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REGULATORY REQUIREMENTS FOR APPROVAL PROCESS OF PROBIOTICS IN CANADA

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ABSTRACT

Probiotics are microorganisms that, when consumed, generally provide a benefit to humans health. Probiotics are gaining popularity as a treatment for millions of individuals around the world taken on a regular basis for alleged health benefits. Lactobacilli, bifidobacteria, and lactococciare the examples of probiotics have long been assumed to be safe where as the most important determinant for probiotics selection is human health safety. The rate of discovery of novel organisms with potential therapeutic benefits for both human and environmental health is at an all-time high because many different types of microbes are used as probiotics, safety is inextricably linked to the nature of the specific microbe being used. Natural health products, such as vitamins, minerals, and herbs, along with probiotics are increasingly popular among Canadians. Recent research has looked into the potential of probiotics to treat or prevent disease, maintain health, and reduce the possibility of future disease, despite the fact that they are currently sold mostly as ingredients in foods or nutritional supplements. This article focuses on Regulatory Requirements for the Approval Process of Probiotics in Canada.

Keywords: Probiotics, Microorganisms, Health Canada, Natural Health Product

INTRODUCTION

Probiotics are living microbes that provide a health benefit to the host when administered in adequate amounts. Probiotics and related terms or representations on food labels and in food advertising should only be used in accordance with specific, validated declarations about the benefits or effects of the probiotic microorganism in the food **[1]**. The probiotic field exemplifies microbiology's ability to translate to humans and animals **[2]**. Probiotics are typically present in dairy products including yoghurt, cheese, and milk-based drinks. Other types of probiotic-containing foods are also obtainable to Canadians in stores and on the internet **[1]**. Health Canada is Canada's regulatory authority, which is responsible for assisting Canadians in maintaining and improving their health. It works to ensure that high-quality healthcare services are available and that health risks are minimized **[3]**. Probiotics in Food and NHP are authorized by Health Canada, where as NHPs include Probiotics along with Vitamins and minerals, Herbal remedies, Homeopathic medicines, Traditional medicines such as traditional Chinese and Ayurvedic (East Indian) medicines, other products like amino acids and essential fatty acids **[4]**. The new regulations dated January 1, 2004, regulate all aspects of Natural Health Products (NHP), including probiotics along with manufacturing, packaging, labeling, distribution, storage, importation, and sale. The new NHPD regulations allow therapeutic claims as well as risk reduction and structure/function claims **[5]**. Health Canada's Natural Health Products Directorate (NHPD) has developed guidelines that all Canadians have ready access to NHP that are safe, potent, and of good quality, while also respecting freedom of choice and conceptual and cultural diversity. According to the NHP Regulations, NHP health claims must be supported by particular standards, and items must be manufactured in approved facilities using good manufacturing practices **[6]**.

Probiotics in Foods

Live bacterial cultures, often known as probiotics, are food components that can be added to food products under Food and Drug Regulations. There are currently no specific regulations governing probiotic bacteria in foods; however, the general provisions of the Food and Drugs Act and Regulations govern the safety of foods and their ingredients, as well as claims made on labels of food and in advertising, including claims about probiotics, which can apply to foods containing microorganisms, and food manufacturers and importers are fully responsible for the safety

of food products they manufacture and sell. All product representations, including claims, must be true and not misleading, deceitful, or likely to provide the wrong impression about a product's character, importance, quantity, composition, merit, or safety, according to the Act. All attributes related to Food and Drugs Act and Regulation are enforced by the Canadian Food Inspection Agency (CFIA). Food products that include probiotic microorganisms are considered food. When a food product is marketed as having a medicinal use or purpose, it is usually classified as a NHP, based on the microorganism and the risks associated with it, as well as the product's marketed medicinal use, as well as the product's history of use and public perception of its intended use **[1]**.

Probiotics in Natural Health Products

Probiotics are available as NHPs in pharmaceutical dosage forms. These Regulations govern the manufacture, packaging, labeling, and importing of NHPs for sale. All NHPs should have product licenses to be marketed in Canada, and all Canadian sites that produce, package, label, or import NHPs should have site licenses. The Probiotics Monograph was developed by Health Canada to assist industry stakeholders obtain product licenses for their probiotics NHPs in different dosage forms. The monograph contains comprehensive information on potential health claims, associated doses, source materials, and required risk data. Probiotic NHPs are not restricted to the claims and doses stated in the monograph; they can also be used for a distinct claim at a different dose.

An NHP containing probiotics could be sold as a food supplement (e.g. fermented food products). The criteria described in Health Canada's guideline document, Classification of Products at the Food-Natural Health Product Interface: Products in Food Formats would be used to determine whether such a product should be classified as a food or an NHP. The Natural Health Products Directorate (NHPD) of Health Canada regulates probiotics as NHPs. The Health Products and Food Branch Inspectorate (HPFBI) are in charge of enforcing the NHP regulations **[1]**. NHPs are naturally occurring compounds and are used to improve or maintain good health. Plants are commonly used; however animals, microbes, and marine sources can also be used. Tablets, capsules, tinctures, solutions, lotions, ointments, and drops are among the many forms available. Complementary and alternative medicines are terms used to describe natural health products. The Regulations make it easier for Canada people

to get a wide choice of safe, effective, and high-quality natural health products **[7]**.

Products authorization in Health Canada

NHPs must be safe, effective, and of good quality to be approved in Canada, and must include full label information to allow consumers to make safe and informed choices. Look for the eight-digit Natural Product Number (NPN) or Homeopathic Medicine Number (DIN-HM) on the label to identify items that have been licensed for marketing in Canada. A NPN or DIN-HM indicates that the product was already approved for marketing in Canada and is safe and efficacious when followed the label's instructions **[6]**.

PRODUCT LICENSING

Application:

An application for a product license must be required to submit to the Minister and include the following data: the applicant's name, address, and telephone number, as well as, if applicable, the applicant's facsimile number and electronic mail address, and, if the applicant is a non-Canadian, the applicant's Canadian representative to whom notices must be sent. For each medicinal ingredient in the NHP, provide information on its proper and common names, quantity per dosage unit, potency (if a potency representation is to be expressed on any label of the NHP), a description of its source material, and whether it is synthetically manufactured. A descriptive list of the non-medicinal ingredients proposed for the NHP, with a statement indicating the ingredient's purpose and each brand name under which the NHP is recommended to be sold; information demonstrating the NHP's safety and efficacy when used according to the recommended conditions of use; the recommended label text for each NHP that is proposed to be used in conjunction; a copy of the requirements to which the NHP will comply. A product number will be assigned to each NHP in respect of product license is issued by minister and if NHP is drug then drug identification number is assigned according to the Food and Drug Regulations. The licensee should notify the Minister of any information on the license that the licensee knows to be incorrect within 60 days of receipt the product license **[9]**.

Specifications

After submission of application, the minister may dispose the application within 60 days after the day on which it is issued if not provided additional information or samples requested by minister respect to NHP. The applicant does not make any false or misleading statements in the application.Before the date on which the license is issued and notice is sent to the applicant minister disposes the application.

The Minister shall notify the applicant of the cause for the refusal if it is refused to issue or amend product license along with reason and applicant can request to reconsider within 30 days of receiving the notice and minister shall give applicant an opportunity, if the requirements are met then reconsideration to issue or amend product license of application takes place by minister. If the Minister has reasonable causes to believe that an NHP is no longer safe when used under the recommended conditions of use, the Minister may request that the licensee provide information and documents demonstrating that the NHP is safe when used under the recommended conditions of use within 15 days of receipt the request **[9]**.

Amendment and Notification

If the licensee makes any of the following modifications to the NHP, the licensee shall not market any lot or batch of the NHP impacted by the change unless the product license is notified to the minister within 60 days of the change being made and amended accordingly: A change in its recommended dose, recommended duration of use, recommended use or purpose, common or proper name of any of its medicinal ingredients; the deletion or amendment of risk information shown on any of its labels, including the deletion or modification of a caution, warning, contra-indication, or known adverse reaction associated with its use; a change in the source material and effectiveness of any of its medicinal ingredients. **[9]**

A change that affects its safety or efficacy but is not caused by a change in the quantity of a medicinal ingredient per dosage unit, the inclusion or substitution of a medicinal ingredient, a change in its dosage form, or a change in its recommended route of administration. One or more of the following modifications to its specifications, namely, the removal of a test method specified in the specifications, the change of a test method specified in the specifications in a way that broadens the purity tolerances of the NHP or the quantity, identity, or potency tolerances of any of its medicinal ingredients, or the modification of a test method specified in the specifications in a way that renders it less precise, accurate, and specific or sensitive. The product number of the NHP; anassertion identifying each change described that has been made; information demonstrating that the NHP is safe and effective after the change; the label text for each NHP that is to be used in conjunction after the change; and a copy of the revised specifications must be submitted to the Minister in an application to modify a product license **[9]**.

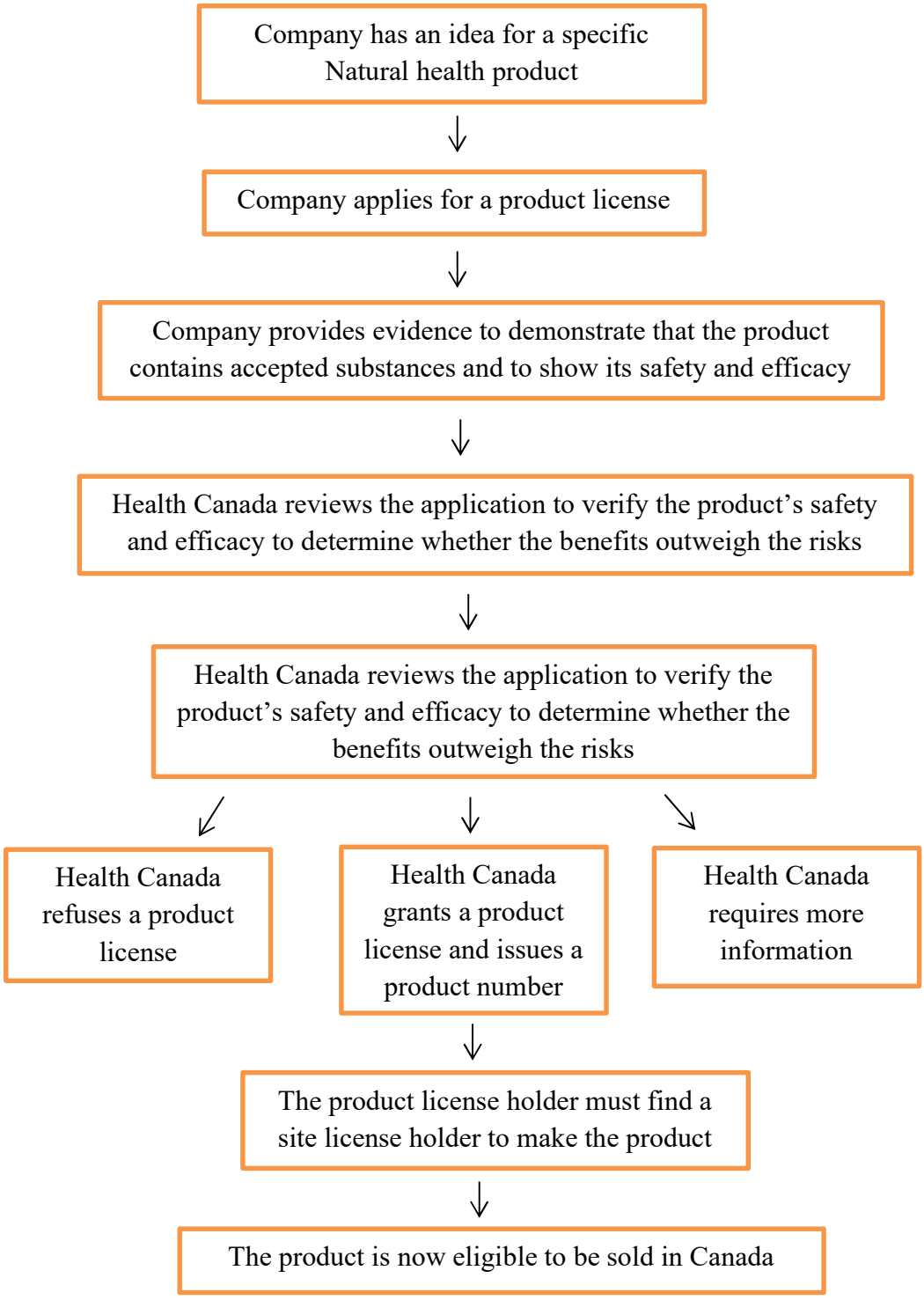

Figure 1: Approval Process for Product License [10]

Records & Suspension or Cancellation

Every licensee who sells an NHP must keep the following records: a list of all ingredients contained in the NHP, as well as records containing adequate information to enable the recall in each lot or batch of the NHP which is made available for sale. The licensee must keep the records for one year after the

expiration date of the NHP to which the record relates. When the licensee contravenes these Regulations or any requirement of the Act relating to the NHP, the product license will be suspended or cancelled along with the notice related to reason to suspension but the product license may not be suspended if the licensee provides the reason for intended suspension within 90 days on which the date the notice is issued and the suspension becomes effective. If the licensee is responded within the time limit then the license is not suspended to the level of intended suspension does not exist or has been corrected and if the minister has valuable reasons which effect purchaser's or consumer's health which leads to no opportunity for licensee to explain related to issue **[9]**.

Site Information

Prior to beginning the sale of the NHP, the licensee must submit the following information to the minister: the person's name, address, and telephone number, as well as, if applicable, the person's facsimile number and electronic mail address, and, if the person conducts the activity in Canada, the number allocated to the site license obtained in respect of that activity; the address of every building in which the NHP is manufactured, packaged, labeled, and stored for importation or distribution. Evidence establishing that the NHP will be manufactured, packaged, labeled, imported, distributed, and stored in accordance with the requirements, if the NHP is imported. If the NHP is one for which a drug identification number has been allocated in compliance with the Food and Drug Regulations and it is already being marketed at the time the product license is issued, the licensee shall provide the information within 30 days along with the day the product license is issued **[9]**.

Reaction and Recall Reporting

A licensee shall submit to the Minister a case report for each severe excepted or unexpected adverse reaction to an NHP that occurs inside or outside of Canada within 15 days of becoming knowing of the reaction. A licensee who sells an NHP shall prepare and maintain an annual summary report that includes a compendious and critical analysis of all adverse reactions to the NHP that have occurred within Canada. All occurrences for which a case report is required within the last 12 months at a dose used or tested for disease diagnosis, treatment, or prevention, or for changing organic functions in humans. If, after reviewing a case report provided or any other safety data relating to the NHP, the Minister has reasonable causes to believe that the NHP may no longer be safe when used under the recommended conditions of use, the

Minister may request that, within 30 days after the day on which the request is received, the licensee provide a summary report prepared and an interim summary report providing a concise and comprehensible description of the NHP. Every licensee who commences a recall of a NHP shall provide the Minister with the information within three days of the recall's inception **[9]**.

CONCLUSION

Probiotics have received increasing attention in the scientific, medical and public sectors in recent years. NHPs are used and marketed for a variety of health reasons, including illness or condition prevention or treatment, risk reduction, and health maintenance. Probiotics and prebiotics, as well as many other related therapies, have benefited from the availability of research on microbiome-targeted nutrition and medicines. The world of probiotics is constantly expanding, not only because of the growing number of people who use probiotics, but also because of the widespread range of probiotic products and novel probiotic strains. By encouraging adherence to a strict scientific definition of probiotics, it is hoped that the underlying principles will assert greater certainty and foster a better understanding within this rapidly evolving field.

Acknowledgements

None

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