa.eu/en/efsajournal/doc/3020.pdf>

Felis GE & Dellaglio F. Taxonomy of Lactobacilli and Bifidobacteria. *Current Issues in Intestinal Microbiology* 2007;(2):44-61.

Gill H, Prasad J. Probiotics, immunomodulation, and health benefits. *Advances in Experimental Medicine and Biology* 2008;606:423-454.

Hawrelak, Jason A. In: Pizzorno JE, Murray MT, editors. *Textbook of Natural Medicine*, Second edition. St. Louis (MI): Churchill Livingstone, 2000. p. 1195-1215.

Hjortmo S, Patring J, Jastrebova J, Andlid T. Inherent biodiversity of folate content and composition in yeasts. *Trends in Food Science and Technology* 2005;16(6-7):311–316.

JC 2009: Justice Canada. *Human Pathogens and Toxins Act* (S.C., 2009, c. 24). Act current to 2013-10-01 and last amended on 2012-06-29 [Internet]. Ottawa (ON): Justice Canada. [Accessed 2013 June 29]. Available from: <http://lois-laws.justice.gc.ca/eng/acts/H-5.67/index.html>

Ledoux D, Labombardi VJ, Karter D. Lactobacillus acidophilus bacteraemia after use of a probiotic in a patient with AIDS and Hodgkin's disease. *International Journal of STD & AIDS* 2006;17(4):280-282.

Lenoir-Wijnkoop I, Sanders ME, Cabana MD, Caglar E, Corthier G, Rayes N, Sherman PM, Timmerman HM, Vaneechoutte M, Van Loo J, Wolvers DA. Probiotic and prebiotic influence beyond the intestinal tract. *Nutrition Reviews* 2007;65(11):469-489.

Lherm T, Monet C, Nougère B, Soulier M, Larbi D, Le Gall C, Caen D, Malbrunot C. Seven cases of fungemia with *Saccharomyces boulardii* in critically ill patients. *Intensive Care Medicine* 2002;28(6):797-801.

Masco L, Ventura M, Zink R, Huy G, Swings J. Polyphasic taxonomic analysis of *Bifidobacterium animalis* and *Bifidobacterium lactis* reveals relatedness at the subspecies level: reclassification of *Bifidobacterium animalis* as *Bifidobacterium animalis* subsp. *animalis* subsp. nov. and *Bifidobacterium lactis* as *Bifidobacterium animalis* subsp. *lactis* subsp. nov. *International Journal of Systematic and Evolutionary Microbiology* 2004;54(4):1137-1143.

Mattarelli P, Bonaparte C, Pot B, Biavati B. Proposal to reclassify the three biotypes of *Bifidobacterium longum* as three subspecies: *Bifidobacterium longum* subsp. *longum* subsp. nov., *Bifidobacterium longum* subsp. *infantis* comb. nov. and *Bifidobacterium longum* subsp. *suis* comb. nov. *International Journal of Systematic and Evolutionary Microbiology* 2008;58(4):767-772.

McFarland L. Systematic review and meta-analysis of *saccharomyces boulardii* in adult patients. *World Journal of Gastroenterology* 2010;16(18):2202-2222.



Miller MW, Yoneyama M, Soneda M. *Phaffia*, a new yeast genus in the Deuteromycotina (Blastomycetes). *International Journal of Systematic Bacteriology* 1976;26(2):286-291.

Morelli L. In vitro selection of probiotic lactobacilli: a critical appraisal. *Current Issues in Intestinal Microbiology* 2000;1(2):59-67.

Péteri Z, Teren J, Vagvolgyi C, Varga J. Ochratoxin degradation and adsorption caused by astaxanthin-producing yeasts. *Food Microbiology* 2007;24(3):205–210.

Picard C, Fioramonti J, Francois A, Robinson T, Neant F, Matuchansky C. Review article: bifidobacteria as probiotic agents -- physiological effects and clinical benefits. *Alimentary Pharmacology & Therapeutics* 2005;22(6):495-512.

Rolfe RD. The Role of Probiotic Cultures in the Control of Gastrointestinal Health. *Journal of Nutrition* 2000;130(Supplement 2S):396S-402S.

Sengun IY, Nielsen DS, Karapinar M, Jakobsen M. Identification of lactic acid bacteria isolated from Tarhana, a traditional Turkish fermented food. *International Journal of Food Microbiology* 2009;135(2):105-111.

Senok AC, Ismaeel AY, Botta GA. Probiotics: facts and myths. *Clinical Microbiology and Infection* 2005;11(12):958-966.

Skerman VBD, McGowan V, Sneath PHA. Approved lists of bacterial names. *International Journal of Systematic Bacteriology* 1980;30(1):225-420.

Schillinger U. Isolation and identification of lactobacilli from novel-type probiotic and mild yoghurts and their stability during refrigerated storage. *International Journal of Food Microbiology* 1999;47(1-2):79-87.

WGO Global Guideline 2011: World Gastroenterology Organisation Global Guidelines. Practice Guideline – Probiotics and Prebiotics. [Accessed 2013 June 29]. Available from: <http://www.worldgastroenterology.org/probiotics-prebiotics.html>

Appendix I

Table 1: Medicinal Ingredients – BACTERIA

Proper and Common names	References
<i>Bifidobacterium adolescentis</i>	Masco et al. 2004; Skerman et al. 1980
<i>Bifidobacterium animalis</i> (including <i>B. animalis</i> subsp. <i>animalis</i> and <i>B. animalis</i> subsp. <i>lactis</i>)	Masco et al. 2004; Skerman et al. 1980
<i>Bifidobacterium bifidum</i>	Skerman et al. 1980
<i>Bifidobacterium breve</i>	Skerman et al. 1980
<i>Bifidobacterium longum</i> (including <i>Bifidobacterium longum</i> subsp. <i>infantis</i> , <i>Bifidobacterium longum</i> subsp. <i>longum</i> and <i>Bifidobacterium longum</i> subsp. <i>suis</i>)	Mattarelli et al. 2008
<i>Lactobacillus acidophilus</i>	Johnson et al. 1980; Skerman et al. 1980
<i>Lactobacillus amylolyticus</i>	Validation List No. 68 1998
<i>Lactobacillus amylovorus</i>	Nakamura 1981
<i>Lactobacillus brevis</i>	Skerman et al. 1980
<i>Lactobacillus buchneri</i>	Skerman et al. 1980
<i>Lactobacillus casei</i>	JCICSB 2008; Skerman et al. 1980
<i>Lactobacillus coryniformis</i>	Skerman et al. 1980
<i>Lactobacillus crispatus</i> ¹	Skerman et al. 1980
<i>Lactobacillus curvatus</i>	Skerman et al. 1980
<i>Lactobacillus delbrueckii</i> (including <i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i> & <i>Lactobacillus delbrueckii</i> subsp. <i>delbrueckii</i>)	Beijerinck 1901; Howey et al. 1990
<i>Lactobacillus farciminis</i>	Validation List no. 11, 1983
<i>Lactobacillus fermentum</i>	Skerman et al. 1980
<i>Lactobacillus gallinarum</i> ¹	Fujisawa et al. 1992
<i>Lactobacillus gasseri</i>	Validation List No. 4 1980
<i>Lactobacillus helveticus</i>	Skerman et al. 1980
<i>Lactobacillus hilgardii</i>	Skerman et al. 1980
<i>Lactobacillus johnsonii</i>	Fujisawa et al. 1992
<i>Lactobacillus kefiranoformis</i>	Fujisawa et al. 1988
<i>Lactobacillus kefir</i>	Validation List no. 11, 1983
<i>Lactobacillus mucosae</i>	Roos et al. 2000
<i>Lactobacillus panis</i>	Wiese et al. 1996
<i>Lactobacillus paracasei</i>	JCICSB 2008; Collins et al. 1989
<i>Lactobacillus paraplantarum</i>	Curk et al. 1996
<i>Lactobacillus plantarum</i>	Skerman et al. 1980
<i>Lactobacillus pontis</i>	Vogel et al. 1994
<i>Lactobacillus reuteri</i>	Validation List No. 8, 1982
<i>Lactobacillus rhamnosus</i>	Collins et al. 1989

Proper and Common names	References
<i>Lactobacillus salivarius</i>	Skerman et al. 1980
<i>Lactobacillus sanfranciscensis</i>	Validation List no. 16, 1984b
<i>Lactococcus lactis</i>	Validation List no. 20, 1985
<i>Leuconostoc citreum</i>	Farrow et al. 1989
<i>Leuconostoc pseudomesenteroides</i>	Farrow et al. 1989
<i>Leuconostoc lactis</i>	Skerman et al. 1980
<i>Leuconostoc mesenteroides</i>	Skerman et al. 1980
<i>Oenococcus oeni</i>	Dicks et al. 1995
<i>Pediococcus acidilactici</i>	Skerman et al. 1980
<i>Pediococcus pentosaceus</i>	Skerman et al. 1980
<i>Propionibacterium freudenreichii</i> (including <i>Propionibacterium freudenreichii</i> subsp. <i>shermanii</i>)	Skerman et al. 1980
<i>Propionibacterium acidipropionici</i>	Skerman et al. 1980

¹For “source of probiotics” claim only

Table 2: Medicinal Ingredients – BACTERIA and FUNGI

Proper and Common names	Strain	References
<i>Lactobacillus johnsonii</i> ¹	La1	Euzéby 2012; Pridmore et al. 2004; Sanders 1999
<i>Lactobacillus johnsonii</i> ¹	Lj1	Euzéby 2012; Reid 1999; Sanders 1999
<i>Lactobacillus johnsonii</i> ¹	NCC 533	Euzéby 2012; Pridmore et al. 2004
<i>Lactobacillus rhamnosus</i> ²	GG	Euzéby 2012; Hawrelak et al. 2005; Gilliland 2001; Reid 1999, Skerman et al. 1989
<i>Saccharomyces boulardii</i> ³		McFarland 2010; NCBI 2009; Malgoire et al. 2005; McCullough et al. 1998; Meyen ex E.C. Hansen 1883
<i>Saccharomyces cerevisiae</i>		McFarland 2010; NCBI 2009; Malgoire et al. 2005; McCullough et al. 1998; Meyen ex E.C. Hansen 1883;

¹*Lactobacillus johnsonii* Fujisawa et al. 1992 (Lactobacillaceae) (NCBI 2009; Bisby et al. 2006; Skerman et al. 1989)

²*Lactobacillus rhamnosus* (Hansen 1968) Collins et al. 1989 (Lactobacillaceae) (NCBI 2009; Bisby et al. 2006; Skerman et al. 1989)

³*Saccharomyces boulardii* Seguela, Bastide & Massot 1984 (Saccharomycetaceae) is not a valid proper name for a genetically distinct subtype within the species of *Saccharomyces cerevisiae* (Posteraro et al. 2005). This name is still used in the scientific literature however and pending a more thorough review, will continue to be accepted as a proper name in probiotic products to prevent confusion with non-probiotic subtypes of *S. cerevisiae* (McFarland 2010; NCBI 2009; Bisby et al. 2006; Malgoire et al. 2005; de Llanos et al. 2004; van der Aa Kühle et al. 2003; McCullough et al. 1998; Skerman et al. 1989).



Table 3: Medicinal Ingredients – FUNGI

Proper and Common names	References
<i>Debaryomyces hansenii</i>	Lodder 1952
<i>Kluyveromyces lactis</i>	van der Walt 1971
<i>Kluyveromyces marxianus</i>	van der Walt 1971
<i>Saccharomyces bayanus</i>	Saccardo 1895
<i>Saccharomyces cerevisiae</i> (including <i>Saccharomyces boulardii</i>)	Meyen ex E.C. Hansen 1883
<i>Saccharomyces pastorianus</i>	Reess 1870
<i>Schizosaccharomyces pombe</i>	Lindner 1893
<i>Xanthophyllomyces dendrorhous</i>	Golubev 1995

Table 4: The following live microorganisms are excluded from this monograph

Proper and Common names	References
<i>Escherichia coli</i>	Skerman et al. 1980
<i>Bacillus coagulans</i>	Skerman et al. 1980
<i>Bacillus subtilis</i>	Skerman et al. 1980
<i>Clostridium butyricum</i>	Skerman et al. 1980
<i>Enterococcus faecium</i>	Schleifer et al. 1984
<i>Streptococcus salivarius</i>	Skerman et al. 1980