NEWSletter

Volume I, Issue No. 1 July 1997

Inside ...

Welcome to the PMPRB NEWSletter

In our desire to keep our stakeholders better informed, we are introducing the PMPRB NEWSletter.

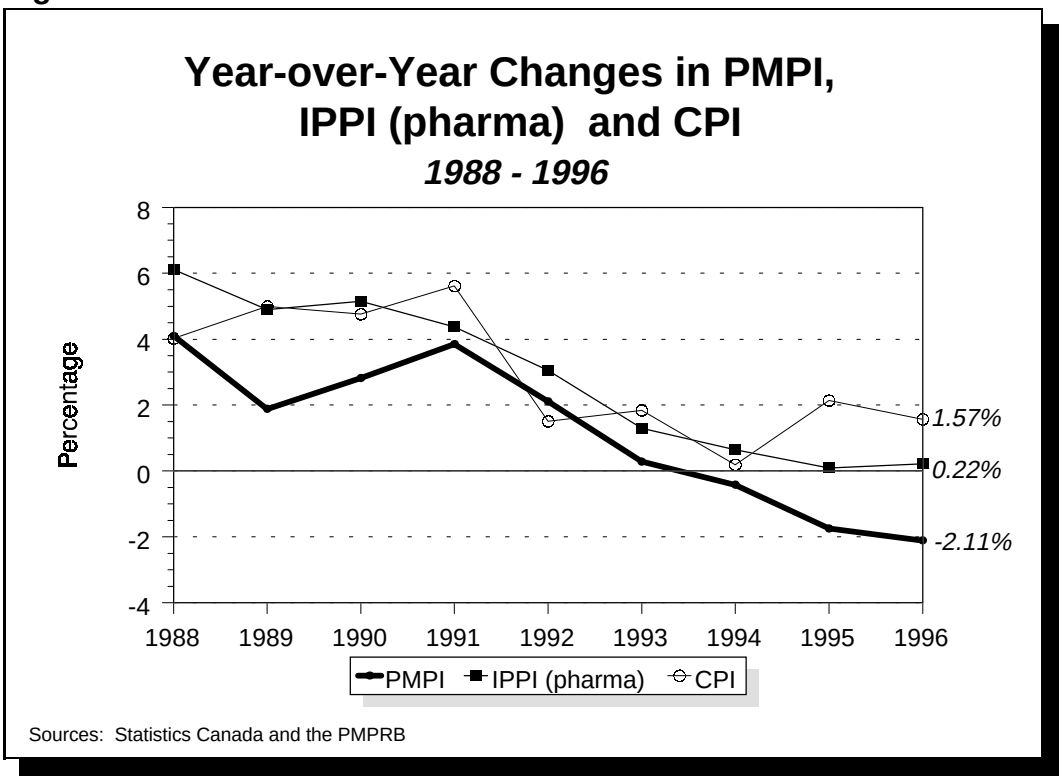
NEWSletter is intended to provide you with current information on drug prices, our activities and a better mix of news from the PMPRB. It will be published twice a year.

We hope NEWSletter will meet your information needs. We look forward to receiving your comments.

Price and Expenditure Trends -- Patented and All Drugs

For the third consecutive year, manufacturers' prices of patented drug products declined in 1996. Prices of patented drugs, as measured by the Patented Medicine Price Index (PMPI), fell by 2.11% from their level in 1995. In contrast, the manufacturers' price index for all drug products, including both patented and non-patented drugs, increased slightly in 1996. This represents the third consecutive year when price increases for all drugs, as measured by Statistics Canada, have been below one percent, as shown in Figure 1.

Figure 1



This decline in the prices of patented drugs comes at a time when total expenditures on drugs, including both patented and non-patented drugs, are still rising.

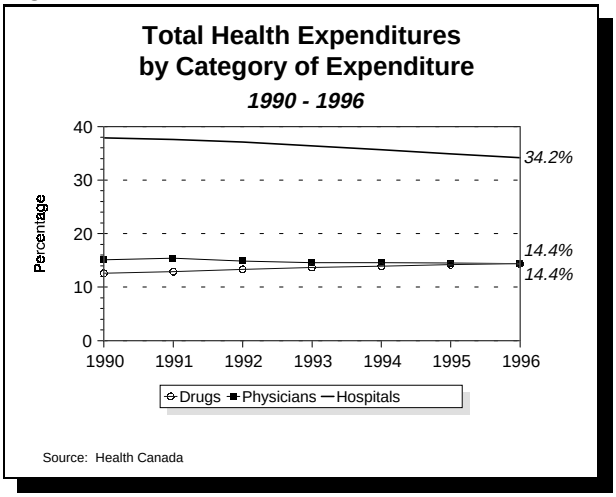
Health Canada estimates that total expenditures on drugs increased to $10.8 billion in 1996. Drug spending has increased faster than other key health sectors, going up from 9.8% of total health expenditures in 1983, to 12.6% in 1990 and 14.4% in 1996. As shown in Figure 2, Health Canada reported that total drug expenditures went up 2.7% in 1996. There are several factors which explain why total drug expenditures continue to rise while prices of patented drugs have fallen:

- Patented drugs only represent about 46% of sales of all drugs.

- Total expenditures on drugs include wholesale costs and pharmacists' dispensing fees, which are not included in the PMPI.

- Increased expenditures are largely a result of increased use of prescription drugs in Canada and the impact of prescribing newer, more expensive drugs. These factors may lead to greater total expenditures even if actual price levels do not change or even fall. This demonstrates that total expenditures on drugs by Canadians continue to increase at a faster rate than prices and that utilization and prescribing patterns are the major factors behind these expenditure increases.

Figure 2



The *Patent Act* provides that the PMPRB shall consider changes in the Consumer Price Index (CPI) in determining if a price of a patented drug product is excessive. The CPI, published by Statistics Canada, measures changes in consumer prices. The PMPRB Guidelines provide that the prices of patented drug products may not increase by more than the CPI. In 1996, the CPI increased at 1.6% while the PMPI declined by 2.1%. Since the creation of the PMPRB, with the exception of 1992, increases in manufacturers' prices for patented drugs have been kept below the rate of inflation.

For more information on the PMPI and other price indices, please refer to the PMPRB previous Annual Reports.

1996 Annual Report to be released in the Fall

The Annual Report of the PMPRB is normally tabled in Parliament in June, prior to the summer recess. This year, dissolution of Parliament for the June 2 election pre-empted the tabling of the ninth Annual Report.

The *Patent Act* provides for the Minister of Health to table the Annual Report in Parliament within thirty sitting days from the date of receipt of the document. **The Annual Report will be submitted to the newly appointed Minister, the Honourable Allan Rock, this summer with a view to having the Report tabled during the Fall session.**

In the interim, statistics on price trends and R&D in Canada in 1996 are included in this issue of the NEWSletter.

If you want to know more, please contact Sylvie Dupont-Kirby by telephone: (613) 954-8299, fax: (613) 952-7626, e-mail: pmprb@pmprb-cepmb.gc.ca, or access the PMPRB's new website at http://www.pmprb-cepmb.gc.ca.

New Drug Products in 1996

Eighty-four new patented drug products (DINs) were introduced in Canada in 1996. Close to half of the 80 new drug products for human use, 37 DINs, were presentations of 21 new active substances (NASs). For 10 of the 21 NASs, patentees submitted that they should be reviewed as category 2 drugs, breakthrough or substantial improvement. After review, the PMPRB's Human Drug Advisory Panel (HDAP) recommended that three NASs, (4 DINs), were category 2 drugs with the remainder of the NASs being grouped into category 3, drugs providing moderate, little or no improvement over existing drugs.

Ethyol, Norvir and Reopro were the three drugs (4 DINs) classified as breakthrough or substantial improvement (category 2) products. Here are the "Factors Considered" by the HDAP in making its recommendations.

ETHYOL (amifostine) 500 mg lyophilized powder for injection
DIN 02218054
ATC CLASS V03AF

Indication: Cytoprotective agent against the cumulative toxicities associated with cisplatin and haematological toxicities associated with cyclophosphamide as well as platinum anticancer agents in patients with advanced solid tumours of non germ cell origin.

Factors Considered: At the time of this review, no alternative therapies have been proven to be effective as a cytoprotective agent against the cumulative renal toxicities associated with cisplatin and the haematological toxicities associated with cyclophosphamide and platinum anticancer agents. Issuance of the Notice of Compliance (NOC) by the Health Protection Branch is evidence that the efficacy of amifostine in this patient population has been adequately proven. Ethyol is therefore the first drug product available in Canada to be demonstrated to be effective for this indication. Co-administration of amifostine with cisplatin should reduce its adverse effects and allow more patients to successfully complete their chemotherapy.

NORVIR (ritonavir) 100 mg capsule, 80 mg/mL liquid
DINs 02229137, 02229145
ATC CLASS J05AX

Indication: In combination with reverse transcriptase inhibitor nucleoside analogues for the treatment of HIV infection when therapy is warranted.

Factors Considered: There is evidence to support that protease inhibitors (ritonavir, saquinavir, indinavir) in combination with reverse transcriptase inhibitor nucleoside analogues are a substantial improvement in the management of HIV disease. Although the protease inhibitors have not been compared head-to-head with nucleoside analogues, the significant effect of protease inhibitors on viral load observed is considered a substantial reduction; this in combination with the increase in CD4 cell count and increase in short term survival in advanced HIV disease support a category 2 classification of the protease inhibitors.

Factors Not Considered: The clinical significance of the differences between the three protease inhibitors currently available on the Canadian market has not been evaluated in this review. Since the three agents were introduced within weeks of one another, it is not necessary to demonstrate that Norvir, the first patented protease inhibitor, is a substantial improvement over the other protease inhibitors to classify it as a category 2 drug product.

REOPRO (abciximab) 2 mg/mL injection
DIN 02216973
ATC CLASS B01AC

Indication: As adjunct to percutaneous transluminal coronary angioplasty (PTCA) or atherectomy for the prevention of acute cardiac ischemic complications in patients at high risk for abrupt closure of the treated coronary vessel.

Factors considered: Abciximab is a new molecular entity and among the first monoclonal antibody drug therapies to be approved by the Health Protection Branch for sale in Canada. Good clinical evidence is available to show a substantial reduction in the number of events following PTCA in high risk patients compared to ASA and heparin. The most obvious clinical benefit is the delay in the need for coronary artery bypass graft (CABG) procedures. There is currently no direct comparator for abciximab available on the Canadian market.

Factors Not Considered: While ticlopidine (Ticlid) may be a potential alternative therapy for this indication, it was not considered in this evaluation of abciximab.

Health Canada adopts the WHO ATC system

Health Canada has recently announced its decision to adopt the World Health Organization's (WHO) Anatomical Therapeutic Chemical (ATC) system as the primary therapeutic classification system within their revamped Drug Product Database (DPD). The PMPRB has used the ATC system for many years and has developed and maintained a Canadianized version.

PMPRB staff are currently working with staff of the Therapeutic Products Directorate to assign the WHO ATC codes to all DINs in the DPD. A regularly updated ASCII file of the DPD is accessible on the Therapeutic Products Directorate website. It is intended for users who download data into their own systems. The Directorate reports that it is working to improve access to this important source of information on Canadian drug products through development of query capability at the Website and a CD ROM version of the DPD.

Although the PMPRB will no longer publish a Canadianized version of the ATC, the classification system will remain an integral part of the PMPRB's review procedures for new patented drug products. The last published edition, the 1995 ATC, can continue to serve as guide to the selection of therapeutic comparators until such time as the WHO ATC classification is fully implemented within the DPD. PMPRB staff will remain available to answer queries regarding the ATC classification of new patented drug products and offer assistance to any organization making the transition from the Canadian to the WHO ATC codes.

If you have any questions or require additional information, please contact Pat Carruthers-Czyzewski, by telephone: (613) 954-7624, fax: (613) 952-7626, or
e-mail: psa@pmprb-cepmb.gc.ca

Parliamentary Review of Bill C-91

The Standing Committee on Industry of the House of Commons conducted public hearings on its review of Bill C-91 during March and April and released its report on April 24, 1997. The Chairperson and Vice-Chairperson of the Board appeared before the Committee on March 4 and the PMPRB submitted a number of documents to the Committee during its review. The Government's response to the Committee's Report, issued on April 25, 1997, noted the concerns of Canadians about drug costs and their impact on the health care system. Among other things, it acknowledged the need to strengthen the PMPRB and to work with provincial and territorial authorities to examine broadening its mandate to include non-patented drugs. Ministers also agreed to work with the PMPRB to review the mechanisms for regulating the prices of patented drugs and to improve the transparency of the price review process.

The PMPRB looks forward to working with the federal and provincial governments in meeting these challenges.

Exchange Rates

The methodology for calculating exchange rates for purposes of the PMPRB's International Price Comparisons is described in Schedule 3 of the *Compendium of Guidelines, Policies and Procedures*. The following table provides the average 36-month exchange rates for new drug products introduced between December 1996 and October 1997.

Month of Introduction	France	Germany	Italy	Sweden	Switzerland	United Kingdom	United States
Dec 96	0.25777500	0.88851667	0.00084761	0.18536667	1.06540833	2.10177163	1.36200747
Jan 97	0.25916389	0.89274444	0.00085008	0.18660000	1.07279444	2.10660245	1.36375932
Feb 97	0.26010278	0.89532222	0.00085167	0.18774167	1.07772500	2.10991470	1.36509496
Mar 97	0.26096111	0.89741111	0.00085325	0.18882778	1.08199722	2.11407929	1.36577510
Dec 96	0.26202778	0.90046667	0.00085586	0.19000833	1.08668333	2.12169701	1.36634918
May 97	0.26292778	0.90324444	0.00085869	0.19112778	1.08993333	2.12956699	1.36721293
Jun 97	0.26366667	0.90559722	0.00086108	0.19191389	1.09197500	2.13706296	1.36808057
Jul 97	0.26399722	0.90657778	0.00086169	0.19232500	1.09225000	2.14311671	1.36844488
Aug 97	0.26408889	0.90663889	0.00086147	0.19250833	1.09176111	2.14787383	1.36865321
Sep 97	0.26420278	0.90665278	0.00086069	0.19266667	1.09156667	2.15402786	1.36897363
Oct 97	0.26411389	0.90600278	0.00085939	0.19268611	1.09119167	2.15892720	1.36896080

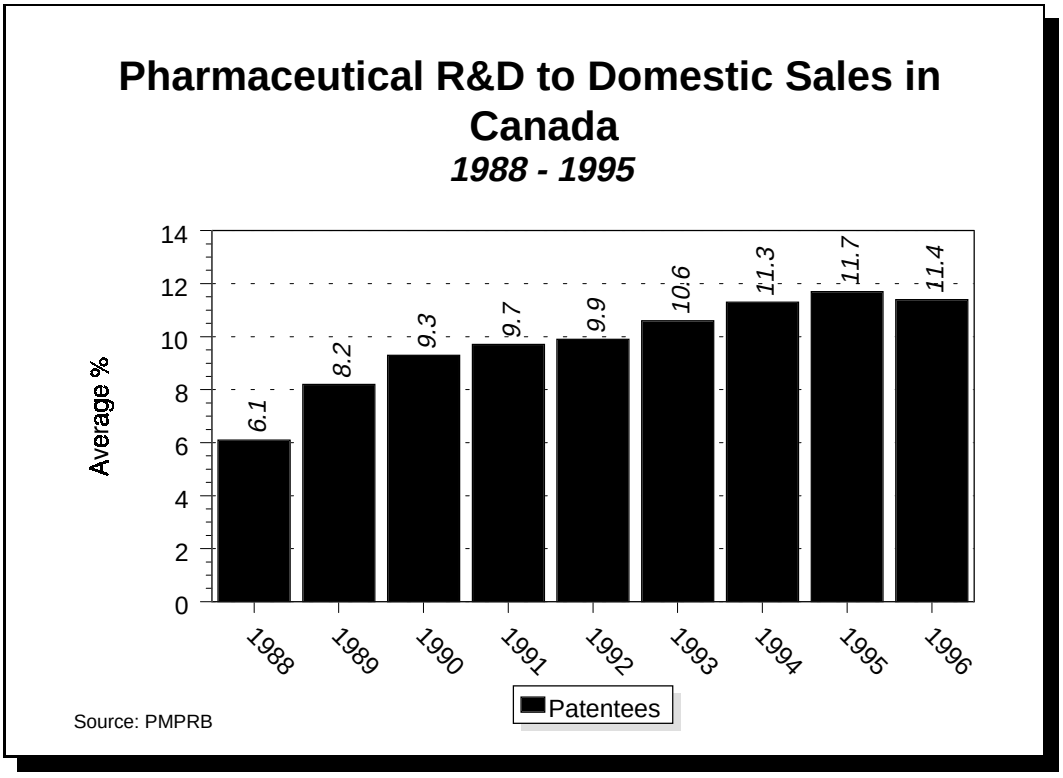
If you have any questions or require additional information, please contact Arlene Lang by telephone: (613) 957-3570, fax: (613) 952-7626, or by e-mail: c&e@pmprb-cepmb.gc.ca. Patentees can contact the Compliance Officer assigned to their company.

Research & Development in 1996

R&D spending by pharmaceutical patentees in Canada continues to increase, reaching $665.3 million in 1996, an increase of $40 million or 6.4% from 1995.

But while R&D expenditures are up, the ratio of R&D spending to sales fell in 1996 for the first time since the PMPRB began reporting. In 1996 the overall ratio, based on the 72 patentees reporting to the PMPRB was 11.4%, down from 11.7% in 1995. The R&D to sales ratio for members of the Pharmaceutical Manufacturers Association of Canada (PMAC) was 12.3%, down from 12.5% in 1995.

Figure 1



The proportion of pharmaceutical R&D spending on basic, applied and other R&D continues to remain unchanged, with basic research spending comprising just under 22%, down slightly from 1995. The largest share of R&D spending continued to be on applied research at $396.4 million or 62.9% of the total. Other qualifying research expenditures was $97.1 million or slightly over 15% of total R&D spending in 1996.

Canada's International Ranking on R&D

The PMPRB has recently circulated a discussion paper comprising R&D spending by brand name pharmaceutical companies in Canada to the seven countries listed in the *Patented Medicines Regulations.* The paper, *A Comparison of Pharmaceutical R&D Spending in Canada and Selected Countries*, reports on the period 1988 to 1995.

While total pharmaceutical R&D expenditures grew faster in Canada than in any of the comparator countries, it continued to trail other countries with respect to the amount spent on

R&D and the average R&D-to-sales ratio. The R&D-to-sales ratio in Canada increased to 11.7% by 1995, reaching the same level as Italy but remaining substantially behind all other countries. The average R&D-to-sales ratio for the seven countries was 20.1% in 1995.

A summary of this comparative study is available on our website: http://www.pmprb-cepmb.gc.ca. If you have any questions on R&D, or need additional information, please contact Dr. Ronald J. Corvari, by telephone: (613) 952-3305, by fax: (613) 952-7627, by e-mail: pmprb@pmprb-cepmb.gc.ca.

PMPRB wired!

Long awaited, the PMPRB web site is here. If you want to know more about the PMPRB and you have access to the Net, look for our site at **http://www.pmprb-cepmb.gc.ca**.

We look forward to hearing from you.

What you want to watch for ...

- *The Difficulty in Assessing the Relative Therapeutic Merit of New Antineoplastic Drugs*, in an upcoming edition of the Canadian Journal of Clinical Pharmacology.
- *A Comparison of Pharmaceutical Research and Development Spending in Canada and Selected Countries*, August 1997
- 1996 PMPRB Annual Report, Fall 1997
- Speech by Dr. Robert G. Elgie, Chairperson of the PMPRB, to C-PIC '97, October 21, 1997, on the future role of the PMPRB

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Mandate of the PMPRB

The PMPRB was created in 1987 under the *Patent Act* to protect consumer interests by regulating manufacturers' prices of patented drugs.