NB: This document was developed by Legislative Renewal staff as a working document for internal purposes, with a focus on content rather than presentation. However, it is being made available to the public to provide background information.

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EXECUTIVE SUMMARY

Drugs available on prescription in Canada are listed in Schedule F to the Food and Drug Regulations. The decision to add or delete a substance from Schedule F is a scientific one, made by the Therapeutic Products Directorate. The actual addition or deletion of a substance from the Schedule requires the implementation of the federal regulatory process, which is lengthy and involves several levels of approval including that of the Special Cabinet Committee of Council. It has been argued that this decision, which does not have broad public policy implications and is more administrative in nature is not the type Cabinet should be concerned with.

A prescription regimen is a proven risk management tool, and for this regimen to function properly, a list of substances which require a prescription needs to be maintained. There is a strong case for the maintenance of an administrative list of prescription substances, with the legal basis for the prescription status residing in the Notice of Compliance document.

1. ISSUE

The purpose of this Issue Analysis Summary is to determine whether Schedule F could be replaced by a more appropriate framework for listing and delisting drugs that require a prescription.

2. BACKGROUND AND ISSUE ANALYSIS [1]

Schedule F to the *Food and Drugs Regulations* is a list of drugs of prescription status. Part I of Schedule F lists drugs intended for human or veterinary use which require a prescription. Part II of Schedule F lists drugs which may be sold without a prescription when the drug is intended for veterinary use and is so labelled, but does require a prescription when sold for human use. It has to be noted that drugs listed on Part I of Schedule F may not be imported for personal use.

The regulations do not require a prescription in the case of a sale to a practitioner, drug manufacturer, wholesale druggist, registered pharmacist, a certified hospital or a government department. The practical result of the regulations, therefore, is to prohibit, except on prescription, the sale of these drugs to the public for human use.

The decision to add a drug substance to Schedule F is made by the Therapeutic Products Directorate based on established science factors and the use of risk management principles. The decision to delete a substance from Schedule F is made on a similar basis. The amendment requires the implementation of the federal

[1] From "Schedule F - The Listing and Delisting of Prescription Drugs", Draft Policy, Bureau of Policy and Coordination, May 10, 1999.

regulatory process which in turn demands several levels of approval including that of the Special Committee of Council (SCC), one of the permanent committees of Cabinet.

The regulatory process for adding or removing a drug from Schedule F status has consisted of publications in Part I and Part II of the *Canada Gazette*, both of which require approval by the Special Committee of Council. The length of time it took to deschedule a drug has prompted the Therapeutic Products Directorate to redesign the process to make it more efficient and timely without compromising the health and safety of Canadians. Once a drug has been approved for non-prescription use through the submission review process the decision has never been overturned as a result of consultation or subsequent approval by the Special Committee of Council.

Any delay in Schedule F deletions deprives the public of easier access to the product. It can also create economic hardship and uncertainty for drug manufacturers. Companies must keep inventories of both the prescription product and the non-prescription labelled product until Schedule F is amended. If manufacturers are unable to predict when the regulatory amendment will come into effect, it becomes very difficult for them to maintain adequate appropriately labelled supplies.

Further, manufacturers could lose substantial sales as a result of a delay. For example, an allergy product received approval for non-prescription status but the manufacturer was unable to sell its product without a prescription during the spring allergy season due to delays in processing the regulatory amendment to Schedule F of the *Food and Drug Regulations*.

Schedule F originated in 1952 with 10 entries - it now contains over 900 substances. It has become unwieldy and difficult to administer, with negative consequences for both consumers and producers.

Both the regulators and stakeholders desire a predictable and efficient process for the timely addition to and deletion from a clear and current list of drug substances requiring a prescription.

2.1 Process to Amend Schedule F

2.1.1 Federal Regulatory Process

Regulations are policy instruments which may be enacted under an authority granted by a statute approved by Parliament. Regulation-making authority may be granted to the Governor in Council (Cabinet) or, in some cases, to the Minister under whose responsibility the statute in question is held. In the case of a Schedule F amendment, the authority is granted to the Governor in Council. Regulations typically consist of detailed, technical requirements through which the general principles of the statute are

put into force. Regulation-making authority is seen as an essential element of effective policy-making in that it frees up Parliament to consider broader public policy issues while delegating to the executive branch of government the detailed rule making that implements the intent of the statute.

All amendments to federal regulations must follow the process contained in the Federal Regulatory Policy[2] and the Statutory Instruments Act. The policy stipulates *inter alia* that Canadians be consulted on any proposed changes. The consultation includes pre-publication in Canada Gazette Part I of the text of the proposed regulatory change, along with a Regulatory Impact Analysis Statement (RIAS) that explains and justifies the proposal to Canadians. Before a proposal is pre-published, approval must be sought and obtained from multiple parties within government including the Special Committee of Council, the committee mandated by Cabinet to monitor and approve regulatory initiatives.

Regulators may request an exemption from pre-publication. Requests for exemption are considered on a case-by-case basis by the Special Committee of Council in accordance with established criteria. These criteria include regulations that respond to emergencies where there are major risks to health, safety or security, and regulations where the cost of prepublication is likely to outweigh any benefits to be gained from additional consultation.

Based on the comments received following pre-publication, the proposal is amended as appropriate and submitted for a second time through the government approval process. The regulation becomes law once it is approved by the Special Committee of Council and published in Canada Gazette Part II.

At the present time, all amendments to Schedule F must follow this process. However, before that process is initiated, the addition or removal of a drug substance to Schedule F is subject to a rigorous scientific review based on risk management principles, as required under the new drug provisions of the *Regulations*.

2.1.2 Scientific Review and Processing

The process to amend listings on Schedule F begins at the Therapeutic Products Directorate Sub-committee on Drug Schedule Status based on recommendations from the appropriate review Bureau. The recommendation from the Bureau is based on a formal risk-benefit assessment of information supplied either by a manufacturer or from post-marketing surveillance studies on a nonprescription product.

The decision to add or delete a substance is based on established factors. Factors to add a substance to Schedule F, therefore requiring a prescription for human use, are

[2] Federal Regulatory Process, Treasury Board of Canada Secretariat. (http://www.tbs-sct.gc.ca/ri-qr/index.html).

provided in Appendix A. These factors are based on the need to control access by the general public to certain drug products that require information and advice from a practitioner and a pharmacist in order to ensure that the drug is used safely and to maximize its effect.

The criteria for removing a substance from Schedule F are provided in Appendix B. These criteria reflect that, over the life of a drug, there is an increase in knowledge concerning the risk profile of the drug that may allow prescription controls to be removed. The additional knowledge supports the principle that the general public should be able to self-diagnose a health condition and select an appropriate treatment without the advice and counsel of a medical practitioner.

Alternatively, where the use of a nonprescription drug raises a new safety issue, a request for an exemption from pre-publication can be requested and if approved, the proposed regulatory amendment to add the substance to Schedule F is published directly in *Canada Gazette* Part II.

2.1.2.1 Additions to Schedule F

In the case of a new drug substance, a Notice of Compliance (NOC) is issued if the submission has been found to be in compliance with the requirements of the *Regulations*. The Notice of Compliance (NOC) may be issued with the stipulation that the drug product be labelled with a "Pr" symbol, signifying that it may only be sold if the consumer presents a prescription from a licensed practitioner. *However, the drug substance is not added to Schedule F until a regulatory amendment is developed and processed through the federal regulatory process as described above.* The Bureau of Policy within the Therapeutic Products Directorate prepares a regulatory amendment adding the drug substance to Schedule F. In an attempt to make the most efficient use of resources, requests for additions are held until a substantial number are accumulated and then processed as a package. However, a significant period of time may elapse between the issuance of a NOC containing prescription requirements and the official listing of the relevant substance on Schedule F. A manufacturer who has received a NOC can market the Schedule F drug even if the drug has not yet been listed on Schedule F. Between the moment when the NOC is issued and the moment when the drug is listed on Schedule F, there is a period where the drug could legally be sold without a prescription. Although this situation has not resulted in reported cases of drugs not yet scheduled being sold freely, the gap between the issuance of a NOC and the Schedule F listing should be closed.

2.1.2.2 Deletions from Schedule F

After a period of time, the manufacturer may make a submission to market a prescription drug as nonprescription or over-the-counter (OTC) medication. Even though the submission may be found in compliance with the *Regulations*, *a NOC cannot be issued until the drug substance in question is removed by regulation from*

Schedule F. This is because issuance of a Notice of Compliance at that stage would contravene the *Regulations* that prescribe prescription status. That decision, by virtue of the fact that Schedule F is a regulation, has been delegated by Parliament to the Governor in Council, who is advised by the Special Committee Council members.

The decision to "switch" the drug substance in question is referred to the Drug Scheduling Status Committee. The committee applies the criteria for removing a substance from Schedule F. If found acceptable, a recommendation is made to BPC that a regulatory amendment be prepared to remove the substance in question from Schedule F. If not, the request is returned to the sponsoring Bureau for further review or information.

2.2 Issues to Consider

2.2.1 Process Issues

It is perceived by stakeholders that the processing of changes to Schedule F is cumbersome and an inefficient use of resources. The scheduling of substances is a risk management tool designed to control sale through a prescription and is based on a risk assessment by the Therapeutic Products Directorate after a review of data submitted by a manufacturer. By virtue of the fact that scheduling changes must be made by way of a regulation, the ultimate control over which drug products are prescription or non-prescription lies in the hands of the Special Committee of Council.

It could be argued that this is not the type of control Parliament had in mind when it enacted regulations to control the sale of drugs through prescription requirements. In essence, the determination whether a drug is prescription or non-prescription should be a scientific decision rather than a potentially political one. It can be argued that this decision, which does not have broad public policy implications and is more administrative in nature, is not one that Cabinet should be concerned with.

As well, credibility may be lost if the Therapeutic Products Directorate is viewed as having little control over a benefit/risk decision which rests within its mandate as the national regulatory body for safe, efficacious and quality therapeutic products.

The time required to process a Schedule F amendment through the Federal Regulatory Process varies greatly and is unpredictable. Thus, manufacturers cannot be given any assurance as to when the amendment will become law. Consequently, when a manufacturer has made the scientific case for switching their product from prescription to non-prescription, they are unable to predict when they will be able to begin selling the non-prescription product because it is not known when the schedule amendment will become law. As a result, manufacturers are unable to predict how long they will have to maintain inventories of prescription products, or when those products can be re-labelled as over-the-counter (OTC) products. Advertising campaigns cannot begin

since no direct to consumer advertising is permitted until descheduling occurs. They have to continue to supply the prescription product until it is de-scheduled, and the day it is, they have to start supplying the non-prescription labelled product. This uncertainty can result in a loss of revenue for producers.

New drugs may reach the market once a Notice of Compliance (NOC) is issued upon completion of the submission review, as opposed to when the substance is formally listed on Schedule F through the regulatory process. This practice could technically lead to problems enforcing the Schedule F regulations since the substance is not officially listed. However, if the issuance of the NOC were to wait until the regulatory amendment was passed, as is the case with drugs being switched from prescription to over the counter products, the manufacturer's ability to recoup development costs may be greatly reduced. In addition, it would delay the access to a potential beneficial therapy for Canadians.

Linked to the length of time it takes to implement an amendment are the resources used, not only within the Therapeutic Products Directorate but throughout the entire process. As an effort to reduce the human resource impact on the Directorate, new substances are grouped together in one regulation produced annually.

The last official consolidation of the *Regulations* was in 1976. Unofficial versions of the *Regulations* are updated yearly by the Department of Health. Therefore, there is no recent consolidation of Schedule F available for reference other than *Canada Gazette*, Part II.

If each new substance required its own regulation it is estimated that at least two full time employees would be needed to be dedicated full time to keep the list current.

2.2.2 Description of Substances Issues

The naming of substances and how they are listed has caused problems for many of the users of Schedule F. The manner in which substances are listed is inconsistent: in addition to textual listing of substances, which sometimes creates a problem when international nomenclature does not exist for a drug, Schedule F still has some class listings, which are not user-friendly.

Also, principles applied to the control of a drug substance have resulted in the restriction of the availability of all products containing the particular chemical entity. Innovation in the pharmaceutical industry and the review of risk management principles has led to the availability without prescription of several products for specific ailments or at specific dosage strengths while all other products containing that substance remain on prescription. Extensive textual modifications to the basic name listing are required to accommodate these changes.

2.3 Consultations

The following is a summary of the comments that were received on Schedule F during the national and internal Legislative Renewal consultations:

On the principle of Schedule F:

- *HPB has no alternative but to restrict drug access based on medical prescription and on an approval process similar to the one currently used to demonstrate efficacy and safety.*

On where should the list of prescription drugs reside:

- *The procedure for removing a drug from Schedule F has been very time consuming. In our company's experience, it has taken 18 to 24 months to change from Schedule F after all other regulatory requirements were met. Removal of Schedule F from the Food & Drugs Act would make it easier to make approved switches available to the public.*

- *We agree that removing Schedule F from legislation would assist the descheduling process of a prescription product to nonprescription status. The present process is lengthy and unnecessarily restrictive for those products in the queue. The decision as to whether or not a product can be sold with or without a prescription should be based purely on science without any political input. These switched products should be made available for sale in the self-medication marketplace sooner. In addition to the time required in the descheduling process, the initial stage of having a drug reviewed by Health Canada in an OTC switch submission is also unnecessarily long. An administrative list of prescription only products could replace Schedule F.*

- *In terms of the administrative processes of descheduling, it may be worthwhile investigating the possibility of having the National Drug Scheduling Advisory Committee (NDSAC) making these decisions. They are an already established group of experts involved in drug schedule harmonization.*

- *Health Canada should work to eliminate duplication between national and provincial services and standards, wherever possible. An example is Schedule F and the duplication of schedules at the federal and provincial level. Schedule F should be removed from the legislation.*

- *Schedule F should be removed from the Food and Drugs Act. The requirement for a regulatory amendment when descheduling individual therapeutic products is unnecessary and wasteful. Descheduling would be more accurately represented as an administrative process with Schedule F being replaced by an administrative list of products required to be sold by prescription only.*

- *A regulatory amendment should be unnecessary for the descheduling of individual products from Schedule F. Descheduling would be more accurately represented as an administrative process rather than an amendment to the regulations.*

- *The submission requirements and administrative processes involved in descheduling have already been subjected to the full and usual consultative processes of Government. To require each individual recommendation for descheduling to undergo the same degree of public notification and consultation constitutes a form of wasteful duplication and adds nothing to the accountability of Canada's drug regulation system.*

- *The determination of whether a therapeutic product is prescription or nonprescription should be a scientific decision rather than a political one. A scientific decision requires technical expertise and*

knowledge and is based on a risk-benefit assessment of the information.

- *The public notification and consultation process does not add value to the descheduling of products. The Special Committee of Council has never denied a switch application but has always deferred to the recommendations of the scientific experts. The requirement for a regulatory amendment is, therefore, wasteful and unnecessary.*

- *The current system subjects consumers to unnecessary delays for access to safe, cost-effective therapeutic products. Although there is no value added by the public notification and gazetting process, consumers are denied access to potentially beneficial products while these processes are undertaken. The time frame for descheduling products under the current system has historically run up to 15 months.*

- *The current system results in the unnecessary delay of economic benefits to the Canadian healthcare system. The movement of a prescription drug to OTC status eliminates the involvement of the primary healthcare sector and physician fees. There is a tremendous economic benefit for Canada's health care system as a result of the approval of a product for self-medication on the basis of safety and appropriate risk management tools. Two recent studies on the economics of self-medication showed a value of over $100 million to formal health care in just two categories of treatment.*

- *Canada has lagged behind its major international partners (UK and USA) in switch over the last several years. Removing Schedule F from the legislation would streamline the descheduling process and would permit Canada to regain its leadership in this area.*

On the contents of Schedule F:

- *It is recommended that Schedule F of the Food and Drugs Act be reviewed carefully and amended appropriately as it also contains items and substances that would otherwise be classified as Complementary Health Products.*

On who should be able to prescribe prescription drugs:

- *In their education and clinical training, naturopathic doctors learn to prescribe a comprehensive range of natural medicines, parenteral therapies, and nutritional supplements for effective patient treatment. As documented previously, their education and training are extensive and similar to that of conventional medical doctors, yet they are not considered "practitioners" under the current Food and Drug Act. They are restricted from prescribing a number of remedies that are within their scope of practice and that they are trained to prescribe because these are listed in Schedule I, II, IV, and Schedules D, and F, and in the Controlled Drugs and Substances Act. However, conventional medical doctors are allowed to prescribe these restricted and controlled natural substances without appropriate academic and clinical training in their use.*

- *The definition of "practitioner" under the Food and Drug Regulations means a person authorized by the law of a province of Canada to treat patients with any drug listed or described in Schedule F to the regulations. Naturopathic doctors are licensed to practice currently in four provinces, each with different provincial acts and none which allow them to prescribe controlled or restricted "drugs". The provincial pharmacy regulatory authorities determine where drugs are sold and whether they require a regulated environment of sale and professional intervention. Their drug schedules are linked to the federal schedules that control and restrict drugs making a circular restriction that is irrational.*

- *Naturopathic doctors are restricted from prescribing those substances they are trained to prescribe but that appear on the provincial drug schedules requiring a prescription as a condition of sale, and/or are only available from a pharmacist. These substances which include some botanical medicines, homeopathic preparations, amino acids, naturally occurring hormones, enzymes, minerals, vitamins, and trace minerals, form only a small part of the schedules but are an essential part of full scope naturopathic practice.*

On the criteria for a prescription drug:

- *The Act should also establish criteria for de-listing a product as a prescription drug/product.*

2.4 International Comparison

2.4.1 United States

In the United States, the distinction between prescription and over the counter drugs was first made in regulations promulgated following passage of the *Food, Drug, and Cosmetic Act* (FDCA) of 1938. Prior to these changes all drugs, except narcotics, were available without a prescription. The FDCA (1938) required labelling, indicating directions for use and warnings about dangers from use of the drug.[3] The Food and Drug Administration (FDA) exempted drugs from the labelling requirements where they deemed that consumers were unable to choose the drugs for safe self-medication. Drugs so exempted were required to have labelling which was unintelligible to the "ordinary" consumer.[4] "Thus the distinction between prescription and other drugs resulted from the FDA's judgement that patient labelling for such drugs was not feasible."[5]

The 1951 *Durham-Humphrey Drug Prescription Act* codified and clarified the distinction between prescription and over the counter drugs. Prescription drugs were defined as either: habit forming; not safe for use except under the supervision of a practitioner; or, for use under the professional supervision of a practitioner.[6]

The United States does not maintain a schedule equivalent to Schedule F to the Canadian *Food and Drug Regulations*. However, the FDA maintains an internal administrative list for the purposes of ensuring that incoming drug applications are evaluated by the appropriate division or office of drug evaluation. There are regulatory schedules of controlled substances published in the Federal Register which are used

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[3] Federal Food, Drug and Cosmetic Act, 1938, ch. 675, 502(f).

[4] Supra Note p826.

[5] Supra Note p826.

[6] Sec. 503. (b) of the *Federal Food, Drug, and Cosmetic Act*

principally for the purpose of enforcement of drug abuse policy by the Drug Enforcement Administration.

Individual states may maintain their own schedules of prescription only drugs. These, much like in Canada, may be more restrictive than federal requirements but not more permissive.

2.4.2 Australia[7]

New drug substances contained in products for which registration is sought are evaluated for quality, safety and efficacy by the Therapeutic Goods Administration. The outcome of this process is provided to the National Drugs and Poisons Schedule Committee (NDPSC) for the consideration of appropriate scheduling of that drug substance based on its public health risks and benefits. The NDPSC comprises representatives from the Commonwealth, the states, experts in pharmaceuticals, industry and consumers. It is set up under the authority of the Australian Health Minister.

Scheduling is considered in terms of the classification criteria (detailed in "Guidelines for Classification of Drugs and Poisons"). A new drug substance will usually fulfill the classification criteria of a prescription drug substance. The recommendation of NDPSC is published in the Commonwealth Gazette after the quarterly meeting of the committee. The Gazetting process is similar to Canada's in that the first publication in the Gazette is an advertisement of the decision and there is an appeal period. When the committee meets after the first publication, comments are reviewed and the final decision is gazetted.

The scheduling decision of NDPSC is at a national level. This decision is finalized by an amendment to the Standard for the Uniform Scheduling of Drugs and Poisons. The *Therapeutic Goods Act* does not deal with the scheduling of drugs and poisons because this is a State and Territory function, based on the adoption of the Standard for the Uniform Scheduling of Drugs and Poisons into their respective legislation. For some states the change in the regulations is immediate because the national schedule is referenced in those regulations. For others, it requires an amendment to the regulations.

In relation to the reclassification of a drug substance from a prescription only status to a lower non-prescription classification or exempt from scheduling, NDPSC normally requires at least two years of local clinical use or local post-marketing experience with the drug substance before considering a proposal.

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[7] Excerpt from "Guideline for National Drugs and Poisons Schedule Committee"; Therapeutic Goods Administration, 19 August 1997.

Sponsors of new and existing Agricultural and Veterinary Chemicals and new forms of Agricultural and Veterinary Chemicals are not required to make application for scheduling directly to NDPSC as the National Registration Authority (NRA) provides information for the purpose of scheduling as part of the registration process.

2.4.3 European Union

The European Community Directive on the *Classification for Supply of Medicinal Products for Human Use* (92/26/EEC) classifies medicines into those subject to medical prescription and those not subject to medical prescription. This directive confines itself to a description of the criteria which would be used in order to determine when a medicinal product should be confined to prescription control. The criteria apply to all EC Member States although the procedure for assigning prescription classification remains the responsibility of each Member State.

The convergence that the Directive had tried to achieve with the Member States has not been accomplished. In a report by the European Commission on the impact and implications of the Directive, several issues have been identified that need to be addressed to bring the Directive forward. In addition, various criteria need to be considered in assessing the direction the Commission must go, including: the tradition and practice of each Member State within the EC; questions of price and reimbursement; and, advances in information technology. Until now, there has not been a straightforward mechanism in the EU by which it is possible to switch the status of a medicinal product from prescription to OTC. Yet, there is a mechanism in place for changing a products status from OTC to prescription status[8].

2.4.4 United Kingdom [9]

The Committee on Safety of Medicines reviews evidence to determine whether the control (prescription status) on a product should be changed and makes this recommendation to the Medicines Control Agency. If the proposal is supported, wider consultation begins. Responses to the consultation are examined by the Medicines Commission whose advice is passed on to Ministers. It is for Ministers to determine, in light of the advice received, whether the prescription status should be amended. The proposed amendment must be before Parliament for not less than 21 days before it comes into force.

A list of prescription-only medicines (POM) is maintained via a regulation called the "POM Order." The POM Order should normally be amended regularly twice a year

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[8] Marie Donnelly, New Frontiers for OTC Medicinal Products. *The Regulatory Affairs Journal.* Vol. 9, No. 3, March 1998.

[9] Changing the Legal Classification in the United Kingdom of a Prescription Only Medicine for Human Use. Medicines Control Agency, Medicines Act Leaflet, April 1997.

according to so-called “twin-track” timetables. The entire POM Order is consolidated once every ten years or so. As an interim measure, various updates are issued by the Medicines Control Agency on an annual or semiannual basis. Along with the actual list of ingredients required to be sold by prescription only, the POM Order may also specify other restrictions such as dosage strength, indication, etc.

In order to get an accurate list of which ingredients require a prescription, one must have the most recent POM Order and all of the updates issued since then. Additionally, prescription to OTC switches can only take place when the update is issued.

2.4.5 The Nordic Council on Medicines

The Nordic Council on Medicines is a joint Nordic organization, comprising of Denmark, Finland, Norway and Sweden. The Council is the cooperation body of the Nordic countries, which acts on behalf of all citizens by working for a high quality, harmonised drug market and rational use of drugs. The principles for the classification of the prescription status of a product are in alignment with the EC Directive 92/26/EEC.[10]

2.5 Impact on Government

Schedule F is also used by other government agencies. For instance, prescription drugs are exempt from GST/HST and Revenue Canada uses the list as a reference for assessing taxes and monitoring importation.

2.6 Federal-Provincial-Territorial Considerations

The federal government regulates the process by which therapeutic products can be manufactured, marketed, and sold in Canada. This is done under the statutory authority of the *Food and Drugs Act* (F&DA) and the *Controlled Drugs and Substances Act* (CDSA). Provincial and territorial governments determine the place of sale of therapeutic products. The provinces have legislative power over the establishment, maintenance and management of various health care facilities.[11]

Provincial Pharmacy Acts, enforced by provincial pharmacy regulatory authorities, regulate the profession and the practice of pharmacy and may further specify conditions of sale. Within these Acts, drugs are classified into categories (called drug schedules) with conditions imposed on their sale. Prior to 1995, five provinces had provisions in their Pharmacy Acts controlling the distribution of drugs that provided additional levels

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[10] Nordic-wide validity of prescriptions. NLN publication No. 47, Nordic Council on Medicines, Box 1983, S-751 49 Uppsala, Sweden, 1998.

[11] Canadian Pharmacy Law. Marie Berry. Aurora Professional Press a Division of Canada Law Book Inc., Aurora, ON, 1998.

of control to those already contained in the federal legislation.

In some cases, these extra controls were partially based on the product's registration: those nonprescription drug products assigned a Drug Identification Number (DIN) could only be sold through pharmacies and those with General Public (GP) status, known as proprietary medicines, could be offered for sale to the public in any retail outlet.

This situation created disharmony in how drugs were scheduled and controlled across Canada. As a result, several initiatives were undertaken to examine and harmonize the provincial scheduling systems.

The Final Report "Harmonized Drug Schedules in Canada"[12] was released May 1, 1995 and was subsequently endorsed by the National Association of Pharmacy Regulatory Authorities (NAPRA). Since that time, provincial pharmacy regulatory bodies have been endeavouring to effect the regulatory changes necessary to align the provincial drug schedules to the national four category/three schedule model. The impact of this alignment varies in each province according to the traditional provincial approach to drug scheduling, hence implementation of the national model is at different stages across the country.

2.7 Impact on Stakeholders

Many private health plans use Schedule F as a reference for reimbursing the cost of prescription drugs. There needs to be an up to date list for their purposes.

3. OPTIONS ANALYSIS

The following are some statements which should be taken into consideration when developing and evaluating options of the listing and delisting of prescription drugs.

- A list (or lists) of substances requiring a prescription for human and veterinary use is required in order to effectively administer and enforce the prescription process.
- The listing of substances on this list(s) must be user-friendly, accessible, consistent, accurate and timely.
- The process to amend the list(s) should have acceptable performance standards to ensure consistent and timely amendments.
- Stakeholders want to be consulted when a change is proposed to a substance's

[12] Final Report of the Canadian Drug Advisory Committee, 1995.

prescription status.

- The decision on the prescription status of a substance must be based on science.
- Enforcement for the proper use of substances requiring a prescription must be in place.
- There should be no duplication of resources in enforcing Schedule F principles or maintaining a list, i.e., a harmonised list.

3.1 Option 1 - Status Quo: Maintain a list in regulation using the current regulatory process. A list which is part of the Food and Drug regulations has legal authority.

Pros:

- The regulatory process used to amend Schedule F has a well-established consultation mechanism which allows for broad consultation.
- Since this list is official, many stakeholders reference it in their regulations and procedures.
- Schedule F may be seen by inspectors as a useful enforcement tool: if a substance is listed they can take enforcement action. It is also a reference: if a substance is listed, it is a drug.

Cons:

- History has shown that regulatory process cannot deliver consistent and timely amendments for Schedule F. Delays happened at all stages of the process, mainly due to shifting priorities. Additions to the list are often made one year after the substance is on the market. It is possible to introduce delays in the process with nonscientific issues.
- The lack of control over the process leads the Therapeutic Products Directorate to describe substances rather broadly, thus making the list not very user friendly.
- Resources for enforcing Schedule F prohibitions are few.

3.2 Option 2 - Third Party List: The Food and Drug regulations would reference a third party list, thus making it official. The third party would be responsible for keeping the list up-to-date, consistent with federal policy and ensuring accessibility. A possible choice of a third party to maintain the list is the National Association of Pharmacy

Regulatory Authorities (NAPRA)[13]. Although their present list only identifies prescription and non-prescription substances for human use, NAPRA is actively working with Veterinary licencing body to include veterinary use in their schedules. An appropriate consultation mechanism would have to be established as well as a process for timely changes (i.e., when the NOC is issued) to the list so that the confidentiality of submissions is retained.

Pros:

- This option would significantly free up resources at all levels of the federal government. Amendments could be made in a consistent and timely manner, which makes for a more user friendly list.

Cons:

- Health Canada would be delegating its authority in this area.
- No list exists now which meets the federal government ‘s requirement for human and veterinary use and broad consultation.
- Since alignment with the national model varies in each province according to the traditional provincial approach to drug scheduling, implementation is at different stages across the country.
- Resources for enforcing Schedule F prohibitions are few.

3.3 Option 3 - Administrative Process: Determining or modifying the prescription status of a substance would be done through an open and transparent administrative process rather than by way of regulatory amendments.

> *Currently, the prescription status of a substance is evidenced by a list of ingredients in a Schedule to the regulations (“Schedule F”). Adding or subtracting an ingredient requires a regulatory amendment. This is a burdensome and lengthy process with little value added considering the nature of these decisions and the overall drug review process. Better adapted mechanisms to keep the list of ingredients current could be envisaged.*

The regulations would identify the factors to consider in determining whether a product should be declared a prescription product.

> *This would contribute to greater transparency and consistency.*

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[13] NAPRA is a voluntary umbrella organization of provincial pharmacy licensing bodies formed in 1995 to facilitate the public protection activities of its members in areas of national importance such as harmonized drug scheduling, standards of professional practice and entry to practice standards.

For example, with regard to human drugs:

- they require individualized instructions and / or direct supervision by a qualified health practitioner, adjunctive therapy with scheduled drugs or routine laboratory monitoring;
- there exists a narrow margin of safety between the therapeutic and toxic dosages, especially in populations such as the elderly, children and pregnant/nursing mothers;
- they possess the potential for or are known to cause undesirable or severe side effects at normal therapeutic dosage levels;
- they are known by experimental data to induce toxicity in animals but have not been in clinical use for a sufficient period of time to establish the pattern or the frequency of long-term toxic effects in humans.
- they are indicated for serious disease states often misdiagnosed by the public;
- their use may mask other ailments;
- they have contributed to or are likely to contribute to the development of resistant strains of micro-organisms in humans;
- they possess a sufficient dependence or abuse potential that has led or is likely to lead to harmful non-medical use if distribution is not supervised;
- they possess a potentially high level of risk relative to their expected benefits;
- they have a therapeutic effect based on recently elucidated pharmacologic concepts, the consequences of which have not been adequately established.

For veterinary drugs, the same factors would be considered, with the necessary adjustments. In addition, the following criteria would also apply:

- they are known to be liable to be diverted to humans;
- it is not possible to write directions for use that could be easily followed by a layman;

- they may be hazardous to the administrator;
- they are new antibiotics for veterinary use that can be used in human medicine.

Exceptions would be considered for products which:

- are required to be readily available under emergency circumstances where it is not practical to obtain a prescription (such as adrenalin in insect-bite kits);
- are rarely used without a qualified health practitioner's supervision, and where the need for free availability outweighs the need for protection (such as insulin and nitroglycerin);
- have the potential to produce dangerous interactions with other drugs or food constituents but effective labelling can minimize this risk.

It is recognized that the concept of requiring a prescription for sale of some drugs in Canada is a proven risk management tool. It is also recognized that in order for this tool to be used effectively a list of substances which require a prescription must be kept and maintained. However, this list does not need to be embedded in law. Defining a substance as requiring a prescription can be ensured through the existing labelling regulations and through the Drug Identification Number (DIN) or Notice of Compliance (NOC). For example, the Notice of Compliance would state what the drug status is, and the labelling would require that the symbol “Pr” appears on the label. An administrative list of the prescription drug could be maintained. The legal basis for the prescription status would be the Notice of Compliance document. It would remain an offense to sell to the general public a prescription drug without a prescription.

The delisting of a drug could be done via a Notifiable Change to the NOC, and the consultation with the stakeholders could take place as part of the process for the Notifiable Change.

As illustrated above, the regulations would provide for criteria and procedures to determine whether a product must be treated as a prescription product and to ensure accessibility to this information. For the sake of transparency and consistency, the regulations would identify the factors to consider in determining whether a product should be declared a prescription product:

Pros:

- This option would significantly free up resources.
- There would no longer be delays due to the regulatory process.

- There would no longer be a requirement to amend by regulation what constitutes a scientific and risk decision.

Cons:

- There are no major disadvantages to this option.

APPENDIX A - FACTORS FOR LISTING DRUGS IN SCHEDULE F

Schedule F to the Food and Drug Regulations is a listing of chemical entities or classes of drugs which, with exceptions, are required by regulation to be sold pursuant to a prescription.

The following factors are used to determine whether this level of control over the sale of these drugs is appropriate:

(a) they require individualized instructions and/or direct practitioner supervision, adjunctive therapy with scheduled drugs or routine laboratory monitoring;

(b) there exists a narrow margin of safety between the therapeutic and toxic dosages, especially in populations such as geriatrics, children and pregnant/nursing mothers;

©) they possess the potential or are known to cause undesirable or severe side effects at normal therapeutic dosage levels;

(d) they are known by experimental data to induce toxicity in animals but have not been in clinical use for a sufficient period of time to establish the pattern or the frequency of long-term toxic effects in humans;

(e) they are indicated for serious disease states often misdiagnosed by the public;

(f) their use may mask other ailments;

(g) they have contributed to or are likely to contribute to the development of resistant strains of micro-organisms in humans;

(h) they possess a sufficient dependence or abuse potential that has led or is likely to lead to harmful non-medical use if distribution is not supervised;

(i) they possess a potentially high level of risk relative to their expected benefits;

(j) they have a therapeutic effect based on recently elucidated pharmacologic concepts, the consequences of which have not been adequately established.

FACTORS FOR LISTING DRUGS IN SCHEDULE F, PART I AND PART II

The factors to be considered when placing veterinary drugs on Part I, which has the effect of restricting their availability to that pursuant to a prescription of, or use by, a licensed practitioner in veterinary medicine, are outlined below:

1) veterinary drugs which are known to be liable to be diverted to humans;

2) veterinary drugs for which it is not possible to write directions for use that could be easily followed by a layman;

3) veterinary drugs which may be hazardous to the administrator;

4) new antibiotics for veterinary use which are useful in human medicine;

5) certain veterinary drug dosages or formulations may be listed in Part I and other dosages or formulations may be listed in Part II.

EXCEPTIONS

Exceptions should be considered for drugs which:

(a) are required to be readily available under emergency circumstances where it is not practical to obtain a prescription (such as adrenalin in insect-bite kits);

(b) are rarely used without a practitioner's supervision, and where the need for free availability outweighs the need for protection under Schedule F (such as insulin and nitroglycerin);

©) have the potential to produce dangerous interactions with other drugs or food constituents but effective labelling can minimize this risk.

APPENDIX B - CRITERIA FOR NONPRESCRIPTION STATUS

1. They must be effective.
2. They must be safe.
3. Benefit to risk balance must be very positive.
4. Indicated for conditions which can be self-diagnosed.
5. Indicated for conditions which can be self-treated.
6. Indicated for conditions which can be self-monitored.
7. No claims for Schedule A diseases.

APPENDIX C - History of Schedule F

Prior to a 1939 Amendment to the *Food and Drugs Act,* there does not appear to have been any significant restriction on access to drugs for medical purposes. The 1939 amendment granted the Governor in Council the power to define the conditions of sale of any drug likely to be injurious to health.

> *3. (1) The Governor in Council may make regulations*
>
> *(k) prohibiting the sale or defining the conditions of sale of any substance that may be injurious to health when used as a food or drug or restricting in like manner its use as an ingredient in the manufacture of food or drug.*

This amendment was passed as a result of concern expressed by the Dominion Council of Health over the sale of potent drugs to the general public. It is important to note that the amendment restricts the regulating power to drugs that may be injurious to health.

In 1941 the Dominion Health Council again considered the question of public access to drugs and passed a resolution asking the Federal Government to pass regulations for the control and distribution of several drugs. Subsequently an order in council (P.C. 8443, Oct. 31, 1941) was passed requiring prescriptions to purchase the drugs listed below for human internal use.

aminopyrine
barbiturates
amphetamine (except inhalers)
cinchopen
neocinchopen
phenytoin sodium
dinitrophenols
sulphonamides
thyroid
thyroxin

The regulation appears in Part C. section 5 of the 1942 consolidation of the regulations under the *Food and Drugs Act*. Drugs requiring prescriptions were listed in the regulations themselves, not in an appendix or schedule to the regulations. [14]

Antibiotics, starting with penicillin, became available in the 1940's. These drugs were not considered to be injurious to health and therefore the authority to control them by the amendment of 1939 was in doubt. It is not clear why it was proposed to require

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[14] 1942 Office Consolidation of the Regulations under the *Food and Drugs Act.* (P.C. 9056 October 1942 and P.C. 10993 December 1942)

prescriptions for penicillin and other antibiotics, but to allow for the control of these drugs a regulation was passed in 1946 granting the authority to make regulations in the interest and for the protection of the public health.

> *3. (1) The Governor in Council may make regulations*
>
> *(kk) defining the conditions of sale of any drug in the interest and for the protection of the public health;*

In the consolidation of the *Food and Drugs Act* R.S.C., 1952, c.123 the amendments mentioned above appear, re-lettered, in section 3 of the Act:

> *3. (1) The Governor in Council may make regulations*
>
> *(j) prohibiting the sale or defining the conditions of sale of any substance that may be injurious to health when used as a food or drug or restricting in like manner its use as an ingredient in the manufacture of food or drug;*
>
> *(k) defining the conditions of sale of any drug in the interest and for the protection of the public health;*

In the 1952 consolidation, Section C.01.041 of the drug regulations requires a prescription for the purchase of drugs listed in Appendix IV or Appendix V to the regulations.

> *C.01.041 No person shall sell a drug named or included in Appendix IV or Appendix V to these regulations until he has received a prescription...*

The same section in the current regulations is similar;

> C.01.041. (1) In this section and sections C.01.041.1 to C.01.046, "Schedule F Drug" means a drug listed or described in Schedule F to these Regulations.
>
> 1.1) Subject to sections C.01.043 and C.01.046, no person shall sell a substance containing a Schedule F drug unless
>
> (a) the sale is made pursuant to a verbal or written prescription received by the seller; and ,...

Drug products that contain an active ingredient listed on Schedule F to the *Regulations* may only be sold pursuant to a prescription and be labelled with a “Pr” symbol.

An additional restriction to the Regulations was added later due to reports of certain practices regarding veterinary medicines and external preparations (P.C. 2194, March 27, 1944). This Order in Council revised the original wording to include ‘for internal or external use by man or animal’.

The list of prescription drugs was included in the body of the *Regulations* until 1949. With the approval of Order in Council, P.C. 1949-1526, the list was moved from the text of the *Regulations* to Appendix IV of the Regulations. This is how it was maintained until 1953. [15]

In 1953 the list of prescription drugs was divided into two groups. Products in group one, listed in Appendix IV, were available only with a physician's prescription. Products in the second group, listed in Appendix V, were available without a prescription provided that they were in a form not suitable for human use, and were marked "FOR VETERINARY USE ONLY".

In 1954 the two-tiered classification of prescription drugs was moved from the *Regulations* to the *Food and Drugs Act.* Appendix IV became Part I of the Schedule to the *Act* and Appendix V became Part II of the same schedule. In 1963 the prescription list moved from the Schedule to the *Act* to Schedule F of the *Regulations*, however its structure did not change (P.C. 1963-1119; SOR/63-269).

The current Schedule F contains over 900 entries with approximately 750 on Part I and 150 on Part II.

[15] Drug control in Canada: a chemical and legislative compendium. S. Chapman. Isomer Design, 1993.