Regulations Amending the Food and Drug Regulations (743 — Non-Medicinal Ingredients)

Statutory authority

Food and Drugs Act

Sponsoring department

Department of Health

REGULATORY IMPACT ANALYSIS STATEMENT

(This statement is not part of the Regulations.)

Executive summary

**Issue:** It is currently not a legal requirement for drug manufacturers to list non-medicinal ingredients (NMIs) on the labels of drugs sold in Canada. Certain NMIs present in drugs can cause adverse reactions in individuals with sensitivities or allergies. In a non-prescription environment in which consumers can self-select a drug product without the counsel of a practitioner, it is difficult for them to avoid consuming certain NMIs. In the case of most prescription drug products, a practitioner or pharmacist can counsel patients. This regulatory amendment proposes to require, with some exceptions, the labelling of NMIs on the labels of non-prescription drugs for human use.

The Natural Health Products Regulations and the Cosmetic Regulations have required the mandatory listing of all NMIs since January 2004 and November 2006 respectively. This has created a difference in regulatory requirements in Canada, especially in light of the knowledge that drug NMIs can pose a health risk.

**Description:** Health Canada has determined that the best approach for providing NMI information for drugs is mandatory NMI labelling on the drug’s outer label. Project 743 is a proposed regulatory amendment requiring NMIs to be listed on the outer labels of non-prescription drugs for human use. Project 743 does not apply to prescription drugs, nonprescription drugs only administered under the supervision of a practitioner, low-level disinfectant or veterinary-use drugs. (see footnote 1)

**Cost-benefit statement:** While any costs associated with these regulations would be largely borne by the pharmaceutical industry, these are anticipated to be minimal. Furthermore, costs would be reduced by deferring the implementation of the regulatory amendments to two years after publication in the Canada Gazette, Part II. This transition period would allow the depletion of existing label supplies and allow packaging companies to introduce the changes within a normal label life cycle, hence reducing costs. Many pharmaceutical companies are already in voluntary compliance with this proposal and hence would have minimal additional cost.

This regulatory proposal may result in a positive impact on consumer health and safety as consumers will be provided with ready access to meaningful information concerning the NMI content of non-prescription drugs.

**Business and consumer impacts:** This regulatory proposal would have minimal impact on businesses, both financial and non-financial. This regulatory proposal would...
Certain non-medicinal ingredients (NMIs) present in nonprescription drugs can cause adverse reactions in individuals with sensitivities or allergies and consequently, individuals may wish to avoid consuming certain NMIs for this and other reasons of personal preference. This regulatory amendment proposes to require the labelling of NMIs on the labels of non-prescription drugs for human use (with some exceptions). This may result in a positive impact on consumer health and safety, by allowing individuals to avoid life-threatening allergens and agents for which they have a history of adverse reactions. Furthermore, this enables consumers to make informed choices when purchasing nonprescription medications. While some manufacturers voluntarily list NMIs on the outer labels of non-prescription drugs, not all do so, and currently, it is not a legal requirement. This proposal is similar to mandatory NMI labelling requirements already existing in the United States, Europe and Australia. In Canada, the Natural Health Products Regulations and the Cosmetic Regulations have required the mandatory listing of all NMIs since January 2004 and November 2006 respectively. This has created a difference in regulatory requirements in Canada, especially in light of the knowledge that drug NMIs can pose a health risk.

Health Canada proposes to amend the Food and Drug Regulations (Regulations) to require that all NMIs be listed on the outer labels of drugs for human use. The proposed amendment does not apply to

(i) prescription drugs;

(ii) non-prescription drugs that are only administered under the supervision of a practitioner;

(iii) drugs that are represented as being solely for use as disinfectants on hard non-porous surfaces; nor

(iv) drugs for veterinary use.

Objectives

This proposed regulatory amendment to require the listing of NMIs on the outer labels of non-prescription drugs for human use will assist individuals in avoiding life-threatening allergens and agents for which they have a history of adverse reactions.

This amendment may result in a positive impact on consumer health and safety which in turn may allow for a reduction in the costs to health care systems as a result of reduced adverse drug reaction incidents.

Increased consumer awareness may cause manufacturers to amend product formulations to remove ingredients known to be sensitizers, or ingredients which are otherwise unacceptable.

Description

Three NMI labelling proposals were previously published in the Canada Gazette, Part I, on December 2, 1989, February 5, 1994, and May 22, 1999. Extensive comments were received during the three consultation periods. Overall, stakeholders were in agreement with the principle behind the proposals, but were not in agreement with all the proposals’ details. The following identifies the issues that were raised in previous proposals.

(1) Which drugs?
The current proposal is less prescriptive than the previous three. Its scope is non-prescription drugs for human use. The exemptions are (1) prescription drugs, (2) non-prescription drugs only administered under the supervision of a practitioner, (3) low-level disinfectants, and (4) veterinary drugs.

(2) Which NMIs?

As in the past three proposals, the current proposal mandates that all NMIs be labelled except for the sub-ingredients of flavours and fragrances. In addition, the current proposal excludes pharmaceutical inks from the requirement to list sub-ingredients.

(3) Which labels?

The current proposal is the same as that of the third: NMIs are required to be listed on the outer label.

(4) What names?

The current proposal is less prescriptive than the previous three: the type of NMI names is not specified, thereby allowing the use of proper, common or international nomenclature.

(5) What order?

The current proposal is less prescriptive than the previous three: NMIs are required to be listed in alphabetical order or in descending order of drug proportion.

(6) Drug formulation

The current proposal is less prescriptive than the previous three in that it only focuses on NMI labelling. A staged approach is being taken where a formulation requirement is underway as a separate initiative.

(7) Other technical details

Other technical details were mandated in past proposals, such as how NMIs were to be distinguished on the label from medicinal ingredients and how variations in NMIs among drug lots were to be indicated. The current proposal is not so prescriptive in these areas. All technical details are described below.

The proposed changes to the *Food and Drug Regulations* are as follows:

1. Amend C.01.001(1): Define four terms.

   “flavour” means a non-medicinal ingredient or combination of non-medicinal ingredients added to a drug solely to produce or mask a particular taste. It does not include an ingredient or combination of ingredients that impart only a sweet taste to the drug; *(saveur)*

   “fragrance” means a non-medicinal ingredient or combination of non-medicinal ingredients added to a drug to produce or mask a particular odour; *(parfum)*

   “non-medicinal ingredient” means a substance — other than the pharmacologically active drug — that is added during the manufacturing process and that is present in the finished drug product; *(ingrédient non médical)*

   “pharmaceutical ink” means a non-medicinal ingredient or combination of non-medicinal ingredients used to imprint the drug with marks or symbols; *(encre pharmaceutique)*

2. Amend C.01.004(1):

   2.1. Mandate the following rules regarding NMI labelling:
— list all NMIs on the outer label of the drug; and

— where the outer label is too small, clearly and prominently affix NMI labelling to the product so that it is readily discernible to the purchaser or consumer under the customary conditions of purchase and use.

2.2. Exempt the following from NMI labelling:

— prescription drugs;

— non-prescription drugs only administered under the supervision of a practitioner;

— low-level disinfectants; and

— drugs for veterinary use.

2.3. Mandate the following rules regarding NMI labelling details:

— list NMIs in alphabetical order or in descending order of drug proportion;

— precede NMIs with clear wording that distinguishes them from medicinal ingredients;

— list flavours, fragrances, and pharmaceutical inks, but not their sub-ingredients; and

— use the terms “may contain,” “+/−” or “or” to indicate that lot composition of NMIs varies from one to the other.

3. Amend C.01.004(2): Update to ensure congruence of the numbering of amended subsections in C.01.004(1).

4. Mandate an implementation date of two years following publication of the proposed regulatory amendment in the Canada Gazette, Part II.

**Regulatory and non-regulatory options considered**

Option No. 1: Status quo

The status quo would be that NMIs are not required to be listed on drug labels.

Option No. 1 was rejected because consumers with sensitivities and allergies are not provided with information to pre-empt adverse events caused by NMIs, nor are consumers able to exercise personal preference with respect to certain NMIs. Furthermore, other lower risk regulated product categories covered under the Food and Drugs Act (Act), such as cosmetics, natural health products (NHPs), and foods, have their own NMI labelling requirements and their own food ingredient labelling requirements, respectively. Finally, international regulators such as the United States Food and Drug Administration, the European Medicines Agency, and Australia’s Therapeutic Goods Administration also mandate some degree of NMI labelling for drugs; Canada does not.

Option No. 2: Voluntary labelling

In 1985, voluntary guidelines for the disclosure of selected NMIs were adopted by the Nonprescription Drug Manufacturers Association of Canada (NDMAC). This information was to be made available on the labels of non-prescription drug products.

Since that time, there has been increased voluntary labelling of NMIs on drugs. However, Option No. 2 was rejected because the labelling has been inconsistent in application and selective in disclosure, and thus has not proven to fulfill the information needs of the consumer.

Option No. 3: Partial labelling
Partial labelling is NMI listing of only those ingredients known to cause reactions.

Option No. 3 was rejected because not all potential sensitizing agents are known. The 1994 Regulatory Impact Analysis Statement (RIAS) stated that “[d]etermining and communicating a list of sensitizers to manufacturers for subsequent disclosure would be an unwieldy, time-consuming process, unresponsive to consumers’ needs”. Furthermore, the 1999 proposal stated that “[p]artial label disclosure of only those ingredients known to cause reactions has not been proven to be a reasonable alternative. Not all potential sensitizing agents are identified. Full label disclosure will eliminate the difficulties associated with the identification of ingredients which are suspected or most likely to be the cause of adverse effects, or those which individual consumers may wish to avoid.”

Option No. 4: NMI information disclosure from sources other than a label

Strategies that are designed to provide NMI information to consumers from a source other than a label have been considered. Though considered appropriate for drugs that require the intervention of a practitioner, Option No. 4 was rejected for nonprescription drugs directly accessible to consumers because Option No. 4 does not provide information disclosure to consumers at time of purchase. “All of these could be valuable supplemental methods of making available non-medicinal ingredient information . . . this does not negate the need for ready access to the information by the consumer at the point and time of purchase.” Furthermore, any decision that requires that NMI information be made available through sources other than labelling would not take advantage of the voluntary labelling activity that is presently occurring.

Option No. 5: The current NMI labelling proposal, elaborated above

The current NMI labelling proposal, Option No. 5, is the recommendation. The current proposal addresses comments received in past consultations with stakeholders, specifically much of the technical detail that was the source of stakeholder concern. The recommended option is built on the premise that a performance standard of full NMI labelling take priority over the prescriptive standards in the technical details.

Benefits and costs

The amendment would impact on the following sectors:

Public

Consumers will be provided with ready access to meaningful information concerning the NMI content of non-prescription drugs. The listing of NMI content will allow consumers to make an informed choice when purchasing non-prescription drugs. Furthermore, it is anticipated that mandatory NMI labelling should lead to fewer repeat adverse reactions. By allowing individuals to avoid life-threatening allergens and agents for which they have a history of adverse reactions, this amendment may result in a positive impact on consumer health and safety.

Industry

While any costs associated with these regulations would be largely borne by the pharmaceutical industry, these are anticipated to be minimal. Furthermore, costs would be reduced by deferring the implementation of the regulatory amendments to two years after publication in the Canada Gazette, Part II. This transition period would allow the depletion of existing label supplies and allow packaging companies to introduce the changes within a normal label life cycle, hence reducing cost. Many pharmaceutical companies are already in voluntary compliance with this proposal and hence would have minimal additional cost.

Increased consumer awareness may cause manufacturers to amend product formulations to remove ingredients known to be sensitizers, or ingredients which are otherwise unacceptable. This would result in increased availability of products which are less likely to cause undesirable side effects.

Provincial health care systems
There are no expected costs for the provincial health care systems. However, there may be a reduction in the costs to health care systems as a result of reduced adverse drug reaction incidents, meaning there may be a decrease in practitioner visits due to a decrease in adverse reactions.

Federal Government

There would be minimal increases in Government costs to ensure compliance.

In sum, the benefits of the proposed amendment outweigh and justify the costs. There is general support for NMI labelling in the industry, and the recommended option builds upon the progress made by the previous three regulatory proposals described below.

Rationale

The current NMI labelling proposal is less prescriptive than previous ones with respect to the manner of compliance. An NMI labelling strategy does not require the rigid and prescribed manners of labelling that were proposed in 1989, 1994, and 1999, none of which built upon industry’s 1985 voluntary labelling guidelines and all of which ruled out many reasonable alternatives. The current proposal amends much of the technical detail that was the source of stakeholder concern while ensuring that NMI information is made available to consumers.

(1) Prescription drugs

NMIIs listed on the manufacturers’ labels of prescription drugs generally do not reach the consumer, because prescription drugs are routinely repackaged and relabelled for the individual patient by the pharmacist. The responsibility for the selection of the medication most often lies with the individual who writes the prescription. This individual is a practitioner who is familiar with the health status of the consumer in question, and is well-positioned to contextualize risk involved (including risks relating to allergens and sensitizers) in prescribing a specific treatment to a patient. Finally, NMI information for prescription drugs is typically available by means of the product monograph and the Compendium of Pharmaceuticals and Specialties. A product monograph is a factual, scientific document about a drug that (a) describes the drug’s properties, claims, indications, and conditions of use, and (b) contains any other information that may be required for optimal, safe, and effective use of the drug; the product monograph is devoid of promotional material. “Part I: Health Professional Information” of the product monograph requires an alphabetical listing by proper or common name of all NMIIs for each strength of each dosage form of the drug. Access to information is being facilitated through Health Canada–authorized product monographs which are now starting to be posted on Health Canada’s Web site. Therefore, prescription drugs are exempt from Project 743.

(2) Non-prescription drugs only administered under the supervision of a health care practitioner

NMIIs listed on the manufacturers’ labels of non-prescription drugs only administered under the supervision of a practitioner would not reach the intended recipient, the patient, because these drugs are administered to the patient in non-self-care settings such as hospitals. The practitioners who administer these drugs are well-positioned to contextualize the risk involved. Furthermore, NMI information for non-prescription drugs only administered under the supervision of a health care practitioner is typically available to practitioners through the product monographs and through the Compendium of Pharmaceuticals and Specialties. Consequently, these drugs are exempt from Project 743.

(3) Low-level disinfectants

Low-level disinfectants are disinfectants that kill pathogenic and potentially pathogenic microorganisms on hard non-porous inanimate surfaces. The issue of labelling for these products will be examined and addressed under a separate policy initiative, and therefore, these drugs are exempt from Project 743.

(4) Veterinary-use drugs

The scope of this proposal is human-use drugs, the decrease in the potential for adverse reactions in humans, and personal choice in self-care. Veterinary-use drugs are outside of this scope;
Consultation

NMI labelling has been the subject of extensive informal discussions and formal consultations with interested parties:

— January 15, 1988: Information Letter No. 733 was published and distributed to all drug manufacturers, health professional associations, and public advocacy groups;

— July 14, 1988: Recommendations were tabled in the fourth report to the House of Commons by the Standing Committee on National Health and Welfare;

— December 2, 1989: The first prepublication of the proposed regulatory amendment in Canada Gazette, Part I. This proposal applied to both prescription and non-prescription drugs for human use and parenteral veterinary use, and mandated that the name and quantity of each NMI in a drug be submitted to and reviewed by Health Canada. Furthermore, it required NMIs to be listed by proper name, in descending order of quantity, on both inner and outer labels. Sub-ingredient listing was not required for flavours and fragrances;

— September 28, 1990: A meeting with representatives of the pharmaceutical industry, consumer organizations, and health professional organizations to present a revised regulatory proposal and to solicit comments;

— Extensive correspondence with all stakeholders, including pharmaceutical manufacturing organizations, individual pharmaceutical manufacturers, pharmaceutical licensing bodies, individual pharmacists, organizations of the profession of pharmacy, provincial ministries of health, consumer advocacy groups, organizations of the profession of medicine, and individual practitioners about the status of and revisions to the NMI initiative;

— September 1992: Questions included in a survey of practitioners and pharmacists conducted for the Health Protection Branch (HPB) to determine the usefulness of NMI information in their practices;

— February 5, 1994: The second prepublication of the proposed regulatory amendment in the Canada Gazette, Part I. This revised proposal addressed many of the concerns raised from the 1989 Canada Gazette, Part I prepublication. It differed from the first proposal in that it required NMIs to be listed in alphabetical order by proper name or common name, on the inner or outer label of prescription drugs, and on the outer label of non-prescription drugs;

— May 22, 1999: The third prepublication of the proposed regulatory amendment in the Canada Gazette, Part I. This revised proposal addressed many of the concerns raised from the 1994 Canada Gazette, Part I prepublication. The third proposal differed from the second proposal in that it applied exclusively to non-prescription drugs for human use. Its exemptions were (1) prescription drugs; (2) non-prescription drugs not for self-care, provided that all NMIs by proper or common names were available from the distributor upon request; (3) disinfectants on inanimate surfaces for the prevention of disease on premises in which food is manufactured, prepared or kept; and (4) veterinary drugs. Furthermore, it permitted NMIs to be listed in alphabetical order by proper names or common names, or in descending order of their proportion in the drug. Finally, the third proposal required NMIs to be listed solely on the outer label;

— Various meetings and discussions with industry associations and representatives;

— August 14, 2006: A letter to stakeholders was sent and posted on the Health Canada Web site. The letter outlined the approach to the fourth NMI regulatory proposal and provided a 60-day comment period. The comments received were considered in drafting the current proposal.

As a result of these consultations, the regulatory proposal has received support from the medical profession, consumer groups and health organizations. The pharmaceutical manufacturing sector has agreed with the general principle of full mandatory disclosure of NMIs.
Implementation, enforcement and service standards

This amendment does not alter existing compliance mechanisms under the provisions of the Food and Drugs Act and the Food and Drug Regulations enforced by the Health Products and Food Branch Inspectorate (HPFBI).

Implementation of the regulatory amendments will be deferred to two years after publication in the Canada Gazette, Part II. This transition period would allow the depletion of existing label supplies and allow packaging companies to introduce the changes within a normal label life cycle, hence reducing cost. Many pharmaceutical companies are already in voluntary compliance with this proposal and hence would have minimal additional cost.

Performance measurement and evaluation

Not applicable.

Contact

Refer to Project No. 743
Bureau of Policy, Science and International Programs
Therapeutic Products Directorate
Health Canada
Holland Cross, Tower B, 2nd Floor
1600 Scott Street
Address Locator: 3102C5
Ottawa, Ontario
K1A 0K9
Telephone: 613-948-4623
Fax: 613-941-6458
Email: regaff-affreg@hc-sc.gc.ca

PROPOSED REGULATORY TEXT

Notice is hereby given that the Governor in Council, pursuant to subsection 30(1) (see footnote a) of the Food and Drugs Act (see footnote b), proposes to make the annexed Regulations Amending the Food and Drug Regulations (743 — Non-Medicinal Ingredients).

Interested persons may make representations concerning the proposed Regulations within 75 days after the date of publication of this notice. All such representations must cite the Canada Gazette, Part I, and the date of publication of this notice, and be addressed to Policy Division, Bureau of Policy, Science and International Programs, Therapeutic Products Directorate, Department of Health, 1600 Scott Street, Holland Cross, Tower B, 2nd Floor, Address Locator: 3102C5, Ottawa, Ontario K1A 0K9 (fax: 613-941-6458; e-mail: regaff-affreg@hc-sc.gc.ca).

Ottawa, May 28, 2009

PAUL SHUTTLE
Assistant Clerk of the Privy Council

REGULATIONS AMENDING THE FOOD AND DRUG REGULATIONS (743 — NON-MEDICINAL INGREDIENTS)

AMENDMENTS

1. Subsection C.01.001(1) of the Food and Drug Regulations (see footnote 2) is amended by adding the following in alphabetical order:

   “flavour” means a non-medicinal ingredient or combination of non-medicinal ingredients added to a drug solely to produce or mask a particular taste. It does not include an ingredient or combination of ingredients that impart only a sweet taste to the drug; (saveur)
“fragrance” means a non-medicinal ingredient or combination of non-medicinal ingredients added to a drug to produce or mask a particular odour; (parfum)

“non-medicinal ingredient” means a substance — other than the pharmacologically active drug — that is added during the manufacturing process and that is present in the finished drug product; (ingrédient non médical)

“pharmaceutical ink” means a non-medicinal ingredient or combination of non-medicinal ingredients used to imprint the drug with marks or symbols; (encre pharmaceutique)

2. (1) Section C.01.004 of the Regulations is amended by adding the following after subsection (1):

(1.1) In addition to the requirements of subsection (1), when a drug is intended for human use, its outer label must contain a list of all non-medicinal ingredients, or, if the outer label is too small, the list must appear on a tag, tape or card that is attached to the package.

(1.2) The non-medicinal ingredients must be listed in alphabetical order or in descending order of predominance by their proportion in the drug, preceded by words that clearly distinguish them from the medicinal ingredients.

(1.3) In the case of flavour, fragrance or pharmaceutical ink, the expressions “flavour/saveur”, “fragrance/parfum” and “pharmaceutical ink/encre pharmaceutique”, respectively, may be included in the list to indicate that such ingredients have been added to the drug, instead of listing those ingredients or combinations of them individually.

(1.4) When the composition of the drug varies from one lot to another, the outer label must include a reference to all non-medicinal ingredient alternatives that may be present in the drug, preceded by the symbol “+/−” or “±” or the expression “or/ou” or “may contain/peut contenir”.

(1.5) Subsections (1.1) to (1.4) do not apply to

(a) a drug that is required to be sold pursuant to a prescription;

(b) a drug that is not required to be sold pursuant to a prescription but is administered only under the supervision of a practitioner;

(c) a drug that is represented as being solely for use as a disinfectant on hard non-porous surfaces; or

(d) a drug for veterinary use.

(2) The portion of subsection C.01.004(2) of the Regulations before paragraph (a) is replaced by the following:

(2) In addition to the requirements of subsection (1) and, if applicable, subsections (1.1) to (1.4), the outer label of a drug must show all of the following information:

COMING INTO FORCE

3. These Regulations come into force two years after the day on which they are registered.

Footnote 1

For details on the reasoning behind the proposed exemptions for these products, please see the “Rationale” section of the Regulatory Impact Analysis Statement (RIAS).

Footnote a

S.C. 1999, c. 33, s. 347


6/26/2009