PUBLIC POLICY SOURCES

Number 55

A Cure Worse than the Illness

Canada's Proposed Regulatory Framework for Natural Health Products in Light of International Evidence

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Contents

THE FRASER INSTITUTE

A FRASER INSTITUTE OCCASIONAL PAPER

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This study was made possible through the generous support of the Lotte & John Hecht Memorial Foundation.

Editing and design: Kristin McCahon and Lindsey Thomas Martin
Printed and bound in Canada.
ISSN 1206–6257.

Date of issue: February 2002

Executive summary

The Canadian government created the Natural Health Products Directorate (NHPD) in 1999 and provided it with some $7 million over three years to establish the new office and another $3 million to fund research on natural health products (NHPs) and complementary medicines. The NHPD was charged with creating a new regulatory framework for NHPs and, after several years of public consultations, the directorate's proposals were published in the Canadian Gazette, Part 1 (December 22, 2001).

From the Canadian federal government to the World Health Organization, the main stated reason for increasing regulatory standards for NHPs is that more and more people are using them. Is this a good enough reason to spend millions of dollars to create a new regulatory body and a new regulatory framework? Are more and more people being harmed by NHPs?

This study examines these and several other issues surrounding the regulation of natural health products. It provides a summary of the reforms being proposed by the NHPD, compares them to the current regulatory framework for drugs, and considers whether the NHPD's proposals conform to the Government of Canada's regulatory policy. It examines the manufacture of natural health products in Canada, the risks posed to Canadians' health by such products and looks at how the way in which drugs are regulated is relevant to the NHPD's proposals. It also gives an overview of how other countries are dealing with this issue and offers recommendations as to how the government should proceed with the regulation of NHPs.

The Government of Canada's regulatory policy

In order to satisfy the Canadian government's regulatory policy, a department must draft a regulatory impact analysis statement (RIAS) to accompany any regulatory proposal. A RIAS is supposed to describe the proposed regulations, the alternatives considered, a cost-benefit analysis, the results of consultations with stakeholders, the department's response to any concerns raised and the means of monitoring and enforcing the proposed regulations.

However, the NHPD's RIAS dismisses any alternatives to regulation and its cost-benefit analysis includes no cost estimates or a valuation of the benefits of regulation. It simply states that the costs imposed on manufacturers would eventually be passed on to consumers and that, for example, consumer confidence could "possibly [result] in an increase in consumer self-medication and a possible decrease in medical problems and associated costs" (Natural Health Products Directorate 2001: 4927).

Protecting consumers

In 2001, adverse reactions to herbal preparations amounted to only 0.38% of all adverse reactions reported in the United Kingdom. In Australia, NHPs accounted for 1.16% of the total adverse reactions to NHPs and drugs in 2000. In the United States, dietary supplements represented only 7.4% of the American government's safety advisories in 2001. As well, statistics on poisonings in the United States support the view that NHPs are not substances that require extensive regulatory intervention: in 1998, 45 people died from a reaction to Aspirin, there

were 10 fatalities as a result of homeopathic or dietary supplements and two deaths from vitamins.

Another issue must also be considered. More onerous regulations can mean that approval times for products take longer. As there are potential costs to rushing the approval process (in terms of safety and other concerns), there are also costs to delaying it (lives that could have been saved or improved if the drug had been publicly available). There has been no attempt by the NHPD to weigh these costs in its decision to regulate NHPs.

International evidence

In most countries, an NHP is considered a drug when the manufacturer claims that it improves health and a food when no such claim is made. Most countries state that they wish to ensure public access to these products and, therefore, they require lower standards of efficacy for NHPs than drugs though they demand the same levels of evidence with respect to quality and particularly safety for both types of substance. All countries require manufacturers of drugs and NHPs to meet good manufacturing practices. No country has undertaken a serious cost-benefit review of their regulatory practices regarding NHPs.

Recommendations

Enforce current regulations

Canada already has regulations to deal with the contamination and adulteration of NHPs. Instead of pumping money into new directorates or regulations, there should be greater enforcement of the current regulations, more spot checks of products on the shelves. And, this is a function that does not even need to be conducted by government. The vast majority of NHPs can be monitored through self-regulation—producers of organic food, for example, have developed standards and certify products that meet them.

Allow the free flow of information

There are many sources of reliable information on NHPs. If multiple certification bodies or random-testing programs were allowed to proliferate, there would be even more. The manufacturers of the vast majority of NHPs, which pose minimal safety risks, should be permitted to make health claims about their products. For the small percentage of NHPs that are toxic and high-risk, there could be somewhat stricter regulations. Restrictions on advertising for NHPs and prescription drugs should be lifted to increase the amount of information available to consumers.

Let the market provide information on the interaction between drugs and herbs

Some NHPs produce adverse reactions when mixed with pharmaceutical drugs. It is unreasonable to expect all foods or drugs to be labelled with every possible contraindication. The market should be left to determine what is the right amount of information. Already, there are many recognizable and reliable sources on the contraindications of NHPs. It is hard to see how increased labelling requirements will improve the situation.

Measure the costs and benefits of regulating NHPs

The analysis of the costs and benefits of the proposed regulatory reforms provided by Health Canada in its regulatory impact analysis statements (RIAS) is of limited value. There must be concrete data to support the claim that the situation will be improved by the regulations and that their costs are worthwhile.

1 Introduction

In 1997, the Fraser Institute calculated that 73% of Canadians had used at least one complementary medicine at some point in their lives and that 50% had used one in that year. While chiropractic and relaxation techniques were the more common therapies, herbal remedies, folk remedies and homeopathy were in the top 10. In total, it was estimated that Canadians spent $3.8 billion that year on complementary medicine; about $128 per capita on appointments with providers, vitamins and supplements, special diet programs and books, equipment, and so on (Ramsay, Walker and Alexander 1999).

Since then, public opinion polls have shown that a majority of Canadians consume natural health products (NHPs) in the form of traditional herbal products, vitamins and mineral supplements, traditional Chinese, Ayurvedic and other medicines and homeopathic preparations. A report prepared for Agriculture and Agrifood Canada estimated that employment in the NHP industry—retailers, distributors and manufacturers—was about 18,600, including full-time and part-time workers. It determined that the total market for natural health products far exceeded $1 billion. (Strategic Policy Choices 1998: 4)

The genesis of the Natural Health Products Directorate

"Canadians from all walks of life have made it clear that they want freedom of choice in making health decisions. They want enhanced access and choice to a full range of natural health products, along with an assurance of safety and quality," states the welcome page of Health Canada's Natural Health Products Directorate Web site (http://www.hc-sc.ga.ca/hpb/onhp).

The home page then explains how, in 1997, Health Canada responded to these concerns by establishing an advisory panel to provide direction and advice. In November 1997, federal Health Minister Allan Rock asked the Standing Committee on Health to conduct a full public review on the issues surrounding the manufacture, distribution, and use of NHPs.

There was much discussion in meetings of the Standing Committee on Health 1997/1998 (SCH) about the "need" to separate the regulation of NHPs from the regulation of foods and drugs. Many witnesses to the committee spoke of their support for a third regulatory category for NHPs. In the end, the SCH provided 53 recommendations on the regulation of NHPs in its report, *Natural Health Products: A New Vision* (Standing Committee on Health 1998).

One of the SCH's recommendations was that Health Canada, in conjunction with a new separate NHP expert advisory committee, set out an appropriate definition and amend the Food and Drugs Act accordingly. Also among the SCH's recommendations was the suggestion that the government consider creating a new regulatory authority for NHPs that reported to the Health Protection Branch. Eventually, the Office of Natural Health Products was created in 1999 and provided with some $7 million in funding over three years to establish the new office and another $3 million to fund research on NHPs and complementary medicines.

"The creation of the new Office of Natural Health Products is a major step forward for consumers," said Rock when he accepted the SCH's recommendations. "For the first time, there will be a dedicated group of professional experts who will treat the evaluation of health products with the distinctiveness and flexibility it deserves." He added that the new office would provide Canadi-

an consumers with the assurance of safety while enhancing consumer access and choice to a full range of natural health products. He also spoke of his desire for "a fresh approach to the regulation of such products." (Office of Natural Health Products Web site, welcome page)

Now called the Natural Health Products Directorate (NHPD), one of the office's missions is to design a regulatory framework for NHPs within Health Canada. The NHPD is intended to become a new regulatory authority, separate from the Therapeutic Products Program and Food Directorate. Currently, it reports to the assistant deputy minister of the Health Protection Branch. According to its Web site, it is staffed with a small core of those with expertise and experience in NHPs and it drew further expertise from an expert advisory committee and other external groups in order to develop its proposed regulatory framework, which was published in the *Canadian Gazette*, Part 1 (December 22, 2001).

As has been shown by numerous studies, including a recent publication by Laura Jones and Stephen Graf of the Fraser Institute, regulation is expensive. Jones and Graf estimated that regulation cost $3,425 per Canadian in 1997 (Jones and Graf 2001: 24). Contrary to the claim by the NHPD and the federal health minister, many people are concerned that increased regulation of NHPs will result in less access to these products. There are at least two ways in which this could happen: if the costs of regulation are passed on to consumers in the form of higher prices or if prescriptions become required for people to get what they once could purchase off the shelf.

The demand for increased regulation

Although Health Canada and the NHPD have followed through on the promise to consult regularly with Canadians as they move to implement the recommendations of the federal standing committee on health, there are still skeptics who question Health Canada's intentions, alleging that it is under the thumb of pharmaceutical companies.

Initially, this concern and others were included in the SCH's report, *Natural Health Products: A New Vision*, in the form of two minority reports: one written by members of the Reform party, the other by members of the NDP (Standing Committee on Health 1998: http://www.parl.gc.ca/InfoComDoc/36/1/HEAL/Studies/Reports/healrp02/reform-e.htm and http://www.parl.gc.ca/InfoComDoc/36/1/HEAL/Studies/Reports/healrp02/20-ndp-e.htm).

Among the Reform party's criticisms of the standing committee's report was concern about the "paternal" attitude of the federal government regarding the perceived need to "protect Canadians from the unknown evils of NHPs" despite an "incredibly safe historical pattern of use of NHPs." Included among the concerns of the NDP was a "crisis of confidence in the Health Protection Branch" and the need to "respect the expressed wishes of Canadians concerned about freedom of choice and access to natural health products."

On the Internet, several people are less polite and constrained in their criticism of the NHPD and Health Canada. They are worried about their access to NHPs, despite the presence on the NHPD's expert advisory committee of well-known providers of alternative and complementary medicine such as Dr. J. William LaValley, founder and chair of the complementary medicine section of the Nova Scotia Medical Association. One critic has referred to the NHPD as the new Health Protection Branch "hoax" and has accused LaValley and the other members of the expert panel of "sleeping with the enemy" (Rona 1997).

There may be no more malevolent a motive on the part of the NHPD and its expert advisory committee than satisfying public opinion. A 1997 Ipsos-Reid poll on alternative medicine use asked Canadians how they viewed the regulation of these therapies (Ipsos-Reid 1997: 3). It found that 67% of Canadians felt that "the government should regulate alternative medicines and practices in the

same way that they regulate other drugs and practices to make sure they are safe and really do what it is they claimed they will do." More affluent Canadians (74% with annual household incomes of $60,000 or more), residents of Quebec (72%) and Canadians aged 18 to 34 (71%) were more likely to believe that the government should regulate alternative medicines.

In contrast to these findings, the Angus Reid Group conducted a study for Health Canada in 2000, using 16 focus groups to estimate Canadians' views of NHPs. Participants tended to be unfamiliar with the standards and regulations currently in place for NHPs. While most participants said they would be disturbed if government played no role in regulating industry, they expressed mixed views regarding whether government should get more involved in regulation. According to the report, there was a general cynicism about government and a belief that too much regulation would increase the cost and affect the accessibility of NHPs. Many participants indicated that it was not necessary for the government to regulate NHPs to the same extent as prescription drugs (Angus Reid 2000: 15–16).

However, if one looks around the world at the regulatory practices of other countries, it is clear that Health Canada is merely following suit. Most developed countries—Australia, the United Kingdom and Germany, for example—regulate NHPs, herbal preparations, dietary supplements and similar products quite strictly. Canada's move in this direction must be considered within this international context.

The regulation of natural health products

From Health Canada to the World Health Organization, the main stated rationale for increasing regulatory standards for NHPs is that more and more people are using them. But, is this a good enough reason to spend millions of dollars to create a new regulatory body? Are more and more people being harmed by NHPs?

This study examines these and several other issues surrounding the regulation of natural health products. Section 2 provides a summary of the reforms being proposed by the NHPD and compares them to the current regulatory framework for drugs. Section 3 considers whether the NHPD's proposals conform to the Government of Canada's regulatory policy. Section 4 examines the natural health products industry in Canada, the risks posed to Canadians' health by such products and looks at how the way in which drugs are regulated is relevant to the NHPD's proposals. Section 5 gives an overview of how other countries are dealing with this issue and Section 6 offers recommendations as to how the government should proceed with the regulation of NHPs.

2 Proposed regulatory framework of the NHPD

While the Natural Health Products Directorate has published a proposed regulatory framework, natural health products will continue to be regulated either as foods or drugs until the new regulatory framework is established. This could take at least another year. Therefore, this section outlines the current regulations and how NHPs are treated under them—the rules applying to foods being less onerous than those for drugs. The section then highlights the similarity of the NHPD's proposals with the current drug regulations and examines whether they conform to the Government of Canada's regulatory policy.

Current regulations

The Food and Drugs Act (FDA) applies to all foods, drugs, cosmetics, and medical devices sold in Canada, whether manufactured in Canada or imported. The act and regulations specify safety and compositional, nutritional and labelling requirements for these products. For the discussion of NHPs, the act's sections on foods and drugs are most relevant.

According to the FDA, a "drug includes any substance or mixture of substances manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state, or its symptoms, in human beings or animals, (b) restoring, correcting or modifying organic functions in human beings or animals, or (c) disinfection in premises in which food is manufactured, prepared or kept" (Health Canada 1981: 1).

A "food includes any article manufactured, sold or represented for use as food or drink for human beings, chewing gum, and any ingredient that may be mixed with food for any purpose whatever" (Health Canada 1981: 1).

Part 1, section 3, of the act states that no one shall sell or advertise any food, drug, cosmetic, or device "to the general public as a treatment, preventative or cure for any of the diseases, disorders or abnormal physical states referred to in Schedule A." This schedule includes some 50 ailments, including arthritis, asthma, cancer, depression, and heart disease. It was intended to encourage individuals to seek medical attention for serious conditions and to prevent fraudulent health claims.

In the SCH meetings, many witnesses testified that, if there was evidence to support a claim, then it should be permissible to make a claim, even for conditions on Schedule A. The SCH recommended that Schedule A be reviewed and the transition team (that bridged the gap between the SCH report and the creation of the NHPD) recommended that all diseases on this schedule be removed. Another suggestion was for Health Canada to develop policy guidelines that differentiated between various types of claims.[1] Currently, any health claim puts most products, whether they are a food or natural health product, into the drug category. (There are exceptions.)

Since the issue of Schedule A concerns many of the products currently governed by the FDA and not just natural health products, the NHPD has referred the issue to Health Canada's Legislative Renewal initiative. The initiative is part of Health Canada's efforts to update and improve the laws that guide its work in health protection; it started in 1997 and was expected to be complete within two to three years. For now, the schedule remains.

Food

Part 1, section 4 of the FDA, prohibits the sale of an article of food that has in or on it any poisonous or harmful substance; is unfit for human consumption; consists in whole or in part of any filthy, putrid, disgusting, rotten, decomposed or diseased animal or vegetable substance; is adulterated; or was manufactured, prepared, preserved, packaged or stored under unsanitary conditions.

Section 5 requires truth in the labelling of a food:

> (1) No person shall label, package, treat, process, sell or advertise any food 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.
>
> (2) An article of food that is not labelled or packaged as required by, or is labelled or packaged contrary to, the regulations shall be deemed to be labelled or packaged contrary to subsection (1).

Similar sections also apply to drugs. Therefore, many witnesses to the SCH testified that the current regulations are sufficient to protect consumers from two of the most important concerns about NHPs: adulteration (the addition of substances other than those that appear on the product's label) and contamination (manufacture of the product in unsanitary conditions). These witnesses argued that a new regulatory body and its associated costs were unnecessary; that the FDA already protects consumers from unsafe products and fraudulent claims, whether they are treated as foods or drugs.

What is a food and what is a drug?

Items such as a clove of garlic or fresh cranberries are considered a food—they are grown, sold, or represented for use as food for human beings. However, when they are professed to help lower cholesterol or prevent colds, as garlic is, or when they are "prescribed" as a treatment for urinary tract problems, as cranberries are, there are definitional problems. Once something like garlic is put into the form of a pill, it is considered a drug since it is not likely that a pill is being sold for use as food.

Under the current regulations, the manufacturers, distributors, or retailers of the food garlic or cranberry cannot make any health claims or provide any information about how best to use them for medicinal purposes. People have to learn about the medicinal uses of such products by word of mouth or from other sources such as the Internet. Producers of the drug garlic or cranberry can make claims once their manufacturers show Health Canada's Therapeutic Products Program enough scientific evidence to support their claims and if they follow the other requirements laid out in the drugs section of the FDA. This can be a lengthy and costly process, as is shown in Section 3 of this study.

The result is that some natural health products are sold as foods, while others are marketed as drugs. Garlic, for example, falls into both categories since it is sold both raw and as a pill. Most witnesses to the SCH felt that NHPs should not be classified as foods (because they are being used to address health and wellness concerns) or as drugs (because they are not generally being used to treat an illness). This grey area is one reason why the NHPD was set up—to accommodate the perceived distinction of NHPs from food and drugs.

Drugs

Part 1, section 8, of the FDA requires that any drug must be manufactured, prepared, preserved, packaged or stored under sanitary conditions and not be adulterated; section 9 requires truth in labelling. Manufacturers of drugs must satisfy many requirements in order to receive a product licence, or DIN (drug identification number), and an establishment licence.

There are eight publications that provide standards for drugs acceptable to Health Canada and

these are detailed in Schedule B: *European Pharmacopoeia*, *Pharmacopée française*, *Pharmacopoeia Internationalis*, *The British Pharmacopoeia*, *The Canadian Formulary*, *The National Formulary*, *The Pharmaceutical Codex: Principles and Practices of Pharmaceuticals* and *The United States Pharmacopoeia*.

A person is permitted to sell any drug described in Schedule C (radiopharmaceuticals) or Schedule D (blood and blood derivatives, insulin, snake venom, etc.) only under special conditions. Schedule F drugs (dopamine, L-tryptophan and its salts, Tamoxifen and its salts, Thalidomide, etc.) are available only by prescription and, for any drug on the list, the regulations permit only the advertising of a product's name, price and quantity to the general public.

Enforcement of the FDA

At first glance, it would not seem that restrictions on the sale of drugs, such as Schedule F, would be related to NHPs. However, several witnesses to the SCH brought up the treatment of L-tryptophan—used for the treatment of depression, insomnia and other ailments—as an example of the, at times, confusing application of the FDA by the drug regulatory body, Health Canada's Therapeutic Products Program (TPP), that makes doing business in NHPs a precarious venture.

One of the main problems with Health Canada is a lack of transparency in their decision-making process. The result is often public confusion as to the reasons for Health Canada's actions. For example, some witnesses to the SCH blamed the removal of L-tryptophan from the general marketplace on a contaminated American shipment of L-tryptophan from Japan in 1989 that reportedly caused about 1,500 cases of eosinophilia-myalgia syndrome, a rare and deadly flu-like condition from which about 40 people died (US Food and Drug Administration 1996: 6) The United States pulled L-tryptophan off the market and Health Canada did the same even though many health experts later determined that the Japanese shipment to the United States had been contaminated and it was likely the contaminant, and not the amino acid, that caused the deaths.

However, at least one witness claimed that L-tryptophan had been removed from the market before this incident. David Chapman, president of Purity Life Health Products Ltd. and director of the Canadian Health Food Association at that time, appeared before the SCH on February 17, 1998.

> There's a bit of misunderstanding here. L-tryptophan was removed from the market before this contamination problem happened. All the amino acids were yanked one day, overnight. From what we understood, it was yanked because some American couple had written a book that made outlandish and outrageous claims for amino acids. At that point, Health Canada's way of handling claims was to haul products off the market … Instead of telling industry to be careful about what claims to make, they just put it to new drug status.[2] Once something goes to new drug status, they really don't want to pull it out. (Standing Committee on Health 1997–1998: February 17, 1998)

Mary Carman, then-director of the bureau of pharmaceutical assessment at the TPP, supported Chapman's testimony, in saying that tryptophan was first licensed in Canada in 1986 (SCH 1997–1998: February 26, 1998). But, whatever the reason for, or timing of, its removal from the general market, the placing of L-tryptophan on Schedule F had implications for consumers. Chapman said that the price per dose went up from $15 to $80. On February 10, 1998, Paul Hogarth, owner and founder of Personal Health and Nutrition at the time, told the SCH that the current regulations were adequate protection from unsafe products, claiming a price increase from $14 for a bottle of tryptophan in the health store to $114 a bottle through a doctor's prescription.

While there is no definitive study verifying that this increase in cost and decrease in availability of tryptophan has had a positive effect on consumer safety, one witness claimed that Health Canada's actions in this instance saved lives: "I was also a

chair of the task force on amino acids for Canada. By putting them into a regulated domain, we prevented several deaths from tryptophan in Canada," said Prof. G. Harvey Anderson, then co-director of the University of Toronto's program in food safety, department of nutritional sciences (SCH 1997–1998: March 19, 1998).

Burden of proof

L-tryptophan was taken off the market and placed into the new drug category. Several witnesses bemoaned this development because, as Donna Herringer, then-vice-president of sales and merchandising at Sears Health Food and Fitness Shop, put it: "new drug status is what we in our industry call that deep, dark hole that nothing ever comes out of" (SCH 1997–1998: February 17, 1998).

One "victim" of the "deep, dark hole" of new drug status is melatonin, which is used most often to treat jet lag and to facilitate sleep. It is not available in Canada. Dann Michols (then the director general of Health Canada's Therapeutic Products Program) explained to the SCH that melatonin, "because it is a hormone, is in the new drug category, and very clearly there are guidelines on what information is required [to get it approved for sale]" (SCH 1997–1998: February 26, 1998).

Carman summarized Health Canada's position on melatonin to the SCH:

> The regulatory regime for a drug in Canada is a pre-market approval process. We do not put together the data. We do not sponsor the data. It would rather compromise our judgment if indeed it were our data. That information on any substantive basis, risk-wise, may or may not be a problem with melatonin, but we're continuing to look at it. We have no quality information on melatonin from any source (SCH 1997–1998: February 26, 1998).

She acknowledged that Health Canada had received animal and laboratory studies, provided either through the literature or the Canadian Health Food Association, but claimed that these were "limited small-scale studies. We couldn't even do a meta-analysis on it for any one indication." She also said there was not enough clinical data to show whether the benefit of any product would outweigh the potential risks.

Chapman contended that the industry had been asking for years for Health Canada to remove numerous products from new drug status, whether they are amino acids, various herbs or melatonin. "In the case of melatonin, we spent a considerable amount of money. We went to leading experts around the world and asked for position papers," he testified. Chapman said they were simply told at a meeting that their submission did not meet Health Canada's requirements "and that was it" (SCH 1997–1998: February 17, 1998).

The problem with meeting the many scientific requirements of proof demanded by the new drug approval process is that the necessary research for a single chemical entity that is patentable must be economically profitable in the end. However, for NHPs, most of their therapeutic effects cannot be attributed to one entity and, even if they can be, the entity is non-chemical and non-patentable. It is not feasible to expect that a company or individual will spend millions of dollars to prove the efficaciousness of a non-patentable substance.

The irony, according to many witnesses to the SCH, is that the current regulations permit Canadians to import a three-month supply of substances such as melatonin for personal use. Besides the irony, however, several witnesses pointed to the impact that such a situation has on the industry. Joel Thuna, then general manager of Global Botanical, said that there is one American company that has "20,000 regular purchasers from Canada. That is a significant number to an industry our size" (SCH 1997–1998: February 24, 1998).

Cost implications

Another concern expressed by witnesses to the SCH was the cost for NHP manufacturers of meeting the more rigorous requirements of the drug

regulations if they wish to make a claim about their product. For example, it can cost more than $143,000 for the evaluation of a product considered to be a new drug (SCH 1998: chapter 9). Currently, it costs $720 for an herbal or homeopathic preparation supported by traditional references.

> To receive an establishment licence, a drug manufacturer, among other things, must follow good manufacturing practices (GMPs) that include several sanitary measures. While this regulation may sound perfectly reasonable, Health Canada charges quite substantial establishment licensing fees to pay for the inspections and other measures needed to make sure that GMPs are being followed in the production of drugs. Currently, producers of NHPs are exempt from these fees and, while the NHPD has not yet determined that it will charge the fees, "Health Canada estimates that, if these exemptions were lifted, revenue for establishment licensing fees on NHPs could amount to $2 million annually." (SCH 1998: chapter 9)

Proposed regulatory framework of the National Health Products Directorate

Since the creation of the Natural Health Products Directorate, there have been numerous public consultations. The NHPD published the document *Proposed Regulatory Framework for Natural Health Products* for public comment in March 2001. The authors of the document express their hope that readers would "discover a progressive system that is appropriate to NHPs: a system that protects consumers' concerns of safety and product quality, without being unduly restrictive to the NHP industry."

While the proposed regulations have a few novel aspects, a "progressive" system is not to be found in the framework described in the *Canada Gazette*, Part 1 of December 2001. The NHPD proposals are unique in that most other countries treat dietary supplements, traditional medicines, and homeopathic products separately, whereas the NHPD's definition of a natural health product includes all of these. As well, the NHPD's definition states that NHPs are products "manufactured, sold or represented for use in (i) the diagnosis, treatment and mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans," a status currently only afforded to drugs.

The main disappointment with the NHPD's proposed framework is that the NHP regulations seem almost identical to the drug regulations of the FDA: Part C, Divisions 1, 1A and 2 in particular (see the Appendix, page 53.)

Definition of a natural health product

It is proposed that natural health products be defined as substances that are manufactured, sold or represented for use in (i) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans; (ii) restoring or correcting organic functions in humans; or (iii) maintaining or promoting health or otherwise modifying organic functions in humans.

Specifically, medicinal ingredients of NHPs would include, alone or in combination: (a) a homeopathic preparation; (b) a substance or substances used as a traditional medicine; and (c) a mineral, a vitamin, an amino acid, an essential fatty acid or other botanical, animal or micro-organism derived substance. NHPs do not include such substances as an antibiotic, a substance included in various schedules of the Controlled Drugs and Substances Act, a substance regulated under the Tobacco Act and others.

Licences for natural health products

The intent of licensing products is to assess and manage the benefits and risks associated with the use of natural health products. The goal is to

ensure accessibility, safety, efficacy, and quality of NHPs. Under the proposed regulatory framework, an NHP could be sold only once it has been assigned a product licence by the Minister of Health (in practice, by the NHPD on the minister's behalf). An applicant would have to provide the following information for a product licence:

- the name, address, telephone number, and other contact information for the applicant and each importer, manufacturer, packager and labeller of the NHP, and the address of each site at which the NHP will be manufactured, packaged or labelled;
- the proper name of each of the medicinal ingredients contained in the NHP, each of their sources, if any, and the strength or potency of each of the NHP's medicinal ingredients;
- a qualitative list of the non-medicinal ingredients the applicant proposes to include in the NHP and the purpose for which they will be included;
- the brand name or brand names of the NHP, if any;
- the recommended conditions of use for the natural health product;
- information that supports the safety and efficacy of the NHP when it is used in accordance with the recommended conditions of use;
- the text of each label that is proposed to be used in conjunction with the NHP; and
- a copy of the specification[4] with which the NHP will comply and an attestation by the applicant that the NHP will be manufactured, packaged, labelled and stored in accordance with the requirements set out by the GMPs.

A 60-day "disposition" clause has been included in the regulations, recognizing that the NHPD should be able to review certain NHP licence applications appropriately within 60 days. The clause would apply to an application that references a monograph in the compendium of monographs developed by the NHPD, which is based on public literature. The development of monographs is ongoing and will include both single- and multi-medicinal ingredient monographs. The monograph will provide support for the safety and the claim of the NHP and, therefore, additional safety and efficacy data would not be required in the application for a product licence. The compendium will be made publicly available and amendments will be made to it as required from time to time. New medicinal ingredient monographs will be added to the compendium as the NHPD determines that the available body of evidence related to their safety and efficacy supports their inclusion.

Health Canada's Therapeutics Products Program (TPP)—which, as the regulator of drugs, is responsible for the regulation of NHPs until the NHPD's regulations are in place—produced guidelines in 1995 on traditional herbal medicines. They stated that "at least two herbal references supporting the intended traditional use of each herbal ingredient must be provided with the application" for a drug identification number; the TPP's 1998 homeopathic policy requires the support of "at least two traditional homeopathic references." Now that herbal medicines and homeopathic remedies are to be considered as NHPs, it is unclear whether the requirements are to become more or less rigorous, given that the NHPD compendium has not yet been published. There are no assurances (notwithstanding an appeals process that has also not yet been developed) that all applications will be duly considered. Numerous instances of bias in Health Canada were claimed by witnesses to the 1997–1998 Standing Committee on Health examining the question of NHPs (melatonin and ma huang, for example).

While there is reference in the regulations to the FDA's Schedule B, the list of recognized publications, there does not appear to be a commitment to expand this list to include publications perhaps better suited to the regulation of NHPs, such as

the three homeopathic pharmacopoeia (American, French and German) in the TPP's homeopathic guidelines or the British Herbal Pharmacopoeia.

Site licences

The goal of a site licensing system is to ensure quality NHPs are being sold and to aid the product recall process when necessary. A site licensing system requires that all persons in the manufacturing and distribution chain have a site licence and that all sites meet the GMPs regarding standards of cleanliness, quality assurance, and record keeping.

In the proposed regulations for NHP site licences, there are only a few obvious differences from the drug regulations. One difference is the number of days (15 for drugs, 60 for NHPs) within which the NHPD should be notified of changes in the application information, the equipment used in manufacturing, and so on. There are also longer time periods provided for NHP licensees to react if the NHPD deems it necessary to suspend or cancel their licence. As well, there is a relaxation of the frequency of licence renewal for NHPs (which is annual for drugs but which gradually decreases to every three years for NHP licence holders in good standing for nine years or more).

The cost concerns of smaller NHP manufacturers, packagers, storers, and handlers are not addressed in the proposed regulations, especially if the NHPD eventually implements cost recovery initiatives similar to those of other Health Canada departments and other countries' regulatory bodies. Currently, NHP producers are exempt from site licensing and inspection fees—which cost thousands of dollars—and the NHPD has said that it will not charge such fees. The directorate has promised further consultations if cost-recovery initiatives are thought necessary.

Good manufacturing practices

Good manufacturing practices (GMPs) are an attempt to ensure product quality control and risk management. They comprise standards and practices for product design, testing, manufacture, storage, handling, and distribution. The NHP guidelines were supposed to allow the industry to develop useful products at a reasonable cost and to accommodate changing scientific developments. The guidelines were also supposed to reflect the various types of NHPs. In February 2001, the NHPD formed working groups made up of industry representatives, consumers, health-care professionals and NHPD personnel to develop GMPs for herbal products, vitamins and minerals, homeopathic preparations, and traditional and cultural medicines. It is disappointing, therefore, to see that the NHPD's proposed GMP regulations for NHPs are virtually identical to the FDA, Division 2.

No one is allowed to sell an NHP unless it has been manufactured, packaged, labelled, imported, distributed and stored in accordance with the GMPs; in premises that are designed, constructed, and maintained in a manner that permits the activity to be conducted under sanitary conditions and that prevents the contamination of, and the addition of, an extraneous substance to the NHP. There are storage and equipment regulations as well as requirements that the personnel be qualified to perform their tasks.

Every NHP must be manufactured, packaged, labelled, and stored in accordance with a written sanitation program that sets out procedures for cleaning of the premises and equipment, the handling of substances and the clothing of the personnel. Almost every step in the process must be approved by a quality-assurance person.

Every NHP must meet the specifications for that NHP before it is made available for sale. If the label of the NHP will bear any use or purpose in respect of the potency of the NHP, detailed information respecting the potency of the product and tolerances for the potency of the NHP are required. Specification also includes a detailed description of the methods used for testing or examining the NHP. Specifications must be in writing and approved by a person responsible for quality assurance.

Every manufacturer who sells a NHP must maintain records at the site at which the person conducts that activity. These include:

- the master production document for the NHP;
- a list of all ingredients contained in each lot or batch of the NHP;
- records of any testing conducted in respect of a lot or batch of raw material used in the manufacture of the NHP;
- records of any testing conducted in respect of a lot or batch of the NHP;
- a copy of the specification for each NHP that the person is manufacturing;
- records demonstrating that each lot or batch of the NHP was manufactured in accordance with GMPs;
- records containing sufficient information to enable the recall of every lot or batch of the NHP that has been made available for sale; and
- a list of all NHPs that are being manufactured at the site.

There is also a detailed list of the records that the packagers, labellers, importers, distributors, and product licence holders of NHPs are required to hold. Other than the fact that there seem to be fewer records that must be kept in the NHP industry than in the drug industry, there are few obvious differences between the NHP and drug GMPs. Two others are that there is no section concerning packaging-material testing for NHPs; and the sections on raw material and finished product testing are more succinct and somewhat less onerous for NHPs than drugs, being summarized in one section (titled Specifications).

Labelling

The intent of labelling is, of course, to provide consumers with as much information as possible about the products they are using. While the NHPD, in its *Building Together: Phase 2 in Developing a Framework for Natural Health Products*, cautioned NHP users that there is a limit to the amount of information that can fit onto a label, there is a lot of labelling information proposed in the NHPD's regulatory framework.

No one will be able to sell an NHP to the public unless it is labelled in accordance with the regulations, which require clearly and prominently displayed in both official languages *at least* the following information:

- the brand name;
- a qualitative list by proper name that sets out in descending order of importance, all the medicinal ingredients that it contains;
- the recommended dose and duration of use, if any;
- the product licence number, lot number, and expiration date;
- if the NHP is sterile, the notations "sterile" and "stérile";
- if the NHP is one which is to be sold on prescription, the symbol "Pr" in the upper left quarter of the principal display panel; and
- the net amount of the natural health product in the immediate container in terms of weight, measure, or number.

These are only some of the small package labelling requirements. For a general package, the information required is much greater. Basically, the labelling requirements for NHPs are the same as those for drugs. There does not appear to be an allowance for NHP producers who may not wish to put therapeutic claims on their products (and thereby not be subjected to the NHP regulations, presumably).

Reporting adverse reactions

"Adverse reaction" means a noxious and unintended response to a natural health product that occurs at any dose used or tested for the diagnosis, treat-

ment or prevention of a disease or for modifying an organic function.

Once a product licence is granted, product licence holders will be required to comply with the adverse reaction system. The NHPD is proposing exactly the same system as is currently used for drugs and it has stated that will be considering alternative means to report adverse reactions, such as a toll-free telephone line.

The regulations require that every licensee provide the minister with a case report for each serious expected or unexpected adverse reaction to the NHP that occurs inside or outside Canada within 15 days of becoming aware of the reaction. If, after reviewing a case report or any other safety data relating to the NHP, the minister has reasonable grounds to believe that the NHP is not safe when used under the recommended conditions, the minister may require the licensee to provide, within 30 days, a detailed report about the adverse reactions that have occurred. As well, licensees are annually to prepare and maintain a summary report that contains a concise and critical analysis of all adverse reactions to the NHP that have occurred inside during the previous 12 months.

Reporting and analysis of adverse reactions is, arguably, the one recommendation that should have been implemented years ago, at the beginning of the whole discussion of regulating herbal medicines, homeopathic products, traditional remedies, or whatever the name assigned to what are now considered NHPs.

Other issues

Part 4 of the proposed regulatory framework deals with clinical trials. According to the NHPD, this component has been developed to recognize the generally accepted principles of good clinical practice. There was no mention of these regulations in any of the NHPD's public consultation documents in 2001.

Another item of note is that the proposed NHP regulations contain a page of references to sections of the Food and Drug Regulations that are applicable to pressurized containers, cautionary statements and child-resistant packages, medicinal ingredient representations, inspectors, imported NHPs, export certificates, sampling of articles, standards and grades, tablet disintegration times, NHPs recommended solely for children, and prescription NHPs.

3 Adherence of the proposed NHP regulations to the Government of Canada's regulatory policy

According to the Privy Council Office Web site, the government's regulatory policy provides the guiding principles for the development of regulations and it imposes certain requirements (see Government of Canada 2001). These include:

(1) that regulatory authorities demonstrate both that a problem or risk exists and that federal intervention is justified;

(2) that all possible means—whether regulatory or non-regulatory—of addressing the problem or risk have been considered;

(3) that stakeholders—industry, labor, consumer groups, professional organizations, other governments and interested individuals—be consulted on all phases of the identification of problems and the development of the regulatory solution;

(4) that intergovernmental agreements be respected and that opportunities for intergovernmental co-ordination have been exploited;

(5) that benefits and costs of the regulatory interventions under consideration be assessed, that the benefits justify the costs and that limited government resources are used where they will do the most good;

(6) that adverse impacts on the economy are minimized;

(7) that systems are in place to manage regulatory resources effectively;

(8) that compliance and, when appropriate, enforcement policies be implemented; and

(9) that the regulators have the resources for monitoring compliance and enforcing the regulations.

In December 2000, the Auditor General's report included two chapters relevant to the topic of NHP regulation: Federal Health and Safety Regulatory Programs and Canadian Food Inspection Agency (Auditor General 2000: chapters 24–25). Many of the concerns that the Auditor General had regarding federal health and safety regulatory programs and the Canadian Food Inspection Agency (CFIA) stemmed from its finding of "many instances where the regulatory authorities have not met the expectations of the government's regulatory policy."

This section examines how previous attempts by Health Canada to regulate herbs failed to meet the principles of the federal government's regulatory policy. It also looks at the NHPD's current effort in this context: how it, too, fails to meet the principles. Finally, it discusses in more detail the Auditor General's report and its relevance to the proposals put forward by the NHPD and Health Canada.

Health Canada's attempt to regulate herbs and botanicals

In order to satisfy the government's regulatory policy, a department must draft a regulatory impact analysis statement (RIAS) to accompany any regulatory proposal. A RIAS is supposed to describe the proposed regulations, the alternatives considered, a cost-benefit analysis, the results of consultations with stakeholders, the department's response to

any concerns raised and the means of monitoring and enforcing the proposed regulations.

Almost a decade ago, Health Canada attempted to amend the Food and Drug Act specifically to prohibit certain herbs and botanicals from being sold as foods. The department prepared a RIAS and it was pre-published in the *Canada Gazette*, Part 1, December 19, 1992, concerning the Food and Drug Regulations—Amendment (Schedule No. 705). This RIAS manifests a lack of risk assessment and cost-benefit analysis that, still today, is problematic and should worry government, industry, and consumers alike. Unfortunately, this is a problem at the international level, with no country, it seems, taking the time to evaluate the actual risks posed to their citizenry by NHPs or whether the expenditures to regulate these risks are being well spent. (For more information, see Section 4 of this study.)

The 1992 RIAS sponsored by the then-Department of National Health and Welfare described the concern "that some herbs and botanical preparations with potentially harmful properties could be marketed to the public." It listed 64 substances that, in its opinion, should be categorized as "adulterants" when found in food and seven substances that the department believed should have cautionary labelling. For a number of reasons, a public uproar ensued and Schedule 705 became, for Health Canada's critics, the epitome of regulation gone wrong.

Health Canada seems to have learned something from this experience and has, in the process of creating the NHPD, consulted the public and various stakeholders extensively (fulfilling guiding principle number 3). It also changed from a herbs-that-are-unsafe-as-foods approach (a "blacklist") to a NHPs-shouldn't-be-regulated-as-strictly-as-drugs approach that often mentions the right of consumers to make informed decisions about how they manage their health care. Lessons that do not seem to have been learned, however, include the consideration of alternatives to regulation and the measurement of the anticipated impact of regulations.

Alternatives to regulation not considered

The 1992 RIAS included the discussion of one option—that of listing the substances in question as adulterants in food—it did not consider any alternatives to this type of regulation. The 2000 Report of the Auditor General (Office of the Auditor General of Canada and the Commissioner of the Environment and Sustainable Development 2000) stated that "there is still a tendency for the government to regulate, not to find alternative solutions" and the more recent process of creating the NHPD affirms this notion.

According to the 2001 RIAS, a number of options were explored by a variety of committees. The NHPD dismissed concepts such as voluntary standards, which would be a move towards deregulation of these products, because this

> is not in line with consumer demands for higher safety assurances, more complete and accurate labelling, and consistency of product. In similar Health Canada initiatives, such as nutritional labelling, efforts to introduce voluntary standards have met with limited success. (Natural Health Products Directorate 2001: 4925)

Another alternative that the NHPD dismissed is the adoption of the American system, because the United States exists as an "anomaly," classifying many NHPs as dietary supplements, whereas countries such as Australia and those of the European Union consider these products to be drugs.

The NHPD refers to the SCH recommendations, which were accepted in their entirety by the government: they focused on a separate regulatory regime and authority for NHPs, based on the unique nature of these health products. It was decided the most effective regulatory mechanism was to create a new set of regulations specific to NHPs that would be situated under the Food and Drugs Act.

No assessment of costs and benefits

As well, neither the 1992 RIAS nor the NHPD process included any in-depth cost-benefit analysis.

The 1992 RIAS simply stated that the costs "are not anticipated to be greater than those for administering the existing regulations," that the "cost to the industry is anticipated to be small" and that the "costs will be increased primarily for individuals or firms" selling the seven products requiring cautionary labelling as "labels for these products will have to be changed." There are no dollar figures given for these "small" costs and no discussion of the extra monitoring and other expenses (in capital and human resources) of restricting access to a total of 71 herbs and botanicals (not just the seven needing new labels but the 64 "adulterants" as well).

As for the benefits, the 1992 RIAS states that "the proposed amendment will help to alleviate any confusion about the safe use of herbs and botanical preparations as foods" (Department of National Health and Welfare 1992: 3909–10). No quantifiable benefits of the proposed regulations are indicated: no cost per life saved or number of illnesses prevented, for example.

The 2001 RIAS is similarly devoid of numbers. It states that the NHPD undertook a cost-benefit analysis of the proposed regulations prior to the first draft of the regulatory framework and used the results to develop the subsequent drafts and the regulations in the *Gazette* but the results are not included in the statement. All that is indicated in the RIAS is that, in a competitive market, the costs imposed on manufacturers would be passed on to the retailers, who would then pass them on to consumers. As well, Health Canada's costs were expected to increase as the NHP regulations, at least initially, would not be administered on a cost-recovery basis.

Another interesting aspect regarding costs is that the 2001 RIAS also states:

> Manufacturers recognized that those NHP manufacturers who also manufacture drugs (and, therefore, hold valid establishment licences) would not incur significant costs for any additional NHP specific requirements. Manufacturers of NHPs only would probably incur some substantial costs. (Natural Health Products Directorate 2001: 4927)

Health Canada believes the benefits of regulations to be that consumers would have more information and, therefore, would be able to make informed decisions. As well, consumer confidence in the safety and efficacy of NHPs would be increased, "possibly resulting in an increase in consumer self-medication and a possible decrease in medical problems and associated costs" (Natural Health Products Directorate 2001: 4927). Practitioners would also have more confidence in NHPs and would be better able to make product recommendations to their patients. "Industry may benefit from a resulting increase in long-term, stable demand for NHPs and will be generally better able to compete domestically and internationally through knowledge that Canadian NHPs meet regulatory requirements" (Natural Health Products Directorate 2001: 4927).

In sum, Health Canada concludes that the benefits outweigh the costs of adopting the NHPD's regulatory framework.

Auditor General's 2000 *Report*

The Auditor General estimated that $1.2 billion was spent in 1999/2000 on administering major federal health and safety regulatory programs (Office of the Auditor General of Canada and the Commissioner of the Environment and Sustainable Development 2000).[5] This estimate does not include spending by some government agencies in this area nor does it include the costs incurred by industry to comply with the requirements of these programs and the costs incurred by consumers, so the actual costs are probably much higher. In a study of the total cost of regulation for all levels of government in Canada, the Fraser Institute estimated that compliance costs for the private sector ($103 billion in 1997/1998) were almost 20 times

larger than the governments' administration costs ($5.2 billion) (Jones and Graf 2001).

The Auditor General could not comment on the appropriateness of the health and safety expenditures "because performance measurement is weak, there is insufficient information to assess the cost-effectiveness of health and safety regulatory programs." To this point in the process of developing the new regulatory framework, there has been no data collection or performance monitoring system set up to capture the cost-effectiveness of the NHPD. The directorate states that it will do so after it gains some experience under the new framework.

A lack of human resources

In addition to its own assessment, the Auditor General's *Report* refers to a 1999 government assessment of human resource issues in regulatory organizations. The results of the two are consistent and reveal "an aging [inspector] population, many vacancies, few recruits and high attrition rates in some key areas."

SCH witnesses also pointed to what they perceived as a lack of expertise in Health Canada and its various branches to deal with the issues of NHPs such as determining their quality, safety and effectiveness, and monitoring the manufacturing practices of NHP producers. While Health Canada representatives who testified to the SCH denied this characterization of their department, according to the Auditor General, an analysis by the CFIA estimated a shortage of some "500 staff positions across all of the agency's inspection programs." Therefore, regarding the implementation of the proposed framework, more consideration must be given by the NHPD to personnel issues. The NHPD must ask itself how it expects to ensure that all of the proposed regulations will be followed once they are implemented. As well, it must consider ways in which to make sure that there will be consistent enforcement of the regulations across provinces—something many witnesses to the SCH said was currently lacking.

Timeliness in approving NHPs for sale and for acting on compliance concerns is also an important factor. According to the Auditor General's review of the CFIA, "the compliance actions were not sufficient to achieve the agency's goal because of limitations in legislation or a failure by the inspector to take more serious compliance action." The Auditor General also pointed to general findings for federal regulatory programs, including "inadequate information on the incidence of non-compliance and related consequences," "insufficient random inspections to detect and prevent incidents of non-compliance" and an "over-reliance on voluntary compliance with limited verification to demonstrate that this reliance is justified." It will be interesting to see what steps the NHPD takes to avoid these types of weaknesses in the execution of its regulatory framework.

Need for performance measures

Referring specifically to the CFIA, a relatively new government department whose experiences could be useful to the NHPD, the Auditor General noted that the CFIA's "progress toward good performance reporting has been slow and targets have been repeatedly missed." The CFIA's corporate business plan "is not adequate to allow Parliament and the public to later judge how well the agency has actually performed," stated the Auditor General. What assurances can the NHPD give that it will be any more successful at achieving its goals than the CFIA? What performance measures are in place? What public reporting mechanisms are in place?

Allocation of resources on the basis of risk

Since 1988, the Auditor General has "recommended that food inspection resources be aligned on the basis of risk" (Office of the Auditor General 2000: 25-15). The 2000 report stated that "without an overall assessment of risks and decisions on how much risk to accept, the agency cannot determine the number of resources it needs to adequately de-

liver its programs" (Office of the Auditor General 2000: 25-21). The CFIA responded to such criticisms, claiming that "the expectation of the Auditor General, to fully assess this sector in terms of potential hazards and levels of controls currently in place, is neither possible nor reasonable" (Office of the Auditor General 2000: 25-23). However, the CFIA and other national regulatory agencies, such as the NHPD, should at least attempt to adhere to the regulatory policy of the Government of Canada, especially since the cost of complying with regulations is up to 20 times that of administering them.

4 Regulation of prescription drugs and its relevance to natural health product regulation

The Standing Committee on Health stated that the primary objectives of any new natural health products regulatory framework must take into account the well-being of consumers: consumer health should be protected, consumers' access to products respected and product safety and quality should be guaranteed (SCH 1998).

In an apparent effort to meet these objectives, especially that of product safety, the regulatory framework being proposed by the Natural Health Products Directorate is based on a modified version of the existing regulatory framework for approving pharmaceutical drugs in Canada. This section evaluates this decision by examining the way in which drugs are regulated in Canada and several other countries. It looks at what drug regulations cost in terms of product and establishment licensing fees, and the time it takes a regulatory body to evaluate a new drug submission. As well, it discusses whether the current drug regulations prevent adverse reactions and describes some of the unintended consequences of a drawn-out drug approval process.

Cost of drug regulations

As previously stated, the Auditor General estimated that $1.2 billion was spent in 1999-2000 on administering major federal health and safety regulatory programs in Canada and this estimate does not include the costs incurred by the private sector (industry and consumers) as a result of these programs. It was these costs that were of much concern to many of the witnesses to the SCH. They were worried that the introduction of NHP regulations could confer an onerous cost burden upon businesses and consumers in the NHP market; compliance costs and user fees for businesses and higher prices for consumers.

Currently, Health Canada's Therapeutics Products Program (TPP) collects user fees for activities that are considered to have a private benefit, such as the drug review process, adverse reaction monitoring and for-cause inspections, and some post-marketing activities. The NHPD has stated that, at this time,

> no fees will be passed on for the reviewing and approving of licence applications. We recognize that in other areas of the government, and in many other countries, fees are applied for such reviews. If in the future we are required to explore cost recovery, we would do so after further consultation to ensure any impact on the NHP industry is minimized." (Health Canada March 2001a: 8)

Given that public discussion may be forthcoming on the topic of cost recovery by the NHPD, it is worthwhile to look at the current fee structure for drugs in Canada, and for drugs and other health products in various countries. The fees collected by the regulatory agencies in the countries examined ranges from roughly CDN$31.8 million in Australia to approximately CDN$212.9 million in the United States. (Bank of Canada; US Food and Drug Administration 2000: 1) Regulation is not costless.

Canada

The total federal health portfolio is estimated at $2.7 billion for 2001-2002.[6] Health Canada spends 84% of that amount, or $2.4 billion, with the TPP accounting for a net expenditure of $70.5 million (after cost recovery revenues are considered) (Health Canada 2000: 39).

The TPP has operated under partial cost recovery since 1995. The stated objectives of the policy are to promote more efficient use of government services and to foster more business-like and client-oriented practices in the supply of government services. As well, cost recovery applies to services from which a specific subset of the population, rather than the general public, mainly benefits.

According to the TPP, it collected $39.8 million in 1999/2000, which covers approximately 55% of total TPP expenditures (Health Canada February 2001: 2). Among the mandatory costs for drugs—those that are required by regulation—there are fees for the authority to sell drugs, for drug submission evaluation, and for establishment licenses.

The fee for the authority to sell drugs is an annual charge that ranges from $50 for any product with less than $20,000 in annual sales, to $1,000 for drugs listed in Schedule F (prescription-only) of the Food and Drugs Act. It currently costs $250 a year for the authority to sell homeopathic drugs (Health Canada, February 2001: 15).

A drug submission evaluation for simple administrative changes costs $250. A new drug submission that comprises preclinical and clinical data to support a single route of administration, dosage form, and condition of use is $117,000. Submissions comprising published references to support a traditional herbal medicine cost $720. The maximum fee in this category is 10% of the aggregate anticipated sales (Health Canada, February 2001: 16).

The TPP has different annual establishment fees for manufacturers, packagers and labellers, importers and distributors, and wholesalers and distributors. The basic fee for a manufacturer is $6,000 a year plus additional charges for dosage form classes and other categories, which range from $600 to $10,500. The basic packaging and labelling fee is $4,000 a year, plus additional costs ranging from $1,000 to $3,000. The fees continue to get lower in the other two groups. The maximum establishment fee is set at 1.5% of the gross revenue from the sales, testing, and packaging and labelling of drugs) (Health Canada, February 2001: 18).

Currently, NHPs are not subject to establishment licensing fees; however, as mentioned previously, if these fees were required, Health Canada estimates that they could amount to $2 million annually (SCH, 1998: chapter 9).

Australia

The Therapeutic Goods Administration (TGA) that enforces Australia's Therapeutic Goods Act operates on a full cost-recovery basis. In 1998/1999, the TGA collected AUS$40 million[7] from user fees but spent AUS$48 million administering the regulations (they covered the difference using reserves carried over from previous years) (US FDA 2000: 1).

As with other countries, the fees collected go toward the drug review process as well as post-market surveillance. There are more than 90 different fees. Application fees vary with the number of pages and can exceed AUS$150,000 (US FDA 2000: 1). Plant inspection fees are AUS$380 per auditor-hour.

In Australia, a medicinal product is either listed or registered. The listed category is for low-risk products used for minor conditions, while the registered category is for higher-risk products. The following fees are taken from the TGA's *Summary of Fees and Charges at 1 July 2001*.

The registration of a non-prescription medicine (over-the-counter and complementary medicine) entails application and processing fees of AUS$690 each and an annual charge of AUS$500. Then there is a AUS$4,580 evaluation fee per submission if the evaluation documentation does not contain clinical or toxicological data. For a variation of an existing registered medicine, the fee ranges from

AUS$1,650 to approximately AUS$32,000, depending on the page count; and the evaluation for a new product with accompanying data ranges from AUS$4,580 to almost AUS$32,000 per submission.

To list a non-prescription medicine carries a AUS$430 application fee or a AUS$210 processing fee for a variation to an existing listing, and a AUS$370 annual charge. In addition, there are GMP charges and annual GMP licence fees, which are listed as AUS$3,730 for herbal and homeopathic medicinal products.

Germany

There is limited information in English available from the Federal Institute for Drugs and Medical Devices (BfArM), which regulates medicinal product in Germany. Every substance in Germany is considered a medicinal product, whether it is an NHP or a pharmaceutical. However, there are fewer evidentiary requirements for products deemed to be of lesser risk. For the approval of a medicinal product requiring a prescription for use, a fee of DM110,800 ($80,108) is charged; for medicinal products containing known substances, the fee is DM23,000 ($16,629).

United Kingdom

The regulatory body in the United Kingdom is the Medicines Control Agency (MCA) and it operates under full cost recovery. In 1999/2000, the MCA collected £28 million[8] in fees while it spent £36 million, using carry-over revenue (US FDA 2000: 1).

There is a chart of more than 50 different fees that can apply to various aspects of the work associated with drug registration (US FDA, 2000: 1). As an example of the magnitude of the fees, product licences range from more than £1,885 for an abridged simple application to £69,127 for a major application. There are additional inspection fees and licensing fees.

Fees for the homeopathic registration scheme range from £113 if both the formulation and the stock have been assessed before (and there are fewer than five stocks) to £736, which is the standard fee for more than five stocks. Plus, there are periodic fees, which are applied per licence, per period, of £12 for a homeopathic registration and £62 for an herbal.

United States

The Food and Drug Administration (US FDA) is the body that interprets and enforces the Food, Drug and Cosmetics Act in the United States. The budget request for the US FDA for the fiscal year 2002 is US$1.4 billion, an increase of 9.5% over fiscal year 2001. The request includes US$204 million in industry-specific user fees.

Any new submission to the FDA must include an application along with a fee to pay for the review process. In addition, companies must pay an annual fee for each manufacturing establishment and for each prescription drug product marketed. In fiscal year 1999, the US FDA collected almost US$122 million, which covered almost half of the total cost of the FDA's drug review activities. There are four sets of fees faced by companies wanting to market a new drug in the United States. In fiscal year 2001, these costs were: full application fee with clinical data (US$309,647), half-application fee without clinical data (US$154,823), annual establishment fees for manufacturers (US$145,989) and annual product fees (US$21,892) (US FDA 2000: 1).

As most NHP-type products in the United States are sold as dietary supplements,[9] they are not subject to these drug-related fees. "There are no FDA fees for manufacturers or importers of dietary supplements, and the agency does not charge product fees. FDA does not have a procedure to register or approve manufacturers or importers of these products, and FDA does not charge a fee for inspections of manufacturing facilities."[10] The way in which the United States regulates dietary supplements is discussed in Section 4 of this study.

Lessons for Canada

Although the NHPD has stated that it will not charge GMP inspection fees, it is unlikely that this will be the enduring situation. Health Canada al-

ready has cost recovery measures in place for homeopathic and traditional herbal remedies, albeit they are less onerous than those in many other countries. But, countries that regulate NHPs as medicinal products—countries on which Canada seems to be modelling its treatment of NHPs—charge establishment or site licence fees. These fees are thousands of dollars and, even if the NHPD charges lower rates, they likely will still be substantial.

A detailed examination of the impact of such potential costs on the NHP industry should have been included in the regulatory impact analysis statement provided by the NHPD for its proposed regulatory framework. While the industry has been experiencing double-digit growth rates and the total market for natural health products likely far exceeds $1 billion, the composition of the industry is noteworthy:

> More than 70% of retailers in the natural health products industry have sales less than $500,000 a year and more than 70% of manufacturers have sales of less than $1 million … [However,] the very few large companies in the industry control a large share of the total market. This is markedly true for manufacturers where more than 50% of total manufacturing sales are controlled by less than 2% of the total number of manufacturers. (Strategic Policy Choices 1998: 4–5)

GMP inspection fees and other regulatory costs will have less impact on companies such as Natural Factors Nutritional Products Ltd.—which has a sales volume of more than $1 million, a research and development budget of more than $100,000 and more than 100 employees, and which is a subsidiary of Gahler Enterprises Ltd., a pharmaceutical company mainly—than for a company such as Herb Works, which has a sales volume of about $500,000, a research and development budget of approximately $5,000 and five employees (Agriculture and Agri-Food Canada). Such differences must be acknowledged, especially in efforts to include stakeholders in the decision-making process.

It should not be surprising that Roland Gahler, president of Natural Factors, in his written submission to the SCH, supported government initiatives to regulate GMPs "100%" and thought that consumers would be willing to pay more to have all industry standards upgraded (Gahler, 1998: 1–2). It should also not be a surprise that Richard DeSylva, owner and operator of Herb Works, in his testimony to the SCH stated:

> I would suggest, please, leave this industry alone. Let us self-regulate … if there needs to be warning at all, let it be put on the label that these products have not been evaluated by whatever, be it the Health Protection Branch or, who knows, another agency to replace them. (SCH 1997–1998, March 10)

The regulatory uncertainty that has existed for years now regarding NHPs is an impediment to the future of the industry. Many witnesses to the SCH spoke of Health Canada's uneven application of the rules and its flip-flop on several products (taking them off shelves one day only to allow them to be sold another day). Investors take these issues into account in their decision as to where to do business.

What is at stake—Canada's NHP industry

The NHP industry in Canada has great potential. A report prepared for Agriculture and Agri-Food Canada estimated that

> total sales for the natural health product retailers, distributors and manufacturers in 1997 were $680 million, $203 million and $362 million, respectively. Total employment for retailers, distributors and manufacturers was 10,400 (5,800 full-time/4,600 part-time), 2,950 and 5,250, respectively. (Strategic Policy Choices 1998: 4)

These estimates did not include the sales of NHPs in pharmacies, chain drugstores, and other businesses that do not sell them as their primary activity, neither did it include Internet sales.

The same report found that the outlook for employment growth is very positive: "Over the next five-year period, 92% of manufacturers expect a rise in employment, while 90% and 77% of distributors and retailers, respectively, expect an increase in employment (Strategic Policy Choices 1998: 6).

Looking at specific crops: some $35 million worth of ginseng root was grown in Ontario in 1991; $13 million worth of root and about $5 million worth of seeds in British Columbia in 1992 (Small and Catling 1999: 111). There are more than 1,000 cranberry growers in the United States, producing more than $1 billion in sales annually: "With a large potential area of cultivation in the eastern provinces and British Columbia, cranberry could become a much more important Canadian crop" (Small and Catling 199: 164–65). These are only two examples of medicinal crops that could flourish in this country.

Another study conducted for Agriculture and Agri-Food Canada in 1995, explored Canada's potential in the nutraceutical industry by surveying 45 companies. Nutraceuticals are products isolated or purified from foods and are generally sold in medicinal forms not usually associated with food; they have a physiological benefit or provide protection against chronic disease. (National Institute of Nutrition 2000: 3) An example would be any isolated, purified preparation of active food ingredients in dosage form, such as isoflavones from soy and ß-glucan from oat bran (National Institute of Nutrition, 2000: 2).

The survey conducted for Agriculture and Agri-Food Canada identified at least 65 nutraceuticals on the market at that time and 16 of the interviewees named approximately 40 potential nutraceuticals they were researching or intending to research in the future. Among the determinants of market potential listed was supportive legislation. The interviewees believed that consumer awareness is almost a "given" in the international arena and that the Canadian market is "smaller, has less volume potential and is less accessible than some foreign markets" (Culhane 1995: 6).

While the proposed new regulations will allow for health claims on approved NHPs, it will come with a price. Unfortunately, there has not been much research conducted on the effect of regulating NHPs as medicinal products akin to drugs—with less rigorous proof-of-efficacy requirements but with similar quality and safety requirements. For example, there was at least one witness to the SCH who claimed that many NHP manufacturers, labellers and packagers, and distributors went out of business after Australia tightened its regulatory requirements in 1989 with its Therapeutic Goods Act. However, inquiries to Australia's health authorities and to NHP associations and organizations revealed no evidence as to the validity of this claim and similar investigations for other countries found that this type of information is not being collected in any systematic way.

Regulations to protect consumers

The justification for much regulatory activity is the protection of consumers from unsafe products, from defective infant car seats to poorly made hockey helmets to contaminated or adulterated pharmaceuticals and NHPs. While protecting consumers is a noble aim, is a complex and costly regulatory system the best way in which to pursue it? Can complete safety—zero risk—be assured? As well, the concept of protection implies that people are in danger from something from which they need to be protected or saved: What is the threat to consumers' health from the use of NHPs?

Adverse reactions to drugs and NHPs

Despite the amount of regulation and the money spent on it, there are still adverse reactions to approved pharmaceutical drugs. In Canada, for instance, the TPP estimates that "over 51% of approved drugs have serious side effects not detected before marketing approval" (Hogan and Turner

1998: 2). Table 4.1 shows the number of reported adverse drug reactions in Canada, Australia, and the United Kingdom.

Canada fares well relative to Australia and the United Kingdom in that it has, by far, the lowest rates of reported adverse drug reactions. However, there are a few notes of caution regarding such comparisons: different reporting systems and different definitions of what constitutes an adverse reaction will contribute to the variation in ADR rates between countries. As well, the UK Pharmacovigilance Group of the Medicines Control Agency cautions that a report of an adverse reaction does not mean that the medicine or herbal remedy caused it. At a minimum, Table 4.1 shows that thousands of adverse reactions still occur even in the presence of strict regulatory measures, and that these numbers seem to be increasing.

The only country for which data has been collected for a number of years on adverse reactions to herbal preparations is the United Kingdom. Table 4.2 provides a comparison between the number of adverse drug reactions reported in that country and the number associated with herbal preparations. The data clearly show that the potential risk of herbal preparations to consumers' health is much lower than that posed by drugs. In 2001, adverse reactions to herbal preparations amounted to only 0.38% of all adverse reactions reported in the United Kingdom. For the six years from 1996 to 2001, this ratio never went over 0.5%.

The experience in Australia seems to parallel that of the United Kingdom in the one year for which there is data. In 2000, there were approximately 150 adverse reaction reports involving NHPs and 12,744 adverse drug reactions (Australian TGA, Adverse Drug Reactions Unit 2001). NHPs accounted for 1.16% of the total adverse reactions for that year.

More evidence of the relative safety of NHPs comes from the United States. Table 4.3 shows the number of health advisories, "Dear Health Professionals" letters, and other documents issued by the US FDA regarding safety concerns about biologics, dietary supplements, and pharmaceuticals from 1997 to June 2001. Dietary supplements represented 14% of the US FDA's safety advisories or information summaries in 1997 and 7.4% in 2001. In 2000, they represented less than 5%.

Statistics on poisonings in the United States support the view that NHPs are not substances that require extensive regulatory intervention. Table 4.4 shows the reports to American poison control centres for adverse reactions to certain types of drugs, homeopathic remedies and vitamins in 1998.

The number of poisonings reported as being related to Aspirin only is 13,854; if the number of poisonings from Aspirin in combination with other substances is added, the total increases to more than 20,000 exposures. However, looking at incidents with Aspirin only, to avoid additional interpretative complications, the total number of poisonings attributed to homeopathic and dietary supplements is about the same, at 13,722.

The number of cases that exhibited a major medical outcome—a life-threatening, disabling or disfiguring result from the exposure—were 744 for the homeopathic and dietary supplement category and 251 for Aspirin alone (in combination, almost 80 more major medical outcomes would be added). However, 45 people died from the reaction with Aspirin (plus another 10, approximately, from Aspirin combinations); there were 10 fatalities as a result of homeopathic or dietary supplements and two deaths from vitamins. While cough and cold preparations were responsible for almost 100,000 poison exposures, only 199 major reactions and five deaths resulted.

Adverse interactions between herbs and drugs

Adverse reactions from the NHPs themselves are only one health concern. As more and more people use NHPs, it becomes more likely that they will at some point in their life be taking both an NHP and a prescribed medication. There has been a large amount of data compiled on possible interactions between herbs and drugs and most of it is easily

Table 4.1: Reported adverse drug reactions (ADRs) in Australia, Canada and the United Kingdom, 1996 to 2000

	1996	*1997*	*1998*	*1999*	*2000*
Australia					
Total number of ADRs	8,649	9,527	10,909	12,833	12,744
Number of ADRs per 1,000 population	0.47	0.51	0.58	0.68	0.67
Canada					
Total number of ADRs	4,198	4,006	4,663	5,688	7,361
Number of ADRs per 1,000 population	0.14	0.13	0.15	0.19	0.24
United Kingdom					
Total number of ADRs	17,107	16,630	18,061	18,493	33,004
Number of ADRs per 1,000 population	0.30	0.28	0.30	0.31	0.55

Definitions: *Population* refers to the total number of people in a country. According to Canadian authorities, an adverse drug reaction (ADR) is "a noxious and unintended response to a drug which occurs at any dose and requires inpatient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death" (Canadian Food and Drugs Act). ADRs that are monitored include those resulting from the use of prescription, non-prescription, biological (including blood products), complementary medicines (including herbals) and radio-pharmaceutical drug products (*Canadian Adverse Drug Reaction Newsletter*, January1999).

Sources: The Adverse Drug Reactions Unit, Therapeutic Goods Administration (e-mail correspondence); Australian Bureau of Statistics Web site; *Canadian Adverse Drug Reaction Newsletter*, Therapeutic Products Directorate, Health Canada (July 2001, April 2000, April 1999, April 1998 issues); Statistics Canada Web site; The Pharmacovigilance Group, Post Licensing Division, Medicines Control Agency (e-mail); UK government Web site, http://www.statistics.gov.uk/statbase/xsdataset.asp and http://www.statistics.gov.uk.

Table 4.2: Reported adverse reactions to drugs and herbal preparations in the United Kingdom, 1996 to 2001

	1996	*1997*	*1998*	*1999*	*2000*	*2001*
Total number of adverse drug reactions	17,107	16,630	18,061	18,493	33,004	16,449
Number of adverse drug reactions per 1,000 population	0.30	0.28	0.30	0.31	0.55	0.28
Total number of adverse reactions to herbal preparations	36	46	40	60	138	63
Number of adverse reactions to herbal preparations per 1,000 population	0.0006	0.0008	0.0007	0.0010	0.0023	0.0011
Adverse reactions to herbals as a percent of total adverse reactions (to drugs and herbals)	0.21%	0.28%	0.22%	0.32%	0.42%	0.38%

Definition: *Population* refers to the total number of people in a country.

Note: The number of ADRs reported in 2000 is not consistent with the trend from 1996 to 2001 and the data for that year should be considered suspect.

Sources: Pharmacovigilance Group, Post Licensing Division, Medicines Control Agency, London, England, e-mail correspondence (Nov. 5, 2001); UK government Web sites, http://www.statistics.gov.uk/statbase/xsdataset.asp and http://www.statistics.gov.uk (as of Dec. 15, 2001).

Table 4.3: MedWatch Safety Information Summaries, 1997 to 2001

(Number of "Dear Health Professionals" letters, public health alerts, FDA Talk Papers, etc., issued by the US Food and Drug Administration regarding biologics, dietary supplements, and drugs. Includes multiple advisories for some products and some products fall into more than one category.)

	1997	*1998*	*1999*	*2000*	*June 2001*
Biologics	3	6	14	28	3
Dietary Supplements	6	3	4	3	2
Drugs	34	28	25	31	22
Total	43	37	43	62	27

Source: *US Food and Drug Administration MedWatch Safety Information Summaries*, 1997 to June 2001, http://www.fda.gov/medwatch/safety/.

Table 4.4: Reports to US poison control centres for adverse reactions to selected drugs, homeopathic remedies and vitamins, 1998

Substance Implicated in the Exposure	*Number of Exposures*	*Medical Outcome**		
		None	*Major*	*Death*
Aspirin only (adult, pediatric and unknown formulations but not in combination with other substances)	13,854	3,886	251	45
Antidepressants (ex. Amitriptyline, Imipramine, Lithium)	70,060	17,788	3,104	153
Cardiovascular drugs (ex. Beta blockers, antihypertensives)	43,856	16,904	886	127
Cough and cold preparations	99,873	27,445	199	5
Homeopathic and/or dietary supplements	13,722	3,008	744	10
Cocaine	4,286	643	374	70
Marijuana	1,930	164	65	0
Vitamin A	1,555	358	2	0
Vitamin C	2,470	540	1	0
Vitamin E	1,869	423	1	0
Vitamins as a whole (multivitamins, and vitamins A, B3, etc.)	48,741	13,494	26	2

***Note:** Medical outcome data were also collected in categories labelled "minor," "moderate," "unknown, potentially toxic," "unknown, nontoxic" and "unrelated effect," therefore the numbers listed here do not represent the total poison exposure experience.

Source: American Association of Poison Control Centres annual report, 1999.

accessible and from reliable sources. Table 4.5 includes seven of the more well-respected publications on herbals, the number of herbs they describe and the number of herbs that react with drugs.

Many of the herb-drug interactions are positive, with the herb enhancing the beneficial effects of the drug or reducing the drug's side effects; while about the same number enhance the negative side effects of the drug. There are, however, life-threatening interactions as well. Table 4.6 outlines the potential severity of herb-drug reactions.

Given the plethora of information on herbal remedies, it is hard to see what the Canadian government would add in this regard by its proposed regulatory policy. The American Botanical Council (ABC) has even translated the German health department's Commission E monographs; they comprise detailed data on hundreds of herbs. The ABC has published the *Botanical Safety Handbook* that explains more than 500 herbs.

Another ABC publication is Popular Herbs in the US Market: Therapeutic Monographs which, as its name suggests, looks at some of the more popular herbs being sold. For example, there is a monograph on St. John's wort, which is used both internally to help with depressive moods and externally as treatment and post-therapy of acute injuries and contusions. The ABC book lays out the uses, dosage, contraindications, interactions with other drugs—it should not be used at the same time as prescription antidepressants—as well as information on the mode of administration, duration of use, regulatory status in other countries, and additional comments.

Hawthorn berries, used to treat coronary complications and disease, are also in this publication. Under regulatory status, for Canada, it reads: "New drug status; not approved as self-treatment for cardiovascular conditions, is deemed inappropriate" (Blumenthal 1997: 47). While there are warnings about Hawthorn's possible effects on cardiac rate and blood pressure and it is recommended that pregnant women refrain from using it, there are no known interactions with conventional drugs and the Commission E does not note any adverse side effects of Hawthorn.

The benefits and hazards of using NHPs are becoming increasingly well-documented. There is the ABC, http://www.pdr.net (a Web site run by Medical Economics Company Inc., which publishes the *Physician's Desk Reference*), the World Health Organization monographs, Germany's Commission E monographs and many others that provide consumers with a lot of valuable information. They even give the recommended dosages so that people can check the bottle of echinacea they are purchasing to make sure that there is enough active ingredient in it for the NHP to have an effect. They do not provide any way of ensuring that what is in the bottle is what the label says is in the bottle but there are laws in Canada already against the fraudulent labelling and adulteration of foods and drugs. As well, consumers who use a certain brand name and find it ineffective can try another. There are dozens of cough and cold remedies, painkillers, vitamin pills, and other over-the-counter medications from which consumers already have to choose; many vary in their effectiveness. Other than the permitting of some form of health claim—which is not currently allowed for "foods"—government regulation cannot (and should not) change this situation, as private, independent suppliers of these products are responding adequately to consumers' demand for information.

Risk tolerance

The main justification for the regulation of NHPs is that more and more Canadians are using such products to self-medicate or improve their quality of life. None of the regulations proposed by Health Canada, from the 1992 effort to prohibit certain herbs from being sold as foods to the NHPD's current proposals for a regulatory framework, includes a discussion of risk tolerance. What is an "acceptable level" of risk and to what risks should scarce financial and human resources be dedicated?

Table 4.5: Numbers of interactions between herbs and drugs reported by various sources

Publication	*Number of herbs described*	*Number of herbs with interactions*
American Herbal Products Association's Botanical Safety Handbook	540	11
Herb Contraindications and Drug Interactions	207	79
British Herbal Compendium	84	17
European Scientific Cooperative on Phytotherapy (ESCOP) Monographs on the Medicinal Use of Plant Drugs	60	15
The Complete German Commission E Monographs	308	35
Herbal Medicine – Expanded Commission E Monographs	107	42
World Health Organization Monographs on Selected Medicinal Plants	28	14

Source: Mark Blumenthal, "Interactions between Herbs and Conventional Drugs: Introductory Considerations," *HerbalGram* 49 (2000): 52–63.

Table 4.6: Potential severity of reactions between herbs and drugs

Severity of interaction	*Number of interactions*	*Percentage of total interactions*
Beneficial effects or reduction of drug side effects	18	17.0
Innocuous effects	28	26.4
Production of disease or enhancement of side effects	18	17.0
Threat to life through interaction with dangerous drugs	42	39.6
Total	106	100

Source: Mark Blumenthal, "Interactions between Herbs and Conventional Drugs: Introductory Considerations," *HerbalGram* 49 (2000): 52–63.

Table 4.7 shows various death rates for Canada and the United States. It includes deaths from medications, as well as deaths from motor vehicle accidents, accidental falls, and other causes.

Either implicitly or explicitly, the federal government, Health Canada and the Canadian public (in their demand for government regulation) seem to accept the fact that there were 1,197 deaths in 1997 attributed to accidental or purposeful poisoning by drugs, medicaments, and biologicals (table 4.7) and that there were 7,361 reports of adverse drug reactions in 2000 (table 4.1). Motor vehicle accidents and accidental falls claim more lives per year than poisoning by drugs or NHPs in Canada. Given that the limited data available seem to indicate that deaths or adverse reactions due to NHPs are much fewer than those for drugs, how much should be spent on further reducing the risks to Canadians from NHPs?

Ten deaths were attributed to poisonings from homeopathic remedies or dietary supplements in the United States in 1998. The highest number of adverse reactions from NHPs was the rough estimate from Australia of 150 reactions in 2000. Even assuming a worst-case scenario that the number of deaths in Canada from NHPs would equal that of the United States, despite our much smaller population, spending $2.3 million-plus a year[11] to save 10 lives is about $233,333 per life. Taking the Australia figure as an estimate of the adverse reaction rate that Canada experiences (but doesn't keep track of), a $2.3-million-a-year NHPD translates into about $15,556 per adverse reaction avoided.

Drug lag

Even if it were determined that spending $15,556 to save someone from an NHP poisoning is value for money, there is another aspect of regulation that needs to be considered. More onerous regulations tend to mean that approval times for products take longer, hence the product takes longer to reach the marketplace. As there are potential costs to rushing the approval process (in terms of safety and other concerns), there are also costs to delaying it (lives that could have been saved or improved if the drug had been publicly available). There has been no attempt by the NHPD to weigh these costs—using as a proxy the delays that exist in the drug review process—in its decision to regulate NHPs.

The 2000 Auditor General's report pointed to delays in getting new drugs approved by Health Canada:

> For new biological drugs approved in 1999, the department took an average period of 328 days (compared with a performance target of 180 days) to review priority-status submissions and 545 days (compared with a performance target of 300 days) to review non-priority status submissions. (Office of the Auditor General 2000: 24–26)

In the United States, there have been attempts to quantify the costs of this so-called drug lag.

The human cost of drug lag

As do most regulators, the US FDA has an incentive to be overcautious in its approval of new medications and medical devices. A mistake by the agency can result in highly visible victims and severe political repercussions. On the other hand, if the FDA delays or denies a needed therapy, there may be many more people hurt; they, however, are politically invisible. According to the Cato Institute, "by a conservative estimate, FDA delays in allowing US marketing of drugs used safely and effectively elsewhere around the world have cost the lives of at least 200,000 Americans over the past 30 years" (Cato Institute 1997).

Using FDA data, the Competitive Enterprise Institute (CEI) estimated, in 1995, that up to 3,500 kidney cancer victims died waiting for the FDA to approve Interleukin-2, a process which took three and one-half years even though the drug had already been approved in nine European countries. The institute also calculated that the two-year

Table 4.7 Comparison of selected causes of death in the United States and Canada

	Total number of incidences
Deaths in the United States (1998) attributed to ...	
Non-error, adverse effects of medications	106,000
Medication errors in hospitals	7,000
Motor vehicle accidents	43,458
Breast cancer	42,297
AIDS	16,516
Workplace injuries	6,000
Homeopathic/dietary supplement poisoning	10
Deaths in Canada (1997) attributed to ...	
Poisoning from drugs, medicaments and biologicals	1,197
Motor vehicle traffic accidents	2,867
Accidental falls	2,622
Inhalation and ingestion of food or other objects causing obstruction of respiratory tract or suffocation	252

Sources: Deaths per year from medications in the United States are from Barbara Starfield, *Journal of the American Medical Association* 284, 4 (July 26, 2000); US figures for deaths from motor vehicle accidents, breast cancer, AIDS and workplace injuries are from Institute of Medicine, To Err Is Human: Building a Safer Health System (National Academy of Sciences, 2000); US Homeopathic/dietary supplement poisoning are from American Association of Poison Control Centres annual report, 1999. Canadian death statistics are from Statistics Canada, *Mortality—Summary List of Causes, 1997* (Ottawa: Health Statistics Division: Ottawa, July 1999).

approval process for Streptokinase, a drug used for blood clots in heart-attack victims, took 22,000 lives; the nine-month drug lag for Misoprostol (used to stop gastric ulcer bleeding) claimed 8,000 to 15,000 victims (DeFalco 1995: 4). The CEI maintains that, despite stricter regulations for drugs in the United States,

> there has not been any corresponding increase in safety or efficacy of the drugs that have been approved. Even after companies spend millions of dollars on testing, there is always the possibility that the drug or device will be sent back two or three times. Consequently, large drug companies have an advantage over smaller companies with less cash and less ability to wait for several years. (DeFalco, 1995: 4)

In a 1985 article in the *Cato Journal*, Dale Gieringer estimated the net loss of life from the FDA approval lag, as well as the number of lives lost from new drugs. He estimated that the benefits of FDA regulation lie in the range of preventing 5,000 to 10,000 casualties per decade. The cost, however, of FDA delay ranged from 21,000 to 120,000 lives per decade.

Drug lag and natural health products

The relevance of the drug lag to natural health products regulation is that the same lag that now affects the approval of drugs will likely affect the approval of NHPs, given the regulatory framework being proposed by the NHPD. Based on the discussion of the situation in the United States, there are two main concerns for Canada: the financial costs to NHP manufacturers and others, of complying with the regulations and the human cost that may result from an NHP lag (or from the NHPD not approving certain products).

Financial costs

Many of the witnesses to the 1997–1998 Standing Committee on Health voiced fears that smaller manufacturers of natural products would be put out of business if NHPs were regulated as strictly as drugs. The NHPD response to this concern has been vague: "we are working with the industry in the development of the regulatory framework, to ensure it is not overly burdensome or does not result in inappropriate expenses for manufacturers" (Health Canada, March 2001: 8). Efforts by Health Canada to quantify the costs to industry of proposed regulations have been equally nebulous, as has been discussed in Section 2.

Human costs

While NHPs are generally considered to be health-enhancing rather than life-saving remedies, there are substances that have been shown to increase a sick person's chance of survival and there are others that have been shown to reduce the risk of debilitating diseases or birth defects significantly.

Gieringer, in his 1985 article in the *Cato Journal*, also made reference to the regulatory state of vitamins and minerals in the United States at that time:

> In recent years, there has been growing evidence that certain vitamins and minerals may have significant potential for blocking cancer. While the evidence is far from certain, it seems possible that substantial benefits could be obtained from prophylactic use of vitamins and minerals as dietary supplements. Vitamins and minerals are presently [1985] classified as "food supplements" and are exempt from drug regulation … However, it is illegal for manufacturers to make any reference to possible health benefits of vitamins without becoming subject to new drug application approval requirements for proof of efficacy. In prohibiting the advertising of possible anticarcinogenic benefits of vitamins and minerals, present regulations may be having a substantially adverse effect on consumer education and health. For example, *assuming* [emphasis added] that food supplements could reduce risk of cancer by 10 percent, some 3,500 per year could be saved if only 10 percent of the population were persuaded to take them. (Geiringer 1985: 191)

While vitamins and minerals are now considered as dietary supplements in the United States and, therefore, are permitted to make certain health claims—such as "supplement *A* supports the immune system"—this did not happen until 1994. If one looks at the approximately nine years from 1985, when Gieringer wrote his article, to when the Dietary Supplement and Health Education Act was passed, this would mean that some 31,500 cancer victims could potentially have been saved, depending on the accuracy of his initial assumption and assuming that the risk of contracting cancer has not changed over the years.

Another quick illustration would be the use of folic acid,[12] which has been shown to reduce the risk of women giving birth to babies born with a neural tube defect (NTD), such as spina bifida.[13] About 400 babies are born each year with an NTD in Canada, a rate of approximately one per 1,000 births. It is estimated from various studies that folic acid in a vitamin supplement, when taken one month before conception and throughout the first trimester, reduces the risk for an NTD-affected pregnancy by 50% to 75%.

The National Institute of Nutrition (NIN) is a Canadian organization that provides a link between nutrition science, consumers, government and industry. It has conducted research projects for the federal government. On its Web site (http://www.nin.ca) is an abundance of information on many topics, including folic acid. According to the NIN, it was as early as 1964 that

> it was suggested that sub-optimal maternal folate status increased the risk of an NTD-affected pregnancy. During the subsequent decades, several investigations examined the role of periconceptual folate supplementation in the primary occurrence and recurrence of NTDs. Only one study failed to support the protective effect of folic acid-containing vitamin supplements against the first occurrence of NTD. (National Institute of Nutrition 1993)

But, it was only after a couple of clinical trials in the early 1990s that folic acid's benefits were recognized by the Canadian and American governments; a British trial, the results of which were published in the *Lancet* in 1991, and a Hungarian controlled study, the results of which were published in the *New England Medical Journal* in 1992. Since 1992 in the United States and 1993 in Canada, the recommendation in both countries is that women of childbearing age should take 400 mcg (0.4 milligrams) of synthetic folic acid daily. However, manufacturers are still not permitted to make health claims on foods (or NHPs) linking folic acid to the reduced risk of having a child born with a NTD.

Assuming, as did Geiringer, that 10% of pregnant women could be persuaded to take the recommended amount of folic acid if a health claim were permitted, 20 to 30 Canadian babies a year could be spared a neural tube defect.[14] This estimation is for one ailment only and for one type of NHP only. Nonetheless, using the higher-end estimate of 75% of NTDs prevented, the number of babies who could potentially be saved from a debilitating defect is almost half of the total number of adverse reactions to *all* herbal preparations in the United Kingdom in 2001, which was 63. Both estimates are greater than the number of poisoning deaths attributed to dietary supplements in the United States in 1998.

While obviously a rough calculation that entails many assumptions, it is meant to provide a broader basis for discussion about the regulation of NHPs. Many Canadians want to be assured of safety and they believe that numerous and strictly enforced regulations are the way to achieve this ideal of zero risk. However, a scenario in which no one gets sick and no one dies does not exist. There are always trade-offs to consider. In saving two people from being poisoned to death by vitamins, we may, in effect, be "killing" 3,500 others, in that they die of cancer while vitamins are going through the NHP approval process.

5 Regulation of natural health products in other countries

In addition to hearing from Canadian individuals, associations, and businesses, the SCH heard from international witnesses. Specifically, representatives from the regulatory agencies of Australia, Germany and the United Kingdom addressed the committee, explaining how NHPs were regulated in their respective countries. As well, there were witnesses from American firms and organizations. This section looks briefly at the regulatory framework in these countries, the European Union as a whole, as well as at some of the initiatives being coordinated by the World Health Organization.

World Health Organization

Many developed countries have shown a growing interest in alternative or complementary systems of medicine and many developing countries rely more on traditional than on Western medicine. The result has been an increase in international trade in herbal medicines and other types of traditional remedies. From this, the World Health Organization concludes that a stimulus exists to assess and rationalize practices.

Definition of an herbal medicine

WHO defines an herbal medicine as a finished, labelled medicinal product that:

> contains as active ingredients aerial or underground parts of plants or other plant material or combination thereof, whether in the crude state or as plant preparations. Plant material also includes juices, gums, fatty oils, essential oils and any other substances of this nature. Herbal medicines may contain excipients in addition to the active ingredients. Medicines containing plant material combined with chemically defined active substances, including isolated constituents of plants, are not considered to be herbal medicines. (Upton 2001: 2)

WHO has produced several publications on this topic, including *Regulatory Situation of Herbal Medicines: A Worldwide Review* and *Guidelines for the Appropriate Use of Herbal Medicines*. In addition, WHO itself has produced 28 monographs on selected medicinal plants and more than 30 monographs are being prepared. According to WHO, their purpose is to provide scientific information on the safety, efficacy and quality control of widely used medicinal plants; to facilitate the proper use of herbal medicines; to provide models for member states to develop their own monographs on these and additional herbal medicines; and to facilitate information exchange.

Use of herbal medicines

WHO recognizes that plants have been used for health and medicinal purposes for thousands of years and that they are still an integral part of health care:

> It is estimated that 35,000 to 70,000 species have, at one time or another, been used in some cultures for medicinal purposes. A majority of the world's population in developing countries still relies on herbal medicines to meet its health needs … Medicinal plants are important sources for pharmaceutical manufacturing. Medicinal plants and herbal medicines account for a significant percentage of the pharmaceutical market. (World Health Organization Regional Office for the Western Pacific [WHO ROWP] 1998: 1)

Regulatory environment

While WHO is not a regulatory body, they have produced guidelines that the organization would like countries' regulatory bodies to follow. Despite the relatively safe use of herbal medicines for centuries, WHO notes that herbal medicines are not always safe because they are natural:

> Some have given rise to serious adverse reactions and some contain certain chemicals that may produce long-term side effects such as carcinogenicity and hepatoxicity. Herbal medicines will only benefit the health of human beings when they are used appropriately. Thus, good quality control and standardization of herbs is essential. Furthermore, with the increased use of both herbal medicines and modern western pharmaceutical drugs, there is a need to monitor reactions. (WHO ROWP 1998: 3)

WHO recommends that, in most cases, the use of herbal medicines be guided by qualified practitioners and that people not be left to self-medicate. There are 10 items WHO considers important for governments to include in any regulatory policy (WHO ROWP 1998: 10–13):

(1) recognize the role of herbal medicine in the health-care system;

(2) support the appropriate use of herbal medicine;

(3) improve the training requirements for practitioners and regulators;

(4) establish a framework to oversee the manufacture, processing, storage, distribution, sale, import, export and use of herbal medicines;

(5) set the direction and priorities of research and development;

(6) address the need for, and mechanisms to ensure, a reliable supply of quality herbal medicines;

(7) subscribe to the conservation of medicinal plants, especially endangered species;

(8) identify the cost of any national program and the expected sources of funding ("The cost-benefit of the national herbal medicine policy and program *may* [emphasis added] need to be identified.");

(9) facilitate international cooperation, especially on technical issues; and

(10) monitor and evaluate the national herbal medicines policies.

WHO also details the information that governments should require for the issuance of product licences, for the meeting of GMPs and for other aspects of the regulatory process. These requirements are as rigorous, or even more so, than those being proposed by Canada's NHPD.

Australia

The major legislation dealing with the regulation of therapeutic goods in Australia is the Therapeutic Goods Act 1989 and the Therapeutic Goods Regulations 1990.[15] Most therapeutic goods (medicines and medical devices) are required to be approved and included on the Australian Register of Therapeutic Goods before they can be supplied.

According to the health department, the Therapeutic Goods Act 1989 and associated regulations establish a uniform, national system of regulatory controls to ensure the quality, safety, efficacy and timely availability of therapeutic goods for human use. Responsibility for the regulatory control lies with the Therapeutic Goods Administration (TGA) and the department exerts this control using three main processes: the pre-market evaluation and approval of products, the licensing of manufacturers, and post-market surveillance. In general, therapeutic goods intended for human use must be included in the Australian Register of Therapeutic Goods (ARTG) and, as discussed in Section 3, the TGA

must recover its expenses fully. Therefore, there are various fees charged to those who wish to produce or supply therapeutic products.

Definition of complementary medicine

Complementary medicines (also known as traditional or alternative medicines) include vitamin, mineral, plant or herbal, naturopathic and homoeopathic preparations, and some aroma therapy products. Schedule 14 of the Therapeutic Goods Regulations contains a list of the type of substances or products covered by the term complementary medicines.

Use of complementary medicine

According to the TGA, more than 60% of Australians use at least one complementary health-care product per year, including vitamin and mineral supplements as well as herbal products. Australians spend about AUS$900 million (CDN$716.4 million) per year in the complementary medicines sector: AUS$621 million is spent on complementary medicines and AUS$309 million on complementary therapies.

Also according to the TGA, in both Australia and America, the person most likely to use complementary health-care products is female, aged between 30 and 50 years, has tertiary qualifications, earns more than AUS$50,000 a year and is employed in a professional or managerial position. The two main reasons given for turning to complementary health-care products are that they are natural alternatives or users are dissatisfied with other treatments. The most common reason given for using complementary medicines was to prevent illness, in particular to avoid respiratory conditions, such as colds.

Regulatory environment

Any product that is regarded as being a therapeutic good (with a few exceptions) must be entered on the ARTG before it can be supplied in Australia. This applies equally to complementary, prescription, and other over-the-counter remedies. All therapeutic goods supplied in Australia are required to meet GMP standards, even if they are manufactured in another country. Australian manufacturers must be licensed to perform manufacturing of the type proposed.

The ARTG's listed category is for those products made with low-risk ingredients that may be used only for minor, self-limiting conditions. Listed medicines only contain well-known established ingredients, usually with a long history of use, such as vitamin and mineral products or sunscreens. Sponsors must hold appropriate evidence to support claims they make about their products (self-assessment). Listed products are identified by an AUST L number.

Medicines assessed as having a higher level of risk must be registered (not listed). Also, there is a list of serious diseases, disorders and conditions about which claims may be made only after evaluation of the product and any claims through registration of the product. The definition of a serious disease, disorder, or condition is one that cannot or should not be diagnosed or treated except under medical advice. The registrable disease list includes infectious diseases, including sexually transmitted diseases, cardiovascular diseases, insomnia, musculoskeletal diseases, endocrine diseases and conditions, respiratory diseases, and so on.

Registered medicines are evaluated as either high-risk (prescription) or low-risk (non-prescription). Registration applications undergo a rigorous and detailed scientific evaluation, with sponsors required to provide comprehensive safety, quality, and efficacy data. All medicines that are registered must display an AUST R number on the label as proof of registration.

Complementary medicines may be either listed or registered, depending on their ingredients and the claims made. Most complementary medicines are listed in the ARTG.

The evaluation of medicines and medical devices for safety, quality, and, where appropriate, efficacy is undertaken by the TGA with advice from expert committees as required. Sponsors

of products carry the primary responsibility to ensure that claims made about products are true, valid, and not misleading, under the self-assessable listing system for medicines. However, should a question arise about the appropriateness of evidence supporting a claim, the final evaluation of that evidence will be made by the TGA. Claims that are included in the ARTG at the time of listing or registration are not automatically approved for use in advertising, as registrable claims may require recommendation from the Therapeutic Goods Advertising Code Council for approval.

In certain circumstances, individuals may be granted permission to use medicines that have not yet been approved for entry in the ARTG under the Special Access Scheme (SAS). Arrangements can be made to provide a three-month supply of an unapproved therapeutic good for a single patient, on a case-by-case basis.

Europe

The general situation in Europe, with the European Union, is that there is an attempt to harmonize regulations surrounding herbal medicines and other natural health products. As a result, regulation will likely become stricter, rather than more lax. There is recognition that there are many well-known, traditionally used medicinal plants that have only slight pharmacological effects and, therefore, likely have few serious side effects. However, the focus is on a scientific approach to the assessment of a natural health product's safety, efficacy and quality. Most traditional[16] medicines must carry a disclaimer, such as "This product is traditionally used for … If symptoms persist, see your physician."

If claims of illness prevention or treatment are made, most countries classify the natural product as a medicinal product and regulate it as such, requiring clinical studies or bibliographic evidence as proof of efficacy and support for the product's traditional use and safety record. In most of the countries that accept bibliographic references in the herbal medicine licensing process, ESCOP (European Scientific Cooperative on Phytotherapy), *European Pharmacopoeia* and WHO monographs may be used as a summary of bibliographic data. As well, most regulators consider material from the EMEA (European Medicines Evaluation Agency) Ad Hoc Working Group as a recognized bibliographic source. All countries require manufacturing according to GMPs (for finished products, not raw material suppliers) and adverse reactions are tracked by pharmacovigilance programs.

The move toward harmonization in Europe has been slow. While most countries regard NHPs as medicinal products, there are large differences in how they classify the products, grant licences for them, determine efficacy and treat retail distribution. The example often given in the literature is that garlic (allium sativum) is licensed for coughs and colds in Germany and for the prevention of arteriosclerosis in the United Kingdom. So far, only three products have been approved for consistent indications throughout Europe: two psyllium (Ispaghula) husk products and one valerian root preparation (Upton 2001: 16; Valverde 1998: 60).

Germany

In January 1978, the Second Medicines Act came into force, setting new standards for the granting of marketing authorization. Under this new regulation, proof of quality, safety and efficacy became an essential pre-condition for the registration of medicines, including herbals.

To meet the requirements of the act, the German authorities were obliged to carry out a review process. The two steps of the procedure were first a review of active principles, which resulted in monographs, and, second, a product-specific verification of pharmaceutical quality and conformity with the published monographs. The concept underlying the procedure was to establish clear, *a priori* criteria for active ingredients and to make it transparent to industry which products would

have a chance to be authorized. The review of herbal remedies was done by a pluridisciplinary commission of experts, called Commission E, with pharmacists, pharmacologists, toxicologists, clinical pharmacologists, biostatisticians, medical doctors from hospitals, and general medical practitioners. This commission was responsible for the evaluation of more than 300 medicinal plants and these monographs cover most of the ingredients of industrially prepared herbal medicines on the market (World Health Organization 1998: 14–15).

The monographs formed the basis for the marketing authorization and review decisions of the Federal Institute for Drugs and Medical Devices. The so-called "positive monograph" covered all relevant indications for the package leaflet or consumer information, such as composition of the drug, indications, contraindications, warnings and dosage. There were also a substantial number of "negative monographs," where there were risks from active ingredients or an absence of reasonable proof of efficacy, and marketing authorizations of a number of herbal remedies were withdrawn or modified because of serious risks to public health (WHO 1998: 15).

The work of all review commissions, including Commission E, regarding the evaluation of bibliographic data and the preparation of monographs was finished with the fifth amendment of the Medicines Act. The main reason for "finishing" the process was that most of the relevant active principles were covered by monographs and the remaining products could be assessed more economically on a case-by-case basis. The commissions are now advisory boards to the health authority in making decisions on the registration of new drugs and in the individual assessment of medicinal products already on the market (WHO 1998: 15).

Definition of an herbal medicine

In terms of legal status, herbal medicines are considered as medicines or drugs. Herbal medicinal products contain as active ingredients only plants, parts of plants or plant materials, or combinations thereof, whether in crude or processed form. Chemically defined, isolated constituents of herbal origin (such as menthol or digitoxin) are not classified as herbal medicinal products (Valverde 1999: 72).

Use of herbal medicines

According to the World Health Organization's *Regulatory Situation of Herbal Medicines: A World Review,* the German herbal medicines market was worth some US$1.7 billion in 1989, which was equal to 10% of the total pharmaceutical market in Germany. Estimates of drug sales in West Germany indicate that herbal remedies made up 23% of the nonprescription market, or US$2.5 billion, in 1994 (Keller 1996: 938).

WHO's *Regulatory Situation of Herbal Medicines* also cites a representative study carried out by the Allensbach Institute among the German population in June 1989. It showed 58% of the population had taken such remedies, 44% of them within the previous year. It could also be shown that, over the years, the number of younger people using natural medicines had increased significantly. According to the Allensbach study, natural medicines were generally considered to be more harmless than chemical drugs.

Regulatory environment

The Federal Institute for Drugs and Medical Devices, Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), is responsible for the assessment of medicines and the verification of submitted dossiers with respect to quality, safety, and efficacy. As previously stated, there is a fee charged for the approval of a prescription medicinal product and for products containing known substances.

For well-known substances such as herbal medicines, bibliographic data and monographs such as those developed by the Commission E constitute acceptable evidence of safety and efficacy. Homeopathic products that make no claims need registration only, rather than BfArM approval, provided that adequate quality is demonstrated. There are

no differences between the GMP requirements for herbal medicinal products and pharmaceuticals, and product authorization for all medicinal products is limited to five years.

In August 1994, the fifth amendment of the German Medicines Act became effective. It provides a new procedure with respect to proof of quality, safety, and efficacy, widening the scope of existing legislation for products already on the market, including herbal medicines. Traditional usage instead of reasonable proof of efficacy is accepted for a certain category of products, mostly sold outside pharmacies. Many products with a negative assessment by Commission E are included in this regulation. All these products have to be labelled as "traditionally used." The BfArM has compiled lists stating which preparations are allowed to refer to this regulation and which traditional indications can be claimed. "Non-traditional" indications will be admissible as before, provided that these are based on monographs or on individual clinical studies with defined preparations (WHO 1998: 16).

Herbal medicines are distributed through over-the-counter sales in pharmacies and other distribution channels and on medical prescription through pharmacies. They are reimbursable by the health insurance system unless special criteria for their exclusion apply. For example, specified indications such as common cold or laxatives, or substances with a negative assessment by Commission E (WHO 1998: 14).

United Kingdom

The requirements of the licensing system in the United Kingdom are set out in the Medicines Act 1968. The Medicines Control Agency (MCA) has the main responsibility of interpreting and enforcing the act. It has been operating under full cost-recovery since the early 1990s.

Without the appropriate licence, it is an offence to manufacture, sell, supply, export, or import a medicine into the United Kingdom. However, exemptions from licensing for certain herbal remedies are contained in the Medicines Act. A plant-based remedy does not require licensing if the plant has been subjected only to minimal processing, such as drying and crushing, in the production of the remedy; if the remedy is sold or supplied by its botanical name with reference to the process of manufacture; and if it is sold or supplied without any written therapeutic recommendation (WHO 1998: 23). St. John's wort, for example, is not licensed in the United Kingdom and, therefore, cannot make claims, despite much research as to its effectiveness in treating certain conditions and evidence of contraindications with some conventional drugs. (House of Lords 2000: chapter 5.91).

Even those herbal remedies that are exempt from the regulation to obtain a market authorization (licence) are considered to be medicinal products and, therefore, they are regulated as such with respect to labelling, advertising, and so on.

Definition of a herbal medicine

The Medicines Act defines a herbal remedy as a

> medicinal product consisting of a substance produced by subjecting a plant or plants to drying, crushing or any other process, or of a mixture whose sole ingredients are two or more substances so produced, or of a mixture whose sole ingredients are one or more substances so produced and water or some other inert substance. (Valverde 1998: 74)

Use of herbal medicines

A telephone survey conducted for the BBC in 1999 found that 34% of respondents had used herbal medicine in the 12 months prior to the interview; 17% had used homeopathy (House of Lords 2000: chapter 1.17). The Royal Pharmaceutical Society of Great Britain, in a submission to the House of Lords committee on science and technology, cited a 1999 report that estimated retail sales of complementary medicine (herbals, homeopathic preparations, and

aromatherapy essential oils) to be £93 million in 1998: £50 million from herbals, £23 million from homeopathy, and £20 million from essential oils. The report also showed that total revenue was up 50% from 1994 and that overall retail sales were predicted to reach £109 million in 2000 and £126 million in 2002 (House of Lords 2000: chapter 1.20).

The Royal Pharmaceutical Society and the Proprietary Association of Great Britain contend that the total annual sales of herbal products (retail, direct sales, Internet sales, and mail order) was as much as £240 million a year (House of Lords 2000: chapter 5.86).

Regulatory environment

A review of herbal medicines was completed in 1990. Herbal medicines indicated for conditions capable of self-diagnosis were granted a licence once sufficient evidence of efficacy was established. The product labels for these products were required to include the statements "a herbal remedy traditionally used for the symptomatic relief of …" and "if symptoms persist consult your doctor." Combination products containing a large number of herbal ingredients or mixtures of herbal and other ingredients were not accepted, and licence holders were invited to consider to which ingredients the therapeutic claim related and to adjust the formulations (WHO 1998: 23).

While, in principle, the MCA accepts bibliographic evidence as proof of efficacy, there is no simplified procedure for proof of efficacy. As to the issue of quality, producers of herbal medicinal products must adhere to GMPs and the MCA carries out regular inspections.

Medicines that are considered safe enough to be sold to the public without the supervision of a pharmacist are listed in the general sales list. While there is an exemption from licensing for certain herbal remedies, toxic plants are not included in the general sales list category of medicines; therefore, they are either available in a pharmacy only or their dose or route of administration for use is limited outside a pharmacy setting. There is a list of plants that may only be sold or supplied in a pharmacy. Other lists indicate which plants may be sold by practitioners to a particular person following a personal consultation but which are for sale only in a pharmacy.

United States

The Food and Drug Administration (US FDA) is primarily responsible for interpreting and enforcing the Food, Drug, and Cosmetic Act (FDC Act). When the FDC Act was enacted in 1938, it only required proof of safety and the submission of a new drug application for any new drug. In 1962, the act was amended to require that new drugs be proven both safe and effective: all human testing of new drugs, all drug-related advertising, and all labelling had to be approved by the US FDA prior to the drug being marketed and GMPs were introduced (Miller 2000: 14–15) .

The US FDA regulates as drugs any products that claim to treat, cure, mitigate, or prevent a disease. For any herbal medicine to make a health claim, the same evaluative procedures must be followed as for a chemical drug, which generally require costly and lengthy double-blind, placebo-controlled human clinical trials to prove efficacy. Homeopathic products are regulated as drugs in the United States but any drugs listed in the *Homeopathic Pharmacopoeia of the United States* are exempt from the pre-market US FDA review of safety and efficacy (Valverde 1998: 176).

In 1994, the Dietary Supplement Health and Education Act (DSHEA) amended the FDC Act. As a result of these provisions, dietary ingredients used in dietary supplements are no longer subject to the pre-market safety evaluations required of other new food ingredients or for new uses of old food ingredients. They must, however, meet the requirements of other safety provisions. (US FDA 1995: 1).

The provisions of DSHEA define dietary supplements and dietary ingredients, establish a new framework for assuring safety, outline guidelines

for literature displayed where supplements are sold, provide for use of claims and nutritional support statements, require ingredient and nutrition labelling and grant the US FDA the authority to establish GMP regulations. The law also requires formation of an executive-level Commission on Dietary Supplement Labels and an Office of Dietary Supplements within the National Institutes of Health (US FDA 1995: 1).

Definition of dietary supplements

According to the US FDA, the DSHEA defines a dietary supplement to be a product (other than tobacco) that is intended to supplement the diet and that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by humans to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients. Dietary supplement status falls into the US FDA's classification of food (rather than drug).

Use of dietary supplements

According to the National Nutritional Foods Association's Web site, sales of dietary supplements reached $16.8 billion in 2000. Of this, vitamins accounted for 36% of sales, herbs and botanicals 25%, meal supplements 12%, specialty and other products 10%, sports nutrition 9%, and minerals 8%.

Total retail sales of herbal products in the United States in 1997 were estimated to be almost US$4 billion (Brevoort 1998: 33). The five top-selling herbal supplements in natural food stores that year were echinacea (12% of total sales), garlic (9%), gingko biloba (7%), goldenseal (6%) and saw palmetto (5%) (Brevoort 1998: 40). In 1998, St. John's wort bumped goldenseal out of the top 5.

The results of two surveys taken in the United States, one in 1990 and one in 1997, were published in the *Journal of the American Medical Association*. The results showed that almost 34% of Americans had used a complementary medicine in the year prior to the survey in 1990; this percentage had increased to 42% in 1997. Only 2.5% of respondents had used herbal medicine in 1990 but 12.1% claimed to use it in 1997. The percent of respondents using homeopathy increased from 0.7% in 1990 to 3.4% in 1997 (House of Lords 2000: chapter 1.23).

Regulatory environment

Under the DSHEA, herbs and other botanicals, vitamins, and minerals fall under the definition of a dietary supplement that is presented in a dosage form such as capsules, tablets, or liquids and labelled as a dietary supplement. Dietary supplements can include foods. For example, an herbal tea can be either a conventional food or a dietary supplement, depending on the intended use of the product—but a dietary supplement cannot be represented for use as a conventional food or as the sole item of a meal or diet. Any product that has been approved and marketed as a drug first cannot then be sold as a dietary supplement.

Dietary supplement ingredients that were marketed prior to the implementation of the DSHEA (October 15, 1994) are considered to be safe unless the US FDA proves otherwise. While pre-market approval by the US FDA for new supplement ingredients marketed after October 15, 1994 is not required, evidence of a product's safety (published scientific studies, a history of use, and so on) must be submitted to the agency at least 75 days prior to the product's marketing (Valverde 1998: 183).

Dietary supplement products are required to be prepared, packaged, and stored in accordance with GMPs modelled after those applied to food products. The ingredients, any plants or parts of plants and their quantity, must be truthfully and accurately listed on the product label and the product must not be adulterated with other substances. If the supplement claims to conform to the standard listed in an official compendium[17] for which there is an official specification and it fails to meet that standard, the product is regarded as mislabelled and the US FDA can have the product removed from the market. This also applies to a product that is not

covered by an official compendium but that fails to have the identity, strength, quality, and purity it claims to have on its label (WHO 1998: 10).

According the US FDA, a statement on the label of a dietary supplement is allowed if the benefit being claimed is related to a classical nutrient deficiency, if the role of the nutrient or dietary ingredient is described, or if the documented mechanism of action to maintain a function is characterized. For example, a product may not carry the claim "cures cancer" or "treats arthritis." Appropriate health claims authorized by the US FDA—such as the claim linking folic acid and reduced risk of neural tube birth defects and the claim that calcium may reduce the risk of osteoporosis—may be made in supplement labelling if the product qualifies to bear the claim. But, it must be clearly stated that the benefit claimed has not been evaluated by the US FDA and that the product is not intended to diagnose, treat, cure, or prevent any disease

The DSHEA puts the burden of proof onto the US FDA. The agency may remove a dietary supplement from the market if it can demonstrate that the product presents a significant risk of injury or illness when the product is used as directed on the label or, if there is no label, under normal conditions of use. An actual injury or illness need not occur in order for the FDA to act.

The DSHEA provides that retail outlets may make available "third-party" materials to help inform consumers about any health-related benefits of dietary supplements but the information must not be false or misleading; cannot promote a specific supplement brand; must be displayed with similar materials to present a balanced view; must be displayed separately from the supplements; and may not have other information attached (product promotional literature, for example). The Federal Trade Commission Act governs the advertising of herbal and dietary supplement products and the FTC requires that any representations, expressed or implied, about the efficacy, performance, safety, or benefits of a product be substantiated by scientific evidence.

Summary

Lessons for Canada

In most countries, NHPs are considered as drugs when there are health claims made about them and as foods when there are not. Homeopathic remedies are generally considered separately from herbal medicines.

Most countries state that they wish to ensure public access to these products and, therefore, they require lower standards of efficacy for NHPs than drugs but they demand the same levels of evidence for the quality and, particularly, the safety of both types of substance. All countries require manufacturers of drugs and NHPs to meet GMPs. In an international context, then, the NHPD's proposed regulatory framework is not particularly unique nor is it exceptionally rigid with respect to the efficacy, GMP, and other requirements that NHP manufacturers, packagers, labellers and distributors will be expected to meet.

The rigour with which herbal and other natural products are regulated in most countries even adds a strange quirk to the issue: If Canada chose to regulate NHPs with the laxity that their apparent safety seems to warrant, how would this affect Canada's NHP exports? Most likely, NHP exporters would voluntarily adopt European standards, as it would be in their own best interest to do so. However, in a session of the British House of Lords' Science and Technology Committee, there was concern voiced about the treatment of imports from the United States. Herbal products in the United States are generally sold as dietary supplements and, therefore, they are produced without the regulatory controls applied to medicinal products (House of Lords 2000: chapter 5.94).

Such trade issues are being debated as Europe attempts to harmonize its NHP and drug regulations. Many manufacturers will simply continue to sell their products nationally, forgoing the opportunity of marketing their products to all of Europe. They will only go to the trouble of meeting the regulatory requirements of another country if there is a

profit motive to do so. But, a consequence of the increased supply of regulation may be that manufacturers have to meet costlier and more time-consuming regulations at home, as their nation attempts to match the EC or other international standards. This could lead to the unintended result that NHPs—even high-quality, effective ones—become less accessible to the public as some manufacturers become unable to meet the increasing costs of the regulatory process.

Recommendations

Government regulation is warranted when the benefits to be derived from it are greater than its costs. With respect to natural health products, the numbers simply do not justify stricter regulations.

Proponents of more government in this area point to the amount of money spent on NHPs and other complementary or alternative medicines. They pinpoint one or two ineffective NHPs as proof

Table 5.1: The regulatory attitudes of selected nations towards therapeutic goods

Monopolistic	
Only the practice of modern, scientific medicine by authorized professionals is recognized as lawful, specifically excluding, or maintaining sanctions against, all other forms of healing	Algeria, Austria, Belgium*, Czechoslovakia, France*, Italy, Netherlands* (Countries vary in their enforcement of these medical laws)
Tolerant	
Only "modern" medicine is recognized although the practice of other forms of medicine is tolerated by law	Australia, Canada, Denmark, Germany, Israel, New Zealand, Nigeria, Scandinavian countries, United Kingdom, United States
Inclusive	
Systems that recognize the value of, and allow the practice of, a varying number of healing disciplines	Hong Kong, India, Thailand
Integrated	
Systems in which there is an official promotion of the integration of two or more systems of healing within a single recognized service: i.e. the integrated training of licensed medical professionals	China, Korea

* In these countries, the value of alternative health care is beginning to be acknowledged and a variety of health disciplines is, in point of fact, tolerated.

Source: Adapted from Roy Upton, "Regulation of Botanical Products in the European Market," Speaking notes. *American Herbal Pharmacopoeia* (2001): 26.

that people are wasting lots of money on "snake-oil" products. What about losses in productivity, in work time, because people are taking echinacea for what they think is a cold instead of an antibiotic for their bronchitis? What about people who use alternative therapies instead of getting "needed" chemotherapy and radiation treatment for cancer? Will such delays in medical treatment increase hospital costs, physician costs, patient pain and suffering?

While these may be valid questions, the data do not indicate an overall problem. There is no systematically collected data showing that people en masse are using alternative therapies and, in doing so, not getting the conventional care they may need. For the most part, the use of NHPs is not a life and death issue.

Despite their widespread use, relatively few people have adverse reactions from them and even fewer people have died as a result of using them. Over a period of six years, adverse reactions to herbal preparations never amounted to more than 0.5% of all adverse reactions reported in the United Kingdom. In Australia, NHPs accounted for 1.16% of the total adverse reactions in 2000. In the United States, safety advisories warning about dietary supplements made up a very small number of all safety advisories issued by the US FDA about biologics, dietary supplements, and pharmaceuticals every year from 1997 to 2001. As well, in the United States, the number of people who were reported to have died from Aspirin poisoning in 1998 was more than four times the number of people reported to have died that year from poisonings attributed to homeopathic or dietary supplements.

Regarding effectiveness, even if it were the government's responsibility to determine effectiveness, they would not be able to do so. Effectiveness is a subjective concept: what works on one person may not work as well on another person. Government regulation—no matter how strict—cannot assure an objective ideal of effectiveness. In attempting to do so, the government may be allowing thousands of people to die from cancer or babies to be born with a neural tube defect, while NHPs such as vitamins are going through the approval process. As well, the government would be spending more than $15,000 per adverse reaction avoided and more than $2.3 million a year to save 10 lives. The funds allocated to the NHPD could be better spent.

In addition, the adverse drug reaction data indicates that governments can only protect us to a limited extent—they cannot eliminate all of the risks associated with medicinal or any other products. People have life-threatening allergic reactions to peanut butter. Grapefruits contain a bioflavinoid called naringenin that negatively affects the ability of the liver to metabolize certain drugs; Valerian, an herb known for its soothing effect on the nerves, intensifies the effect of prescription sedatives and, therefore, can prove harmful (National College of Naturopathic Medicine 1999). No matter how much regulation is imposed, these types of risks will still exist.

Lastly, there is great debate as to how to define and then ensure the quality of a natural health product. For example, many traditional Chinese medicines are combinations of many substances, the overall result of which is an intended physiological effect; in isolation, any one substance in the combination may not have a health impact. The active ingredients, therefore, can be hard to determine and test. It is not a simple task to purify or make an extract of a single active ingredient even in the case of a single plant, which has a complex chemical composition.

6 Recommendations

It is interesting that, in the presentations to the SCH, there was discussion about the need for a program of certification of botanical identity, so that when consumers buy a product they can be assured that what is in the bottle is what the label says is in the bottle. Given that many of the adverse reactions (including death) from NHPs were apparently the result of adulteration and contamination, it seems that such a technique may be useful in either helping the government enforce the current food and drug regulations or helping the NHP industry to regulate itself.

There seem to be three main concerns about natural health products: contamination and adulteration of substances, a lack of information available to consumers, and interactions between herbs and pharmaceutical drugs.

(1) Enforce current regulations

Part 1, section 4, of the Canadian Food and Drug Act prohibits the sale of a food that has in, or on, it any poisonous or harmful substance, is adulterated or was manufactured, prepared, preserved, packaged, or stored under unsanitary conditions, and so on. Section 5 states that is illegal to label, package, treat, process, sell, or advertise any food 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.

There are already regulations to deal with the contamination and adulteration of NHPs. There is no need to create a new level of bureaucracy. Instead of pumping money into new directorates or regulations, there should be greater enforcement of the current regulations, more spot checks of products on the shelves. And, this is a function that does not even need to be conducted by government. The vast majority of NHPs can be monitored through self-regulation—the organic food industry, for example, has developed standards and certifies products that meet them. The Canadian Health Food Association (CHFA) has a code of ethics for its members and has initiated a random-testing program.

The CFHA membership includes retailers, wholesalers, and distributors in a range of sectors, including vitamins, herbals, homeopathics, sports and nutrition supplements, and packaged and organic foods. The random-testing program is designed to "increase retailer and public confidence in the quality and safety of products sold by CHFA member companies" (Canadian Health Food Association 2001).

According to the association's Web site (http://www.chfa.ca/), a category of NHPs is randomly selected each quarter from retail shelves for testing against label claims. An independent laboratory performs the analysis on unidentified, coded products so as to ensure impartiality. Unsatisfactory results are discussed with the relevant supplier, with the option of re-testing prior to the results being released to the members of the CHFA.

Given the relatively safety of NHPs, a self-regulation program in which the results are also made available to consumers would adequately address contamination, adulteration, and truth-in-labelling concerns.

(2) Allow information to flow freely

Even with the status quo—no health claims being permitted on NHP labels unless they receive a DIN (drug identification number)—there are multiple

sources of reliable information on most NHPs that are being sold in the marketplace. Health Canada, other countries' governments, the World Health Organization, the CHFA, the American Botanical Council, and several other organizations provide everything a person needs to know to use an herbal or other natural product as safely and as effectively as possible.

If multiple certification bodies or random-testing programs were allowed to proliferate, even more information would be generated, with annual checklists, reports, and so on being made publicly available on a regular basis. In this scenario, the vast majority of NHPs, which pose minimal safety risks, could be permitted to make claims. There would be unsubstantiated claims, claims backed up by a certification body, and products without claims at all. With the information available to them, consumers would be left to sort out the therapeutic assertions. Already, these same consumers choose mechanics for their cars, builders for their homes and vitamins—all of which are regulated to some degree but which vary greatly in cost, quality, and effectiveness.

For the perhaps 7% to 8% of NHPs that may merit being categorized as high-risk products,[18] perhaps Health Canada had the right idea back in 1992—prohibit these from being sold as foods. For these substances that are toxic and potentially dangerous (even when used appropriately), there could be stricter regulations enforced by the Therapeutic Products Program—there is no need for an extra bureaucracy. Evidence on safety could be supported using monographs and scientific data available from other countries. Quality and efficacy should not be the regulator's main objectives with these products for the reasons discussed above.

In contemplating a renewed role for the regulator, there are sections of the current Food and Drugs Act that should either be removed or revised significantly. For example, Schedule A, which lists the conditions for which it is prohibited to make treatment claims, should be removed so as to offer consumers the opportunity to take more control over their own health. As well, the restrictions on advertising for NHPs and prescription drugs should be reconsidered if increasing the amount of information available to consumers is considered a priority.

(3) Let the market provide information on interactions between pharmaceuticals and herbs

There has been increasing evidence that some NHPs produce adverse reactions when mixed with pharmaceutical drugs. They can magnify the side effects of medications, creating a health danger to consumers. Given this, it might seem—at first glance—desirable to require NHPs to have on their labels such contraindications as these. However, where does the line get drawn?

As stated earlier, grapefruit can hinder the ability of the liver to metabolize certain drugs. Other regular foods, such as fibre in large amounts, can decrease the absorption and distribution of any drug, especially anti-depressants (National College of Naturopathic Medicine 1999). It is unreasonable to expect all foods or drugs to be labelled with every contraindication possible. It is also hard to see how NHP manufacturers, which tend to be smaller companies, could afford to research all of the potential interactions between herbs and drugs.

Consumers should be asking their health-care practitioners about the products they are taking, practitioners should be aware of the latest medical data, and NHP and drug manufacturers should provide as much research on the effects of their products as they can. What the right amounts of information are, the market should be left to determine. Already, there are many recognizable and reliable sources on the contraindications of NHPs. Increased labelling requirements are unlikely to improve the situation.

(4) Measure the costs and benefits of regulating NHPs

The regulatory reform efforts of Health Canada have supplied regulatory impact analysis statements of limited value with respect to the costs and benefits of the proposed reforms. Statements such as "the costs should not be greater than it currently costs to run the system" and "costs placed on industry to comply with the regulations would eventually be passed on to the consumer" are not acceptable. There must be data to support the claim that the situation will be improved by the expenditure. A RIAS should answer several questions, including, but not limited to the following:

- What health risks do Canadians face from NHPs? How many adverse reactions have there been? How many deaths have there been?
- Could the risk from NHPs be diminished by the improved enforcement of current laws?
- How many lives will the proposed NHP regulations save? How many illnesses will the regulations prevent? How many low-quality NHPs will be taken off the market?
- What are the human resource needs expected to be to enforce the proposed regulations?
- Are cost-recovery fees expected at some point? If so, how much does Health Canada expect them to be? For what size of firms will they be affordable? How many NHP producers may not be able to afford to comply with the regulations implemented?

The directorate published the text of its proposals and its regulatory impact analysis statement in the *Canada Gazette*, Part 1, on December 22, 2001. The *Gazette* is the official newspaper of the Canadian government and is published under the authority of the Statutory Instruments Act; it has three parts. After Part 1 has been issued, there is a period of 90 days in which people have to submit their comments to the NHPD, therefore, anyone wishing to comment on the directorate's proposals has until mid-March 2002 to do so. The rules for submissions are included in the December 22 *Gazette* along with the NHPD's proposals. After consideration of the comments received, the framework will be formally adopted and published in the *Canada Gazette*, Part 2. Part 3 of the *Gazette* contains the most recent acts of Parliament and their enactment proclamations.

While time is running out for Canadians and other interested parties to affect how NHPs are regulated in Canada, there is still the opportunity to do so. It is hoped that this publication will aid people in their thoughtful consideration of the issues and provide them with information to critically analyze the regulatory framework being proposed by the directorate.

Appendix

The following sections from the Food and Drugs Act are included as an appendix to this study for comparative purposes. These are *not* all of the relevant sections but will serve as examples of the similarity between the regulation of drugs and the Natural Health Products Directorate's proposed regulatory framework.

Part C, Drugs, Division 1

C.01.003. No person shall sell a drug that is not labelled as required by these regulations.

C.01.004. (1) The inner and outer labels of a drug shall show

(a) on the main panel: (i) the proper name, if any, of the drug which, if there is a brand name for the drug, shall immediately precede or follow the brand name in type not less than one-half the size of that of the brand name, (ii) if there is no proper name, the common name of the drug, (iii) where a standard for the drug is prescribed in Division 6 of this Part, a statement that the drug is a Canadian Standard Drug, for which the abbreviation C.S.D. may be used, (iv) where a standard for the drug is not prescribed in Division 6 of this Part but is contained in a publication mentioned in Schedule B to the Act, the name of the publication containing the standard used or its abbreviation as provided in Schedule B or, if a manufacturer's standard is used, a statement setting forth the fact that such a standard is used, and (v) in both official languages, the notation "sterile" if the drug is required to be sterile by these regulations.

(c) on any panel (i) the name and address of the manufacturer of the drug, (ii) the lot number of the drug, (iii) adequate directions for use of the drug, (iv) a quantitative list of the medicinal ingredients of the drug by their proper names or, if they have no proper names, by their common names, and (v) the expiration date of the drug.

Assignment and Cancellation of Drug Identification Numbers

C.01.014. (1) No manufacturer shall sell a drug in dosage form unless a drug identification number has been assigned for that drug and the assignment of the number has not been cancelled pursuant to section C.01.014.6.

C.01.014.1 (1) A manufacturer of a drug, a person authorized by a manufacturer or, in the case of a drug to be imported into Canada, the importer of the drug may make an application for a drug identification number for that drug.

(2) An application under subsection (1) shall be made to the director in writing and shall set out the following information:

(a) the name of the manufacturer of the drug as it will appear on the label;

(b) the pharmaceutical form in which the drug is to be sold;

(c) in the case of any drug other than a drug described in paragraph (d), the recommended route of administration;

(d) in the case of a drug for disinfection in premises, the types of premises for which its use is recommended;

(e) a quantitative list of the medicinal ingredients contained in the drug by their proper names or, if they have no proper names, by their common names;

(f) the brand name under which the drug is to be sold;

(g) whether the drug is for human use, veterinary use or disinfection in premises;

(h) the name and quantity of each coloring ingredient that is not a medicinal ingredient;

(i) the use or purpose for which the drug is recommended;

(j) the recommended dosage of the drug;

(k) the address of the manufacturer referred to in paragraph (a) and, where the address is outside the country, the name and address of the importer of the drug;

(l) the name and address of any individual, firm, partnership, or corporation, other than the names and addresses referred to in paragraphs (a) and (k), that will appear on the label of the drug;

(m) the written text of all labels and package inserts to be used in connection with the drug and of any further prescribing information stated to be available on request; and

(n) the name and position of the person who signed the application and the date of signature.

Adverse Drug Reaction Reporting

C.01.016. (1) No manufacturer shall sell a drug unless the manufacturer, with respect to any adverse drug reaction or any serious adverse drug reaction known to the manufacturer that occurs after this section comes into force, furnishes to the director

(a) a report of all information in respect of any serious adverse drug reaction that has occurred in Canada with respect to the drug, within 15 days after receiving the information; and (b) a report of all information in respect of any serious unexpected adverse drug reaction that has occurred outside Canada with respect to the drug, within 15 days after receiving the information.

(2) The manufacturer shall, on an annual basis and whenever requested to do so by the director, conduct a concise, critical analysis of the adverse drug reactions and serious adverse drug reactions to a drug referred to in subsection (1) and prepare a summary report in respect of the reports received during the previous twelve months or received during such period of time as the director may specify.

(3) Where, after reviewing any report furnished pursuant to subsection (1) and any available safety data relating to the drug, the director considers that the drug may not be safe when used under the recommended conditions of use, the director may, for the purpose of assessing the safety of the drug, request in writing, that the manufacturer submit (a) case reports of all adverse drug reactions and serious adverse drug reactions to that drug that are known to the manufacturer; and (b) a summary report prepared pursuant to subsection (2).

(4) The manufacturer shall submit the case reports and summary report referred to in subsection (3) within 30 days after receiving the request from the director.

C.01.017. The manufacturer shall maintain records of the reports and case reports referred to in section C.01.016 for auditing purposes.

Division 1a, Establishment Licences

Notification

C.01A.013. Every person who holds an establishment licence shall notify the minister in writing within 15 days after (a) there is any change to the information referred to in any of paragraphs C.01A.005(a), (b), (e), (f), (h) and (i), and subparagraphs C.01A.005(g)(i) and (ii); or (b) an event occurs that results in their being in contravention of any of the applicable requirements of Divisions 2 to 4, where it may affect the quality, safety or efficacy of a drug fabricat-

ed, packaged/labelled, tested as required under Division 2 or stored by them.

Suspension

C.01A.016. (1) Subject to subsection (3), the minister may suspend an establishment licence in respect of any or all matters indicated in subsection C.01A.008(2) if the minister has reasonable grounds to believe that (a) the licensee has contravened any provision of the act or these regulations; or (b) the licensee has made a false or misleading statement in the application for the establishment licence.

C.01A.017. (1) The minister may suspend an establishment licence without giving the licensee an opportunity to be heard if it is necessary to do so to prevent injury to the health of the consumer, by giving the licensee a notice in writing that states the reason for the suspension.

(2) A licensee may request of the minister, in writing, that the suspension be reconsidered.

(3) The minister shall, within 45 days after the date of receiving the request, provide the licensee with the opportunity to be heard.

Division 2, Good Manufacturing Practices

C.02.002. In this Division, "specifications" means a detailed description of a drug, the raw material used in a drug or the packaging material for a drug and includes (a) a statement of all properties and qualities of the drug, raw material or packaging material that are relevant to the manufacture, packaging and use of the drug, including the identity, potency and purity of the drug, raw material or packaging material, (b) a detailed description of the methods used for testing and examining the drug, raw material or packaging material and (c) a statement of tolerances for the properties and qualities of the drug, raw material or packaging material.

Sale

C.02.003. No distributor referred to in paragraph C.01A.003(b) and no importer shall sell a drug unless it has been fabricated, packaged/labelled, tested and stored in accordance with the requirements of this Division.

Premises

C.02.004. The premises in which a lot or batch of a drug is fabricated or packaged/labelled shall be designed, constructed and maintained in a manner that (a) permits the operations therein to be performed under clean, sanitary and orderly conditions; (b) permits the effective cleaning of all surfaces therein; and (c) prevents the contamination of the drug and the addition of extraneous material to the drug.

Equipment

C.02.005. The equipment with which a lot or batch of a drug is fabricated, packaged/labelled or tested shall be designed, constructed, maintained, operated and arranged in a manner that (a) permits the effective cleaning of its surfaces; (b) prevents the contamination of the drug and the addition of extraneous material to the drug; and (c) permits it to function in accordance with its intended use.

Personnel

C.02.006. Every lot or batch of a drug shall be fabricated, packaged/labelled, tested and stored under the supervision of personnel who, having regard to the duties and responsibilities involved, have had such technical, academic and other training as the director considers satisfactory in the interests of the health of the consumer or purchaser.

Sanitation

C.02.007. (1) Every person who fabricates or packages/labels a drug shall have a written sanitation program that shall be implemented under the supervision of qualified personnel.

(2) The sanitation program referred to in subsection (1) shall include (a) cleaning procedures for the premises where the drug is fabricated or packaged/labelled and for the equipment used in the fabrication or packaging/labelling; and (b) instructions on the sanitary fabrication and packaging/labelling of drugs and the handling of materials used in the fabrication and packaging/labelling of drugs.

Records

C.02.020. (1) Every fabricator, packager/labeller, distributor referred to in paragraph C.01A.003(b) and importer shall maintain on their premises in Canada, for each drug sold, (a) master production documents for the drug; (b) evidence that each lot or batch of the drug has been fabricated, packaged/labelled, tested and stored in accordance with the procedures described in the master production documents; (c) evidence that the conditions under which the drug was fabricated, packaged/labelled, tested and stored are in compliance with the requirements of this Division; (d) evidence establishing the period of time during which the drug in the container in which it is sold will meet the specifications for that drug; and (e) adequate evidence of the testing referred to in section C.02.018.

Notes

1 The Foods Directorate defines the three types of claims as follows (Health Canada, Foods Directorate 2000: 2):

- **Structure-function** claims, which describe the effect of a food, drug, or diet on a structure of physiological function in the body. For example, "Calcium helps build strong bones."
- **Risk-reduction** claims, which describe the relationship between the consumption of a food, drug, or diet and the reduction in the risk of developing a chronic disease or abnormal physiological state by significantly altering a risk factor or factors recognized to be involved in its development. For example, "Diets high in calcium may help reduce the risk of osteoporosis."
- **Treatment** claims, which describe how a drug (and only a drug) can cure, treat, mitigate, or prevent illnesses.

2 A new drug is one that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use as a drug.

3 All of the information in this section is taken from the Canadian Food and Drug Act, the Natural Health Products Directorate public consultation document Proposed Regulatory Framework for Natural Health Products (March 2001) and the NHPD's Natural Health Products Regulations in the *Canada Gazette*, Part 1 (December 22, 2001).

4 Specification means a detailed description of the product: the identity, purity and potency of the NHP, including statements that indicate the tolerances for the identity, purity and potency of the NHP. As well, it includes a description of the methods used for testing or examining the NHP and any specification (or change to it) must be approved by a quality assurance person.

5 The major health and safety programs in Canada are administered by the Canadian Food Inspection Agency, Health Canada, Environment Canada, Transport Canada, the Canadian Nuclear Safety Commission and the National Energy Board.

6 The health portfolio comprises Health Canada ($2.3 billion), the Canadian Institutes of Health Research ($430.5 million), Hazardous Materials Information Review Commission ($2.9 million) and the Patented Medicines Prices Review Board ($4.1 million) (Health Canada, Foods Directorate 2000: 1).

7 At the time of writing, one Australian dollar was roughly equivalent to CDN$0.8 (Bank of Canada 2001)

8 At the time of writing, one British pound was roughly equivalent to CDN$2.26 (Bank of Canada, 2001)

9 Dietary supplements include products that are intended to supplement a person's diet and contain a vitamin, mineral, herb, or other botanical, an amino acid, or a concentrate, metabolite, constituent, extract, or combination of any of these ingredients.

10 E-mail correspondence from Industry Activities Staff, Centre for Food Safety and Applied Nutrition, U.S. Food and Drug Administration, August 21, 2001.

11 The NHPD was allocated $7 million over three years. Its $3 million research budget is not included in this example.

12 According to the National Institute of Nutrition in Canada, folate and folacin are descriptors for a group of compounds having the activity of folic acid. This B vitamin is required by cells for growth and cell division. This is why it is important during pregnancy, fetal growth, and lactation. (For more information, see http://www.nin.ca/Publications/NinReview/summer93_p.html.)

13 A neural tube defect is caused when the brain and spinal cord do not develop correctly. Spina bifida describes a group of birth defects caused by the failure of the lower portion of the neural tube to close so that the spinal cord and back bones do not develop properly.

14 This calculation is based on the estimate that folic acid in a vitamin supplement, when taken one month before conception and throughout the first trimester, has been proven to reduce the risk for an NTD-affected pregnancy by 50% to 75%. There are 400 babies born in Canada per year with an NTD; therefore, between 200 and 300 of these could be prevented. The assumption that 10% more women would take the recommended folic acid supplement if they knew it was beneficial to do so means that 20 to 30 incidences of NTDs could be avoided each year.

15 All of the information on the regulation of complementary medicines in Australia comes from the health department's Therapeutic Goods Administration Web site, unless indicated otherwise.

16 A product must have been used for at least 30 years to be considered traditional.

17 Official compendia include the *US Pharmacopoeia*, the *Homeopathic Pharmacopoeia* of the United States or the *National Formulary*.

18 Figures cited by Del Anderson, president of Added Dimensions, in his testimony to the Standing Committee on Health on March 18, 1998.

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Cynthia Ramsay is a Vancouver-based consultant specializing in health economics. She wrote *Beyond the Public-Private Debate: An Examination of Quality, Access and Cost in the Health-Care Systems of Eight Countries*, which was released in July 2001 by Western Sky Communications Ltd. She has just completed writing a chapter for a forthcoming book (spring 2002) on the health-care system and she is in the midst of preparing a report for the Commission on the Future of Health Care in Canada, headed by the Hon. Roy Romanow. In addition to consulting, Ms. Ramsay is co-owner and publisher of the *Jewish Western Bulletin*, British Columbia's only Jewish community newspaper.

From 1993 to 1998, Ms. Ramsay was senior health economist at The Fraser Institute in Vancouver. She wrote the Institute's study on medical savings accounts for Canada, was co-author of numerous editions of the Institute's annual waiting list survey (*Waiting Your Turn: Hospital Waiting Lists in Canada*) and is co-editor of the Institute's book, *Healthy Incentives: Canadian Health Reform in an International Context*. Ms. Ramsay has written numerous articles that have contributed to the Canadian health-care debate and she has spoken to groups in Canada and the United States on the necessity of market-based health-care reform.

From 1990 to 1992, Ms. Ramsay worked for Statistics Canada as an economic analyst. She received her BA (Honours) in economics from Carleton University in Ottawa, Ontaria, and her MA in economics from Simon Fraser University in Burnaby, British Columbia.