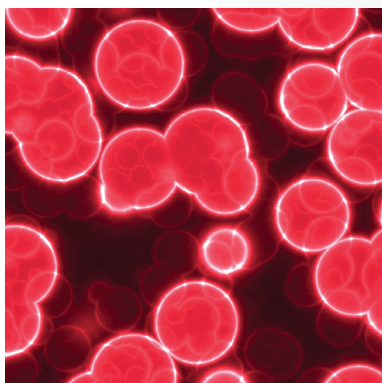


April 2012

Access Delayed, Access Denied 2012

Waiting for New Medicines in Canada

by Mark Rovere and Brett J. Skinner



Key findings

- On average, Canadians wait over two years for access to new drugs because of federal delays in approving them and provincial delays in authorizing reimbursement.
- Health Canada took longer to approve new medicines than the European Medicines Agency in all five years studied—2006, 2007, 2008, 2009, and 2010.
- Health Canada took longer to approve new medicines than the American Food and Drug Administration (FDA) in six of the last seven years studied—2004 to 2010.
- On average, only 23% of the new drugs that Health Canada certified as safe and effective between 2004 and 2010 have been declared eligible for reimbursement under provincial public drug programs as of January 1st, 2012.
- Private-sector drug insurance plans have provided reimbursement for 84% of new drugs approved by Health Canada from 2004 to 2010 (as of January 1st, 2012), and have covered them more rapidly than public drug insurance.

Studies in Health Policy

April 2012

Access Delayed, Access Denied 2012 Waiting for New Medicines in Canada

by Mark Rovere and Brett J. Skinner

Summary

Federal and provincial government policies create unnecessary delays for patients wanting access to new medicines.

The federal government does not allow patients to use new drugs until Health Canada has reviewed each product's safety and effectiveness. The latest data show that in 2010 Health Canada took 527 days on average to approve new drugs, up from 472 days in 2009. Health Canada took longer to approve new drugs than regulators in Europe in all five years studied (2006 to 2010) and longer than the American FDA in six of the last seven years studied (2004 to 2010). Relative to other countries, Canadian patients wait too long for government permission to use new drug treatments. International safety standards are similar, so the federal government could speed up access to new drugs by harmonizing with European and American regulatory processes through mutual recognition of drug approval decisions.

Provincial public drug plans refuse to pay for most new drugs, even after Health Canada has approved them as safe and effective. The latest data show that, only 23% of the new drugs approved by Health Canada each year from 2004 to 2010 were eventually covered by provincial public drug programs as of January 1, 2012. By contrast, 84% of these same drugs were covered under private-sector drug insurance plans over the same period and coverage occurred far more rapidly than under public drug plans. Provincial governments could improve access for patients and save money by replacing existing public drug programs with a means-tested subsidy for people with low incomes to aid the purchase of private drug insurance.

Contents

Highlights / 2

Introduction / 3

Global factors affecting access to new medicines / 4

Delays caused by the federal government / 6

Delays caused by provincial governments / 10

Total delay for access to new medicines / 12

Denials of reimbursement by provincial governments / 14

Comparing coverage delays in public and private drug insurance / 16

Policy options / 26

Appendix / 27

References / 32

About the authors / 38

Acknowledgments / 39

Publishing information / 40

Supporting the Fraser Institute / 41

Purpose, funding, & independence / 42

About the Fraser Institute / 43

Editorial Advisory Board / 44

Highlights

- On average, Canadians wait over two years for access to new drugs because of federal delays in approving them and provincial delays in authorizing reimbursement.
- Health Canada took longer to approve new medicines than the European Medicines Agency in all five years studied—2006, 2007, 2008, 2009, and 2010.
- Health Canada took longer to approve new medicines than the American Food and Drug Administration (FDA) in six of the last seven years studied—2004 to 2010.
- On average, only 23% of the new drugs that Health Canada certified as safe and effective between 2004 and 2010 have been declared eligible for reimbursement under provincial public drug programs as of January 1st, 2012.
- Private-sector drug insurance plans have provided reimbursement for 84% of new drugs approved by Health Canada from 2004 to 2010 (as of January 1st, 2012), and have covered them more rapidly than public drug insurance.

Introduction

This edition of *Access Delayed, Access Denied* is the Fraser Institute's sixth annual report measuring delays in the approval of new drugs by Health Canada and rates of coverage for new drugs under provincial public drug plans, relative to private-sector drug plans. This report provides patients with 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 financially sustainable policy alternatives that give consumers greater choice.

Access Delayed, Access Denied 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 rigour 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 (EMA).

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 and 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

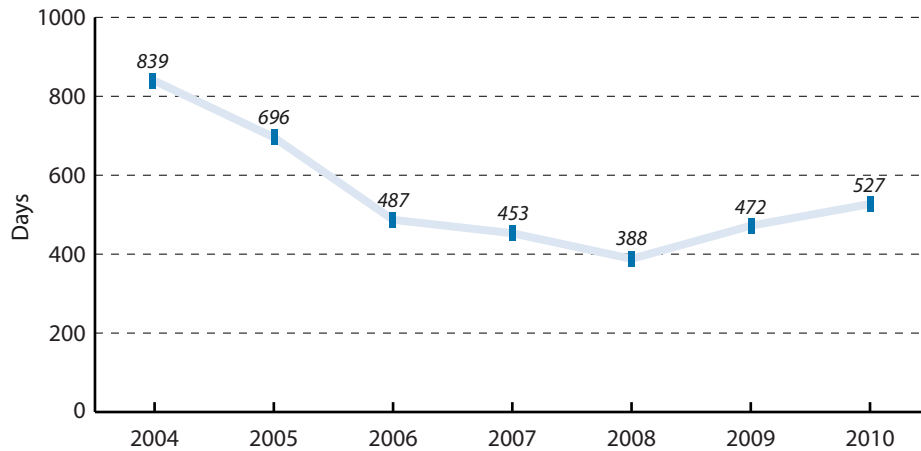
After the development phase is over, the first segment of the wait for new medicines that is affected by public policies and institutional performance in Canada is the wait for the federal government to approve the safety and effectiveness of new drugs. Before any new drug is legally allowed to be sold in Canada, it must first receive official approval from Health Canada, which 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. Because marketing approval for new drugs occurs at the national level and applies to all drugs sold in Canada, any delay caused by Health Canada's drug review process affects the wait time for access to new medicines for all Canadians, regardless of whether they are publicly insured, privately insured, or uninsured.

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 (EMA). Since 2004, the equivalent authority to approve pharmaceutical and biological medicines in the United States has been Center for Drug Evaluation and Research (CDER), which is 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.

Drug approval times in Canada, 2004–2010

In 2004, Health Canada took 839 days (on average) to issue a Notice of Compliance (NOC) (figure 1). In comparison, Health Canada took 696 days to grant market authorization for new medicines in 2005, 487 days in 2006, 453 days in 2007, 388 days in 2008, 472 days in 2009, and 527 days in 2010. These data suggest that Health Canada's approval times improved significantly from 2004 to 2008, but increased in both 2009 and 2010.

Figure 1: Weighted average delay (days) for Health Canada to grant regulatory and marketing approval for new drugs (NDS), 2004–2010



Sources: Health Canada, 2011a, 2011b; calculations by authors.

Drug approval times in Canada and the European Union, 2006–2010

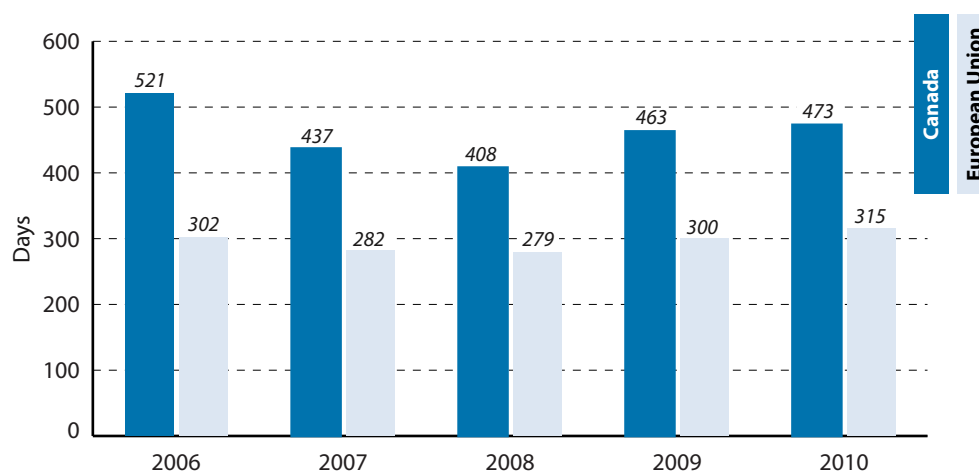
The Canadian data presented here are different from the Canadian data shown in the previous section because the data in the previous section are weighted by biologic and pharmaceutical drug type. Unfortunately, the EMA data available for this study were not detailed enough to permit the calculation of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

The data indicate that, in all five years observed, Health Canada took longer (on average) than the European Medicines Agency (EMA), its European equivalent, to grant market approval for new drugs (figure 2). In 2006, Health Canada took 521 days (on average) to approve new medicines, while the EMA took 302 days. In 2007, Health Canada took 437 days (on average) to grant market authorization for new medicines, while the EMA took 282 days. In 2008, Health Canada took 408 days (on average) to approve new medicines, while the EMA took 279 days. In 2009, Health Canada took 463 days (on average) to certify new medicines, while the EMA took 300 days. Likewise, Health Canada took 473 days (on average) to certify new medicines in 2010, while the EMA took 315 days.

Drug approval times in Canada and the United States, 2004–2010

The Canadian data presented here are different from those in 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

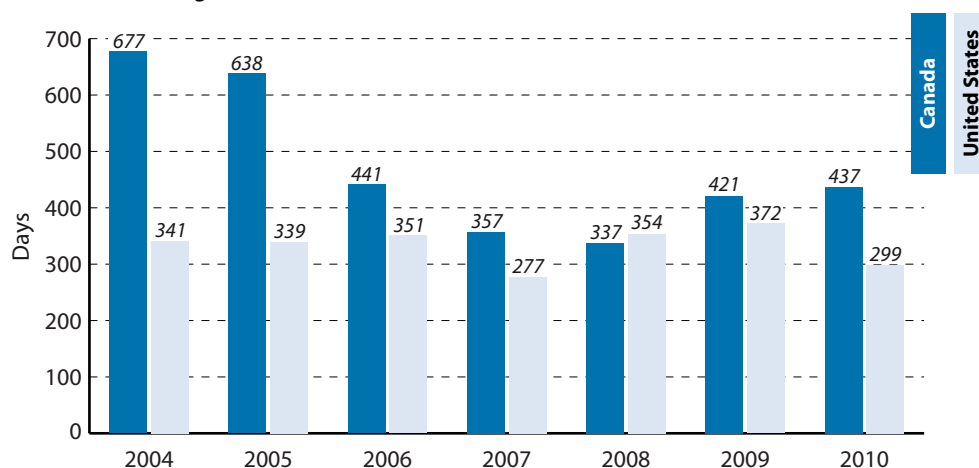
Figure 2: Non-weighted consolidated average delay (days) for regulatory and marketing approval of new drugs, Canada and the European Union, 2006–2010



Sources: Health Canada, 2010, 2011; EMA, 2007, 2008, 2009, 2010, 2011; calculations by authors.

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 status (priority or non-priority). However, the US data do not allow weighting by drug type (biologic or pharmaceutical). Figure 3 shows the differences between median approval times (weighted average medians) in Canada and the United States for new drug applications between 2004 and 2010. 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.

Figure 3: Weighted average median delay (days) for regulatory and marketing approval of new drugs, Canada and the United States, 2004–2010



Sources: Health Canada, 2008, 2009, 2011a; US FDA, 2009a, 2010, 2011; calculations by authors.

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. In contrast, in 2008, Health Canada took less time than the FDA to grant market approval for new drugs. As figure 3 shows, Health Canada took 337 days to approve new drugs in 2008 while the FDA took 354 days. However, the most recent data indicate that Health Canada took longer to approve new drugs in both 2009 and 2010. In 2009, Health Canada's median approval time was 421 days compared to the FDA's median approval time of 372. Similarly, Health Canada took 437 days to approve new medicines in 2010 while the FDA took 299 days. Thus, although Health Canada's median approval time was slightly shorter than the FDA's in 2008, it took longer than the FDA to grant market authorization for new drugs in six of the last seven years observed in this study.

Delays caused by provincial governments

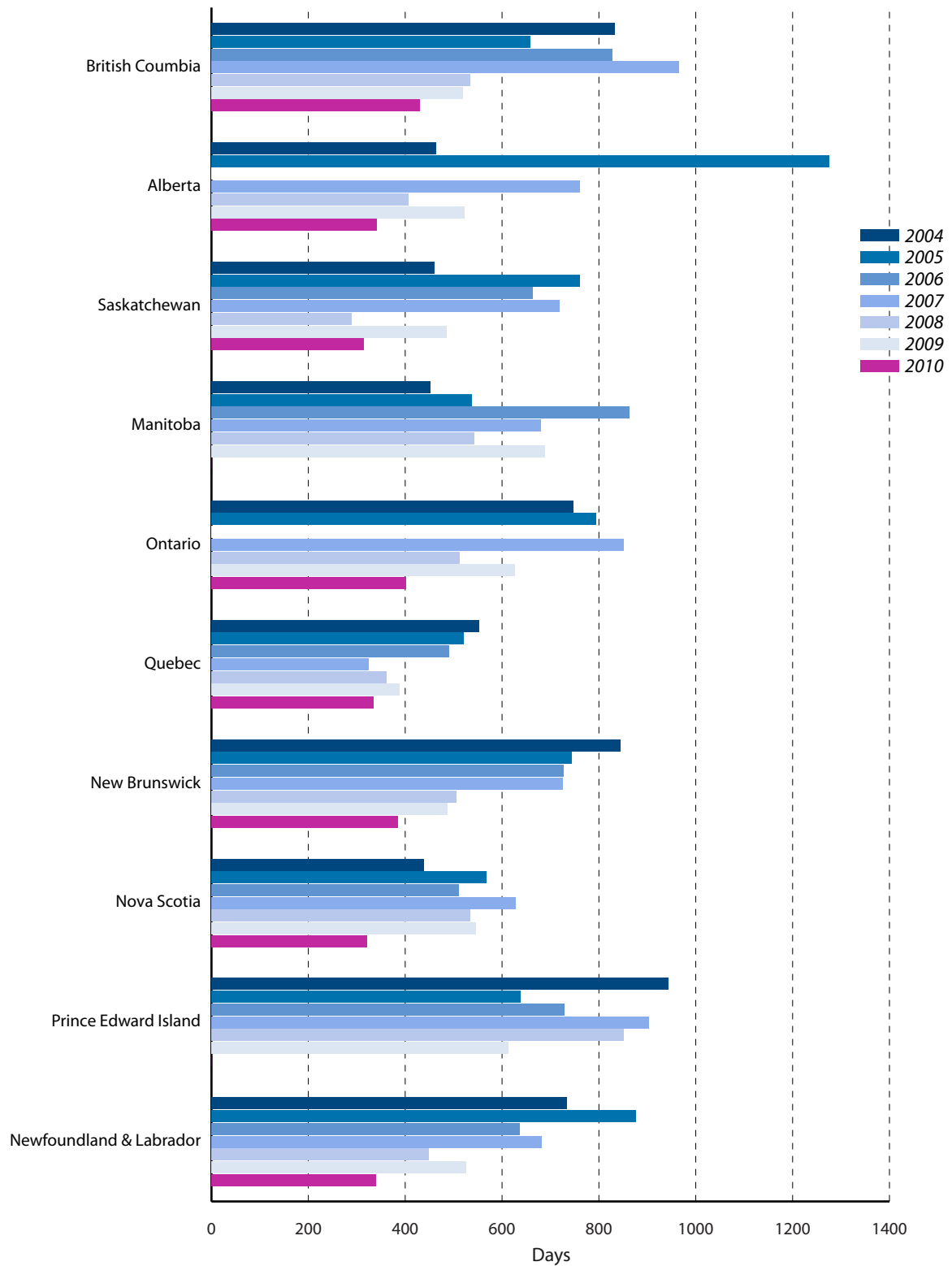
The second segment of the wait for new medicines that is affected by government policies and institutional performance is the time spent by the federal, provincial, and territorial (FPT) governments in deciding whether to reimburse a new drug under their respective publicly funded drug-insurance programs. Each jurisdiction determines eligibility for reimbursement 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, 2004–2010

Federal, provincial, and territorial authorities have three options when determining 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 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 but 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 647 days; the average for new drugs that received market approval in 2005 was 737 days; the average for new drugs approved in 2006 was 682 days; the average for new medicines approved in 2007 was 724 days; the average for new drugs approved in 2008 was 499 days; the average for new drugs approved in 2009 was 541 days; and the average for new drugs approved in 2010 was 359 days (figure 4).

Figure 4: Weighted average time (days) between Health Canada's regulatory and marketing approval and provincial approval for public reimbursement for new medicines, by province, 2004–2010



Sources: Health Canada, 2011b; Brogan Inc., 2012; 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 5 shows the consolidated average wait for access to new medicines, measured in days, for the years 2004, 2005, 2006, 2007, 2008, 2009, and 2010. This wait time is measured in days and is presented as a weighted average for pharmaceutical and biological drugs, including all new drugs classified by Health Canada as new drug submissions (NDS) and excluding supplemental new drug submissions (SNDS).

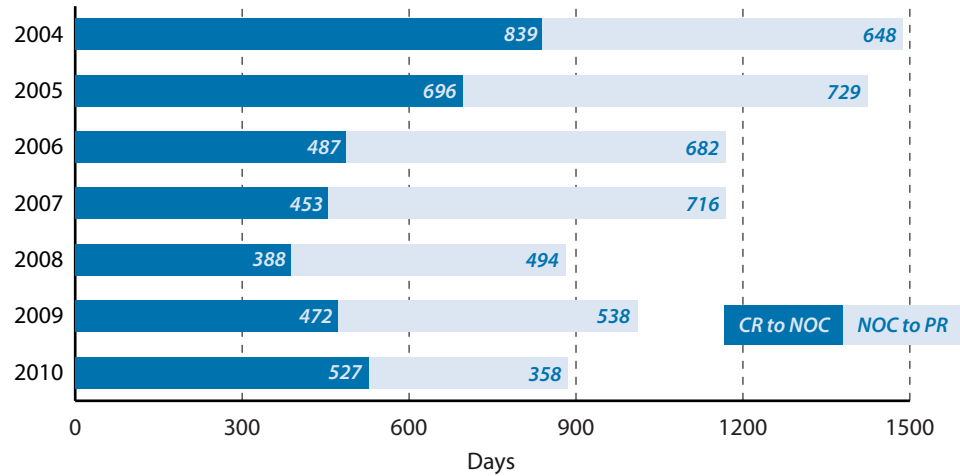
National delay

Reading left to right in figure 5, 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, but slightly longer in 2009 and 2010. 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, 388 days in 2008, 472 days in 2009, and 527 days in 2010.

Provincial delay

The second segment of the bar in figure 5 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 fluctuated since 2004. Patients relying on public drug programs waited approximately 648 days on average for drugs that were approved by Health Canada in 2004, before they were given approval for public reimbursement. However, for new drugs approved by Health Canada in 2005, the average wait for reimbursement approval increased to 729 days. The average wait for provincial reimbursement fell to 682 days for new drugs approved in 2006, but increased to 716 days for new drugs approved in 2007. The average wait for provincial reimbursement of new drugs certified by Health Canada in 2008 fell to 494 days; but increased to 538 days for drugs certified in 2009. The most recent data indicate that the average wait for public reimbursement of new drugs certified by Health Canada in 2010 decreased to 358 days.

Figure 5: Weighted average total delay (days) for access to publicly insured new medicines in Canada, by wait segment, averaged across all provinces, 2004–2010



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 in 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, 2011a, 2011b; Brogan Inc., 2012; calculations by authors.

Total delay

Adding together the wait times from the first and second segments, the total average wait for patients dependent on public drug programs for insured access to new medicines was 885 days (approximately 2.4 years) for new drugs approved by Health Canada in 2010. The total average wait has significantly decreased from an average of 1,487 days (approximately 4.1 years) in 2004. While this is 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.

Denials of reimbursement by provincial governments

It is important to examine not only provincial delays in determining eligibility for reimbursement but outright denials of public reimbursement as well. Although most provinces have reduced the number of days that patients must wait to have new drugs declared eligible for public reimbursement, 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. The rates for approving reimbursement are estimated by calculating the number of full or partial reimbursement approvals recorded in each province (as of January 1, 2012) as a percentage of the total number of drugs already approved as safe and effective—that is, drugs issued a NOC—by Health Canada in each year.

Our 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 January 1, 2012, 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 19.3% of new drugs certified in 2005, 31.0% of new drugs certified in 2006, 28.4% of new drugs certified in 2007, 31.6% of new drugs certified in 2008, 19.1% of new drugs certified in 2009, and 11.7% of new drugs certified in 2010 (table 2A). The coverage rate averaged across all years is less than 24%.

In contrast, our analysis shows that the majority of new drugs that are approved by Health Canada as safe and effective are eventually covered by at least one private insurer. As table 2B shows, averaged across all provinces, 97.9% of all new drugs that Health Canada approved as safe and effective in 2004 were covered by at least one private insurer as of January 1, 2012. Likewise, 90.9% of new drugs certified in 2005, 82.0% of new drugs certified in 2006, 79.5% of new drugs certified in 2007, 81.3% of new drugs certified in 2008, 82.2% of new drugs certified in 2009, and 77.3% of new drugs certified in 2010 were covered by at least one private insurer (averaged across all provinces) as of January 1, 2012. The coverage rate averaged across all years is over 84%.

Table 2A: Number of drugs approved for public reimbursement, as a percentage of NDS-class drugs approved by Health Canada (NOCs), by province, 2004–2010, as of January 1, 2012

	2004		2005		2006		2007		2008		2009		2010	
	Nº	%	Nº	%	Nº	%	Nº	%	Nº	%	Nº	%	Nº	%
BC	10	21.3	2	4.5	9	18.0	11	25.0	9	28.1	11	24.4	3	6.7
AB	8	17.0	4	9.1	12	24.0	6	13.6	10	31.3	8	17.8	5	11.1
SK	13	27.7	11	25.0	18	36.0	11	25.0	10	31.3	8	17.8	6	13.3
MB	9	19.1	5	11.4	11	22.0	9	20.5	6	18.8	2	4.4	n/a	n/a
ON	8	17.0	7	15.9	11	22.0	16	36.4	10	31.3	14	31.1	4	8.9
QC	20	42.6	14	31.8	24	48.0	22	50.0	16	50.0	18	40.0	12	26.7
NB	11	23.4	12	27.3	23	46.0	17	38.6	12	37.5	6	13.3	4	8.9
NS	9	19.1	13	29.5	16	32.0	10	22.7	9	28.1	8	17.8	4	8.9
PE	9	19.1	8	18.2	13	26.0	11	25.0	8	25.0	5	11.1	n/a	n/a
NL	11	23.4	9	20.5	18	36.0	12	27.3	11	34.4	6	13.3	4	8.9
Prov. avg.		23.0		19.3		31.0		28.4		31.6		19.1		11.7
Total NDS NOCs	47		44		50		44		32		45		44	

Note: Provinces often take more than a year to decide whether 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 IMS Brogan.

Source: Health Canada 2011b; IMS Brogan, 2012; calculations by authors.

Table 2B: Number of drugs covered by at least one private insurer, as a percentage of NDS-class drugs approved by Health Canada (NOCs), averaged across all provinces, as of January 1, 2012

	2004		2005		2006		2007		2008		2009		2010	
	Nº	%	Nº	%	Nº	%	Nº	%	Nº	%	Nº	%	Nº	%
	46	97.9	40	90.9	41	82.0	35	79.5	26	81.3	37	82.2	34	77.3
Total NDS NOCs	47		44		50		44		32		45		44	

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

Source: Health Canada 2011; IMS Brogan, 2012; calculations by authors.

Comparing coverage delays in public and private drug insurance

This study compares the delays in reimbursing patients for purchases of new drugs under private drug-insurance plans with the delays 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 approval for reimbursement for new drugs. Only those drugs that received a Notice of Compliance from Health Canada in 2006, 2007, and 2008 are used for comparison as they will provide a comprehensive dataset.

There are a number of new drugs that were approved by Health Canada in 2006, 2007, and 2008 that have been claimed for reimbursement by private insurers but have yet to be approved for reimbursement by public drug plans. Tables 3A to 5B include all new drugs (NDS) in IMS Brogan's database that received market approval by Health Canada in 2006, 2007, and 2008. Pharmaceutical and biologic drugs are separated by drug type and are listed in alphabetic order. Tables 3A to 5B 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 are aggregated across all provincial public drug plans and private drug insurers, and are current up to January 1, 2012.

Drugs approved for public reimbursement in 2006

Only 22 (62.9%) of the 35 new pharmaceutical drugs that received market approval by Health Canada in 2006 have been approved for public reimbursement by at least one of the provincial drug plans as of January 1, 2012 (table 3A). In contrast, the data indicate that 31 (88.6%) of the new pharmaceutical drugs approved by Health Canada in 2006 have been claimed for reimbursement by at least one private insurer. Likewise, public drug programs (at least one) have approved only 5 (33.3%) of the 15 new biologic drugs that were issued a Notice of Compliance from Health Canada in 2006 as of January 1, 2012; compared to 9 (60.0%) that have been claimed by at least one private insurer (table 3B).

Table 3A: Pharmaceutical drugs, 2006—first listing on a public drug insurance plan (aggregated across all provincial drug plans), first claim with a private drug insurance plan (aggregated across insurance companies and provinces), and the difference in days between first listing on a public drug plan and first claim with a private insurance plan, for all new pharmaceutical drugs that received a Notice of Compliance from Health Canada in 2006, as of January 1, 2012

NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2006	Delay (in days) between NOC and first listing on public drug plans (aggregated across all provinces)	Delay (in days) between NOC and first claim on private drug plans	Difference in days
ABRAXANE	Not listed	363	N/A
ACTONEL PLUS CALCIUM	266	36	230
ACTONEL SACHET KIT	Not listed	66	N/A
ACZONE	Not listed	Not claimed	N/A
ALTACE HCT	328	7	321
ALVESCO	148	22	126
ARESTIN MICROSPHERES	Not listed	1043	N/A
AZILECT	174	41	133
BARACLUDE	236	110	126
BIPHENTIN	413	148	265
CHILDRENS IBUPROFEN	Not listed	524	N/A
DUOTRAV	198	54	144
EXJADE	256	37	219
FOSAVANCE	333	47	286
FOSRENOL	839	120	719
IBUPROFEN LIQUID FILLED CAPSULES	Not listed	149	N/A
NEXAVAR	560	25	535
NORLEVO	1062	1117	-55
PMS-URSODIOL	Not listed	558	N/A
PMS-URSODIOL C	136	159	-23
PREXIGE	Not listed	22	N/A
PREZISTA	194	34	160
REVATIO	257	46	211
SEBIVO	Not listed	133	N/A
SOMATULINE AUTOGEL	411	312	99
SONOVUE	Not listed	Not claimed	N/A
SUTENT	201	56	145
TESTIM	504	385	119
TOBRAMYCIN FOR INJECTION	1392	886	506
TROSEC	264	247	17
TRUVADA	268	102	166
VANTAS	Not listed	Not claimed	N/A
VESICARE	352	170	182
VOLUVEN	Not listed	Not claimed	N/A
ZYTRAM XL	Not listed	85	N/A

Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Table 3B: Biological drugs, 2006—first listing on a public drug insurance plan (aggregated across all provincial drug plans), first claim with a private drug insurance plan (aggregated across insurance companies and provinces), and the difference in days between first listing on a public drug plan and first claim with a private insurance plan, for all new biological drugs that received a Notice of Compliance from Health Canada in 2006, as of January 1, 2012

NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2006	Delay (in days) between NOC and first listing on public drug plans (aggregated across all provinces)	Delay (in days) between NOC and first claim on private drug plans	Difference in days
ADVATE	Not listed	Not claimed	N/A
APIDRA	1027	1017	10
GAMMAGARD	Not listed	639	N/A
GARDASIL	Not listed	36	N/A
IGIVNEX	Not listed	Not claimed	N/A
MENACTRA	Not listed	177	N/A
MENOPUR	1490	32	1458
MYOZYME	543	1078	-535
ORENCIA	358	49	309
QUIXIL	Not listed	Not claimed	N/A
ROTATEQ	Not listed	64	N/A
SANDOGLOBULIN NF	Not listed	Not claimed	N/A
TYSABRI	734	116	618
VIVAGLOBIN	Not listed	Not claimed	N/A
WILATE	Not listed	Not claimed	N/A

Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Drugs approved for public reimbursement in 2007

Of the 35 new pharmaceutical drugs that received market approval by Health Canada in 2007, 24 (68.6%) have been approved for public reimbursement by at least one of the provincial drug plans as of January 1, 2012; compared to 30 (85.7%) that have been claimed for reimbursement by at least one private insurer (table 4A). Similarly, public drug programs (at least one) have approved 4 (44.4%) of the 9 new biologic drugs that were issued a Notice of Compliance from Health Canada in 2005 as of January 1, 2012; compared to 5 (55.6%) that have been claimed by at least one private insurer (table 4B).

Table 4A: Pharmaceutical drugs, 2007—first listing on a public drug insurance plan (aggregated across all provincial drug plans), first claim with a private drug insurance plan (aggregated across insurance companies and provinces), and the difference in days between first listing on a public drug plan and first claim with a private insurance plan, for all new pharmaceutical drugs that received a Notice of Compliance from Health Canada in 2007, as of January 1, 2012

NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2007	Delay (in days) between NOC and first listing on public drug plans (aggregated across all provinces)	Delay (in days) between NOC and first claim on private drug plans	Difference in days
ATRIANCE	Not listed	1011	N/A
ATRIPLA	231	15	216
AVAMYS	538	77	461
BICILLIN L-A	597	336	261
CAMPRAL	444	164	280
CELSENTRI	527	66	461
CHAMPIX	250	82	168
CHILDRENS MOTRIN COLD	Not listed	Not claimed	N/A
CO CITALOPRAM	Not listed	Not claimed	N/A
CUBICIN	1478	374	1104
CYMBALTA	214	-49	263
DERMOTIC OIL EAR DROPS	Not listed	112	N/A
DUODOPA	Not listed	Not claimed	N/A
ELOXATIN	Not listed	95	N/A
EMEND	343	59	284
ERAXIS	Not listed	991	N/A
EXELON PATCH 5	186	54	132
INVEGA	692	44	648
ISENTRESS	146	9	137
JANUVIA	292	20	272
MEZAVANT	203	143	60
MIRANOVA	Not listed	Not claimed	N/A
MYCAMINE	255	590	-335
OMNARIS	660	126	534
PMS-PAROXETINE	228	55	173
RALIVIA	Not listed	68	N/A
RASILEZ	322	21	301
SEASONALE	543	260	283
SEROQUEL XR	249	32	217
SPRYCEL	128	32	96
SUBOXONE	381	25	356
THELIN	247	77	170
TORISEL	Not listed	Not claimed	N/A
XOLEGEL	Not listed	695	N/A
ZELDOX	280	154	126

Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Table 4B: Biological drugs, 2007—first listing on a public drug insurance plan (aggregated across all provincial drug plans), first claim with a private drug insurance plan (aggregated across insurance companies and provinces), and the difference in days between first listing on a public drug plan and first claim with a private insurance plan, for all new biological drugs that received a Notice of Compliance from Health Canada in 2007, as of January 1, 2012

NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2007	Delay (in days) between NOC and first listing on public drug plans (aggregated across all provinces)	Delay (in days) between NOC and first claim on private drug plans	Difference in days
CNJ-016	Not listed	Not claimed	N/A
ELAPRASE	714	345	369
EXUBERA	Not listed	Not claimed	N/A
HEPAGAM B	Not listed	241	N/A
LUCENTIS	128	63	65
NATRECOR	Not listed	Not claimed	N/A
OCTAPLEX	Not listed	Not claimed	N/A
PRIORIX-TETRA	1251	378	873
ROTARIX	1180	-62	1242

Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Drugs approved for public reimbursement in 2008

Only 15 (60.0%) of the 25 new pharmaceutical drugs that received market approval by Health Canada in 2008 were approved for public reimbursement by at least one of the provincial drug plans as of January 1, 2012; compared to 22 (88.0%) that have been claimed by at least one private insurer (table 5A). Likewise, as of January 1, 2012, public drug programs (at least one) have approved only 1 (14.3%) of the 7 new biologic drugs that were issued a Notice of Compliance from Health Canada in 2008, compared to 5 (71.4%) of the 7 that have been claimed by at least one private insurer (table 5B).

Table 5A: Pharmaceutical drugs, 2008—first listing on a public drug insurance plan (aggregated across all provincial drug plans), first claim with a private drug insurance plan (aggregated across insurance companies and provinces), and the difference in days between first listing on a public drug plan and first claim with a private insurance plan, for all new pharmaceutical drugs that received a Notice of Compliance from Health Canada in 2008, as of January 1, 2012

NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2008	Delay (in days) between NOC and first listing on public drug plans (aggregated across all provinces)	Delay (in days) between NOC and first claim on private drug plans	Difference in days
ADALAT XL PLUS	206	35	171
AERIUS DUAL ACTION 12 HOUR	Not listed	18	N/A
ALREX	Not listed	92	N/A
ALTARGO	Not listed	Not claimed	N/A
CATENA	Not listed	69	N/A
CLINDESSE	339	14	325
COVERSYL PLUS	Not listed	Not claimed	N/A
GEN-CLOZAPINE	97	182	-85
INTELENCE	188	27	161
NEVANAC	Not listed	144	N/A
OLMETEC	216	-39	255
OLMETEC PLUS	192	112	80
PRADAX	1044	100	944
RELISTOR	Not listed	77	N/A
RETISERT	Not listed	120	N/A
REVLIMID	368	14	354
SIMVASA	Not listed	489	N/A
STALEVO	226	192	34
TASIGNA	878	98	780
VOLIBRIS	195	299	-104
WINDEX ANTIBACTERIAL DISINFECTANT	Not listed	Not claimed	N/A
XAMIOL	237	82	155
XARELTO	198	23	175
YAZ	190	21	169
ZEFTERA	340	353	-13

Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Table 5B: Biological drugs, 2008—first listing on a public drug insurance plan (aggregated across all provincial drug plans), first claim with a private drug insurance plan (aggregated across insurance companies and provinces), and the difference in days between first listing on a public drug plan and first claim with a private insurance plan, for all new biological drugs that received a Notice of Compliance from Health Canada in 2008, as of January 1, 2012

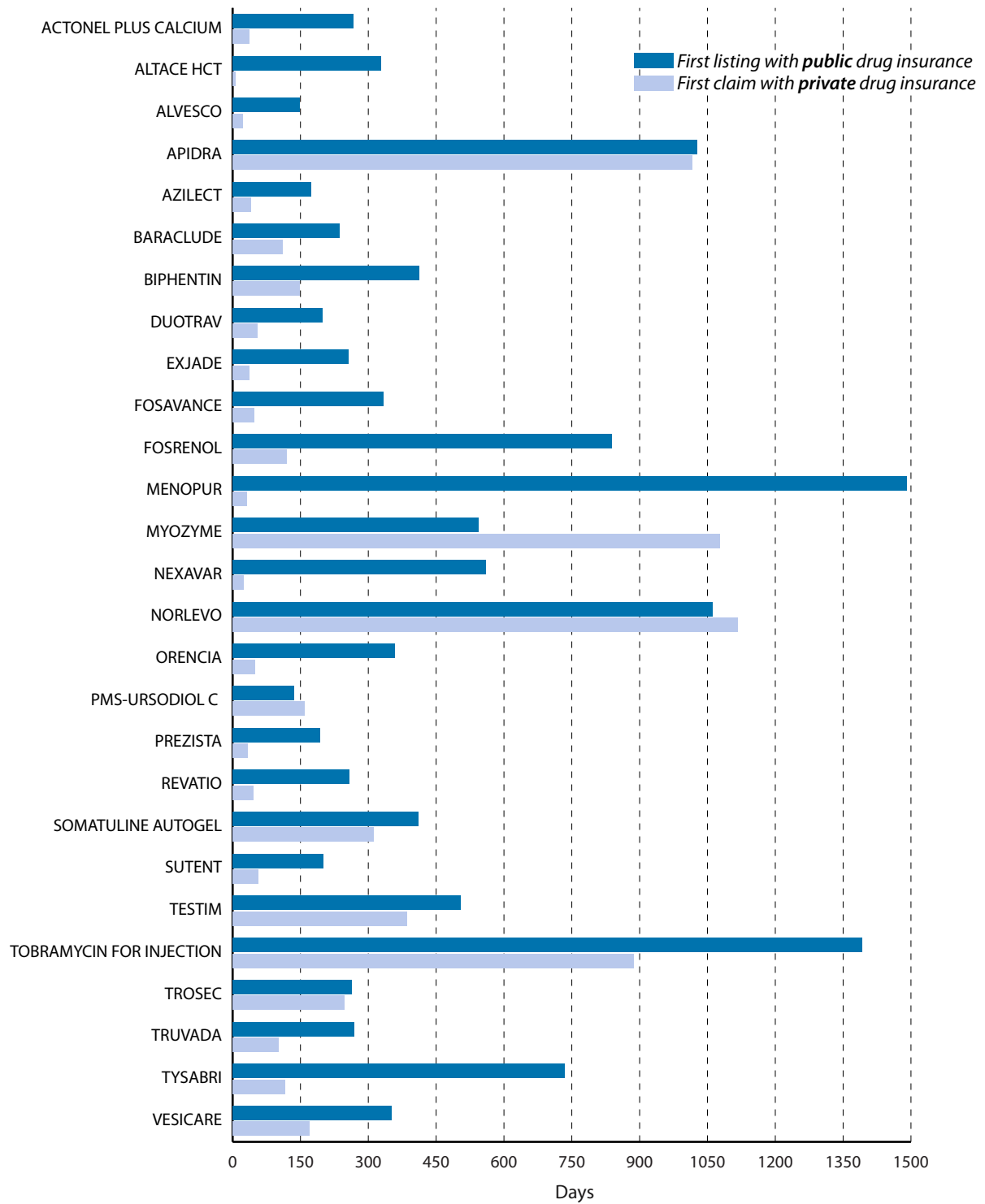
NDSs that were issued a Notice of Compliance (NOC) by Health Canada in 2008	Delay (in days) between NOC and first listing on public drug plans (aggregated across all provinces)	Delay (in days) between NOC and first claim on private drug plans	Difference in days
PRIVIGEN	Not listed	Not claimed	N/A
STELARA	232	39	193
SYNFLORIX	Not listed	263	N/A
VECTIBIX	Not listed	153	N/A
ZOSTAVAX	Not listed	19	N/A
BOOSTRIX - POLIO	Not listed	175	N/A
MIRCERA	Not listed	Not claimed	N/A

Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Differences between provincial drug plans and private insurance in providing coverage

Figures 6, 7, and 8 display 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 that received a Notice of Compliance from Health Canada in 2006, 2007, and 2008 (pharmaceutical and biological) that have been approved for reimbursement by at least one public and private drug insurance plan as of January 1, 2012. In some extreme cases, such as the biological drug Menopur (figure 6), the difference in reimbursement approval between public and private drug insurance was 1,458 days (approximately 4 years). In general, the data indicate that private drug insurance (at least one insurer) covers new drugs approved by Health Canada much earlier than any provincial public drug plan (with the exception of PMS-Ursodiol C, Norlevo, and Myozyme in figure 6; Mycamine in figure 7; and GEN-Clozapine, Volibris, and Zeftera in figure 8).

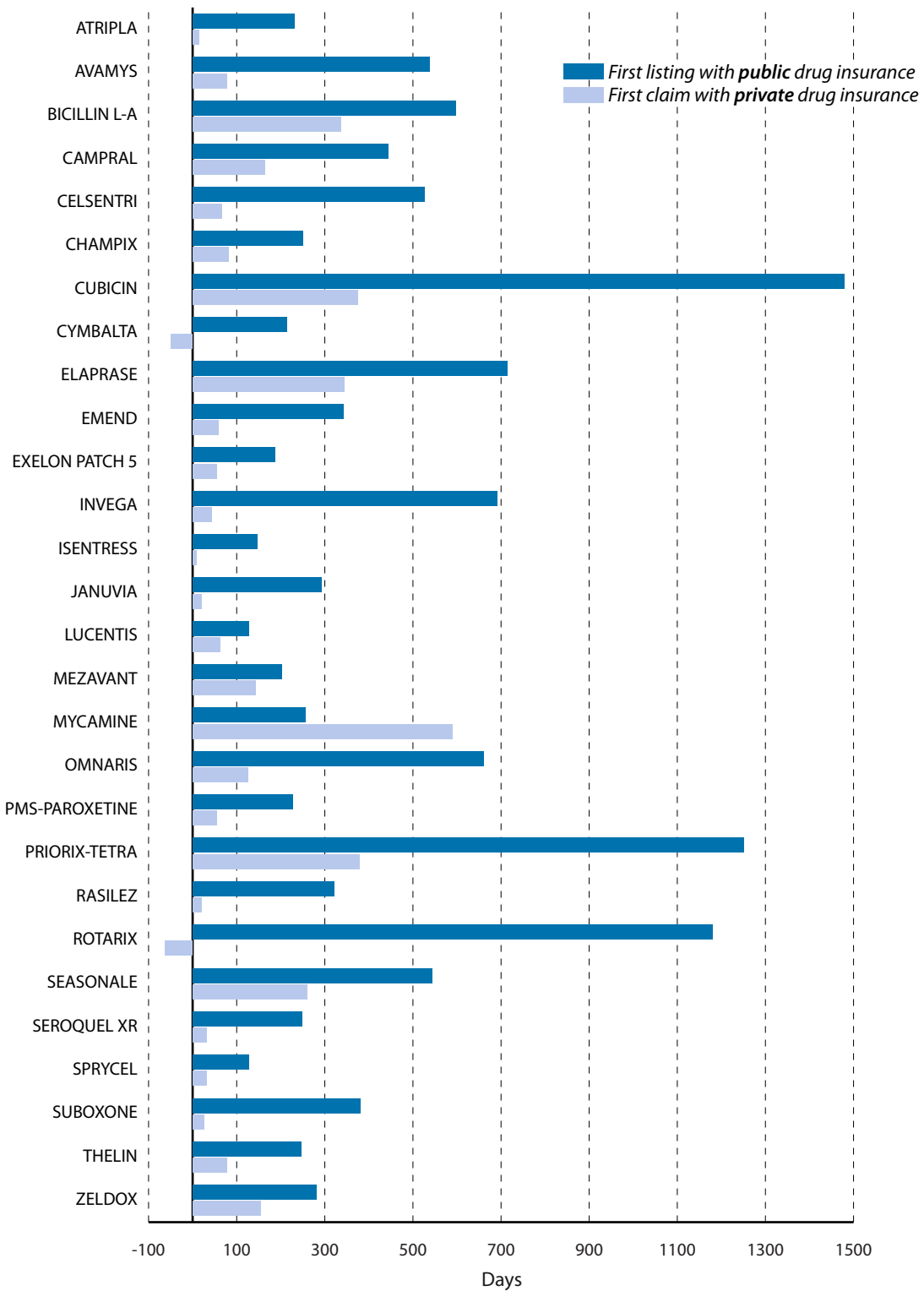
Figure 6: Difference (in days), 2006, between the first listing with a public insurance plan and the first claim with a private insurance plan for new drugs that received a Notice of Compliance (NOC) from Health Canada, aggregated across all provinces and drug plans



Note: includes only drugs approved for reimbursement by at least one public and private insurer as of January 1, 2012.

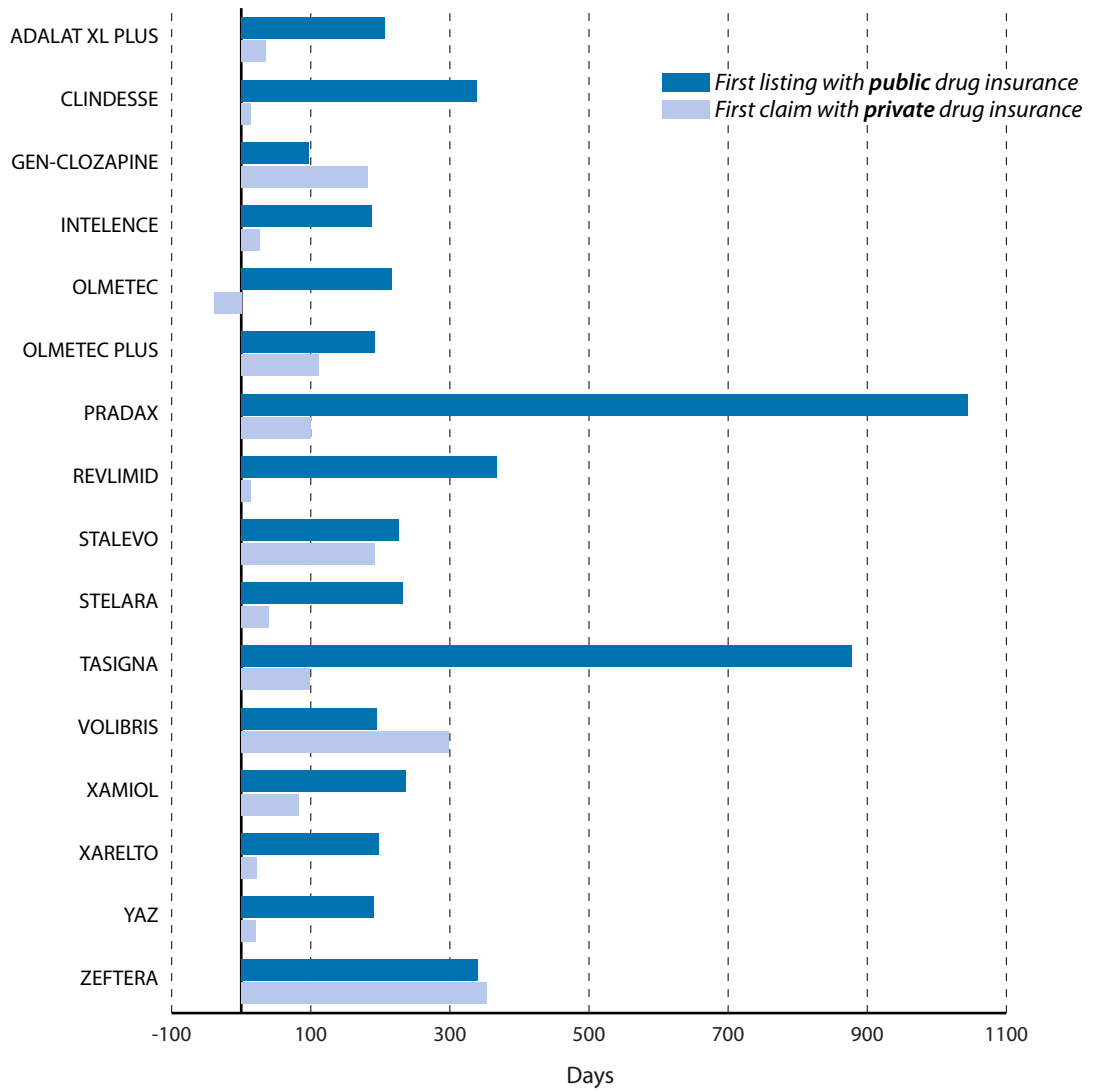
Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Figure 7: Difference (in days), 2007, 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 (NOC) from Health Canada, aggregated across all provinces and drug plans



Note: includes only drugs approved for reimbursement by at least one public and private insurer as of January 1, 2012.
 Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Figure 8: Difference (in days), 2008, 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 (NOC) from Health Canada, aggregated across all provinces and drug plans



Note: includes only drugs approved for reimbursement by at least one public and private insurer as of January 1, 2012.

Sources: Health Canada, 2011b; IMS Brogan, 2012; calculations by authors.

Policy options

Mutual recognition of drug approvals in cooperation with other jurisdictions

International safety standards are similar, so the federal government could speed up access to new drugs by harmonizing with European and American regulatory processes through mutual recognition of drug-approval decisions. In an effort to reduce the time taken to review new medications, Canada's Smart Regulation strategy proposed a form of mutual recognition to reduce persistent delays in the drug-approval process (EACSR, 2004). Similar thinking was reflected in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The intention of the international conference on harmonization was to establish international technical requirements and guidelines for increasing the efficiency of the drug development by reducing unnecessary duplications (thus reducing costs), while also accelerating market approval so that new drug products were made available to patients as soon as possible (ICH, 2009).

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 drug programs. Provincial governments could improve access for patients and save money by replacing existing public drug programs with a means-tested subsidy for people with low incomes to aid the purchase of private drug insurance. Quebec has already taken initial steps towards this policy. Economic theory and evidence, and actual Canadian experience, suggest that such a policy alternative would achieve better access to prescription drug coverage and would contain costs, while reducing government-imposed restrictions on consumer choice.

Appendix

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. 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 issuing 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, 2004, 2005a, 2005b, 2006a, 2006b, 2006c, 2007, 2008, 2009, 2010, and 2011](#)).

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 ([EMA, 2005, 2007, 2008, 2009, 2010, 2011](#)). The FDA and the EMA publish separate data for the time spent by 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 from the FDA and the EMA.

Prior to 2008, annual reports from Health Canada’s Therapeutic Products Directorate and Biologics and Genetic Therapies Directorate published both average and median figures for drug-approval wait times. However, in 2008 and subsequent annual reports, Health Canada only published 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 EMA 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 EMA 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 (priority or non-priority review). The Canadian figures published by Health Canada are separated according to submission status (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 data from Health Canada is weighted by drug type (biological and pharmaceutical drugs) and by submission status (priority and non-priority). As drug types are already consolidated by the FDA, the US data is only weighted by submission status.

The fourth main source of data cited in this paper is IMS Brogan ([IMS Brogan, 2012](#)). IMS Brogan 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. IMS Brogan'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 (EMA) and the US Food and Drug Administration (FDA) but under different terminology. The Canadian and international classifications are briefly described in [tables 6, 7, and 8](#).

Table 6: 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 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 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, rather than the 300 days assigned to 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 7: 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 the FDA's requirements for marketing approval, the sponsor submits to the 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 NDAs 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). The 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 the FDA's 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 biologic 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.

Source: US FDA, 1996, 2009b.

Table 8: Classifications of new applications for drug-market authorization 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 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 (c.f. 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.

References

Adams, Christopher P., and Van V. Brantner (2003). New Drug Development: Estimating Entry from Human Clinical Trials. FTC Working Paper No. 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.

Canada's Research-Based Pharmaceutical Companies (2005). *Rx&D 2005 NOC Survey: Results and Key Messages*. Canada's Research-Based Pharmaceutical Companies.

Danzon, P.M. (1993). Health Care. *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 and Therapeutics* 69, 5 (May): 297–307.

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.

DiMasi, J.A., R.W. Hansen, H.G. Grabowski, and L. Lasagna (1995). Research and Development Costs for New Drugs by Therapeutic Category: A Study of the US Pharmaceutical Industry. *PharmacoEconomics* 7, 2: 152–69.

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] (2007). *Annual Report of the European Medicines Agency 2006*. EMA. <http://www.emea.europa.eu/pdfs/general/direct/emeaar/EMA_Annual_Report_2006_full.pdf>.

European Medicines Agency [EMA] (2008). *Annual Report of the European Medicines Agency 2007*. EMA. <<http://www.emea.europa.eu/pdfs/general/direct/emeaar/AnnualReport2007.pdf>>.

European Medicines Agency [EMA] (2009). *Annual Report of the European Medicines Agency 2008*. EMA. <<http://www.ema.europa.eu/pdfs/general/direct/emeaar/AnnualReport2008.pdf>>.

European Medicines Agency [EMA] (2010). *Annual Report of the European Medicines Agency 2009*. EMA. <http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2010/05/WC500090712.pdf>.

European Medicines Agency [EMA] (2011). *Annual Report of the European Medicines Agency 2010*. EMA. <http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2011/06/WC500108076.pdf>.

External Advisory Committee on Smart Regulation [EACSR] (2004). *Smart Regulation: A Regulatory Strategy for Canada*. Report to the Government of Canada (September). <<http://www.regulatoryreform.com/pdfs/Canada%20Smart%20Regulation%20Report%20Sept%202004.pdf>>.

Food and Drugs Act, R.S.C. 1985, c. F-27. <<http://laws.justice.gc.ca/en/F-27/index.html>>. Last updated March 1, 2010.

Graham, John R. (2005a). *A Lethal Guardian: The Canadian Government's Ban on Prescription Drugs*. Fraser Institute Digital Publication. 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. Fraser Institute.

Health Canada (2001). *How Drugs Are Reviewed in Canada*. Health Products and Food Branch, Therapeutic Products Directorate. <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/fs-fi/reviewfs_examenfd_e.html>.

Health Canada (2002). *Special Access Programme – Drugs*. *Drugs and Health Products*. Government of Canada.

Health Canada (2003). *Therapeutic Products Directorate (TPD) – 2003 Annual Submission Performance Report—Part I*. Government of Canada.

Health Canada (2004). *Therapeutic Products Directorate – 2004 Annual Submission Performance Report – Part I; Biologics and Genetic Therapeutics Directorate – 2004 Annual Submission Performance Report – Part II*. Government of Canada.

Health Canada (2005a). *Therapeutic Products Directorate (TPD) – 2005 Annual Submission Performance Report – Part I; Biologics and Genetic Therapeutics Directorate – 2005 Annual Submission Performance Report – Part II*. Government of Canada.

Health Canada (2005b). *Regulatory Review of Pharmaceuticals, Biologics and Medical Devices: 2005 Annual Summary of Performance*. <http://www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/performance_rendement_2005_e.html>. Last updated July 25, 2006.

Health Canada (2006a). *Access to Therapeutic Products: The Regulatory Process in Canada*. Health Canada, Health Products and Food Branch. Government of Canada.

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

Health Canada (2006c). *Priority Review of Drug Submissions*. Health Canada, Health Products and Food Branch: Therapeutic Products Directorate.

Health Canada (2007). *2006 Annual Drug Submission Performance Report: Part I Therapeutic Products Directorate (TPD); Part II Biologics and Genetic Therapies Directorate (BGTD)*. Health Canada, Health Products and Food Branch.

Health Canada (2008a). *2007 Annual Drug Submission Performance Report: Part I Therapeutic Products Directorate (TPD); Part II Biologics and Genetic Therapies Directorate (BGTD)*. Health Canada, Health Products and Food Branch.

Health Canada (2008b). Special Data Request. Detailed drug product data matching the Brogan Inc. (2007) dataset, which was used to measure provincial reimbursement delays and rates.

Health Canada (2009a). *2007 Annual Drug Submission Performance Report: Part I Therapeutic Products Directorate (TPD); Part II Biologics and Genetic Therapies Directorate (BGTD)*. Health Canada, Health Products and Food Branch.

Health Canada (2009b). Special Data Request. Detailed drug product data matching the Brogan Inc. (2008) dataset, which was used to measure provincial reimbursement delays and rates.

Health Canada (2010). *2009 Annual Drug Submission Performance Report: Part I Therapeutic Products Directorate (TPD); Part II Biologics and Genetic Therapies Directorate (BGTD)*. Health Canada, Health Products and Food Branch.

Health Canada (2011a). *2010 Annual Drug Submission Performance Report: Part I Therapeutic Products Directorate (TPD); Part II Biologics and Genetic Therapies Directorate (BGTD)*. Health Canada, Health Products and Food Branch.

Health Canada (2011b). Special Data Request. Detailed drug product data matching the IMS Brogan (2012) dataset, which was used to measure provincial reimbursement delays and rates.

IMS Brogan (2012). Special data request by authors.

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use [ICH] (2009). *History and Future of ICH*.

Ministry of Health and Long-Term Care (2011). *Ontario Drug Benefit Program*. Publicly Funded Drug Programs. Government of Ontario.

Newhouse, J.P., and Insurance Experiment Group (1993). *Free For All? Lessons from the RAND Health Insurance Experiment*. RAND. Harvard University Press.

Romanow, Roy (2002). *Building on Values: The Future of Health Care in Canada – Final Report*. Commission on the Future of Health Care in Canada. Government of Canada.

Rovere, Mark (2008). Subsidization in Saskatchewan: Drug Cost Coverage Should Be Means Tested, Not Aged-Based. *Fraser Forum* (June): 18–19.

Skinner, Brett J. (2005). *Universal Drug Benefits for Seniors: Unnecessary, Unsustainable, and Unfair*. Fraser Institute.

Skinner, Brett J. (2006, June 21). Sure, It's Cheap to Make Drugs. But the Cost of Discovering and Developing Them Is Enormous. *Globe and Mail*.

Skinner, Brett J., and Mark Rovere (2008a). *Access Delayed, Access Denied 2008: Waiting for New Medicines in Canada*. Fraser Institute.

Skinner, Brett J., and Mark Rovere (2008b). *Canada's Drug Price Paradox 2008*. Fraser Institute.

Skinner, Brett J., and Mark Rovere (2009). *Access Delayed, Access Denied 2009: Waiting for New Medicines in Canada*. Fraser Institute.

Skinner, Brett J., and Mark Rovere (2010). *Access Delayed, Access Denied 2010: Waiting for New Medicines in Canada*. Fraser Institute.

Skinner, Brett J., and Mark Rovere (2011). *Access Delayed, Access Denied: Waiting for New Medicines in Canada, 2011 Report*. Fraser Institute.

Skinner, Brett J., Mark Rovere, and Courtney Glen (2007). *Access Delayed, Access Denied: Waiting for Medicines in Canada*. Fraser Institute.

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

US Food and Drug Administration [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 [FDA] (2009a). *New Drug Application (NDAs) & Biologic License Applications (BLAs)*. Center for Drug Evaluation and Research. <<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM123957.pdf>>.

US Food and Drug Administration [FDA] (2009b). *Drugs@FDA Glossary of Terms*. US Department of Health and Human Services. <<http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm>>. Last updated January 7, 2010.

US Food and Drug Administration [FDA] (2010). *2010 FDA Budget Summary. FY 2010 Congressional Justification; Narrative by Activity, Human Drugs*. <<http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/BudgetReports/2010/default.htm>>.

US Food and Drug Administration [FDA] (2010). *2010 FDA Budget Summary. FY 2010 Congressional Justification; Narrative by Activity, Human Drugs*. <<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM245582.pdf>>.

World Medical Association [WMA] (1964). *World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*.

About the authors

Mark Rovere

Mark Rovere is Associate Director of the Health Policy Research Centre at the Fraser Institute. He holds an Honours Bachelor's degree and a Master's Degree in Political Science from the University of Windsor. Since joining the Institute, Mr Rovere has contributed research and writing to numerous studies on a range of health and pharmaceutical policy issues, including Canadian pharmaceutical pricing, access to new medicines, government drug expenditures, Canadian and American prescription drug spending, and the sustainability of public health care in Canada. His recent commentaries have appeared in such newspapers as the *National Post*, *Calgary Herald*, *Montreal Gazette*, *Vancouver Sun*, *Windsor Star*, and *Toronto Sun*. He also regularly appears on radio shows across the country to discuss the Institute's health policy research, and has appeared on a number of television news programs including *CBC News Hour*, *CTV News*, *SUN TV's Daily Brief*, and *CPAC's Prime Time Politics*. Mr Rovere has also written regularly for the *Fraser Forum* on health and pharmaceutical policy. He is currently a Ph.D. student in Health Services Research at the Institute of Health Policy, Management, and Evaluation at the University of Toronto.

Brett J. Skinner

Dr. Brett J. Skinner was the Fraser Institute's Director of Health Policy Research (February 2004 to February 2012) and was also the Institute's President and CEO (January 2010 to February 2012). Dr. Skinner has a B.A. from the University of Windsor, an M.A. through joint studies at the University of Windsor and Wayne State University (Detroit), and a Ph.D. from the University of Western Ontario (London), where he has lectured in both the Faculty of Health Sciences and the Department of Political Science. Dr. Skinner has been author or co-author of approximately 50 major original pieces of applied economics and public policy research. In 2003, he was a co-winner of the Atlas Economic Research Foundation's Sir Antony Fisher Memorial Award for innovative projects in public policy. Dr. Skinner's book, *Canadian Health Policy Failures: What's Wrong? Who Gets Hurt? Why Nothing Changes*, was a finalist for Atlas' 2009 Fisher book prize. His research has been published through several think-tanks including the Fraser Institute (Vancouver), the Atlantic Institute for Market Studies (Halifax), the Pacific Research Institute (San Francisco), the American Enterprise Institute (Washington, D.C.) and the Israel National Institute for Health Policy Research (Israel). His work

has also been published in several academic journals including *Economic Affairs*, *Pharmacoeconomics*, and *Alimentary Pharmacology & Therapeutics*. Dr. Skinner appears, and is cited frequently as an expert, in the Canadian, American, and global media. He has presented his research at conferences and events around the world, including testifying before the House of Commons Standing Committee on Health in Ottawa, and briefing bi-partisan Congressional policy staff at the US Capitol in Washington, D.C.

Acknowledgments

The Fraser Institute would like to thank our anonymous donors for the support that made this project possible.

Any remaining errors, omissions, or mistakes are the sole responsibility of the authors. As the authors have worked independently, the views and analysis expressed in this document are their own, and do not necessarily represent the views of the supporters, trustees, or other staff of the Fraser Institute.

Publishing information

Distribution

These publications are available from <<http://www.fraserinstitute.org>> in Portable Document Format (PDF) and can be read with Adobe Acrobat® 7 or Adobe Reader®, versions 7 or later. Adobe Reader® X, the most recent version, is available free of charge from Adobe Systems Inc. at <<http://get.adobe.com/reader/>>. Those who have trouble viewing or printing our PDF files using applications from other manufacturers (e.g., Apple's Preview) should use Reader® or Acrobat®.

Ordering publications

For information about ordering the printed publications of the Fraser Institute, please contact the publications coordinator:

- ◆ e-mail: sales@fraserinstitute.org
- ◆ telephone: 604.688.0221 ext. 580 or, toll free, 1.800.665.3558 ext. 580
- ◆ fax: 604.688.8539.

Media

For media enquiries, please contact our Communications Department:

- ◆ 604.714.4582
- ◆ e-mail: communications@fraserinstitute.org.

Copyright

Copyright © 2012 by the Fraser Institute. All rights reserved. No part of this publication may be reproduced in any manner whatsoever without written permission except in the case of brief passages quoted in critical articles and reviews.

Date of issue

April 2012

ISSN

ISSN 1918-2090 Studies in Health Policy

Citation

Rovere, Mark, and Brett J. Skinner (2012). *Access Delayed, Access Denied 2012: Waiting for New Medicines in Canada*. Fraser Institute. <<http://www.fraserinstitute.org>>.

Editing, typesetting, and design

Lindsey Thomas Martin

Cover design

Bill Ray

Images for cover

© KHZ, Fotolia (“Blood Cells”)

© Emrah Turudu, iStockphoto (“Test Tube”)

© Vasiliy Yakobchuk, iStockphoto (“Brain”)

Supporting the Fraser Institute

To learn how to support the Fraser Institute, please contact

- ◆ Development Department, Fraser Institute
Fourth Floor, 1770 Burrard Street
Vancouver, British Columbia, V6J 3G7 Canada
- ◆ telephone, toll-free: 1.800.665.3558 ext. 586
- ◆ e-mail: development@fraserinstitute.org

Lifetime patrons

For their long-standing and valuable support contributing to the success of the Fraser Institute, the following people have been recognized and inducted as Lifetime Patrons of the Fraser Institute.

Sonja Bata	Serge Darkazanli	Fred Mannix
Charles Barlow	John Dobson	Con Riley
Ev Berg	Raymond Heung	Catherine Windels
Art Grunder	Bill Korol	
Jim Chaplin	Bill Mackness	

Purpose, funding, & independence

The Fraser Institute provides a useful public service. We report objective information about the economic and social effects of current public policies, and we offer evidence-based research and education about policy options that can improve the quality of life.

The Institute is a non-profit organization. Our activities are funded by charitable donations, unrestricted grants, ticket sales, and sponsorships from events, the licensing of products for public distribution, and the sale of publications.

All research is subject to rigorous review by external experts, and is conducted and published separately from the Institute's Board of Trustees and its donors.

The opinions expressed by the authors are those of the individuals themselves, and do not necessarily reflect those of the Institute, its Board of Trustees, its donors and supporters, or its staff. This publication in no way implies that the Fraser Institute, its trustees, or staff are in favour of, or oppose the passage of, any bill; or that they support or oppose any particular political party or candidate.

As a healthy part of public discussion among fellow citizens who desire to improve the lives of people through better public policy, the Institute welcomes evidence-focused scrutiny of the research we publish, including verification of data sources, replication of analytical methods, and intelligent debate about the practical effects of policy recommendations.

About the Fraser Institute

Our vision is a free and prosperous world where individuals benefit from greater choice, competitive markets, and personal responsibility. Our mission is to measure, study, and communicate the impact of competitive markets and government interventions on the welfare of individuals.

Founded in 1974, we are an independent Canadian research and educational organization with locations throughout North America and international partners in over 85 countries. Our work is financed by tax-deductible contributions from thousands of individuals, organizations, and foundations. In order to protect its independence, the Institute does not accept grants from government or contracts for research.

Nous envisageons un monde libre et prospère, où chaque personne bénéficie d'un plus grand choix, de marchés concurrentiels et de responsabilités individuelles. Notre mission consiste à mesurer, à étudier et à communiquer l'effet des marchés concurrentiels et des interventions gouvernementales sur le bien-être des individus.

Peer review—validating the accuracy of our research

The Fraser Institute maintains a rigorous peer review process for its research. New research, major research projects, and substantively modified research conducted by the Fraser Institute are reviewed by a minimum of one internal expert and two external experts. Reviewers are expected to have a recognized expertise in the topic area being addressed. Whenever possible, external review is a blind process.

Commentaries and conference papers are reviewed by internal experts. Updates to previously reviewed research or new editions of previously reviewed research are not reviewed unless the update includes substantive or material changes in the methodology.

The review process is overseen by the directors of the Institute's research departments who are responsible for ensuring all research published by the Institute passes through the appropriate peer review. If a dispute about the recommendations of the reviewers should arise during the Institute's peer review process, the Institute has an Editorial Advisory Board, a panel of scholars from Canada, the United States, and Europe to whom it can turn for help in resolving the dispute.

Editorial Advisory Board

Members

Prof. Armen Alchian	Prof. Jack L. Granatstein
Prof. Terry L. Anderson	Prof. Herbert G. Grubel
Prof. Robert Barro	Prof. James Gwartney
Prof. Michael Bliss	Prof. Ronald W. Jones
Prof. James M. Buchanan [†]	Dr. Jerry Jordan
Prof. Jean-Pierre Centi	Prof. Ross McKittrick
Prof. John Chant	Prof. Michael Parkin
Prof. Bev Dahlby	Prof. Friedrich Schneider
Prof. Erwin Diewert	Prof. Lawrence B. Smith
Prof. Stephen Easton	Mr. Vito Tanzi
Prof. J.C. Herbert Emery	

Past members

Prof. Friedrich A. Hayek ^{*†}	Prof. George Stigler ^{*†}
Prof. H.G. Johnson [*]	Sir Alan Walters [*]
Prof. F.G. Pennance [*]	Prof. Edwin G. West [*]

* deceased; † Nobel Laureate