Contact
Regulatory Affairs

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Provincial and Territorial Deputy Ministers of Health
Provincial and Territorial Drug Program Managers
Deans of Pharmacy
Registrars of Provincial Medical and Pharmacy Associations
Industry Associations
Consumer Associations
Regulatory Associations
Health Professional Associations
Other Interested Parties

Dear Madam/Sir:

Re: Amendment to the *Food and Drug Regulations*, Project No. 743, Non-medicinal Ingredients

This provides you with an opportunity to comment on the

- Regulatory Requirements for Advertising
- Special Access to Drugs & Health Products
- Substances: Problematic Use
- Veterinary Drugs
- Legislation & Guidelines
- Reports & Publications

- **Emergencies & asters**
- **Environmental & rkplace Health**
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- **Government alth Partners**
- **Need ger xt?**

Therapeutic Products Directorate's (TPD) proposal to amend the *Food and Drug Regulations* (Regulations) to require that non-medicinal ingredients (NMIs) be listed on the outer labels of nonprescription drugs for human use. This requirement would enable the consumer to avoid ingredients to which they are sensitive or allergic, and would permit the consumer to exercise personal preferences with respect to specific ingredients. When NMI labelling information is available at the point of purchase of nonprescription drugs, the consumer is more able to make informed choices with respect to their health.

Strategy

Health Canada is implementing a broad strategy to make NMI information available to consumers and to health care practitioners. The strategy is tailored to specific types of drugs: prescription drugs, nonprescription drugs only administered under the supervision of a health care practitioner, and nonprescription drugs.

Drugs that require the intervention of a health care practitioner

NMI information for drugs that require the intervention of a health care practitioner, those being *prescription drugs* and *nonprescription drugs only administered under the supervision of a health care practitioner*, is typically available to health care practitioners through the *Compendium of Pharmaceuticals and Specialties* (CPS) and through Product Monographs (PMs).

A PM 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 PM is devoid of promotional material. "Part I: Health Professional Information" of the PM requires an alphabetical listing by proper or common name of all NMIs for each strength of each dosage form of the drug (see point 3.12 of http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/monograph/pm_mp_e.html). "Part III: Consumer Information" of the PM, also used in patient package inserts (PPIs), refers to NMI information in Part I of the PM. Access to information will be facilitated through Health Canada-authorized PMs once publically available. For more information on the public availability

of PMs, refer to http://hc-sc.gc.ca/dhp-mps/prodpharma/activit/proj/monograph-rev/pm_notice_mp_avis_trans_e.html.

Therefore, the NMI information strategy for drugs that require the intervention of a health care practitioner is the CPS and PMs.

Drugs directly accessible to the consumer

NMI information for *nonprescription drugs directly accessible to consumers* will be increasingly available to the consumer on outer labels of nonprescription drugs. Currently, many manufacturers already voluntarily label NMIs on these drugs.

The NMI information strategy for drugs directly accessible to the consumer is mandatory NMI labelling on the drug's outer label, or Project 743.

Project 743

Project 743 is a proposed regulatory amendment requiring NMIs to be listed on the outer labels of nonprescription drugs for human use. Project 743 does not apply to prescription drugs, nonprescription drugs only administered under the supervision of a health care practitioner, low-level disinfectant drugs, nor veterinary-use drugs.

1) Prescription drugs

NMIs on the manufacturers' labels of *prescription drugs* would not reach the intended recipient, the consumer, because prescription drugs are routinely repackaged and relabelled for the individual patient by the pharmacist. Therefore, prescription drugs are exempt from Project 743.

2) Nonprescription drugs only administered under the supervision of a health care practitioner

NMIs on the manufacturers' labels of *nonprescription drugs only administered under the supervision of a health care 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. These drugs are therefore exempt from Project 743.

3) Low-level disinfectant drugs

Low-level disinfectant drugs are disinfectants that kill pathogenic and potentially pathogenic microorganisms on hard non-porous inanimate surfaces. Low-level disinfectant drugs are lower risk products than drugs which are used in or on the body, therefore they 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, therefore they are exempt from Project 743.

Comparison of NMI labelling proposals

Three NMI labelling proposals were previously prepublished in *Canada Gazette*, Part I (CG I). They were prepublished on December 2, 1989, February 5, 1994, and May 22, 1999; they can be accessed via the *Canada Gazette* website at http://canadagazette.gc.ca/index-e.html. 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' technical details.

1) Which drugs?

The scope of the first and second proposals was prescription and nonprescription drugs for human use and parenteral veterinary use. The scope of the third proposal was nonprescription drugs for human use. Its exemptions were (1) prescription drugs; (2) nonprescription 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.

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

2) Which NMIs?

The three past proposals mandated that all NMIs be labelled, except for the sub-ingredients of flavours and fragrances.

The current proposal does the same.

3) Which labels?

The first proposal required NMIs to be listed on the inner and outer labels. The second proposal required NMIs to be listed on the inner or outer label of prescription drugs, and to be listed on the outer label of nonprescription drugs. The third proposal required NMIs to be listed on the outer label.

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 first proposal required NMIs to be listed by proper name or, if none, by common name. The second and third proposals required NMIs to be listed by proper names or common 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 first proposal required NMIs to be listed in descending order of quantity of NMIs in the drug. The second proposal required NMIs to be listed in alphabetical order by proper names or common names. The third proposal required NMIs to be listed in alphabetical order

by proper names or common names, or in descending order of their proportion in the drug.

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

All three past proposals mandated that the name and quantity of each NMI in a drug be submitted to and reviewed by Health Canada.

The current proposal is less prescriptive than the previous three in that it only focusses on NMI labelling. A staged approach is being taken where an NMI 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, how variations in NMIs among drug lots were to be indicated, and when the proposed regulation would come into force. These types of technical details are found in the original 1989, 1994, and 1999 CG I prepublications at http://canadagazette.gc.ca/index-e.html.

The current proposal also mandates other technical details; they are described below.

Current NMI labelling proposal

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 manner of labelling that was proposed in 1989, 1994, and 1999, which did not build upon voluntary labelling already in existence and which ruled out many reasonable alternatives. In the current proposal, NMI information is made available to consumers, plus much of the technical detail that was the source of stakeholder concern has

been amended.

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

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

- "flavour" means any non-medicinal ingredient or combination of non-medicinal ingredients in a drug used solely to impart a taste to the drug, but does not include an ingredient or combination of ingredients that imparts only a sweet taste to the drug; *(saveur)*
- "fragrance" means any non-medicinal ingredient or combination of non-medicinal ingredients in a drug used solely to impart a smell to the drug; *(parfum)*
- "non-medicinal ingredient" means any substance in a drug that does not contribute to the drug's pharmacological activity, but is used in the manufacture of a drug and present in the dosage form in which the drug is to be sold; *(ingrédient non médicinal)*

2. Amend C.01.004:

2.1 Mandate the following rules regarding NMI labelling.

- list all NMIs on the outer label of the drug
- if 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
- nonprescription drugs only administered under the supervision of a health care practitioner
- low-level disinfectant drugs
- 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 which distinguishes them from medicinal ingredients
- list specific flavours and fragrances, but not their sub-ingredients (i.e. the general term “flavouring agent” is not acceptable, but the term “grape flavour” is)
- 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): Mandate that NMIs be listed on the outer labels of drugs.

4. Mandate an implementation date of two years following publication of the proposed regulatory amendment in CG II.

Options Considered

Option #1: Status quo

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

Option #1 was rejected because consumers with sensitivities and allergies are not provided with information to preempt adverse events caused by NMIs, nor are consumers able to exercise personal preference with respect to certain NMIs. Furthermore, other lower risk product categories covered under the *Food and Drugs Act*, such as cosmetics, natural health products (NHPs), and foods, have their own NMI labelling requirements and their own food ingredient labelling requirements, respectively; drugs do not. Finally, international regulators such as the US, the EU, and Australia also mandate some degree of NMI labelling for drugs; Canada does not.

Option #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 nonprescription drugs.

Since the publication of Information Letter (IL) No. 733 and the three previous CG I prepublications, there has been increased voluntary labelling of NMIs on drugs. However, Option #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 #3: Partial labelling

Partial labelling is the NMI listing of only those ingredients known to cause reactions.

Option #3 was rejected because not all potential sensitizing agents are known. Objections to a partial listing strategy are found in past proposals. 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” (CG I, February 5 1994, p863). 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” (CG I, May 22 1999, pp1527-1528).

Option #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 health care practitioner, Option #4 was rejected for nonprescription drugs directly accessible to consumers because Option #4 does not provide information disclosure to consumers at time of purchase. “All of these could be valuable supplemental methods of making available nonmedicinal ingredient information ... this does not negate the need for ready access to the information by the consumer at the point and time of purchase” (CG I,

December 2 1989, p5221). 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 #5: The current NMI labelling proposal, elaborated above

The current NMI labelling proposal, Option #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.

Benefits and Costs

The amendment would impact on the following sectors:

Public

Consumers would be provided with ready access to NMI information, which would allow consumers to make an informed choice when purchasing nonprescription drugs. Furthermore, it is anticipated that mandatory NMI labelling may lead to fewer repeat adverse reactions.

Industry

The major costs associated with these regulations would be incurred by the pharmaceutical industry. However, the cost would be minimized by deferring the implementation of the regulatory amendments to two years after publication in CG 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 not have any 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 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 physician visits due to a decrease in adverse reactions.

Federal government

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

Compliance and Enforcement

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

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 CG I;
- **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 physicians about the status of and revisions to the NMI initiative;

- **September 1992:** Questions included in a survey of physicians 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 CG I. This revised proposal addressed many of the concerns raised from the 1989 CG I prepublication;

- **May 22, 1999:** The third prepublication of the proposed regulatory amendment in CG I. This revised proposal addressed many of the concerns raised from the 1994 CG I prepublication;

- Various meetings and discussions with industry associations and representatives.

This letter is being sent by email to stakeholders, and is also being posted on the Health Canada website at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/legislation/acts-lois/notice-avis/index_e.html and the Consulting With Canadians website at http://www.consultingcanadians.gc.ca/cpcPubDepartments.jsp?DeptID=73&lang=en&Type=current.

Any comments regarding this proposed amendment should be addressed as follows within **60** days following the date of posting of this letter on the Health Canada website.

Project No. 743
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Yours sincerely,

Original signed by

Omer Boudreau
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Important Notices