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Federal Regulation of Pharmaceuticals in the United States and Canada

PATRICIA I. CARTER*

I. INTRODUCTION

Since the 1930s, the pharmaceutical industries in Canada and the United States have been subject to increasing federal regulation designed to protect public health and safety. The development of these two drug regulatory systems has often paralleled each other. While there are many similarities between these two regulatory schemes, there are also significant and deliberate differences. This Article will examine these similarities and differences.

This discussion begins with a review of the historical development of drug regulation in the United States and Canada. Section III follows with an analysis of the basis for federal jurisdiction, and a comparison of the administrative and regulatory framework within which the pharmaceutical regulations operate in each country. Section IV explains some of the most important areas of drug regulation, such as the approval process for new

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drugs, administrative inspections, labeling requirements, and good manufacturing practices. In some of these key areas, such as the new drug approval process, the regulations in the United States and Canada are very similar. In other areas, however, there are distinct differences in approach. Section V follows with an examination of certain issues currently affecting pharmaceutical regulation. The first of these is the North American Free Trade Agreement (NAFTA), which has had considerable impact on Canadian drug regulation, particularly in the area of patents. A second issue is the struggle in both the United States and Canada with federal budget deficits and the resulting search for methods to streamline the regulatory processes. Some of these efforts have impacted pharmaceutical regulation. Finally, this paper concludes with an analysis of the relationship between government regulators and the regulated industry from the standpoint of cultural and philosophical differences between the United States and Canada.

II. HISTORICAL DEVELOPMENT OF PHARMACEUTICAL REGULATION

Drug regulation, often paired with food regulation, has a long tradition in North America. Drug laws in both the United States and Canada have their roots in English law and arose from a common concern about safety and fraud prevention. In the 19th century, there was widespread adulteration of food and drugs. Nonetheless, it was not until 1862, after a druggist’s assistant in a small English town poisoned 400 people by accidentally putting arsenic in some peppermint lozenges, that the British Parliament passed the Bill for Preventing Adulteration of Articles of Food and Drink. The history of drug regulation has often repeated this pattern of enacting legislation in response to public outcry following drug-related tragedies.

Canada’s first legislation “to prevent the Adulteration of Food, Drink and Drugs” was the Inland Revenue Act of 1875, which focused on concerns about adulterated alcohol. Food and

3. See id. at 209.
4. See infra notes 24, 34–37 and accompanying text.
5. See ROBERT EMMET CURRAN, CANADA’S FOOD & DRUG LAWS 143–45 (1953).
Federal Regulation of Pharmaceuticals

Drug regulation soon gained an importance independent of adulterated alcohol and were removed from the Inland Revenue Act and enacted into separate legislation as The Adulteration Act of 1884 ("Adulteration Act"). The Adulteration Act set standards for strength, quality and purity, and made it a criminal offense to manufacture or sell adulterated food or drugs. Other members of the Commonwealth modeled their food and drug legislation on the Adulteration Act. When the United States enacted its first national food and drug act, adulteration was treated in a manner substantially similar to the Canadian model.

In the United States, the first national food and drug legislation was the Pure Food and Drug Act of 1906 ("Pure Food and Drug Act"). The Pure Food and Drug Act passed with overwhelming support in Congress, despite opposition from food and drug manufacturers concerned that it would curtail business. Like the Adulteration Act, the U.S. law required all drugs to meet standards for strength, quality and purity. The prohibition on misbranding barred any false or misleading statements on the label regarding the drug or its ingredients. For a small number of drugs considered especially dangerous, the law required the label to state the ingredients and quantities.

The Pure Food and Drug Act had significant problems. While the Act gave consumers some protection from fraudulent patent medicines, it did not adequately assure safe and effective

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6. See id. at 145.
7. See id. at 147.
8. See id.
9. See id.
12. See Pure Food and Drug Act of 1906; see also James Harvey Young, Drugs & the 1906 Law, in Safeguarding the Public: Historical Aspects of Medicinal Drug Control 148, 150 (John B. Blake ed., 1970).
13. See Pure Food and Drug Act of 1906; see also Young, supra note 12, at 148.
14. See Pure Food and Drug Act of 1906; see also Young, supra note 12, at 148.
products. The Act did not authorize the ban of unsafe drugs, or cover cosmetics. Additionally, labels for most drugs were not required to identify the contents. Moreover, therapeutic claims were exempt from the requirements regarding false and misleading statements.

In 1912, the U.S. Congress passed the Sherley Amendment, which attempted to remedy the problem of therapeutic claim exemptions by prohibiting therapeutic claims that were false or misleading; however, it also added the requirement that the claim be fraudulent. This requirement of fraudulent intent shifted the burden of proof to the government and effectively nullified the Sherley Amendment.

The sulfanilamide disaster of 1937 brought public and congressional attention to the limitations of the U.S. food and drug regulations. Sulfa drugs were in widespread use in the United States during the 1930s, and one sulfa drug manufacturer decided to produce a liquid form using antifreeze. No clinical tests were made prior to its marketing, and 107 reported deaths resulted. Congress was finally spurred into action, and passed the Food, Drug and Cosmetic Act of 1938 (FDCA). The FDCA addressed the common industry practice of making false therapeutic claims by eliminating the need to prove fraud and also authorized factory inspections, seizures and injunctions. The FDCA also heralded the modern age of drug regulation by requiring the drug manufacturer to submit a New Drug Application (NDA) to the Food and Drug Administration (FDA) before the FDA would allow the product to enter the stream of interstate commerce. Unless the FDA issued an order within a specified period of time stating that the NDA was insufficient to establish the safety of the

17. See id. at 6.
18. See id. at 4.
20. See Young, supra note 12, at 149.
21. See id.
23. See id.
drug, the NDA would be automatically approved and the drug could proceed to market.26

The FDCA required that new drugs be adequately tested and shown to be safe, i.e., nontoxic when used in accordance with the conditions set forth on the label.27 The FDCA required that labels provide adequate directions for use to the consumer.28 However, the directions for use of some drugs were so complex that it was not feasible to include this information on the labeling.29 This problem was resolved by the Durham-Humphrey Amendment of 1951, which exempted certain drugs from the labeling requirement.30 These drugs, which could be safely used only under the supervision of a physician, required instead, the legend: "Caution: Federal law prohibits dispensing without a prescription."31

In Canada, it was not until 1951 that it became mandatory under the Food and Drugs Act that information about new drugs be submitted to the Food and Drugs Divisions of the Department of Health and Welfare (predecessor to the Health Protection Branch) prior to marketing.32 This legislation was prompted by a concern that the clinical testing being conducted was insufficient to ensure safety for human use, and by concerns that many drug manufacturers were using Canada as a testing ground for American drugs.33

The next major revision to the drug laws of both the United States and Canada came in 1962 as the result of another drug-related tragedy, this time involving thalidomide. Thalidomide was a sleeping pill developed and widely used in Europe.34 A researcher, conducting an investigative study of thalidomide drug use in the United States, discovered that severe birth defects could

27. See NIELSON, supra note 16, at 6.
28. See id. "Label" includes the package insert and any other written, printed or graphic materials accompanying the drug. See id.
29. See id. at 7.
30. See id.
33. See id.
34. See NIELSON, supra note 16, at 8.
result if pregnant women took the drug in their first trimester.\textsuperscript{35} The study showed that over 1000 children were born in Europe with severe birth defects as a result of their mothers ingesting thalidomide during pregnancy.\textsuperscript{36}

The U.S. Congress responded to this tragedy by passing the 1962 Kefauver-Harris Amendments, which substantially broadened the powers of the FDA. The 1962 Amendments required drug manufacturers to prove all new drugs to be both safe and effective by “substantial evidence,” before the FDA would grant marketing approval.\textsuperscript{37} Good Manufacturing Practices (GMP) were established, and any drug manufactured without adherence to these standards was presumed adulterated.\textsuperscript{38} The FDA was given authority over prescription drug advertising.\textsuperscript{39} The modern procedures for New Drug Applications (NDA) and for Investigational New Drugs (IND) were established.\textsuperscript{40}

Similarly the Canadian Food and Drugs Act was revised 1963 in response to the thalidomide experience.\textsuperscript{41} The Canadian law paralleled that of its U.S. counterpart, requiring manufacturers to submit “substantial evidence of the clinical effectiveness of the new drug . . . under the conditions of use recommended.”\textsuperscript{42}

\section*{III. CURRENT REGULATORY FRAMEWORK}

\subsection*{A. Federal Jurisdiction}

In both the United States and Canada, the regulation of pharmaceuticals by the federal government is based on Constitutional authority, but the source of that authority differs just as the Constitutions of the two countries differ. The subject of pharmaceutical regulation is not specifically addressed in the constitutions of either the United States or Canada. Federal authority for pharmaceutical regulation must therefore be found under other federal powers.

\begin{itemize}
\item[35.] See id.
\item[36.] See Marlin, supra note 25, at 176. See generally TEMIN, supra note 10, at 123–24.
\item[37.] See NIELSON, supra note 16, at 8.
\item[38.] See id. at 9.
\item[39.] See id. Advertising of Over the Counter (OTC) drugs was, and continues to be, supervised by the Federal Trade Commission (FTC). See id.
\item[40.] See id.
\item[41.] See LEXCHIN, supra note 32, at 183.
\item[42.] See id.
\end{itemize}
Like the British Constitution, the Canadian Constitution is both written and unwritten. The written portion comprises primarily the British North America Act of 1867 (BNA) and the Statute of Westminster of 1931. The BNA divides the legislative powers between the federal and provincial governments according to subject matter. The federal and provincial governments are each given exclusive jurisdiction over certain enumerated subjects. In a "deliberate departure" from the U.S. Constitution, which reserves to the states or to the people those powers not specifically enumerated, Canada's BNA grants these residual powers to the federal government. The federal government of Canada is empowered to exercise this residual power to make laws necessary for "peace, order and good government."

Three categories of legislative subject matter found in the BNA have been analyzed with respect to identifying the constitutional authority for Canada's food and drug laws. Section 91 of the BNA enumerates subjects for which Parliament has exclusive authority, including regulation of trade and commerce, and the criminal law. In addition, the preamble to section 91 provides Parliament with the residual power "to make laws for the peace, order and good government of Canada" in relation to all matters not exclusively assigned to the provinces under section 92.

Although the Canadian Food and Drugs Act has not been subjected to frequent judicial scrutiny, its constitutionality was directly challenged in Standard Sausage Co. Ltd. v. Lee. This case involved a prosecution for food adulteration, in which the British Columbia Court of Appeal unanimously held the Food and Drugs Act to be constitutionally valid as a criminal law under

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43. See CURRAN, supra note 5, at 30.
44. See ROBERT J. JACKSON & DOREEN JACKSON, POLITICS IN CANADA 181-83 (1994).
45. See id. at 182.
47. Canadian Embassy, Canada's Constitution 2 (May 1997).
48. U.S. CONST. amend. IX.
49. See The British North America Act, 1867, 30 Vict., ch. 3 § 91.
50. See id. at §§ 91(2), 91(27).
51. See id. at § 91; see also id. at § 92.
52. See Standard Sausage Co. Ltd. v. Lee [1934] 1 D.L.R. 706; see also CURRAN, supra note 5, at 38.
BNA section 91(27), and alternatively, valid as a law concerning the "peace, order and good government of Canada" under the preamble to BNA section 91. The court broadly interpreted the term "criminal law" to include any law with penal consequences for its violation. Nevertheless, Parliament cannot, under the guise of criminal law legislation, appropriate jurisdiction which the BNA allocated to the exclusive jurisdiction of the provinces. This provides some limitation on Parliament's otherwise expansive powers to legislate under this broadened definition of criminal law.

The constitutionality of the Food and Drugs Act was reaffirmed in 1987 in the case of C.E. Jamieson v. Canada. In this case, a pharmaceuticals manufacturer was held in violation of the "new drug" regulations. The Canadian Federal Trial Court set out a two-step test for judicial review of legislation in the context of the constitutional division of powers: First, the courts must determine the "pith and substance (that is, the dominant subject matter) of the legislation"; second, the courts must assign the subject matter to one of the classes of subjects listed in the BNA under either section 91 or section 92. The Jamieson court determined the "pith and substance" of the Food and Drugs Act to be regulation of public safety. It considered the "trade and commerce" category as a possible basis for jurisdiction, but determined that since the regulations were not "aimed directly" at "international and interprovincial trade and commerce," these were not sustainable on that basis.

In following the reasoning of Standard Sausage, the court found that the Food and Drugs Act "resides squarely within Parliament's legislative jurisdiction over criminal law." Moreover, in line with the reasoning of Standard Sausage, the court also held that the Act was within Parliament's power "to make laws for the Peace, Order and Good Government of Canada," because these are "matters of national interest and
concern."\textsuperscript{62}

In the United States, the FDCA "rests upon the constitutional power resident in Congress to regulate interstate commerce."\textsuperscript{63} The FDCA prohibits the movement in interstate commerce of adulterated and misbranded food, drugs, devices and cosmetics, and prosecutes offenders for shipping such goods across state lines.\textsuperscript{64} At first glance, this appears to be a major difference between the United States' FDCA and Canada's Food and Drugs Act. In Canada, the Food and Drugs Act is a federal criminal law, which applies to all food and drugs sold in Canada, regardless of its origin.\textsuperscript{65} In contrast, the FDCA relies on the commerce clause and therefore drug manufacturers operating entirely within one state would not be subject to these regulations. However, if any ingredient, container or label used was acquired outside the state, that would constitute interstate commerce and thus the FDA would have jurisdiction.\textsuperscript{66} Therefore, in practice, federal law in the United States can regulate the vast majority of pharmaceuticals as well.

\section*{B. Agency Structure and Scope}

Health and Welfare Canada is the department of the Canadian federal government responsible for "promoting and preserving the health, safety and well-being of all Canadians."\textsuperscript{67} The Health Protection Branch (HPB) of Health and Welfare Canada oversees the "availability, use, manufacture and sale" of food, drugs, cosmetics and medical devices.\textsuperscript{68} In the United States,

\begin{itemize}
  \item \textsuperscript{62} Id. at 54–75.
  \item \textsuperscript{63} United States v. Walsh, 331 U.S. 432, 434 (1947).
  \item \textsuperscript{64} See 21 U.S.C. § 331 (1994); see also Wassenaar, supra note 2, at 210.
  \item \textsuperscript{65} See Ron O. Read, Food Safety and Regulations—A Canadian Perspective, 36 FOOD DRUG COSMETIC L.J. 120 (1981).
  \item \textsuperscript{66} See e.g., Daniel v. Paul, 395 U.S. 298, 305 (1969) (holding that a substantial portion of the food at a snack bar had moved in interstate commerce, based on principal ingredients in the food items having probably been obtained from out of state sources); Katzenbach v. McClung, 379 U.S. 294 (1964) (holding that where Ollie's Barbecue Restaurant had obtained four to six percent of its food from outside Alabama, that a substantial portion of the food served moved in interstate commerce); Gregory v. Meyer, 376 F. 2d 509, 511 (5th Cir. 1967) (holding that where a restaurant used products which had moved in interstate commerce, this fact provided an adequate basis for coverage under the commerce clause).
  \item \textsuperscript{67} EILEEN MCMAHON, NEW DRUG APPROVAL IN CANADA 80 (1994).
  \item \textsuperscript{68} HEALTH PROTECTION BRANCH, HEALTH PROTECTION & DRUG LAWS 9 (1991) [hereinafter HPB].
\end{itemize}
the Food and Drug Administration (FDA) performs these functions.

The scope of responsibility of the HPB is broader than that of the FDA. The HPB is also responsible for the control of environmental hazards, an area overseen by the Environmental Protection Agency (EPA) in the United States. The HPB also acts as a national center for the identification, control and prevention of human disease. As such, the HPB has a role similar to the United States' Center for Disease Control (CDC). Finally, the HPB regulates activities related to controlled drugs and narcotics, a task handled by the U.S. Drug Enforcement Agency (DEA).

Within the HPB, the Therapeutic Products Directorate is responsible for overseeing the availability and use of drugs before they are marketed. The Therapeutic Products Directorate evaluates new drug submissions, determines potential health hazards, inspects drug manufacturing plants, authorizes emergency drug sales, and reviews drug advertising. The HPB has the authority to bring criminal charges against drug manufacturers for non-compliance with Canadian laws and regulations.

In the United States the Department of Health and Human Services (DHHS) is responsible for pharmaceutical regulation. The FDA, an independent agency within DHHS, was established by the FDCA to regulate the importation, manufacture, distribution and sale of drugs in the United States. A Commissioner who is appointed by the President and approved by the Senate heads the agency. Within the FDA, the Bureau of Drugs regulates human prescription and over-the-counter drug products. The mission of the Bureau of Drugs is very similar to

69. See id.
70. See id.
71. See id. at 11.
72. See id. As of May 1, 1997, the Drugs Directorate merged with the Medical Devices Bureau and was renamed the Therapeutic Products Directorate. See Therapeutic Products (Drugs) Programme (visited Aug. 8, 1997) <http://www.lpinelane.com/canada.htm>.
73. HPB, supra note 68, at 11-12.
74. See NiELSON, supra note 16, at 3.
75. See id.
76. See id.
77. See SCI. & TECH. COMMITTEE, supra note 26, at 1; See also Quirk, supra note 10, at 201.
that of the Therapeutic Products Directorate; it evaluates new drug submissions for safety and efficacy, conducts research, monitors the quality of marketed drugs through product testing and surveillance, and monitors prescription drug advertisements and labeling.\textsuperscript{78} Like the HPB, the FDA has authority to bring criminal charges against drug manufacturers for non-compliance.

\section*{C. Delegation of Authority}

The FDA's enforcement authority flows from Congress' delegation of the power to regulate food and drugs in interstate commerce to the Secretary of DHHS.\textsuperscript{79} The Secretary has, in turn, delegated this authority to the Commissioner of the FDA.\textsuperscript{80} Statutory empowerment of the Secretary thus effectively empowers the FDA to enforce food and drug laws and regulations.

The non-delegation doctrine generally prohibits such delegation of congressional legislative authority. Such delegation is permissible, however, if the statute delegating these powers includes "standards."\textsuperscript{81} The concept of "standards" has been broadly interpreted by the courts, as requiring only "public interest" or "reasonableness" as the basis for agency actions.\textsuperscript{82} The FDCA satisfies this requirement by establishing standards of reasonableness for the FDA's actions, in light of its primary objective of protecting consumers.\textsuperscript{83} In practice, Congress does not take the time to provide detailed instructions to agencies and relies instead on the agency's own expertise.\textsuperscript{84}

The Canadian Parliament has the constitutional authority to regulate pharmaceuticals for public health and safety, and to prevent deceptive and dishonest practices. As enacted by Parliament, the Food and Drugs Act delegates to the Governor-in-Council, an advisory body similar to the U.S. President's Cabinet, far-reaching powers to regulate and control the manufacture and sale of drugs in Canada.\textsuperscript{85} While the Food and Drugs Act provides

\begin{itemize}
\item \textsuperscript{78} SCI. \& TECH. COMMITTEE, supra note 26, at 3.
\item \textsuperscript{80} See 21 C.F.R. § 5.10; see also Quirk, supra note 10, at 201.
\item \textsuperscript{81} See CHARLES H. KOCH, ADMINISTRATIVE LAW \& PRACTICE 39 (1985).
\item \textsuperscript{82} See id. at 39. According to Koch, in the United States, the non-delegation doctrine "has had no practical force." Id. at 40.
\item \textsuperscript{84} See id. at 41.
\item \textsuperscript{85} See CURRAN, supra note 5, at 157. An act of the Governor in Council is an act of
\end{itemize}
the framework, the details are provided in regulations published in
the Canada Gazette. Unlike the broad standards provided by
legislation in the United States, the Canadian Food and Drugs Act
clearly specifies what matters can be handled through delegated
regulations.

The delegation of legislative authority in Canada is
sometimes seen as open to abuse. However, under Canada’s
system of “responsible government,” safeguards exist in the
delegation process. The regulations originate in an operating unit
of the HPB. The Canadian Department of Justice first considers
the regulations. Following discussion and revision in the Justice
Department, the Minister of Health and Welfare, reviews the
proposed regulations and then presents them to the Governor-in-
Council. Rarely are the regulations discussed in detail at this
stage, but are read into the minutes of the Privy Council and
signed as an Order-in-Council. The Minister is ultimately
responsible to Parliament for the regulations originating in his or
her department. As a member of Parliament, the Minister is also
answerable to his or her constituency. In addition, the validity of
any regulation is open to challenge in court.

the Governor General (the representative of the Queen) on the advice of the Cabinet.
See id. at 159.
86. See HPB, supra note 68, at 14.
87. See CURRAN, supra note 5, at 159.
88. See id. Since the publication of the Gagnon Report (see infra note 167) in 1992,
the pharmaceutical industry has been asking that the Therapeutic Products Directorate
be made an independent operating agency, “at arm’s length from the federal
government,” reporting directly to the Minister rather than the HPB. See MCMAHON,
supra note 67, at 81; Larry Johnsrude, Companies Urge Ottawa to Speed Up Approval of
New Drugs, MONTREAL GAZETTE, Jan. 18, 1995, at B4. The American concept of an
independent administrative agency, however, is not totally applicable in the Canadian
regulatory agencies in Canada are more dependent on the administrative and political
support of the ministers and departments than is the situation in the United States. See
id.
89. See Wassenaar, supra note 2, at 211.
90. See id.; HPB, supra note 68, at 14.
91. See id.
92. See Wassenaar, supra note 2, at 211.
93. See CURRAN, supra note 5, at 160.
94. See id. However, court challenges to the Food & Drugs Act regulations have
been rare. See Michael Gagnon, The Case of the Elusive Regulations, 1 LEGAL MED. Q.
D. The Regulatory Process

The U.S. rulemaking process requires a hearing to provide industry and consumer representatives with a public forum. However, the definition of "hearing" in American administrative law varies. This right of the public to participate in the rulemaking process is guaranteed for all legislative rulemaking; however, the extent of participation provided for need only be "reasonable under the circumstances." The federal Administrative Procedures Act (APA) requires that the minimum amount of public participation in rulemaking consist of notice and an opportunity to submit written comments. Most rules are made through informal rulemaking procedures. Notice usually involves publication of the proposed rule in the Federal Register. Comments are usually written, but an agency may also elect to hear testimony at a public legislative-type hearing.

Under the FDCA, Congress allowed for informal notice-and-comment rulemaking generally, but also provided for formal rulemaking upon request from an adversely-affected party. The first part of the process follows notice-and-comment procedures: The Secretary of DHHS publishes the proposed regulation in the Federal Register to allow "all interested persons an opportunity to present their views . . . orally or in writing." Adversely-affected parties have thirty days from the publication of the proposed regulation to request a public hearing. This public hearing will

96. See Administrative Procedures Act, 5 U.S.C. § 553 (1994). The term "informal rulemaking" is used to refer to this notice-and-comment process, although the term does not appear in the Administrative Procedures Act (APA). See generally KOCH, supra note 81, at 215.
97. See KOCH, supra note 81, at 67.
98. See id.
99. See id. "An agency's choice of rulemaking procedure is virtually unreviewable." Id. at 215.
102. See 21 U.S.C. § 371(e)(1). Agency rulemaking is not a democratic process; the agency is not bound to follow the dictates of the comments received. See Natural Resources Defense Council, Inc. v. EPA, 822 F.2d 104, 122 n.17 (D.C. Cir 1987).
103. See 21 U.S.C. § 371(e)(2). However, as interpreted by the courts, this statute does not require a public hearing in every case in which an adversely-affected party objects to the proposed regulation. See Pineapple Growers Ass'n v. FDA, 673 F.2d 1083 (9th Cir. 1982).
be a "full-fledged, trial-type hearing."104 Following the hearing, final rules are published in the Federal Register, and later codified in the Code of Federal Regulations.

U.S. agencies also issue handbooks and guidelines containing informative, but not binding rules.105 Although FDA guidelines do not have the force of law, they do represent a statement of the FDA's formal position on the subject, and obligate the FDA to act in a manner consistent with that policy.106 These internal pronouncements are not subject to the notice-and-comment rulemaking requirement.107

In Canada, major policy initiatives and proposals for regulatory amendments are communicated to the drug industry, health professionals and the public through Information Letters distributed by the HPB or through publication in the Canada Gazette.108 Final regulations are also published in the Canada Gazette.109 Unlike the more strict administrative procedures in the United States, regulations made under Canada's Food and Drugs Act do not require any form of public hearing or formal inquiry.110 Elected officials, the HPB, trade associations, or consumers may initiate changes in regulations.111 When a regulation is proposed, the government is under no obligation to provide a "comment period" for those affected by the regulation.112 The industry or public may elect to submit comments, but as with the FDA, the HPB is not required to follow the dictates of those comments. Nevertheless, as a general policy, Health and Welfare Canada discusses proposed regulations with the affected trade or industry.113

104. See Independent Cosmetic Mfrs. & Distrib., Inc. v. HEW, 574 F.2d 553, 572 (D.C. Cir. 1978) (dissenting opinion) (stating that the legislative history "clearly indicates that a full-fledged, trial type hearing was intended, and the FDA regulations carry out this intention.").

105. See 21 C.F.R. § 10.90. See generally KOCH, supra note 81, at 68.

106. See Southeastern Minerals, Inc. v. Harris, 622 F.2d 758, 768 (5th Cir. 1980).


108. See HPB, supra note 68, at 14.

109. See id.


111. See Morrison, supra note 110, at 639.

112. See id.

113. See CURRAN, supra note 5, at 160.
Like the FDA, the HPB also publishes informative handbooks, or Guidelines.\textsuperscript{114} This literature provides the industry and public with interpretations, additional information and examples on topics such as the conduct of clinical studies, Good Manufacturing Practices (GMP), and preparation of human and investigational new drug submissions.\textsuperscript{115} Like their U.S. counterparts, these Guidelines do not have the binding force of laws or regulations.\textsuperscript{116}

IV. OVERVIEW OF KEY AREAS OF REGULATION

A. New Drug Approval

The FDA’s “most formidable” power lies in its regulatory authority to approve new drugs.\textsuperscript{117} No new drug may enter the U.S. market without FDA approval as to both safety and effectiveness.\textsuperscript{118} Similarly, in Canada, no new drug may be marketed without the approval of the HPB.\textsuperscript{119}

1. Definition of “New Drug”

The definition of “new drug” is substantially the same in the United States and Canada. Regulations promulgated under the Canadian Food and Drugs Act define a “new drug” as any drug that has not been sold in Canada “for sufficient time, and in sufficient quantity, to establish its safety and effectiveness under its recommended conditions for use.”\textsuperscript{120} Similarly, the FDCA defines a “new drug” as any “drug not generally recognized among experts... as safe and effective under the conditions prescribed, recommended or suggested in the labeling thereof,” or which has been recognized as safe and effective under such conditions based on research but “has not, otherwise than in such investigations, been used to a material extent or for a material time under such

\textsuperscript{114} See Wassenaar, \textit{supra} note 2, at 213–14.
\textsuperscript{115} See HPB, \textit{supra} note 68, at 15, 69–70 (listing Guidelines and other publications of the Therapeutic Products Directorate).
\textsuperscript{116} See \textit{id.} at 15.
\textsuperscript{117} See NIELSON, \textit{supra} note 16, at 27.
\textsuperscript{118} See \textit{id.} at 28. FDA approval is required before the new drugs can be imported or transported in interstate commerce. \textit{See id.}
\textsuperscript{119} See HPB, \textit{supra} note 68, at 5.
\textsuperscript{120} \textit{Id.} at 25.
conditions."\textsuperscript{121}

2. New Drug Approval Process

The Canadian new drug approval process is substantially similar to the U.S. process. In fact, the Canadian process was modeled after that of the United States.\textsuperscript{122} The new drug approval process in both countries consists of four phases: Pre-Clinical, Clinical, NDA Review and Marketing.

This is illustrated in the diagram below:

### U.S. and Canadian Process for New Drug Approval

<table>
<thead>
<tr>
<th>Pre-Clinical Phase</th>
<th>Clinical Phase</th>
<th>NDA/NDS Phase</th>
<th>Marketing Phase</th>
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<td>Animal Testing</td>
<td>Human Testing I II III</td>
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<td>NDA or NDS Submission</td>
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<tr>
<td>NDA or NDS Approval</td>
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### Timeline

**Pre-Clinical Phase**

The United States new drug approval process begins when the drug manufacturer completes initial laboratory research, including studies on animals, and determines that the new drug looks promising for the treatment of a specific disease.\textsuperscript{123} If these pre-clinical studies indicate it is reasonably safe to initiate human clinical trials, the drug’s "sponsor" (usually the manufacturer) will

\textsuperscript{123} See NIELSON, *supra* note 16, at 28.
then file a Notice of Claimed Investigational Exemption for a New Drug (IND) with the FDA. This IND application provides notice that clinical (human) trials will be conducted, contains information about the pre-clinical results, outlines the proposed clinical studies, identifies experienced clinical investigators who will conduct the trials and provides other information about the manufacturing and testing processes. Additionally, the sponsor must provide the results of any foreign clinical experience.

Canada uses essentially the same process. To perform clinical trials, the drug sponsor must file an Investigational New Drug Submission (INDS) with the Therapeutic Products Directorate containing information very similar to an IND supplied to the FDA. However, the HPB does not require the submission of foreign clinical data. This omission has generated criticism of the HPB's process, that the drug sponsor may be aware of adverse reactions or poor results in clinical trials outside of Canada, yet is not obligated to report this information.

In the United States, clinical studies may start thirty days after receipt of the IND notice unless the FDA issues an objection. In Canada, the Therapeutic Products Directorate sends the drug sponsor a letter acknowledging receipt of the IND. If there is no negative response from the Therapeutic Products Directorate within sixty days, clinical trials may commence.

Clinical Phase

During the Clinical Trials phase, a Phase I Study is first conducted on a relatively small number of healthy human volunteers, to identify the safe dosage range and obtain other basic

126. See HPB, supra note 68, at 26.
127. See LEXCHIN, supra note 32, at 188.
128. See Nicholas Regush, How a Suspect Arthritis Drug Evaded Government Checks, MONTREAL GAZETTE, Oct. 25, 1982, at A1 (telling the story of the drug Oraflex, in which the drug manufacturer failed to inform the Therapeutic Products Directorate of eight deaths in Britain connected with the drug, or about suspected adverse reactions documented in a U.S. study).
129. See NIELSON, supra note 16, at 29.
130. See MCMAHON, supra note 67, at 29–30.
131. See id.
information. If these results indicate the drug can safely be tested on humans, a Phase II Study follows to test the drug's effectiveness on a limited number of patients with specific medical conditions. Finally, provided there are no major safety concerns raised by the Phase II Study, the drug is tested for safety and efficacy in wider clinical use. The Phase III Study will also attempt to identify the optimal dosage level.

**NDA Phase**

In the United States, once the research has been completed, the sponsor may submit a *New Drug Application* (NDA) to the FDA. The NDA has become the principal regulatory device for controlling pharmaceutical companies in the United States. An NDA is an extensive document, including extremely detailed safety and effectiveness data and statistical analyses. The FDA reviewers thoroughly "examine the clinical, chemical, statistical and pharmacological data submitted by the sponsor." Often, the FDA reviewers will require the drug sponsors to submit additional information. The FDA can refuse to accept the NDA application if, within sixty days of receipt, the FDA determines it to be substantially deficient. The FDA will approve a new drug only if the drug's sponsor provides substantial evidence of safety and effectiveness. Similarly, in Canada, once the research is completed, the drug's sponsor may submit a *New Drug Submission* (NDS) to the Therapeutic Products Directorate.

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132. See 21 C.F.R. § 312.1(a)(2). See also Gibbs, supra note 125, at 204; NIELSON, supra note 16, at 29.
133. See 21 C.F.R. § 312.1(a)(2). See also Gibbs, supra note 125, at 204; NIELSON, supra note 16, at 29.
134. See 21 C.F.R. § 312.1(a)(2). See also Gibbs, supra note 125, at 204; NIELSON, supra note 16, at 29.
135. See 21 C.F.R. § 312.1(a)(2). See also Gibbs, supra note 125, at 204; NIELSON, supra note 16, at 29.
137. See id.
138. See Gibbs, supra note 125, at 205; see generally 21 C.F.R. § 56.
139. See Gibbs, supra note 125, at 205.
141. See Gibbs, supra note 125, at n. 68.
143. See HPB, supra note 68, at 26.
are so similar to the United States' process that the Therapeutic Products Directorate will even accept a copy of a FDA New Drug Application, including clinical evidence, in lieu of a Canadian NDS application.\textsuperscript{144} Canada and the United States do not reciprocate with regard to application approval, however. Each country conducts its own investigation after the application is received.\textsuperscript{145}

\textit{Marketing Phase}

Once the FDA approves the NDA, the drug may be marketed in the United States. The product, however, may still be classified as a new drug for many years, and the manufacturer is under a continuing obligation to report any adverse reactions to the FDA.\textsuperscript{146} Similarly, in Canada, once the Therapeutic Products Directorate is satisfied with the NDS, it will issue a Notice of Compliance that allows the drug to be marketed.\textsuperscript{147} The drug will remain classified as a new drug at the discretion of the HPB, until it has been in use "for sufficient time and in sufficient quantity to assure the HPB that it is safe and effective," which takes about five years.\textsuperscript{148} During this period, the drug manufacturer is required to report any adverse reactions occurring in Canada.\textsuperscript{149}

The HPB also issues a Drug Identification Number (DIN).\textsuperscript{150} The DIN is required for every drug on the Canadian market and provides information to HPB regarding the drug's manufacturer, use, effect and ingredients.\textsuperscript{151} This requirement applies not just to \textit{new} drugs, but to \textit{all} drugs; therefore, manufacturers of drugs that had been marketed in Canada for years prior to the DIN requirement had to apply for DIN numbers for those drugs and pay an associated fee.\textsuperscript{152} Undoubtedly because of the expense to manufacturers, the DIN regulations have been challenged as "\textit{ultra vires} the Canadian Parliament."\textsuperscript{153}

\begin{itemize}
\item \textsuperscript{144} See Curran, \textit{supra} note 122, at 648.
\item \textsuperscript{145} See id.
\item \textsuperscript{146} See 21 C.F.R. § 310.300; 21 C.F.R. § 310.303; see also NIELSON, \textit{supra} note 16, at 31.
\item \textsuperscript{147} See HPB, \textit{supra} note 68, at 27.
\item \textsuperscript{148} LEXCHIN, \textit{supra} note 32, at 190.
\item \textsuperscript{149} See id.
\item \textsuperscript{150} See C.R.C. C.0.014(1). See generally HPB, \textit{supra} note 68, at 27.
\item \textsuperscript{151} See C.R.C. C.01.014.1(1); C.R.C. C.01.014.1(3). See also McMACHON, \textit{supra} note 67, at 63–66; Curran, \textit{supra} note 122, at 650.
\item \textsuperscript{152} See C.R.C. C.01.014(1); McMACHON, \textit{supra} note 67, at 63.
\item \textsuperscript{153} C.E. Jamieson & Co. v. Canada [1987] 12 F.T.R 167.
\end{itemize}
Canada, however, has upheld the regulation. The United States has no comparable numbering system.

3. Approval Times

The development of a new drug is a long and expensive process. The FDA is famous for both the stringency and the slowness of its new drug approval process. However, the NDA approval time has improved dramatically in the past ten years. NDAs submitted in 1987 took an average of thirty-three months to be reviewed. The average time for NDAs submitted in 1992 had decreased to nineteen months, representing a remarkable forty-two percent reduction. The average review time in 1997 had decreased to fifteen months. The fastest reviews are for NDAs to which the FDA assigns a priority status (ten months less than the average review time) and for NDAs submitted by experienced sponsors (four months less than the average review time). Much of the improvement since 1992 can be credited to the Prescription Drug User Fee Act (PDUFA). This gave the FDA

154. See id.
155. See Curran, supra note 122, at 650.
156. In the United States, it takes between $300 million and $500 million for a single drug to complete the FDA approval process. See VanHuysen, supra note 15, at 478–79. From pre-IND application studies to final marketing approval, the entire research and development period lasts an average of between eight and one half and fourteen and one half years. See id. at 485. The President and CEO of Glaxo Wellcome, Inc., the world's largest pharmaceutical company, has stated that the cost of developing a new drug in Canada is C$450 million and takes an average of 10 years. See Paul Lucas, Canada's Global Success Demands Better Field for Pharmaceuticals, CANADIAN SPEECHES: ISSUES OF THE DAY, Jan./Feb., 1997, at 47.
157. See Testing Testing, THE ECONOMIST, Feb. 1, 1997, at 81 [hereinafter ECONOMIST]; see also Quirk, supra note 10, at 206. Under 21 U.S.C. § 355(c) (1994), the FDA has only 180 days to act on a completed NDA; however, this deadline is easily evaded "by asking the companies for 'voluntary' extensions, or declaring the NDA incomplete pending further information." Quirk, supra note 10, at 208.
158. See U.S. GENERAL ACCOUNTING OFFICE, FDA DRUG APPROVAL: REVIEW TIME HAS DECREASED IN RECENT YEARS 4 (GAO/PEMD-96-1, Oct. 1995) [hereinafter GAO/PEMD-96-1]. Nearly half of all NDA's submitted are not approved for marketing, either because the FDA determined they were not safe and effective, or because the sponsor did not pursue the application. See id. at 10.
159. See id.
161. See GAO/PEMD-96-1, supra note 158 at 4–5. Only 17% of all NDAs are given priority status, meaning that they represent an important therapeutic advance. See id. at 11.
162. See infra Section V.B.1.
the ability to collect user fees from the drug industry to help finance the computerization of the review process. Computerization alone accounted for an eleven month reduction in NDA approval time.

In the 1970s, the Canadian drug review system was faster than its U.S. counterpart. But in 1993, while the United States was improving its review process time, Canada's review time slipped to an average of thirty-four months, making it one of the slowest drug regulatory systems in the world. According to one government study, the Therapeutic Products Directorate was so bogged down in bureaucracy, it lacked the flexibility to approve new drugs quickly. Canada, however, instituted a fast-track review for drugs identified as having an important therapeutic benefit, such as treatment for AIDS. Additionally, in the last few years, the HPB has improved its new drug approval time to more closely mirror that of the United States.

Speeding up the approval process means making needed drugs available to patients sooner. This objective, although laudable, must be tempered with concerns for safety; faster is not better if it compromises patient safety. While the timeliness of the new drug approval process is an issue in both the United States

163. ECONOMIST, supra note 157, at 81. Until a pilot study in 1994, NDAs had to be sent to the FDA as large bundles of papers. See id.

164. See id.

165. See COMPTROLLER GENERAL, FDA APPROVAL—A LENGTHY PROCESS THAT DELAYS THE AVAILABILITY OF IMPORTANT NEW DRUGS, GAO-HRD-80-64 (1980) at 7 [hereinafter GAO-HRD-80-64]. For drugs approved between July 1975 and February 1978, which were classified as "important new drugs," the approval time was 16 months in Canada, compared to 23 months in the United States. See id.

166. See Ian Austen, Faster Drug Approvals Might Pose Safety Risks: Study, MONTREAL GAZETTE, January 19, 1995, at E3. The British review board, for example, takes a maximum of 80 days for review of new products, and turns around the majority of applications within 60 days. See id.

167. See McMATH, supra note 67, at 85-87 (Appendix II: Executive Summary of "Review of the Canadian Drug Approval System," a government-sponsored report by Dr. Denis Gagnon, Université Laval). See also Larry Johnsrude, supra note 88, at B4 (quoting industry representatives' concerns about the slowness of the drug approval process).

168. See Austen, supra note 166, at E3. More than 90% of Canadian applications are for drugs that are either variations of current medicines or offer little significant medical benefit. See id.

169. Paul Lucas, of the multi-national pharmaceutical company Glaxo Wellcome, stated in a 1997 speech that "[i]n Canada, while considerable improvement has been made, it still takes 18 months or longer for a new drug to be approved by the Health Protection Branch." Lucas, supra note 156, at 47.
and Canada, Canada seems to take a more conservative approach and is more willing to forego speed to ensure safety.\textsuperscript{170} This is corroborated by a 1995 study which found that “there is some evidence that approval procedures may be more stringent in Canada than in the United Kingdom or the United States.”\textsuperscript{171}

Even while maintaining a conservative new drug approval process, the Canadian fast-track review for important drug breakthroughs will effectively give priority to drugs whose quick approval will make the most difference to patients.

\textbf{B. Inspections and Seizures}

In Canada, federal inspectors are given very broad discretionary powers to enter and inspect any premises where regulated activities occur. Under the Canadian Food and Drugs Act, inspectors from the HPB Field Operations Directorate have the authority to enter and inspect drug manufacturing and storage locations to monitor compliance with the Act and HPB regulations.\textsuperscript{172} These inspections may be performed “at any reasonable time,” and inspectors may enter any place where the inspector “believes on reasonable grounds” that “any article to which [the Food and Drugs Act applies] is manufactured, prepared, preserved, packaged, or stored.”\textsuperscript{173} Furthermore, the inspector may examine any articles, take samples, examine and make copies of any books or other records.\textsuperscript{174} The inspector may also, on reasonable grounds, “seize and detain for such time as may be necessary any article [connected with] contravention of the Food and Drugs Act.”\textsuperscript{175} The HPB inspector need not obtain a search warrant before entering the premises.\textsuperscript{176} In \textit{Jamieson}, a

\begin{itemize}
  \item \textsuperscript{170} \textit{See}, e.g., Austen, \textit{supra} note 166, at E3; \textit{see also} Nicholas Regush, \textit{Prescription-Drug Safety Rules are Slipping}, \textit{MONTRÉAL GAZETTE}, June 6, 1992, at B1.
  \item \textsuperscript{171} Austen, \textit{supra} note 166, at E3. This study was conducted by Dr. Joel Lexchin, and published in the International Journal of Health Services. \textit{See id}. Furthermore, in a review of 15 drug applications that Canada had rejected as not safe and effective, the U.S. approved nine, but later rescinded or limited approval of four of those. \textit{See id}. Britain approved ten of these drugs, later changing its mind about seven of them. \textit{See id}.
  \item \textsuperscript{172} \textit{See} HPB, \textit{supra} note 68, at 38.
  \item \textsuperscript{173} Food and Drugs Act, R.S.C., ch. F-27, § 23 (1997) (Can.).
  \item \textsuperscript{174} \textit{Id}.
  \item \textsuperscript{175} \textit{See} id.
  \item \textsuperscript{176} \textit{See} W. Wassenaar, \textit{Canada: Evolution of Drug Regulation Within the Health Protection Branch}, 35 \textit{FOOD DRUG & COSM. L.J.} 451, 453 (1980). There is an exception in the regulations for “dwelling houses,” the entry of which does require a search warrant. \textit{See} Food and Drugs Act, R.S.C., ch. F-27, § 23(1.1) (1997) (Can.).
\end{itemize}
drug manufacturer challenged the HPB's authority for warrantless searches under the Canadian Charter of Rights and Freedoms. The Charter guarantees that "[e]veryone has the right to be secure against unreasonable search and seizure." The Jamieson court held that the "pivotal word in section 8 of the Charter is 'unreasonable'. Reasonable searches and seizures [such as those authorized under the Food and Drugs Act] ... are constitutionally valid if otherwise lawful." Warrantless search and seizure by a public health and safety inspector of business activities subject to government regulation are likely to be considered reasonable because those businesses have "a lowered expectation of privacy."

In the United States, the inspection powers of government agencies are generally more limited than in Canada. Section 8 of Canada's Charter of Rights and Freedoms is very similar to the U.S. Constitution's Fourth Amendment guarantee of "[t]he right of the people to be secure ... against unreasonable searches and seizures, ... and no Warrants shall issue, but upon probable cause. ..." Nevertheless, until the late 1960s, administrative inspections were considered exempt from this requirement. The U.S. Supreme Court later rejected this concept. Although government inspections for public health and safety purposes are less intrusive than criminal police searches, the individual's privacy interests were deemed protected by the warrant requirement. There are exceptions, however; for example, government inspectors may enter a place of business that is open to the public and act on their observations. Another exception applies to closely regulated businesses. Using language very similar to that of the Canadian court in Jamieson, and in the same year, the U.S. Supreme Court held that the business owner in a closely regulated

180. Id. at 175. Nevertheless, in Jamieson, the court found the particular product seizure in question to be unreasonable. See id. at 171.
181. U.S. Const. amend. IV.
185. See McWalters v. United States, 6 F.2d 224 (9th Cir. 1925).
industry "has a reduced expectation of privacy."186 Legislation may legitimately provide for warrantless inspection of closely regulated businesses by the relevant government agency.187 Where close scrutiny and frequent inspection are essential to enforcement, these objectives would be frustrated by a warrant requirement. Moreover, when one chooses to engage in a pervasively regulated business, it is with the knowledge that such inspections may occur.188 This Colonnade-Biswell exception for closely-regulated businesses is a narrow one, and in most cases a warrant is still required for administrative inspections. The Ninth Circuit Court of Appeals recently held, however, that FDCA drug regulations relate to a "closely regulated business" within the Colonnade-Biswell exception, and a warrant for inspection of a drug manufacturer is not required.189

C. Labeling

When the FDA reviews an NDA, in addition to the clinical evidence, it also considers what information should be required on the product's labeling. The principal requirement is that the product must be "indicated for" only those uses for which there is substantial evidence of safety and effectiveness.190 The labeling must also provide the physician with all medically relevant information regarding appropriate use of the product, including dosage, directions for administration, and all known precautions, warnings, and contraindications.191 FDA regulations require a rather rigid format which all manufacturers must follow.192 The final product labeling must accompany the product in the form of a package insert, which is usually provided to the physician but not the patient.193

Canadian regulations also require approved labeling prior to marketing, but the requirements are not as detailed. The label

188. See Biswell, 406 U.S. 311.
190. See Gibbs, supra note 125, at 211.
191. See 21 C.F.R. § 201.56(d)(1). See generally Gibbs, supra note 125, at 206, 211–12.
192. See Gibbs, supra note 125, at 212 (citing as examples, 21 C.F.R. §§ 201.13(a); 201.316(b); and 801.420(c)(3), which provide detailed requirements for particular drugs).
193. See id.
must contain only the name of the drug, adequate directions for use, a quantitative list of the active ingredients, expiration date, potency of the drug, and method of administration if other than oral.\textsuperscript{194} The main panel of the label must also clearly show the DIN, which is not required in the United States.\textsuperscript{195} Another difference between the United States and Canada is in the language requirements. In Canada, all drug labels must be in two languages, one of which must be either French or English.\textsuperscript{196} In addition, the \textit{Charter of the French Language} requires that all drugs sold in Quebec be labeled in French and that no other language be more prominent.\textsuperscript{197}

\textbf{D. Good Manufacturing Practices (GMP)}

The FDA has adopted extensive and detailed regulations regarding Good Manufacturing Practices (GMP) for drugs.\textsuperscript{198} These regulations establish minimum criteria for buildings, personnel, equipment, control of components, processing controls, quality controls and record keeping.\textsuperscript{199} Any drug not manufactured in conformance with GMP standards is presumed adulterated.\textsuperscript{200} This presumption arises out of necessity because the FDA cannot inspect every article manufactured in a substandard facility to assure it is safe. “The risk to public health from impure articles is greater than the financial hardship and the inconvenience suffered by a manufacturer who desires to produce a product under such conditions [which do not conform to GMP].”\textsuperscript{201} The counter-argument is that the GMP standards are unduly harsh for small manufacturers who cannot afford the expense of compliance.\textsuperscript{202} Nevertheless, this argument cannot overcome the strong policy favoring public safety.

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\textsuperscript{194} See MCMAHON, supra note 67, at 75-77.
\textsuperscript{195} See supra notes 150-55, and accompanying text.
\textsuperscript{196} C.R.C. A.01.015. If the drug is for sale without a prescription, adequate directions for use must be shown in both French and English. C.R.C. A.01.015. See MCMAHON, supra note 67, at 75.
\textsuperscript{198} See 21 C.F.R. pt. 211. The GMP requirements originated in the 1962 Kefauver-Harris Amendments.
\textsuperscript{199} See id.
\textsuperscript{200} 21 C.F.R. §§ 211.1-211.208.
\textsuperscript{201} See NIJELSON, supra note 16, at 15.
\textsuperscript{202} See id.
\end{flushleft}
Canada has also adopted its own Good Manufacturing Practices to be followed in the manufacturing of drugs. According to the Food and Drugs Act, "[n]o person shall manufacture, prepare, preserve, package or store for sale any drug under unsanitary conditions."\(^{203}\) The regulations have elaborated on this principle by providing that "no manufacturer or importer shall sell a drug unless it has been produced in accordance with the [GMP] requirements."\(^{204}\) The regulations then proceed to detail those GMP requirements, which cover standards for the premises where the drug is produced, equipment involved, personnel, sanitation, manufacturing controls or procedures, quality control and record keeping.\(^{205}\) The Therapeutic Products Directorate has also published the GMP requirements in the form of a Guideline, which sets out the applicable sections from the regulations and their meaning, interpretation and rationale.\(^{206}\) While Canada's GMP requirements are very similar to those of the United States, Canada has not adopted the policy of presuming a product is adulterated if these standards are not met.

V. SELECTED ISSUES IN U.S. AND CANADIAN PHARMACEUTICAL REGULATION

A. Effect of NAFTA on Canadian Pharmaceutical Regulation

The United States, Canada and Mexico implemented the North American Free Trade Agreement (NAFTA) on January 1, 1994.\(^{207}\) Prior to NAFTA, Canada and the United States had a significant economic and trade relationship, including a significant pharmaceutical trade relationship.\(^{208}\) The United States, however,
desired more intellectual property protection for its exports.\textsuperscript{209} This objective was incorporated into NAFTA, which mandated important changes in the area of patent protection for the pharmaceutical industry.\textsuperscript{210} In turn, the changes Canada made to its patent legislation—in anticipation of and as a result of NAFTA— resulted in the institution of pharmaceutical price controls. In contrast, NAFTA is "unlikely to have any significant impact on the U.S. regulation of pharmaceuticals."\textsuperscript{211}

1. Patent Law

Several Canadian government reports in the 1960s identified Canadian drug prices as among the highest in the world and identified patent protection as a major cause.\textsuperscript{212} In response, the Canadian government passed an amendment to the Patent Act requiring compulsory licensing of drug patents.\textsuperscript{213} Compulsory licensing controls the prices of pharmaceuticals by allowing companies that produce generic-equivalent drugs to enter the market before expiration of the patent on the brand-name drug.\textsuperscript{214} Canadian companies were allowed to market generic versions of patented drugs for a minimal royalty fee (usually four percent of sales). This effectively negated the original drug's patent protection by eliminating the patent-holder's market exclusivity.\textsuperscript{215} Compulsory licensing drove down prices for the patented drugs, ...


\textsuperscript{210} See Noah, supra note 208, at 1296.

\textsuperscript{211} See \textit{id.} at 1315; Arvin P Shroff, \textit{FDA Enforcement Initiatives in the United States \& Abroad}, 49 \textit{FOOD \& DRUG L.J.} 575, 579 (1994).

\textsuperscript{212} See Joel Lexchin, M.D., \textit{Pharmaceuticals, Patents \& Politics: Canada \& Bill C-22} (Feb. 1992) (paper prepared for The Canadian Centre for Policy Alternatives) (reviewing Canada's unique history of using its patent laws to encourage price competition in pharmaceuticals).

\textsuperscript{213} See Act to Amend the Patent Act, the Trade Marks Act \& the Food \& Drugs Act, S.C. 1968-69, ch. 49, § 1 (1968) (Can.).


thus making it more difficult for manufacturers to recoup their substantial research and development expenses.\footnote{216} In contrast, generic equivalents may not be marketed in the United States until the full patent term of the original drug has expired.\footnote{217} Understandably, the patent-holders, usually foreign companies, challenged the granting of many of these compulsory licenses, but the Canadian courts consistently upheld the practice.\footnote{218}

The United States considered Canada’s compulsory licensing scheme as a “trade irritant.”\footnote{219} Although Canada represents only two percent of the world’s pharmaceutical market, multi-national drug companies were “horrified that compulsory licensing would set a precedent.”\footnote{220} It was an issue during the negotiations for the \textit{Free Trade Agreement} (FTA) between the United States and Canada, but it was not specifically addressed in the final text of the FTA.\footnote{221}

By 1987, Parliament concluded that “compulsory licensing had encroached too far into the patentee’s sphere of exclusivity, resulting in a decrease in research and development of new medicines in Canada.”\footnote{222} In an attempt to strike a balance between encouraging pharmaceutical innovation and providing the public with reasonably priced drugs, Parliament passed Bill C-22, which modified the compulsory licensing scheme to grant patent-holders the exclusive right to market the drug for the first seven years of the patent term.\footnote{223} This still allowed compulsory

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\item \footnoteref{216} See Noah, \textit{supra} note 208, at 1300.
\item \footnoteref{218} See Lexchin, \textit{supra} note 212, at 2. These compulsory licenses were heavily litigated. By 1971, of the 69 compulsory licenses issued, 43 were appealed in the courts. \textit{See id.} See also, e.g., Novopharm [1992] 41 C.P.R.3d 384; Novopharm [1989] 27 C.P.R.3d 249.
\item \footnoteref{219} See Lexchin, \textit{supra} note 212, at 4 (quoting the 1985 annual report of a U.S. Trade representative). Drug patents were one of the key agenda items at a summit meeting in 1985 between then-President Ronald Reagan and then-Prime Minister Brian Mulrooney. \textit{See id.}
\item \footnoteref{221} See Lexchin, \textit{supra} note 212, at 4–5. Lexchin’s position is that Mulrooney’s Conservative government bargained away the compulsory licensing system in return for passage of the FTA. \textit{See id.} at 5.
\item \footnoteref{223} \textit{See} An Act to Amend the Patent Act, 1987 S.C. ch. 41 (most commonly referred to as “Bill C-22”). This modified form of compulsory licensing continued to be upheld by
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licensing, but at least guaranteed to the patent-holder an initial period of market exclusivity in which to recoup research and development costs.

NAFTA allows compulsory licensing only under very limited circumstances. In 1993, in anticipation of NAFTA requirements, the Canadian Parliament enacted Bill C-91 to eliminate compulsory licensing. Furthermore, NAFTA required that patent protection be the same for all industries. Bill C-91 also extended patent protection for pharmaceuticals from seventeen to twenty years, the standard for other products, and moved to a first-to-file system. As a result, instead of patent protection being granted for seventeen years from the date issuance, the patent period now runs for twenty years from the date the patent application was filed.

In 1994, the United States increased its patent protection term for prescription drugs from seventeen to twenty years. The patent term can be further extended under the Drug Price Competition & Patent Term Restoration Act, which allows five year extensions of patent protection beyond the twenty year period under limited circumstances (generally related to regulatory delays).

NAFTA specifically permits the extension of a patent term to compensate for delays caused by the regulatory approval process.
process.229 This affords Canada, in light of its lengthy regulatory approval process, the opportunity to follow the U.S. model and adopt a patent term restoration act. Currently, patent terms can be extended in Canada by a specific act of Parliament, but only on a drug-by-drug basis.230 If Canada is unable to reduce its new drug approval times, pressure from the pharmaceutical industry for patent term extension legislation is likely to increase.

Canada's Bill C-91 included a sunset provision and was up for review in 1997.231 In February 1997, a parliamentary committee began reviewing the C-91 legislation.232 Groups both supporting and opposing renewal of C-91 heavily lobbied the committee.233 Generic drug companies would benefit from the repeal of C-91 and a return to compulsory licensing.234 Some public interest groups, fearing escalating drug prices, also favored repeal of C-91.235 The multi-national drug companies were naturally in favor of retaining C-91 and feared a return to compulsory licensing, with its inherent limitations on patent-holder profits.236

229. See NAFTA, art. 1709, ¶ 10. See also Blake et al., supra note 226, at 334.
233. See Beatty, supra note 231. Lobbying groups included the Canadian Drug Manufacturers Association (CDMA), a lobby group for the generic industry; the Pharmaceutical Manufacturers' Association of Canada (PMAC), a lobby group for the brand-name firms; and the Canadian Health Coalition (CHC), which lobbied against the renewal of C-91, with "protecting the public from private greed" as the theme for their campaign. See Walkom, supra note 220, at F4; CATHOLIC NEW TIMES, supra note 232, at 2.
235. See id.
236. The Canadian brand-name pharmaceutical manufacturers claim that they receive less patent protection for their products than in the United States, Japan or the European Community, and therefore Canada is less able to attract pharmaceutical research investment. See Lucas, supra note 156, at 50. "A major product coming off patent has a devastating impact on a company—dramatically eroding sales, virtually overnight." See id. at 49. "Without the 20-year patent protection available in just about every other
Much of the debate surrounding the renewal of Bill C-91 centered on the interpretation of NAFTA. The Industry Minister and Health Minister argued that NAFTA obligations required the renewal of C-91. Other trade experts, however, believed there were loopholes in NAFTA that would allow the government to return to a compulsory licensing system. Still other experts suggested that it would be difficult to convince a court or international dispute panel that compulsory licensing could be made consistent with Canada’s international obligations under NAFTA. In the end, this latter view prevailed, and when the Parliamentary committee released its recommendations to the government in April 1997, it recommended retaining C-91.

2. Canada’s Patent Medicine Price Review Board (PMPRB)

The elimination of compulsory licensing in Canada was expected to cause a dramatic increase in pharmaceutical prices. As a political compromise, the establishment of price controls on patented medicines accompanied the elimination of compulsory licensing. The Patented Medicine Prices Review Board (PMPRB) was established under Bill C-22 in 1987, and was given additional authority under Bill C-91 in 1993. The PMPRB is an independent quasi-judicial body that has the authority to investigate and regulate excessive pricing of patented medicines. Canadian-based research and development.”

236. See id.
237. See Walkom, supra note 220, at F4.
238. See id.
239. See id.
240. See id.
241. See Commons Drug Review Backs National Drug Plan, EDMONTON J., Apr. 25, 1997, at A13. Although review of C-91 was the extent of the committee’s mandate, it also made some other surprise recommendations, including the establishment of a national “pharmacare” program. See id. Drugs are not currently covered under the provincial health plans that provide medical care to all Canadian citizens. The committee also recommended reviewing the C-91 regulations. See id.
242. See Noah, supra note 208, at 1300, n.33 (citing a government source, which estimated that elimination of compulsory licensing would raise Canadian drug expenditures by C$129 million over the first five years).
245. See An Act to Amend the Patent Act, 1993 S.C. ch. 2, § 7(80) to (82) (strengthening the Board’s remedial and punitive powers).
pharmaceutical products in Canada.  

The PMPRB's determination as to whether the price of a drug is excessive is based on a comparison between the Canadian price and the price in other markets, the price of similar medicines within Canada, and changes in Canada's Consumer Price Index.  

The PMPRB may also consider the cost of making and marketing the drug, but will not generally consider research costs. If the PMPRB determines the price of a drug is excessive, it will first try to induce the manufacturer to voluntarily reduce the price. The PMPRB has been successful in most cases in persuading drug manufacturers to comply voluntarily with its guidelines. If necessary, the PMPRB can hold a public hearing after which it can either order the manufacturer to reduce the price or take away the manufacturer's market exclusivity for the drug. The PMPRB can even require the patent owner to reduce the price of another drug or remit money to the government. With these measures, the PMPRB appears to have successfully restrained Canadian drug price increases.

The PMPRB has withstood a number of challenges to its authority. Pharmaceutical companies unsuccessfully argued that establishment of the PMPRB was ultra vires the Parliament of Canada, because the purpose of the PMPRB was to regulate drug prices, and therefore, was a matter of property and civil rights under provincial jurisdiction, rather than a matter relating to federal patent jurisdiction. In Re Manitoba Society of Seniors, the Manitoba Court of Appeals held that the PMPRB's control of excessive prices was incidental to its primary purpose of increasing patent protection for new medicines, and therefore, was within federal jurisdiction.

246. See Smith, supra note 214, at 5–6.
247. S.C. 1993, ch. 2, § 7(85(1)). See also Blake et al., supra note 226, at 328–29.
248. Blake et al., supra note 226, at 329.
249. See GAO/HRD-92-110, supra note 234, at 37.
250. See U.S. GENERAL ACCOUNTING OFFICE, PRESCRIPTION DRUG PRICES: ANALYSIS OF CANADA'S PATENTED MEDICINE PRICES REVIEW BOARD 7 (GAO/HRD-93-51, Feb. 1993) [hereinafter GAO/HRD-93-51]. Compliance with the price guidelines for new drugs has usually been achieved within 90 days of product introduction. See id.  
255. Manitoba Soc'y, 35 C.P.R.3d at 73. The Manitoba Court of Appeal held that
Because the price regulation applies only to patented drugs, some pharmaceutical companies have attempted to avoid the PMPRB by "dedicating" the patent for a drug to the Canadian public.\textsuperscript{256} This method of "donating" a patent to the Canadian people is not mentioned in the Patent Act, but has been recognized by the Commissioner of Patents.\textsuperscript{257} Dedication of patents to the public used to be very rare; however, with the creation of the PMPRB in 1987, "[m]any drug companies suddenly became interested in making a magnanimous dedication of their valuable patent rights to the people of Canada."\textsuperscript{258} The drug companies intended to sacrifice their patent protection to avoid price regulation, gambling that regulatory delays would leave them a few years of market exclusivity before generic versions were approved for sale.\textsuperscript{259} The PMPRB ruled, however, that such patent "dedications" do not avoid the Board's jurisdiction over the prices of these drugs.\textsuperscript{260} Because patent dedication was not mentioned in the Patent Act, but was only an administrative policy, the PMPRB reasoned that the dedication could be ignored.\textsuperscript{261}

In 1996, in \textit{ICN Pharmaceuticals v. PMPRB}, a pharmaceutical company challenged the jurisdiction of the PMPRB, but the Federal Court of Appeal interpreted the Patent Act to give the PMPRB very wide jurisdiction.\textsuperscript{262} According to the \textit{ICN} court, the PMPRB has jurisdiction to monitor prices if there is a patent "pertaining to" the product, even if the patent-holder's use of the product falls outside the patent claims.\textsuperscript{263} The court held that the powers of the PMPRB should be construed broadly because its legislative purpose was to replace the previous price controls under the compulsory licensing system, which itself had been

\begin{itemize}
  \item \"[t]he impugned legislation is in pith and substance in relation to matters within Parliament's exclusive jurisdiction over patents.\" 45 C.P.R.3d at 195.
  \item \textsuperscript{256} See Hore, supra note 243, at 36. See also Blake et al., supra note 226, at 324.
  \item \textsuperscript{257} See Hore, supra note 243, at 36.
  \item \textsuperscript{258} See id.
  \item \textsuperscript{259} See id.
  \item \textsuperscript{260} This PMPRB ruling was upheld in Genentech, Inc. v. Patented Med. Prices Review Bd. [1992] 44 C.P.R. 3d 335 (holding that dedication of patents to the public does not terminate the PMPRB's jurisdiction). See also Hore, supra note 243, at 36.
  \item \textsuperscript{261} See Hore, supra note 243, at 36.
  \item \textsuperscript{262} ICN, 138 D.L.R.4th at 71 (construing the Patent Act, R.S.C. 1985, ch. P-4, §§ 83(1) and 79(2), as amended).
  \item \textsuperscript{263} See id. at 93.
\end{itemize}
construed broadly in the courts. 264

Parliament may also broaden the powers of the PMPRB. In April 1997, the parliamentary committee reviewing the renewal of C-91 recommended greater powers for the PMPRB, including expanding its authority to non-patented drugs. 265

Like its Canadian counterpart, the U.S. government is concerned about increases in pharmaceutical prices. 266 Studies by the U.S. Government Accounting Office have found that the prices of some prescription drugs in the United States are substantially higher than in other countries. 267 In particular, prices for identical prescription drugs are typically higher in the United States than in Canada. 268 A sample of prices for 121 commonly prescribed drugs indicated thirty-two percent higher costs in the United States. 269 This difference is largely attributable to the Canadian government actions to restrain drug prices. 270

As a result, the U.S. Congress considered legislation to regulate drug prices. 271 Some of these bills would have created a federal agency, modeled after Canada's PMPRB. 272 Such a federal board, however, might not be as effective in the United States because the United States, unlike Canada, is home to a

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264. See id.

266. During the 1980s and 1990s, the prices of prescription drugs increased at three times the rate of inflation. See U.S. GENERAL ACCOUNTING OFFICE, PRESCRIPTION DRUG PRICES: OFFICIAL INDEX OVERSTATES PRODUCER PRICE INFLATION 1 (GAO/HEHS-95-90, Apr. 1995) [hereinafter GAO/HEHS-95-90]. The growth in U.S. drugs prices, however, has declined since 1990, consistent with drug manufacturers’ public pledges of self-restraint in pricing. See U.S. GENERAL ACCOUNTING OFFICE, PRESCRIPTION DRUGS: COMPANIES TYPICALLY CHARGE MORE IN THE UNITED STATES THAN IN THE UNITED KINGDOM 3 (GAO/HEHS-94-29, Jan. 1994) [hereinafter GAO/HEHS-94-29].

267. See GAO/HRD-92-110, supra note 234, at 37.
268. See id. at 2.
269. See id.
270. See id. This includes provincial, as well as federal government actions. Provincial actions include the use of concentrated buying power to obtain low prices for the provincial drug plans. See id. at 3. Provincial laws and regulations are beyond the scope of this article.

271. See GAO/HRD-93-51, supra note 250, at 1. At least eleven such bills were introduced in the 102nd Congress, but none were enacted. See id.
272. See id.
strong, research-oriented pharmaceutical industry.\textsuperscript{273} Price restraints might adversely effect pharmaceutical research and development, as well as the availability of new drug products in the United States.\textsuperscript{274} Furthermore, in Canada, the pharmaceutical market is heavily influenced by the provincial drug plans which are among the largest purchasers of drugs, and which require generic-equivalents because they are typically available at a lower price.\textsuperscript{275} In contrast, the U.S. health care market is dominated by private payors without such concentrated buying power and without a uniform demand for the generic products. While it deserves additional study, it is not clear that a Canadian-style price review board would be appropriate for the U.S. regulatory scheme.

**B. Reinventing Drug Regulation: Teaching the Elephant to Dance\textsuperscript{276}**

With the advent of the Clinton Administration’s Reinventing Government Initiative, the FDA became a “priority target” for reform efforts.\textsuperscript{277} Beginning in 1994, the agency undertook a number of self-examination and reform projects.\textsuperscript{278} These included publication of a report, *Reinventing Drug & Medical Device Regulations*, identifying areas of the regulatory process which could be reduced or eliminated without lowering health or safety standards, and the subsequent reforms of the Food and Drug Modernization Act of 1997.\textsuperscript{279}

This initiative has a counterpart in Canada’s Regulatory Efficiency Act, which has similarly tried to streamline processes and reduce bureaucracy in an effort to control the federal

\textsuperscript{273} See GAO/HEHS-94-29, supra note 266, at 2.
\textsuperscript{274} See GAO/HRD-92-110, supra note 234, at 22.
\textsuperscript{275} See id. at 15.
\textsuperscript{278} See id.
deficit. In addition, Canada's Minister of Health and Welfare commissioned a study in 1992 by Dr. Denis Gagnon of the Universit6 Laval, who produced a report containing 152 recommendations for revising the Canadian regulatory model and drug approval processes. The Therapeutic Products Directorate has implemented or plans to implement ninety of these recommendations.

Both countries have adopted new strategies to change the regulation of the drug industry, with an emphasis on reducing the time required for the new drug approval process. Techniques include shifting some of the costs of regulation to industry through user fees, and using non-agency experts to leverage agency personnel.

1. User Fees

Most departments of the Canadian federal government have adopted new cost recovery programs, wherein corporations pay the majority of the costs of services provided to them. In 1995, the Therapeutic Products Directorate followed this trend against strong industry opposition by instituting fees for its services, including issuance of DIN numbers, annual licensing and evaluations of New Drug Submissions. Costs to the pharmaceutical industry are expected to reach C$40 million annually. This user fee system has raised some concerns in Canada that only the large pharmaceutical companies will be able to pay the fees, and smaller companies will not survive. It has also been suggested that pharmaceutical companies are becoming more demanding with respect to approval times from the Therapeutic Products Directorate since they are paying for such services. This has led to concerns that drug safety might be compromised by succumbing to industry pressure to speed up the

280. See McMahon, supra note 209, at 79.
281. See id. at 81, 85-101.
282. See id. at 81.
283. See id. at 47.
284. See id. at 1.
285. See id. at 2.
286. See Maureen Moore, Drugs Weren't Mother Bunny's Cup of Tea, VANCOUVER SUN, Mar. 19, 1997, at A15.
approval process—a charge vehemently denied by the HPB.288

Similarly, the U.S. Congress passed the Prescription Drug User Fee Act of 1992 (PDUFA) to provide the FDA with additional resources to expedite drug reviews and approval.289 Fees are now charged for submission of an NDA, annual licensing for each prescription drug being marketed, and an annual fee for each manufacturer.290 Congress gave the FDA five years to speed up its NDA review process across the board, along with the power to collect more than $300 million from drug companies to help accomplish this goal.291 The money has been used to computerize the system and to hire 600 new reviewers.292 Under PDUFA, the FDA is expected to perform a complete review of an NDA within six months after submission for priority applications, and within twelve months for standard applications.293 The average approval time for priority applications fell short of that goal at 8.9 months for 1997. However, the FDA succeeded in reducing the median approval time for standard applications to twelve months.294 The Clinton Administration maintains that this expedited approval process can be done without any sacrifice in review quality.295

In the United States, concerns about the ability of small drug companies to afford these user fees were addressed by including a small business exception in the PDUFA.296 Pharmaceutical
companies with fewer than 500 employees pay only one-half of the human drug application fee. Full annual licensing fees, however, are still required. The imposition of user fees may ultimately have the effect of inhibiting pharmaceutical research and development, especially among smaller companies. The FDA does have the flexibility, however, to waive the user fees altogether in instances where the fees would be unduly burdensome, e.g., for small businesses or where the fee would create a significant barrier to innovation.

2. Expert Committees

The HPB uses Expert Advisory Committees to augment the expertise of its own staff. These Committees are comprised of individuals with expert knowledge and judgment in specific scientific, technical or medical fields. Typically, an outside expert committee conducts the first review of an NDS. This practice has been criticized as leading to inexpert reviews and conflicts of interest. "Some outside reviewers receive only one or two days’ training and are poorly supervised, . . . [or] have close ties with drug companies—conducting tests for them, preparing their submissions for drug approval or acting as consultants." The use of outside reviewers to speed up the drug approval process has raised concerns that the health and safety of Canadians will be compromised. Furthermore, in July 1997, as part of a deficit-cutting program, Health Canada closed down the Bureau of Drug Research (a division of the Therapeutic Products Directorate), which helped review drug submissions and support government regulators. This led to greater fears that the HPB would become too reliant on outside experts with ties to the pharmaceutical companies, and thus lose its ability to make independent drug assessments. Some health policy consultants

297. See id.
299. See HPB, supra note 68, at 14.
300. See id. at 27.
301. See Regush, supra note 170; Nicholas Regush, Experts Question Objectivity of Private Drug Reviewers, OTTAWA CITIZEN, June 8, 1992, at A4.
302. See Regush, supra note 170.
303. See id.
305. See id. See also Kathryn May, Health Canada Considers Downsizing its Drugs
believe there is too much money at stake in gaining marketing approval for a new drug to trust the pharmaceutical companies to provide unbiased information.\textsuperscript{306}

In the early 1990s, the United States implemented a small-scale trial of outside reviewers, “farming out” the approval process for eight to ten drugs intended to treat non-life-threatening illnesses.\textsuperscript{307} The FDA never implemented this scheme on a wider scale. However, in 1995 and 1996, several FDA reform bills were introduced (though not passed) in Congress which would have encouraged the use of outside experts to perform reviews of drug applications.\textsuperscript{308} Critics of these bills raised the same concerns raised by Canadian commentators: Reviews by private sector experts would result in conflicts of interest, and “potentially reduce the FDA’s role to rubber stamping the outside expert’s recommendations.”\textsuperscript{309} At a minimum, outside experts should be required to disclose any potential conflict of interests. An additional eligibility requirement could be that an outside expert not have worked for a drug company within one year of serving as an outside expert for the FDA.

Despite such concerns, in November 1997, Congress authorized the Secretary of DHHS to enter into contracts for expert review of applications for biological products, where the Secretary determines that such outside expert review will improve the timeliness and quality of the application or submission review process.\textsuperscript{310} This is a first step towards the Canadian model of augmenting the government staff with outside experts. While some concerns remain, proponents argue that the use of outside experts, or even privatization of certain regulatory processes, is the only way to reverse the “risk avoidance and autocratic style of regulation” of the FDA.\textsuperscript{311}

\textsuperscript{306} See Eggertson, supra note 304, at A4.

\textsuperscript{307} See Regush, supra note 301.

\textsuperscript{308} See VanHuysen, supra note 15, at 494–95.

\textsuperscript{309} See id. at 495.


\textsuperscript{311} Elizabeth C. Price, Teaching the Elephant to Dance: Privatizing the FDA Review Process, 51 FOOD & DRUG L.J. 651, 652 (1996). The FDA has been criticized for taking a risk avoidance approach to regulation. It has been suggested that the FDA is overcautious in approving new drugs because a serious mistake will bring the wrath of Congress, consumer groups and the public down on the FDA; whereas, the consequences
C. Relationship Between the Regulator and the Regulated

As a rule, there is compliance with drug laws and regulations in both the United States and Canada; however, the source of the compliance differs. The U.S. drug regulatory system is considered more adversarial compared to the more collegial nature of the Canadian system. This may be attributable to the general sentiment that "Canadians value peace, order and good government," whereas Americans have a "deep suspicion and fear of government." 312

In the early days of food and drug regulation in the United States, the government placed primary emphasis on cooperation with industry, hoping for voluntary compliance that would avoid the need for legal enforcement. 313 By the 1930s, however, a more adversarial relationship between the FDA and the drug industry had developed as a result of increasing noncompliance and other "disreputable practices" of the drug industry. 314 The "psychological climate" had changed, and while cooperation still existed, relations between the FDA and industry had "cooled." 315 This situation has not improved over the years. In 1980, a federal study of the delays in new drug approval cited the "adversarial relationship between the FDA and pharmaceutical industry" as a major factor. 316 A federal court in 1993 characterized the relationship between the FDA and a pharmaceutical business it regulates "as a confrontation between a humorless warden and his uncooperative prisoner." 317

A drug company may be reluctant to file a lawsuit against the FDA to protect its interests, for fear of antagonizing the FDA. 318 The FDA could easily introduce delays into the approval process for any products that the drug company has submitted for approval or retaliate in other ways. A 1991 poll of companies regulated by the FDA revealed that "eighty-four percent of respondents

of delaying approval of a valuable drug tend to be much less public. See id. at 654-60; Quirk, supra note 10, at 217.


313. See Young, supra note 12, at 154.

314. See id. at 155.

315. See id. at 156.

316. SCI. & TECH. COMMITTEE, supra note 26, at v.


318. Price, supra note 311, at 653.
suppressed potentially legitimate complaints against the FDA for fear of retaliation.” In *Washington Legal Found. v. Kessler*, the plaintiff alleged that “few if any companies are willing to challenge the FDA [in court, because the] FDA wields enormous power over drug and medical device manufacturers through its power to grant or deny new product applications. It is evident that manufacturers are most reluctant to arouse the ire of such a powerful agency.”

Another reason for the drug industry’s reluctance to challenge the FDA in court is that they are likely to lose. The courts have generally upheld the rulings of the FDA, and the scope of the FDA’s authority is interpreted broadly because of the court’s sensitivity to matters of public health and consumer protection. The courts commonly defer to the FDA’s expertise and support the agency’s decisions. “No sponsor has successfully sought reversal of an FDA refusal to approve its drug. The lesson has not been lost on the vast majority of applicants who understand that the only way to secure approval of an NDA is to satisfy the agency.”

Foreign drug regulators and industry officials see this adversarial relationship between the FDA and industry as unique to the United States and as an impediment to the regulatory process. Canada has actively avoided creating such an adversarial relationship. Rather, HPB officials “have opted for a co-operative and ‘open door’ policy with Canadian drug

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321. *See Wassenaar, supra note 2, at 210.*
322. *See Price, supra note 311, at 654 (citing, as an example, Unimed, Inc. v. Richardson, 458 F.2d 787 (D.C. Cir. 1972) (deferring to FDA expertise and refusing to reverse an allegedly improper denial of an NDA). See generally United States v. C.R. Bard, Inc., 848 F. Supp. 287, 293 (D. Mass. 1994) (upholding a $30 million penalty against C.R. Bard with the admonition: ‘[This award] should send a message to [drug companies] that to subvert the Food & Drug Administration process intended to assure the safety and effectiveness of medical products is not just wrong, it is dumb.’)."
323. Price, supra note 311, at 654 n. 20 (quoting *PETER BARTON HUTT & RICHARD A. MERRILL, FOOD & DRUG LAW: CASES & MATERIALS* 534 (2d ed. 1991)). Peter Barton Hutt was general counsel at the FDA in the 1970s. *See Quirk, supra note 10, at 210.*
324. See GAO-HRD-80-64, supra note 165, at 38 (comparing drug regulation in Britain, Canada, West Germany, Switzerland, Norway and Sweden).
325. *See Janis Apse, Drug Regulation: Federal Perspectives—Outer Limits, 1 LEG. MED. Q 242 (1977).*
company officials instead of a tougher adversarial stance." The HPB is proud of the congenial relationship it has with representatives of Canadian drug subsidiaries of U.S. companies. The HPB holds to the philosophy of voluntary compliance, and most drug manufacturers and distributors comply with the legislation. The HPB has chosen to rely on persuasion, education and cooperation, rather than litigation, to achieve its objectives. The HPB's objective of protecting the health and safety of the public is not perceived as being at odds with the aims and objectives of the drug industry.

In order to avoid litigation when there is a compliance problem, the HPB first consults with manufacturers, and attempts to persuade them to comply with the law. "However, when a violation is serious, or when repeated violations that are less serious come to the attention of the HPB, the violator may be prosecuted." Nevertheless, lawsuits are filed only as a last resort. HPB representatives emphasize the lack of any type of formal hearing in the regulatory process, and perceive this as a method of avoiding the confrontational atmosphere that exists in the United States. The HPB's approach to compliance procedures assures that there is little food and drug litigation in Canada. "Everything is done in the quiet, unobtrusive Canadian way."

Some commentators have criticized the HPB's use of selective enforcement policies, arguing that it results in the denial of due process to some companies and agency decisions which are not subject to judicial review. Large corporations have the resources to withstand a compliance challenge, either by curing the

326. Id.
327. See Regush, supra note 170, at A1.
328. HPB, supra note 68, at 39.
329. See Curran, supra note 122, at 645.
330. See CURRAN, supra note 5, at 161.
331. See Curran, supra note 122, at 645; HPB, supra note 68, at 39.
332. See HPB, supra note 68, at 39.
333. See Curran, supra note 122, at 645.
334. See Morrison, supra note 110, at 640; Wassenaar, supra note 2, at 211.
335. See Curran, supra note 122, at 645. In fact, there are relatively few lawyers in Canada who specialize food and drug law. See id. at 644. See generally James A. Robb, Comments & Views from the Perspective of a Canadian Food Lawyer, 30 FOOD DRUG & COSM. L.J. 659 (1975).
336. Wassenaar, supra note 2, at 211.
337. See Wassenaar, supra note 176, at 454–55.
fault or defending the allegations. Small companies, on the other hand, are more likely be forced to pay the fine or go out of business. This implies a certain amount of coercion in the HPB’s “voluntary compliance” approach. The fear of retaliation that exists in the drug industry in the United States is not altogether absent in the Canadian system. The HPB, like the FDA, is able to use the threat of prosecution and public exposure to coerce drug companies to follow the agency’s dictates.

Because prosecution under the Food and Drugs Act is so rare in Canada, the exceptions are particularly conspicuous. Canadian drug companies consider it a public relations disaster to be listed in the HPB bulletin as having been convicted under the Food and Drugs Act.

In addition to the problems of due process raised by selective enforcement, the “collegial attitude” itself is also viewed by some as a major defect in Canada’s regulatory system. “Many American consumer advocates and sources within the FDA . . . say this [collegial] attitude is ‘naïve and very dangerous,’ especially when Canadian branch-plant operations are controlled by foreign head offices.” A senior FDA source has been quoted as saying “[t]he companies will try to get away with everything they can. None of this nice guy stuff is going to work when millions of dollars in potential profits are involved.”

While the American system appears to be more adversarial, and the Canadian system more collegial, the end result in each system is very similar. In most cases there is “voluntary” compliance by industry, whether out of cooperative public-health goals or due to direct or indirect coercion from the regulatory agency. Moreover, in both countries, to some degree, the

338. See Robb, supra note 335, at 665.
339. Id.
340. See Wassenaar, supra note 176, at 458.
341. See Robb, supra note 335, at 661–62. “The public relations consequences of this type of charge are difficult, if not impossible, to overcome.” Id. See also Genentech, Inc. v. Patented Med. Prices Review Bd., 44 [1992] C.P.R.3d 335, 337 (holding that the drug company’s mere participation in a PMPRB hearing “would damage their reputation in the eyes of the public, as evidenced by the negative media coverage” and “any adverse determination by the Board would lead to . . . stigmatization of the applicants . . . and would irreparably harm the [drug company’s] goodwill”).
342. See LEXCHIN, supra note 32, at 187.
344. Id.
regulated fear the power of the regulators. Regulation is, in any
system, liable to be coercive to some degree, and even Canadian
experts view this as "legitimate coercive intervention in . . . the
public interest."345

VI. CONCLUSION

The pharmaceutical regulatory systems in the United States
and Canada are very similar in many respects. This is not a
surprise considering the common history and development of the
two systems, as well as their common goal of protecting the public
from unsafe drugs. Many of the substantive regulations are the
same in both countries, as seen in the new drug approval process
and administrative inspections. With the ratification of NAFTA,
many of the differences that did exist have now been eliminated.
The drive for efficiency and cost-savings may lead to the
elimination of remaining differences. For example, the United
States is considering legislation that would follow Canada's model
of drug price regulation. Similarly, the United States is now taking
steps toward the Canadian practice of using outside experts in the
new drug review process.

While the two countries have substantively similar
regulations, distinctions appear primarily in the areas of
constitutional and administrative law. These distinctions stem
from differences between the parliamentary system of Canada and
the U.S. system with its separate executive and legislative
branches. As discussed, the U.S. rulemaking system is more open
to participation than the Canadian system. Nevertheless, there is a
perception that the U.S. system is adversarial and the Canadian
system is collegial. Ultimately in both systems there is mostly
voluntary compliance with the regulations, and some degree of
coercion by the regulatory agency. In summary, while there are
some important differences between the regulatory systems of the
United States and Canada, their goals and means of effectuating
them are very much aligned.