Future medicines:
Regulations , Decision Makers and Patient Concerns

CAPT ACTP
Canadian Association for Population Therapeutics

Annual meeting ,Ottawa,Ont. April 19,2011

Université de Montréal

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Disclaimer

The views offered here are personal and primarily reflect my experience both as a concerned citizen and health care professional

Conflicts of interest to declare: None

Canada Fact Sheet 2007-2008

Note: All figures are estimates based on sources reviewed from Health Canada and CIHI

Human drug products registered : **18-20,000**

Medical devices registered : **40,000**

User fees as % of regulatory services costs: **25 %**

Annual marketed products ADR reports : **20,000**

Annual Clinical trial apps. & amends: **2600**

Annual number of CT-ADR reports in Canada: **46,000**

Annual drug expenditures in Canada: **$30 billions**

% of Canada's population lifetime exposure to drug products: **> 90%**

Where would you look for information on drug regulation in Canada ?

H

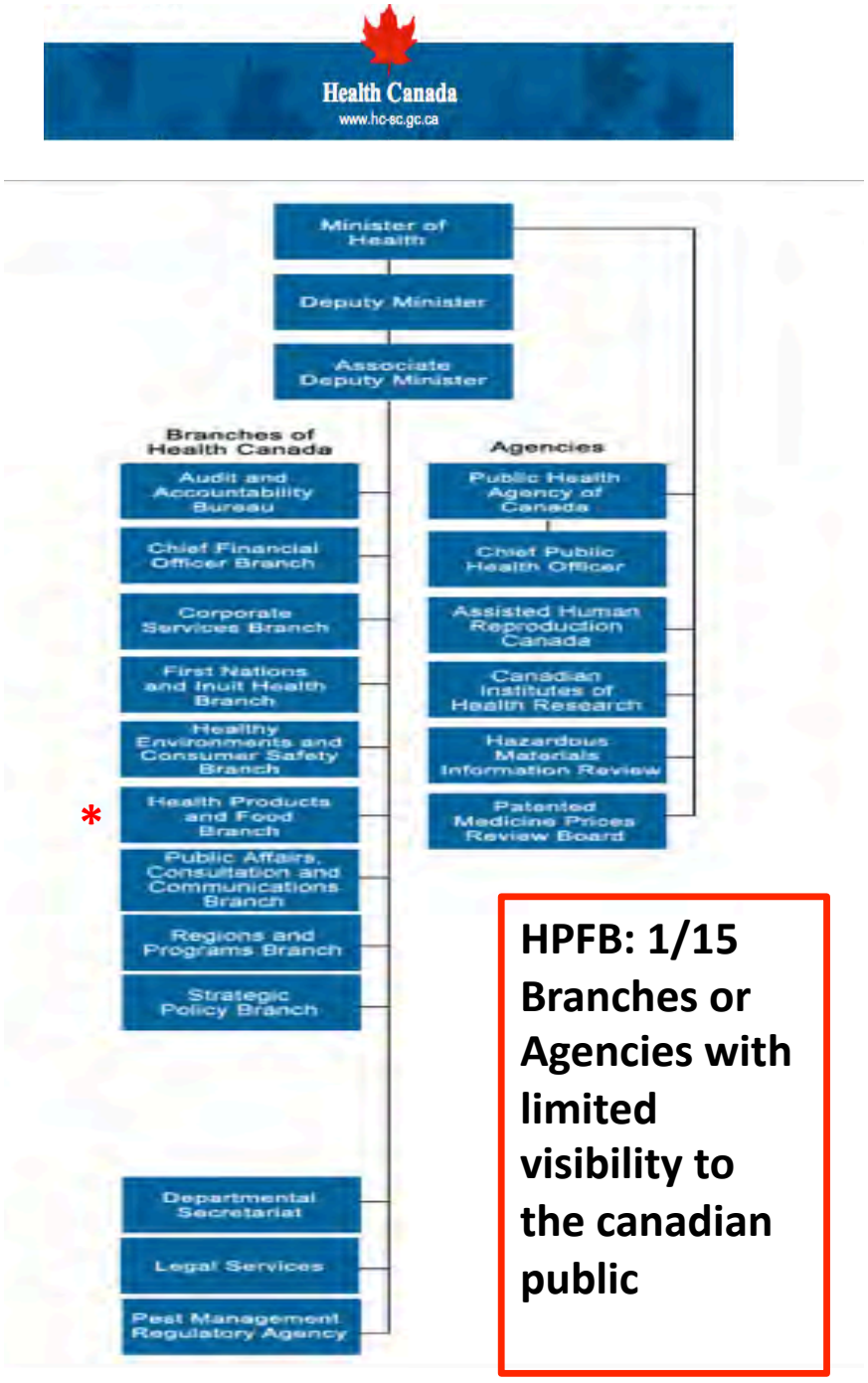
- Hazardous Materials Information Review Commission
- Health Canada
  - Interagency Advisory Panel on Research Ethics
- House of Commons
- Human Resources and Skills Development Canada (HRSDC)
  - Canada Employment Insurance Commission
  - Federal Labour Standards Review Commission
  - National Seniors Council
  - Pension Appeals Board
  - Policy Research Initiative
  - Service Canada

T

- Tax Court of Canada
- Taxpayers' Ombudsman - Canada Revenue Agency (CRA)
- Telefilm Canada
- Translation Bureau - Public Works and Government Services Canada
- Transport Canada
  - Canada Lands Company Limited
  - Marine Services On-line
- Transportation Appeal Tribunal of Canada
- Transportation Safety Board of Canada
- Treasury Board of Canada Secretariat
  - National Joint Council

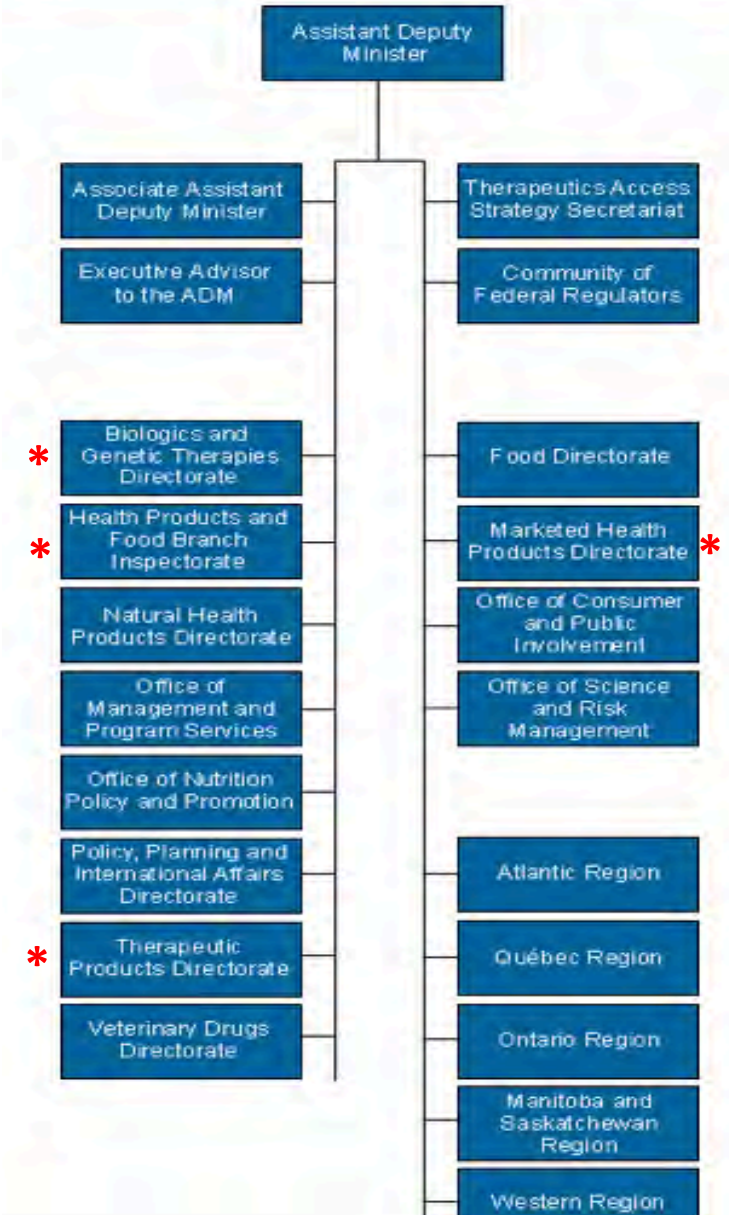
W

- Western Economic Diversification Canada

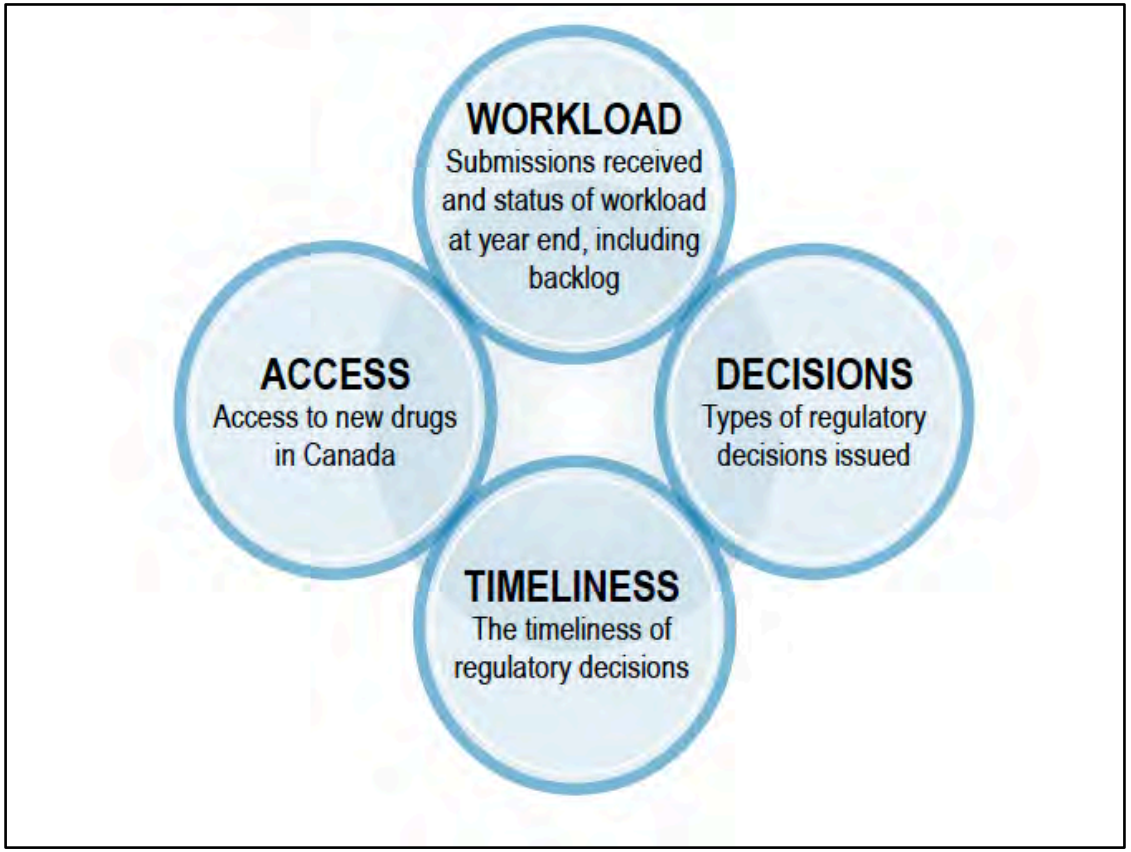


HPFB: 1/15 Branches or Agencies with limited visibility to the canadian public

Health Products and Food Branch



HPFB: Performance reporting framework for reviewing drugs and medical devices



Source: HPFB Performance report,2006-2007

WORKLOAD
Submissions received and status of workload at year end, including backlog

Workload

Submissions received

In 2006, we received the highest number of submissions for pharmaceutical and biologic drugs in the past six years.

Figure 1 **Submissions received for pharmaceuticals**

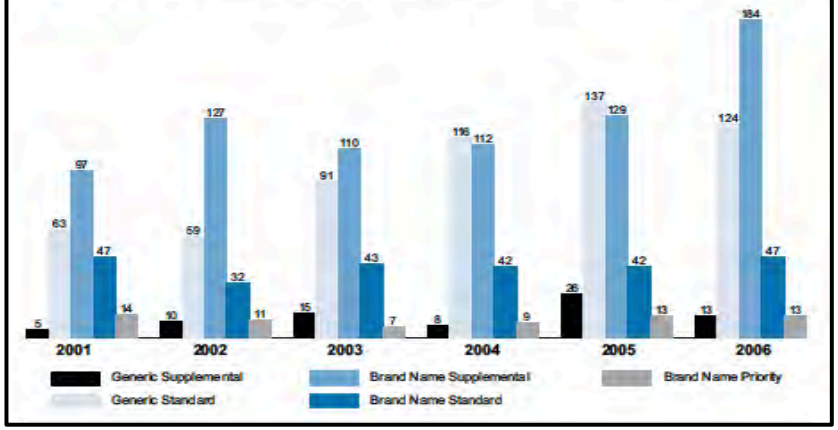


Figure 2 **Submissions received for biologic drugs**

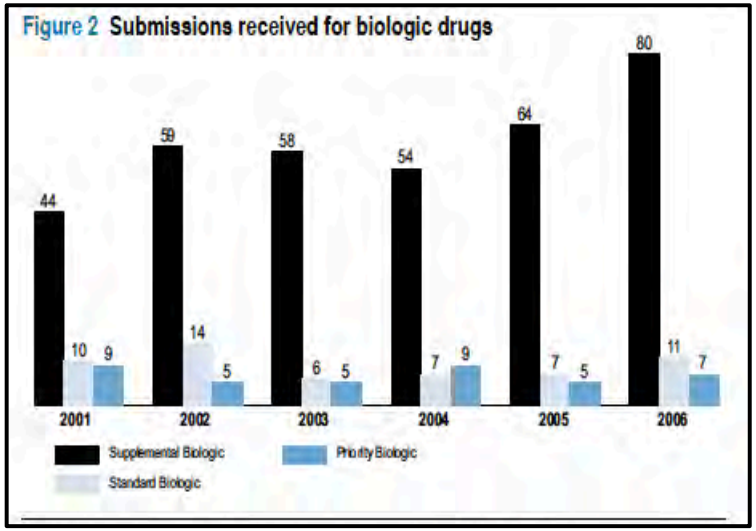
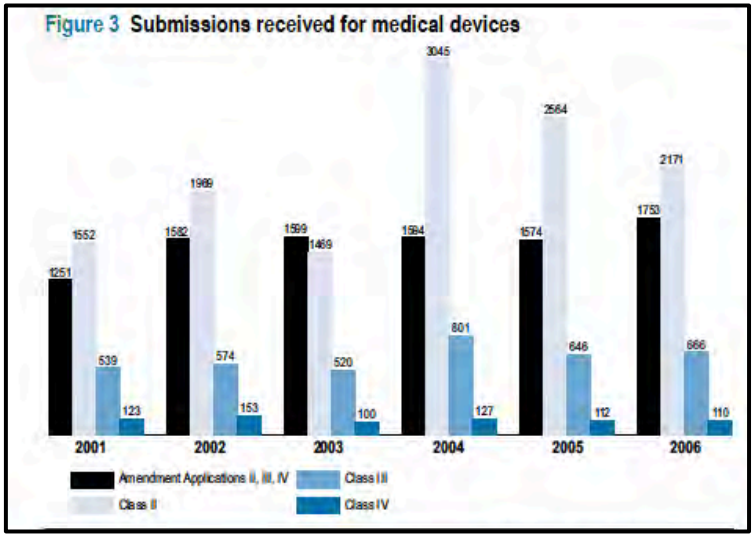


Figure 3 **Submissions received for medical devices**

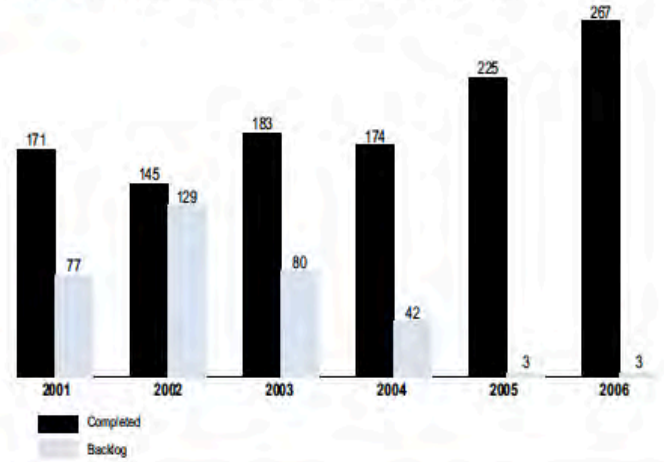


In 2006, HPFB received 1,686 pharmaceutical drug clinical trial applications and 272 biologic CTAs. It also received 931 pharmaceutical drug clinical trial application amendments (CTA-A) and 287 biologic CTA-As.

Source: HPFB Performance report,2006-2007

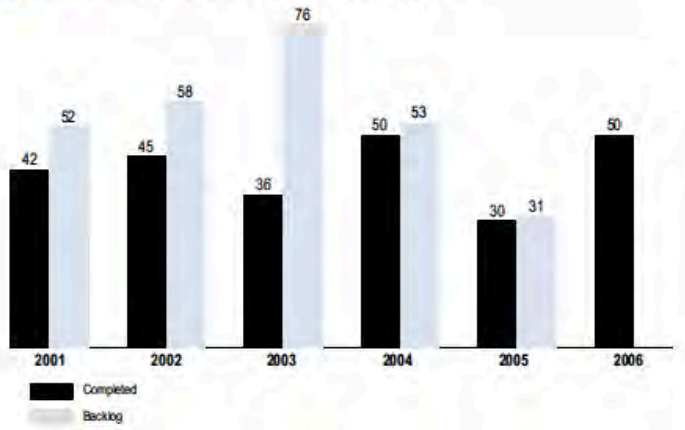
WORKLOAD
Submissions received and status of workload at year end, including backlog

Figure 4 Workload for pharmaceuticals (on December 31)



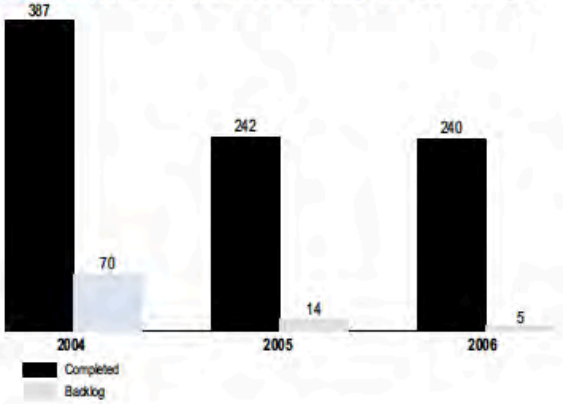
Backlog for pharmaceutical drugs remained at 1 percent of the total review workload (3 of 267 submissions).

Figure 5 Workload for biologics (on December 31)



At the end of 2006, there was no backlog for the 50 biologic drugs submissions, compared to 51 percent of the workload in backlog (or 31 of 61 submissions) in 2005.

Figure 6 Workload for medical devices (on December 31)



At the end of 2006, the backlog for medical devices remained at 2 percent (5 of 245 submissions). This was an improvement from 2004, which ended with a 15 percent backlog.

No application backlog (2006)

Source: HPFB Performance report,2006-2007

Therapeutic access strategy performance targets -2003

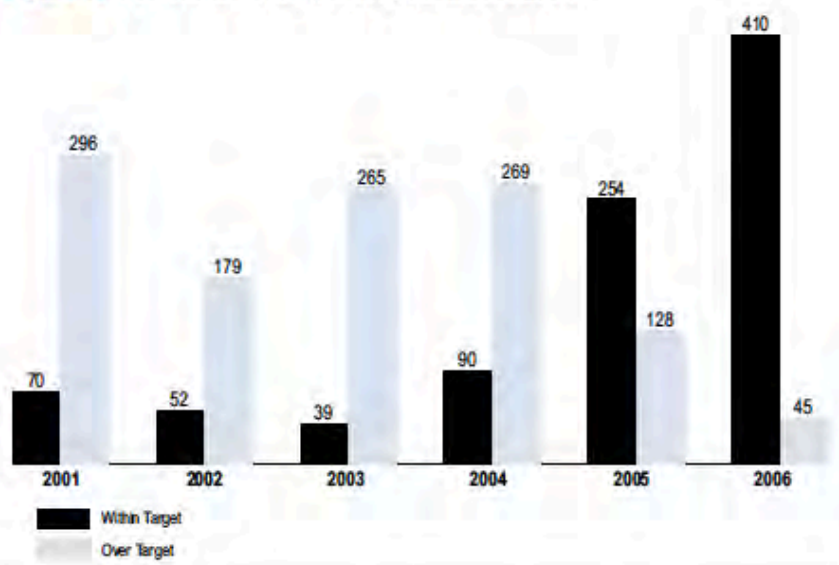
Performance Targets	
Drugs (Pharmaceutical and Biologic)	**Target Times** (Calendar days)*
• Brand Name Priority/Priority Biologic	• 180 or 200**
• Brand Name Standard/Standard Biologic	• 180 or 300
• Brand Name Supplemental/Supplemental Biologic	• 180 or 300
• Generic Standard	• 180
• Generic Supplemental	• 180 or 300
Medical Devices	**Target Times** (Calendar days)
• Priority (Class III and IV)	• 45
• Class II	• 15
• Class III	• 75
• Class IV	• 90
• Amendment applications (Class II, III, IV)	• same target times as Class II, III, IV

*Performance targets do not include screening the submissions for new drugs
**Target times vary depending on the submission class

TIMELINESS

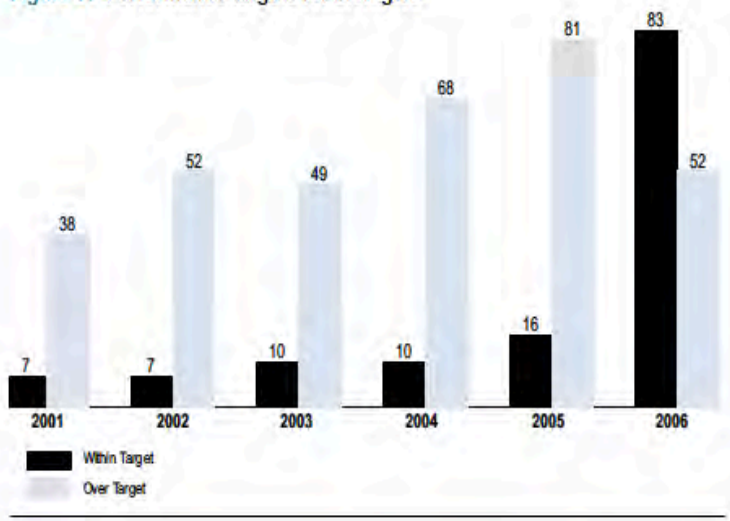
The timeliness of regulatory decisions

Figure 10 Performance targets for pharmaceuticals



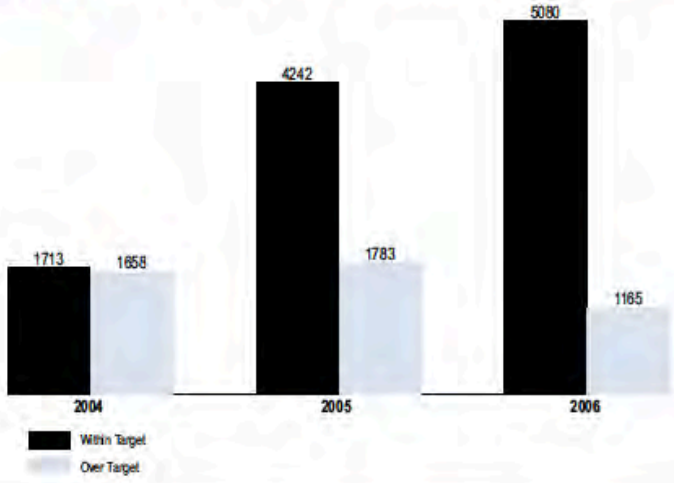
In 2006, significant progress has been made in meeting performance targets, with 90 percent of regulatory decisions issued on time for pharmaceutical drugs, compared with 13 percent in 2003.

Figure 11 Performance targets for biologics



In 2006, the number of decisions made on time for biologics rose significantly compared with 2005, from 16 percent to 61 percent.

Figure 12 Performance targets for medical devices



In 2006, we made considerable progress in meeting performance targets for medical devices, with 81 percent of regualtory decisions issued on time, compared with 51 percent in 2004.

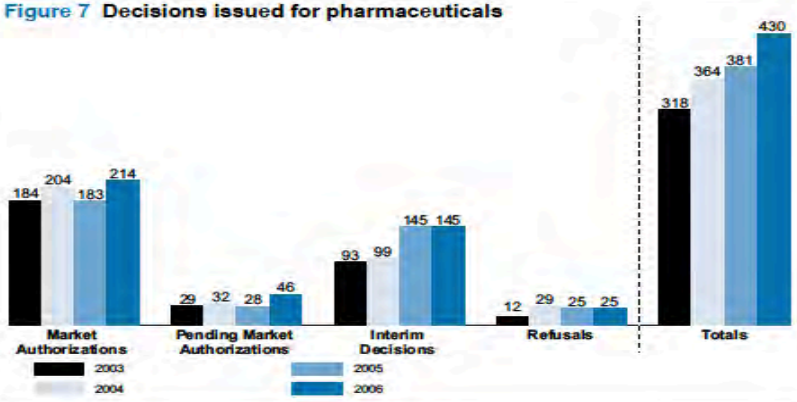
Source: HPFB Performance report,2006-2007

DECISIONS
Types of regulatory decisions issued

Decisions

Types of regulatory decisions issued

Figure 7 Decisions issued for pharmaceuticals



In 2006, regulatory decisions issued for submissions of pharmaceutical drugs increased by 13 percent compared with 2005, from 381 to 430.

Figure 8 Decisions issued for biologics

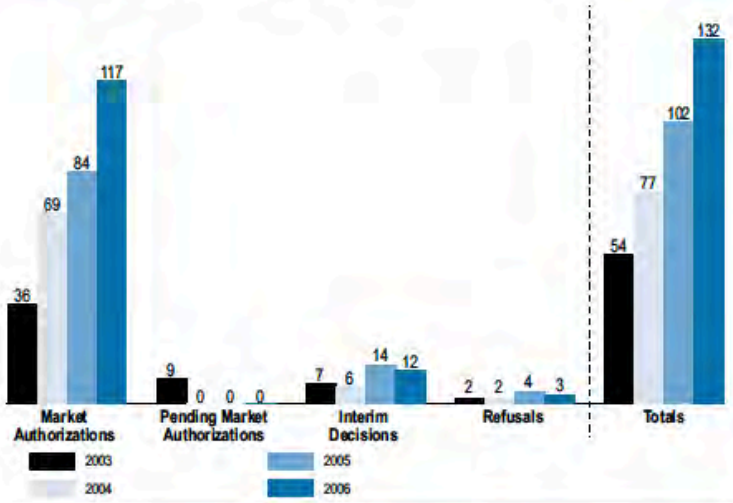
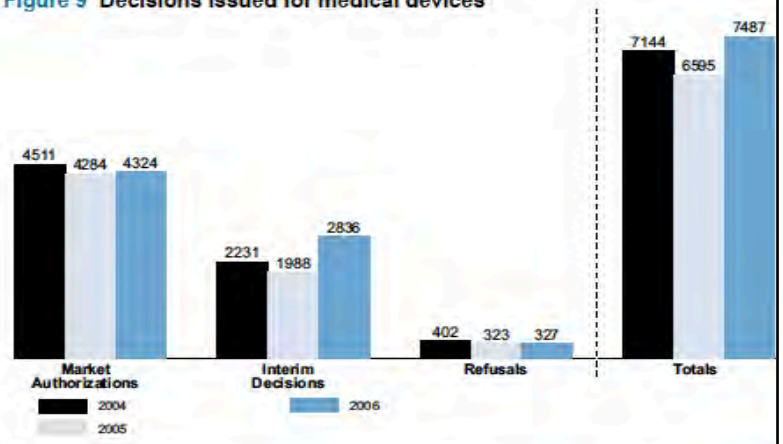


Figure 9 Decisions issued for medical devices



In 2006, regulatory decisions issued for medical device submissions increased by 14 percent compared with 2005, from 6,595 to 7,487.

Source: HPFB Performance report,2006-2007

Table 1. Drug Approval Time by Year

	Canada			US			
Year	No.	Median (d)	Range (d)	No.	Median (d)	Range (d)	p Value
≤1992[a]	39	1057	158–5118	62	713	87–3726	0.070
1993	30	862	295–4633	23	668	319–3497	0.13
1994	25	876	90–4035	18	392	178–1203	0.0058
1995	24	628	143–2306	28	455	96–2716	0.11
1996	29	567	185–1937	47	455	42–3053	0.15
1997	39	490	227–2454	43	405	78–1619	0.021
1998	25	518	301–1048	34	361	98–774	<0.0001
1999	33	577	224–1183	34	364	178–1233	0.0024
2000	24	646	209–1884	23	476	170–1655	0.28
≥2001[b]	27	704	179–1803	25	393	72–1421	0.046
TOTAL	295	650	90–5118	337	458	42–3726	<0.0001

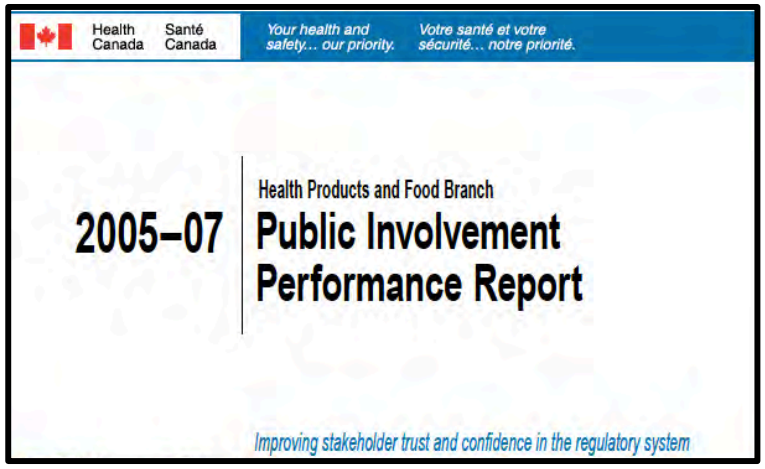
[a]Thirty-nine drugs approved in Canada in the decade had a pre-1992 US approval date, and 9 approved in the US in the decade had a pre-1992 Canadian approval date.
[b]Six drugs approved in the US in the decade had a Canadian approval date in early 2002.

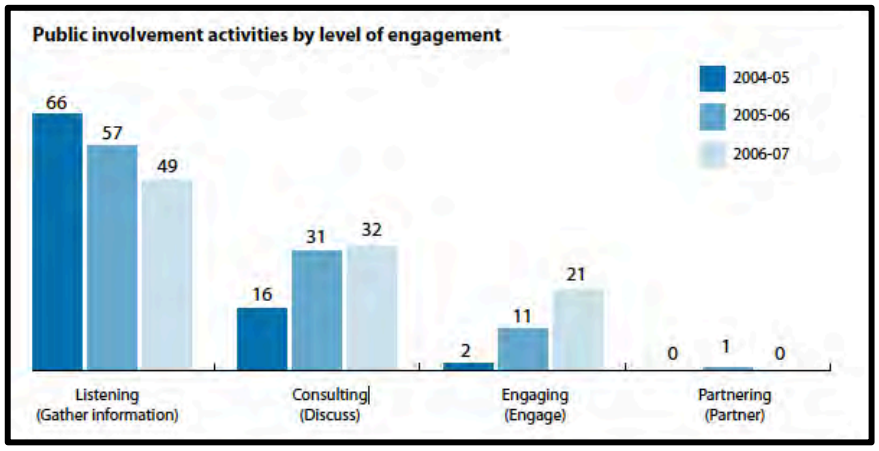
The Annals of Pharmacotherapy,2003 October, Volume 37

- **New drug approval times were significantly slower***
- **Across all drug categories and review type (priority/standard)**
- **Discontinuations for safety reasons (2.0%) vs US (3.6%)**

Note:*Latest data published which may not reflect current trends

What about public involvement ?





Methods of public involvement activities

Face-to-face	2004-05	2005-06	2006-07
Consensus conference	0	1	0
Public forum	0	2	0
Symposium	0	1	0
Workshop	12	5	8
Technical consultation	2	14	20
Focus group	3	6	5
Bilateral meeting	0	4	6
Public meeting	2	6	2
Roundtable	2	4	3
Dialogue	0	3	1
Electronic dialogue	0	1	3
Working group	0	2	1
Advisory body	0	3	5
Other	0	2	6
Other			
Mail-out for feedback	24	11	9
Web posting for feedback	32	24	27
Canada Gazette, Part 1	5	4	3
Survey	1	5	0
Other	1	1	3

What about resources ?

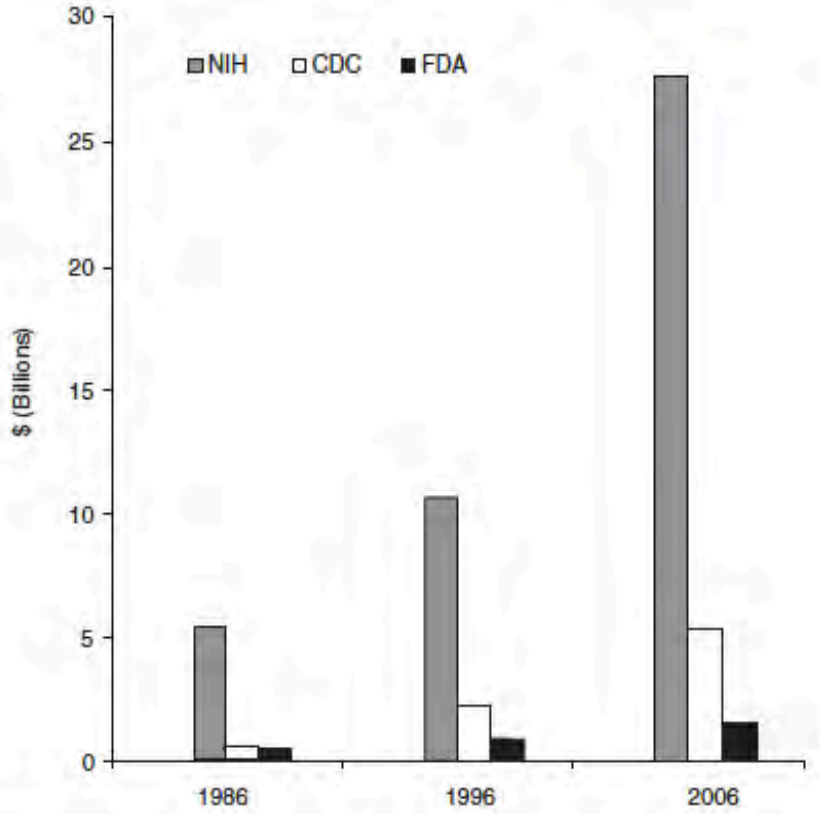
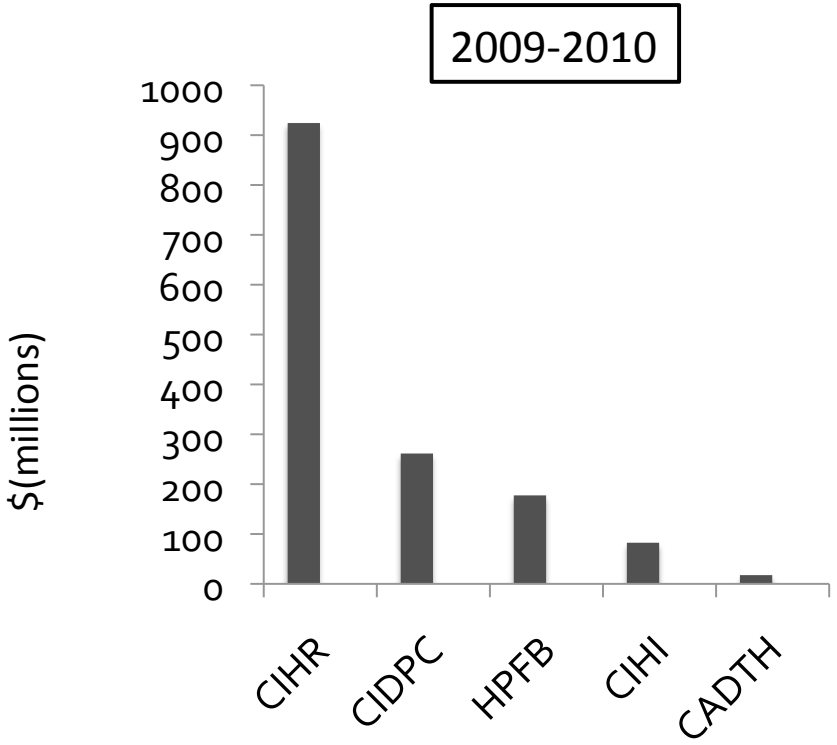
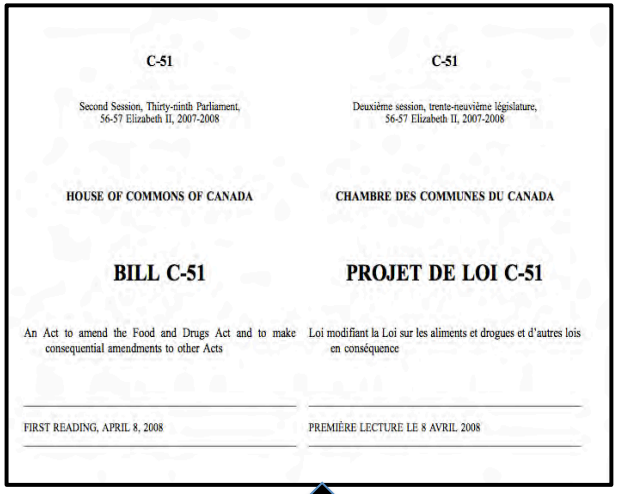


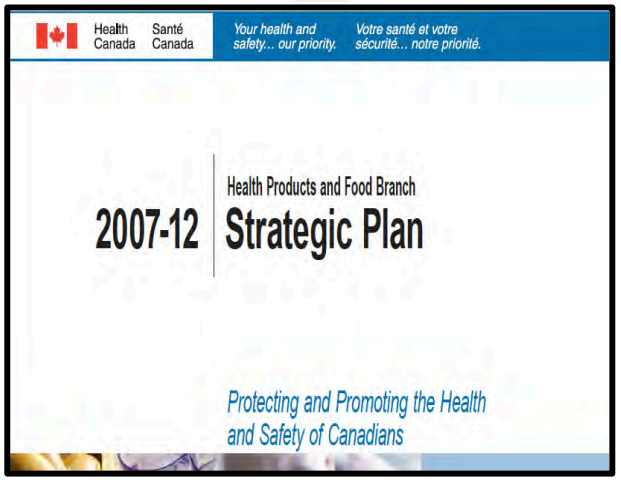
FIGURE 2-1 Comparison of NIH, CDC, and FDA budgets between 1986, 1996, and 2006. In 1986, FDA's budget was $416.7 million, CDC's was $429.4 million, and NIH's was $5.1 billion. In 1996, FDA's budget was $865 million, CDC's was $2.2 billion, and NIH's was $10.2 billion. In 2006, FDA's budget was $1.5 billion, CDC's was $5.2 billion, and NIH's was $27.7 billion.
SOURCE: Coalition for a Stronger FDA, 2007.



Treasury board of Canada main estimates for operating capital; $924,326 for CIHR,$261,298 for CIDPC ,$176,853 for HPFB,$81,746 for CIHI and $ 16,903 for CADTH

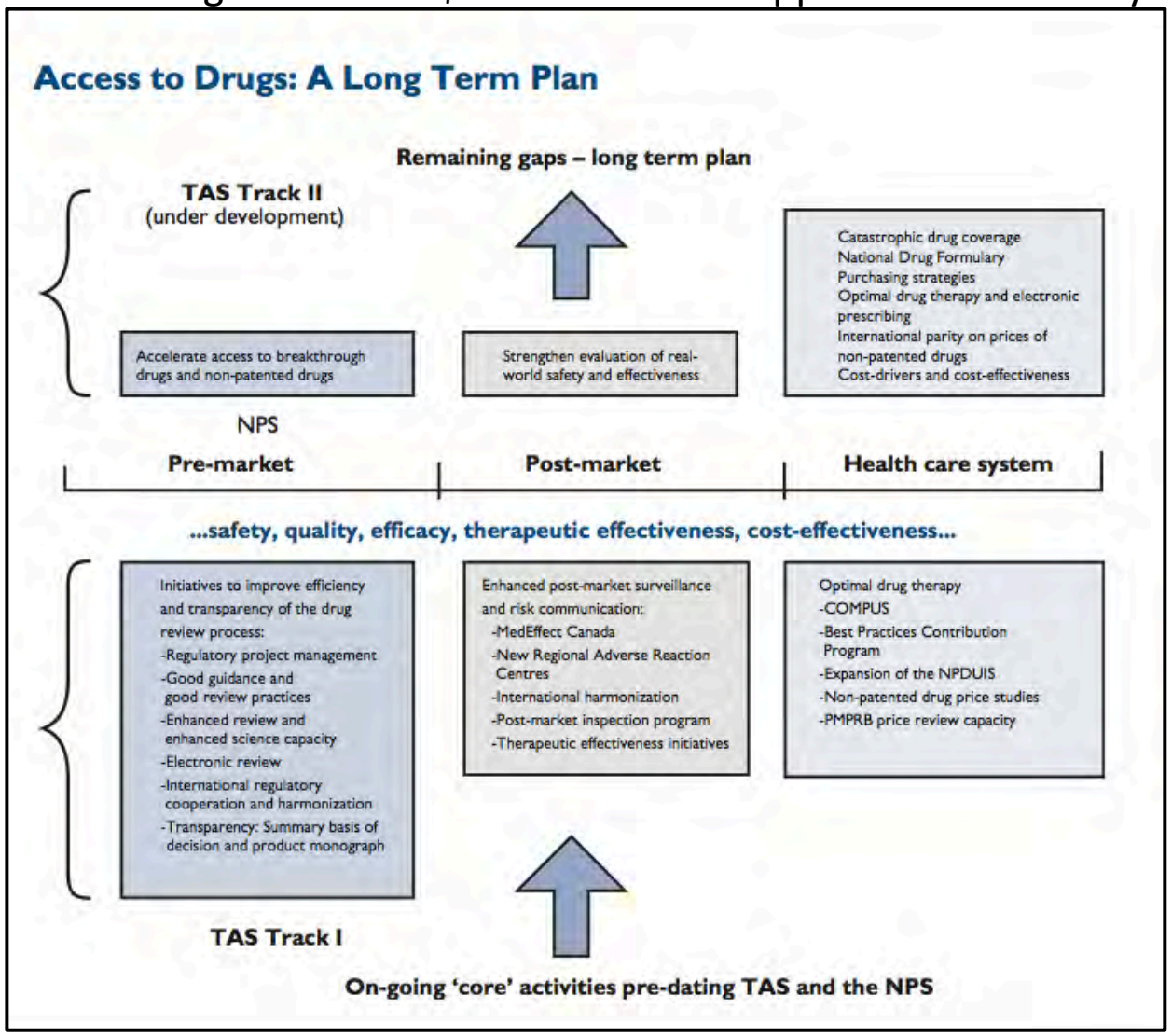
Nearly a decade of planning for change....





The Therapeutic Access Strategy Plan

Federal budget of 2003 : $190 millions in support of TAS over 5 yrs



Source: Regulation and Beyond: Progress on Health Canada's Therapeutic Access Strategy,2005

Health Canada's TAS objectives

Federal budget of 2003 : $190 millions in support of TAS over 5 yrs

To make pre-market regulatory decision-making more efficient, timely and transparent, while maintaining high standards of safety

To pay greater attention to safety and therapeutic effectiveness once products reach the market

To promote optimal drug use, including better practices in prescribing drugs, better management of products and drug plans, and making medicines more affordable

December 2007

Speaking at the Salvation Army Christmas Toy Depot in Ottawa, Prime Minister Harper noted that there has been a sharp rise in the number of product recalls involving unsafe toys, food and drugs in recent years. ***"Canadians rightly expect their federal government to police the safety of the products they bring into their homes,"***

Establishment of the Drug Safety and Effectiveness Network (DSEN) as a 'horizontal initiative'

Budget: $32 million over 5 yrs and $10 million on-going

Partnering Agencies

HC: Health Products, Consumer Products, Food Safety, and Pesticide Regulation
CFIA: Food Safety
PHAC: Health Promotion, Chronic Disease Prevention and Control, and Infectious Disease Prevention and Control
CIHR: Strategic Priority Research

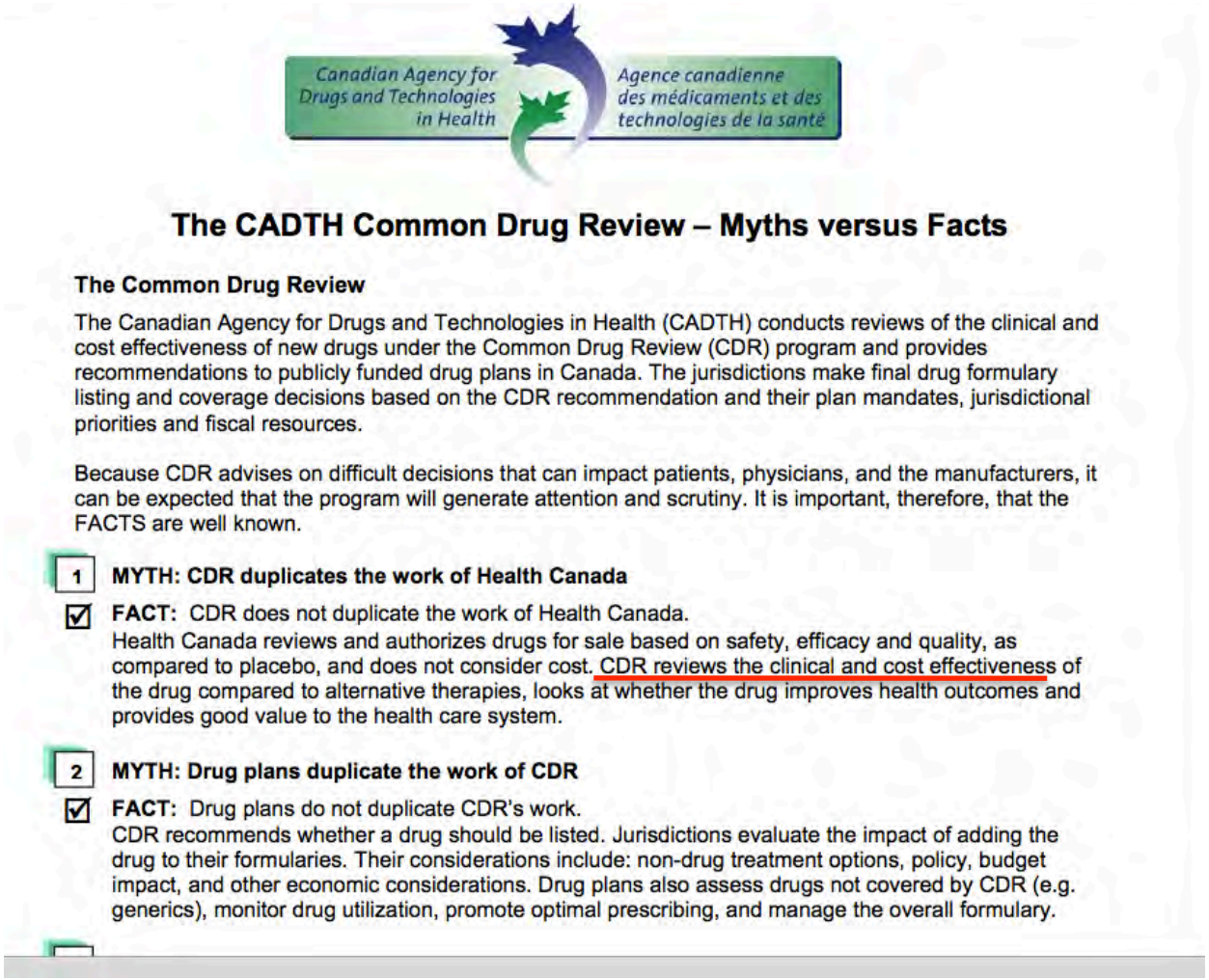
New agencies have surfaced in the last decade

DSEN (2007): The key objectives for establishing the DSEN are ***to increase the available evidence on drug safety and effectiveness available*** to regulators, policy-makers, health care providers and patients; and, to increase capacity within Canada to undertake high-quality post-market research in this area.
Source: www.cihr-irsc.gc.ca

CADTH-CDR (2003): The Canadian Agency for Drugs and Technologies in Health (CADTH) is a national body that provides Canada's federal, provincial and territorial health care decision makers with credible, ***impartial advice and evidence-based information about the effectiveness and efficiency of drugs*** and other health technologies.Source: www.cadth.ca

NDPUIS (2001):To provide access to ***standardized information on prescription drug use and costs from across jurisdictions***;Information that will facilitate informed management of drug plans;Information that will support exploration and analysis of interplay among plan design, formulary listings and drug utilization;Analysis on the impact of policy decisions on utilization;Trends on utilization over time and across jurisdictions.Source: www.cihi.ca

Drug review responsibilities are fragmented



Canadian Agency for Drugs and Technologies in Health

Agence canadienne des médicaments et des technologies de la santé

The CADTH Common Drug Review – Myths versus Facts

The Common Drug Review

The Canadian Agency for Drugs and Technologies in Health (CADTH) conducts reviews of the clinical and cost effectiveness of new drugs under the Common Drug Review (CDR) program and provides recommendations to publicly funded drug plans in Canada. The jurisdictions make final drug formulary listing and coverage decisions based on the CDR recommendation and their plan mandates, jurisdictional priorities and fiscal resources.

Because CDR advises on difficult decisions that can impact patients, physicians, and the manufacturers, it can be expected that the program will generate attention and scrutiny. It is important, therefore, that the FACTS are well known.

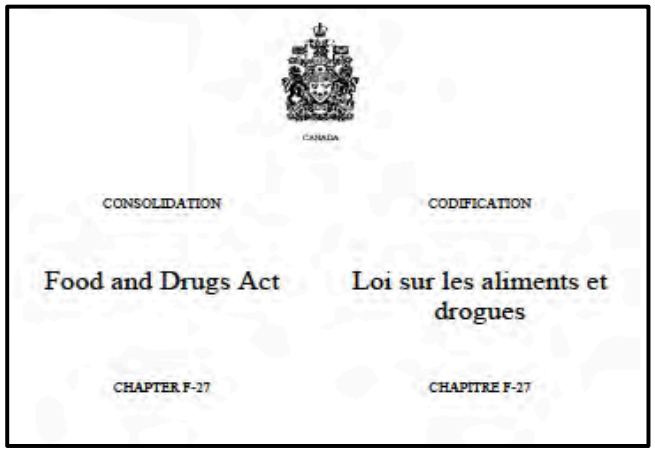
1 **MYTH: CDR duplicates the work of Health Canada**

☑ **FACT:** CDR does not duplicate the work of Health Canada.
Health Canada reviews and authorizes drugs for sale based on safety, efficacy and quality, as compared to placebo, and does not consider cost. CDR reviews the clinical and cost effectiveness of the drug compared to alternative therapies, looks at whether the drug improves health outcomes and provides good value to the health care system.

2 **MYTH: Drug plans duplicate the work of CDR**

☑ **FACT:** Drug plans do not duplicate CDR's work.
CDR recommends whether a drug should be listed. Jurisdictions evaluate the impact of adding the drug to their formularies. Their considerations include: non-drug treatment options, policy, budget impact, and other economic considerations. Drug plans also assess drugs not covered by CDR (e.g. generics), monitor drug utilization, promote optimal prescribing, and manage the overall formulary.

The Food and Drug Act has not been amended in the last 50 years


CANADA

CONSOLIDATION

CODIFICATION

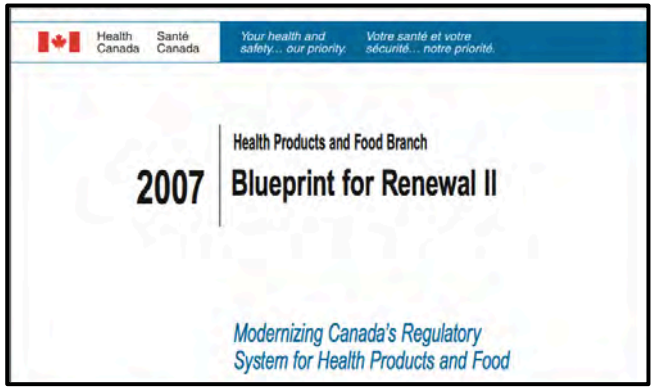
Food and Drugs Act

Loi sur les aliments et drogues

CHAPTER F-27

CHAPITRE F-27

- Patent Medicine Act-1909
- Food and Drugs Act-1920
- F&DA Act Amendment-1951

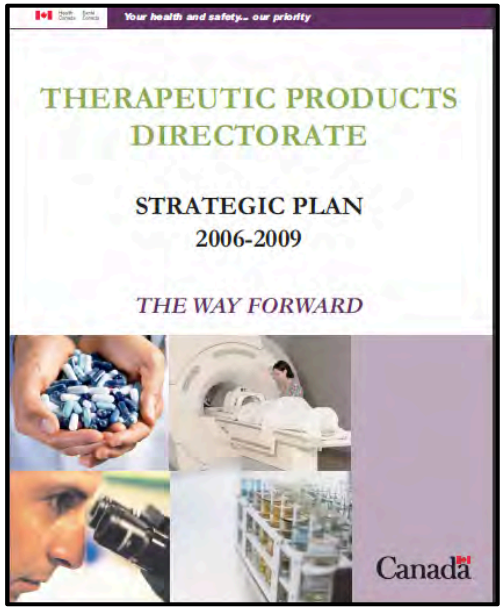

Health Canada Santé Canada

Your health and safety... our priority. Votre santé et votre sécurité... notre priorité.

Health Products and Food Branch

2007 Blueprint for Renewal II

Modernizing Canada's Regulatory System for Health Products and Food



A change process aimed at the "big picture" challenge and trends affecting TPD business, such as legislative reform, technology changes, evolving science, international collaboration, and the expectations of Canadians for information, openness and transparency

1. Strategic Objective: **Modernized Regulatory Framework**
2. Strategic Objective: **Performance Sustainability**
3. Strategic Enabler: **Governance**
4. Strategic Enabler: **People**
5. Strategic Enabler: **Relationship Management**

Key objectives of legislative reform of the Food and Drug Act in Canada

- A “life cycle” regulatory approach to health products that would encompass all stages of product development and enable ‘progressive licensing’
- A more transparent and consistent system of categorizing ‘therapeutic products’ and assessing their benefits and risks
- A proactive regulatory system which is much more engaged with the public and health care professionals of Canada
- Improved generation, dissemination and response to new safety and effectiveness data for health products
- A more open and transparent regulatory system
- Increased focus on Regulatory science
- Building expertise in areas of health care innovation
- Small and medium business assistance

The last attempt at FD&A legislative reform in Canada was on a good start..

C-51

Second Session, Thirty-ninth Parliament,
56-57 Elizabeth II, 2007-2008

HOUSE OF COMMONS OF CANADA

BILL C-51

An Act to amend the Food and Drugs Act and to make consequential amendments to other Acts

FIRST READING, APRIL 8, 2008

C-51

Deuxième session, trente-neuvième législature,
56-57 Elizabeth II, 2007-2008

CHAMBRE DES COMMUNES DU CANADA

PROJET DE LOI C-51

Loi modifiant la Loi sur les aliments et drogues et d'autres lois en conséquence

PREMIÈRE LECTURE LE 8 AVRIL 2008

Until it went sailing in the eye of the storm…

Canadian's Health at stake ?

It's time for Canada to change !

Taking it to the streets...

Partnerships to Build and Sustain a Regulatory Science Infrastructure (NIH-FDA,February 24,2010)

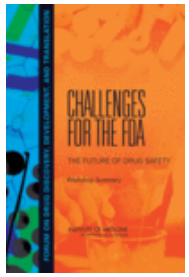
A first-of-its-kind collaboration between NIH and FDA with a joint leadership council to enable the agencies to work together to improve regulatory science, beginning with what is a small but very important program of grants to advance important research in regulatory science.

It's … an important first step to strengthen regulatory science as an organized research endeavor and as a catalyst to advance science at FDA more broadly. Moreover, as Secretary Sebelius noted at the announcement,collaboration between NIH and FDA, including support for regulatory science, will go a long waytowards fostering access to the safest and most effective therapies for the American people

"With our Critical Path Initiative, FDA will continue to partner with academic groups, patient advocacy groups, and industry to bring innovation to fields such as genomics, imaging, and informatics, so they can be applied to gaps in drug and diagnostic development"

Engaging the community: USA

Institute of Medicine (IOM) sponsored workshops



Challenges for the FDA: The Future of Drug Safety. September 2007

Building a National Framework for the Establishment of Regulatory Science for Drug Development – October 2010

Evaluation of Biomarkers and Surrogate Endpoints in Chronic Disease–May 2010

Public Health Effectiveness of the FDA 510(k) Clearance Process: Balancing Patient Safety and Innovation – October 2010

Conclusions

<u>The last decade</u>: Formulating the plan for change !

- Significant improvements in the performance targets of HPFB together with the formulation of a solid set of recommendations for change but continued underfunding
- Emergence of new agencies that can contribute to the assessment of drug safety and effectiveness
- An increased risk of fragmentation of efforts due to the lack of coordinated efforts
- A failure to modernize the Food and Drug Act , appropriately support and empower the Canadian food and drug regulatory authority in a manner consistent with the US or the European Union

Conclusions

The next decade: Executing the plan for change !

- Modernization of the Food and Drug Act and establishment of **CAFDA*** working in close cooperation with CIHR,CADTH,CIHI and other key stakeholders
- An increased focus on regulatory science and initiatives to sustain the discovery and development of innovative therapies in Canada
- Greater transparency and timely access to comprehensive information on consultations, assessments and regulatory decisions
- Greater involvement of health care professionals and the Canadian public

***CAFDA: « CANADIAN Food and Drug Agency »**

Thank You!

" A key challenge for FDA is that the agency is often forced to "take limited data … based on small numbers of people's response to a given therapeutic approach—and determine what will happen when this therapy is unleashed to very large numbers of people "

Jeff Drazen , Editor NEJM