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Health Products and Food Branch

Regulatory Review of Pharmaceuticals, Biologics and Medical Devices

2005 Annual Summary of Performance

Canada

Health Products and Food Branch

Regulatory Review of Pharmaceuticals, Biologics and Medical Devices

2005 Annual Summary of Performance

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Executive Summary

All drugs and medical devices sold in Canada must be approved by Health Canada. In 2003, Health Canada launched the Therapeutics Access Strategy, a five-year, $190 million initiative with a vision to improve timely access for Canadians to safe, effective and affordable drugs and other therapeutic products.

These investments have supported: streamlining the pre-market review process so that submissions are being managed as projects; additional scientific review capacity; and new tools to enhance infrastructure in support of more efficient and transparent decision-making.

Significant progress has been made in eliminating the review backlog and towards issuing review decisions within performance targets. As of December 31, 2005, the backlog of submissions for new pharmaceutical drugs was at a record low, with just one percent of the total workload in backlog. Sixty-six percent of regulatory decisions were issued on time for new pharmaceutical drugs in 2005, compared with 13% in 2003[1]. Consistent with internationally comparable performance targets, Health Canada expects to meet its goal of issuing 90% of decisions on time for submissions for new pharmaceutical drugs in 2006.

There was a sharp jump in the number of interim decisions issued for submissions for new pharmaceutical drugs in 2005, growing from 93 to 145. Such decisions are applied to submissions requiring additional information which the manufacturer is expected to provide within a specified period of time. The next area of focus will be to establish processes, guidance, and work collaboratively with manufacturers to improve the quality of submissions received at the outset of the review process.

Compared with the year 2003, median market authorization times have improved for new pharmaceutical drugs, dropping by 33% and 29% respectively, for Brand Name Priority and Standard drugs[2]. Median approval times for Generic Standard drugs dropped by 26% since 2003, with the number of approvals rising from 57 to 77.

Steady progress continues for biologics. As of December 31, 2005, 55% of the backlog had been eliminated since the baseline date of March 31, 2003, with 16% of review decisions issued on time. By the end of the year, the number of submissions in backlog for new biologic drugs reached a low not observed in five years (at 31 compared with 76 in 2003). It is expected that further elimination of the backlog will enable progress in meeting the overall goal of issuing 90% of decisions on time for submissions for new biologic drugs in 2007.

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[1] In most cases throughout this report, 2003 is referenced as a baseline year (or year of comparison) since new funding was introduced in 2003 through the Therapeutics Access Strategy.

[2] Note that *median* is used instead of average to reduce the skewing of approval times by 'older' submissions that were in backlog and have since been authorized for the marketplace.

The number of decisions for Biologics grew by 89% since 2003 (from 54 to 102) with approvals growing by 87% (from 45 to 84). The number of approvals for Priority Biologics more than doubled from five to 13, with the median time to approval decreasing from 31.5 to 20 months, or by 36% since 2003. Median authorization times went up for Standard Biologics, rising from 28.8 to 38.3 months in 2005.

Eighty percent of the total backlog of medical device submissions was cleared by December 31, 2005 compared with 2004, with 70% of decisions rendered on time.

The total number of medical devices issued market authorization in 2005 was 4284, up by 32% since 2003. For Class IV devices, median days to approval declined from 132 (in 2003) to 109 days in 2005.

New performance information contained in this report highlights that in 2005 Health Canada approved 24 new medicines never before available in this country. Know as New Active Substances, the majority of these drugs are indicated for cancer treatments, but also include drugs for the treatment of HIV infection, infertility and diabetes among other disease conditions (*see Table 2-A*).

Introduction

The *2005 Annual Summary of Performance* provides an outline of Health Canada's pre-market regulatory review performance of therapeutic products intended for human use, including pharmaceuticals, biologics and medical devices[3]. This report is not intended to replace the more detailed quarterly and annual Drug Submission Performance Report[4].

HPFB is a science-based organization within Health Canada that carries out federal responsibilities for the regulation of therapeutic products and food. HPFB evaluates and monitors the safety, efficacy and quality of thousands of human and veterinary drugs, medical devices, natural health products and other therapeutic products available to Canadians. For more information, go to http://www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/index_e.html

Before a therapeutic product is authorized for sale in Canada, the manufacturer must file a submission to Health Canada's Health Products and Food Branch (HPFB) that provides substantial scientific evidence of its safety, efficacy and quality, as required by the *Food and Drugs Act and Regulations*. This evidence is reviewed by skilled scientists to determine whether the potential risks from the product are acceptable when balanced against the benefits for the product's proposed use. If the evidence of safety, efficacy and quality is satisfactory, the product is granted authorization for sale in Canada[5].

Since this report was introduced in 2004, further additions have been made to increase the scope of performance information, including two new tables in the *Access* section which highlight new therapeutic drug products approved by Health Canada in 2005 as well as a sample of drugs added to provincial and territorial drug plans.

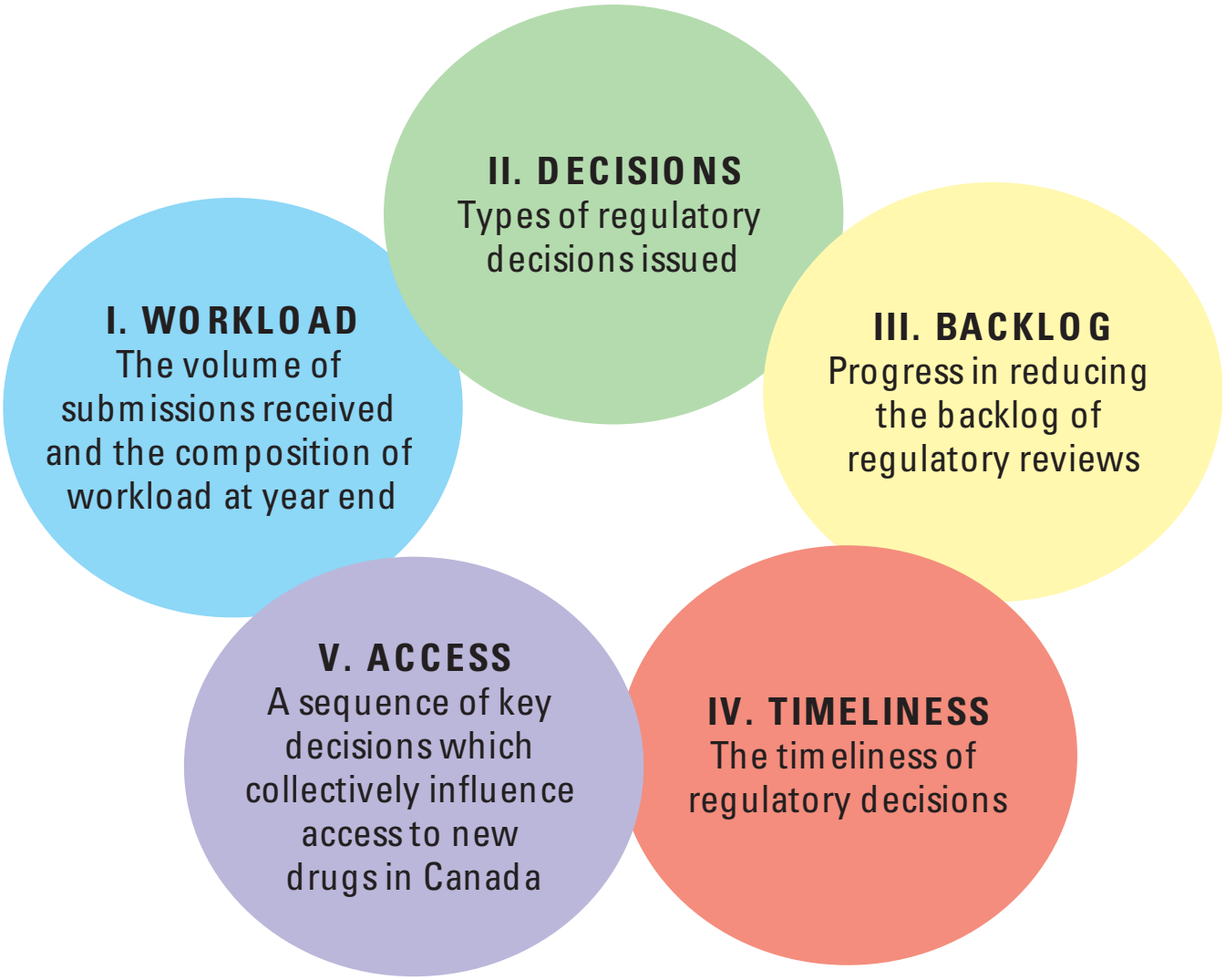
[3] Definitions of these products can be found in Annex A.

[4] The *Drug Submission Performance Report* uses different definitions and terminology to outline performance statistics and is therefore not directly comparable. For more information, refer to: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/docs/perform-rendement/index_e.html

[5] Cost-effectiveness considerations are examined by organizations outside of HPFB (refer to Section V: Access to New Drugs in Canada).

Review Performance Reporting Framework

This report is organized into five sections that summarize data on regulatory review performance for new drugs and medical devices[6] including: workload, decisions, backlog, timeliness and access to new drugs in Canada. Definitions of the terms used throughout the report are provided in *Annex A*.



[6] For consistency and to simplify terminology, medical device applications are referred to as 'submissions' throughout the report.

I. Workload

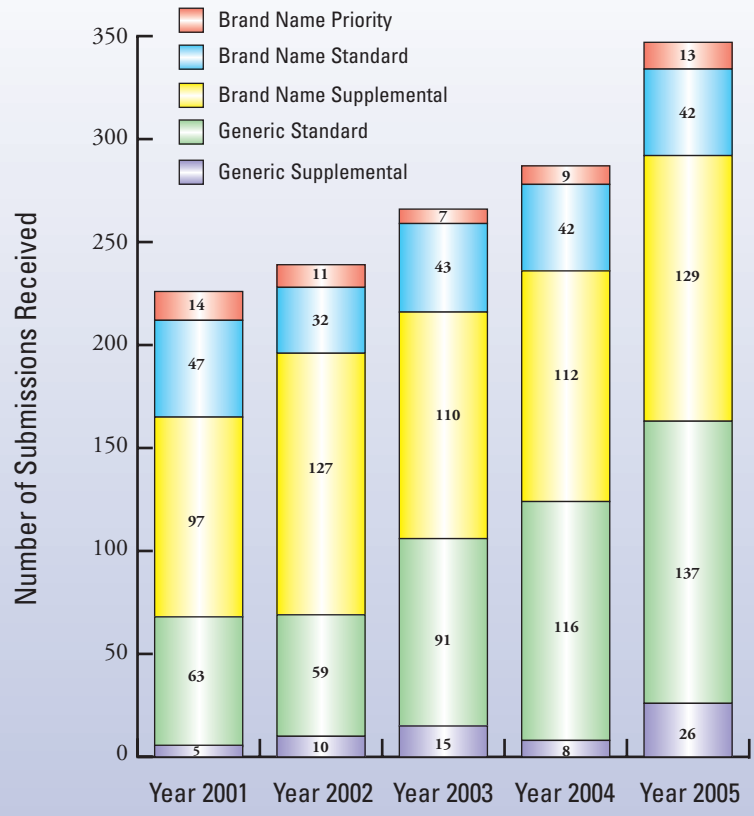
Number of Submissions Received Annually for New Drugs and Medical Devices

The year 2005 marked the highest number of submissions received for both pharmaceuticals and biologics in the past five years. The number of submissions received for new pharmaceutical drugs increased by 54% since 2001 – from 226 to 347 (*see Chart 1-A*). This can be explained by the increase in new therapeutic uses for marketed drugs as well as the expiration of patented drugs (and subsequent entry of generic drugs).

Submissions for Brand Name Priority pharmaceuticals rose from seven in 2003 to 13 in 2005. This increase is attributed to the rise in the number of submissions under consideration for Notices of Compliance with Conditions (growing from one in 2003 to five in 2005); the highest number of such submissions received to date[7].

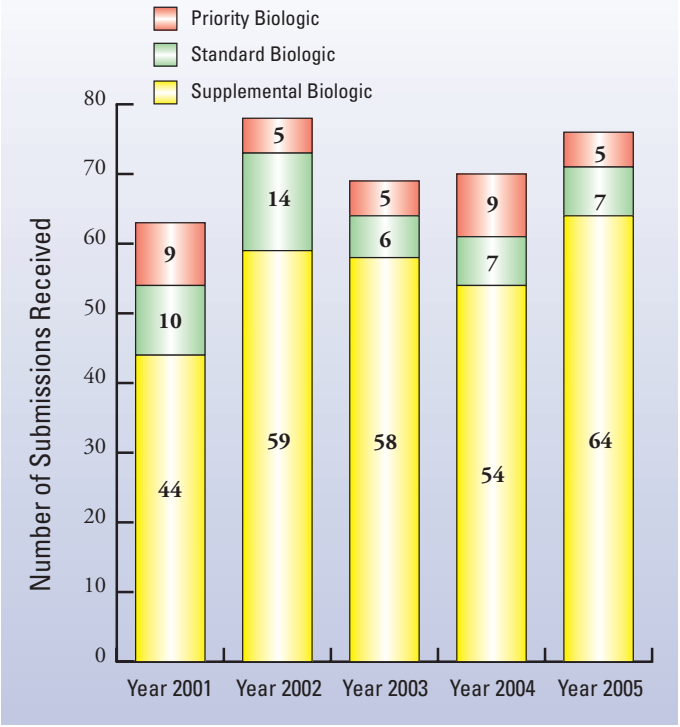
Since 2002, submissions for Generic Standard pharmaceutical drugs have been increasing, more than doubling from 59 to 137 by 2005. This increase in generic submissions is representative of the significant growth in the Canadian generic drugs sector (and the expiration of many patents). Generic Supplemental submissions more than tripled since 2004 (from eight to 26).

Chart 1-A: Number of Submissions Received for New Pharmaceutical Drugs



[7] See Annex A for a definition of the Notice of Compliance with Conditions decision type.

Chart 1-B: Number of Submissions Received for New Biologic Drugs



In 2005, the total number of submissions received for new Biologic drugs increased by 27% since 2001, with submissions for Supplemental Biologics growing by 45% (from 44 to 64). *See Chart 1-B.*

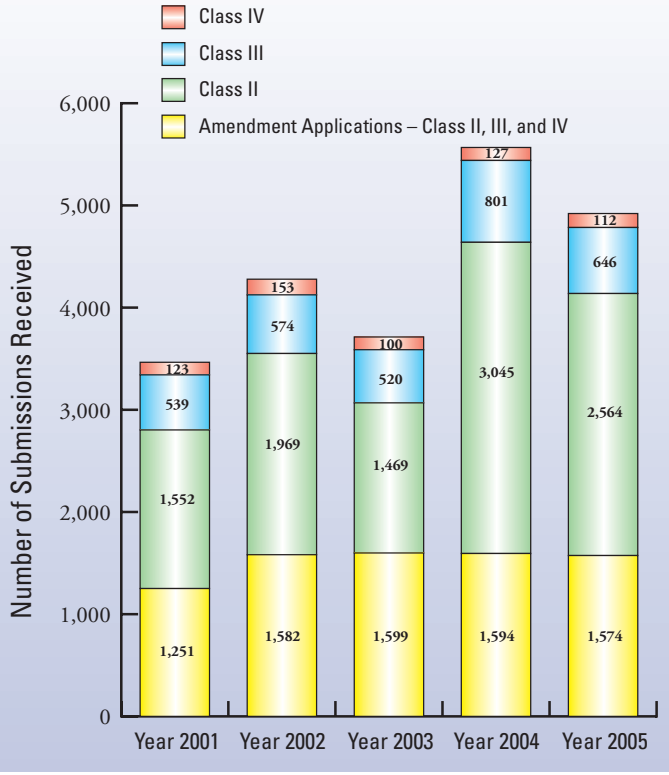
These figures do not include applications for clinical trials, which are scientific studies that use test populations and are designed to test the safety, efficacy and quality of drugs on human subjects. Clinical trials in Canada must be conducted in accordance with internationally accepted principles of Good Clinical Practice. In 2005, HPFB received 1743 Clinical Trial Applications (CTAs) for new pharmaceutical drugs and 239 CTAs for new biologic drugs. A significant number of CTA Amendments were received in 2005, totaling 902 and 316 for new pharmaceutical and new biologic drugs, respectively.

Close to 5000 (4896) medical device submissions were received in 2005, up from 3465 in 2001 (an increase of 41%). *See Chart 1-C.*

In addition to review of submissions for new drugs and medical devices, the HPFB review workload includes various other types of submissions that are not covered in this report.[8]

HPFB received 131 Investigational Testing Applications in 2005 for clinical trials using medical devices on human subjects.

Chart 1-C: Number of Submissions Received for Medical Devices



[8] Other submission types not included in this report are Notifiable Changes, Drug Identification Number Applications and Faxback Amendment Applications (for medical devices).

End-of-Year Workload Status of Submissions for New Drugs and Medical Devices

This section provides data on the number and composition of new drug and medical device submissions at the end of 2005. Backlog refers to submissions which have exceeded their review time performance target without the issuance of a regulatory decision.

The Therapeutics Access Strategy, launched in 2003, has lead to substantial improvements in the efficiency and responsiveness of the drug review system. New investments have supported streamlining the drug review process so that submissions are being managed as projects. Additional scientific review capacity is in place, including the development of an 'ever-green' database of external expertise to enable more timely and well-informed decision-making.

By December 31, 2005, the end-of-year workload for new pharmaceutical drugs included an all-time low of backlog submissions, with just one percent of the workload in backlog (or three of 228 submissions). *See Chart 2-A.*

The total number of submissions in workload (including backlog) at the end of 2005 was the lowest it has been over the past five years for new biologic drugs (dropping by 46% since 2003), in spite of the 14% increase in the number of submissions received (since 2004). *See Chart 2-B.*

The end-of-year workload for new biologic drugs consisted of 51% of the workload in backlog (or 31 of 61 submissions).

Chart 2-A: End-of-Year Workload Status of Submissions for New Pharmaceutical Drugs

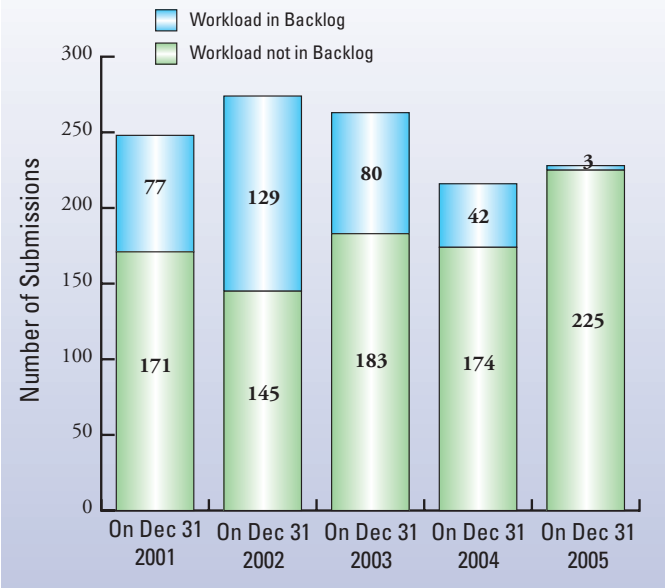
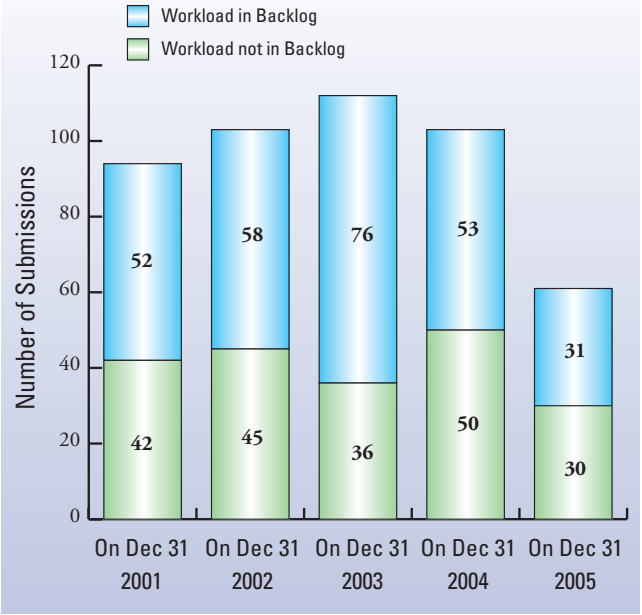
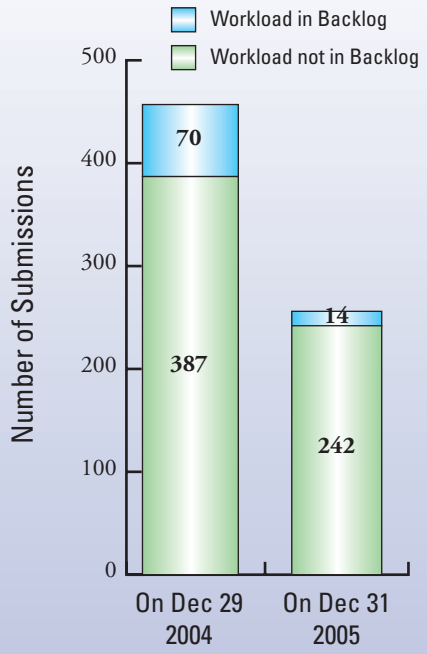


Chart 2-B: End-of-Year Workload Status of Submissions for New Biologic Drugs



The 2005 end-of-year workload for medical devices comprised 14 submissions – or five percent of (256) submissions in backlog. This was an improvement from 2004, when 15% of the total workload was in backlog (*See Chart 2-C*). Overall, there was a decrease in the total end-of-year workload of medical device submissions since 2004. Increased use of project management practices, combined with a 12% reduction of incoming submissions from 2004 to 2005 may account, in part, for this observation.

Chart 2-C: End-of-Year Workload Status of Medical Device Submissions



In 2004, the Office of the Auditor General released a report along with recommendations concerning Health Canada's regulatory program for medical devices. Recommendations ranged from timely access to medical devices, to post-market activities and performance measurement. HPFB is undertaking a thorough review of the medical devices program and is responding to all eight recommendations. The report is available at http://www.oag-bvg.gc.ca/domino/reports.nsf/html/20040302ce.html

II. Decisions

Regulatory Decisions Issued for Submissions for New Drugs and Medical Devices[9]

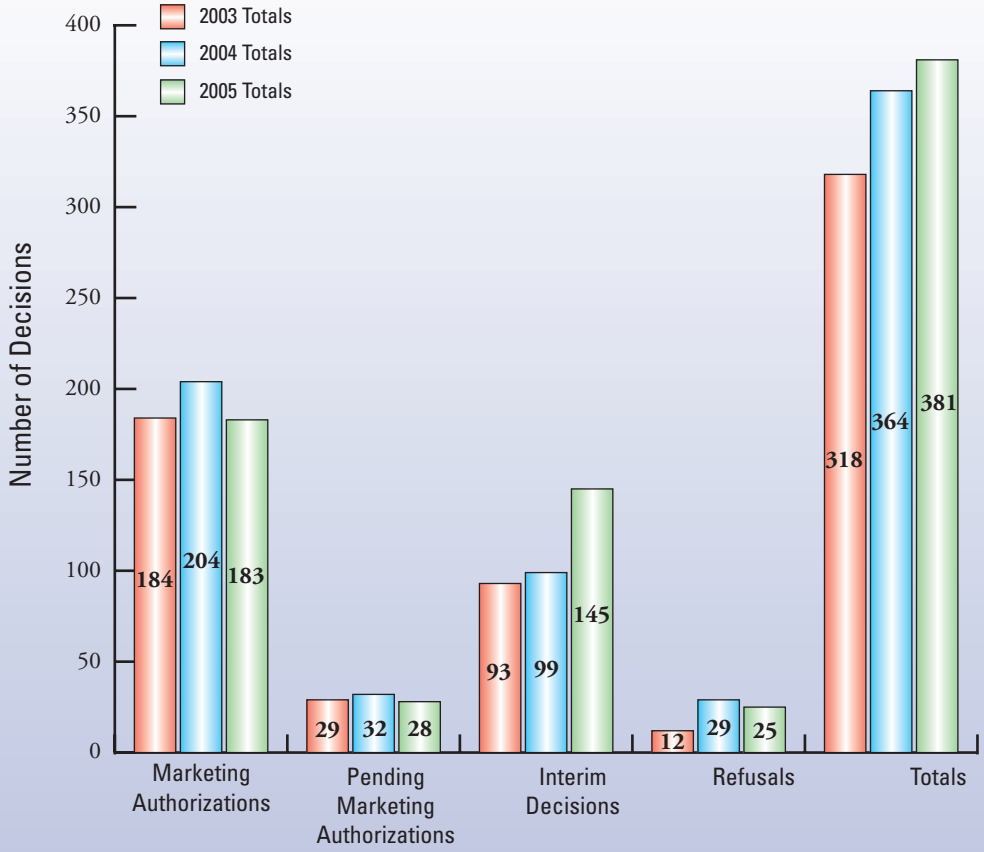
The total number of regulatory decisions issued for submissions for new pharmaceutical drugs in 2005 increased by 20% compared with 2003 (from 318 to 381). *See Chart 3-A.*

The number of interim decisions issued increased by 56% since 2003 (from 93 to 145). Interim decisions are given to submissions that contain deficiencies with respect to the regulatory requirements for market authorization. Following an interim decision, the manufacturer is provided with a notice of the information required and a time period in which to respond with the missing documentation. HPFB is examining its processes and working with manufacturers to increase the receipt of high quality submissions at the outset of the review process, in support of minimizing the number of interim decisions.

The Good Guidance and Good Review Practice initiatives underway are intended to promote good quality submissions as well as a high quality review process.

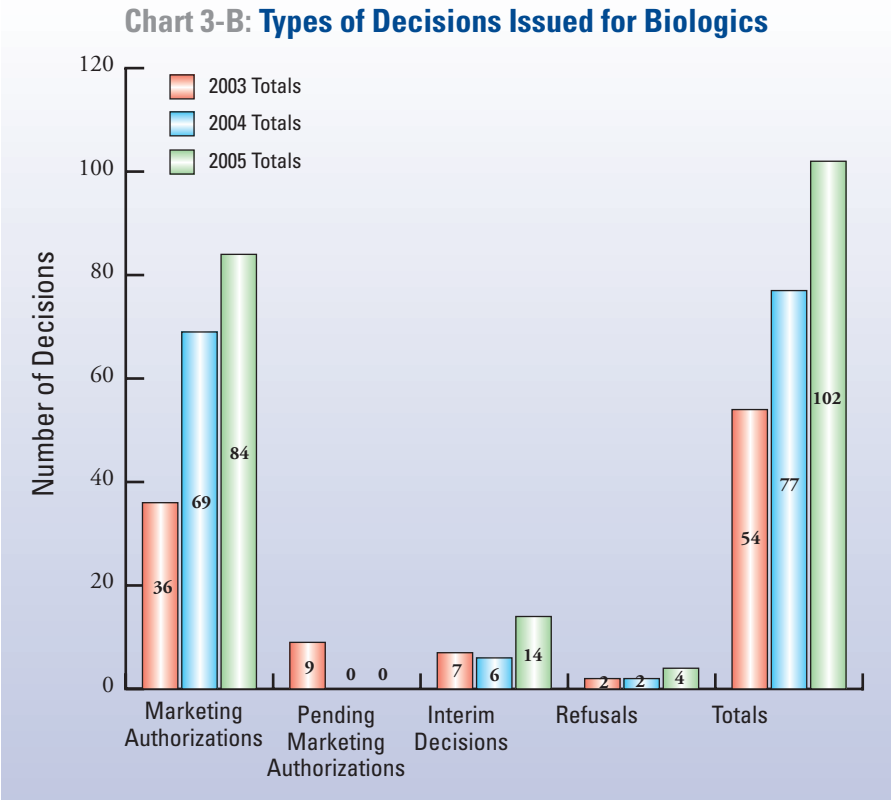
Refusals increased from 12 to 25 since 2003.

Chart 3-A: Types of Decisions Issued for Pharmaceuticals



[9] See Annex A for definitions of regulatory decisions for submissions for new drugs and medical devices.

Chart 3-B: Types of Decisions Issued for Biologics

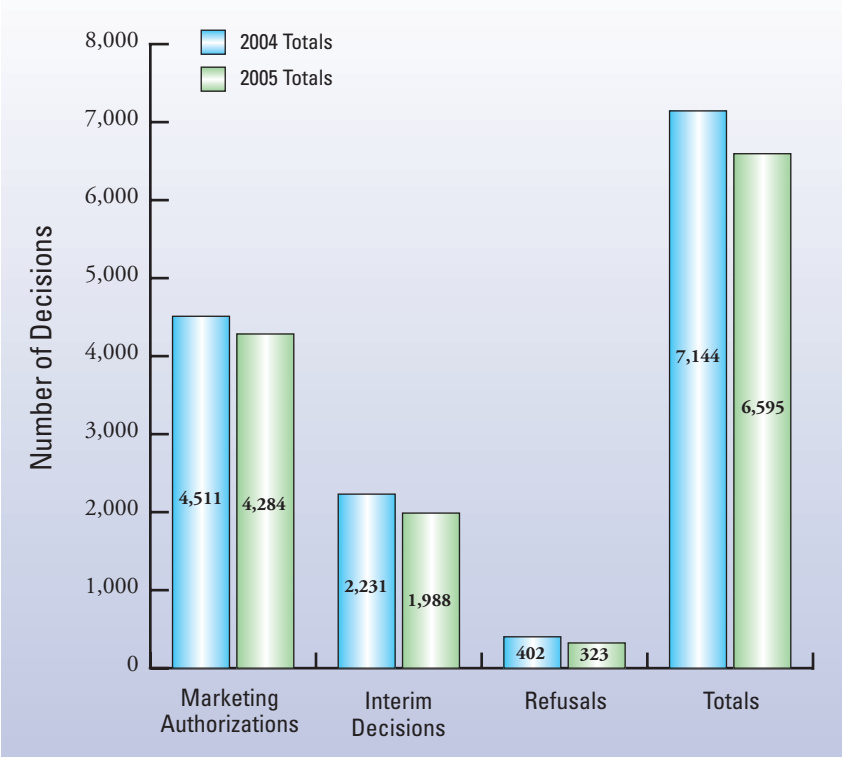


The total number of regulatory decisions issued for new biologic drugs increased by 89% in 2005 compared with 2003 (from 54 to 102 decisions). The number of market authorizations more than doubled since 2003, growing from 36 to 84. Interim decisions doubled from seven to 14 (*see Chart 3-B*).

The total number of decisions issued for medical device submissions decreased by eight percent in 2005 compared with 2004, from 7144 to 6595[10] (*see Chart 3-C*). This observation is consistent with the decline in medical device submissions received in 2005 – a 12% reduction since 2004 (*see Chart 1-C*).

All decision types decreased, with the greatest drop in Interim Decisions.

Chart 3-C: Types of Decisions Issued for Medical Devices



[10] Equivalent data from previous years is not available.

III. Backlog

Progress in Backlog Reduction of Submissions for New Drugs and Medical Devices

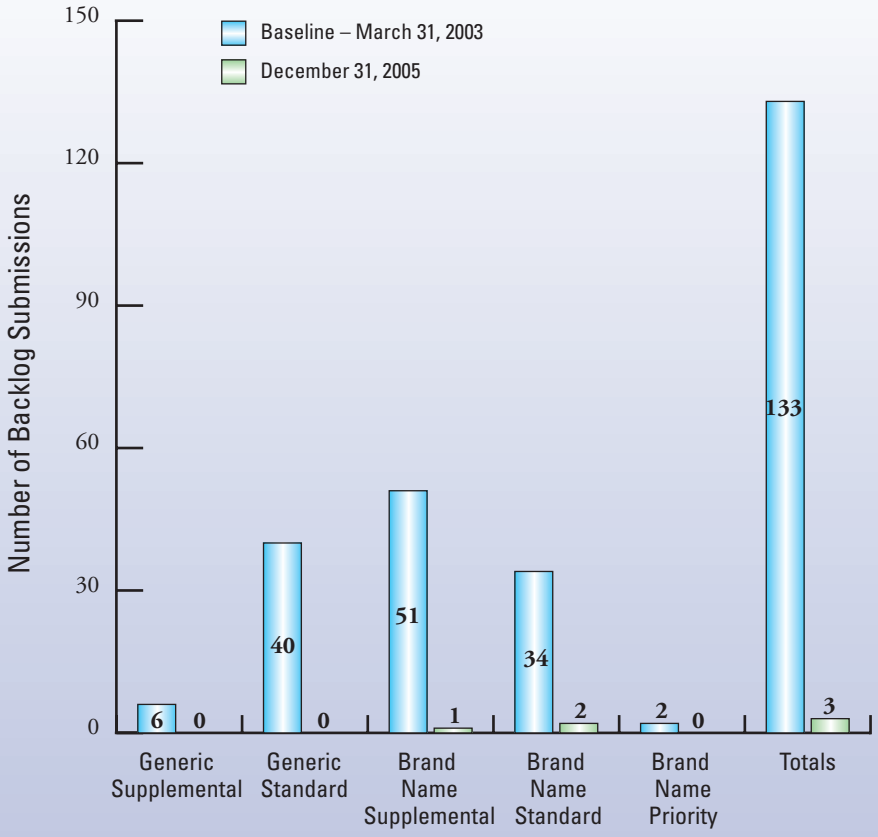
For many years, a large backlog existed for pharmaceutical drugs. One of the key goals of the Therapeutics Access Strategy was to eliminate this chronic backlog and ensure that it did not return.

Substantial progress has been made in this regard. Between the baseline date of March 31, 2003 and December 31, 2005, 98% of the backlog had been eliminated (*see Chart 4-A*).

Ninety percent of the backlog of submissions for new pharmaceutical drugs was eliminated as of March 31, 2005, with further progress achieved by the end of the year.

Health Canada aims to have no more than 10% of its workload in backlog at any given time. This 10% threshold recognizes that there may be exceptional situations where a submission will not be able to meet its performance target.

Chart 4-A: Progress in Backlog Reduction of Submissions for New Pharmaceutical Drugs



Backlog reduction of submissions for new biologic drugs continues to improve, with 55% of the total backlog removed by December 31, 2005 since the baseline date of March 31, 2003 (*see Chart 4-B*).

HPFB continues to work with colleagues in other countries to identify opportunities for cooperation. Best practices are being explored to increase the efficient use of foreign reviews in the Canadian review process.

Chart 4-B: Progress in Backlog Reduction of Submissions for New Biologic Drugs

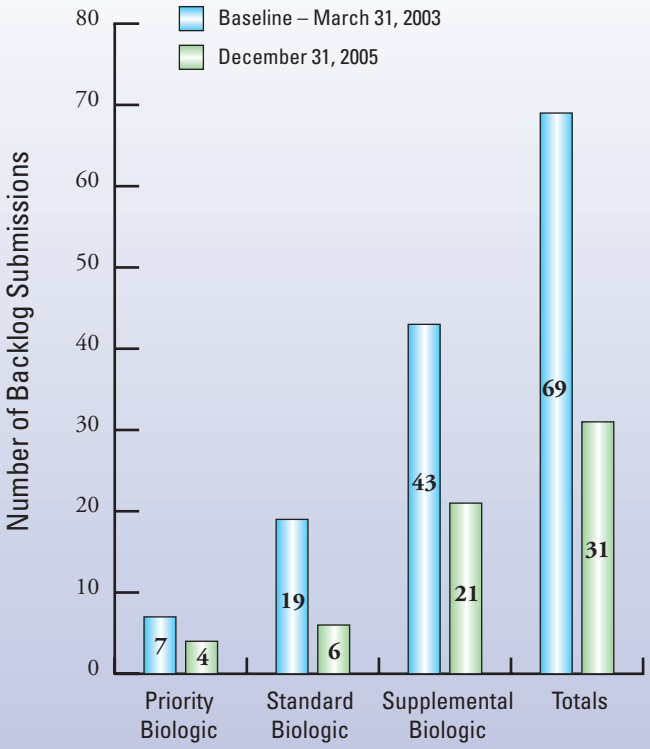
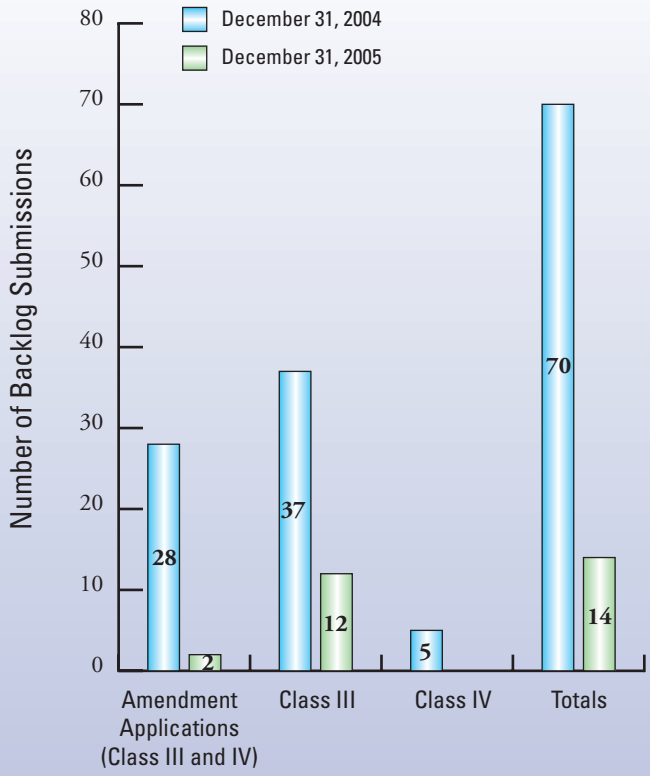


Chart 4-C: End-of-Year Backlog of Submissions for New Medical Devices



By December 31, 2005, 80% of the total backlog of medical device submissions was eliminated compared with the previous year. No Class IV submissions remained in backlog. The backlog of Class III and Amendment Applications had been reduced by 68% and 93%, respectively (*see Chart 4-C*).

This accomplishment is a result of an increased focus on more effective workload management and increased review capacity (achieved through contracting and staffing).

IV. Timeliness

Performance for Review of Submissions for New Drugs and Medical Devices

Performance targets differ by the type of submission. Different classes of therapeutic products have different target times for completion of reviews. For example, target review times are significantly shorter for all classes of medical devices than for other therapeutic products.

Performance Targets for First Review Cycle Concerning Market Authorization[11]

Submission for New Drug (Pharmaceutical and Biologic)	**Target Times (Calendar days)***
Brand Name Priority/Priority Biologic	180 or 200**
Brand Name Standard/Standard Biologic	180 or 300
Brand Name Supplemental/Supplemental Biologic	180 or 300
Generic Standard	180
Generic Supplemental	180 or 30

Medical Device Application	**Target Times (Calendar days)**
Priority (Class III and IV)	45
Class II	15
Class III	75
Class IV	90
Class II, III, and IV Amendment Applications are the same as above	

*Performance targets do not include screening of submissions for new drugs.

**Target times vary depending on the submission class.

[11] For further information on performance targets, refer to *The Guidance for Industry on the Management of Drug Submissions* available at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/mgmt-gest/mands_gespd_e.html and *The Management of Applications for Medical Device Licences and Investigational Testing Applications* available at http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/pol/mdlapp_demhim_pol_e.html

The following charts provide performance information for all review decisions concerning submissions, including market authorizations, pending authorizations, refusals and interim decisions.

As part of the Therapeutics Access Strategy, HPFB has a goal to meet 90% of review performance targets for new drugs in 2006 for pharmaceuticals and in 2007 for biologics.

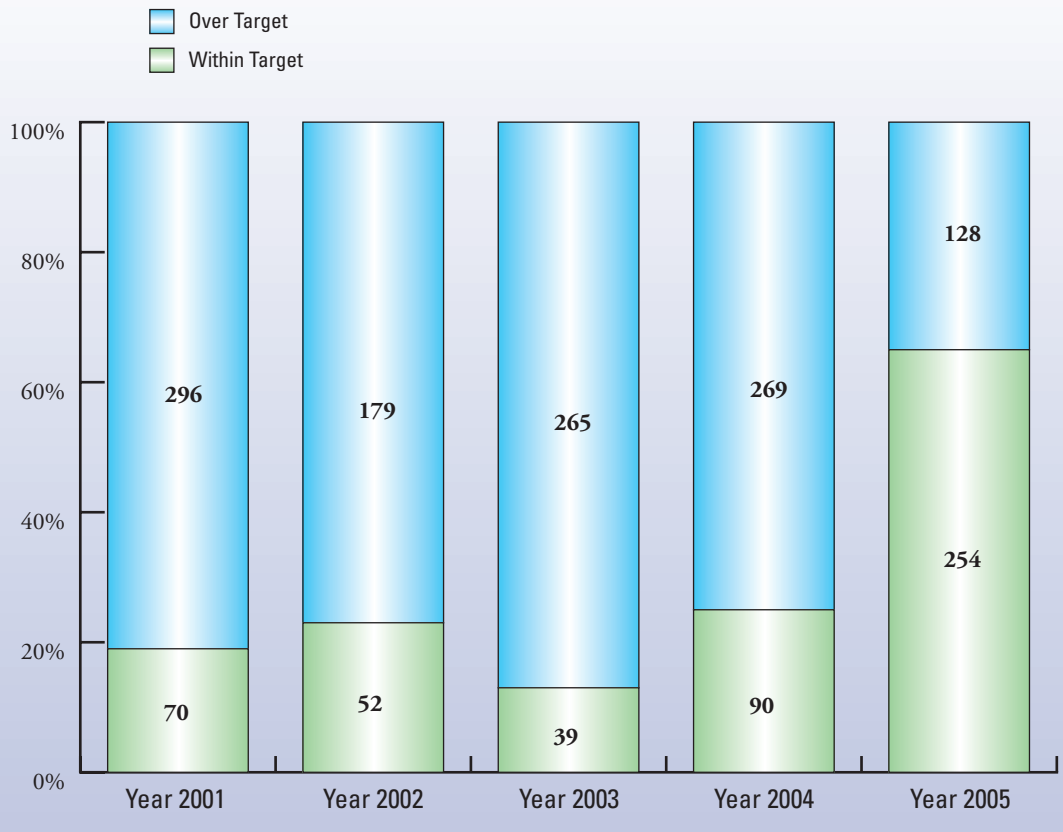
To sustain a high level of performance (i.e. 'review on time'), the backlog must be kept at a very low level.

Backlog (unlike performance) is calculated on a given day, and can change in number and composition of submissions throughout the year. In this report, performance is calculated for the entire year, which is why a 98% elimination of backlog does not imply 98% performance (or 98% of decisions issued on time).

Significant progress has been made in meeting performance targets, with 66% of regulatory decisions issued within time targets for submissions for new pharmaceutical drugs in 2005, compared with 13% in 2003 (*see Chart 5-A*)[12].

The elimination of the chronic backlog has enabled further progress in meeting performance targets.

Chart 5-A: Performance for Submissions for New Pharmaceutical Drugs



[12] Cancellations are excluded from Charts 5-A, B and C.

Due to continued efforts to clear the backlog, the number of decisions made within target for new biologic drugs rose only slightly in 2005 compared with 2004, from 13 to 16% (*see Chart 5-B*). Although the performance improvement is modest, the total number of decisions taken in 2005 was at a five year high (at 97 decisions) – 24% higher than 2004 (the second highest year) – and it is expected that further elimination of backlog will lead to an improvement in performance over time.

In 2005, 70% of regulatory decisions issued for medical device submissions were made within time targets[13]. *See Chart 5-C.*

Chart 5-B: Performance for Submissions for New Biologic Drugs

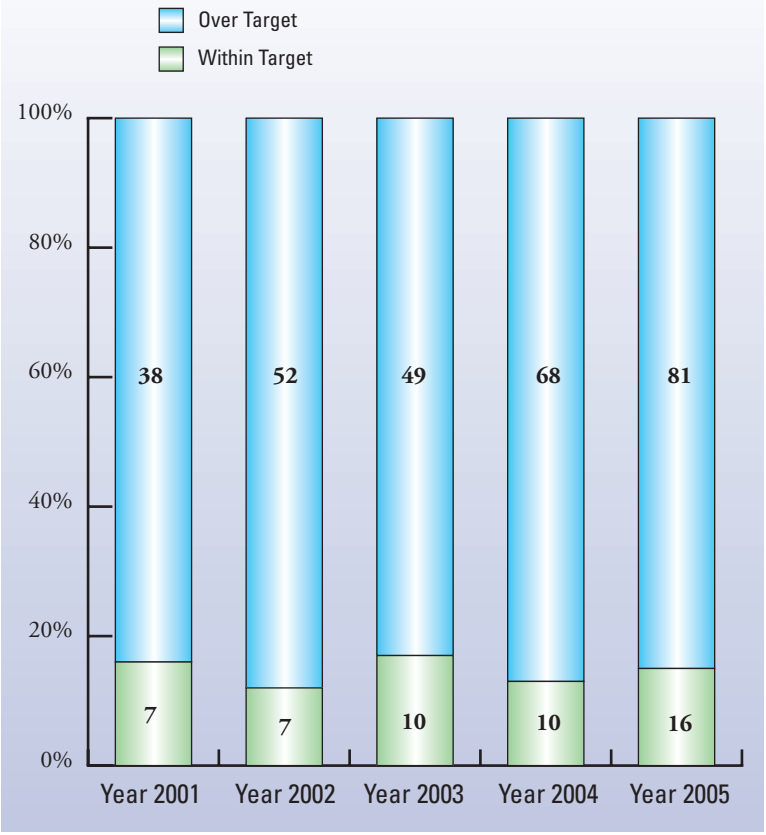
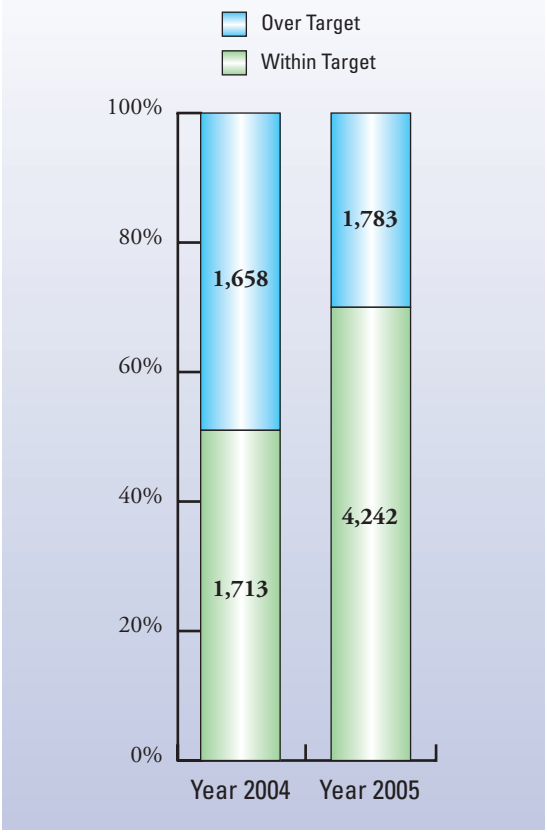


Chart 5-C: Performance for Submissions for Medical Devices



[13] Data for medical devices covers the third and fourth quarter (last six months) and not the full year of 2004. Validated data on medical devices review performance prior to 2004 is not available.

[14] Note: Due to limitations in data collection systems for medical device submissions, the performance calculations presented for 2005 in Chart 5-C are missing more than 500 interim decisions. Ongoing efforts will be made for continuous improvements to the quality of such performance information for future editions of this report.

Market Authorization Times

Canada's time to market authorization includes the time from the receipt of a submission to authorization, including the company time required to respond to questions and deficiencies. It is common for more than one review cycle to have taken place before a new therapeutic product is authorized for market access.

In 2005, 210 new pharmaceutical drugs were issued market authorization in Canada, a slight decrease from the 2003 total of 212 (*see Charts 6-A, B, C, D and E*). Since the introduction of the Therapeutics Access Strategy in 2003, market authorization times have improved for new pharmaceutical drugs, as outlined below.

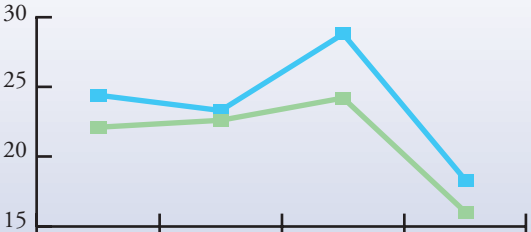
Chart 6-A: Market Authorization Times for Brand Name Priority Pharmaceuticals

	2002	2003	2004	2005
Number Approved	9	7	6	9
Average Months	10.6	12.1	8.9	10.7
Median Months	9.4	12.7	7.6	8.4

Since 2003, median times for Brand Name Priority Pharmaceuticals have decreased, dropping by 34% between 2003 and 2005 (or from 12.7 to 8.4 months).

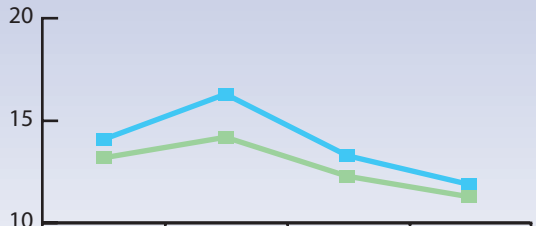
Median times for Brand Name Standard Pharmaceuticals have improved compared with 2003, dropping by 29%. The number of Brand Name drugs approved decreased from 29 in 2003 to 24 in 2005.

Chart 6-B: Market Authorization Times for Brand Name Standard Pharmaceuticals



	2002	2003	2004	2005
Number Approved	24	29	36	24
Average Months	24.4	23.2	28.8	18.3
Median Months	22.1	22.6	24.2	16.0

Chart 6-C: Market Authorization Times for Brand Name Supplemental Pharmaceuticals

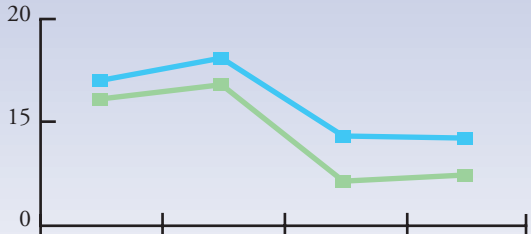


	2002	2003	2004	2005
Number Approved	68	110	101	91
Average Months	14.1	16.3	13.3	11.9
Median Months	13.2	14.2	12.3	11.3

Since 2003, the time to approval has decreased for Brand Name Supplemental drugs, with median times dropping by 21%. The number of approvals has also declined from 110 in 2003 to 91 in 2005.

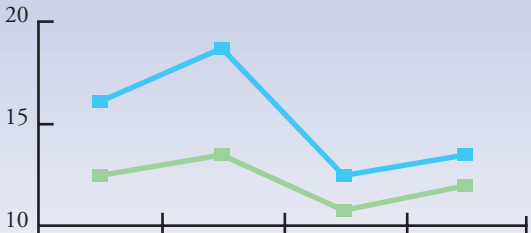
The number of generic standard drugs approved has risen compared with 2003, from 57 to 77 in 2005. Approval times have declined since 2003, with a 26% reduction in median months (from 16.8 to 12.4 months in 2005).

Chart 6-D: Market Authorization Times for Generic Standard Pharmaceuticals



	2002	2003	2004	2005
Number Approved	57	57	83	77
Average Months	17.0	18.1	14.3	14.2
Median Months	16.1	16.8	12.1	12.4

Chart 6-E: Market Authorization Times for Generic Supplemental Pharmaceuticals

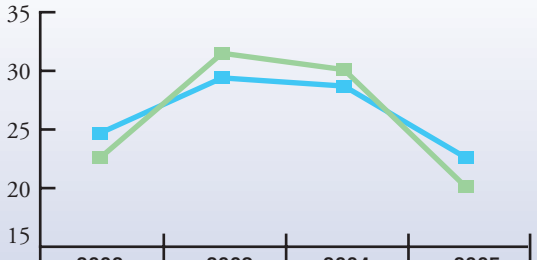


	2002	2003	2004	2005
Number Approved	4	10	10	9
Average Months	16.1	18.7	12.5	13.5
Median Months	12.5	13.5	10.8	12.0

An 11% reduction in median time to approval was observed for Generic Supplemental drugs in 2005 compared with 2003.

A total of 84 new biologic drugs were authorized for the Canadian market in 2005, increasing from 45 in 2003, an 87% increase (*see Charts 7-A, B and C*).

Chart 7-A: Market Authorization Times for Priority Biologics

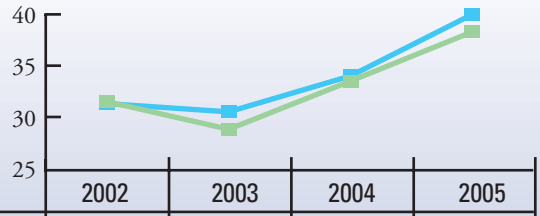


	2002	2003	2004	2005
Number Approved	5	5	6	13
Average Months	24.7	29.4	28.7	22.6
Median Months	22.6	31.5	30.1	20.1

For Priority Biologics, median authorization times improved by 36%, since 2003, dropping from 31.5 to 20.1 months in 2005 – with more than double the number of approvals (from five in 2003 to 13 in 2005).

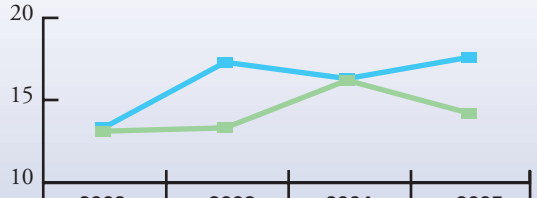
Median approval times for Standard Biologics increased by 33% since 2003 (from 28.8 to 38.3 months), reflecting the reduction in backlog submissions. It is expected that market authorization times will decrease once the backlog is eliminated and further developments are made towards a more efficient review process and higher quality incoming submissions.

Chart 7-B: Market Authorization Times for Standard Biologics



	2002	2003	2004	2005
Number Approved	7	7	8	11
Average Months	31.3	30.5	34.0	40.4
Median Months	31.5	28.8	33.5	38.3

Chart 7-C: Market Authorization Times for Supplemental Biologics

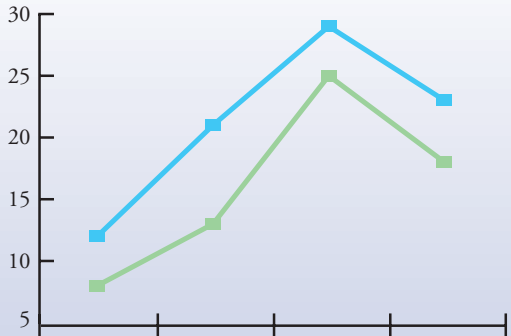


	2002	2003	2004	2005
Number Approved	39	33	55	60
Average Months	13.3	17.3	16.3	17.6
Median Months	13.1	13.3	16.2	14.2

Sixty Supplemental Biologics were approved in 2005, an increase from 2003, when 33 were approved. Median times increased by seven percent since 2003 (from 13.3 to 14.2 months).

The total number of medical devices issued market authorization in 2005 was 4284, up from 3242 in 2003, a 32% increase (*see Charts 8-A, B and C and Table 1-A*).

Chart 8-A: Market Authorization Times for Class II Medical Devices

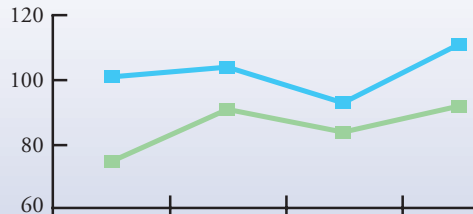


	2002	2003	2004	2005
Number Approved	1,725	1,478	2,745	2,396
Average Days	12	21	29	23
Median Days	8	13	25	18

The number of approvals for Class II medical devices rose by 62% since 2003, (from 1478 to 2396). Median days to approval also increased, from 13 days in 2003 to 18 days in 2005.

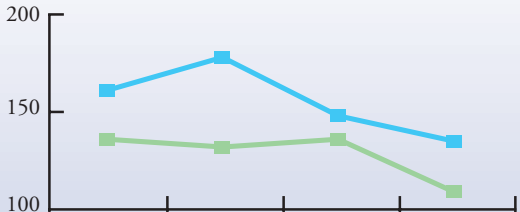
The number of approvals for Class III devices rose by 10% since 2003 (from 554 to 607).

Chart 8-B: Market Authorization Times for Class III Medical Devices



	2002	2003	2004	2005
Number Approved	455	554	613	607
Average Days	101	104	93	111
Median Days	75	91	84	92

Chart 8-C: Market Authorization Times for Class IV Medical Devices



	2002	2003	2004	2005
Number Approved	106	111	106	99
Average Days	161	178	148	135
Median Days	136	132	136	109

For Class IV medical devices, the number of approvals and the median approval times decreased since 2003, by 11% and 17%, respectively.

Table 1-A: Market Authorization Times for Amendment Applications

	Amendment Applications (Class II, III and IV)		
Year	Number Approved	Average Days	Median Days
2002	1082	8 (Class II) 60 (Class III) 115 (Class IV)	4 (Class II) 33 (Class III) 45 (Class IV)
2003	1099	7 (Class II) 79 (Class III) 110 (Class IV)	4 (Class II) 56 (Class III) 103 (Class IV)
2004	1044	18 (Class II) 67 (Class III) 69 (Class IV)	19 (Class II) 68 (Class III) 85 (Class IV)
2005	1182	13 (Class II) 84 (Class III) 95 (Class IV)	10 (Class II) 74 (Class III) 70 (Class IV)

V. Access to New Drugs

Table 2-A: New Active Substances that Received Market Authorization in 2005

The following table displays *New Active Substances* which received market authorization by Health Canada in 2005. A New Active Substance includes chemical or biological substances which have not been previously authorized for sale in Canada as a drug and therefore not been previously available for therapeutic use in humans[15]. The order of products listed is alphabetical, by *Therapeutic Use*, followed by the *Market Authorization Date*.

	Brand Name, Active Ingredient (s) & Description	Market Authorization Date	Therapeutic Use
1	**SOMAVERT** (pegvisomant) – for the treatment of acromegaly, which is a disease caused when the body produces too much growth hormone. SOMAVERT blocks the effect of too much growth hormone and improves the symptoms of acromegaly. (Priority Biologic)	Oct 17 2005	Acromegaly
2	**MACUGEN** (pegaptanib sodium) – for the treatment of the wet form of age-related macular degeneration. This disease leads to vision loss resulting from damage to the central part of the retina (called the macula), at the back of the eye. The macula enables the eye to provide the fine central vision that is needed for driving a car, reading fine print and other similar tasks. (Brand Name Priority Pharmaceutical)	May 2 2005	Age-related macular degeneration
3	**LYRICA** (pregabalin) – is used for the symptomatic relief of neuropathic pain associated with Diabetic peripheral neuropathy (pain from damaged nerves due to diabetes) and Postherpetic neuralgia (persisting pain following healing of the rash due to shingles). (Brand Name Standard Pharmaceutical)	Jun 3 2005	Analgesic
4	**TRAMACET** (tramadol hydrochloride / acetaminophen) – for the short-term (five days or less) management of acute pain. (Brand Name Standard Pharmaceutical)	Jul 20 2005	Analgesic
5	**ENABLEX** (darifenacin hydrobromide) – for the treatment of overactive bladder. (Brand Name Standard Pharmaceutical)	Nov 14 2005	Overactive Bladder
6	**VELCADE** (bortezomib) – for the treatment of adults with cancer of the bone marrow (multiple myeloma). (Brand Name Standard Pharmaceutical)	Jan 27 2005 (Conditionally Cleared)	Cancer
7	**ZEVALIN** (ibritumomab tiuxetan) – to treat certain types of B-cell non-Hodgkin's lymphoma. This is a cancer of certain white blood cells called B-lymphocytes. ZEVALIN is used if an earlier treatment has not worked, or has stopped working. (Priority Biologic)	May 10 2005	Cancer
8	**TARCEVA** (erlotinib) – for treatment of non-small cell lung cancer at an advanced stage if chemotherapy has not been effective. (Brand Name Priority Pharmaceutical)	Jul 7 2005	Cancer

[15] This table does not include new therapeutic uses for substances previously approved in Canada.

Table 2-A: New Active Substances that Received Market Authorization in 2005 *(cont'd)*

	Brand Name, Active Ingredient (s) & Description	Market Authorization Date	Therapeutic Use
9	**BEXXAR THERAPY** (tositumomab) – for the treatment of patients with CD20 positive relapsed or refractory, low grade, follicular, or transformed non-Hodgkin's lymphoma, including patients with rituximab-refractory non-Hodgkin's lymphoma. (Priority Biologic)	Aug 18 2005	Cancer
10	**AVASTIN** (bevacizumab) is used in combination with a specific type of chemotherapy for treatment of people diagnosed with metastatic colorectal cancer for the first time. Metastatic colorectal cancer is cancer of the colon or rectum that has spread to other organs in the body. (Priority Biologic)	Sep 9 2005	Cancer
11	**ERBITUX** (cetuximab) – for patients with metastatic cancer of the large intestine or rectum that express Epidermal Growth Factor Receptor, who have previously received irinotecan-based chemotherapy or who are intolerant to irinotecan. ERBITUX can be used alone, or in combination with irinotecan. (Priority Biologic)	Sep 9 2005	Cancer
12	**MABCAMPATH** (alemtuzumab) – for the treatment of patients with B-cell chronic lymphocytic leukemia (B-CLL) when other previous treatments, such as alkylating agents and fludarabine, have been unsuccessful. B-CLL is a blood cancer affecting a certain type of white blood cells, called B-lymphocytes. (Standard Biologic)	Nov 30 2005	Cancer
13	**KEPIVANCE** (palifermin) – used to decrease the incidence, duration, and severity of oral mucositis (severe mouth ulcerations) that are a side effect of some cancer treatments. KEPIVANCE is used to treat the mouth and throat soreness thereby improving the patient's ability to swallow, eat, drink, talk and sleep. (Priority Biologic)	Dec 9 2005	Cancer
14	**XYREM** (sodium oxybate) – oral solution for the treatment of cataplexy (sudden loss of muscle strength) in patients with narcolepsy. (Brand Name Standard Pharmaceutical)	Aug 5 2005	Cataplexy (sudden loss of muscle strength)
15	**LEVEMIR – Flexpen/Innolet/Penfill** (insulin detemir) – for the treatment of patients with diabetes mellitus. LEVEMIR is a long-acting human insulin analogue which lowers blood glucose. LEVEMIR has a flat and predictable profile for blood glucose control. The effect lasts up to 24 hours depending on the dose. (Standard Biologic)	Sep 29 2005	Diabetes
16	**PANTOLOC M** (pantoprazole magnesium) – for the treatment of conditions where a reduction of gastric acid secretion is required such as duodenal ulcer, gastric ulcer, reflux esophagitis, symptomatic gastroesophageal reflux disease, Helicobacter pylori associated duodenal ulcer. (Brand Name Standard Pharmaceutical)	Apr 22 2005	For reduction of gastric acid secretion
17	**APTIVUS** (tipranavir) – is a medicine to treat adults with Human Immunodeficiency Virus (HIV), the virus that causes AIDS (Acquired Immune Deficiency Syndrome). It must always be taken with Norvir® (ritonavir) and with other anti-HIV medicines to treat people with HIV infection. (Brand Name Priority Pharmaceutical)	Nov 21 2005	HIV

Table 2-A: New Active Substances that Received Market Authorization in 2005 *(cont'd)*

	Brand Name, Active Ingredient (s) & Description	Market Authorization Date	Therapeutic Use
18	**EMTRIVA** (emtricitabine) is a type of medicine called an HIV nucleotide analog reverse transcriptase inhibitor. It is always used in combination with other anti-HIV medicines to treat adults with HIV infection. (Brand Name Standard Pharmaceutical)	Nov 21 2005	HIV
19	**ZEMPLAR** (paricalcitol) – is a synthetic vitamin D analogue is used to replace the body's naturally produced active form of vitamin D. It is used in hemodialysis patients for the prevention and treatment of secondary hyper-parathyroidism – high levels of parathyroid hormone which can cause bone problems associated with chronic renal failure (long term kidney failure). (Brand Name Standard Pharmaceutical)	Mar 31 2005	Hyperparathyroidism (high levels of parathyroid hormone which can cause bone problems)
20	**COVERSYL** (perindopril arginine) – for initial treatment of mild to moder-ate essential hypertension. It may be used alone or in association with other drugs, particularly thiazide diuretics. (Brand Name Standard Pharmaceutical)	Aug 23 2005	Hypertension
21	**INOMAX** (nitric oxide) – is used for babies who have been born near or at term and who have been diagnosed with a condition called hypoxic respiratory failure. A baby with hypoxic respiratory failure has less blood flow through the lungs, and low amounts of oxygen in the blood. Some medical conditions, such as pulmonary hypertension (high blood pressure in the lung), meconium aspiration (fecal material that blocks the lungs) and infection, may cause hypoxic respiratory failure. (Brand Name Priority Pharmaceutical)	Sep 23 2005	Hypoxia (low oxygen levels)
22	**LUVERIS** (lutropin alfa) – is one option available to help women with hypgonadotropic hypogonadism to achieve development of ovarian follicles. LUVERIS is a gonadotrophin hormone produced by DNA technology. LUVERIS is for use in association with Gonal-F (follitropin alpha for injection) to stimulate follicular development necessary for the recruitment, growth and maturation of the ovarian follicles which contain eggs known as ova or oocytes. (Standard Biologic)	Jun 24 2005	Infertility
23	**LEUKOSCAN** (sulesomab) – An antibody is a natural substance made by the body which binds to foreign substances to help remove them from the body. Humans produce many different kinds of antibodies. LEUKOSCAN is a special kind of antibody which binds to the surface of certain kinds of blood cells called leukocytes. It is produced in mice and purified so it can be used in humans. When combined to the radioactive technetium isotope and injected, it finds an abnormal accumulation of white blood cells and attaches to them. This helps the doctor make a diagnosis and evaluate the extent of the illness. The doctor does this by using a special imaging camera that reveals areas of radioactivity. (Standard Biologic)	Jan 17 2005	Osteomyelitis (Bone Infection)
24	**RAPTIVA** (efalizumab) – for the treatment of adults who have moderate to severe chronic plaque psoriasis, which is the most common form of psoriasis. (Standard Biologic)	Oct 24 2005	Psoriasis

Table 2-B: Access to New Drugs in Canada

The time it takes for the public to have access to new therapeutic products in Canada is determined by many factors, including:

(1) Global marketing strategies of individual manufacturers, which influence where and when they file their regulatory submissions; and, whether and when they will market launch their product in Canada following a market authorization decision by Health Canada.

(2) The length of time HPFB takes to review a submission and authorize sale of the product.[16]

(3) Decisions taken by other bodies including pricing decisions by the Patented Medicine Prices Review Board (PMPRB).[17]

(4) Formulary listing recommendations by the Common Drug Review (CDR).

(5) Formulary listing decisions taken by individual federal, provincial, and territorial drug plans and privately financed drug plans.[18]

The following table displays key decisions that influence access to new drugs in Canada. The drugs listed are those which were subject to a formulary listing recommendation by the Common Drug Review (CDR) in 2005. The table does not describe every drug which received market authorization by Health Canada in 2005. In particular, generic and over-the-counter drug products, medicines for use in hospitals, blood products and vaccines are not included.

For the drugs listed in Table 2-B, the therapeutic use sought and approved in the United States may differ from the therapeutic use sought and approved in Canada. Different countries vary in the approach to measuring market authorization times, reflecting differences in legislation, policy and processes.

Drugs are listed alphabetically followed by market authorization date.

As part of the National Pharmaceuticals Strategy, in October 2005, Health Ministers directed the CDR to expand its scope to include recommendations for reimbursement to all drugs, and agreed to work towards a common national formulary, which is expected to lead to more consistent access to drugs across Canada. For more information, go to http://www.scics.gc.ca/cinfo05/830866004_e.html

[16] Note that HPFB has mechanisms in place such as the Special Access Program, that enable interim access to new drugs or medical devices. For more information, refer to http://www.hc-sc.gc.ca/dhp-mps/acces/index_e.html

[17] More details on the role of the PMPRB and CDR are provided in Annex B.

[18] Federal, provincial, and territorial governments manage drug formularies and assess the drugs for which reimbursement from government plans is available. In some cases, drugs have a restricted status limiting coverage to particular types of patients or situations. Note that Quebec is not part of the CDR.

Table 2-B: **Access to New Drugs in Canada** *(cont'd)*

New Drug Trade Name (Active Ingredient (s)) & Therapeutic Use	**Health Canada** a. Filing Date b. Market Authorization Date	**Market Notification Date** (Date of first sale)	**PMPRB Price Decision** a. Under PMPRB Jurisdiction b. Status	**CDR** a. Filing Date b. Recommendation & Decision Date	**US FDA** a. Filing Date b. Approval Date
1. Avodart (Dutasteride) – for Benign prostatic hyperplasia	a. Dec 3 2001 b. Jul 22 2003	Nov 14 2003	a. Jan 7 2004 b. Within guidelines, Nov 2004	a. Aug 24 2004 b. To list on Jan 20 2005	a. Dec 21 2000 b. Nov 20 2001
2. Aldurazyme (Laronidase) – for enzyme replacement therapy	a. Dec 18, 2002 (Priority) b. May 31 2004	Aug 12 2004	Not under PMPRB jurisdiction	a. Feb 3 2005 b. *Not to list* on Jul 14 2005	a. Jul 26 2002 (rolling Biologic License Application – Priority & Orphan designation) b. Apr 30 2003
3. Amevive (Alefacept) – for moderate to severe chronic plaque psoriasis	a. Nov 21 2001 b. Oct 6 2004	Oct 12 2004	a. Oct 12 2004 b. Within guidelines Mar 2005	a. Nov 16 2004 b. *Not to list* on May 26 2005	a. Aug 6 2001 b. Jan 30 2003
4. Ciprodex (Ciprofloxacin hydrochloride / dexamethasone) – for Acute otitis media with otorrhea & acute otitis externa	a. Nov 22 2002 b. May 10 2004	May 13 2004	Not under PMPRB jurisdiction	a. Jun 11 2004 b. *Not to list* on Jan 26 2005	a. Sep 25 2002 b. Jul 18 2003
5. Ebixa (Memantine hydrochloride) – for moderate to severe dementia of the Alzheimer type	a. Jun 26 2003 b. Dec 8 2004	Dec. 16, 2004	a. Mar 3 2004 b. Within Guidelines, Dec 2004	a. Dec 21 2004 b. *Not to list* on Nov 23 2005	a. Dec 19 2002 for *Namenda* b. Oct 16 200
6. Fabrazyme* (Agalsidase beta) – Fabry Disease	a. Aug 7 2000 (Priority) b. Jan 23 2004	Apr 8 2004 for DIN 02248966 Sep 17 2004 for DIN 02248965	Not under PMPRB jurisdiction	a. Feb 24 2004 b. *Not to list* on Nov 24 2004; resubmitted on Dec 10 2004 and recommended not to be listed on May 18 2005	a. Jun 2000 (Priority & Orphan designation) b. Apr 24 2003

* Federal, provincial and territorial governments, along with two drug companies, are participating in a three-year post-market study on Fabry's disease treatments. As part of this study, eligible Canadian patients with Fabry's disease will gain access to enzyme replacement therapy either – Fabrazyme or Replagal. For more information, go to http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/2006/2006_48_e.html

Table 2-B: **Access to New Drugs in Canada** *(cont'd)*

New Drug Trade Name (Active Ingredient (s)) & Therapeutic Use	**Health Canada** a. Filing Date b. Market Authorization Date	**Market Notification Date** (Date of first sale)	**PMPRB Price Decision** a. Under PMPRB Jurisdiction b. Status	**CDR** a. Filing Date b. Recommendation & Decision Date	**US FDA** a. Filing Date b. Approval Date
7. Gynazole.1 (Butoconazole Nitrate) – for vaginal infection	a. Jun 30 2001 b. Dec 23 2003	Apr 20 2004	a. Apr 27 2004 b. Within guidelines, Nov 2004	a. Jun 30 2004 b. *Not to list* on Jan 26 2005	a. *Information not available on FDA website.* b. Feb 7 1997 for *Femstat One*
8. Humira (Adalimumab) – Rheumatoid arthritis	a. May 15 2002 b. Sep 24 2004	Sep 24 2004	a. Sep 29 2004 b. Within guidelines, Mar 2005	a. Sep 24 2004 b. To list on Feb 11 2005	a. *Information not available on FDA website.* b. Dec 31 2002
9. Kivexa (Abacavir Sulfate /Lamivudine) – HIV infection	a. Oct 31 2003 b. Jul 25 2005	Aug. 17 2005	a. Aug 17 2005 b. Within guidelines	a. July 26 2005 b. To list on Dec 6, 2005	a. Oct 8 2003 for Epzicom b. Aug 2 2004
10. Lantus (Insulin glargine) – Antidiabetic agent (Type 1 & 2)	a. Aug 20 1999 b. Apr 3 2002	July 24 2002	a. Nov 28 2004 b. Within guidelines Feb 2005	a. Feb 11 2005 b. *Not to list* on Sep 28 2005	a. Apr 23 1999 b. Apr 20 2000
11. Myfortic (Mycophenolate Sodium) – Prophylaxis of organ rejection in allogeneic renal transplants	a. Aug 25 2003 b. Feb 4 2005	Feb 11 2005	Not under PMPRB jurisdiction	a. Mar 3 2005 b. To list on Jul 8 2005	a. Apr 30 2003 b. Feb 27 2004
12. Norprolac (Quinagolide Hydrochloride) – Hyperprolactinemia	a. Feb 22 1994 b. Jun 25 1996	Dec 29 2004	Not under PMPRB jurisdiction	a. Dec 16 2004 b. *Not to list* on Sep 28 2005; resubmitted Nov 23 2005 and currently under review	*Information not available on FDA website*
13. Relpax (Eletriptan Hydrobromide) – migraine therapy	a. Mar 21 2003 b. Aug 5 2004	Oct 13 2004	a. Nov 1 2004 b. Within guidelines, Mar 2005	a. Sep 21 2004 b. *Not to list* on Mar 23 2005	a. Oct 27 1998 b. Dec 26 2002

Table 2-B: **Access to New Drugs in Canada** *(cont'd)*

New Drug Trade Name (Active Ingredient (s)) & Therapeutic Use	**Health Canada** a. Filing Date b. Market Authorization Date	**Market Notification Date** (Date of first sale)	**PMPRB Price Decision** a. Under PMPRB Jurisdiction b. Status	**CDR** a. Filing Date b. Recommendation & Decision Date	**US FDA** a. Filing Date b. Approval Date
14. Sensipar (Cinacalcet Hydrochloride) – Secondary hyper-parathyroidism in chronic kidney disease	a. Nov 14 2003 (Priority) b. Aug 9 2004	Sep 16 2004	a. Aug 30 2005 b. Within guidelines, Sep 2005	a. Aug 20 2004 b. *Not to list* on Mar 23 2005	a. Sep 8 2003 (Priority & Orphan designation) b. Mar 8 2004
15. Strattera (Atomoxetine Hydrochloride) – attention deficit hyperactivity disorder	a. July 30 2002 b. Dec 24 2004	Feb 24 2005	a. Feb 24 2005 (10 and 18 mg/cap); and Mar 3 2005 (25, 40 and 60 mg/cap) b. Under investigation	a. Jan 25 2005 b. *Not to list* on Sep 28 2005	a. Oct 12 2001 b. Nov 26 2002
16. Tarceva (Erlotinib Hydrochloride) – non-small cell lung cancer	a. Oct 25 2004 (Priority) b. Jul 7 2005	July 19 2005	a. Jul 20 2005 b. Within Guidelines	a. Jul 19 2005 b. To list on Dec 6 2005	a. Jan 2004 (Priority rolling review) b. Nov 18 2004
17. Telzir (Fosamprenavir Calcium) – HIV infection	a. May 23 2003 b. Dec 10 2004	Dec 22 2004	a. Feb 28 2005 b. Within Guidelines, Sep 2005	a. Jan 24 2005 b. To list on Jun 16 2005	a. Feb 3 2003 for *LEXIVA* 700 mg Tablets b. Oct 20 2003
18. Viread (Tenofovir Disoproxil Fumarate) – HIV infection	a. Dec 28 2001 (Priority) b. Mar 18 2003	Mar 15 2004	a. Mar 15 2004 b. Advance Ruling Certificate, Jun 3 2004	a. Feb 23 2004 b. *Not to list* on Aug 25 2004; resubmitted on Aug 11 2005 and recommended for listing on Mar 15 2006	a. May 1 2001 (Priority) b. Oct 26 2001
19. VFEND (Voriconazole) – Invasive aspergillosis	a. Sep 3 2003 b. Aug 20 2004	Nov 12 2004	a. Nov 15 2004 b. Within guidelines, Mar 2005	a. Oct 25 2004 b. To list on Apr 14 2005	a. Nov 17 2000 b. May 24 2002
20. Yasmin (Drospirenone /Ethinyl Estradiol) – oral contraceptive	a. Sep 2 1999 b. Dec 10 2004	Dec 22 2004	a. Dec 22 2004 b. Within guidelines, July 2005	a. Jan 20 2005 b. To list on Jun 16 2005	a. May 17 1999 b. May 11 2001

Table 2-C: Additions to Provincial and Territorial Drug Plans

Table 2C provides information about the timing of listing decisions by federal, provincial and territorial drug plans on two drugs subject to a formulary listing recommendation by the CDR[19].

Federal, provincial and territorial governments continue to make final formulary listing decisions, taking into account recommendations provided by the CDR[20]. Each drug plan differs with respect to the conditions for which benefits are provided. More information on individual drug plans may be found by consulting with the provincial and territorial health ministries.

Once a product has received market authorization from Health Canada and a decision on pricing from the PMPRB, the remaining time to drug plan listing is determined by:

(1) The decision taken by the manufacturer regarding *when* to file a given submission with the CDR, this may be influenced by the manufacturer's marketing strategy;

(2) The time it takes the manufacturer to prepare a given submission for the CDR and each province and territory to which it also submits – submissions may differ by province and territory; and

(3) The time taken by the CDR and the province or territory to review the submission and make a listing decision.

Health Canada's non-insured health benefits formulary for First Nations and Inuit (managed by the First Nations and Inuit Health Branch – or FNIHB) provides coverage for prescription and over-the counter medications that are not covered by other private or provincial/territorial health insurance plans.

[19] Information in Table 2-C was provided by Brogan Inc. See http://www.broganinc.com/

[20] Quebec is not part of the CDR.

Table 2-C: Additions to Provincial and Territorial Drug Plans *(cont'd)*

Table 2C Legend:

EDS – Exception Drug Status – restricted coverage under certain circumstances (as outlined within the drug plan)

FB – Full Benefit Status – full coverage (subject to a deductible and may apply to specific health conditions or age groups as outlined within the drug plan)

LU – Limited Use Status – restricted coverage under certain circumstances (as outlined within the drug plan)

SA – Special Authorization Status – restricted coverage under certain circumstances that may require the attending clinician to submit a formal request for such coverage (as outlined within the drug plan)

X – Not Listed – where the drug has not been listed on a drug plan (either following a review or with a review still pending)

New Drug Trade Name, (Active Ingredient (s)) & Therapeutic Use	a. Listing Status on Provincial and Territorial Drug Plans (as of April 13, 2006) b. Number of days from Market Authorization date to Listing										
i. Health Canada Market Authorization date **ii. CDR** Recommendation & Decision Date	**BC**	**AB**	**SK**	**MB**	**ON**	**QC**	**NB**	**PEI**	**NS**	**NF**	**Health Canada FNIHB**
1. Axert (Almotriptan Malate) – for the acute treatment of migraine headache in adults i. Sep 29, 2003 ii. To list on May 27, 2004	a. FB on Aug 15/ 05 b. 686	a. SA on Jul 1/04 b. 276	a. EDS on Oct 1/ 04 b. 368	x	x	a. FB on Jun 30/04 b. 275	a. SA on May 31/05 b. 610	x	a. EDS on Jul 1/ 04 b. 276	x	a. FB on Oct 1/ 04 b. 368
2. Combigan Ophthalmic Solution (Brimonidine Tartrate / Timolol Maleate) – Glaucoma/ ocular hypertension i. Dec 9, 2003 ii. To list on May 24, 2004	a. FB on Aug 15/05 b. 615	a. SA on Jan 1/ 05 b. 389	a. FB on Oct 1/ 04 b. 297	a. FB on Sep 1/ 04 b. 267	a. LU on Nov 4/04 b. 331	a. FB on Oct 6/ 04 b. 302	a. FB on Sep 23/05 b. 654	x	a. FB on Aug 1/05 b. 601	a. FB on Oct 14/04 b. 310	a. FB on Oct 1 /04 b. 297

Annex A: Definitions

These plain language definitions are intended for general understanding and are not necessarily the formal definitions used by Health Canada or those that appear in the legislation or regulations.

1. Therapeutic Product Types

The following therapeutic product types are described in this report.

(a) Pharmaceuticals: drugs that are mostly synthetic products that are made from chemicals. Pharmaceuticals include prescription and non-prescription drugs such as antibiotics, disinfectants, as well as low risk products such as sunscreens, antiperspirants and toothpaste.

(b) Biologics: drugs that are made from biological starting material, including those produced using recombinant DNA procedures. They include vaccines, blood and blood products and many hormonal products such as insulin. Radiopharmaceuticals (drugs that contain radioactive components) are included as part of this product group in this report as they are regulated by the same program within the HPFB.

(c) Medical Devices: any article or instrument used in the diagnosis, treatment, mitigation, or prevention of a disease, disorder, or abnormal physical state, and in restoring, correcting, or modifying body functions in humans or animals. Devices range from band-aids to pacemakers and also include those used in the prevention, diagnosis, and care of pregnancy.

2. Submissions for New Drugs and Medical Devices

The focus of this report is on submissions for new drugs and medical device applications. Definitions are provided below.

I. Submission for New Drugs: *include the following submission types for pharmaceuticals and biologics, where 'brand name' and 'generic' refers to pharmaceuticals.*

(a) Priority (Brand Name or Biologic): submissions for products intended for the treatment,

prevention, or diagnosis of serious, life-threatening, or severely debilitating illnesses or conditions where: no product is presently marketed in Canada or; the new product represents a significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies. Submissions granted priority review status are subject to the same quality, safety, and efficacy requirements as non-priority submissions – with shorter performance target times. In this report, priority includes submissions under advance consideration for a Notice of Compliance with Conditions (refer to Regulatory Decision Types below for more information).

(b) Standard (Brand Name or Biologic): a submission that contains scientific information about the product's safety, efficacy, and quality and is typically 100 to 800 binders of data. It includes: the results of both the pre-clinical and clinical studies; details regarding the production of the drug; its packaging and labelling; information regarding therapeutic claims; conditions for use; and side effects.

(c) Supplemental (Brand Name, Generic, or Biologic): submissions to support proposed changes to already authorized products. Such changes might include: changes to the dosage form or strength of the drug product; labelling; recommended route of administration; and expanded indications (claims or conditions of use) for the drug product.

(d) Generic Standard: submissions that demonstrate that the proposed generic product is as safe and efficacious, and manufactured to the same quality standards, as the brand name product. Typically between 10 and 20 binders of data, the submission includes scientific information that shows how the generic product performs compared with the brand name product, as well as details regarding production, packaging, and labelling.

II. Medical Device Submissions: *includes the application types listed below.*

(a) Medical Device Applications: medical devices are categorized into four classes based on the classification rules of the Medical Devices Regulations. Class I devices present the lowest potential risk (e.g. thermometers) and do not require a medical device licence for their sale in Canada. Class II, III, and IV devices range from low, moderate, to high risk, respectively, and manufacturers must obtain a medical device licence before their products can be legally sold in Canada. As the class of the device increases, more data is required from the manufacturer in support of safety and effectiveness of the device.

(b) Medical Device Amendment Applications: changes to a licensed medical device (Class II, III, or IV) – such as a change in design, indications, or additions/deletions of identifiers.

3. Regulatory Decision Types

For this report, four decision types are provided, including: market authorizations; pending market authorizations; interim decisions; and refusals. Further detail on each decision type is outlined below.

I. Market Authorizations: *apply to submissions for new drugs and medical device applications that have been authorized for sale in Canada.*

(a) Notice of Compliance: : if, at the completion of a review of a submission for a new drug, HPFB concludes that the benefits outweigh the risks and that the risks can be mitigated and/or managed, the product is issued a Notice of Compliance (NOC). This allows the manufacturer to sell the product in Canada.

(b) Notice of Compliance with Conditions (NOC/c): may be granted to provide earlier market access to potentially life-saving drugs. Eligibility is restricted to drugs intended for the treatment, prevention, or diagnosis of serious, life-threatening, or severely debilitating illnesses or conditions where promising clinical evidence indicates that the product provides an effective treatment where: no alternative therapy is available on the Canadian market; or the new product represents a significant improvement in the benefit/risk profile over existing products. An NOC/c provides the manufacturer authorization to market a drug with the condition that it undertakes additional studies to confirm the clinical benefit. Conditions associated with approval allow HPFB to monitor the safety and effectiveness of the drug through enhanced post-market surveillance.

(c) Medical Device Licence: upon completion of a medical device application review, HPFB concludes that the evidence exists to support the safety and effectiveness of the device as required by the regulations; a Medical Device Licence is issued, allowing the manufacturer to sell the device in Canada.

(d) Medical Device Licence with Conditions: HPFB may issue a Medical Device Licence with Conditions when there is reasonable assurance that the device is safe and effective, but where supplemental information would further support this conclusion. Such information must be submitted within a prescribed timeframe.

II. Pending Market Authorizations: *apply to those submissions for new drugs that have been provided with an 'issuable' NOC but are not yet authorized for sale due to outstanding regulatory issues that require resolution.*

(a) Issuable NOC (Patent): HPFB may issue an NOC that is on hold due to the Patented Medicines (Notice of Compliance) Regulations.

(b) Issuable NOC (Rx to OTC): HPFB may issue an NOC that is on hold due to a change in status of the drug, from prescription to over-the-counter.

III. Interim Decisions: *apply to submissions for new drugs and medical device applications that contain deficiencies and are insufficient in complying with regulatory requirements for market authorization. These regulatory decisions (described below) have provided the manufacturer with a notice of the information required and a time period in which to respond with the missing documentation.*

(a) Notice of Deficiency: If a major deficiency is detected that prevents completion of the scientific review of a submission for a new drug, HPFB can issue a Notice of Deficiency (NOD). The manufacturer is provided with a specified period in which to respond with the required information.

(b) Notice of Non-Compliance: If, upon completion of the new drug review, the submission is found to be insufficient in complying with the requirements set out in the *Food and Drugs Act and Regulations*, a Notice of Non-Compliance (NON) may be issued. This notice outlines all the outstanding issues and requests for information that HPFB has about the submission. The manufacturer has a specified period in which to respond with the required information.

(c) Additional Information Letter: If, during the course of the scientific review of a medical device application, there remains insufficient information to determine whether the device meets the safety and effectiveness requirements, an Additional Information Letter may be issued, providing the manufacturer with a specified period in which to respond with the required information.

IV. Refusals: *are final decisions where the manufacturer has been provided with the opportunity to improve the submission or application but has been unable to satisfy the requirements of the Food and Drugs Act and Regulations. In the case of a refusal, a manufacturer may re-file a new application at a future time, without prejudice. Refusal decision types are outlined below.*

(a) Notice of Deficiency Withdrawal Letter: May be issued if the manufacturer fails to submit the requested information in response to a NOD within the required time period, or the response contains unsolicited information, is incomplete or deficient.

(b) Notice of Non-Compliance Withdrawal Letter: May be issued if the manufacturer fails to submit the requested information in response to a NON within the required time period, or the response contains unsolicited information, is incomplete or deficient.

(c) Refusal Letter: May be issued if the manufacturer fails to submit the requested information in response to an Additional Information Letter within the required time period, or the response contains unsolicited information, is incomplete or deficient.

Annex B: The Role of the Patented Medicine Prices Review Board and the Common Drug Review

Price Review – The Patented Medicine Prices Review Board

The Patented Medicine Prices Review Board (PMPRB) is an independent quasi-judicial administrative agency, responsible for regulating the prices that patentees charge, the "factory-gate" price for prescription and non-prescription patented drugs sold in Canada to wholesalers, hospitals, or pharmacies for human and veterinary use, to ensure that they are not excessive. The PMPRB regulates the price of each patented drug product, including each strength of each dosage form of each patented medicine sold in Canada.

Under the *Patented Medicines Regulations*, patentees are required to file price and sales information twice a year for each strength of each dosage form of each patented medicine sold in Canada for price regulation purposes. Patentees are also required to file research and development expenditures once a year for reporting purposes. Manufacturers must inform the PMPRB of their intention to sell a new patented medicine but are not required to obtain approval of the price before they do so.

In October 2005, as part of the National Pharmaceuticals Strategy, First Ministers gave the PMPRB responsibility to monitor and report on the prices of non-patented (prescription) drugs. For more information, go to http://www.scics.gc.ca/cinfo05/830866004_e.html

Common Drug Review – The Canadian Agency for Drugs and Technologies in Health *(formerly known as the Canadian Coordinating Office for Health Technology Assessment)*

The Canadian Agency for Drugs and Technologies in Health (CADTH) is Canada's health technology agency whose goal it is to increase access to and use of evidence as a basis for informed decisions about technology use in Canada's publicly funded health care system.

The broad mandate of CADTH includes the Common Drug Review (CDR), a single process to assess new drugs for potential coverage by participating federal, provincial and territorial drug benefit plans. CADTH develops evidence-based clinical and pharmacoeconomic reviews which are used by the Canadian Expert Drug Advisory Committee (CEDAC), an independent advisory body of professionals in drug therapy and evaluation, as the basis for its formulary listing recommendations to the participating drug plans. CDR commenced in 2004. Federal, provincial, and territorial governments continue to make final formulary listing decisions, taking into account recommendations provided by CDR.