

Access Delayed, Access Denied

Waiting for Medicines in Canada

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Executive summary

This report analyzes the total time patients must wait in Canada to gain access to newly invented pharmaceutical and biological medicines, also known as patented drugs. [1] The purpose of this report is twofold: (1) to draw attention to the impact that Canadian public policies and institutions have on the time it takes for patients to gain access to new medicines; and (2) to contribute to the policy discussion about the relative performance of government drug-insurance programs in providing timely coverage for new medicines compared to private-sector drug insurance in Canada.

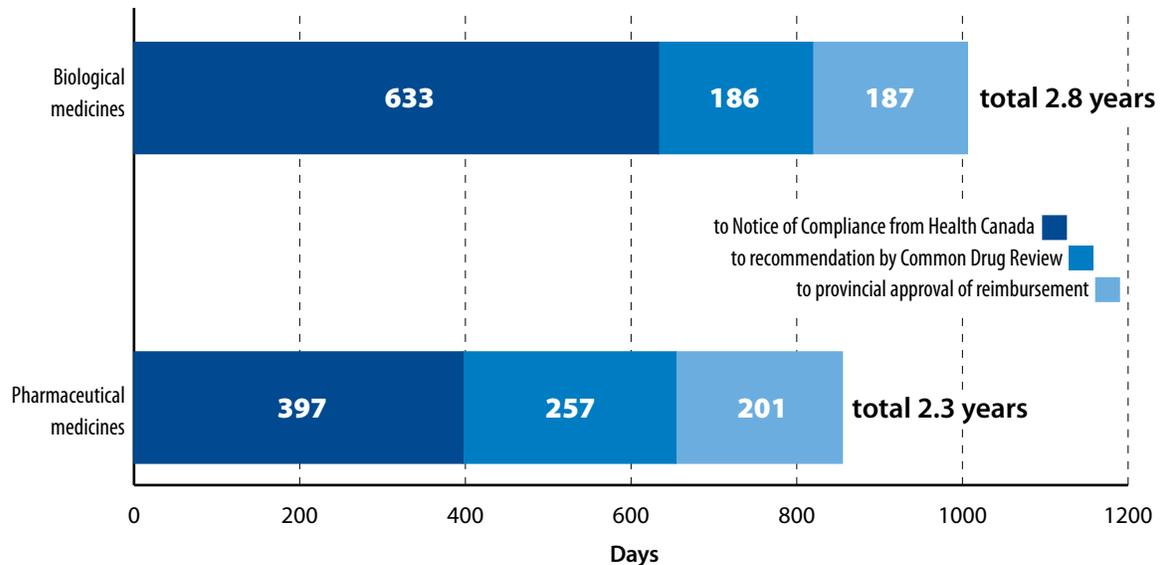
Research indicates that it takes over 10 years to develop the average drug [DiMasi et al., 2003, 1995]. Various government policies are responsible for extending the time that patients must wait for access to a new medicine after it has been developed. An estimate of the total time spent waiting for access to new medicines in Canada after they have been developed can be calculated by adding:

- 1 the time it takes for Health Canada to certify that a new drug is safe and effective and allowed to be sold in Canada;
- 2 the time spent waiting for the national Common Drug Review (CDR) to issue its recommendation that a new drug should become eligible for public reimbursement in the provinces;
- 3 the time spent waiting for the provincial programs to finally make a decision about reimbursement for a new drug.

Figure 1 shows the consolidated average wait for access to new medicines in Canada, broken down by each of the three segments described above. The wait is measured in days and presented separately for pharmaceuticals and biologics. Reading left to right; the first segment of the bar represents the Health Canada approval time. For new biological medicines, the time spent during this segment was 633 days, on average, in 2005 compared to 397 days, on average, for new pharmaceutical medicines. The data for the period from 2001 to 2005 suggest that Health Canada's approval times have improved for pharmaceuticals since 2003 but have gotten longer for biologics. Comparing the wait internationally (averaged across both biological and pharmaceutical medicines, and across all drug submission types) suggests that Health Canada's performance also improved relative to Europe's in 2005 but has been longer than that in both the United

[1] The Fraser Institute has previously published on the issue of wait times for medicines in Canada [see Graham, 2005].

Figure 1: Total time (days) spent waiting after a new drug has been developed before patients have access to new pharmaceutical and biological medicines in Canada, by wait segment, averaged across all new drug-submission classes, 2004–2005



Sources: Health Canada, 2006a; Brogan Inc., 2006a; authors' calculations.

States and Europe in the majority of the five years studied. This segment of the wait for access to new medicines equally affects all patients in Canada, whether they pay for their drugs through private insurance, out-of-pocket expenditure, or public drug programs. Improving the efficiency and capacity of Health Canada to conduct new drug reviews can reduce the time spent waiting for marketing approval.

The second and third segments of the bar represent a single period of waiting for those who are dependent on public drug programs, or for anyone needing drugs that are only administered on an in-patient basis and cannot afford to pay cash. The wait for a CDR reimbursement recommendation is presented separately from the wait for provincial approval of reimbursement. This allows the reader to identify the contribution of both jurisdictions to the overall time before reimbursement of a drug is approved. Notably the CDR's contribution to the wait time for new pharmaceuticals is 257 days compared to 186 days for new biologics. By comparison, the wait for provincial approval of reimbursement adds, on average, another 201 days for pharmaceuticals and another 187 days for biologics. The total average wait for approval of reimbursement is 458 days for pharmaceuticals and 373 days for biologics. In other words, patients who are dependent on public drug benefits or who need drugs that are delivered only through in-patient settings must wait more than a year after Health Canada has certified a new drug as safe and effective before they finally have access to it. Added together, the total

average wait for patients dependent on public drug benefits in Canada for access to new biological medicines is 1,006 days or approximately 2.8 years; and for access to new pharmaceutical medicines, the wait is 855 days or approximately 2.3 years.

There is also a significant number of drugs that are approved by Health Canada as safe and effective but never declared eligible for reimbursement by the CDR or the provinces. The CDR approved slightly less than half (11 of 23) of the pharmaceuticals and only about 30% (4 of 13) of the biologicals that it reviewed during 2004 and 2005. Quebec, the only province not participating in the CDR, approved more new pharmaceuticals (12) than the CDR itself and nearly as many biologicals (3). All other provinces approved significantly fewer new pharmaceuticals and biologicals for reimbursement than the CDR itself recommended.

New drugs covered by private insurance, however, are generally eligible for reimbursement as soon as Health Canada has certified that the drugs are safe and effective for use by Canadians. However, private insurance sometimes has annual coverage limits that might expose patients to significant out-of-pocket costs in rare cases involving very expensive drugs. Instead of, and sometimes in addition to, annual expenditure caps, private insurers also apply user fees like deductibles and copayments. By creating a price at the point of consumption, user fees rationalize patients' demand for drugs and encourage cost-efficient substitution between treatment alternatives.

Introduction

This report analyzes the total time patients must wait in Canada to gain access to newly invented pharmaceutical and biological medicines, also known as patented drugs. [1] Pharmaceutical medicines are chemically based while biological medicines use organic material in their structure. The purpose of this report is twofold: (1) to draw attention to the impact that Canadian public policies and institutions have on the time it takes for patients to gain access to new medicines; and (2) to contribute to the policy discussion about the relative performance of provincial drug-insurance programs in providing timely coverage for new drugs compared to standard access to new drugs in private-sector drug insurance in Canada.

The information contained in this report is designed to be easily accessible to the reader. It will be an annual publication to ensure that public attention to this important topic is sustained. The report provides patients with some of the information they need to determine whether the time that they wait for access to new medicines is unnecessarily long in Canada, and whether publicly funded and managed drug-insurance programs provide greater benefit than privately funded and managed alternatives. It is our hope that the report will encourage governments to work harder to reduce any unnecessary delays in approving access to new medicines. We also hope that the report encourages policy-makers to give fair and honest consideration to policy alternatives that rely more on a properly regulated, competitive, private insurance market, which could produce better outcomes for patients and for taxpayers than current public drug-insurance programs while achieving the same social goals.

The report focuses on new patented medicines because this class of drugs is uniquely affected by public policies that delay access for patients. Because government approval of generic drugs is based on the assumption that generics are copies of new drug inventions that had previously been approved, there is no substantive delay observed or expected before the public has access to generic products and this class of drugs is not studied here. Because there are distinct differences observed in the time it takes for new pharmaceutical and biological medicines to be approved, the report also examines the impact of delays affecting access to these two classes of patented medicines separately whenever possible.

The findings presented here may differ from those of other studies due to differences in methodology. For instance, some studies separate the wait time for access to “new active substances” (NAS)—i.e., a drug molecule that has never been invented before—from other types of new drug-submission classes (e.g., modifications of pre-

[1] The Fraser Institute has previously published on the issue of wait times for medicines in Canada [see Graham, 2005].

viously approved molecules). By comparison, this paper looks only at an aggregate average of the time spent waiting for access to medicines across all new drug-submission classes. This is done to make the data comparable to other international jurisdictions where the data is not separately available (from centralized sources) by new drug-submission classes that are equivalent to Canada's.

There are four segments in the total time spent waiting for access to new medicines in Canada; each is affected by a different set of public policies, which in turn affect various patient populations differently. This report measures the length of time patients must wait during each of these segments as a result of current public policies and proposes market-based, private-sector alternatives that could help quicken access to new medicines once they have been developed.

1 The global wait for development of new drugs

The first waiting period for access to new medicines is the time it takes to develop a new drug. This period is measured from the patented discovery of a new drug molecule until the first time an application is submitted for marketing approval anywhere in the world. The longest period within the drug development phase involves clinical testing of a newly invented medicine among volunteer patients. Clinical testing of new drugs involves thousands of patients, often located across international jurisdictions, over many years. No drug is submitted for marketing approval anywhere in the developed world without having first completed successful clinical tests.

The costs and time spent in the development of new drugs is affected mostly by universal scientific standards of experimental research. These standards determine for example, how many patients must be enrolled in the testing of a new drug in order for researchers to have confidence in the statistical results and conclusions. There are also scientific standards for the design and conduct of clinical drug testing in patient populations as well as ethical standards about the treatment and use of human and animal subjects. These standards have international acceptance and affect the absolute minimum period of time it takes to complete clinical testing of the safety and effectiveness of any new medicine.

While these rules and regulations are set at the national level, drug development occurs on a global basis. The United States and Europe are the largest markets for drug sales in the world [IMS Health Inc., 2006a & 2006b]. And since January 1, 2005, the US Food and Drug Administration (US FDA) and the European Medicines Agency (EMA) have engaged in a successful pilot project to harmonize American and European scientific standards for the clinical development of new medicines [EMA, 2005]. Because of this, pharmaceutical and biotech companies conduct clinical trials to meet the standards of both the US FDA and the EMA, knowing that the results will then allow their prod-

ucts to be marketed in the most important markets first. Therefore, in practical effect FDA and EMEA safety standards largely determine the actual minimum global length of time it takes to develop new medicines. If Canadian safety regulations are in various ways more strict than those applied by the United States and Europe, [2] then the development phase in Canada can be delayed beyond the minimum waits that affect American and European patients.

In this, the first edition of this report, we have not identified the ways that Canadian public policies might uniquely lengthen the development segment of the wait for access to new medicines in Canada, either by requirements that are stricter than the minimum scientific standards or than the European and American standards. In future reports, we will investigate this question further and collect data that will allow us to identify and quantify any extra waiting time that might be caused by Canadian policies affecting this segment.

For the purposes of this report, the global development time is assumed to be a function of factors outside of Canada's control and therefore the time associated with this segment is presented for completeness but is not the focus of the main policy discussion in this paper nor part of the overall length of time measured here to represent the wait for access to new medicines. This paper is concerned with government policies that can contribute to an unnecessary further delay in access to new medicines—even after the lengthy period of time it takes to develop them in the first place.

2 The national wait for marketing approval from Health Canada

The next segment of the wait for new medicines, and the first segment affected by government policies and institutional performance in Canada, is the wait for drug safety and efficacy (or marketing) approval. This period is measured between the date at which an application is made for marketing approval of a new drug in Canada to the date at which Health Canada issues a Notice of Compliance (NOC) certifying that a new drug is safe for sale and effective for treatment.

This segment is directly affected by the time spent by Health Canada in reviewing applications for marketing approval before it certifies new drugs. Before any new drug is legally allowed to be sold in Canada, it must first receive the official approval of Health Canada. This process involves a scientific review of published clinical research conducted on new drugs and the issuance of an official decision—the Notice of Compliance—certifying that a drug is safe for sale to Canadians and that the drug's efficacy

[2] Health Canada's regulations require minimum compliance with international standards for clinical research on new medicines but do not exclude stricter regulations as deemed necessary by the government of Canada [Health Canada, 2006b].

has been proven up to acceptable scientific standards for health treatments. [3] Marketing approval for new drugs occurs at the national level and, therefore, any delay caused by inefficiencies in Health Canada's process of reviewing applications and granting marketing approval affects the wait time for access to new medicines for the entire Canadian patient population.

3 The national wait for reimbursement recommendation by the CDR

The next segment of the wait for new medicines, and the second segment affected by government policies and institutional performance in Canada, is the time spent by the Common Drug Review (CDR) before it issues a recommendation that a new drug should be reimbursed by federal, provincial and territorial (FPT), publicly funded drug programs. The period is measured from the date at which Health Canada issues a NOC for a new drug to the date at which the CDR issues a reimbursement recommendation.

The Common Drug Review (CDR) is part of the Canadian Agency for Drugs and Technologies in Health (CADTH). It was established in September 2003 and is managed by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA). The CDR is a single process for reviewing new drugs and providing listing recommendations to participating publicly funded FPT drug-benefit plans in Canada. All jurisdictions participate except the province of Quebec [CADTH, 2006].

According to Health Canada, the CDR was set up to reduce duplication and provide equal access to high-level evidence and expert advice, thereby contributing to the quality and sustainability of Canadian public drug plans. The CDR was also supposed to streamline the approval of reimbursement by consolidating the submission process for pharmaceutical manufacturers [Health Canada, 2006e]. Once Health Canada has issued an NOC, manufacturers must apply to the CDR for a reimbursement evaluation. The CDR process involves a systematic review of the available clinical evidence, a pharmacoeconomic evaluation, and the issuance of a recommendation by the Canadian Expert Drug Advisory Committee [CEDAC] that the drug be listed, not listed, or listed with conditions under participating FPT drug plans [CADTH, 2006].

4 The wait for eligibility for provincial reimbursement

The next segment of the wait for new medicines, and the third segment affected by government policies and institutional performance in Canada, is the time spent waiting for provincial reimbursement eligibility. This period is measured from the date at

[3] For general information about Canada's review process, please see Health Canada, 2001.

which CDR issues its recommendation about reimbursement of a new drug to the date at which each provincial government drug plan issues an official notice that a new drug is eligible for public reimbursement.

After the CDR issues its recommendation that federal, provincial, and territorial (FPT) governments should pay for a new drug through their public drug plans, the new drug must receive additional approval from FPT government agencies before it finally becomes eligible for public reimbursement under FPT health and drug insurance programs. CDR recommendations are not binding on FPT drug benefit plans, which make their own decisions about listing and coverage based on a number of considerations: the CDR recommendation; advice and budget impact information prepared by drug-plan staff; and the plan's mandate, priorities, and resources (CADTH, 2006). Because of this, the wait for access to new medicines differs from jurisdiction to jurisdiction.

The wait for public reimbursement most heavily affects recipients of public drug benefits who lack the financial resources to pay privately but it also affects those who pay privately for drugs. In Canada, provincially funded and managed health-insurance plans generally cover the costs of health care delivered in hospitals and physicians' clinics for the entire population. Private payment for these services is illegal. Therefore, drugs administered to in-patients in hospitals or clinics are paid for through publicly funded health-insurance programs. However, public reimbursement of drug expenses for out-patients (i.e. patients who do not require hospitalization) is not available on a universal basis and only particular sub-populations (e.g., seniors, welfare recipients, military, aboriginals) are eligible.

The bulk of the Canadian population pays for drugs administered on an out-patient basis through private insurance or cash expenditure but private insurance does not generally cover any drugs administered on an in-patient basis (i.e. in a hospital). Private insurers in Canada generally grant automatic reimbursement to out-patients for any drug that has been approved by Health Canada. This means that access to drugs for out-patients with private insurance or those with the ability to pay cash is not affected by delays in approving provincial reimbursement. But for drugs administered on an in-patient basis, all those who lack the means to pay cash, whether they have public or private insurance, are equally affected by government reimbursement delays or denials. Further, it is possible that, when drug makers know that their product must be delivered on an in-patient basis, they will not bring a product to market at all in the absence of public reimbursement, because there will not be enough cash-paying patients to make it economical. In this case, everyone is affected by delays in approving provincial reimbursement [for an example, see Skinner, 2006].

1 The global wait for new drug development

Issuance of new drug patent to first international application for marketing approval

Governments across the world regulate drugs to ensure the safety of the product. For example, Health Canada has a national mandate to ensure the safety of drugs sold in Canada and therefore regulates which products are allowed to be sold, and under what conditions. Canadian regulations fall under the Food and Drugs Act 1985 [Canada, DOJ, 1985]. In order to obtain marketing approval for a drug, manufacturers must provide Health Canada with evidence of its successful clinical testing in patients. Health Canada uses the Therapeutic Products Directorate (TPD) to approve new pharmaceutical medicines and the Biologic and Genetic Therapies Directorate (BGTD) to approve new biological medicines.

International scientific standards for clinical trials are established by the World Medical Association Declaration of Helsinki [World Medical Association, 1964]. These are generally interpreted as the minimum global standard. Actual standards for demonstrating the safety of drug products are set by national governments through domestic regulation and determine the number, length, and rigour of clinical trials that will be required. For instance, Health Canada’s regulations require minimum compliance with international standards for clinical research on new medicines but do not exclude stricter regulations as deemed necessary by the government of Canada [Health Canada, 2006b].

Nevertheless, because of the importance of the American and European markets, throughout the world, the actual minimum time spent during drug development is determined by the length of time it takes to satisfy the requirements of the US Food and Drug Administration (US FDA) and the European Medicines Agency (EMA) for clinical testing. The most recent research indicates that, on a global basis, the process of developing a new drug takes, on average, approximately 10 years [DiMasi et al., 2003, 1995]. [4] This time is measured from the point that a drug discovery is patented until an application is made for marketing approval with the US FDA (table 1).

Table 1: Estimated time spent (in months) from issuance of new drug patent to application for US FDA marketing approval, for drugs approved between 1985 and 2000.

Patented discovery to start of human clinical trials	52.0
Start of human clinical trials to new drug application for US FDA marketing approval	72.1
Total	124.1 (10.3 years)

Source: DiMasi et al., 2003, 1995.

[4] Evidence also indicates that the cost of developing a new patented drug ranges between \$521 million (US\$2000) and \$2,119 million (US\$2000) depending on the company and the drug; the average is \$868 million (US\$2000) [Adams and Brantner, 2006].

2 The national wait for marketing approval from Health Canada

Canadian application for marketing approval to Notice of Compliance

The next segment of the wait for new medicines, and the first segment affected by government policies and institutional performance in Canada, is the wait for drug safety and efficacy (or marketing) approval. This segment is directly affected by the review time spent by Health Canada to certify that new drugs are safe and effective before allowing them to be sold on the market. [5]

In Canada, the time spent waiting for marketing approval for a new drug is measured from the date at which an application for government approval of a new medicine is recorded or filed in the Central Registry (CR) of Health Canada's Therapeutic Products Directorate (TPD) or Biologic and Genetics Therapies Directorate (BGTD) following the completion of clinical testing. The period ends when Health Canada issues an official Notice of Compliance (NOC). International systems for drug approval in Europe and the United States measure the same period but use different terminology for describing start and end dates.[6]

The following sub-sections present the findings on Health Canada's performance in approving drugs according to the following: changes in drug-approval times within Health Canada from 2001 to 2005 comparing new pharmaceutical and biological medicines; comparison of Health Canada's performance on drug-approval times relative to the FDA and the EMEA for new pharmaceutical and biological medicines together from 2001 to 2005.

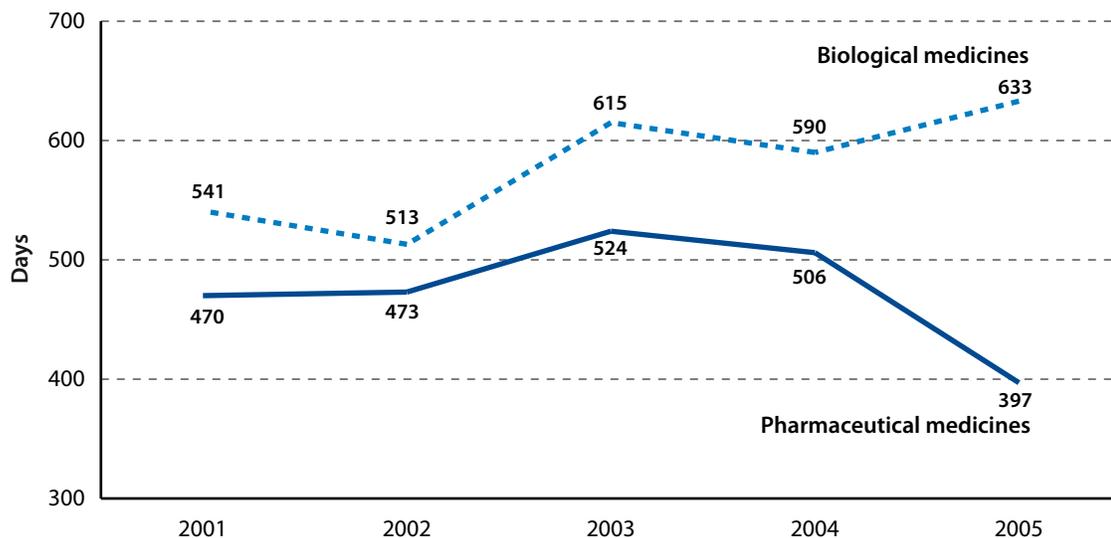
-
- [5] In Canada, this falls under the authority of Health Canada, Health Products and Food Branch: Therapeutic Products Directorate (TPD) for pharmaceutical medicines; and Biologic and Genetics Therapies Directorate (BGTD) for biological medicines. The equivalent authority in the United States lies with the Department of Health and Human Services (HHS), Food and Drugs Administration (FDA): Center for Drug Evaluation and Research (CDER) for pharmaceutical and biological medicines as of 2004; and formerly the Center for Biologics Evaluation and Research (CBER) for biological medicines prior to 2004. As of 1999, responsibility for both pharmaceutical and biological medicines was centralized for all countries that are members of the European Union through the European Medicines Agency (EMA).
- [6] There are differences in how the time is reported that affect how this period is compared across international jurisdictions. See the Appendix (pages 33–37) for a discussion of this issue, information on data sources, and other explanatory notes on the different classes of drug submissions in Canada, Europe, and the United States.

Changes in drug-approval times in Canada, 2001–2005

In this section, aggregate delays in approving drugs are presented across all types of new drug submissions including new active substances (NAS), new drugs submissions (NDS) and supplementary new drug submissions (SNDS) (see appendix for definitions of these terms). The data presented will be used to measure the average time spent waiting for Health Canada to issue an approval across all new non-generic drug submission classes. However, the data is separated by pharmaceutical and biological medicines for comparison.

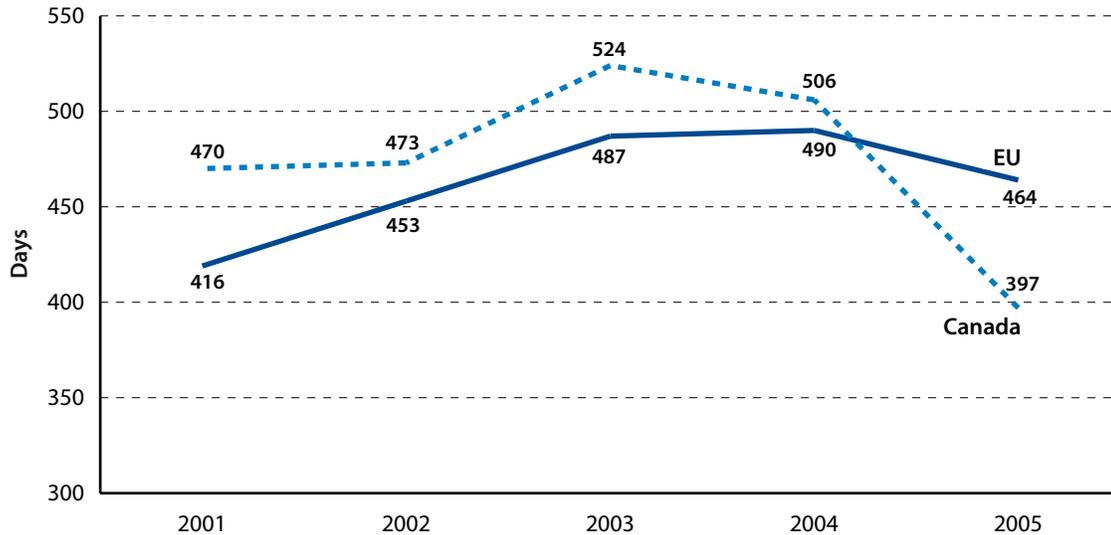
Figure 2 shows the average approval time in days for new pharmaceutical and biologic medicines for the years 2001 to 2005. Approval times for both types of medicines fluctuated over the five-year period. Average approval times for pharmaceuticals took fewer days than biologics in every year monitored. This difference is partially, but not totally explained by the fact that most biological medicines are classified as new active substances [NAS] drugs and the evidence indicates that approval times can be longer for this class of drug submission. 2002 was the year with the least disparity in approval times with pharmaceutical medicines averaging 473 days and biologics averaging 513 days, a difference of 40 days. In contrast, by 2005 approval times were 236 days apart, as average approval times for pharmaceuticals dipped to 397 days and average approval times for biologics peaked at 633 days.

Figure 2: Average time (days) spent waiting for Health Canada to approve new pharmaceutical and biological medicines, averaged across all new drug-submission classes, 2001–2005



Source: Health Canada, 2006a.

Figure 3: Average time (days) spent waiting for government approval of new pharmaceutical medicines, averaged across all new drug-submission classes, Canada and European Union, 2001–2005



Source: Health Canada, 2006a; EMEA, 2006.

Drug-approval times in Canada and Europe, 2001–2005

Figure 3 displays the average number of days spent waiting for approval of new medicines in Europe and Canada for the years 2001 to 2005. The data presented only show time spent in both jurisdictions for the approval of new pharmaceutical medicines. Separate European data for biological medicines was not available. The data indicate that Health Canada took longer on average to approve new pharmaceuticals compared to European Medicines Agency (EMA), its European counterpart, in four of the five years used for comparison. In 2005, Health Canada’s performance improved significantly relative to its European counterpart. This is an encouraging development and future editions of this report will monitor this comparison to see if it reflects a trend or a one-time occurrence.

Drug-approval times in Canada and the United States, 2001–2005

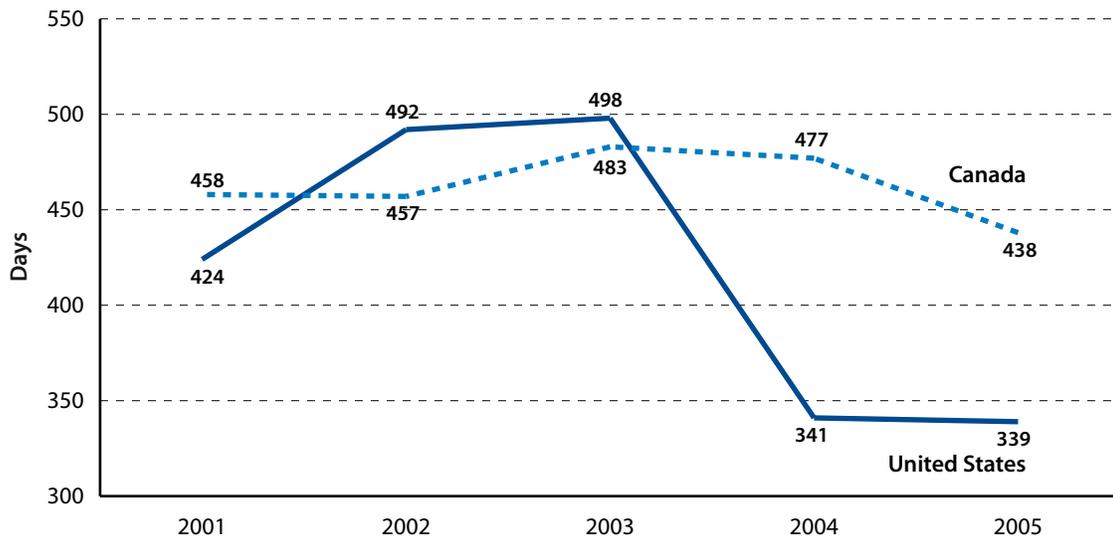
The United States only publishes median figures for drug-approval times. Figures for pharmaceutical and biological medicines are published in separate tables in some years (2001–2003) and aggregated in other years (2004–2005). As well, figures for drugs having priority review status are published separately from those with non-priority status. Canada also publishes median drug-approval times. The Canadian data are aggregated

by Health Canada according to the priority or non-priority review status of the drugs, and reported separately by drug submission class. In order to make the two sets of data comparable, it was necessary to aggregate the separately reported medians by calculating a weighted median proportional to the number of drugs approved in each sub-set as a percentage of the total number of drugs approved overall [see Esmail and Walker, 2006, for methodology].

Figure 4 displays the difference between median approval times in Canada and those in United States for all new drug applications between 2001 and 2005. The delays are presented as consolidated figures across all classes of new drug applications and are an aggregate including both pharmaceutical and biological medicines.

The data show that time for drugs approvals in Canada were longer than those in the United States in three of the five years studied. Health Canada took a shorter time than the US FDA to approve drugs in 2002 and 2003 but a longer time in 2001, 2004, and 2005. The widest gap was in 2004, when new drug approvals took 136 days longer in Canada than in the United States. In 2005, the Health Canada’s median approval time still lagged that of the US FDA by a great deal but the gap had decreased to 99 days.

Figure 4: Median time (days) spent waiting for government approval of new pharmaceutical and biological medicines, across all new drug-submission classes, average weighted by submission class, Canada and United States, 2001–2005



Source: Health Canada, 2006a; US FDA, 2006.

Conclusion

The data from 2001 to 2005 suggest that Health Canada's approval times, when averaged across all drug submission types, have improved for pharmaceuticals since 2003 but have gotten longer for biologicals. Health Canada's performance across all drug submissions also improved relative to Europe in 2005, but has been poorer than the performance of both the US FDA and the EMEA in the majority of the years studied.

3 The national wait for reimbursement recommendation by the Common Drug Review

Notice of compliance to recommendation by Common Drug Review

The next segment of the wait for new medicines, and the second segment affected by government policies and institutional performance in Canada, is the time spent by the Common Drug Review (CDR) to issue a recommendation that a new drug should or should not be reimbursed by federal, provincial and territorial (FPT), publicly funded drug programs. The period is measured from the date at which Health Canada issues a NOC for a new drug and the date at which the CDR issues a reimbursement recommendation.

Data source

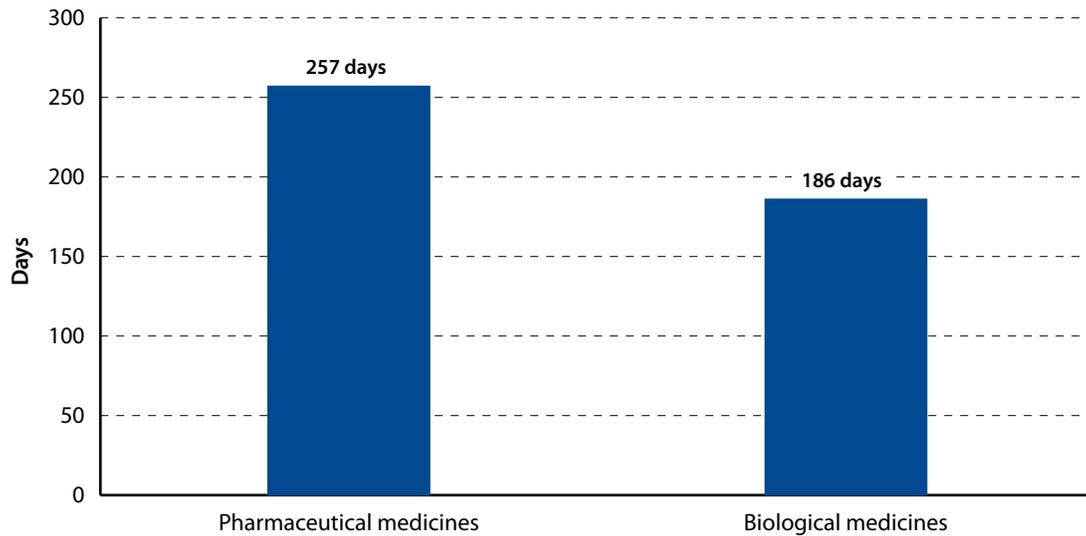
Brogan Inc., a private consulting and data firm, generously made available to us their data-set containing the date when the NOC was issued for every new drug submission, the date of the reimbursement recommendation by the CDR, and the date of the final reimbursement decision by each province for these drugs. Brogan's data cover all new drug-submission classes. Data covering the first two full years after the introduction of the CDR (2004–2005) are presented in the following graphs showing separate data for pharmaceutical medicines and biological medicines where possible. Brogan's data-set appears to be missing a small percentage of data but this is not expected to affect the averaged results in a statistically significant way.

Time spent waiting for recommendation by the CDR, 2004–2005

The data presented in this section examine only those drugs that were submitted to the CDR for reimbursement review during 2004 and 2005. The data available from Brogan Inc. was based on a sample of 23 submissions made to the CDR for new pharmaceutical medicines and 13 for new biological medicines. [7] Figure 5 shows the times spent in days waiting for CDR to issue a recommendation over the period from 2004 to 2005. This data is averaged across all drugs that received a recommendation, positive or negative, during this period. The average time spent waiting for the CDR to issue a recommendation on the pharmacoeconomic value of pharmaceutical medicines that

[7] This sample excludes any drugs for which the Brogan database did not contain full data. The actual total number of drugs reviewed by CDR is larger.

Figure 5: Time (days) spent waiting from Notice of Complicance to positive recommendation by the Common Drug Review, averaged across all new drug-submission classes, 2004–2005



Source: Brogan Inc., 2006.

have already been approved as safe and effective by Health Canada is an additional 257 days. The equivalent figure for biological medicines is 186 days, on average. As the data show, the time spent in CDR is longer for pharmaceutical medicines than for biological medicines. This is the reverse of the comparable figures for the time spent waiting for Health Canada to issue a NOC, where the wait was longer for biologicals.

4 The wait for eligibility for provincial reimbursement

Recommendation by CDR to decision on provincial reimbursement

The final segment of the wait for new medicines affected by government policies and performance is the wait for approval of provincial reimbursement. Once certified safe for sale by Health Canada's NOC, new drugs must receive additional approvals from federal, [8] provincial, and territorial (FPT) government agencies before they become eligible for public reimbursement under FPT health and drug-insurance programs. FPT drug agencies issue decisions about the eligibility for reimbursement of new medicines separately from CDR. Therefore, the wait time for access to new medicines differs by jurisdiction.

FPT authorities have three options when deciding about eligibility for reimbursement under public drug plans. First, they can declare a drug ineligible for public reimbursement. Second, they can declare a drug eligible for full reimbursement (F) of its costs without conditions. Third, FPT authorities can declare a new medicine eligible for reimbursement with restrictions (R).

In this study, only the performance of provincial reimbursement authorities will be compared on the basis of how long it takes each jurisdiction to approve new medicines for public reimbursement. Second, each province will be compared on the basis of how many new medicines they actually approve for reimbursement. Finally, the number of drugs approved by each jurisdiction will be compared to the number of drugs approved by CDR to see if the provincial authorities are actually following the recommendations of the CDR.

Time spent waiting for provincial reimbursement in Canada, 2004–2005

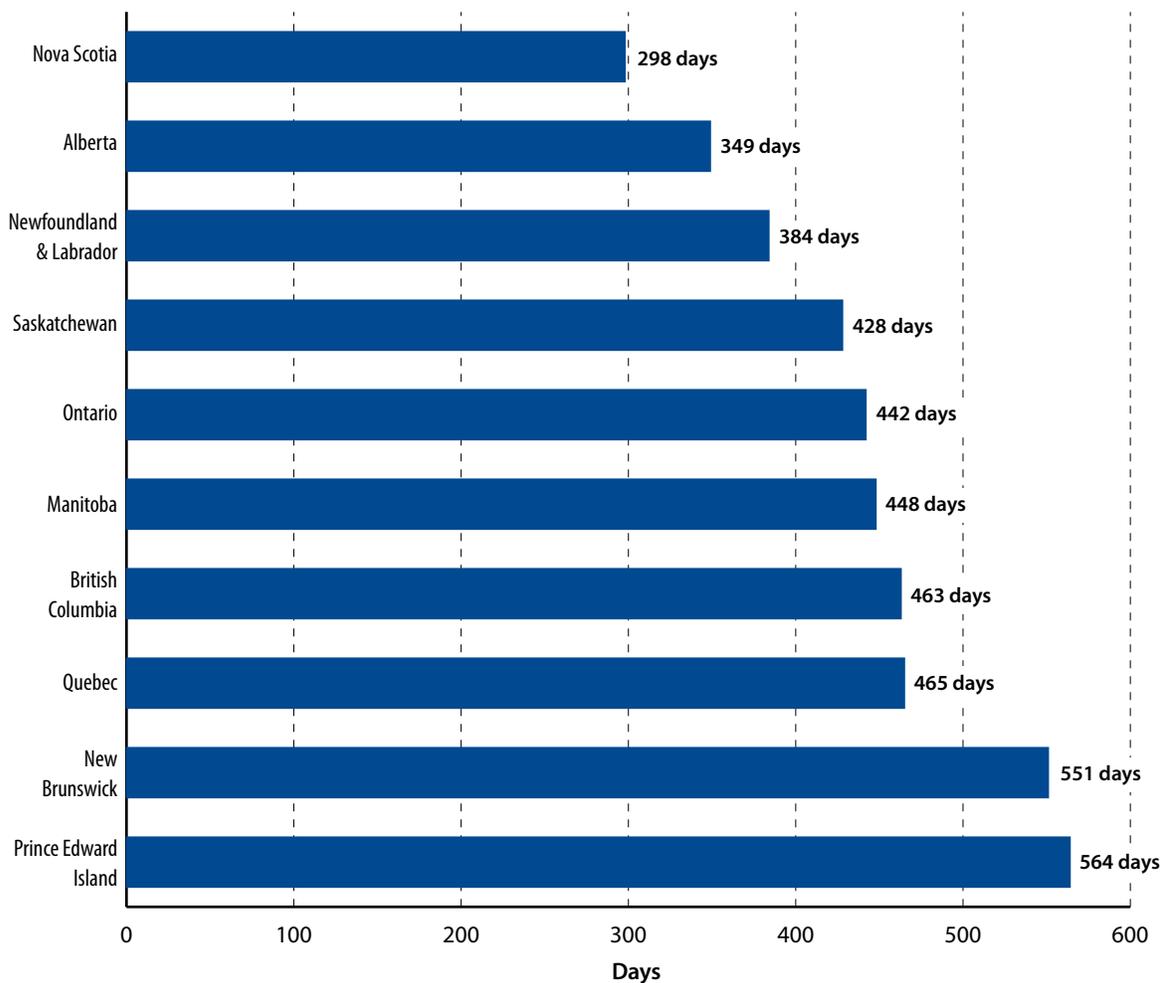
Figure 6 compares the time (in days) spent waiting for each province to issue a reimbursement approval, averaged across all drugs that received a positive approval and aggregating decisions for both full and restricted reimbursement. The period measured is between the date when Health Canada's issues a NOC for each drug and the date when a provincial reimbursement (PR) decision is issued, as evidenced by the publishing of the drug's listing in the provincial formulary. Quebec does not participate in the CDR process and the time spent waiting for a CDR recommendation is the same for

[8] The Government of Canada, through various programs, provides prescription-drug coverage for about one million Canadians who are members of eligible groups. These groups include First Nations and Inuit, members of the military, Veterans, members of the RCMP, and inmates in federal penitentiaries.

every province that does participate because CDR is a national agency, so presenting the differences in the overall wait are sufficient for comparison across all provinces.

It is notable that even though Quebec does not participate in the CDR, it is still among the slowest provinces when it comes to approving new medicines for reimbursement. This suggests that the added layer of bureaucracy introduced to the reimbursement process by the CDR has not increased the overall time it takes to reach a decision on provincial reimbursement, because all other provinces are participating in the CDR and seven of them are making faster decisions on average than Quebec.

Figure 6: Comparison of the average number of days spent waiting in Canadian provinces between Notice of Complicance and provincial reimbursement decision for new pharmaceutical and biological medicines reviewed by the Common Drug Review, 2004–2005



Note: Quebec does not participate in the CDR.
Source: Brogan Inc., 2006.

Table 2 displays the consolidated, average wait for approval of reimbursement between NOC and PR across all provinces and all new pharmaceutical and biological medicines submitted for review to the CDR in 2004 and 2005. Quebec is excluded from the calculation of the average NOC to CDR segment because it does not participate in the CDR but it is included in the overall NOC to PR delay. The data show that the average time spent waiting for provinces to approve new drugs for reimbursement in Canada after Health Canada has declared them safe and effective for sale was 439 days in 2004 and 2005.

Figure 7 (p. 20) compares the number of reimbursement approvals issued by each province for drugs that were reviewed by the CDR in 2004 and 2005. The data show that Quebec approved more new medicines for public reimbursement than all other provinces. In fact, Quebec approved double the number of new drugs approved by seven of the other provinces and 50% more than Saskatchewan, the province with the next highest number of new drug reimbursement approvals.

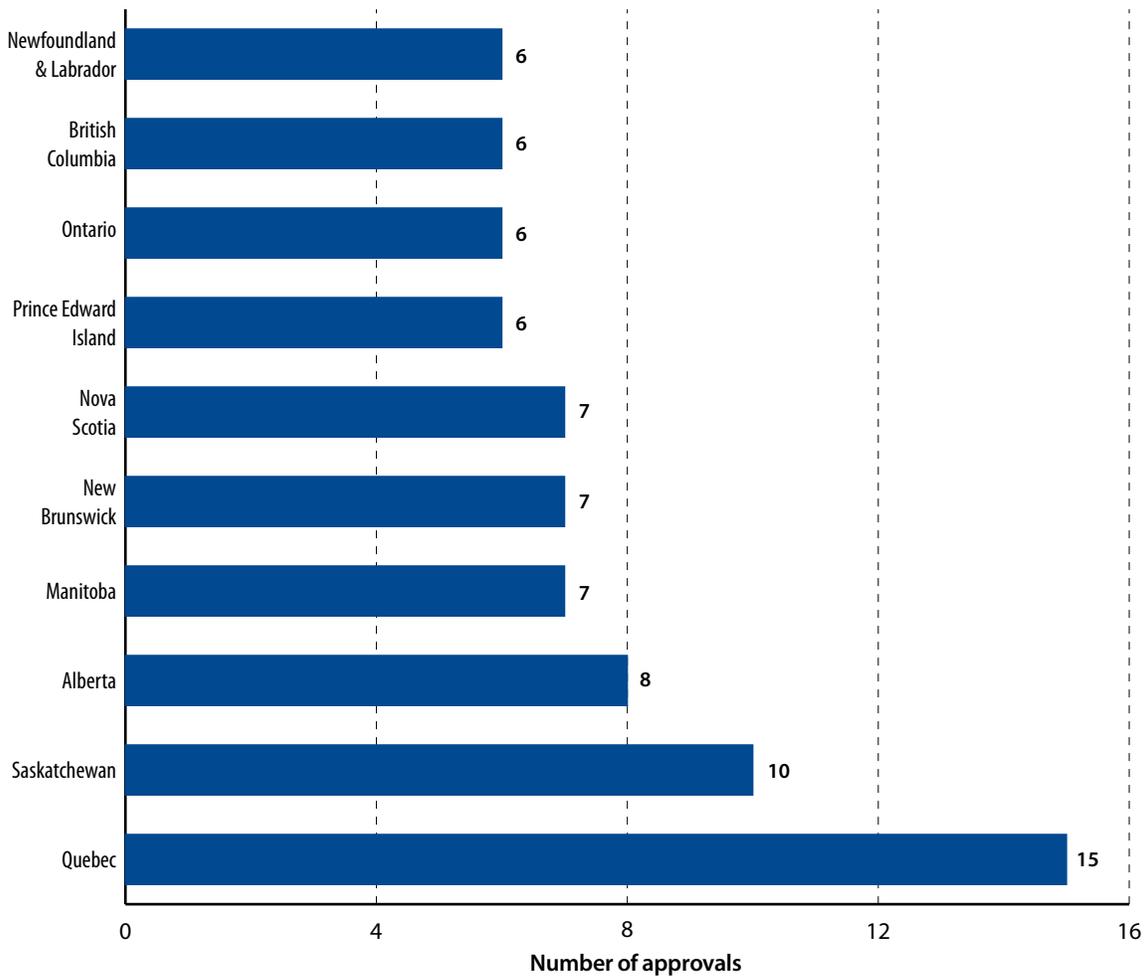
Figure 8 (p. 21) shows the number of new pharmaceutical and biological drugs approved in each province and by the CDR, as a percentage of the total number of new drugs reviewed by the CDR in 2004 and 2005. The data indicate that the CDR approved slightly less than half (11 of 23) of the pharmaceuticals and only about 30% (4 of 13) of the biologicals that it reviewed during 2004 and 2005. It is worth noting that Quebec, the only province not participating in the CDR, approved more new pharmaceuticals (12) than the CDR itself and nearly as many biologicals (3). All other provinces approved significantly fewer new pharmaceuticals and biologicals for reimbursement than the CDR itself recommended.

Table 2: Average time spent waiting between NOC and PR for new pharmaceutical and biological medicines submitted for review to CDR, 2004–2005

	Average wait (days) for pharmaceutical medicines	Average wait (days) for biological medicines
NOC to CDR	257	186
CDR to PR	201	187
NOC to PR	458	373
<i>weighted average, pharmaceutical and biological medicines</i>		439

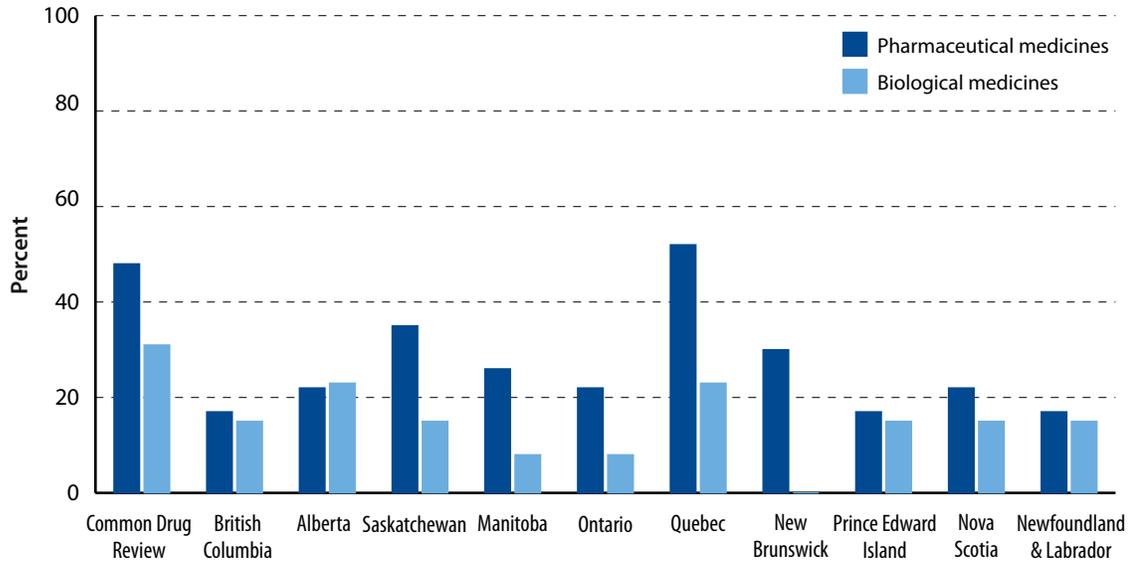
Source: Brogan Inc., 2006; authors' calculations.

Figure 7: Comparison of the number of provincial reimbursement approvals issued by Canadian provinces for new pharmaceutical and biological medicines reviewed by the Common Drug Review, 2004–2005



Note: Quebec does not participate in the CDR.
Source: Brogan Inc., 2006.

Figure 8: Provincial reimbursement approvals and positive reimbursement recommendations by the Common Drug Review as a percentage of total new pharmaceuticals and biologicals submitted for approval of reimbursement, including both full and restricted reimbursement decisions, 2004–2005



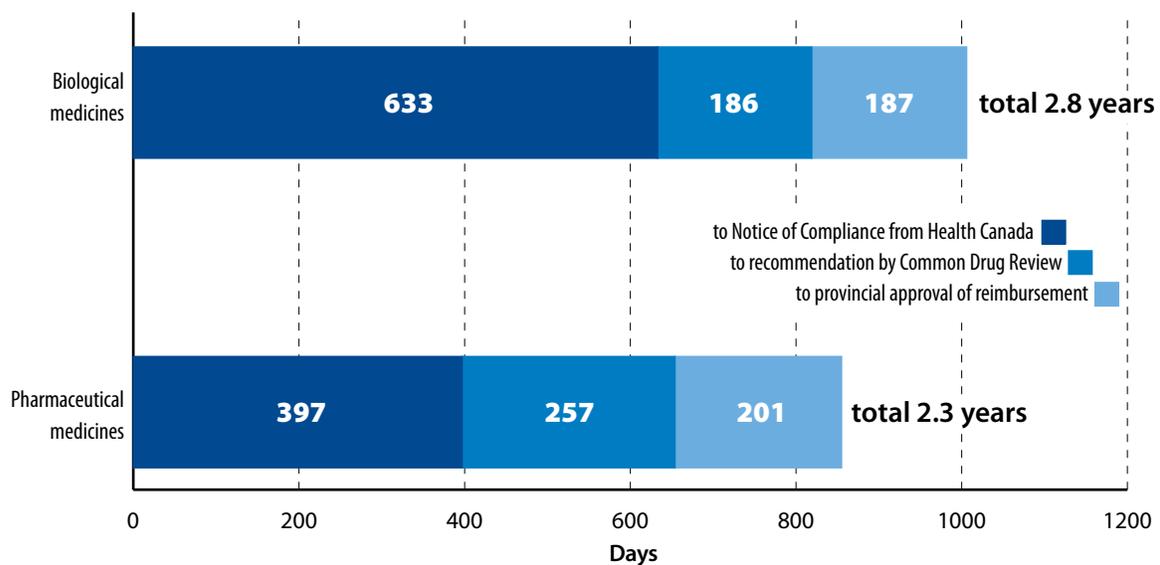
Source: Brogan Inc., 2006.

5 Total time spent waiting for access to new medicines

An estimate of the total time spent waiting for access to new medicines after they have been developed can be calculated by adding the time it takes for Health Canada to issue a safety approval (CR to NOC), the time spent during the CDR reimbursement recommendation delay (NOC to CDR), and the provincial reimbursement delay (CDR to PR). The wait times observed for new pharmaceuticals and new biologics are distinct and should be measured separately. Figure 9 shows the consolidated average wait for access to new medicines, measured in days; pharmaceuticals and biologics are shown separately.

Reading left to right, the first segment of the bar represents the time needed for Health Canada to certify that new drugs are safe and effective before allowing them to be sold on the market. For new biological medicines, the time spent during this segment was 633 days on average in 2005 compared to 397 days on average for new pharmaceutical medicines. This segment of the wait for access to new medicines affects all patients in Canada equally, whether they pay for their drugs through private insurance, out-of-pocket expenditure, or public drug programs. Only improving the efficiency and capacity of Health Canada to conduct new drug reviews can reduce the time spent in marketing approval.

Figure 9: Total time (days) spent waiting after a new drug has been developed before patients have access to new pharmaceutical and biological medicines in Canada, by wait segment, averaged across all new drug-submission classes, 2004–2005



Sources: Health Canada, 2006a; Brogan Inc., 2006a; authors' calculations.

The second and third segments of the bar represent a single period of waiting for those who are dependent on public drug programs, or for anyone needing drugs that are only administered on an in-patient basis and cannot afford to pay cash. The wait for a CDR reimbursement recommendation is presented separately from the wait for provincial approval of reimbursement to allow the reader to identify the contribution of both the CDR and the provinces themselves to the overall time before reimbursement of a drug is approved. Notably the CDR's contribution to the wait time for new pharmaceuticals is 257 days compared to 186 days for new biologics. By comparison, the the wait for provincial approval of reimbursement add, on average, another 201 days for pharmaceuticals and another 187 days for biologics. The total average wait for approval of reimbursement is 458 days for pharmaceuticals and 373 days for biologics. In other words, patients who are dependent on public drug benefits or who need drugs that are delivered only through in-patient settings must wait more than a year after Health Canada has certified a new drug as safe and effective before they finally have access to it. If private insurers were to rely on CDR recommendations to guide their own coverage decisions, then this delay could also affect those with public or private insurance coverage who lack the financial capacity to pay out-of-pocket for access to new medicines.

The total average wait for patients dependent on public drug benefits in Canada for access to new biological medicines is 1,006 days, or approximately 2.8 years; and for access to new pharmaceutical medicines the wait is 855 days, or approximately 2.3 years. There is also a significant number of drugs that are approved by Health Canada as safe and effective but never declared eligible for reimbursement by the CDR or the provinces.

Discussion and policy options

Solutions for shorter drug-approval times—harmonization, competition, and user fees

The data presented in this paper confirms other research showing that Canadian patients suffer from delayed access to new medications because of a slow drug-safety approval process at Health Canada that is inefficient relative to comparable systems in other countries. The result is that Canadian patients wait significantly longer than patients in other countries to have access to the latest advances in medicines.

While a complex and thorough review of a new drug submission is necessary given the sometimes quite serious health risks involved with new medications, delays in approving drugs can also prevent safe and effective medications from being available to Canadian patients earlier, resulting in unnecessary negative health impacts (Jones, 2002). Data are not available to produce an accurate estimation of the precise number of mortalities or morbidities that are due to delayed access to new medications in Canada. However, evidence exists supporting the assertion that any decrease in negative health outcomes resulting from avoiding the harmful side effects of new medicines is likely to be off-set many times over by the lost positive outcomes that would have occurred if the government had allowed patients to use new drugs sooner [Graham, 2005a]. Such improvement in access to new drugs is important. According to a recent study on the safety and efficacy of the US FDA, more rapid access to drugs on the American market enabled by the introduction of performance-based user fees paid by manufacturers to the FDA has saved the equivalent of 180,000 to 310,000 life-years [Philipson et al., 2005].

Although Canada has managed to speed up its drug approvals since the late 1980s, research shows that a considerable “drug lag” persists relative to comparable jurisdictions. For instance, one study showed that between 1992 and 2001, Health Canada not only approved significantly fewer drugs than the United States Food and Drug Administration (FDA) but took, on average, 189 days longer to approve them [Rawson and Kaitin, 2003].

Numerous studies have been conducted on the time required for approval of new drugs in Canada compared to times in similar jurisdictions such as Australia, Sweden, the United Kingdom, and the United States. The studies consistently identify Canadian approval times as either similar to (1996–1998), or longer than (1999–2001), those in Australia and significantly longer than those in Sweden, the United Kingdom, and the United States [Rawson, 2000b]. In another study, the median approval time of new drugs in Canada was shown to be almost 200 days longer than in the United States [Rawson and Kaitin, 2003].

Joel Lexchin has also compared delays in approving drugs in Canada and the United States. Lexchin used Canadian and American issues of the *Medical Letter*, a publication evaluating new drugs marketed in both the United States and Canada, to collect data and identify disparities between drugs approved in each of the two countries. He identified 37 new drugs approved in the United States between May 12, 2003 and June 21, 2004. Of those 37 drugs, 32 were not available in Canada. By late July 2005, 12 of the 32 drugs had finally been approved in Canada, yet for the 20 drugs still not approved, the median time to approval in Canada was 714 days. Lexchin identified the drug approval process in the United States as being, on average, 7.8 months faster than in Canada [Lexchin, 2006].

A number of factors affect a country's review and approval process, such as regulations, access to data from other countries, policies, procedures, and resources [Rawson, 2003]. According to Health Canada's Therapeutic Products Directorate, there are two reasons for Canada's slower approval times: a lack of resources and delayed submission by pharmaceutical companies. Drugs are submitted for review later in Canada than in comparable jurisdictions and, as a result, Health Canada feels obliged to review all available pre-marketing studies as well as post-marketing data from markets where the new drug is already in use. Of the 78 drugs approved in Canada between 1999 and 2001, 29% had been submitted at least six months earlier in the United States [Rawson, 2003]. Pharmaceutical companies tend to submit new drugs to Health Canada an average of six to nine months after they file a new drug submission with the US FDA [Lexchin, 2006].

While Lexchin acknowledges the substantial difference between drug approval times in different jurisdictions such as Canada and the United States may result from a difference of original filing dates, he argues that this is not the sole factor responsible. Rather, regulatory delays in Canada are thought to be attributed to a lack of human resources, poor coordination between assessments of chemistry and manufacturing data and of safety and efficacy data, delays due to "company time," or receiving requested additional information from manufacturers and the "bureaucratic rigidity" of Health Canada and the Therapeutic Products Directorate [Lexchin, 2004].

It has been argued that Health Canada's slower approval times may be indicative of a much more rigorous and safe scientific review, one that might ultimately lead to fewer drug recalls than in the United States. However, Canada's External Advisory Committee on Smart Regulation argues that this is not the case. Longer approval times in Canada simply give Canadian officials more time to consider American or international post-market data on adverse reactions among patients in their scientific review prior to issuing their own decisions. This means that when international jurisdictions recall a drug for safety reasons, the same drug is often still waiting for its initial approval in Canada. Knowing this, Health Canada would not grant the initial approval in the first place, thereby artificially reducing its recall rate [EACSR, 2004].

The timeliness with which a regulatory agency approves new drugs may be directly influenced by the human resources available to review applications [Rawson, 2002a]. Yet, Canada's approach to drug approval has essentially followed the American approach, although Health Canada has far fewer resources. The number of staff in Canada (159) is less than 10% of those in the United States (1,610) [Rawson, 2002a]. It is unnecessarily expensive and time consuming for Health Canada to duplicate the American approval process. Canada is a much smaller country and, as such, has a much smaller regulatory agency. For instance, the US FDA's 2002 budget for the evaluation of human medicines reached approximately US\$220 million whereas Health Canada's was approximately US\$40.9 million. Yet, Health Canada attempts to review a roughly similar number of new drugs [EACSR, 2004].

However, Canada's longer approval times cannot be attributed only to its having fewer resources, given that both Sweden and the United Kingdom have regulatory agencies staffed at lower levels than the Therapeutic Products Directorate (TPD) and yet manage to consistently review and approve drugs in a time frame similar to the United States FDA [Rawson, 2000b]. Research indicates that Canada's human resources for the review and approval of new active substances are, in actuality, quite substantial (159), approximately twice those in Australia (76), over 2.5 times those in the United Kingdom (60) and 3.5 times those in Sweden (46) [Rawson, 2002a].

Harmonization—cooperation with other jurisdictions

Health Canada could speed up its regulatory process by taking advantage of the regulatory knowledge and capacity of other jurisdictions, rather than attempting to duplicate the American process. A consolidation of resources through the sharing of data, workload, and processes would be of great benefit. For example, if Canada entered into agreements of "mutual recognition" with other countries, new medications already approved in those countries could be introduced to the Canadian market far more rapidly. In an effort to reduce the time taken to review new medications, Canada's recent Smart Regulation strategy proposed a form of mutual recognition to reduce persistent delays in the drug approval process [EACSR, 2004].

User fees

There are other measures that can be taken to improve Canada's regulatory productivity. For instance, revitalization of Canada's user-fees program could be a solution. Health Canada collects fees from drug companies wishing to have their products reviewed. If the user-fees program were combined with strictly enforced and appropriate targets that Health Canada must meet before receiving the increased revenue, this might succeed in reducing delays, as has been the case in the United States. According to Graham, a decade of user fees intended to increase the budget available to Health Canada has failed to improve its performance in comparison to most comparable countries

that also have user fees because the fees are not linked to performance. [Graham, 2005a]. By contrast, the establishment of user fees in the United States has resulted in the vast majority of review targets established under the Food and Drug Modernization Act of 1997 being met [Berndt et al., 2005]. In return for levying user fees, the US FDA is required to meet a number of performance goals intended to speed up drug approvals. Since the establishment of user fees in the United States, drug-approval times have been reduced dramatically from a median of 22 months in 1992 to a median of less than 12 months in 1999, as the fees enabled the US FDA to increase their review staff and achieve much faster review times [Philipson et al., 2005].

Competition

The European Union, on the other hand, has a policy of regulatory competition whereby central regulators and the national regulators of member states compete for user fees charged to manufacturers to cover the costs of regulatory approval. Upon approval by any one regulator, regulators in other participating countries must lift bans on the marketing of the new medicines. Competition for user fees has created incentive for countries to be more efficient in their approval of new drugs and, as a result, improved the productivity of new drug approvals in the European Union [Graham, 2005a].

Solution to delays in approving public reimbursement— universal compulsory private insurance

The data presented in this paper confirms other research showing that even after waiting too long for Health Canada to approve medicines relative to other countries, provincial governments further delay access to new drugs by refusing to declare them eligible for reimbursement under public drug programs that cover prescription medications or in taking a long time to declare that such drugs are eligible for reimbursement.

The rationale behind the Common Drug Review (CDR) was to reduce bureaucratic redundancy by replacing the various provincial agencies for approving reimbursement with a new, centralized, national process. However, the provinces have not eliminated their reimbursement approval processes, and so the CDR has only added another layer of bureaucracy. The data presented in this study, however, do not indicate that the introduction of the CDR has slowed the decision-making process on reimbursements but do suggest that it has resulted in fewer approvals overall.

Until recently, pharmaceutical companies wishing to have a new drug listed for public reimbursement were faced with the onerous task of submitting applications to nearly 20 provincial and territorial drug plans, a process that resulted in costly duplications, delays, and discrepancies among provinces and territories. A lack of collaboration among the provinces and territories as well as differing provincial budgets

and mandates led to the new medications being available in some provinces but not others, denying many Canadians access to new and innovative medications. Formulary decisions made in one province or territory had little or no bearing on the decisions made in others [West et al., 2002].

Data measuring the CDR's rate in approving drugs for reimbursement and the subsequent adoption by public drug programs in the provinces suggest that the CDR is being used as a cost-containment mechanism to ration access to new medicines, not to improve the efficiency of the reimbursement process. Provinces are replicating the review processes undertaken by the CDR and choosing not to reimburse a number of the new medications that have been given positive listing recommendations by the CDR [Laudrum, 2005].

Research presented in this paper on reimbursement performance demonstrates that only a small percentage of new drugs were successful in obtaining the CDR's reimbursement approval. Furthermore, only a small percentage of new drugs were successful in obtaining provincial reimbursement even when they received a positive recommendation from the CDR. Importantly, there is also wide variation in the decisions taken by the provinces despite the introduction of the Common Drug Review in 2003. If the CDR's reviews are based on objective scientific considerations and not on rationing decisions driven by costs alone, then there should not be such variation in reimbursement decisions among the provinces.

The centralization of regulatory review commonly fosters rationing in the decision-making process [Morgan et al., 2006]. This can be seen not only in Canada but also with the Pharmaceutical Benefits Scheme in Australia, the Pharmaceutical Management Agency in New Zealand, and the National Institute for Clinical Excellence in the United Kingdom [Pollard, 2006; Sundakov, 2005]. Cost-containment measures force provincial governments to restrict their drug expenditures through policies that control and influence the availability, use, and pricing of newly approved medications. Because budget pressures are different in each province, there are large variations in the number of drugs listed as well as the time taken to list new medications for reimbursement. As a result, access to drugs varies from province to province and all Canadians do not receive equal access to drugs approved by Health Canada [West et al., 2002]. For instance, of the 132 innovative drugs introduced in Canada between March 1999 and February 2001, 72 were listed on the Quebec formulary in an average time of 336 days, while only 37 were listed in Ontario in an average time of 455 days [Rawson, 2002b]. Given that the structure of the scientific review of new medications in each province is consistent, there is a clear duplication of effort, which is a waste of valuable time and resources [West et al., 2002]. Additionally, there is a governance problem related to the CDR. By introducing a centralized CDR, governments can accept the advice of a non-governmental agency when it recommends against reimbursing a new drug while shifting responsibility away from themselves, and ignore the agency's advice when it recommends in favour of public reimbursement.

In an evaluation of centralized review processes such as the CDR, Morgan and colleagues define what they consider the three standards that must be met for centralized review agencies to be deemed legitimate. First, the agency must demonstrate a “rigour of process” by setting and consistently maintaining high standards. Second, there must be “clarity of roles”: a clear definition of the roles and responsibilities of experts is widely believed to improve the review process. Lastly, there must be transparency of information and decision-making rationales. Accountability and understanding is increased when those affected understand the rationale and reasoning for decisions [Morgan et al., 2006].

An evaluation of the CDR makes it very clear that none of these standards have been met. Members of CDR’s evaluation committee remain anonymous, there is no clarity in the roles and responsibilities of those involved, nor is there any means to hold them accountable for decisions made. While reimbursement decisions are posted on the CDR’s website, they are not written for the general public but rather for manufacturers and experts. As well, only pharmaceutical manufacturers may appeal a decision by the CDR, and appeals are heard by the same panel that made the initial recommendation [Laudrum, 2005]. Finally, the CDR as a quasi-governmental agency is not formally part of the federal or the provincial governments. Therefore, it is not directly responsible to the public. As a result, there is very little transparency, accountability, and understanding, especially for patients directly affected.

The CDR would not be necessary in a well-regulated market for universal private insurance

The rationale offered by governments to justify the CDR is that such an agency is necessary in order to contain the growth in government expenditure on drugs. But there are several problems with government-run drug-insurance programs that are not found in private insurance. If drug insurance were delivered through a properly regulated, private, competitive market, there would be no need at all for agencies like the CDR and patients would have improved access to new medicines.

Public drug-insurance programs are notorious for restricting access to new medicines in a misguided attempt at cost control. When government health insurance attempts to provide equal access and 100% insurance coverage for any medical need on a universal basis, then the system becomes financially unsustainable. Therefore, when governments are committed to enforcing egalitarian access to all services large and small, they inevitably deny everyone access to the more expensive medical goods and services—which are usually the latest and most advanced technologies—including patented medicines. This means that under a government health-insurance monopoly like that which exists in Canada, patients go without if they do not have the option to buy private insurance or pay directly for the latest developments in health technology.

It is only because governments use rationing as a form of misguided cost control that the creation of central planning agencies like CDR are thought to be necessary.

Government interference in health-care markets through government health- and drug-insurance programs also distorts the efficient allocation of medical resources. Government health- and drug-insurance programs are not able to optimize the efficiency benefits of new medical technologies like pharmaceuticals because such programs lack appropriate incentives for patients and providers using medical goods and services. Central planning is unable to compensate for this deficiency.

Any kind of insurance (private or government) insulates the consumer from price to some degree and this can distort supply-and-demand decisions. But unlike private-sector insurance, elected officials who are highly sensitive to political pressures run government programs. Political pressures create powerful incentives for politicians to reduce any out-of-pocket expense toward zero and to base premiums on heavy cross-subsidization according to income instead of on expected use or, even, equal risk-pooling (i.e., community rating). [9] The resulting absence of price signals for consumers removes the necessary economic incentives to influence the demand for goods and services. Exposure to price helps to control price inflation and creates incentives for the efficient allocation of resources matching the individual needs and preferences of patients [Herrick, 2006]. The politicization of central-planning decisions regarding allocation distorts investment and spending decisions. Political pressures and the impossibly large information requirements needed to plan patients' individual health-care needs and preferences are insurmountable structural obstacles faced by government health insurance and drug programs but not by private-sector insurers, who are better able to react to price signals and changes in supply and demand.

Canadian government health insurance is also divided into silos. Government insurance covers 100% of the cost of medical services delivered by hospitals and physicians but does not generally cover the cost of out-patient goods and services except for certain sub-populations like seniors, the disabled, and social-welfare recipients. And when government insurance does cover out-patient health care, it does not pay 100% of the costs. This lack of comprehensive coverage makes the out-of-pocket cost of competing health-care options much different and can therefore create inappropriate incentives to consume inefficient combinations of medical care that receive a government subsidy rather than more efficient combinations of care that do not receive a subsidy or, at least, a full subsidy. Drugs are the primary example of a medical technology that is demonstrably more efficient at improving health outcomes but which, as a result of the lack of comprehensive insurance coverage offered under government programs, is

[9] The experience with government health care in Europe, where user fees are common and community risk rating is increasingly being adopted, suggests that economic realities can lead to rational policy changes.

made comparatively more expensive. This creates a disincentive for both patients and physicians to substitute drugs for less efficient treatment technologies. [10]

Decisions by government about drug-insurance coverage can also have negative side effects. For instance, the refusal of a large, public drug program to reimburse purchasers of certain drug products can also amount to a barrier to market access for some drug makers and destroys the business case for bringing new medicines to market in the first place. Canada represents only 2% of the global market for drugs [IMS Health Inc., 2006 a, b] and public drug programs account for about half the market for prescription drugs in the country [CIHI, 2006]. Therefore, when a province decides not to reimburse purchasers of a drug, it essentially blocks access for that product to half of an already small market. Doing so might reduce the size of the market to the point where it is not feasible to incur the costs of introducing a product to the market, especially if other public policies might be also making the market unattractive. For example, lengthy drug-safety approvals can further delay market access, reducing the effective patent period left on a new drug, and price controls might reduce the profit potential once a drug finally makes it to market. In this way, market distortions caused by the reimbursement decisions of large, public drug programs can have the indirect effect of reducing access for everyone, not just the recipients of public drug benefits. [11]

Instead of implementing new, centralized, unaccountable bureaucracies like the CDR, governments should dramatically reduce the scope of public subsidies for health care that cause distortions in the market and reduce patients' access to new medicines. Economic evidence suggests that private-payment health systems (a combination of private insurance and out-of-pocket spending) are better structured to encourage the rational demand for, and allocation of, health technology and capture overall efficiency gains [Danzon, 1993; Newhouse et al., 1993].

Research conducted for this study indicates that private drug-insurance programs in Canada are generally structured without formularies listing specific drugs as eligible for reimbursement. Instead, some private plans have made certain broad categories of drugs, such as the so-called "lifestyle" drugs, ineligible for coverage. However, in almost all private plans, outside of such broad exclusions, every drug that receives a NOC from Health Canada is eligible for reimbursement immediately. Therefore, for new "medically necessary" drugs, private insurers cover close to 100% of drugs for which NOCs have been issued and the delay to approval of reimbursement is practically non-existent. Most private plans have instead imposed an annual coverage limit for insured drug expenditures combined with various kinds of deductibles and co-payments to introduce incentives for the insured to control costs and allocate resources

[10] Research shows drug therapies are actually under used as cost-efficient substitutes because of flawed insurance designs [Kleinke, 2004].

[11] For a recent example, see Skinner, 2006 regarding the drug, *Erbitux*.

efficiently. Some private plans have no annual limits at all but use co-payments to a greater degree instead. In short, the kind of centrally planned rationing that is necessary to keep public drug-insurance programs in Canada from sliding into financial unsustainability is generally not used by the private drug insurance industry [see also Graham and Tabler, 2005].

Moving to a regulated, competitive, private market for health insurance like that in Switzerland [Skinner, 2005; Esmail, 2006] would introduce the benefits of competitive markets while ensuring universal coverage of the population. Such a health-insurance model would also be more comprehensive (including drugs, for instance) than Canada's current patchwork of public programs and would eliminate the incentives for governments to ration access to medicines.

Appendix: Classes, data sources, and comparability

Classes of new drug submissions

New drugs fall under different classifications defined by the Therapeutic Products Directorate (TPD) and the Biologic and Genetic Therapies Directorate (BGTD). Table 3 (p. 35) shows the classes of drug submissions used by TPD and BGTD and their corresponding definitions. In Canada, non-generic, new drug approvals involve new active substances [NAS], new drug submissions [NDS], and supplementary new drug submissions [SNDS]. Similar classifications are used by the US Food and Drug Administration (US FDA) [table 4] (p. 36) and the European Medicines Agency (EMA) [table 5] (p. 37) but under different terminology and the classes of new drug applications in each of the three jurisdictions do not match perfectly.

Data sources and comparability issues

There are three sources of data cited in section 2 of the report. [12] The first source is Health Canada, which is the only source of data on drug approval delays in Canada that comprehensively includes all drugs. Health Canada publishes data on pharmaceutical medicines through the TPD and on biologic medicines through the BGTD. Data published in annual reports on drug approvals by TPD and BGTD is stated in aggregates and is not broken down in detail. Health Canada publishes this data separately by drug submission class, priority (or “fast track”) review status, and therapeutic category. [13] Finally, Health Canada’s published approval times include the entire period between original filing of the new drug-submission application (CR) to the issuance of

[12] Another public source of aggregated Canadian and international data on drug approval times is the industry association, Rx&D, that represents the makers of new drugs otherwise known as brand-name pharmaceutical companies. Rx&D conducts an annual survey of its member companies (representing most but not all of the industry) to collect data on their actual experience with government approval times for a defined basket of specific drug products (i.e. new drug submissions, supplemental drug submissions, and clinical trial applications) [Rx&D, 2005].

[13] Health Canada’s published data on drug-approval delays excludes administrative SNDS applications, which apply to drug products that have already been marketed and have previously received Health Canada’s approval but are now being duplicated by a new manufacturer. This usually results from the buyout or merger of patent-holding drug companies and so there are very few such applications and they do not occur on a regular basis. Because these approvals are merely administrative in nature, they are completed more quickly than standard new drug applications.

the Notice of Compliance (NOC), inclusive of all company time spent to address any deficiencies in the manufacturer's application [14] [Health Canada, 2006a].

The two sources of international comparative data cited in section 2 are the US FDA and the European EMEA. The US FDA and the European EMEA publish data on approval delays that is inclusive of all new drug submission classes, even administrative applications [FDA, 2006; EMEA, 2006]. This will have the effect of reducing the average wait time when calculated across all new drug submissions but probably not that significantly because of the infrequency with which this type of application is submitted. Therefore, a direct comparison of approval delays between Health Canada's data and data from the FDA or the EMEA can produce minor inaccuracies if not treated carefully. Nevertheless, it is the only fully comprehensive data publicly available for this research and reasonable comparisons can be made if conclusions are drawn cautiously from the results.

The US FDA and the EMEA also publish separate data for the time spent by companies to correct the deficiencies in their applications. Health Canada does not do so but, instead, publishes an entire approval delay that includes what they call "company" time. This makes it difficult to accurately compare the direct institutional performance of Health Canada and its international counterparts because it is impossible to determine what part of Health Canada's approval delay is attributable to its own performance and what part to deficient company applications.

The EMEA publishes average figures on drug approval delays but does not include median figures. Unlike Health Canada and the FDA, the EMEA does not publish data that separates priority and non-priority new drug submissions. Also, like the US FDA, the EMEA includes administrative new drug applications in its published figures on drug approval delays and separately publishes both institutional time spent and time spent for companies to correct deficiencies in their applications [EMEA, 2006].

In order to make comparisons of wait times in this study, all data for delays will include both company and government review time. European and Canadian comparisons in this study use averages for approval delays measured in days, while American and Canadian comparisons will use weighted medians. In both cases, figures will be aggregated across all drug-submission categories, incorporating company time spent addressing application deficiencies.

[14] It is unclear whether Health Canada records the filing of a new drug-submission application on the actual date it was delivered to TPD or the date at which a reviewer first sees a file.

Table 3: Classes of new drug submissions used by Health Canada's Therapeutic Products Directorate (TPD) and Biologics and Genetic Therapies Directorate (BGTD)

New Active Substance (NAS)

A New Active Substance is a therapeutic substance that has never before been approved for marketing in any form; a chemical or biological substance not previously approved for sale in Canada as a drug; an isomer, derivative, or salt of a chemical substance previously approved for sale as a drug in Canada but differing in properties with regard to safety and efficacy; and a biological substance previously approved for sale in Canada as a drug but differing in molecular structure, nature of the source material, or manufacturing process.

New Drug Submission (NDS)

New Drug Submission includes all NAS's as well as combinations of previously approved NAS's, and any drug that has not been sold in Canada for sufficient time and in sufficient quantity to establish its safety and effectiveness under use or its recommended conditions for use.

Supplementary NDS (SNDS)

A Supplemental NDS (SNDS) must be filed by the manufacturer if certain changes are made to products that have already been authorized. Such changes might include the dosage form or strength of the drug product, the formulation, method of manufacture, labelling, or recommended route of administration. An SNDS must also be submitted if the manufacturer wants to expand the indications (claims or conditions of use) for the drug product.

Abbreviated NDS (ANDS)

An abbreviated NDS (ANDS) must be filed by a manufacturer wishing approval of a substance that is not a new drug but a generic "copy" of a drug that has been previously approved for sale in Canada.

Priority or Non-Priority review status

Priority review status is "fast-track" status granted to eligible new drug submissions for human use, following review and approval of a request submitted by the manufacturer of the drug. Priority Review status assigns eligible submissions a shortened review target of 180 days, in comparison to 300 days for submissions classed as non-priority. Health Canada believes it is in the best interests of Canadians to review potentially lifesaving drugs as early as possible. Priority review status may be granted to drug submissions intended for the treatment, prevention, or diagnosis of serious, life-threatening, or severely debilitating illnesses or conditions where (a) there is no existing drug on the Canadian market with the same profile or (b) the new product has a benefit/risk profile that is a significant improvement over the profile of existing products.

Source: Health Canada, 2006 b, c, d.

Table 4: Classifications of new drug applications (NDA) used by US FDA's Center for Drug Evaluation and Research (CDER)

New Molecular Entity (NME)

New salt of previously approved drug (not an NME)

New Formulation of previously approved drug (not a new salt or NME)

New combination of two or more drugs

Already marketed drug product—duplication by new manufacturer

New indication for already marketed drug

Already marketed drug not previously approved by NDA

Review Priority Classification

The Review Priority Classification is a determination that is made based on an estimate of the therapeutic preventive or diagnostic value of the drug submitted. The designations "Priority" (P) and "Standard" (S) are mutually exclusive. Both original NDAs and effectiveness supplements receive a review priority classification but manufacturing supplements do not.

Priority review (P)

Priority review is granted when a drug product, if approved, would be a significant improvement over marketed products in the treatment, diagnosis, or prevention of a disease. Improvement can be demonstrated by, for example: (1) evidence of increased effectiveness in treatment, prevention, or diagnosis of disease; (2) elimination or substantial reduction of a treatment-limiting drug reaction; (3) documented enhancement of patient compliance; or (4) evidence of safety and effectiveness in a new subpopulation.

Standard review (S)

All non-priority applications will be considered standard applications.

The Center for Biologics Evaluation and Research's definition of priority review

The Center for Biologics Evaluation and Research (CBER) definition of a priority review is stricter than the definition that CDER uses. The biological drug, if approved, must offer a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious or life-threatening disease.

Source: US Food and Drug Administration [US FDA], 1996.

Table 5: Classification of new drug market authorization applications (MAA) by the European Medicines Agency (EMA)

New Active Substance [NAS]

A new chemical, biological, or radiopharmaceutical active substance includes:

- a chemical, biological, or radiopharmaceutical substance not previously authorized as a medicinal product in the European Union;
- an isomer, mixture of isomers, a complex or derivative or salt of a chemical substance previously authorized as a medicinal product in the European Union but differing in properties with regard to safety and efficacy from that chemical substance previously authorized;
- a biological substance previously authorized as a medicinal product in the European Union, but differing in molecular structure, nature of the source material, or manufacturing process;
- a radiopharmaceutical substance, which is a radionuclide, or a ligand, not previously authorized as a medicinal product in the European Union, or the coupling mechanism to link the molecule and the radionuclide has not been authorized previously in the European Union.

Extensions

- different salt/ester complex/derivative (with the same therapeutic moiety): Evidence that there is no change in the pharmacokinetics of the moiety, pharmacodynamics, and/or in toxicity which could change the safety/efficacy profile (otherwise, to be considered as a new active substance);
- different route/pharmaceutical form (for parenteral administration, it is necessary to distinguish between intraarterial, intravenous, intramuscular, subcutaneous, and other routes): (i) new route of administration; (ii) new pharmaceutical form (same route);
- different strength, same route/pharmaceutical form and posology: Bioavailability (cf. guideline);
- suprabioavailable products: (i) same dosage intervals but reduced doses intended to achieve same plasma/blood concentrations as a function of time; bioavailability studies may suffice (see paragraph 5 of Bioequivalence guideline);
- active substances associated in a different proportion/different posology or if one or more is intended for modified release.

Orphan

A medicinal product shall be designated as orphan where it can be established that:

- it is intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the Community at the time when the application is made, or it is intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition in the Community and that without incentives it is unlikely that the marketing of the medicinal product in the Community would generate sufficient return to justify the necessary investment; and
- there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.

Source: European Medicines Agency [EMA], 2005.

References

- Adams, Christopher P., and Van V. Brantner (2003). *New Drug Development: Estimating Entry from Human Clinical Trials*. FTC Working Paper 262. Federal Trade Commission.
- Adams, Christopher P., and Van V. Brantner (2006). Estimating the Cost of New Drug Development: Is It Really \$802 Million? *Health Affairs* 25, 2: 420–28.
- Anis, A.H. (2000). Pharmaceutical Policies in Canada: Another Example of Federal-Provincial Discord. *Canadian Medical Association Journal* 162, 4 (February): 523–26.
- Berndt, Ernst R., et al. (2005). Industry Funding of the FDA: Effects of PDUFA on Approval Times and Withdrawal Rates. *Nature Reviews* 4 (July): 545–54.
- Blouin, Dan (2004). Canada Signs Agreement to Potentially Share Drug Information with the US and Australia. *Canadian Medical Association Journal* 171, 2 (July 20): 121.
- Brogan Inc. (2005). *Formulary Updates 2004*. <<http://www.broganinc.com/news/archive04.html#04>>, as of May 2006.
- Brogan Inc. (2006a). Special data request.
- Brogan Inc. (2006b). *Formulary Updates 2005*. <<http://www.broganinc.com/news/archive05.html#05>>, as of May 2006.
- Brown, Jeffrey R., Norma B. Coe, and Amy Finkelstein (2006). *Medicaid Crowd-Out of Private Long-Term Care Insurance Demand: Evidence from the Health and Retirement Survey*. NBER working paper W12536. National Bureau of Economic Research. <http://www.nber.org/~afinkels/papers/Brown_Coe_Finkelstein_Medicaid_crowd_out.pdf>.
- Canadian Agency for Drugs and Technologies in Health [CADTH] (2006). Common Drug Review. <<http://www.cadth.ca/index.php/en/cdr>>, as of May 9, 2006.
- Canadian Institute for Health Information [CIHI] (2006). *Drug Expenditure in Canada 1985-2005*. National Health Expenditure Database. CIHI.

- Danzon, P.M. (1993). Health Care Industry. *Concise Encyclopedia of Economics: The Library of Economics and Liberty*. <<http://www.econlib.org/library/enc/HealthCareIndustry.html>>.
- DiMasi J.A. (2001). Risks in New Drug Development: Approval Success Rates for Investigational Drugs. *Clinical Pharmacology & Therapeutics* 69, 5 (May): 297–307.
- DiMasi, J.A., et al. ([1995]). Research and Development Costs for New Drugs by Therapeutic Category: A Study of the U.S. Pharmaceutical Industry. *Pharmacoeconomics* 7, 2: 152–69.
- DiMasi, J.A., H.G. Grabowski, and J. Vernon (2004). R&D Costs and Returns by Therapeutic Category. *Drug Information Journal* 38, 3: 211–23.
- DiMasi, J.A., R.W. Hansen, and H.G. Grabowski (2003). The Price of Innovation: New Estimates of Drug Development Costs. *Journal of Health Economics* 22, 2: 151–85.
- Dranove, D., and D. Meltzer (1994). Do Important Drugs Reach the Market Sooner? *The RAND Journal of Economics* 25, 3: 402–23.
- EKOS Research Associates (2005). *Evaluation of the First Year of Operation for the Common Drug Review*. Canadian Coordinating Office for Health Technology Assessment.
- Esmail, Nadeem (2006). Like Clockwork: The Swiss Health Insurance System. *Fraser Forum* (June): 23–25.
- Esmail, Nadeem, and Michael Walker (2006). *Waiting Your Turn: Hospital Waiting Lists in Canada, 16th Edition*. The Fraser Institute.
- Glen, Courtney, and Brett J. Skinner (2006). The Common Drug Review: Governments Avoiding Accountability for Rationing. *Fraser Forum* (June): 16–19.
- Gould, M. (2004). CDR: Will It Increase Review Times? *The NOC* 61 (Spring): 16–19.
- Graham, Janice (2005). Smart Regulation: Will the Government's Strategy Work? *Canadian Medical Association Journal* 173, 12 (December 6): 1469.
- Graham, John R. (2005a). *A Lethal Guardian: The Canadian Government's Ban on Prescription Drugs*. Fraser Institute Digital Publication (April). The Fraser Institute.

- Graham, John R. (2005b). Approving New Medicines in Canada: Health Canada Needs a Dose of Competition. *Fraser Forum* (June): 9–11.
- Graham, John R., and T. Tabler (2005). *Canadian Pharmacare: Performance, Incentives, and Insurance*. Fraser Institute Digital Publication (March). The Fraser Institute.
- Han, D., and E.C.Y. Wang (2005). The Value of Medicines in Canada. *Canadian Journal of Clinical Pharmacology* 12, 1 (Winter): 10–21.
- Herrick, Devon M. (2006). *Update 2006: Why Are Health Costs Rising?* Brief Analysis 572 (September 21). National Center for Policy Analysis. <<http://www.ncpa.org/pub/ba/ba572/ba572.pdf>>.
- IMS Health Inc. (2006a). *IMS Drug Monitor: Canada*. <http://www.imshealthcanada.com/htmen/3_2_29.htm>.
- IMS Health Inc. (2006b). *IMS Health Reports Global Pharmaceutical Market Grew 7 Percent in 2005, to \$602 Billion*. News Release (March 21, 2006).
- Jones, Laura (2002). Can the Drug Approval Process be Reformed to Save Lives. *Fraser Forum* (February): 14–16.
- Kleinke, J.D. (2004). Access Versus Excess: Value-Based Cost-Sharing for Prescription Drugs. *Health Affairs* 23, 1 (January/February): 34–47.
- Laudrum, K. (2005). Under Review: Is the Common Drug Review Meeting Expectations? *Canadian Healthcare Manger* 12, 2: 12–14.
- Lexchin, J. (2004). Drug Regulation: New Directions in Drug Approval. *Canadian Medical Association Journal* 171, 3 (August 3): 229–30.
- Lexchin, J. (2006). *A Comparison of New Drug Availability in Canada and the United States and Potential Therapeutic Implications of Differences*. <<http://www.elsevier.com/locate/healthpol>>, last updated October 2006.
- Lo Sasso, Anthony T., and Bruce D. Meyer (2006). *The Health Care Safety Net and Crowd-Out of Private Health Insurance*. Working paper W11977. National Bureau of Economic Research. <<http://www.nber.org/papers/w11977>>.

- McMahon, Megan, et al. (2006). *The Common Drug Review: A NICE Start for Canada?* <<http://www.elsevier.com/locate/healthpol>>, last updated October 2006.
- Menon, Devidas (2001). Pharmaceutical Cost Control in Canada: Does It Work? *Health Affairs* 20, 3 (May/June): 92–102.
- Milne, Celia (2003). *Under the Microscope*. Canadian Healthcare Manager [online]. <http://www.chmonline.ca/issue/article.jsp?content=20030827_113450_3480>, last updated July 2006.
- Morgan, Steven G., et al. (2006). Centralized Drug Review Processes in Australia, Canada, New Zealand and the United Kingdom. *Health Affairs* 25, 2 (May/April): 337–47.
- Newhouse, J.P., et al. (1993). *Free For All? Lessons From The RAND Health Insurance Experiment*. RAND. Harvard University Press.
- Osteoporosis Canada [COPN] (2006). *Coping: The E-newsletter of the Canadian Osteoporosis Patient Network*. <<http://www.osteoporosis.ca/local/files/home/PDFs/COPNnews01-06.pdf>>, last updated May 2006.
- Philipson, Tomas J., Ernst R. Berndt, Adrian H. B. Gottschalk, and Matthew W. Strobeck (2005). *Assessing the Safety and Efficacy of the FDA: The Case of the Prescription Drug User Fee Acts*. NBER working paper 11724. National Bureau of Economic Research.
- Pollard, Stephen (2006). NICE is Nasty. *Fraser Forum* (March): 7–9.
- Rawson, Nigel S.B. (2000a). Drug Approval Times. *Canadian Medical Association Journal* 162, 13 (June 27): 1804.
- Rawson, Nigel S.B. (2000b). Time Required for Approval of New Drugs in Canada, Australia, Sweden, the United Kingdom and the United States in 1996–1998. *Canadian Medical Association Journal* 162, 4 (February 22): 501–04.
- Rawson, Nigel S.B. (2002a). Human Resources for the Approval of New Drugs in Canada, Australia, Sweden, the United Kingdom and the United States. *Canadian Journal of Clinical Pharmacology* 9, 2 (Summer): 73–78.
- Rawson, Nigel S.B. (2002b). Issues in the Approval of, Access to, and Post-Marketing Follow-Up of New Drugs in Canada: A Personal Viewpoint. *Health Affairs* 11: 335–40.

Rawson, Nigel S.B. (2003). Timeliness of Review and Approval of New Drugs in Canada from 1999 through 2001: Is Progress Being Made?" *Clinical Therapeutics* 25, 4 (April): 1230–47.

Rawson, Nigel S.B. (2005). Assessing Prescription Medications for Priority Regulatory Review. *Regulatory Toxicology and Pharmacology* 42: 70–76.

Rawson, Nigel S.B., and Kenneth I. Kaitin [2003]. Canadian and US Drug Approval Times and Safety Considerations. *Annals of Pharmacotherapy* 37 (October): 1403–08.

Reichert, Janice M. (2003). Trends in Development and Approval Times for New Therapeutics in the United States. *Nature Reviews* 2 (September): 695–702.

Rx&D (2005). Rx&D Notice of Compliance Survey 2005. Canada's Research-Based Pharmaceutical Companies [Rx&D]. <http://canadapharma.org/Pubs/NOC_Survey/2005-NOC-Survey-Binder.pdf>.

Skinner, Brett J. (2006). "Sure, It's Cheap to Make Drugs. But the Cost of Discovering and Developing Them Is Enormous. *Globe and Mail* (June 21). Online Edition. <<http://www.globeandmail.com>>.

Skinner, Brett J. (2005). Why Medicare Fails to Provide Access to Medically Necessary Health Care. *Fraser Forum* (October): 10–13.

Skinner, Brett J., and Mark Rovere (2006). *Paying More, Getting Less 2006: Measuring the Sustainability of Public Health Insurance in Canada*. Fraser Institute Digital Publication. The Fraser Institute.

Sundakov, Alex (2005). *New Zealand Pharmaceutical Policies: Time to Take a Fresh Look*. Castalia Advisory Group.

West, Roy, et al. (2002). Cost-Effectiveness Estimates Result in Flawed Decision-Making in Listing Drugs For Reimbursement. *Canadian Journal of Public Health* 93, 6 (November/December): 421–25.

World Medical Association [WMA] (1964). *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*. <<http://www.wma.net/e/policy/b3.htm>>.

Government sources

Canada

Canada, Department of Justice [DOJ] (1985). Food and Drugs Act [R.S., 1985, c. F-27], Food and Drug Regulation, Part C Drugs. <<http://laws.justice.gc.ca/en/F-27/index.html>>.

External Advisory Committee on Smart Regulation [EACSR] (2004). *Smart Regulation: A Regulatory Strategy for Canada*. Report to the Government of Canada (September). <http://epe.lac-bac.gc.ca/100/206/301/pco-bcp/committees/smart_regulation-ef/2006-10-11/www.pco-bcp.gc.ca/smartreg-regint/en/08/index.html>.

Health Canada (2001). *How Drugs Are Reviewed in Canada*. Health Products and Food Branch, Therapeutic Products Directorate. <<http://www.hc-sc.gc.ca/hpb-dgps/therapeut/>>.

Health Canada (2003a). *Biologics and Genetic Therapies Directorate - 2003 Annual Submission Performance Report*. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demandedocs/perform-rendement/ar-ra/bgtd_dpbtg_annual_annuel_03_e.html>, last updated April 28, 2004.

Health Canada (2003b). *Therapeutic Products Directorate - 2003 Annual Submission Performance Report*. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demandedocs/perform-rendement/ar-ra/tpd_dpt_annual_annuel_03_e.html>, last updated April 28, 2004.

Health Canada (2004a). *Biologics and Genetic Therapeutics Directorate - 2004 Annual Submission Performance Report*. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demandedocs/perform-rendement/ar-ra/bgtd_dpbtg_annual_annuel_04_e.html>, last updated May 24, 2005.

Health Canada (2004b). *Therapeutic Products Directorate - 2004 Annual Submission Performance Report*. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demandedocs/perform-rendement/ar-ra/tpd_dpt_annual_annuel_04_e.html>, last updated May 24, 2005.

Health Canada (2005a). *Biologics and Genetic Therapeutics Directorate - 2005 Annual Submission Performance Report*. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demandedocs/perform-rendement/ar-ra/bgtd_dpbtg_annual_annuel_05_e.html>, last updated March 14, 2006.

Health Canada (2005b). *Therapeutic Products Directorate - 2005 Annual Submission Performance Report*. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demandedocs/perform-rendement/ar-ra/tpd_dpt_annual_annuel_05_e.html>, last updated March 14, 2006.

Health Canada (2005c). *Regulatory Review of Pharmaceuticals, Biologics, and Medical Devices: Annual Summary of Performance*. <http://www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/performance_rendement_2004_e.html>, last updated September 12, 2005.

Health Canada (2006a). *2005 Annual Drug Submission Performance Report: Part I Therapeutic Products Directorate [TPD]; Part II Biologics and Genetic Therapies Directorate [BGTD]*. Health Products and Food Branch.

Health Canada (2006b). *Access to Therapeutic Products: The Regulatory Process in Canada*. Health Canada, Health Products and Food Branch. <http://www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/access-therapeutic_acces-therapeutique_e.html#2.1>, last updated June 28, 2006.

Health Canada (2006c). *Priority Review of Drug Submissions [Therapeutic Products]*. Health Products and Food Branch [HPFB]: Therapeutic Products Directorate [TPD]. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demanded/pol/prds_tppd_pol_2006_e.html>, adopted 1996; last updated January 10, 2006.

Health Canada (2006d). *Priority Review of Drug Submissions*. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demanded/pol/prds_tppd_pol_2006_e.html>.

Health Canada (2006e). *Common Drug Review*. <http://www.hc-sc.gc.ca/hcs-sss/pharma/mgmt-gest/cdr-emuc/index_e.html>, last updated October 1, 2004.

European Community

European Medicines Agency [EMA] (2005). *The Rules Governing Medicinal Products in the European Community: Volume 2a, Procedures for Marketing Authorization*, Chapter 1 Marketing Authorisation (November). European Commission Enterprise Directorate-General, Consumer Goods, Pharmaceuticals.

European Medicines Agency [EMA] (2006). *Annual Report 2005*. <<http://www.ema.eu.ent/>>.

United States

US Food and Drug Administration [US FDA] (1996). Manual of Policies and Procedures. MAPP 6020.3. Center For Drug Evaluation And Research [CDER].

US Food and Drug Administration [US FDA] (2002). *The FDA and the Drug Development Process: How the FDA Insures that Drugs Are Safe and Effective*. FDA fact sheet. FDA.

US Food and Drug Administration [US FDA] (2006). New Drug Approval Reports. Center for Drug Evaluation and Research [CDER]. <<http://www.fda.gov/cder/rdmt/default.htm>>.

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