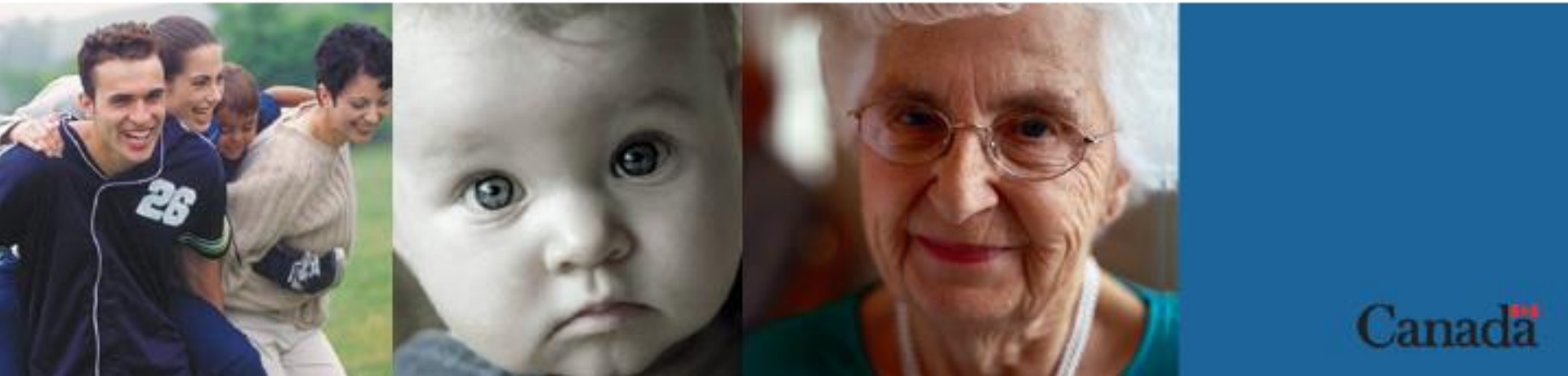
Health Canada Santé Canada

Helping the people of Canada maintain and improve their health

Aider les Canadiens et les Canadiennes à maintenir et à améliorer leur état de santé

Prescription Drug List Switch Guidance Document

February 20, 2014
Kyra Paterson, Natural Health Products Directorate, Health Canada



Presentation Overview

- Background – Prescription Drug List
- Policy Statement/Scope of Guidance Document
- Overview of Drug Scheduling
- How to Submit a Switch Submission
- Data Requirements for Switches – Overview
- Developing Non-prescription Rationale
- Minimum Data Requirements – Safety
- Additional Data Requirements – Safety
- Minimum Data Requirements – Efficacy
- Labelling
- Consumer Use Studies
- Relevant Links

Background – Prescription Drug List

- As part of the *Jobs, Growth and Long-term Prosperity Act* (Bill C-38), which received Royal Assent on June 29, 2012, the Government amended the *Food and Drugs Act* to give the Minister of Health the power to establish a list that sets out prescription drugs.
- Amendments to the *Food and Drug Regulations* (FDR) were made in June 2013 to remove Schedule F.
- The amendments created the Prescription Drug List (PDL), a web-based administrative list that is not set out in regulation.
  - The PDL came into effect December 2013.
- Additions to, and removals from, the PDL follow an administrative process, rather than the regulatory process required with the former Schedule F.
- Changes to the PDL will take much less time than changes to Schedule F.

Background – Prescription Drug List (2)

- The PDL is divided into two:
  - a list of medicinal ingredients that, when found in a drug, require a prescription for **human** use; and
  - a list of medicinal ingredients that, when found in a drug, require a prescription for **veterinar**y use.
- Drugs that were listed on Schedule F were transferred to the PDL.
- The PDL is accessible via the Health Canada website.

Background – Prescription Drug List (3)

- Health Canada looks at 3 broad principles and their associated factors when determining whether a medicinal ingredient should be sold on prescription.
- In contrast to the former Schedule F factors which were listed in policy, the 3 broad principles are set out in the FDR.
- These principles encompass the Schedule F factors that HC has considered in making decisions about prescription status for over 20 years.
- **The science has not changed** – only the process to add/remove medicinal ingredients from the PDL has changed.
- An explanatory guidance document has been developed to make the decision-making process more transparent.
- Only a “practitioner” as defined by the FDR can prescribe ingredients on the PDL.

Switch Guidance Document

- The “Data Requirements for Switching Medicinal Ingredients from Prescription to Non-prescription Status” guidance document provides information to help sponsors determine the evidence to submit to Health Canada in order to apply to switch a medicinal ingredient from prescription to non-prescription status.
- This guidance document is commonly referred to as the “Switch Guidance Document”.
- The process to add/remove ingredients from the PDL is outlined in the PDL Q’s and A’s on the Health Canada website.

Policy Statement

- The evidence that can be provided to support the safety and efficacy of a medicinal ingredient in a non-prescription product, when previously it was required to be sold on prescription, varies depending on:
  - whether the conditions of use of the medicinal ingredient will change, and the degree to which they will change;
  - whether there is experience in other jurisdictions with the proposed product's conditions of use, and the extent of this experience;
  - the knowledge gathered thus far in the product's life-cycle when sold on prescription, and whether that knowledge alters the uncertainty associated with the benefits and harms.

Scope of Guidance Document

- Applies to medicinal ingredients (MI) for human use only.
- Does not apply to:
  - Switch submissions for biologic or radiopharmaceutical products
  - MIs that were deemed exceptions from prescription status – e.g., influenza vaccines (for public health reasons) and nitroglycerin (for emergency use).
- Applies to two types of switches:
  - Full switch: MI + all approved conditions of use previously listed on the PDL are removed from prescription status
  - Partial switch: certain conditions of use are removed from prescription status but the MI and other conditions of use remain on the PDL

Overview of Drug Scheduling

- MIs are given prescription status where control over the sale of the MI is deemed to best protect the health and safety of Canadians.
- Guiding principles governing prescription status are outlined in section C.01.040.3 of the *Food and Drug Regulations*, and are described in the guidance document "*Determining Prescription Status for Human and Veterinary Drugs* (2013)".
- An MI warrants prescription status when the MI, under the specified conditions of use, meets at least one of the PDL principles or factors.

Overview of Drug Scheduling

- Factors that are considered when deciding an MI's prescription status include whether the diagnosis, treatment and monitoring of a condition requires practitioner involvement.
  - Generally, non-prescription products are those that are believed to be safe for use by the public in a self-care environment.
- MIs requiring prescription status at the federal level are listed on the PDL, a web-based administrative list.
  - Qualifiers may be included such as strengths, uses, routes of administration or dosage forms.
- Provinces and territories can further restrict the place of sale of drugs
  - Typically based on recommendations made by the National Association of Pharmacy Regulatory Authorities (NAPRA).

How to Submit a Switch Submission

- When an MI has prescription status and a sponsor wants to sell that MI in a non-prescription product, a switch submission must be submitted to Health Canada.
- Switch submissions must include evidence demonstrating that the MI no longer meets any of the PDL principles and factors, can be used safely and is efficacious in a self-care environment.
- The switch of an MI from prescription to non-prescription status will result in the MI being acceptable for sale either as a non-prescription drug or natural health product.

How to Submit a Switch Submission

- If the MI meets the natural health product definition, *Natural Health Products Regulations* apply.
  - Submit product licence application.
- If the MI meets the drug definition, *Food and Drug Regulations* apply.
  - For full switch: submit Supplemental New Drug Submission.
  - For partial switch: submit New Drug Submission.

Drugs	Natural health products
Office of Submissions and Intellectual Property (OSIP) **Therapeutic Products Directorate** **Health Canada** **Finance Building 2** **Address Locator 0201A1** **101 Tunney's Pasture Driveway** **Ottawa, Ontario, K1A 0K9** **Telephone: 613-957-3123** **Fax: 613-941-0825**	Please send your submissions by courier service to the Submission Management Division Natural Health Products Directorate Health Canada Qualicum Building Tower A 2936 Baseline Rd. Ottawa, Ontario, K2H 1B3 Fax: (613) 954-2877

Data Requirements for Switches - Overview

The body of evidence for a switch submission must show that the:

- indication for use of the MI is amenable to **self-treatment** and **self-monitoring;**
  - No different than any other non-prescription product submission.
- benefits outweigh the risks;
  - No different than any other product submission.
- prescription MI can be used safety and effectively by the general public in the absence of a practitioner by showing that the product no longer meets any of the PDL principles and factors.

Data Requirements for Switches - Overview

- Consumer use studies such as label comprehension, self-selection, and actual use may be required for indications, directions of use, and/or warnings or contraindications that:
  - Have never before been marketed for sale in a self-care environment (in Canada or elsewhere);
  - Are considered complex for the self-care environment and therefore present a possible risk of misuse.
- In cases where conditions of use are complex or new to the self-care environment, if the associated risks can be adequately mitigated through cautionary labelling, then consumer use studies will not be required.
- Sponsors may choose to follow methodologies for consumer use studies suggested by other regulatory agencies.

Additional Requirements for Partial Switches

- Additional efficacy and safety evidence must be submitted when the modifications involve a new indication, target population, route of administration, or dose/dosage regime.
- Additional chemistry and manufacturing data will be required when there are changes made to the dose/dosage unit, formulation or dosage form.

Developing Non-prescription Rationale

- The characteristics of a non-prescription product outlined in the guidance document should be used to demonstrate that the PDL principles and factors no longer apply:
  - The use of the product is amenable to self-diagnosis.
  - The use of the product is amenable to self-treatment.
  - The use of the product is amenable to self-monitoring.
  - The use of the product is associated with an adequate margin of safety.
  - The consequences of misuse of the product are minor.
  - The use of the product does not lead to dependence.
  - The use of the product does not have potential for diversion, addiction or abuse leading to harmful nonmedical uses to either the individual or the public at large.
  - There is adequate market experience with the drug.
  - The use of the product does not present a significant risk to human, animal or public health.

Minimum Data Requirements - Safety

Full and Partial Switches:

- Product Monograph (Health Canada (HC) and published in Compendium of Pharmaceuticals and Specialities),
- Clinical trial adverse reactions not captured by above,
- Domestic post marketing surveillance information for prescription product,
- Periodic safety update reports submitted to HC, where available
- Regulatory status in specified countries
- Post marketing surveillance information outside of Canada as a prescription and/or non-prescription product

Minimum Data Requirements - Safety

Full and Partial Switches – additional safety evidence can include:

- Safety evaluations from a regulatory body with standards similar to those of Canada (e.g., United States, Australia, European Union), including any available safety information from the World Health Organization or other international health organization;
- Summary of reports from Poison Control Centres to provide information about accidental overdose or intended overdose and/or incorrect/misuse/abuse of the product;
- Published literature containing safety information.

Additional Safety Req's for Partial Switches

- Consumer use studies may be required, depending on the severity and likelihood of the risks:
  - The risk associated with the general public intentionally misusing the product with therapeutic intent based on knowledge of its prescription use; and
  - The risk of a consumer taking both the prescription and non-prescription products at the same time, particularly in vulnerable sub-populations such as children and the elderly.
- Up-to-date prescribing information in Canada will be required to fully understand these risks.
- In case where these risks can be adequately mitigated through cautionary labelling, consumer use studies will not be required.
- A scientific/clinical justification must be submitted in instances where these potential risks do not warrant consumer use studies or cautionary labelling.

Minimum Data Requirements - Efficacy

Full switches:

- Product Monograph
- Clinical trials (e.g., phase IV) not captured by above
- Efficacy data may be required if the data in support of the prescription drug was generated by investigations not meeting present day standards for safety and efficacy evaluations.

Partial switches:

- Clinical trials
- Bioequivalence studies
- Effectiveness evaluations from other regulatory bodies with standards similar to those of Canada (examples provided)

Labelling

- Safety evidence will assist in developing the label cautionary statements, in addition to supporting the safe use of the product in a self-care environment.
- Label components include inner and outer labels and package inserts.
- Non-prescription drugs also require a Product Monograph as part of the label component.
- Labelling requirements outlined sections 3, 9, and 10 of the *Food and Drugs Act*, as well as in the *Food and Drug Regulations* for non-prescription drugs and *Natural Health Products Regulations* for natural health products.

Labelling

- Section 3 of the *Food and Drugs Act*:
  - Prohibits the sale of drugs, including non-prescription drugs and natural health products, that are labelled, or that are advertised to the general public, for the treatment, prevention or cure of the diseases, disorders, or abnormal physical states listed on Schedule A.
  - Regulatory amendment to the *Food and Drug Regulations* and *Natural Health Products Regulations* permits the labelling and advertising of Schedule A preventative health claims for non-prescription drugs and natural health products
- Section 9 of the *Food and Drugs Act*:
  - Prohibits the labelling of drugs in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.
- Section 10 of the *Food and Drugs Act*:
  - Sets out labelling requirements with respect to standards that have been prescribed for drugs.

Appendix - Consumer Use Studies

- Consumer use studies are valuable in substantiating that the product can safely be used in the non-prescription setting.
- Types: 1) label comprehension, 2) actual use study, 3) self-selection
- Label comprehension study:
  - Assesses consumer understanding of the communication elements of a label based on language, layout and graphics.
- Self-selection study:
  - Test whether consumers can apply the label information to their personal medical situations and make correct decision to use or not use the product (self-selection decision).
- Actual use study:
  - Determines the safety and effectiveness of the product under proposed non-prescription conditions of use based on consumer compliance with respect to warning(s), dosage instructions and other advice.

Relevant Links

- *Canada Gazette*, Part II – amendment to *Food and Drug Regulations*: http://www.gazette.gc.ca/rp-pr/p1/2012/2012-12-22/html/reg2-eng.html
- Prescription Drug List: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/pdl-ord/pdl_list_fin_ord-eng.php
- PDL Q's and A's: http://www.hc-sc.gc.ca/dhp-mps/consultation/drug-medic/pdl_qa_ldo_qr-eng.php
- Determining Prescription Status for Human and Veterinary Drugs Guidance Document: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/pdl-ord/pdl_gd_ord_ld-eng.php
- Draft Data Requirements for Switching Medicinal Ingredients from Prescription to Non-prescription Status: http://www.hc-sc.gc.ca/dhp-mps/consultation/natur/consult_prescription-ordonnance-eng.php