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Access Delayed, Access Denied

Waiting for New Medicines in Canada

2010 Report

by Dr. Brett J. Skinner and Mark Rovere

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Editor's Note

Despite what many American pundits, politicians, and activists claim, Canada's health care system is anything but a model to be emulated. This paper explores the total time patients in Canada are forced to wait to gain access to new pharmaceutical and biological medicines, also known as patented drugs.

Executive summary

This is the Fraser Institute's fourth annual report on the amount of time patients must wait for access to new medicines in Canada.[1] The 2010 edition of this study uses the most recent data available, covering the years 2004, 2005, 2006, 2007, and 2008. This edition replicates and adapts the method previously used by Skinner et al. (2007) and Skinner and Rovere (2008a; 2009) to estimate the total amount of time patients must wait for access to new patented prescription medicines in Canada. Like the 2009 report, this edition focuses narrowly on the wait for access to new drugs classified by Health Canada as new drug submissions (NDS) and excludes supplemental new drug submissions (SNDS).

The purpose of this report is (1) to draw attention to the impact that Canadian public policies and institutions have on lengthening the time it takes before patients have access to newly invented, patented prescription drugs; and (2) to offer alternative policy options that could improve access to new drugs in Canada.

Access delayed

After a new drug is developed and ready for use by patients, various government policies extend the time that patients must wait for access to it. An estimate of the total additional time that Canadians must wait for access to new medicines because of government policies and institutional performance can be calculated by adding:

the national delay the time spent waiting for Health Canada to certify the safety and effectiveness of new drugs and approve them for use in Canada; and,

the provincial delay the time spent waiting for provincial drug insurance programs to approve the public reimbursement of new drugs.

Figure 1 shows the consolidated average wait time for access to new medicines in Canada, broken down by each of the two segments described above. This wait time is measured in days and is presented as a weighted average for

1 The first annual report that used this methodology was Skinner et al. (2007). However, John R. Graham (2005a) published an earlier Fraser Institute study on wait times for access to new medicines in Canada, using a slightly different method of analysis.

pharmaceutical and biological drugs,[2] including all new drugs classified by Health Canada as new drug submissions (NDS) and excluding supplemental new drug submissions (SNDS).[3]

National delay

Reading left to right in figure 1: the first segment of the bar represents the average time taken by Health Canada to certify that new drugs are safe and effective. Delays in approval of new drugs by Health Canada were shorter in 2008 than in the previous four years. In 2004, Health Canada took an average of 839 days to approve new medicines, compared to 696 days in 2005, 487 days in 2006, 453 days in 2007, and 388 days in 2008. These data suggest that Health Canada's approval times have steadily improved relative to the agency's performance in the previous four years.

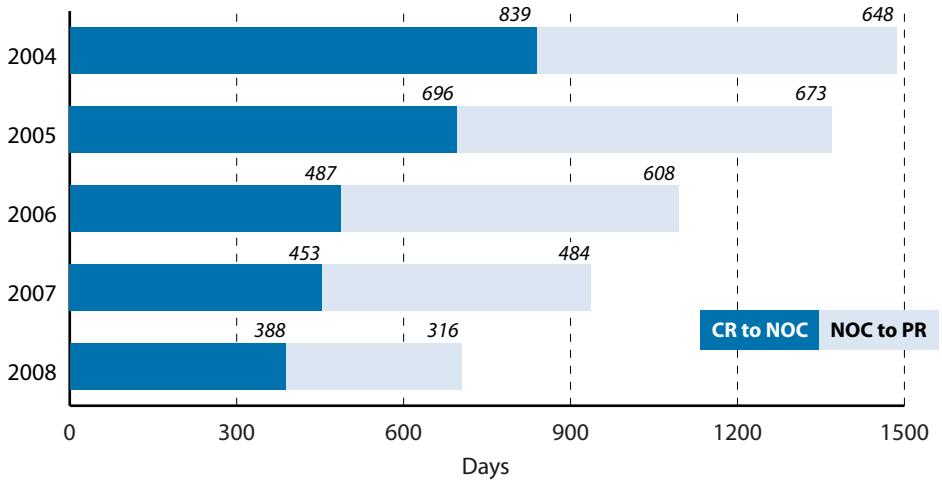
Provincial delay

The second segment of the bar represents the average wait time for insured access to new medicines for patients who are covered under provincial publicly funded drug programs. The delay between Health Canada's certification of new drugs and provincial reimbursement for them has generally decreased since 2004. In 2004, patients relying on public drug programs waited approximately 648 days on average before new drugs were given approval for public reimbursement. However in 2005, the average wait for reimbursement approval increased to 673 days. The average wait for provincial reimbursement fell to 608 days in 2006, to 484 days in 2007, and to 316 days in 2008. On average, the wait for provincial reimbursement approval of new medicines has improved over time.

2 "Pharmaceutical" drugs are chemical-based products; "biological" drugs are biochemical based products. According to the US Food and Drug Administration (2009b), "Biologics products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources—human, animal, or microorganism—and may be produced by biotechnology methods and other cutting-edge technologies."

3 There are three classes of under which new drugs may be submitted by manufacturers for market approval: new active substance (NAS), new drug submission (NDS), and supplemental new drug submission (SNDS) (for details, see Appendix—classes, data sources, and comparability).

Figure 1: Weighted average total delay (days) for access to publicly insured new medicines in Canada, by wait segment, averaged across all provinces, 2004–2008



Abbreviations: **CR**: the date the drug manufacturer's application for marketing approval is recorded or filed in Health Canada's Central Registry. **NOC**: the date Health Canada issues an official Notice of Compliance, certifying that the new drug is safe and effective and is legally approved for sale is Canada. **PR**: the date on which the first public reimbursement of the new drug is recorded in the formularies of each provincial drug program.

Sources: Health Canada, 2009a, 2009b, 2010; Brogan Inc., 2009; calculations by authors.

Total delay

Adding together the wait times from the first and second segments discussed above, the total average wait for patients dependent on public drug programs for insured access to new medicines was 704 days (1.9 years) in 2008. The total average wait has significantly decreased from an average of 1,487 days (approximately 4.1 years) in 2004. While this represents an improvement, overall waits for access to new medicines remain significant. One underappreciated consequence of this delay is that in the meantime, patients are not experiencing the potential health benefits that may result from earlier access to innovative new drug treatments.

Access denied

Despite improvements in the speed at which decisions are made about national and provincial drug approvals, most of the drugs that are approved by Health Canada as safe and effective are not declared eligible for reimbursement under provincial drug plans. Averaged across all provincial public drug programs, as of December 31, 2009, only 23.0% of all drugs that Health Canada approved as safe and effective in 2004 had actually been approved for reimbursement (fully or partially) by the provinces; compared to 16.2% of new drugs certified in 2005, 28.0% of new drugs certified in 2006, 19.1% of new drugs certified in 2007, and 20.3% of new drugs certified in 2008.

Introduction

[***Editor's Note*** Despite what many American pundits, politicians, and activists claim, Canada's health care system is anything but a model to be emulated. This paper explores the total time patients in Canada are forced to wait to gain access to new pharmaceutical and biological medicines, also known as patented drugs.]

This annual report provides patients with some of the information they need to determine whether the time they wait for access to new medicines in Canada is unnecessarily long, and whether publicly funded and managed drug insurance programs provide adequate benefits and choice for patients. We hope that this report will encourage policy makers to consider policy alternatives that empower consumers with greater choice. This 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 drugs that have previously been approved, there is no substantive delay (observed or expected) before the public has access to generic products; consequently, this class of drugs is not studied in this report.

Global factors affecting access to new medicines

It takes a long time to develop a new drug. The development period for new drugs is measured from the patented discovery of a new drug molecule to the first time an application is submitted for marketing approval anywhere in the world. Governments around the world regulate drugs to ensure the safety of the product. For example, Health Canada has a national mandate to ensure the safety of all drugs sold in Canada and thus it regulates which products are allowed to be sold and under what conditions. Health Canada approves new pharmaceutical medicines through the Therapeutic Products Directorate (TPD) and approves new biological medicines through the Biologics and Genetic Therapies Directorate (BGTD). Canadian regulations fall under the 1985 *Food and Drugs Act*.

In order to obtain marketing approval for a drug, manufacturers must provide Health Canada with evidence of its successful clinical testing. The longest period within the drug-development phase involves clinical testing of a new medicine on volunteer patients. Clinical testing of new drugs involves thousands of patients who are often located across international jurisdictions and monitored over many years. No drug is submitted for marketing approval anywhere in the developed world without having first completed successful clinical tests.

The cost of, and time spent in, the development of new drugs is affected 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 with respect to 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. 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. In practice, actual standards for demonstrating the safety of drug products are set by national governments through domestic regulation. These standards determine the number, length, and rigor of the required clinical trials. 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, 2006a). 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 clinical testing time necessary to satisfy the requirements of the US Food and Drug Administration (FDA) and the European Medicines Agency (EMEA).

The most recent research indicates that, on a global basis, the process of developing a new drug takes, on average, about 10 years (DiMasi, 2001; DiMasi et al., 1995, 2003; Adams and Brantner, 2006). The process is measured from the time a drug discovery is patented to the time an application for FDA marketing approval is made (table 1). Moreover, this lengthy development process comes with a steep price. The cost of developing a new patented prescription drug ranges from $521 million to $2,119 million, depending on the company and the drug. The average cost is $868 million (above figures adjusted to 2000 US dollars) (DiMasi, 2001; DiMasi et al., 1995, 2003; Adams and Brantner, 2003, 2006).

For the purposes of this report, the global development time for new medicines is assumed to be a function of factors outside of Canada's control; 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 is it part of the overall wait time for access to new medicines measured here. This paper is primarily concerned with government policies that contribute to an unnecessary delay in access to new medicines after the lengthy period of time it takes to develop them in the first place.

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

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

Source: DiMasi et al., 1995, 2003.

Delays caused by the federal government

After the development phase is over, the first segment of the wait for new medicines that is affected by public policies and institutional performance in Canada is the wait for the federal government to approve the safety and effectiveness of new drugs. Before any new drug is legally allowed to be sold in Canada, it must first receive official approval from Health Canada. Health Canada reviews published clinical research conducted on new drugs before it certifies that a drug is safe for sale in Canada and that the drug's effectiveness has been scientifically demonstrated.[1] Because marketing approval for new drugs occurs at the national level, any delay caused by Health Canada's drug review process affects the wait time for access to new medicines for all Canadians.

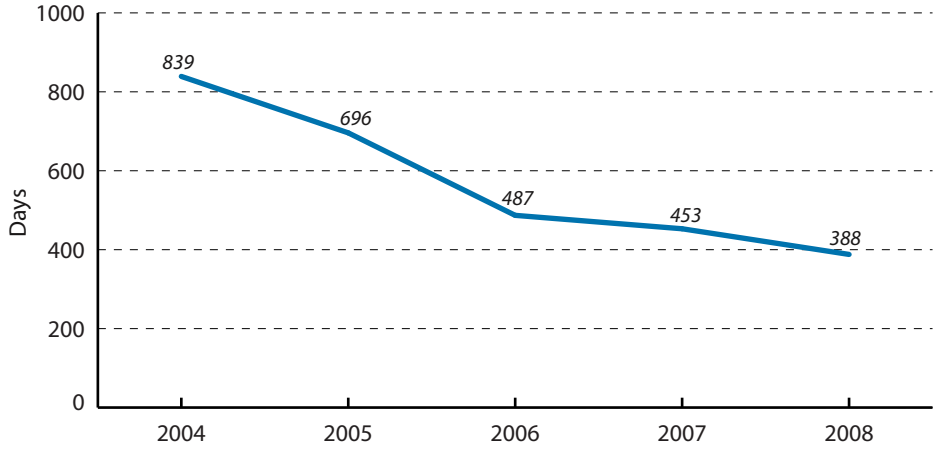
In Canada, the time patients spend waiting for the federal government's approval of a new drug is measured from the date the drug manufacturer's application for approval is recorded or filed in the Central Registry (CR) of Health Canada's Therapeutic Products Directorate (TPD) or Biologics and Genetics Therapies Directorate (BGTD) following the completion of clinical testing. This approval period ends when Health Canada issues an official Notice of Compliance (NOC), certifying that the new drug is safe and effective. Drug approval systems in Europe and the United States measure the same period but use different terminology for describing the start and end dates. As of 1999, responsibility for approving both pharmaceutical and biologics medicines was centralized for all European Union countries in the European Medicines Agency (EMEA). Since 2004, the equivalent authority to approve pharmaceutical and biological medicines in the United States has fallen under the Department of Health and Human Services (HHS) with the Center for Drug Evaluation and Research (CDER), a part of the Food and Drugs Administration (FDA). Prior to 2004, the Center for Biologics Evaluation and Research (CBER) was the approving authority for biological medicines.

1 For general information about Canada's review process, see Health Canada (2001).

Drug approval times in Canada, 2004–2008

In 2004, Health Canada took 839 days (on average) to issue a Notice of Compliance (NOC) (figure 2). In comparison, Health Canada took 696 days to grant market authorization for new medicines in 2005, 487 days in 2006, 453 days in 2007, and 388 days in 2008. This data suggests that Health Canada's approval times have improved significantly over the study period (2004 to 2008).[2]

Figure 2: Weighted average delay (days) for Health Canada to grant new drugs (NDS) regulatory / marketing approval, 2004–2008



Sources: Health Canada, 2009a, 2010; calculations by authors

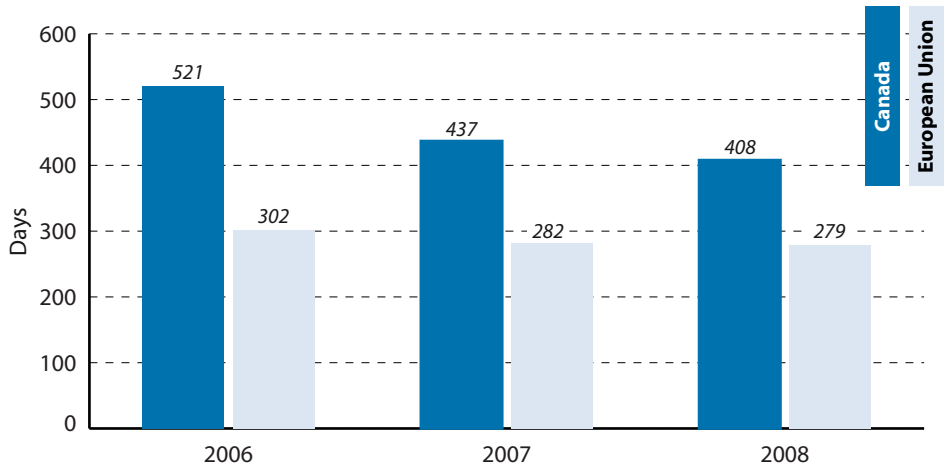
Drug approval times in Canada and the European Union, 2006–2008

The Canadian data presented here are different from the Canadian data shown in the previous section because the data in the previous section are weighted by biologic and pharmaceutical drug type. Unfortunately, the EMEA data available for this study were not detailed enough to permit the calculation of an average that is weighted by drug type. To make the Canadian and European data comparable, the data for Health Canada and the EMEA are shown as non-weighted, consolidated averages across biologic and pharmaceutical drug types.

2 The data indicate that from 2004 to 2008, Health Canada consistently received a higher number of new drug submissions for both biologic and pharmaceutical medicines. Thus, Health Canada's improvement in the approval delay for new drugs (2004-2008) is not due to fewer drugs being submitted for review. Instead, the data indicate that Health Canada's performance has improved over the observed period.

The data indicate that, in all three years observed, Health Canada took longer (on average) than the European Medicines Agency (EMEA), its European equivalent, to grant market approval for new drugs (figure 3 , which shows the average number of days spent waiting for the approval of new medicines in the European Union and Canada in 2006, 2007, and 2008, the only years for which comparable data are available because of changes in data reporting by the European Medicines Agency). In 2006, Health Canada took 521 days (on average) to approve new medicines, while the EMEA took 302 days. In 2007, Health Canada took 437 days (on average) to grant market authorization for new medicines, while the EMEA took 282 days. Likewise, Health Canada took 408 days (on average) to approve new medicines in 2008, while the EMEA took 279 days.

Figure 3: Non-weighted consolidated average delay (days) for regulatory/marketing approval of new drugs, Canada and the European Union, 2006–2008



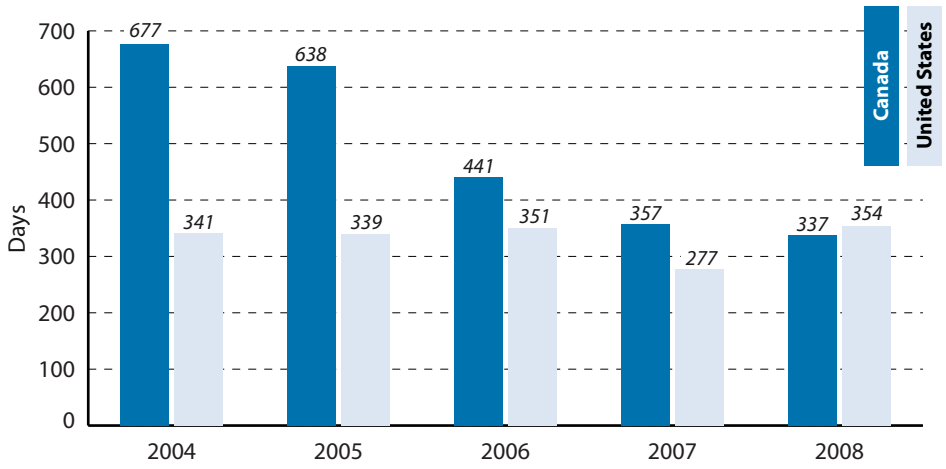
Sources: Health Canada, 2009a, 2010; EMEA, 2007, 2008, 2009; calculations by authors.

Drug approval times in Canada and the United States, 2004–2008

The Canadian data presented here are different from the previous sections because they are based on a different method of aggregating the statistics. In the previous sections, the statistics were aggregated on the basis of averages. However, the United States (FDA) only publishes median figures for drug approval times. Fortunately, Health Canada also publishes median figures, making comparisons to the US data possible. The data for both Canada and the United States are detailed enough to permit a calculation of a weighted average of the medians according to drug submission category (priority or non-priority). However, the US data does not allow weighting by drug

type (biologic or pharmaceutical). Figure 4 displays the differences between median approval times (weighted average medians) in Canada and the United States for new drug applications between 2004 and 2008. The data indicate that, from 2004 to 2007, Health Canada took longer (on average) than the FDA to grant marketing approval for new drugs. In 2004, Health Canada took approximately 677 days to approve new drugs, while the FDA took 341 days. In 2005, Health Canada's median approval time to grant market authorization for new drugs was 638 days, while the FDA's median approval time was 339 days. In 2006, Health Canada took 441 days to approve new drugs, while the FDA took 351 days. In 2007, Health Canada's median approval time to grant market authorization for new drugs was 357 days, while the FDA's median approval time was 277 days. However, the most recent data indicate that in 2008, Health Canada took less time than the FDA to grant market approval for new drugs. As figure 4 shows, Health Canada took 337 days to approve new drugs in 2008 while the FDA took 354 days. It should be noted that the FDA took longer to approve new drugs in 2008 than it did in any other year observed in this report.

Figure 4: Weighted average median delay (days) for regulatory/marketing approval of new drugs, Canada and the United States, 2004–2008



Sources: Health Canada, 2009a; US FDA, 2009a; calculations by authors.

Delays caused by provincial governments

The second segment of the wait for new medicines that is affected by government policies and institutional performance is the time spent by the federal,[1] provincial, and territorial (FPT) governments to decide whether to reimburse a new drug under their respective publicly funded drug insurance programs. Each jurisdiction determines reimbursement eligibility through its own government agency; consequently, the wait time for access to new medicines differs by jurisdiction. This wait is measured from the date on which Health Canada issues a Notice of Compliance (NOC) for a new drug to the date on which the first public reimbursement (PR) of the same drug is recorded in the formularies of each federal, provincial, and territorial drug program.

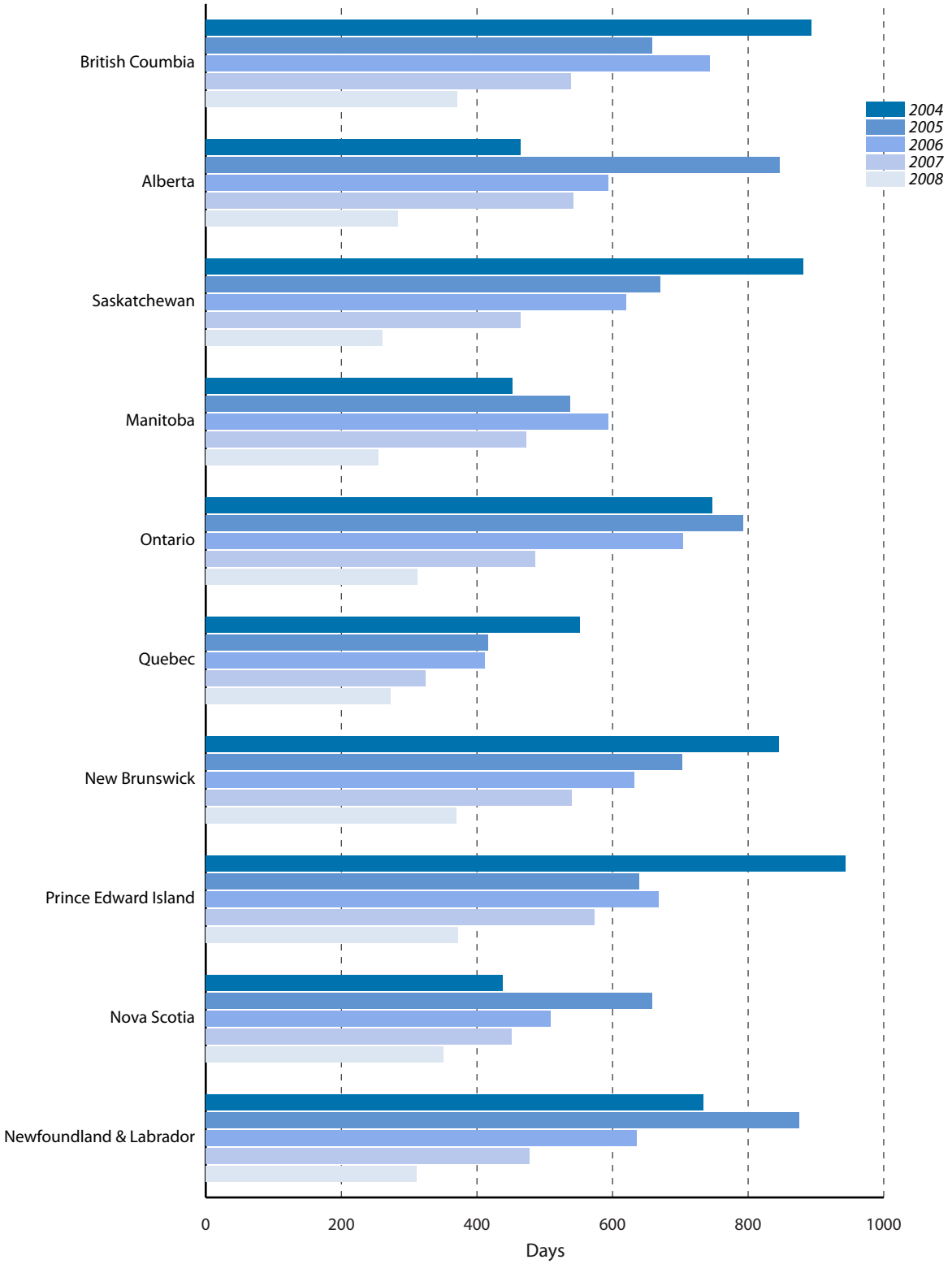
Provincial reimbursement delays, 2004–2008

FPT authorities have three options when determining reimbursement eligibility under public drug plans. First, they can declare a drug ineligible for public reimbursement. Second, they can declare a drug eligible for full reimbursement without conditions. Third, they can declare a new medicine eligible for reimbursement with restrictions. The analysis presented here considers any type of approval (full or restricted) to be an approval for the purpose of measuring and comparing performance between jurisdictions. The analysis does not present data on reimbursement delays for federal or territorial government drug programs. This analysis is focused only on the performance of provincial drug plans.

The average time taken by the provinces to grant reimbursement eligibility for new drugs that were approved by Health Canada in 2004 was 648 days; the average for new drugs that received market approval in 2005 was 673 days; the average for new drugs approved in 2006 was 608 days; the average for new medicines approved in 2007 was 484 days; and the average for new drugs approved in 2008 was 316 days (figure 5).

1 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.

Figure 5: Weighted average time (days) between Health Canada regulatory/marketing approval and provincial public reimbursement approval for new medicines, by province, 2004–2008



Sources: Health Canada, 2009b; Brogan Inc., 2009; calculations by authors.

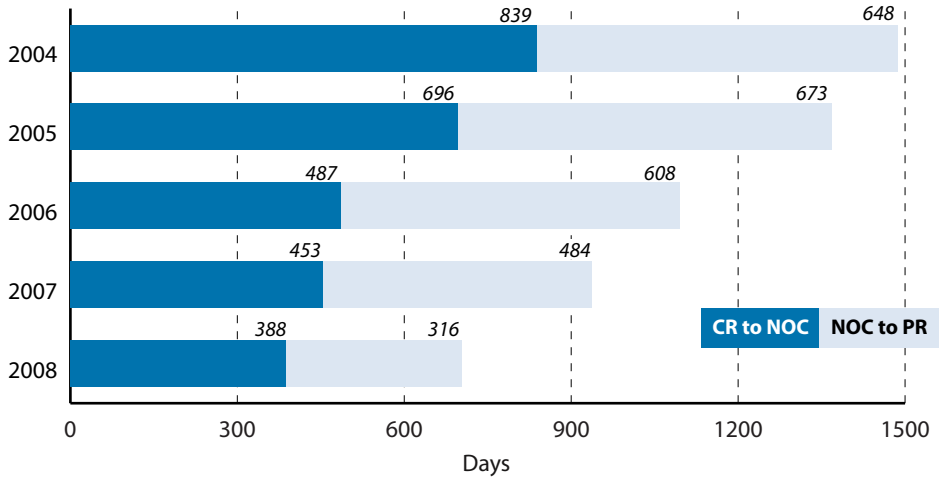
Total delay for access to new medicines

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 taken by Health Canada to issue a safety approval (CR to NOC) and the provincial reimbursement delay (NOC to PR). Figure 6 shows the consolidated average wait for access to new medicines, measured in days, for the years 2004, 2005, 2006, 2007, and 2008. 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 patients to use them. 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 approval. The length of time taken by Health Canada to grant marketing approval for new medicines has decreased over the last five years (figure 6).

The second segment of the bar represents the period of waiting for those who are dependent on public drug programs. As figure 6 shows, the time spent by the provinces to grant eligibility for the public reimbursement of new drugs decreased over the five-year period.

The total average wait for publicly insured access to new medicines approved by Health Canada in 2004 was 1,487 days (4.1 years); compared to 1,369 days (3.8 years) for drugs approved for sale in 2005; 1,095 days (approximately 3 years) for drugs that were granted market authorization in 2006; 937 days (approximately 2.6 years) for drugs that received a NOC in 2007; and 704 days (1.9 years) for drugs approved for sale in 2008. Nevertheless, wait times for these drugs remain significant.

Figure 6: Weighted average total delay (days) for access to publicly insured new medicines in Canada, by wait segment, averaged across all provinces, 2004–2008



Abbreviations: **CR**: the date the drug manufacturer's application for marketing approval is recorded or filed in Health Canada's Central Registry. **NOC**: the date Health Canada issues an official Notice of Compliance, certifying that the new drug is safe and effective and is legally approved for sale is Canada. **PR**: the date on which the first public reimbursement of the new drug is recorded in the formularies of each provincial drug program.

Sources: Health Canada, 2009a, 2009b, 2010; Brogan Inc., 2009; calculations by authors.

Denials of reimbursement by provincial governments

It is important to examine provincial reimbursements, not just in terms of delays, but also in terms of denials of access. Although most provinces have reduced the number of days that patients must wait to have new drugs publicly reimbursed, this does not necessarily mean that the overall percentage of drugs that eventually become eligible for reimbursement has remained the same. Provincial agencies could be taking less time to review and grant reimbursement approval for new drugs because fewer drugs are ultimately being accepted for reimbursement. Reimbursement approval rates are estimated by calculating the number of full or partial reimbursement approvals recorded in each province (as of December 31, 2009) as a percentage of the total number of drugs already approved as safe and effective (i.e., drugs issued a NOC) by Health Canada in each year.

The analysis shows that most of the drugs that are approved by Health Canada as safe and effective are not declared eligible for reimbursement under provincial drug plans. Averaged across all provincial public drug programs, as of December 31, 2009, only 23.0% of all drugs that Health Canada approved as safe and effective in 2004 had actually been approved for reimbursement (fully or partially) by the provinces; compared to 16.2% of new drugs certified in 2005, 28.0% of new drugs certified in 2006, 19.1% of new drugs certified in 2007, and 20.3% of new drugs certified in 2008 (table 2).

Table 2: Public reimbursement approvals, as a percentage of NDS-class drugs approved by Health Canada, by province, 2004–2008, as of December 31, 2009

	2004		2005		2006		2007		2008	
	Number of drugs approved	Drugs approved as a % of NOCs	Number of drugs approved	Drugs approved as a % of NOCs	Number of drugs approved	Drugs approved as a % of NOCs	Number of drugs approved	Drugs approved as a % of NOCs	Number of drugs approved	Drugs approved as a % of NOCs
AB	8	17.0%	2	4.4%	11	21.6%	4	9.1%	6	18.8%
BC	10	21.3%	2	4.4%	8	15.7%	5	11.4%	5	15.6%
MB	9	19.1%	5	11.1%	8	15.7%	7	15.9%	3	9.4%
NB	11	23.4%	10	22.2%	20	39.2%	10	22.7%	8	25.0%
NL	11	23.4%	9	20.0%	18	35.3%	8	18.2%	8	25.0%
NS	9	19.1%	7	15.6%	16	31.4%	8	18.2%	6	18.8%
ON	8	17.0%	7	15.6%	11	21.6%	8	18.2%	4	12.5%
PEI	9	19.1%	8	17.8%	12	23.5%	6	13.6%	2	6.3%
QC	20	42.6%	13	28.9%	22	43.1%	22	50.0%	14	43.8%
SK	13	27.7%	10	22.2%	17	33.3%	6	13.6%	9	28.1%
Provincial average		23.0%		16.2%		28.0%		19.1%		20.3%
Total NDS NOCs	47		45		51		44		32	

Note: Provinces often take more than a year to decide whether or not to make a new drug eligible for public reimbursement. Therefore, more new drugs that were approved by Health Canada in the observed years could eventually be granted eligibility for public reimbursement in the future. The delay will be captured in future reports and will be reflected in the percentages shown above

Note: Total NDS NOCs include all available data from Brogan Inc.

Source: Health Canada 2009b; Brogan Inc., 2009; calculations by authors.

Coverage and reimbursement by private drug insurance

This is the first year that this study has compared the reimbursement delays and coverage of new drugs under private drug-insurance plans with delays and coverage measured under public drug plans. Using this data, we are able to measure the difference (in days) taken by both public and private drug insurance schemes to grant reimbursement approval for new drugs.[1] Only those drugs that received a Notice of Compliance from Health Canada in 2004 are used for comparison as they will provide the most comprehensive dataset.[2] Tables 3a and 3b include all new drugs (NDS) that received market approval by Health Canada in 2004 that are available in Brogan Inc.'s database. Pharmaceutical and biologic drugs are separated by drug type and are listed in alphabetic order.

The tables display the delay (in days) for each new drug between Health Canada's Notice of Compliance and the drug's first listing (reimbursement) on any provincial public drug plan; and the delay (in days) between market approval and the drug's first paid claim registered with any private drug insurer. The data is aggregated across all provincial public drug plans and private drug insurers, and is current up to December 31, 2009.

As tables 3a and 3b show, there are a number of new drugs that were approved by Health Canada in 2004 that have been claimed for reimbursement by private insurers, but have yet to be approved for reimbursement by public drug plans. According to the data provided by Brogan Inc., 20 (61%) of the 33 new pharmaceutical drugs that received market approval by Health Canada in 2004 were approved for public reimbursement by at least one of the provincial drug plans as of December 31, 2009. In contrast, the data indicate that all 33 (100%) new pharmaceutical drugs approved by Health Canada in 2004 have been claimed for reimbursement by at least one private insurer. Likewise, as of December 31st 2009, public drug programs (at least one) have approved only 4 (33%) of the 12 new biologic drugs that were issued a Notice of Compliance from Health Canada in 2004, compared to 11 (92%) of the 12 that have been claimed by at least one private insurer.

Tables 3a and 3b also show the difference in reimbursement delays (in days) between public and private drug-insurance plans. As above mentioned, the difference in delays is based on the first date on which a specific drug was listed on any provincial formulary (public drug plan) and the first date on which a reimbursement claim was made by any private insurer across Canada. As

1 See Appendix: data sources and comparability issues.

2 As noted above, provincial drug plans often take years to issue public reimbursement approval.

Table 3a: Pharmaceutical drugs—first listing on a public drug insurance plan (aggregated across all provincial drug plans) and first claim with a private drug insurance plan (aggregated across insurance companies and provinces), for all new pharmaceutical drugs that received a Notice of Compliance from Health Canada in 2004, as of December 31, 2009.

NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2004	Delay (in days) between NOC and 1st Listing on Public Drug Plans (aggregated across all provinces)	Delay (in days) between NOC and 1st Claim on Private Drug Plans	Difference in Days
ADDERALL XR	866	24	842
ACTIVELLE	Not listed	345	N/A
AVANDARYL	Not listed	586	N/A
BONVIVA	Not listed	1000	N/A
CIPRALEX	1411	61	1350
CIPRO XL	147	20	127
CIPRODEX	1331	59	1272
CLIMARA PRO	1761	1545	216
CLOBEX	Not listed	146	N/A
EBIXA	301	16	285
FACTIVE	Not listed	385	N/A
FASLODEX	Not listed	134	N/A
FROVA	Not listed	1244	N/A
LEVITRA	Not listed	16	N/A
MULTIHANCE	672	904	–232
NUVARING	873	247	626
OXYTROL	224	121	103
PENLAC	Not listed	104	N/A
PREFESTA	Not listed	92	N/A
PREVACID	Not listed	132	N/A
PREVACID FASTAB	1177	34	1143
RELPAX	300	99	201
SENSIPAR	667	80	587
SONOVUE	Not listed	541	N/A
STRATTERA	285	61	224
TELZIR	173	69	104
TEVETEN PLUS	246	63	183
TIAZAC XC	142	145	–3
VFEND	285	–44	329
VIGAMOX	143	63	80
YASMIN 21	173	28	145
ZAVESCA	Not listed	517	N/A
ZYMAR	214	–144	358

Sources: Health Canada, 2009b; Brogan Inc., 2009.

shown in table 3, there is a significant difference in the time that it takes to approve a new drug for public reimbursement compared to the time that it takes before a new drug is claimed for reimbursement through a private insurance plan. The drugs *Multihance* and *Tiazac XC* are the only two drugs that were listed for reimbursement on at least one provincial formulary (public drug plan) before a claim was submitted to a private insurance plan. It should be noted that the drugs *Vfend* and *Zymar* have negative delays between Health Canada's Notice of Compliance and the date on which a claim was made to a private insurer. A negative delay indicates that a patient had access to a drug before Health Canada's approval though the Special Access Programme (SAP). The SAP authorizes access to a drug that has not been approved by Health Canada for patients with a serious life-threatening condition (Health Canada, 2002).

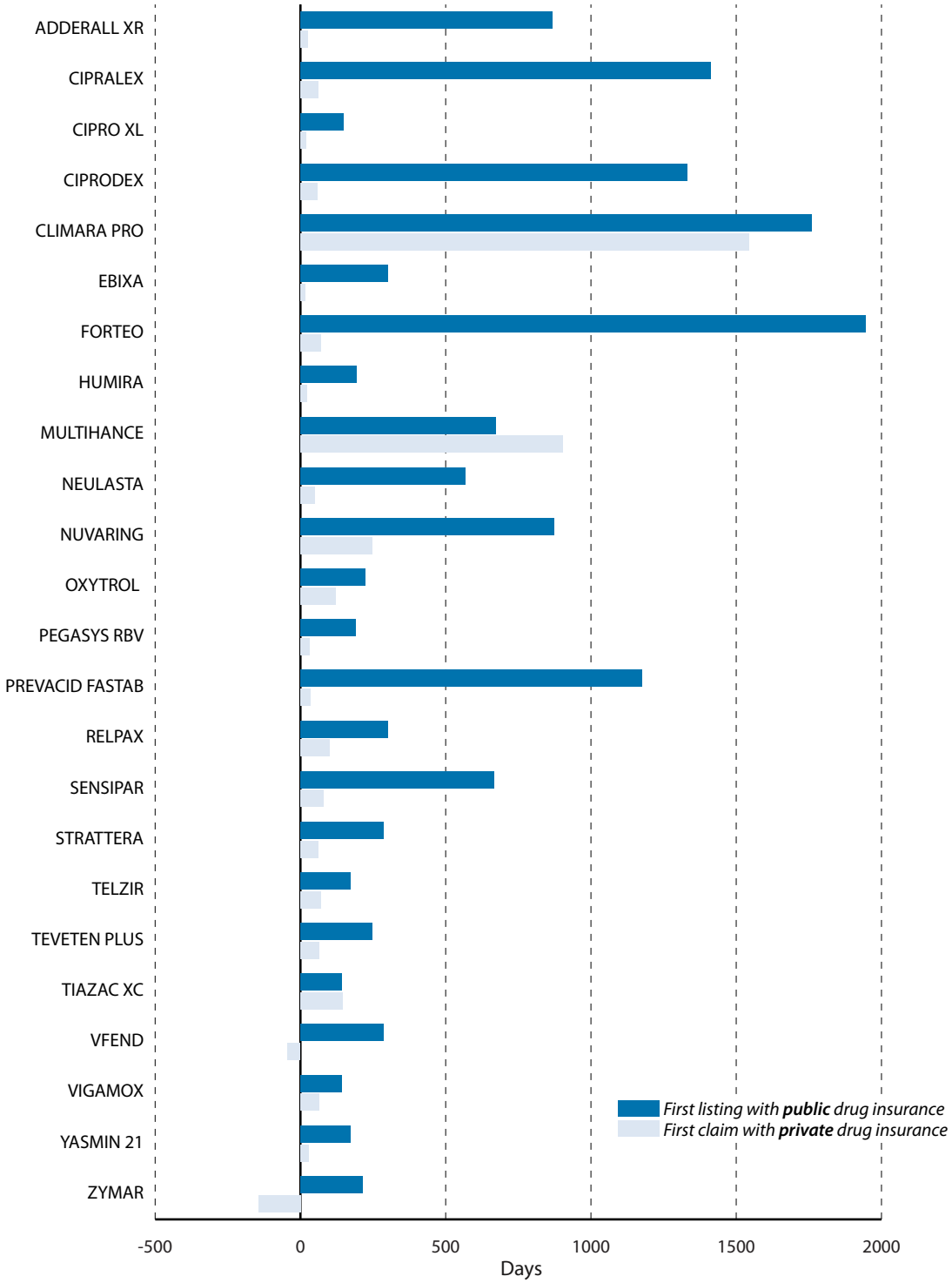
Figure 7 displays the difference in days between the first claim that was made with a private insurance plan and the first listing of the drug with a public insurance plan (aggregated across provinces) for all drugs (pharmaceutical and biological) that have been approved for reimbursement by at least one public and private drug insurance plan as of December 31, 2009. In some extreme cases, such as the biological drug *Forteo*, the difference in reimbursement approval between public and private drug insurance was over 1,800 days. In general, the data indicate that private drug insurance (at least one insurer) listed new drugs that were approved by Health Canada in 2004 much earlier than any provincial public drug plan (with the exception of *Multihance* and *Tiazac XC*).

Table 3b: Biological drugs—first listing on a public drug insurance plan (aggregated across all provincial drug plans) and first claim with a private drug insurance plan (aggregated across insurance companies and provinces), for all new biological drugs that received a Notice of Compliance from Health Canada in 2004, as of December 31, 2009.

NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2004	Delay (in days) between NOC and 1st Listing on Public Drug Plans (aggregated across all provinces)	Delay (in days) between NOC and 1st Claim on Private Drug Plans	Difference in Days
ALDURAZYME	Not listed	65	N/A
AMEVIVE	Not listed	245	N/A
FABRAZYME	Not listed	434	N/A
FORTEO	1946	69	1877
HUMIRA	192	23	169
INFANRIX-HEXA	Not listed	1608	N/A
MYOBLOC	Not listed	Not claimed	N/A
NEULASTA	568	48	520
OVIDREL	Not listed	61	N/A
PEGASYS RBV	189	32	157
REPLAGAL	Not listed	397	N/A
XOLAIR	Not listed	92	N/A

Sources: Health Canada, 2009b; Brogan Inc., 2009.

Figure 7: Difference (in days) between the first listing with a public insurance plan and the first claim with a private insurance plan for new drugs that received a Notice of Compliance from Health Canada in 2004, aggregated across all provinces and drug plans



Note: includes only drugs approved for reimbursement by at least one public and private insurer as of December 31, 2009.

Sources: Health Canada, 2009b; Brogan Inc., 2009.

Conclusions

- In total, Canadians wait nearly two years (on average) for access to publicly insured drugs.
- Health Canada's approval times have improved since 2004, relative to the agency's own performance.
- Health Canada's performance was worse than that of the European EMEA in all three years studied (2006, 2007 and 2008).
- Health Canada's performance was worse than that of the American FDA in four of the last five years studied (2004 to 2008).
- Only a small percentage of the new drugs that Health Canada certifies as safe and effective are finally declared eligible for reimbursement under provincial public drug programs.
- The provincial governments take a significant amount of time to approve the few drugs that they declare eligible for public reimbursement.
- Private drug insurance in Canada covers significantly more new drugs than public drug insurance.
- Private drug insurance in Canada covers new drugs more rapidly than public drug insurance.

Policy options—improving access to new drugs

Mutual recognition of drug approvals and cooperation with other jurisdictions

Health Canada essentially duplicates the new drug approval process of the FDA in the United States. 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 to all participating countries. For example, if Canada entered into agreements of "mutual recognition" with other countries, new medications already approved in those countries could be introduced into the Canadian market far more rapidly and vice versa. 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).

Similar thinking is reflected in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). In the 1980's, the European Community (the predecessor of the European Union) initiated discussions to develop a single market for pharmaceuticals. During this time, bilateral discussions between Europe, Japan and the United States (representing over 80% of the world's pharmaceutical market) were also taking place about harmonizing the approval process for new medicines. Although the regulatory agencies of Europe, Japan and the United States all had the same central objective of evaluating the quality, efficacy, and safety of new medicinal products, they found it necessary to duplicate many expensive and time-consuming tests before granting market authorization in their respective countries. However, this became inefficient as the cost of research and development (for new drugs) and health care costs in general increased significantly over time, and patients did not have access to the newest medicinal products that were available in other countries (ICH, 2009). Thus, the intention of the international conference on harmonization (ICH) was to establish international technical requirements and guidelines for increasing the efficiency of the drug development process by reducing unnecessary duplications (thus reducing costs),

while also accelerating the market approval so that new medicinal products were made available to patients as soon as possible (ICH, 2009).

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use

The ICH is made up of six parties representing industry associations (brand-name drug companies only) and regulatory agencies of the United States, Japan, and Europe; and Observers, which include the European Free Trade Association (EFTA), Health Canada, and the World Health Organization (WHO). Although the observers do not vote on issues, they are present at all conferences and contribute to regulatory consultations. In addition, the Observers act as a link to non-ICH countries and regions (ICH, 2009).

Since its inception, the ICH has developed over 50 harmonized guidelines. The guidelines are intended to eliminate duplication in the drug development and marketing approval process, with the goal that a single set of studies can be produced to show the "quality, safety, and efficacy of a new medicinal product" (ICH, 2009). For instance, under the guidelines, a Common Technical Document (CTD) has been established so that a common application is used for medicinal product submissions to all member regulatory authorities (ICH, 2009).

Importantly, the guidelines are meant to be followed within the standards determined by regional requirements. In general, the guidelines are used by the drug industry as a way of reducing duplication by using a single set of data and universal application to show safety and efficacy, and to apply for licensing (ICH, 2009). ICH guidelines range from the amount of animal testing required during clinical trials to post-marketing safety data.

Although the ICH reduces duplication and costs, a drug must still be approved by the regulatory agency of each member and observer country. In other words, a drug approved by the EMEA (in the European Union) must still be submitted for approval to the FDA if a drug manufacturer would like the drug sold in the United States.

Although Health Canada is an Observer at the International Conference on Harmonization (ICH) and has implemented a number of guidelines established by the ICH, it still lags behind its international counterparts on harmonization efforts.

Replace government drug programs with subsidized access to private insurance

Data presented in this study indicate that private drug insurance in Canada tends to cover a wider range of new medicines and approves their coverage at a much faster rate than public drugs programs. One way to improve access

to new medicines without increasing the burden on taxpayers would be to replace existing public drug plans with a properly regulated and competitive private-sector insurance market in which universal access to catastrophic drug insurance would be facilitated through means-tested subsidies for those with low incomes. Economic theory and evidence, and actual Canadian experience, suggest that such a policy alternative would be expected to achieve universal access to prescription drug coverage and would contain costs, without restricting consumer choice through central planning.

Research suggests that private-payment health systems (a combination of private insurance and out-of-pocket spending) are better structured to encourage the efficient demand for, and supply of, health technology (cf. Danzon, 1993; Newhouse and the Insurance Experiment Group, 1993). By creating a price at the point of consumption, co-payments encourage patients to make cost-efficient choices between alternative treatments (e.g., invasive surgery, non-invasive surgery, prescription drugs, natural remedies). Consumer sensitivity to prices in turn creates incentives for health-care providers to supply and use resources efficiently. This creates incentives for drug manufacturers to invest efficiently in the development of new drugs. It is also common for private-sector insurers to employ deductibles that appropriately restrict insurance coverage to a range of expenses considered individually unaffordable for consumers. Private-sector insurers sometimes impose annual coverage limits that might expose patients to significant cash costs in unusual cases involving very expensive drugs. Yet, in a competitive private-sector insurance market where individuals buy insurance directly, patients who prefer higher insurance coverage limits can opt to pay higher premiums to cover the risk of such extraordinary expenses. Under a system with means-tested subsidies for those with low incomes, maximum coverage limits for subsidized populations would have to be determined through public decision-making processes.

Importantly, it is essential that recipients are means-tested before qualifying for public subsidies. A historic feature of provincial drug-benefit programs in Canada is preferential treatment based on age (Graham and Tabler, 2005). Although some provinces have introduced means-testing in accordance with age-based eligibility, other provinces grant automatic eligibility for publicly funded drug programs once their citizens turn 65 years of age. For instance, in Ontario, seniors with a valid Ontario health card do not need to apply for publicly funded drug coverage: residents of Ontario aged 65 and older simply take their prescriptions to a pharmacy and inform the pharmacist that they are eligible for the Ontario Drug Benefit Program [ODB] (Ministry of Health and Long-Term Care, 2002). Even though the ODB requires seniors to contribute through minimal co-payments (a maximum of $6.11 and a minimum of $2 per prescription) and annual deductibles (a maximum of $100 per person for a couple with a combined income of $24,175 or

more), research shows that very few seniors (and the entire population more generally) actually experience catastrophic drug costs or lack the financial means to pay for it themselves. Skinner found that between 1997 and 2002, only 3% of Canadian households spent more than 5% of their annual income on prescription drugs (Skinner, 2005). Likewise, the Romanow Commission on the Future of Health Care in Canada concluded that, in 2002, only 3% of the general population in the province of Manitoba exceeded the catastrophic threshold of $1,500 (Romanow, 2002). Looking at seniors more specifically, a more recent analysis of the province of Saskatchewan shows that, in 2006, elderly families (65 years of age or older) only spent 1.4% of their median after-tax income on prescription drugs (Rovere, 2008). In other words, a very small percentage of seniors (or the general population) actually experience catastrophic drug costs.

Therefore, instead of automatically providing comprehensive public drug insurance to people based on age, means-tested subsidies should be provided to those with low incomes regardless of age to purchase catastrophic drug insurance in a private, competitive, insurance market. This would benefit recipients by giving them the choice of selecting the drug plan that meets their individual medical needs and financial abilities, while providing significant savings to taxpayers. Research shows that this approach could save taxpayers more than CA$4 billion (2005 dollars) annually (Skinner, 2005). Allowing the private insurance market to compete through price and service, thus eliminating government monopolies on drug prices and coverage (Skinner and Rovere, 2008b) is the best policy choice for improving access to the newest prescription drugs.

Appendix—classes, data sources, and comparability

Data sources and comparability issues

There are four main sources of data cited in this report. The first source is Health Canada, which is the only source of data on drug safety approval times in Canada that comprehensively includes all drugs.[1] Health Canada publishes data on pharmaceutical medicines through the Therapeutic Products Directorate (TPD) and on biologic medicines through the Biologics and Genetic Therapies Directorate (BGTD). Data published in annual reports on drug approvals by the TPD and the BGTD are stated in aggregates and are not broken down in detail. Health Canada publishes this data separately by drug submission class, priority (or "fast track") review status, and therapeutic category. Health Canada's published approval times include the entire period between the original filing of the new drug submission application (CR) and the issuance of the Notice of Compliance (NOC), inclusive of all company time spent to address any deficiencies in the manufacturer's application. It is unclear whether Health Canada records the filing of a new drug submission application on the actual date it was delivered to the TPD or the date on which a reviewer first saw the file (Health Canada, 2001, 2003, 2004a, b, 2005a, b, c, 2006a, b, c, 2007, 2008a, 2009a). The two sources of international comparative data on drug safety approval times cited are the United States Department of Health and Human Services, Food and Drug Administration (US FDA, 1996, 2002, 2009a) and the European Medicines Agency (EMEA, 2005, 2007, 2008, 2009). The FDA and the EMEA publish separate data for the time spent by

1 Another public source of aggregated Canadian and international data on drug approval times is the industry association, Rx&D, which 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 drug products (i.e., new drug submissions, supplemental drug submissions, and clinical trial applications) (Canada's Research-Based Pharmaceutical Companies, 2005).

companies to correct the deficiencies in their applications. Health Canada does not do so; instead, it publishes an entire approval delay that includes what they call "company" time. In order to make the data comparable among countries, "company" time was included in the total approval delay for the FDA and the EMEA.

In previous years Health Canada published both average and median figures for drug approval wait times. However in this year's annual reports, Health Canada published only median figures. A special data request was made to Health Canada to obtain average approval times in order to compare wait times between Canada and the European Union. The FDA only publishes median figures. The EMEA only publishes average figures. As a result, Canadian and European data were compared using averages, while Canadian and American data were compared using medians. Unlike Health Canada and the FDA, the EMEA does not publish approval wait-time data that separates priority and non-priority new drug submissions.

In the US data, drug types (pharmaceutical and biological medicines) are aggregated but the data is separated by submission status type (priority or non-priority review). The Canadian figures published by Health Canada are separated according to submission status type (priority or non-priority review); however, unlike the American data, the Canadian figures are reported separately by drug type. In order to make the two sets of data more comparable, it was necessary to aggregate the separately reported medians by calculating a weighted median proportional to the number of drugs approved in each subset as a percentage of the total number of drugs approved overall. The Health Canada data is weighted by drug type (biological and pharmaceutical drugs) and by submission status type (priority and non-priority). As drug types are already consolidated by the FDA, the US data is only weighted by submission status type.

The fourth main source of data cited in this paper is Brogan Inc. (Brogan Inc., 2009). Brogan Inc. is a private consulting and data firm that collects information that permits the measurement of public and private reimbursement delays and the rate of positive reimbursement approvals in each of the provinces. Brogan Inc.'s database contains the date on which Health Canada issued a NOC for each new drug and the first date on which public reimbursement of a drug was approved in each of the provinces, as well as a classification of whether reimbursement was full, restricted, or declined. The database also provides the first date on which a paid claim for a new drug was registered for private insurers; however it does not provide the name of the private insurer. Using this database, comparisons can be measured between the date on which the private and public drug insurance plans approve a drug for reimbursement after it has received market authorization by Health Canada.

Canadian and international definitions of classes for new drug submissions

In Canada, new drugs fall under different classifications defined by Health Canada's Therapeutic Products Directorate (TPD) and the Biologics and Genetic Therapies Directorate (BGTD). In Canada, non-generic new drug approvals involve new active substances (NAS), new drug submissions (NDS), and supplemental new drug submissions (SNDS). Similar classifications are used by the European Medicines Agency (EMEA) and the US Food and Drug Administration (FDA) but under different terminology. The Canadian and international classifications are briefly described in the following tables.

Table 4: Classes of new drug submissions used by Health Canada's Therapeutic Products Directorate (TPD) and the 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 NASs, as well as combinations of previously approved NASs, 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.

Supplemental 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, labeling, or recommended route of administration. An SNDS must also be submitted if a 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 a "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 interest of Canadians to review potentially life-saving 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, 2006a

Table 5: Classifications of new drug applications (NDA) used by the FDA's Center for Drug Evaluation and Research (CDER)

New Molecular Entity (NME)

A New Molecular Entity is an active ingredient that has never before been marketed in the United States in any form.

New Drug Application (NDA)

When the sponsor of a new drug believes that enough evidence on the drug's safety and effectiveness has been obtained to meet FDA's requirements for marketing approval, the sponsor submits to FDA a new drug application (NDA). The application must contain data from specific technical viewpoints for review, including chemistry, pharmacology, medical, biopharmaceutics, and statistics. If the NDA is approved, the product may be marketed in the United States. For internal tracking purposes, all NDA's are assigned an NDA number.

Supplement

A supplement is an application to allow a company to make changes in a product that already has an approved new drug application (NDA). CDER must approve all important NDA changes (in packaging or ingredients, for instance) to ensure the conditions originally set for the product are still met.

Abbreviated New Drug Application (ANDA) Number

This six-digit number is assigned by FDA staff to each application for approval to market a generic drug in the United States.

Biologic License Application (BLA)

Biological products are approved for marketing under the provisions of the Public Health Service (PHS) Act. The Act requires a firm that manufactures a biologic for sale in interstate commerce to hold a license for the product. A biologics license application is a submission that contains specific information on the manufacturing processes, chemistry, pharmacology, clinical pharmacology, and the medical affects of the biologic product. If the information provided meets FDA requirements, the application is approved and a license is issued allowing the firm to market the product.

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.

Sources: US FDA, 1996, 2009b

Table 6: Classifications of new drug market authorization applications by the European Medicines Agency (EMEA)

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 that has not been authorized previously in the European Union.

Extensions

An extension of a new drug is defined according to the following:

- 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 that 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.

Source: European Medicines Agency, 2005

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