CADTH

An Inside Look at the Early History of the CADTH Common Drug Review in Canada

Elaine MacPhail and Barb Shea

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ABOUT CADTH
CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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CADTH Evidence Driven.

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Abbreviations List

ACHS	Advisory Committee on Health Services
ACP	Advisory Committee on Pharmaceuticals
BCANS	Bureau of Cardiology, Allergy and Neurological Sciences
BMS	Bristol-Myers Squibb
CAC	COMPUS Advisory Committee
CBN	Common Briefing Note
CADTH	Canadian Agency for Drugs and Technologies in Health
CAPIA	Canadian Agency for Pharmaceutical Information Assessment
CCOHTA	Canadian Coordinating Office for Health Technology Assessment
CDFS	Canadian Drug Formulary Service
CDR	Common Drug Review
CDRC	Common Drug Review Committee
CED	Committee to Evaluate Drugs (Ontario)
CEDAC	Canadian Expert Drug Advisory Committee
CMAJ	*Canadian Medical Association Journal*
COI	conflict of interest
COMPUS	Canadian Optimal Medication and Prescribing Utilization Service
DERP	Drug Effectiveness Review Project
F/P/T	federal, provincial, and territorial governments
HESA	House of Commons Standing Committee on Health
HTA	health technology assessment
HTF	Health Transition Fund
HTS	Health Technology Strategy
JAMA	*Journal of the American Medical Association*
JODR	Joint Oncology Drug Review
NEJM	*New England Journal of Medicine*
NICE	National Institute for Health and Care Excellence (UK) (formerly the National Institute for Clinical Excellence)
NIHB	Non-Insured Health Benefits
NOC	Notice of Compliance
NPS	National Pharmaceuticals Strategy
OWI	One World Inc.
PAC	Pharmaceutical Advisory Committee
PBAC	Pharmaceutical Benefits Advisory Committee (Australia)
PBS	Pharmaceutical Benefits Scheme (Australia)
pCODR	pan-Canadian Oncology Drug Review
PIC	Pharmaceutical Issues Committee
PHARMAC	Pharmaceutical Management Agency (New Zealand)
PRA	Provincial Reimbursement Advisor
Rx&D	research-based pharmaceutical companies
SMC	Scottish Medicines Consortium
TPD	Therapeutic Products Directorate

Foreword

It is with great pleasure we present this inside account of the early history of the Common Drug Review (CDR) in Canada. We are grateful to CADTH for providing support to enable this first-hand look back in time when governments in Canada successfully worked together to achieve a common and significant health care goal.

This account has been written to preserve the history of CDR for CADTH and its stakeholders; to provide an overview of the early years (up to 2008); and to provide an understanding of why CDR was established and why it operates as it does.

Over the years, many individuals and teams contributed to the development and delivery of CDR. No matter the role and responsibility, without these respective efforts this account could not be told. We acknowledge all who contributed.

We were the first two full-time staff hired to work on CDR at the Canadian Coordinating Office for Health Technology Assessment (CCOHTA); CCOHTA was re-branded to CADTH in 2006. Elaine began in March 2002 as Coordinator of the Interim CDR and Barb began in January 2003 as Director of CDR. The perspective we bring to this history is that of two "insiders," reflecting our personal involvement. While some of the history is based on our memory, we have gathered information from a variety of sources, including publicly available media releases and reports, and CDR documents (however, without conducting a systematic literature search). Briefing notes, minutes, and background documents from CADTH's archives inform the bulk of this historical document. We have included a bibliography that references additional documents that provide additional insights into the early history of CDR. Our goal is to paint a picture that outlines the challenges and successes, and gives voice to critics and supporters.

This account, we hope, will have something for everyone who is interested in the history of CDR. Chapters 1 and 2 illustrate the Canadian environment in pharmaceuticals management leading up to the announcement of a common process to evaluate drugs in 2001. As well, CCOHTA/CADTH's role and response to becoming the host of a common drug review is covered along with the atmosphere and collaboration among the federal, provincial, and territorial (F/P/T) governments at the time. Chapters 3, 4, and 5 describe the creation and early growth of the single common drug review serving 18 drug plans. Pivotal events in those early years have been captured. Each stone laid in the foundation of the program was developed, designed, and agreed to by representatives of 18 drug plans. No small feat. It is our intent to give a sense of the tremendous amount of cooperation, persistence and desire by F/P/T governments to work together on a common goal.

We hope you enjoy reading CDR's history as much as we enjoyed researching and writing it.

Elaine MacPhail

Barb Shea

CHAPTER 01

Chapter 01

Before the Common Drug Review

Publicly funded drug plans began emerging in Canada in the 1970s. They came into existence one by one, each with unique drug benefits and levels of financial assistance. The processes and decisions about which drugs would be listed as benefits varied from drug plan to drug plan. As time went on there were calls for more consistency and more coordination across the country. It was in the 1990s that designs for the number of common initiatives regarding pharmaceuticals management started to take shape. CCOHTA was a young agency at that time and it wasn't long before it was in the thick of issues related to drug assessments.

In Canada, the power and responsibility of governance is divided between the federal and provincial and territorial governments. The provinces and territories are responsible for the delivery of health services. In the mid-1950s, the federal government enacted legislation that required provinces and territories to deliver fully publicly funded coverage for health services provided in hospitals. In the 1960s it enacted legislation that ensured health services provided by doctors would be publicly funded as well. The provision of and financial assistance for other services, such as prescription medications provided outside of hospitals, is the responsibility of and determined by each individual government.

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1.1

The Drug Review Process Before the Common Drug Review

Each drug plan designed its own system of review for deciding which drugs would be listed on its formulary.

The Early Years of Drug Plans

Publicly funded drug plans (pharmacare programs) began to emerge primarily in the 1970s across Canada. One by one they appeared in the provinces and territories, as governments put plans in place to help residents defray rising drug costs. The federal government established separate plans to provide drug benefits to a number of groups including veterans; Status Indians and Inuit; members of the armed forces and the Royal Canadian Mounted Police; inmates in federal jails; and refugees. Each drug plan, provincial, territorial and federal, was designed differently based on the responsible government's direction. In the provinces and territories, some governments funded drugs only for certain populations, such as seniors and social assistance recipients, while others covered their entire populations.

Each drug plan designed its own system of review for deciding which drugs would be listed on its formulary (the list of drugs it covers). Most provinces set up committees made up of members who brought different expertise and perspectives to the drug reviews and to recommendations on which drugs were to be listed. Normally recommendations required approval by the Minister of Health or someone who was delegated the responsibility.

In order to have their drugs considered for listing, pharmaceutical manufacturers would make a written submission to each drug plan. As the drug plans were not coordinated in their set up or design, the requirements for a submission varied from plan to plan; thus, pharmaceutical manufacturers had to prepare a different submission for each plan. Figure 1.1 illustrates how different drug submissions would go to each of the plans before CDR. Manufacturers were critical, saying it made little sense to have different requirements across the country. They called on drug plans to work together to streamline the process.

Commitment to Work Together Over Time

There was much effort among governments to work together in the area of prescription medications. We know that as early as the mid-1970s, provincial publicly funded drug plans shared experiences and discussed such concepts as establishing a Canadian Drug Formulary Service (CDFS). Consensus was not reached on the proposal and it did not move forward. In the early 1990s a working group of provincial, territorial, and federal representatives proposed the creation of the Canadian Agency for Pharmaceutical Information Assessment (CAPIA). The agency was not created.

Over the years, government leaders, academics and researchers, policy analysts, and patient advocates published papers, held conferences and made many calls for a more coordinated approach to the management and coverage of prescription medications across Canada. While a great deal of work went into this effort, seemingly to the result of little or no action, some work did create incremental change and provided a foundation of sorts to subsequent effort. For example, some of the guiding principles for the proposed CAPIA included minimizing the duplication of efforts, using acceptable standards and guidelines to collect and evaluate information, and creating transparency of the activities. Those principles were ultimately incorporated into the Common Drug Review (CDR).

The Calls for Change Grow Louder

Starting in the mid-1980s, the rising cost of drugs, both to drug plans and to individuals, became a focus of attention. Drug plan budgets began to form a significant and growing portion of overall health care costs due to an increased use of drugs and the introduction of new drugs that were seen as very expensive at the time. Between 1985 and 1998, drug expenditure in Canada increased by 226% — approximately double the increase in total expenditure on health care. Prescribed and non-prescribed drugs comprised the second largest share of health care expenditures, and for the first time surpassed the cost of physician services.[1]

Different drug plans made different decisions on whether or not to cover a particular drug. This led to many people questioning why this was happening. In the 1990s patient advocacy groups were becoming better organized and connected across the country, and were more knowledgeable of how drugs were approved for sale and coverage. They were frustrated when learning a drug was covered by a plan in one province but not in another. They frequently lobbied governments to provide affordable and equitable access to drug treatments across Canada. The pharmaceutical industry representatives asked why their drug was approved for coverage in one province but not in another. Premiers and health ministers were perplexed when an expert committee in one province made a recommendation to cover a drug, while an expert committee in another province made a recommendation not to cover it.

Federal, Provincial, and Territorial Collaboration

In the early 1990s a National Pharmaceutical Strategy[2] was set up to coordinate efforts on a number of pharmaceutical issues and initiatives across Canada. The ultimate goal was to work toward the optimal use of drugs in Canada. The strategy was never formally adopted, but a number of recommendations were rolled into subsequent federal, provincial, and territorial (F/P/T) activities.

Through the 1990s there was a great deal of F/P/T focus on pharmaceutical issues. Several initiatives were implemented, with the federal government and one of the provinces co-leading. Ministry officials from across Canada were members of committees such as the F/P/T Advisory Committee on Health Services (ACHS), which had pharmaceutical issues as part of its mandate, and the Pharmaceutical Issues Committee.

"This work focused attention on pharmaceutical issues, but also created venues where staff from all the provinces worked together and became more attuned to the interest they shared."

— Anne MacFarlane, Assistant Deputy Minister Pharmacare and Intergovernmental Affairs, BC (1997)

In 1996 the F/P/T Ministers of Health directed work to be done on six drug-related issues. Working groups were established to determine where and how governments could collaborate to deal with these issues. For example, the mandate of one group was to explore work that could be done to improve the efficiency of drug plans in Canada. In this regard, it looked at expert advisory committees and pressures that affected listing decisions within drug plans. Those efforts informed the future collaborative work of establishing CDR.[2]

One of the big challenges facing F/P/T collaborations are the associated costs (funding of travel, meetings, undertaking projects); this can then impede participation in some F/P/T groups. The federal government announced The Health Transition Fund (HTF) in 1997, which would cover associated costs. The HTF was a $150 million fund that ran from 1997 to 2001 and supported 140 projects across Canada to test and evaluate innovative ways to deliver health care services, including pharmaceuticals. "These projects generated evidence that governments, health care providers, researchers, and others can use in making informed decisions leading to a more integrated health care system."[3]

Canadian Coordinating Office for Health Technology Assessment

The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) was established in 1989 by F/P/T Ministers of Health as an independent, not-for-profit, and at arms-length-from-governments organization. CCOHTA's goal was "to improve decision-making regarding the use of health technologies so that effective, appropriate, and cost-effective health care is the result."[4] Among its services, CCOHTA provided information and evaluations of health technologies and their impact on health. When first established, CCOHTA did not issue recommendations. Its reports contained a review and summary of the evidence available.

When the proposal for CAPIA failed, CCOHTA was asked to take on a larger role in pharmaceutical assessments. The 1993-1994 Annual Report states "the major challenge facing CCOHTA in 1994-1995 lies in the area of pharmaceuticals, including the coordination of assessment activities, avoidance of duplication, as well as conducting assessments."[5]

CCOHTA became more involved in the review of pharmaceuticals. It established linkages with organizations representing pharmaceutical manufacturers to facilitate mutual understanding about the industry's perspective, about the work CCOHTA was undertaking, and about the data that would be useful for reviews. In 1994 to 1995 it established methodologies for conducting economic pharmaceutical evaluations.

Late in1997 the pharmaceutical manufacturer Bristol-Myers Squibb (BMS) took legal action against CCOHTA. "When the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) was about to release a report saying that all of the different drugs in the statin group were equivalent, Bristol-Myers Squibb (BMS), makers of one of these drugs, objected to the release of the report and went to court to block its publication. The case was eventually thrown out, but not before CCOHTA spent 13% of its annual budget defending itself."[6]

In successfully meeting the legal challenge, the organization became acutely aware of the steps it would need to take in order to successfully defend itself in the future. It was a precedent-setting case. It was apparent CCOHTA's work was and would continue to be under scrutiny.

Momentum Builds

The issue of accessibility to and affordability of prescription medicines in Canada was becoming more and more prominent. Patients and their advocates were lobbying for change and conferences, research papers, and media reports focused on the "patchwork" of drug coverage in Canada. This led to governments across Canada working together in a number of areas of prescription drug management. The question was: what would result from these efforts and would it have staying power?

CHAPTER 02

Chapter 02

Replacing Eighteen Drug Review Processes With One

As a new century got under way, the Premiers' Conference announced that there would be a concerted effort to work together in areas of drug plan coverage. Varied processes, sometimes long established, in each drug plan would need to be merged into one if this was to succeed. There were many details to be examined and many questions to be answered… if this was going to materialize, many people would need to work diligently, collaboratively, and quickly.

Following the Premiers' Conference in August 2000, a press release was issued on a number of health care–related issues. Under the title of Action on Pharmaceutical Management, the press release reads: "In order to ensure Canadians continue to have access to new, appropriate and cost-effective drugs, Premiers agreed to work together and mandated their health ministers to develop strategies for assessing and evaluating prescription drugs. These strategies could include the creation of a common interprovincial/territorial advisory process to assess drugs for potential inclusion in provincial/territorial drug plans. They will be informed by an examination of current provincial/territorial best practices and various means of addressing drug purchasing costs."[7]

The already busy F/P/T activity in pharmaceuticals was about to get busier. Direction on work in this area was coming from the highest levels in governments. The question was whether this attempt to collaborate would be successful. For the next year people on the "inside" focused on strategies that could successfully lead to a transition from the initial 19 separate and, for the most part, different drug review processes (10 provinces, 3 territories, and 6 federal drug plans) to a single common drug review.

Early on in these deliberations Quebec announced it would not participate in efforts toward a common drug review. The province was willing to share information but not to become a participant in a shared review process. The work then focused on 18 drug plans across Canada. Some saw the fact that Quebec did not participate as a weakness of CDR. Over time it was apparent Quebec's decisions on drug coverage were often different from CDR's recommendations (with Quebec often approving coverage and CDR not recommending coverage). The higher rate of approval for coverage in Quebec was attributed, in part, to the pharmaceutical industry presence in that province. Industry and patients in other parts of Canada were critical of their own drug plans for having lower rates of coverage than Quebec.

Many of the drug review processes in Canada had existed for decades. As might be expected, each system gained a level of comfort with its own process and its own experts. There was skepticism from some that a single process could meet everyone's needs. There was tension at times, and some disagreements, but people displayed a commitment to the goal of a single review process.

"The expertise available to conduct evidence-based reviews for each of the drug plans was not consistent. Smaller provinces, in particular, knew they would benefit through having access to expertise available in other provinces. All provinces saw the benefit of no longer duplicating effort."

— Leanne Jardine, Executive Director, Pharmaceutical Services, NB

In August 2001, the Premiers announced they would focus their energy and resources on developing constructive approaches to pharmaceutical management.[8] Health ministers directed their departments to develop an implementation plan for a single common approach to drug reviews in Canada: CDR.[9] The potential benefits of CDR were set out. Aggressive timelines were set for implementation with an interim, shared review process to be established by January 2002.

2.1

Canadian Premiers

41st Annual Premiers' Conference
August 9-11, 2000
Winnipeg, Manitoba

In September 2001 F/P/T health ministers announced a number of initiatives in the area of pharmaceuticals including, "The establishment of a single, common review process for coverage of new drugs in Canada. While decisions on benefit coverage and formulary listing would be retained by individual provinces, territories and the federal government, future cooperation in these areas is both possible and desirable. Ministers also agreed to increase collaboration and further enhance the assessment of cost-effectiveness in the drug review process. While participation in these processes will be optional, information sharing among jurisdictions is expected."[10]

The potential benefits of a common drug review process were percolating through levels of each government. A single process would offer optimal use of resources, higher overall quality of reviews, the potential for more consistency in listing decisions, and the ability to present a consistent approach in addressing pressures from pharmaceutical manufacturers.[11]

Governments were aware that there were a number of factors that were key to setting this program up to be successful, including where CDR would be housed and the infrastructure to support it.

"The major fear would be that the organizational infrastructure necessary to make the process work would not be there and the initiative would (like many similar exercises) simply wither away. For something like a common drug review to work there has to be a strong infrastructure where planning for delivery is strong, target dates are met, quality of reviews are maintained etc. Otherwise, in the demand to list drugs, provinces would do their own reviews and undermine the need for a common drug review."

— Anne MacFarlane, Assistant Deputy Minister Pharmacare and Intergovernmental Affairs, BC (1997)

Agreement was reached, consensus built, and next steps approved in a matter of weeks in late 2001. The speed of these decisions was remarkable when considering there were 18 separate (government) approvals required.

There would be an interim secretariat for CDR. Initially the interim secretariat was to be located with the Non-Insured Health Benefits (NIHB) program, but it was decided that the secretariat would be housed at CCOHTA, if support staff could be hired in time. CCOHTA's Board of Directors supported this new initiative. The board held meetings at short notice to deal with requests and responses to this F/P/T direction. CCOHTA took risks in agreeing to take on CDR at short notice, as to ensure it met early objectives it had to initiate work before any funding was officially approved. CCOHTA senior management, specifically Dr. Jill M. Sanders (President and CEO), Dr. Vicki Foerster (Vice-President of Research), and Mary Gauthier (Manager, Administration and Finance), worked closely with F/P/T representatives to establish the infrastructure needed to sustain the interim and subsequently permanent CDR.

Relatively new drug review efforts in the Atlantic provinces (Atlantic Common Drug Review) and within the federal drug plans were pointing to success in working together.

Despite the fact that previous attempts to work together in the area of pharmaceuticals across Canada had resulted in little or no action, people involved in establishing CDR proceeded with optimism, determination, and a willingness to collaborate on a multitude of issues. There was commitment to a shared goal: a common drug review in Canada.

CHAPTER 03

Chapter 03

Interim Common Drug Review

The interim CDR, housed at CCOHTA, ran from March 2002 until September 2003. It was a distributed review process whereby the participating publicly funded drug plans volunteered to undertake and share a clinical and/or a pharmacoeconomic review of a new drug submission. The CDR Secretariat at CCOHTA coordinated and tracked the process, organized and supported interim CDR Committee (CDRC) meetings, and distributed the reports to the participating drug plans for use by their expert advisory committees to make a listing recommendation. This was an important opportunity to test some of the processes, templates, and guidelines developed by the Pharmaceutical Issues Committee (PIC) Task Group on CDR and to further refine and finalize them for use in the permanent CDR process. During this period, CCOHTA engaged legal advisers to assess the legal risks of CDR to CCOHTA; and subsequently the procedures, underpinned by the principles of rigour, consistency, fairness and transparency, were developed for CCOHTA to use in the permanent CDR.

The interim CDR was launched in March 2002 by all of the F/P/T governments with the exception of Quebec. A total of 18 publicly funded drug plans (9 provincial, 3 territorial, and 6 federal) participated.

Initially, it was anticipated that the interim CDR would be in place until September 1, 2002 when the permanent CDR would be implemented. In fact, the interim CDR operated until September 1, 2003. The activities during the interim CDR expanded beyond sharing drug reviews to include working out the details, getting agreement from participating drug plans, and documenting the procedures for the permanent CDR. The interim CDR Committee (CDRC) with secretariat support from CCOHTA, steered and guided the interim CDR. The Coordinator of the interim CDR came on board on March 4, 2002 to manage, coordinate, and administer the interim process. CCOHTA and the Interim CDRC quickly moved the interim CDR forward, with the first CDRC meeting taking place on March 21, 2004.

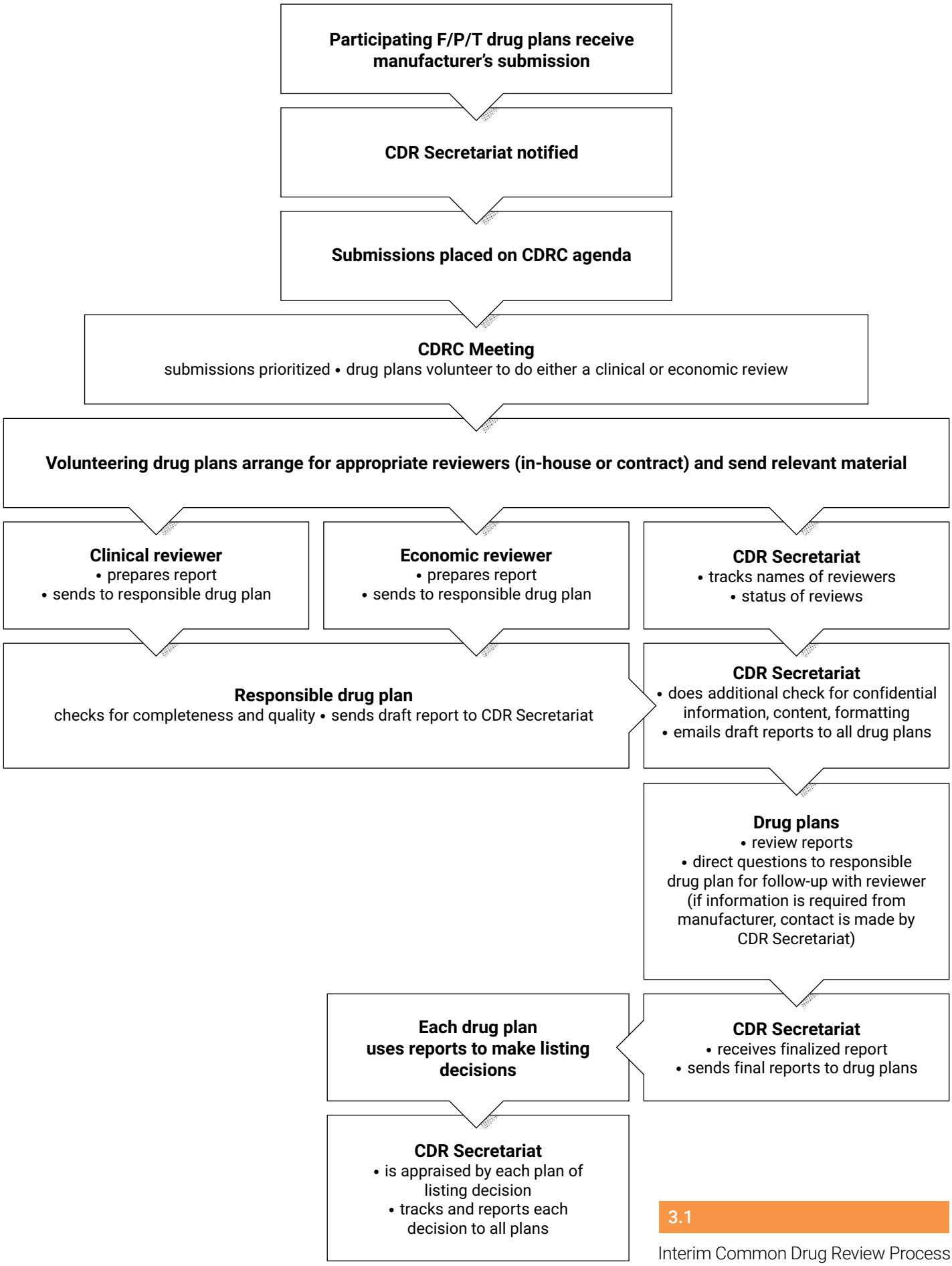
As part of the interim process, manufacturers continued to make submissions to each drug plan for new drugs and new drug combination products approved for sale in Canada. One of the participating F/P/T drug plans volunteered to undertake a clinical and/or a pharmacoeconomic review on behalf of all of the participating plans. The volunteering plan was responsible for managing the review, which included engaging a reviewer(s) and reviewing the report (see Figure 3.1).

The secretariat coordinated the overall process, communicated with the manufacturers if clarifications or information were needed, distributed the reports to all CDRC members, and tracked the status of the reviews. The drug plans provided the reports to their expert advisory committees to use in making listing recommendations. Each drug plan then made its own listing decision based on the expert advisory committee's recommendation and other considerations, such as the plan's mandate, priorities, and resources.

Between March 1, 2002 and September 1, 2003, 31 submissions for new drugs and new combination drugs were reviewed by the drug plans and 62 reports (a clinical and pharmacoeconomic report for each submission) were distributed.[12] The interim CDR provided an opportunity to reduce duplication of efforts, to gain experience with review templates and guidelines, and to continue preparations for a permanent process.

Interim Common Drug Review Committee

The Interim CDRC, chaired by Marnie Mitchell, comprised representatives from each of the participating F/P/T drug plans and observers from Health Canada, Patented Medicine Prices Review Board (PMPRB), and CCOHTA. (Appendix 1 contains the membership of the Interim CDRC.) The individuals on this committee gave unstintingly of their time, effort, and wisdom in developing and supporting CDR. During the interim CDR, the Interim CDRC, supported by the interim CDR secretariat, met every two weeks usually by teleconference. It provided oversight for the review of new drugs and it provided guidance for finalizing the underpinning documents for the permanent CDR, including CDR procedures, manufacturers' submission requirements, terms of reference for the Canadian Expert Drug Advisory Committee and the permanent CDRC, and conflict of interest guidelines. In addition, members volunteered to serve on various working groups that formed to further explore and recommend approaches for addressing CDR-related issues or needs.



3.1

Interim Common Drug Review Process

Preparing for the Permanent Common Drug Review

Beyond the undertaking and sharing of drug reviews, the following are some of the other major activities that took place during the interim CDR in preparation for the permanent CDR. The participating drug plans had already done much of the groundwork before the establishment of the interim CDR. During the interim CDR remaining tasks were tackled and steps were taken to establish the infrastructure and put into operation the permanent process.

Finding an Office for the Permanent CDR and Establishing a Business Case to Support it

The PIC Task Group on CDR identified finding a place to house the permanent CDR as one of the key needs. The Task Group suggested that the office could be located in an existing organization that would be a good fit with the proposed CDR, or that a new independent CDR organization with F/P/T governance could be established. To this end, Bob Nakagawa was contracted by PIC to prepare a paper, *The Development of a Single Common Drug Review for coverage of New Drugs in Canada: A Business Case Analysis, April 2002.*[13]

The Business Case Analysis:

- Provided an evaluation of the capacity and implications of establishing a single common drug review process within an existing or newly established organization. This included the entity's capacity to deal with industry lobbying and possible litigation, synergies or threats to its business lines, and the relationship required to work with current expert committees or new expert or steering committees specific to a common drug review process.
- Included a detailed evaluation and costing of resource requirements (human, financial, infrastructure, and leadership).
- Analyzed funding options, such as shared costs by F/P/T governments or a cost-recovery funding approach.
- Assessed the feasibility of implementing CDR by June 2002.
- Discussed the rationale for establishing a CDR process.

Following the analysis of six potential host sites, it was concluded that "CCOHTA is an attractive host site for the CDR office function. The mission of the organization provides for a good alignment with the CDR function. It has F/P/T governance and both the business and professional infrastructure to support CDR. There is an extremely good fit between the current activities of CCOHTA and the activities of CDR. The addition of CDR responsibilities will nicely complement the existing activities of CCOHTA."[13] The business case analysis also showed that several funding models could support the CDR function; that with the interim office currently located at CCOHTA, it would be feasible to establish the permanent process at CCOHTA, but not likely until the fall of 2002; and that a transition period would be necessary as a CDR process would have significant impact on existing drug plan processes.

Note

In recognizing the rapid evolvement of and sometimes change in scientific evidence, the Premiers (in January 2002) had requested probationary coverage for new drugs subject to ongoing assessment of cost-effectiveness upon the implementation of the permanent CDR. Ultimately, there was a decision not to include probationary coverage in the business case analysis as the conditions and parameters for probationary coverage would be complex and difficult to implement; no relevant models of doing this existed elsewhere in the world; and the participating drug plans already had a host of other details to manage in establishing and implementing CDR. To this day, despite international discussions, the practicalities of probationary coverage remain a challenge.

On September 5, 2002, the F/P/T Health Ministers approved a permanent CDR process to be housed at CCOHTA. Being part of a not-for-profit organization at arms-length from government allowed CDR flexibility to move more quickly in some directions such as increased transparency.

"Housing CDR at CCOHTA, a non-profit organization outside of government, was a strength as it removed the workings from government bureaucracy."

— Mike Tierney, former Vice-President, CDR (2006-2008)

Examining Potential Legal Liability to CCOHTA

Upon being selected to house the permanent CDR, CCOHTA asked its legal advisers to assess the potential legal liabilities resulting from housing and delivering CDR.

CCOHTA was particularly conscious of potential litigation after legal action taken by BMS to prevent CCOHTA from releasing a report on statins. While the courts rejected BMS' attempt, this court case was costly to CCOHTA. CCOHTA not only incurred significant legal costs, which consumed a substantial part of its budget, but lost productivity as a result of the demands on staff time and energy that were diverted to this court case.[14]

The legal advisers considered this case and other cases where the publicly funded drug plan processes had been challenged. They concluded that there were two legal bases for potential challenges to the CDR process:

- Publication — An application could be brought to restrain publication or for damages as a result of publication of misleading or inaccurate information. The legal basis for such a claim would be defamation, malicious falsehood, and/or negligent misrepresentation.
- Procedure — An application could be brought for judicial review based on alleged unfairness in the decision-making process.

CCOHTA could obtain insurance for publication challenges, but not for procedural unfairness.[15] This advice was critical in developing the procedures and processes for the permanent CDR. Great care was taken to establish procedures that would treat all stakeholders fairly.

Developing Procedures for a Permanent Common Drug Review

Although the general purpose, scope, and some of the templates and guidelines had been worked out by the Task Group on CDR before implementation of the interim CDR, the details of its permanent procedures were finalized during its interim phase. The secretariat worked closely with the Interim CDRC to establish procedures that CCOHTA could implement, building on the collaborative work of the participating drug plans and using legal advice to mitigate risks. International organizations were consulted. Personnel at the UK National Institute for Clinical Excellence (now the National Institute for Health and Care Excellence [NICE]), the Scottish Medicines Consortium (SMC), the Australian Pharmaceutical Benefits Scheme (PBS) and Pharmaceutical Benefits Advisory Committee (PBAC), and the New Zealand Pharmaceutical Management Agency (PHARMAC) shared

a wealth of information about their experiences, proving most helpful to this work. Input through consultations with industry and patient and public stakeholders, obtained during the interim CDR, further contributed to developing procedures.

With the goals of creating rigorous, consistent, and evidence-based reviews and recommendations, and using the lessons learned from domestic and international drug review processes and advice from a wide range of stakeholders, the following aspects of the program were decided:

- Maintain an evidence-based approach, using the best available evidence. Publicly available studies in peer-reviewed journals would be preferred but unpublished studies would also be allowed.
- Use standardized templates and guidelines to facilitate consistent, rigorous, and documented processes for reviews. This would illustrate that CDR had taken all reasonable steps to ensure the accuracy of its reports and publications, and to minimize bias.
- Employ checks and balances in the procedures, for example:
  - Reviewers — at least two reviewers would be involved in the clinical and economic reviews.
  - Experts — at least one clinical expert would provide input and advice for each review, and methodological and economic experts would be consulted as needed.
  - Manufacturers — would be informed of information that CDR and CEDAC would be considering by receiving a list of studies selected for the systematic review. They would be able to review, correct, and comment on draft CDR clinical and economic reports before they would be used by CEDAC.
  - CEDAC — this committee of experts established to make recommendations on drug coverage would also provide advice on conducting comprehensive and accurate reviews.
  - Manufacturers — would have the right to request reconsideration if they believed the CEDAC recommendation was not supported by available evidence or if they believed there was procedural unfairness.
  - Drug plans would have the opportunity to request clarification of CEDAC recommendations.

Other facets of the program that were put in place included:

- Submission guidelines for manufacturers were created that outlined a list of requirements that each manufacturer would need to include in its submission. The requirements were publicly available and applied consistently to all manufacturers.
- Conflict of Interest (COI) Guidelines and a Code of Conduct were established to dictate impartiality and no personal interest declarations for everyone involved in the review of the evidence, including CEDAC members.
- Confidentiality Guidelines were put in place to prevent the unauthorized use, disclosure, publication, or dissemination of manufacturers' confidential information that would be used in the review of a drug submission.
- Manufacturers were scheduled opportunities to provide input in the review of their drugs by filing a submission, commenting on draft reports, and requesting reconsideration of CEDAC recommendations.

- CEDAC would be able to only make recommendations or provide advice; participating drug plans/jurisdictions would make listing and coverage decisions.
- CEDAC would give reasons for its recommendations.
- Transparency was an important objective. Policies and procedures would be documented and published; the status of reviews would be tracked on the Web; recommendations and reasons for the recommendations would be made public.
- Timeliness was another important objective. Target timelines would be published and would facilitate verifiable consistency in review time from one submission to the next. If there were delays, those would be noted in the public status reports.

Given CCOHTA's experience with the BMS challenge and how extensive documentation contributed to CCOHTA's defence, it was clear that all communications about a submission under review or any unique situations should be documented and kept on file. While this would add time and effort to an already bustling process, this information proved essential on several occasions.

"The clearly defined processes and adherence to them put us in a stronger position to deal with any challenges."

— Mike Tierney, former Vice-President, CDR (2006-2008)

Over time there would be many revisions and adjustments to the procedures and submission requirements. Any small change in one document had a domino effect — it became a challenge to make sure that all changes were consistently reflected in all of the CDR documents.

Establishing Canadian Expert Drug Advisory Committee

The Task Group on CDR envisioned a national drug expert advisory committee that would receive and consider the results of the CDR drug reviews as well as other factors and develop listing recommendations for consideration by each of the plans. This national committee, drawing on expertise from across Canada, would provide a consistent approach that was predicted to reduce administrative costs and to reduce inequities of access among jurisdictions. The Task Group engaged Bob Nakagawa to develop a document describing the policy implications for the establishment of a national drug expert advisory committee.

The report *Policy Implications of the Establishment of a Canadian Expert Drug Advisory Committee March 2002,*[16] laid the groundwork for establishing CEDAC. It itemized the policy implications for a spectrum of issues and identified a series of tasks and decisions that needed to be addressed to create this committee.

During the interim CDR, the Interim CDRC and CCOHTA collaborated on the following to establish CEDAC: finalizing the CEDAC terms of reference and committee remuneration;

3.2

The first CEDAC (Appendix 2 for list of members and backgrounds)

Dr. Anne Holbrook, Dr. Ken Bassett, Dr. Laurie Mallery, Dr. Bruce Carleton, Dr. Andreas Laupacis (Chair), Dr. John Conly (Vice-Chair), Dr. Braden Manns, Dr. Margot Burnell, Dr. Dale Quest, Dr. Tom Paton.

Missing: Dr. Mike Evans.

incorporating the role of a national drug expert advisory committee into the procedure for CDR; expanding the duties of the CDR office to support CEDAC; striking a nominating committee to recruit a chair and members of the committee; and developing communications about the committee and its role.

The First Canadian Expert Drug Advisory Committee

More than 40 nominations were received for the first CEDAC. The nominations came from a variety of groups and organizations, including drug plans, industry, academic institutions, and other professional organizations. It was rewarding to receive nominations of so many talented and experienced men and women from across the country. They let their names stand for an effort that was yet to be proven and was bound to be controversial. The nominating committee had a challenging task of proposing a slate of potential members from this large pool of qualified nominees to the CCOHTA Board of Directors.

The first chair and members of CEDAC were announced by the F/P/T Conference of Deputy Ministers of Health in September 2003.[17] (Appendix 2) Their mandate was to make evidence-based recommendations of either list, list with criteria, or do not list to each of the participating F/P/T publicly funded drug plans regarding the listing of drugs on their formularies. This independent 11-member advisory body with membership from across Canada was accountable to CCOHTA's Board of Directors. While the

inclusion of public or patient members on CEDAC was discussed, it was concluded that the first CEDAC members would require expertise in drug therapy and drug evaluation. Thus, in accordance with the CDEC terms of reference, the first members had health care backgrounds, including some with expertise in health economics. CEDAC was sometimes referred to, internally, as a "committee of thoroughbreds." In describing the committee, Dr. Jill M. Sanders, President and CEO of CCOHTA/CADTH (1997-2010), said "CEDAC brings together a depth of expertise and experience in drug evaluation far greater than any individual jurisdiction could assemble. As the first truly national committee of drug evaluation experts, CEDAC is an important new resource for publicly funded drug plans that will greatly enhance decision-making and enable participating plans to focus on the most therapeutically beneficial and cost-effective drugs for the benefit of patients."

Developing Processes and Guidelines for Reviewers

As noted, the interim CDR provided an opportunity to test the templates for reviewing the clinical and economic evidence and the guidelines for reviewers, developed by the Task Group on CDR. Although the use of templates and guidelines helped with standardization, the reports produced for the 31 drugs during the interim CDR still varied in approaches used, rigour, and quality. Thus, CDR staff took on the task of refining the templates and guidelines for the review of clinical data so that the reports generated for the permanent CDR process by CCOHTA and contract staff would be credible, would be of a consistently high rigour and quality, and would be informative for CEDAC and drug plans.

As background for developing the review process, the CDR staff used feedback from reviewers, drug plans, and expert advisory committee members involved with the interim CDR process. They looked at how international organizations such as NICE, PBS and SMC conducted reviews and how findings were reported. They also used the extensive experience that CCOHTA had amassed in doing health technology assessments since its inception and obtained input and guidance from methodologists.

This research led to the decision that the systematic review process with a meta-analysis, wherever appropriate and feasible, should be used for clinical reviews rather than just a critical review or a narrative review. This was a major decision and not everyone was convinced at the beginning. One reason for making this choice was to be able to more credibly defend the reviews if questioned.

Reviewers would assess manufacturer-submitted published and unpublished studies as well as any studies identified through a comprehensive literature search by CCOHTA information specialists. Not everyone agreed that unpublished studies should be allowed as they were not peer-reviewed; however, proponents for their use pointed out that they may contain relevant information that was not otherwise available. An annotated template for reports and guidelines for reviewers, undertaking systematic reviews, facilitated consistent clinical reviews.

The pharmacoeconomic reviews would be a critique of the manufacturer-submitted pharmacoeconomic evaluation and it was agreed that the template used during the interim process, with a few minor changes, would be used until further experience was gained.

The clinical and pharmacoeconomic review templates have evolved over the years, but they remain the underpinning for the consistent and rigorous approach used by reviewers.

Holding Pre-Implementation Meeting in St John's in October 2002[18]
On October 16-17, 2002, CCOHTA and drug plan representatives met in St. John's to discuss plans for the implementation of the permanent CDR at CCOHTA. Dr. Jill M. Sanders chaired this meeting. This was an opportunity to review some of the proposed procedures and processes for the permanent CDR and to assess what remained to be done for its launch. While a great deal of work had been completed, the meeting attendees identified 50 action items, with the majority of them and their implementation resting with the CDR secretariat and CCOHTA.

Holding Consultations With Industry and Public Stakeholders
A key activity that had been contemplated throughout the development of CDR was consultation with stakeholders. The Task Group on CDR and subsequently the Interim CDRC and CCOHTA agreed on the importance of consulting with the stakeholders, particularly once the drug plans were more clear about their expectations for a common drug review and when procedures were drafted. Correspondence that CCOHTA and drug plans received from industry and patient groups further fuelled the need for consultation. The correspondence ranged from questions about the proposed CDR to advice on what it should look like, to concerns that CDR would be another barrier to access, to comments that CDR was "fatally flawed."

On January 14, 2003, CCOHTA hosted a daylong meeting with industry and industry consultants to provide an overview of the proposed CDR process and to receive feedback before the processes were finalized. About 100 people, including industry representatives, drug plan representatives, and CCOHTA staff attended. A professional facilitator encouraged discussion and comments at the meeting and also asked attendees to provide written comments to CCOHTA. Twenty-five organizations,[19] mostly pharmaceutical manufacturers, provided written comments. The hundreds of comments and suggestions brought forward through this consultation touched on all aspects of the proposed CDR process, including submission guidelines, number of reviewers per submission, privacy and confidentiality, transparency, and an appeal process. All issues were considered and many resulted in some significant changes to the process, ranging from having at least two reviewers per clinical or pharmacoeconomic review to greater transparency and a priority review process.

"It was a frosty day in January 2003 that the full public journey really began. I remember it like it was yesterday. There was a willingness to listen and to admit that CDR did not have all of the answers. There was a problem solving approach — this was crucial to success."

— George Wyatt, Managing Director and Founder, Wyatt Health Management

On March 4, 2003, CCOHTA hosted a consultation meeting for public stakeholders. Invitations were extended to umbrella organizations that represented a range of stakeholders, including patients. Thirteen stakeholders (groups and individuals) along with CCOHTA and drug plan personnel attended. Again the objective of the meeting was to share an overview of the proposed CDR process and to receive feedback and input from the public stakeholders before processes were finalized. Comments included a need for health care consumers to be fully engaged in all aspects of decision-making about drug coverage and concerns about equity of coverage, accessibility, and timeliness. CCOHTA committed to ongoing communications with the public stakeholders as the process evolved.

Formation of Submission Working Group and Appeal Process Working Group
The consultation process yielded voluminous and varied feedback, with the majority of the input being about submission requirements and the most contentious being about an appeal process. Thus, the Submission Working Group and the Appeal Process Working Group, both comprising CDRC members with CDR support, were established. The efforts of these working groups helped resolve and provide direction for many of the issues raised in the consultations. The submission requirements were clarified and changed in places and were divided into Category 1 (needed for the review of a drug) and Category 2 (needed by drug plans) requirements. After considerable discussion, the reconsideration process was developed as a means for manufacturers to "appeal" CEDAC recommendations quickly and without additional resources.

Over the years, CDR would rely on other working groups for input and advice on a multitude of issues.

Workshop on Preparing Submissions for the Common Drug Review — June 25, 2003
CDR invited manufacturers and consultants who would be preparing submissions for new drugs and new combination drug products to a workshop on June 25, 2003. The workshop provided a detailed walkthrough of the submission requirements for new drugs and new combination drug products, an overview of the review process and timelines, and other relevant information and opportunity for questions.

Administrative and Staffing activities
The first Director of CDR came on board on January 2, 2003 (see Appendix 3 for list of early directors) and was immediately immersed in transitioning the interim CDR to its more permanent state. Many administrative details and staffing initiatives needed to be addressed for a smooth transition.

Staff Recruitment
Hiring qualified staff was a high priority and generated a lot of activity from writing job descriptions to interviewing. CCOHTA found that recruiting staff was a substantial challenge as few people had heard about the fledgling CDR program. Some potential candidates expressed concern that the funding and future of the program was far from certain and they were hesitant to leave the security they had for the unknown. This is a far cry from recruitment years later when there would be many applications for each position. While the plan was to hire some reviewers, it was recognized that there would be a need to contract reviewers across the country to meet the volume of work. To this end, 45 individuals from across Canada responded to a request for expression of interest to conduct clinical or pharmacoeconomic reviews on a contractual basis. Qualified individuals were included in a roster that served as a source of reviewers.

Budget

The annual budget for CDR was set at $2 million and remained at that level until April 1, 2007 when it increased to $5.1 million to cover additional work including new indications for old drugs and increased transparency initiatives.[20] This budget covered financial commitments including staff salaries, office space, CEDAC operations, and all other costs associated with CDR. Participating F/P/T governments provided funding based on a funding agreement of 30% federal and 70% provincial and territorial. The funding in the early days was approved on an annual basis, leading to some uncertainties in planning.

Internal Processes

A consultant worked with CDR to put in place required internal processes for tracking documents, tracking conversations and emails, and developing secure filing systems. CCOHTA understood the importance of accurate records and the pharmaceutical industry called for secure systems to protect the information they would submit to CDR.

Secure Website/Email

CCOHTA obtained advice on developing a secure website/email system. Secure email was selected as the immediate means for exchanging sensitive information because it could be implemented quickly. As secure email was cumbersome to use, the plan included expansion to a secure website in the future.

Communications

CCOHTA took transparency and CDR communications seriously and committed to dialogue and information sharing with industry and other stakeholders. Its communications objectives included:

- ensuring that the CDR roles, objectives, and processes were clearly understood
- ensuring a smooth transition to the permanent CDR
- providing updates on program and policy changes.

While the plan was to use the CCOHTA website and electronic publications as the primary communications vehicles, industry information sessions continued to be held after the launch of the permanent CDR.

CCOHTA and the drug plans received many questions about CDR — often, the same questions. To avoid confusion and to make sure that responses were consistent, CCOHTA and CDRC discussed these at CDRC teleconference calls and meetings and developed common responses that all could use. CCOHTA developed a set of "frequently asked questions" and posted these on the CCOHTA website.

Getting the "Go Ahead" From Federal, Provincial, and Territorial Ministers of Health

At last the much awaited pan-Canadian program that was authorized by the Premiers, designed by the drug plans, and prepared for operation through CCOHTA and drug plan collaboration was ready for sign off by the Deputy Ministers of Health. CCOHTA announced September 1, 2003 as the anticipated date for accepting submissions for the CDR.[21] But alas, it was not to be clear sailing even though everyone thought that all details had been approved. On July 22, 2003, the Deputy Ministers of Health asked that the COI Guidelines, previously approved by CDRC and CCOHTA Board, be tightened. The deputies wanted assurance that conflicts of interest related to a competitor's product and those associated with family members would be declared. They also noted a need for a process to identify and manage COI statements and raised the question about making CEDAC members' COI statements publicly available. The expected time needed to address these requests raised serious concerns that the implementation date would be delayed. A flurry of consultations with the CCOHTA Board of Directors and participating drug plans followed, leading to a revision and tightening of the COI Guidelines and their approval by the Deputy Ministers of Health on August 13, 2003.[22] Considering the review stages and approvals required in carrying out coordinated F/P/T efforts, this turnaround time was quite remarkable.

Implementation of the permanent CDR was given the go ahead.

CHAPTER 04

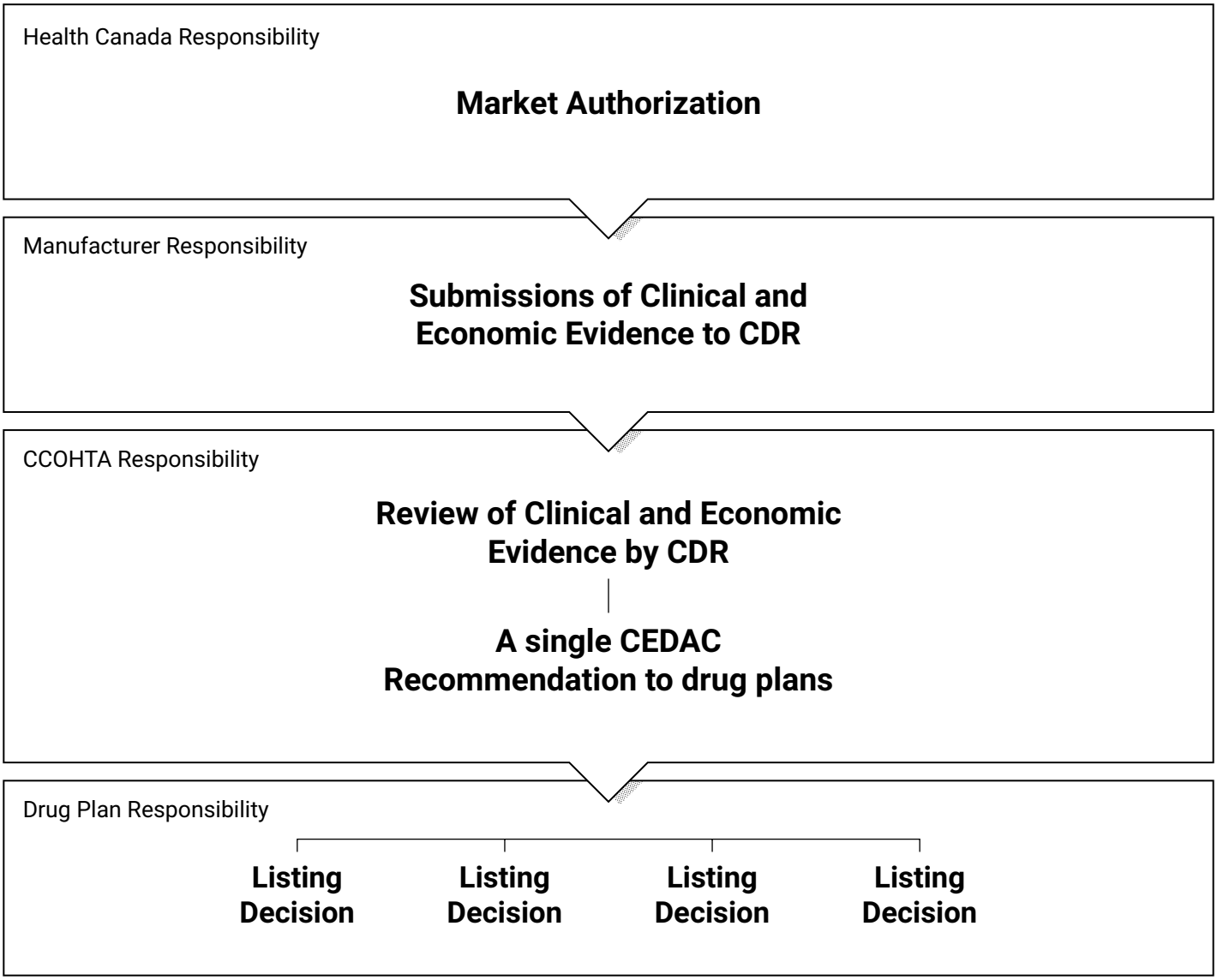
4

Chapter 04

The First Year of the Permanent Common Drug Review (September 2003 to December 2004)

At last everything was in place — the procedures and supporting documents had been finalized. Staff had been hired. The Deputy Ministers of Health announced the establishment of CEDAC. CDR was officially open for business on September 1, 2003. Everyone was eagerly awaiting the first drug submission — it did not arrive until December 15, and then four more submissions arrived by December 24. Meanwhile the reviewers readied themselves to take on systematic reviews, CEDAC had its orientation meeting, and a storm erupted over a phrase excerpted from an internal intergovernmental letter. The phrase was “no means no.”

With the arrival of the first five almost concurrent submissions, CDR was launched onto a treadmill — producing quality reviews under aggressive time frames. During the first year the relevance and effectiveness of all the procedures were tested and the internal systems were tried out. Adjustments and revisions were made as needed. All stakeholders — drug plans, industry, patient groups, the public, and others — as well as CCOHTA were becoming accustomed to this new entity.



4.1

Process for Formulary Listing Decisions in Canada After the Implementation of CDR

Open for Business

CDR was officially open for business on September 1, 2003. This pan-Canadian initiative became the single process for reviewing new drugs and providing formulary listing recommendations to all publicly funded F/P/T drug benefit plans in Canada, with the exception of Quebec (see Figure 4.1). Its stated objectives included:

- greater efficiency and reduced duplication of effort
- enhanced consistency of rigorous drug reviews across Canada
- equal access to timely, evidence-based information and expert advice for all participating jurisdictions
- maximized use of limited resources and expertise from across the country.

Drugs eligible for submission to CDR by manufacturers included new drug and new combination drug products that had received a Health Canada Notice of Compliance (NOC). Generally, any drugs that were submitted for coverage decisions to any of the drug plans were to be submitted to CDR. This included oral cancer drugs and HIV/AIDS drugs, but did not include hospital drugs.

Drug plans could also ask CDR to undertake the review of any drug as well as a new drug or a new combination product.

Based on the average number of new drugs approved for marketing by Health Canada, CDR anticipated 25 new drug submissions per year. CDR expected the first submissions to arrive soon after September 1, 2003 and hopefully at the rate of about two per month — but, alas the first submission, brimonidine tartrate/timolol maleate (Combigan) did not arrive until December 15, 2003. And then four more submissions atazanavir (Reyataz), gefitinib (Iressa), norelgestromin/ethinyl estradiol (Evra), and almotriptan malate (Axert) arrived by December 24, 2003.

Quite a Christmas present for CDR staff!

Although CDR had some dedicated staff it needed to contract work to additional clinical and economic reviewers to meet the aggressive time frames that had been agreed upon and made public. Within days of receiving the submissions, CDR established contracts with reviewers using the roster of individuals who had responded to an earlier call for expression of interest and with clinical expert consultants who would advise on the reviews.

Clinical and Economic Reviewers

CDR staff reviewers were assigned as the primary reviewers for each of the submissions and contractors were secondary reviewers. The learning curve was steep and immediate for all. The first five submissions, which included two priority review submissions, were quite different from one another and presented unique challenges. For the first few months CDR reviewers met daily to discuss their projects and to collectively solve issues that they had encountered in the review process.

The reviewers regularly faced new methodological challenges, such as indirect comparisons, and learned about new methodologies as they were applying them. They took great pains to ensure the accuracy of their reports. This was the first time in Canada where pharmaceutical manufacturers received draft copies of public drug plan reviewers' assessment reports concerning their drugs and they scrutinized them closely for accuracy, completeness, and tone. Relatively early in the delivery of the program, CCOHTA received a letter from a company that had conducted a pharmacoeconomic review complaining that some of the comments made by the CDR reviewers in their report were offensive. Thereafter, all reports were reviewed more carefully for tone and choice of language as well as content accuracy.

Canadian Expert Drug Advisory Committee Meetings

CEDAC had its first meeting, an orientation, in October 2003 (See Appendix 2 for list of members). The main objective of the meeting was to introduce the CEDAC members to the CDR procedures and review processes as well as their responsibilities as committee members. It was a useful gathering as members also raised questions and concerns in areas such COI and personal liability. All issues were addressed either at the meeting or in follow-up actions.

CADTH

4.2

The first submission (Combigan) to CDR is received on December 15, 2003

Back Row: Terri O'Grady, Sarah Vanstone, Stefania Moffatt, Elaine MacPhail, Cheryl Holmes, Barb Shea.

Front Row: Stan Bardal, Vijay Shukla, Mike Gaucher.

CEDAC had its first working meeting in April 2004. It reviewed and provided recommendations for the first five new drug submissions received by CDR. Each drug — Combigan, Reyataz, Iressa, Evra, and Axert — was unique and required unique consideration. The varied backgrounds and perspectives of the members led to robust deliberations for these drugs (as well as for future submissions) and resulted in recommendations that were not always unanimous — a healthy outcome.

First Set of Recommendations Issued

The first CEDAC recommendations and reasons for recommendations were released and posted publicly on the CCOHTA website on May 27, 2004. This was a groundbreaking step as up to this time, publicly funded drug plans did not share their expert advisory committee recommendations or reasons for recommendations publicly. CEDAC took great care in crafting the recommendations and the reasons for them to be as informative as possible and yet contain no confidential information. In the following statement, Andreas Laupacis reflected the sentiments of many who had worked to establish the CDR process: "I'm also very proud of the fact that the Reasons for Recommendation are publicly available…With CEDAC, we can refer people to the website and discuss what's on that site. My sense is that the recommendations are thoroughly read by the pharmaceutical industry and policy-makers. I think that's a big plus, and I'm proud of it."[23]

Manufacturers and drug plans received the first set of recommendations and reasons for recommendations with the accidental inclusion of happy faces on them. Clicking on the happy face caused a comment — generally of an editorial nature — to open up. This technical glitch occurred because CDR did not have a process in place for checking for and removing hidden data. While humorous in this case, this incident was a trigger for CDR to develop processes for "cleaning" documents before they were issued and subsequently posted.

CEDAC Meeting Proceedings

Andreas Laupacis, the first CEDAC Chair, provided able leadership, and the committee tackled its responsibilities with enthusiasm, dedication, compassion, and a commitment to excellence. Notwithstanding their mandate and endorsement of an evidence-based approach, CEDAC members agonized over some "do not list" recommendations, particularly for new drugs indicated for a condition with no or limited treatment options, but for which there was poor or limited evidence. Almost all of the members were actively seeing and treating patients, and thus, had an understanding of and empathy for patients with unmet needs. The chair reported that on one occasion he lost sleep because of a "do not list" recommendation. "I had a very restless sleep that night, constantly fretting about the conflict between making societal recommendations on the basis of evidence and concern for individuals with a terminal disease."[23]

CEDAC sought advice from an ethicist in regard to the "do not list" recommendations, as these recommendations might result in the drugs not being accessible (i.e., unaffordable) to patients. After gaining an understanding of the CDR procedures and CEDAC's role and deliberative process, the ethicist advised it was ethical and within CEDAC's mandate to recommend "do not list" when evidence was lacking or did not support listing the drug. The ethicist also noted that the CEDAC recommendations and reasons were well written and fair, but could be criticized on lack of public involvement.[24]

One of the tenets of CDR was fairness and steps were in place to mitigate bias and undue influence, which included CEDAC. These were based on international models and legal advice. Manufacturers and CEDAC members could not discuss a submission while it was under review. Interactions between CEDAC and the CDR review teams and the drug plans about the submission reviews were also limited. CDR reviewers and external experts could attend CEDAC meetings by invitation to answer questions or provide clarifications. CDRC members could attend as observers but not participate in the discussion or deliberations. The need for more interaction between CEDAC and the CDR review team and drug plans, so that each could serve the other better, quickly became apparent. As the roles and needs became better understood, the interaction increased without compromising responsibilities or CDR objectives.

CEDAC provided strong leadership for enhancing the CDR review process. It encouraged the CDR team and clearly articulated ways in which the CDR reports could better meet the committee's, and therefore the drug plans', needs. The culture of CCOHTA included its willingness to change and evolve with new practices and methodologies.

Efforts to Involve the Public/Consumers in the Common Drug Review Begin

Patient and public/consumer groups were asking for greater involvement in the CDR process from the time of the earliest announcement about the program. CDR and drug plans acknowledged the need for public-consumer involvement. This concept was also supported by CEDAC and this was reflected in a 2005 *Provincial Reimbursement Advisor* article, which quoted Andreas Laupacis, the CEDAC Chair, as stating, "But I do think there is room for increased engagement between the public (which, again, I see as different from disease advocates) and CEDAC."[23] Work on how to involve the public/consumers actually began soon after the permanent CDR was implemented and a discussion paper on options was prepared for both the CDRC and the CCOHTA Board in April 2004. At its April 2004 meeting, the CCOHTA Board gave approval in principle to investigate options. This initiated the effort that would eventually lead to the appointment of public members to CEDAC in 2006 and to the implementation of patient involvement in 2010 — perhaps not as quickly as many would have liked.

Stakeholder Outreach Activities

CDR considered stakeholder outreach activities to be very important. It invested time and effort in meetings and presentations to industry, patient/consumer groups, and numerous and varied organizations.

CCOHTA and industry continued to meet regularly through the Research-Based Pharmaceutical Companies (Rx&D)/CDR Liaison Committee, a committee of Rx&D member company representatives and CCOHTA personnel, which was established in 2003.[25] These meetings provided a forum for an open exchange of information and perspectives. Some of the issues raised in the meetings by industry led to refinements of CDR procedures. In 2004, representatives from BIOTECanada joined this committee.

Merger of CDRC and PAC to form ACP (October 25, 2004)

At the request of the F/P/T Pharmaceutical Issues Committee (PIC), CCOHTA took steps to the merge two jurisdictional advisory committees — the CDRC, providing advice related to CDR, and the Pharmaceutical Advisory Committee (PAC), providing advice related to health technology assessment of drugs — to form the Advisory Committee on Pharmaceuticals (ACP).[26] Given that both former committees had mandates related to pharmaceuticals, jurisdictions felt that merging the two would lead to more coordinated advice to CCOHTA's CDR and health technology assessment (HTA) directorates and it would reduce the amount of time drug plan staff would spend attending CCOHTA advisory committee meetings. CCOHTA saw the merger as a means to reduce the amount of time and effort that its staff spent in supporting two committees. While the streamlining efforts were great in theory, HTA issues were sometimes shortchanged. Inevitably because of the timeline-driven nature of CDR work, CDR agenda items tended to dominate the meetings. This would lead to future work to streamline committee activities.

Year One — Some Notable Events

While these were one-time only events, they are presented because of their impact on the program's evolution.

Governments are accused of inappropriately deferring their decision-making to CCOHTA

While CDR was awaiting its first drug submission, Rx&D generated a flurry of activity about "no means no; yes means maybe." In September 2003, Rx&D had obtained a copy of a letter (dated December 16, 2002) from the then Ontario Minister of Health and Long-Term Care through the Ontario Freedom of Information Act. Rx&D felt that the minister's letter[27] confirmed an agreement among the F/P/T Ministers of Health to collectively and automatically refrain from listing any drugs that received a negative CEDAC recommendation. In a letter that Rx&D sent to all F/P/T Premiers and all F/P/T drug plan managers, as well as to CDR and other organizations, Rx&D argued that this action would take the decision-making about which drugs should be reimbursed out of the hands of elected officials and place it in the hands of a few technical experts.[28] It urged all jurisdictions to provide assurance that CEDAC would not be permitted to dictate pharmaceutical policy in their jurisdictions.[28]

The Rx&D correspondence sparked discussions with CDR and drug plan legal advisers. These discussions confirmed that the ministries must not "fetter their discretion," that is to say, their decision-making responsibilities. A response was sent on behalf of the participating jurisdictions to Rx&D confirming that participating jurisdictions would make their own decisions, based on evidence-based CEDAC recommendations and in consideration of their own factors. This helped to dissipate these Rx&D concerns.[29]

Drug plans request a CDR review of a drug that is administered in hospital. The drug manufacturer challenges CCOHTA on the appropriateness of a CDR review of the drug.
In early 2004, a manufacturer chose not to submit a new drug to CDR for review as it considered the new injectable drug to be a hospital drug. Drug plans felt that they would be the ones funding it, and thus, CDRC on behalf of all participating drug plans submitted a request to CDR to review the drug. As per the CDR procedure for drug plan-filed submissions, the pharmaceutical company was advised of the submission and invited to provide information, which it did, but the company maintained that CDR was not the appropriate venue for its drug.

CDR carried out the review of the available evidence in accordance with its procedures; however, before the final recommendation was issued CCOHTA received a letter from the solicitors for the pharmaceutical company, contending that the CDR process regarding the drug was inappropriate, based primarily on two factors:

- The drug, as a "hospital drug" was not the type of drug which is normally submitted to the CDR for review.
- CEDAC did not adhere to the CDR procedure in that CEDAC entertained a submission from CDRC which the pharmaceutical company felt was not entitled to make a submission and that CEDAC made a recommendation where the process had not been initiated by the pharmaceutical company.

The review of the drug was placed on hold pending receipt of legal advice. In the end, CCOHTA legal advisers found that the CDR procedures did not restrict CDRC in filing a submission for a "hospital drug" and that CEDAC could make a recommendation on a CDRC submission. The review of the drug resumed and a final recommendation was issued. Subsequently CDR documents were further clarified.

This marked the beginning of a move for many injectable drugs that would have traditionally been considered hospital drugs to be reviewed through CDR. The use of hospital outpatient departments and the establishment of infusion clinics meant that people requiring certain intravenous products did not need to be admitted as in-patients. Thus, the costs for these drugs for eligible patients were transferred from hospital budgets to the publicly funded drug plans. Drug plans sought the same review process for these drugs as for all other potential drug benefits.

A patient group contends that the CDR process is not the right one for its drug to be reviewed
On July 28, 2004, CDR issued a (non-final) CEDAC recommendations and reasons for recommendations for two agalsidase beta products (Fabrazyme and Replagal) — drugs used in the treatment of Fabry Disease — in confidence to the manufacturers and drug plans as per CDR procedures. Somehow the Fabry Society learned that CEDAC recommendations for both products were "do not list." On September 15, 2004, a delegation of 15 Fabry Society of Canada members and supporters (accompanied by an *Ottawa Citizen* newspaper photographer) made an unannounced appearance at the CCOHTA offices and asked to make a presentation to CEDAC at its in-progress meeting. CCOHTA staff explained that a presentation by patients to CEDAC was not possible

under the current CDR procedure; however, Dr. Jill M. Sanders, then President and CEO of CCOHTA, met with the delegation and committed to provide their written submission to the CEDAC Chair. The main issues that were raised during the meeting with Dr. Jill M. Sanders, and in relation to the submission[30,31] were:

- CEDAC and CDR must allow for direct patient input about their experiences with treatment and the impact of the treatment on their lives.
- CDR cannot and should not be reviewing catastrophic drugs because the traditional pharmacoeconomic models are not suited to the review of therapies that are recognized as very expensive and serving a very small population.
- It is unconscionable for CDR to deny treatment access to Canadian patients with Fabry, while those in other countries (with coverage for these drugs) continue to live healthy, productive lives.

CCOHTA and the CEDAC Chair sent a joint response to the Fabry Society, acknowledging the patients' concerns about access to effective treatments. They also clarified that CCOHTA was acting within its scope and mandate, but that it was collecting information about other models of drug review for future consideration. This appearance by the Fabry Society members and supporters was another example of the growing pressure to include patients and the general public in the CDR process and another prompt for CDR to proceed with steps to engage them.

Another new program, the Canadian Optimal Medication and Prescribing Utilization Service (COMPUS) was launched at CCOHTA.

In March 2004, COMPUS was launched to optimize the prescribing and use of drugs in Canada. It would identify, evaluate, and promote best practices.[32] The F/P/T jurisdictions agreed that CCOHTA, with its evidence-based approach in determining effectiveness and efficiency of drugs, was the most appropriate venue to house such a program. This was a significant and exciting addition to CCOHTA's range of services, and would lead to some reorganization within the CDR Directorate, as the Director of CDR would become Vice-President, responsible for both CDR and COMPUS.

There were now two pan-Canadian programs breaking new ground in the area of pharmaceuticals management. Those involved were optimistic that the outcome of their work had the potential to positively impact the health of Canadians, but with the realistic expectation that there were no quick and easy routes to success.

Impact of the Common Drug Review During its First Year

Between September 1, 2003 and December 31, 2004, CDR received 28 submissions, including 2 resubmissions; and it released 15 final CEDAC recommendations and subsequently received 12 requests for reconsideration. Despite the pressures and challenges that were encountered, CDR staff and CEDAC members met their targeted time frames.

"Timeliness was a big concern for some provinces and the pharmaceutical industry when CDR was being set up — a concern that CDR would take more time than current reviews."

— Leanne Jardine, Executive Director, Pharmaceutical Services, NB

Demands on CCOHTA's Common Drug Review Staff

All CDR staff experienced the unrelenting flow of new submissions. Added to this were frequent requests for reconsideration filed when CEDAC made a "do not list" recommendation. The pressure on reviewers, both experienced and newly recruited, increased in sync with the growing volume of submissions. The hard copy submissions were huge, so looking for specific information was sometimes like looking for a needle in a haystack. The submitted studies were usually designed to obtain regulatory approval (permission to be legally sold) rather than to inform reimbursement recommendations and decisions (become a drug plan benefit). Methodologies were constantly evolving; thus, reviewers often found themselves using old methodologies for reviews already initiated, but at the same time learning new methodologies and using them for their new projects — that is, working in the old and new at the same time.

The pace of the submissions and the overriding commitment to the quality of the review process prompted the implementation of new document management procedures. Based initially on MS Word (tables) and Excel programs, these eventually evolved into more sophisticated project tracking systems. The submissions and CDR review reports were in hard copy; thus, sharing documents with CEDAC meant photocopying, assembling binders, and packing it all up for couriers; all labour-intensive activities. Any documents that had confidential information that needed to be transmitted by email were sent by CDR staff through secure email, which presented a challenge to set up, maintain, and use. From the outset, means of streamlining CDR processes were sought to address these challenges but in some cases would take years.

The newness of the processes, the rigid timelines, and the intense scrutiny from outside fused to create a cohesive CCOHTA staff. They looked to each other for problem solving and moral support. They seemed to thrive in this almost frontier atmosphere — filled with the thrill of trying something new and also with some trepidation.

CCOHTA was growing rapidly at the time CDR was established and as such the new program benefited immensely. CCOHTA invested in core service areas such as human resources, and finance and administration; thus, providing CDR with access to people with specific training in areas such as recruitment and hiring of staff, arranging and administering contracts, managing finances, managing projects, and website maintenance.

Transparency

Those developing CDR procedures and the legal advisers believed that as much transparency as was feasible should be incorporated. During the first year of operation all stakeholders were able to see the degree of transparency that had been implemented. It was greater than in any drug plan review process in Canada. CDR was considered a leader. Through the *CDR Update*, an electronic newsletter, and the CDR-specific site on CCOHTA's website, all stakeholders had access to:

- detailed information about the CDR process — CDR procedures, submission requirements, time frames
- the submission status of every drug under review
- the CEDAC Recommendation and Reasons for Recommendation documents
- the CEDAC meeting schedule, with an estimated date of when drugs would be on the agenda
- the CEDAC members along with their profiles, and in time, a summary of their conflicts of interest
- the terms of reference for CEDAC and jurisdictional advisory committees
- updates of any changes.

In addition, manufacturers could see and comment on the CDR review reports before CEDAC used them in their deliberations. Manufacturers and other stakeholders had feedback opportunities and information sessions.

"Information sessions and constant discussions and ability to change allowed the organization to be successful. If you had done the sessions and gone back into the cave, we wouldn't be here talking today."

— George Wyatt, Managing Director and Founder, Wyatt Health Management

Drug plans, industry, patient groups, and other stakeholders welcomed this new level of transparency; however, they did not always agree on what should be transparent. Industry did not permit CDR to release certain information that many felt would provide a better understanding of the reasons for CEDAC recommendations. Industry members voiced some reservations about posting the reasons for recommendations — as it felt that this was too transparent and only the recommendations should be posted.[31,33,34] In a meeting with CDR personnel, industry representatives raised concerns that if information in the Reasons for Recommendation differed from the information in the Health Canada approvals, it could present a legal or medical problem.[35]

Many people, including CDR and CEDAC members, felt that CDR and CEDAC should be able to provide more details to better explain reasons for recommendations, such as information from unpublished studies; however, CDR and CEDAC were bound by the *CDR Confidentiality Guidelines* that had been agreed upon. Additionally, most medical journals had editorial policies based on the Ingelfinger Rule,[36] which required author-researchers to not release the details of their findings to the mass media before their work was peer-reviewed and published. In correspondence with editors of the *Canadian Medical Association Journal*, *Journal of the American Medical Association,* and the *New England Journal of Medicine*, CDR received confirmation of this approach. While this was disappointing to all who felt that all relevant references for recommendations should

be disclosed, that desire needed to be pitted against the agreed upon *Confidentiality Guidelines* and concerns that manufacturers might not otherwise submit unpublished data. Sometimes unpublished data were all that was available to CDR and CEDAC.

CDR staff and CEDAC members learned that transparency took time and effort. All details had to be checked carefully. In providing reasons for recommendations, CDR staff and particularly CEDAC members expended a great deal of time and effort to craft the wording and ensure that it was adequately informative, accurate and balanced, and that no confidential information was included. Just updating the submission status reports each week demanded time and effort from several staff. Despite the extra work, CDR remained committed to increasing transparency.

Life Under the Microscope

In its first year of operation CDR was under intense scrutiny from all stakeholders. There were those wishing it great success and there were those wishing that it would fail and be scrapped. As a result, those different camps were watching either for major accomplishments or faults. This certainly put pressure on the CDR staff, which strove for excellence and took precautions to avoid any missteps or reasons for public criticism.

The Common Drug Review's Impact on Drug Plans

By generating review reports and providing recommendations, CDR reduced the workloads of participating drug plans. Most representatives from drug plans noted that the CDR process was far more rigorous than what was performed in their jurisdiction before CDR, particularly in smaller jurisdictions that lacked sufficient resources to do such reviews. Generally, the feedback from drug plans was that CDR was meeting the objectives that were collectively agreed upon when CDR was being designed. Their thoughts can be summed up in the following quote: *"Through the Common Drug Review, we have access to some of the best medical minds in the country. The CDR approach reduces duplication and provides drug plans throughout Canada — big and small — with timely, high-quality recommendations that help us do our work. I think we all come out winners by participating in this sort of model,"* Dr. Judith Glennie, former Associate Director, Drug Benefits Management, Ontario Ministry of Health and Long-Term Care.[37]

How F/P/T drug plans handled CEDAC recommendations ranged from no further review by their drug advisory committee, to limited review, to vetting all CEDAC recommendations through the jurisdictional drug advisory committee.[38] The fact that some drug plans were still doing their own reviews was seen as a weakness in the CDR process.

The Common Drug Review's Impact on Industry

In a 2004 *Provincial Reimbursement Advisor* article, *The Common Drug Review — One Year Later*, David Chown states: "The pharmaceutical industry acknowledges that the CDR Directorate has done a good job in designing and implementing a comprehensive, transparent process that is well understood by most stakeholders. However, as individual companies with drugs that have now run the gauntlet first-hand, and collectively via Canada's Research-Based Pharmaceutical Companies (Rx&D), the industry has expressed concerns with several shortcoming of the CDR process."[31]

The listed shortcomings included:

- concerns that CDR is also reviewing safety and efficacy after these factors had already been reviewed by Health Canada
- no identification of reviewers
- at times differing perspectives in reviews (by CDR) and recommendations (by CEDAC)
- negative recommendation may ignore clinical benefit
- no opportunity for face-to-face meetings between industry and CDR once the review is under way
- no withdrawal process, no pre-submission meetings
- lack of patient involvement
- a need for a modified review process for drugs with NOC/c.[31]

During the years that followed CDR's establishment, many of the listed shortcomings would be addressed through revisions and refinements to the CDR process.

It was somewhat of a surprise that industry felt that CDR was duplicating the work of Health Canada.

"The industry felt that CDR was a duplication of Health Canada. Of course, we know now that the two are very different, but that was not the feeling back then and CDR was seen as a delaying tactic because of the duplication."

— George Wyatt, Managing Director and Founder, Wyatt Health Management

Some other stakeholders also had concerns about duplication. CCOHTA took steps to correct this misconception by explaining that CDR considered the relative benefits, safety, and cost-effectiveness of a new drug in relation to existing therapies, which Health Canada did not do.[39] In addition, efforts were made to explain the need for and importance of cost-effectiveness and the concept of "value for money" for reimbursement decisions.

An Action-Filled First Year

The first year of CDR's operation was filled with excitement, some tension, anticipation, and long hours of work as the efforts of dedicated people inside and outside CCOHTA supported the brand new drug review process. As with any start-up program, some unanticipated challenges and events occurred, but dealing with them led to a stronger CDR. And one thing was clear, CDR would need to embrace and adapt to ongoing change — change precipitated by external factors and change due to internal efforts — to enhance the CDR process and products.

CHAPTER 03

Chapter 05

The Early Years (up to 2008)

A rhythm had set in. CDR was beginning to mature and was better supported by more staff. Reviewers and CEDAC members had become more experienced. But by no means did things remain static. Reviewers and CEDAC members continued to be challenged as there was an increasing number of orphan drugs and costly new drugs to review, and new methodologies were being introduced and implemented. Existing drugs with new indications were added to the eligible types of CDR submissions and the review of pre-NOC submissions was explored. The review of cancer drugs was transferred to the Joint Oncology Drug Review (JODR). Public members were appointed to CEDAC. EKOS Research Associates Inc. evaluated the first year of CDR operations and made some recommendations, and the House of Commons Standing Committee on Health undertook an extensive review of CDR. The participating drug plans continued to support and increasingly value CDR. And CDR was increasingly recognized and respected on national and international levels.

The Common Drug Review's Evaluation — 2005

One of the requirements when CDR was established was an evaluation after one year of operation to determine if the program was meeting its objectives. The objectives were:

- provide a consistent and rigorous approach to drug reviews and evidence-based listing recommendations
- reduce duplication of efforts by drug plans
- maximize the use of limited resources and expertise
- provide equal access to the same high-level evidence and expert advice to all participating plans.

In early 2005, EKOS, an Ottawa-based consulting firm specializing in program evaluation and performance measurement, was selected to undertake the independent CDR evaluation. EKOS delivered its final report on September 27, 2005 and CCOHTA released it to the public on October 12, 2005. EKOS' findings showed that drug plans held different views on the value and impact of CDR than the pharmaceutical industry and consumer/patient groups.[40]

The participating drug plans were positive about CDR. From their perspective, CDR had decreased duplication and increased efficiency, consistency, and rigour. The smaller drug plans, in particular, reported a positive impact as they now had access to a large pool of high-level expertise and information.

The pharmaceutical industry rated the performance and value of CDR lower in meeting the objectives and patient advocacy groups rated it lower still. The advocacy groups argued that CDR was preventing timely access to much needed drugs in Canada. EKOS found that the patient advocacy groups had little awareness of the purposes and benefits of an evidence-based review.

Based on their findings EKOS made four recommendations:[40]

- That CDR develops a process to communicate decisions and recommendations in a language that is not difficult for the general public to understand and appreciate.
- That CDR works with the pharmaceutical industry and individual companies toward making the CDR process more transparent for all stakeholders.
- That CDR assesses how best to incorporate public input into the CDR process.
- That CDR explores different approaches for undertaking reviews. Reviews of simpler products/submissions should be completed in less time and be less labour intensive than more complex submissions.

CDR had been previously considering a number of changes and enhancements, many of them in-line with the four recommendations. The evaluation reinforced the need for greater transparency, public involvement and efficiency, and also highlighted the need to move in these directions as quickly as possible. Fulfilling the EKOS recommendations became an important area of focus for CDR during the next few years.

Public Members Appointed to the Canadian Expert Drug Advisory Committee October 2006

While the involvement of patients and/or public in CDR was discussed as early as 2002-2003 when CDR was being developed, it was agreed that this should be pursued after CDR was established and running. With ongoing pressures from the patient

advocacy groups and requests from CEDAC, CDR responded by drafting a discussion paper that led to the CDRC and CCOHTA Board giving directions in April 2004 for CDR to investigate the options for public/consumer involvement in CDR. In December 2004, CDR engaged One World Inc. (OWI), an independent consultant, to deliver a report outlining appropriate models or options for public involvement in CDR. After exploring national and international examples of public and patient involvement, OWI delivered its report on January 31, 2005 in which it offered three options: include public on CEDAC, obtain input from organized groups, and obtain input from public/consumer advisory committees.[41] The foregoing prompted the CCOHTA Board to ask staff for a proposed staged approach to increase public involvement activities in the agency.

Two public members were appointed to CEDAC in October 2006. This was the first step in CADTH's staged approach to greater public involvement in drug reimbursement reviews and decisions. All stakeholders welcomed this change.

"The appointment of the public members was very progressive — this was an important step in including the public voice."

— Mike Tierney, former Vice-President CDR (2006-2008)

The two public members were selected from a large and diverse group of applicants. They were to serve as members of the general public and not as representatives of any specific interest group or organization. Their role was to bring the broader public interest or perspective (including public concerns and values) to the CEDAC deliberations. The public members had full CEDAC membership: they operated under the same terms and conditions as the other CEDAC members.

The first CEDAC public members embarked on their tenure without precedence of such positions on that committee to guide them. Even with an orientation to CDR and CEDAC about their processes and activities, and ongoing support from CEDAC members and CDR staff, the public members did face a significant learning curve. CEDAC deliberations tended to be highly detailed and filled with medical jargon and public members were not expected to have expertise in drug reviews or medical care. Their previous experience with committees and organizations did help them to quickly become active participants in the CEDAC deliberations though. And just as importantly, through sharing and providing feedback about their experiences on CEDAC, they contributed to a better understanding of how public members could participate on this and other reimbursement advisory committees.

CCOHTA Became CADTH

CCOHTA was becoming a larger, more complex organization managing and delivering three major programs by the end of 2004 — HTA, CDR, and COMPUS. "In 2005-2006 CCOHTA took the next step in its evolution, one that culminated in a new brand, a new look, and a new entity — CADTH. The transition from office to agency was a key recommendation of the Canadian Health Technology Strategy (HTS 1.0), which Canada's F/P/T Health Ministers unanimously approved in 2004."[42] CCOHTA became CADTH on April 3, 2006.

House of Commons Standing Committee on Health

In December 2006, the House of Commons Standing Committee on Health (HESA) pursued its study of prescription drugs, commencing with an examination of the status of, and progress made under CDR. HESA issued its report, *Prescription Drugs, Part I — Common Drug Review An F/P/T Process* on December 12, 2007. "During its hearings on CDR from April through June 2007, the committee heard from representatives of federal and provincial governments, the pharmaceutical industry, patient advocacy groups, health professionals, researchers and academics, as well as from CDR officials. The evidence received spanned a number of concerns and included some conflicting views about CDR."[43] HESA also heard and confirmed that the participating drug plans and other stakeholders believed that "CDR was a positive example of intergovernmental cooperation that provides valuable service to the Canadian public."[43] HESA was told that, to dismantle the review process entirely would be unacceptable, both economically and politically.

The HESA review led to extra work at CADTH, with the President and CEO of CADTH, Vice-President of CDR, and Chair of CEDAC all testifying before HESA. Although HESA concluded that further improvements to CDR were necessary and it made five recommendations, these were non-binding on either Health Canada or CADTH. In its response, Health Canada, with input from CADTH, recognized that there is always room for improvement, and pointed out that CADTH already had several initiatives under way that spoke to the recommendations.[44] One of the recommendations was to establish a formal appeal process. The Federal Government and CADTH agreed that there was no need as appeals typically challenge decisions and CADTH provided recommendations, not decisions; thus, leaving the decision-making about reimbursement to individual drug plans. In the end, the HESA report did little to change the course of CDR.

The HESA hearings experience highlighted for CADTH that it needed to more strongly promote the messages of CDR so that politicians, the public, and health care professionals had a better understanding of its work.[34] As Andreas Laupacis noted in a *The Medical Post* article, "One of the limitations of CDR as it exists now is that it has a difficult — some would say impossible — job to do, and little budget to communicate what it is doing and why. What has stymied CDR a bit is that is doesn't have the PR [public relations] capabilities that pharma does. It isn't proactive, out there saying this was not easy but here's how we struggled. One way to overhaul it is to expand its ability to outreach… Unless a committee like this says yes all the time, there's always going to be controversy."[45] These observations prompted an article published in the *Canadian Medical Association Journal*[39] and letters from CADTH personnel to *The Medical Post*[46,47] to help explain CDR's work.

Changes to the Common Drug Review Procedures

Ongoing clarifications and changes to CDR procedures were made following analyses and consultations with stakeholders. The changes below are selected from among many and represent those that had a significant impact on CDR and stakeholders.

Changes to Pharmacoeconomic Requirements

CEDAC soon found that the CDR pharmacoeconomic review reports were not always helpful in informing their recommendations well. The CDR pharmacoeconomic review reports were essentially a critique of the manufacturers' pharmacoeconomic evaluations and so could only be as good or as useful as the manufacturer-generated pharmacoeconomic evaluations. If the pharmacoeconomic submission met the CDR submission requirements, it was deemed complete. It wasn't until the reviewers critiqued the evaluation that they found that sometimes the type of analysis, choice of comparators, modelling techniques, data sources, or assumptions were inappropriate or clinical claims were unsupported. While the reviewers pointed out the shortcomings of the pharmacoeconomic evaluation, this still left CEDAC without sound pharmacoeconomic evidence to inform its recommendations.

As a result, CDR and CEDAC collaborated to develop detailed guidelines and algorithms to help manufacturers provide economic evaluations that better met the needs of CDR and CEDAC. CDR began to request executable economic models so that it could test the validity of concepts and results and could look at other scenarios of relevance by varying parameters. This was a significant request as the economic models were considered confidential and the property of the organization that generated them. Guidance included in the *CDR Submission Guidelines for Manufacturers* streamlined the economic review process, lead to better information for CEDAC, and helped provide clarity for the manufacturers.[48]

Review of Drugs Pre-Notice of Compliance Pilot

The CDR procedures required that to be eligible for review, drugs needed to be approved for sale by Health Canada. This was the norm across Canada before CDR was established. The reasoning behind this was to ensure that review resources were used only on drugs that were available to Canadians since some drugs under review by Health Canada did not meet its standards and were not approved for sale. Patients with life-threatening or other diseases for which drug therapy was unavailable or inadequate and clinicians managing their conditions advocated for quick access to breakthrough drugs. Drug plans, too, saw a need for access to these drugs. Initiating a review of such a drug before it had received its NOC from Health Canada (i.e., pre-NOC), but far enough along in Health Canada's review process, whereby its approval was likely, was seen as a means of accelerating its availability.

In 2005, CDR and the Bureau of Cardiology, Allergy and Neurological Sciences (BCANS) of the Health Canada Therapeutic Products Directorate began collaborating to explore the feasibility and opportunities for pre-NOC reviews by CDR. They launched a joint pilot project to explore mechanisms for sharing information before a drug received an NOC. Beyond the development of a pre-NOC review process, this pilot broke new ground in transparency for CDR and Health Canada. At that time Health Canada did not disclose names of drugs that it was reviewing for market approval; however, under the CDR procedure, all drugs under review by CDR were tracked on its website. This meant that the names of drugs undergoing pre-NOC review were disclosed while Health Canada was still reviewing them and before it gave market approval.[49]

With consent from the manufacturer, Altana Pharmaceuticals Inc., ciclesonide (Alvesco) was selected as the pre-NOC drug submission for the pilot.[50] In the case of Alvesco, the pre-NOC submission was received on July 24, 2006; the NOC was issued on September 11, 2006; and the final CEDAC recommendation was issued on December 20, 2006 — three months after the NOC was issued. This pilot demonstrated that through sharing of information before drug approval, a CEDAC formulary listing recommendation could be available sooner after marketing approval was received. Based on this experience, drug plans supported the collaboration with Health Canada, but not an accelerated review process whereby steps would be eliminated or less time allowed for steps in the process. They agreed that CDR should proceed to develop criteria (to be informed by the then existing priority review criteria for CDR submissions) and processes for pre-NOC submissions. Manufacturers and other stakeholders supported pre-NOC reviews. (On July 1, 2009, CDR launched pre-NOC submissions as another type of CDR submission.[51])

Confidential Drug Prices

The original submission requirements stated that manufacturers needed to provide publicly available current list prices when filing submissions. Some manufacturers asked if this requirement could be changed to allow them to submit a price that was lower than the published list price as this would help make their product more cost-effective and more likely to get a list or list with criteria CEDAC recommendation. The lower price would be available to the drug plans if they listed the drug. This was referred to as "a proposed price" in the May 2006 version of the *CDR Submission Guidelines for Manufacturers*.

Subsequently, manufacturers argued this price should not be disclosed in any publicly available CDR documents, including CEDAC recommendations, as the disclosure of the lower than publicly available list price could affect their market competiveness. While drug plans, CDR, and CEDAC preferred pricing information to be transparent, they agreed (after debate) to maintain the confidentiality of submitted prices that were lower than published list prices, as these prices would mean cost savings to drug plans. However, they required that pharmacoeconomic evaluations be undertaken, using the submitted confidential price. CDR revised relevant sections of its documents in February 2007 to indicate that confidential prices would be handled in the same manner as other confidential information. CEDAC and CDR were clear that in some situations it would be necessary to make reference to the confidential price (without disclosing it) in the reasons for a recommendation, including: to provide clear and rational reasons for a recommendation; to appreciate/recognize that public monies are used to fund drug costs; and to be consistent with the move toward increasing transparency. Many felt that allowing manufacturers to submit confidential prices diminished transparency.

Common Drug Review Expansion to Include the Review of Drugs with New Indications

The planning for this expansion began in September 2004 when the First Ministers agreed to a *10-year Plan to Strengthen Health Care* and directed their health ministers to establish a Ministerial Task Force to develop and implement a National Pharmaceuticals Strategy (NPS).[52] One action in the NPS was to establish a common National Drug Formulary. [53] In response to this commitment, the Common Formulary Task Group was formed in June 2005 to assess the feasibility of expanding CDR into four areas identified by participating drug plans: reviews of new indications for old drugs, cancer drugs, hospital drugs, and drug class reviews. The expansion of CDR to include reviews of new indications for old drugs was selected as the first step, and following a business case analysis[53] this initiative was recommended in September 2006.

CCOHTA received approval and funding for the expansion of CDR from the Conference of Deputy Ministers in April 2007. It estimated that it would take about six months to implement the expansion. Based on the business case analysis, estimating a 40% increase in number of submissions and reconsiderations for this group of drugs, CADTH prepared by finding more staff and office space, making revisions to CDR procedures and submission guidelines, and developing communications strategies for informing stakeholders. CDR was ready for the expansion on October 1, 2007.[54]

Drug Class Reviews

From the time of implementation, the procedure for CDR referred to the eligibility of drug plans to request a class review; however, details for the drug class review process were limited and no drug class reviews were requested at the outset.

Drug plans wanted the drugs listed in their formularies, including the ones that had been listed for long periods of time, to meet current standards of cost-effectiveness. Drug plans saw drug class reviews as one means to keep their formularies based on the most current evidence — a means for formulary modernization.[55] In addition, CEDAC indicated that drug class reviews would provide important information to help them make a more meaningful recommendation for the new drug under review in that particular class. The Common Formulary Task Group which was established to assess the feasibility of CDR expansion also identified drug class reviews as an area for CDR expansion.[53]

The first Drug Class Working Group, comprising CDRC members with CDR secretariat support, met in August 2004. Based on its work, over the next few years, various approaches to develop drug class reviews were tried — they shared drug class reviews that they had generated; they used class reviews developed by the Oregon-led Drug Effectiveness Review Project (DERP); and they worked on formalizing a drug class review process for the drug plans. In 2006, CADTH, CEDAC, and ACP undertook a pilot drug class review project on the triptan medications for migraines. CEDAC used this drug class review in its deliberations and reported that it considered class reviews to be an extremely important and worthwhile undertaking. In 2008, the Therapeutic Review Working Group replaced the Drug Class Working Group, and building on the experiences of the Drug Class Working Group and the learnings from the triptan drug class review, it developed a framework for therapeutic reviews. A key feature of the therapeutic review process was that a drug class review report would be available at the time that CDR was reviewing a new drug submission in that class. On December 7, 2009, CADTH announced a therapeutic review pilot project[56] which resulted in two reports: *Biological Response Modifier Agents (Biologics) for Adults with Rheumatoid Arthritis*[57] and *Third-Line Therapy for Patients With Type 2 Diabetes Inadequately Controlled with Metformin and a Sulfonylurea*.[58] These projects illustrated the tremendous effort and coordination needed to produce a review of a class of drugs to coincide with the review of a new submission.

Interim Joint Oncology Drug Review Launched

Although at the time of CDR implementation some provinces had cancer agencies that reviewed and covered cancer drugs, most of the participating drug plans provided coverage for cancer drugs, primarily oral ones. At CDR's outset, new oral cancer drugs were to be submitted to it for review and for CEDAC listing recommendations. This changed on March 1, 2007 when the Joint Oncology Drug Review (JODR) was launched as an interim project.[59] During the interim process all drugs for active treatment of cancer were submitted to the Ontario Drug Benefit Program. CDR no longer received and processed submissions or provided CEDAC recommendations for oral cancer drugs;

Evaluation of the First Year of Operation for the Common Drug Review

FINAL REPORT

Submitted to:

Canadian Coordinating Office for Health Technology Assessment
600-865 Carling Avenue
Ottawa, ON K1S 5S8

EKOS RESEARCH ASSOCIATES INC.
September 27, 2005

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Previous: Evaluation of the first year of operation for the Common Drug Review.

This evaluation was one of the activities during the first five years of CDR. Fulfilling the EKOS recommendations became an important area of focus for CDR during the next few years.

however, it continued to produce the clinical and pharmacoeconomic review reports when requested. Ontario's Committee to Evaluate Drugs (CED) and the CED Cancer Care Ontario Subcommittee made listing recommendations and each jurisdiction continued to make its own coverage and funding decisions.

The interim JODR was a provincial collaborative for the review of all cancer drugs for reimbursement in Canada. This was a move to provide more consistent cancer care across Canada, as the provinces' cancer agencies each had their own processes for reviewing and recommending cancer drugs for coverage. After a year of operation the interim JODR project was evaluated and subsequently evolved into a new national program, the pan-Canadian Oncology Drug Review (pCODR), which built on some CDR processes. (The interim JODR transitioned to pCODR in 2011.[60])

Increasing Transparency

Despite the strides CDR had made in its transparency efforts, industry, patient groups, and other stakeholders were unrelenting in their requests for more. The EKOS evaluation and HESA reports both recommended greater CDR transparency. Transparency was an ongoing initiative.

Following consultations with all stakeholders, CDR announced a major initiative.[61] Beginning with submissions received on November 29, 2007, it would publicly post the following three documents after the Final CEDAC Recommendation and Reasons for Recommendation were issued:

- Plain language version of the Final Recommendation and Reasons for Recommendation: the plain language version contained the same information as the technical version, but was presented with non-technical language for the general public.
- Summary of the CEDAC discussion regarding the drug under review: a record of the highlights of the relevant CEDAC discussion points.
- Overview of the clinical and pharmacoeconomic reports: approximately a 20-page overview, based on the CDR Clinical Review Report and the CDR Pharmacoeconomic Review Report prepared by CDR reviewers. The overview condensed and paraphrased the lengthy and detailed full CDR reviews.

CDR found this transparency initiative to be labour intensive. Condensing both voluminous clinical and pharmacoeconomic reports into about 20 pages was challenging. Because CDR had assured stakeholders that confidential information in these documents would be handled as per the *Confidentiality* Guidelines, the identification and redaction of confidential content was painstaking and tedious. Translating and writing the CEDAC Recommendations and Reasons for Recommendation into plain language was challenging enough and finding people with skills and qualifications to do this was equally challenging. Furthermore, manufacturers needed to review the documents for accuracy and to identify any missed confidential information within tight time frames, which added to their workload. With the increasing volume of submissions and with the demands of doing therapeutic reviews, CDR had to refocus its resources to these activities. For these reasons, CDR first placed overviews and plain language recommendations and reasons for recommendations on hold and subsequently discontinued them. Eventually the Summary of CEDAC discussion was incorporated into the CEDAC Recommendation and Reasons for Recommendation document under the Summary of Committee Considerations section, and many felt it enhanced the information therein.

Drugs for Rare Diseases

From day one, drugs for rare diseases posed challenges for CDR. Beginning with the review of drugs for Fabry Disease and subsequently with the review of other drugs for rare diseases, CDR reviewers and CEDAC consistently found that the clinical data were limited and tended not to be robust. Although these types of drugs could be shown to affect certain physiological outcomes, their impact on outcomes that were important to patients and clinicians was seldom proven. These drugs were very costly. These factors (the biggest one being lack of good evidence) led CEDAC to recommend "do not list" for many of these drugs. The CEDAC "do not list" recommendations for drugs for rare diseases sparked ongoing criticisms from industry and patient advocacy groups, arguing that CDR was not the appropriate venue for reviewing drugs for rare diseases. At least, they argued, CDR should not be using the same procedures and processes as it does for drugs for more common diseases. A number of other countries had or were developing special review processes and funding for drugs for rare diseases, and there were criticisms that Canada was not keeping up.

For the drug plans, the CEDAC "do not list" recommendations for drugs for rare diseases highlighted the need for a comprehensive, long-term national drug benefit framework to address the pressures their ministries were facing from constituents. Drug plans faced the challenge of distributing limited resources fairly. Thus, they felt that their decisions about funding these very expensive drugs should be evidence-based and they considered the CDR process appropriate and sound in this regard. Yet they struggled with the knowledge that those living with rare diseases had few if any treatment options and that the new drugs, even those without good evidence, offered hope. They were caught between making evidence-based decisions and finding a way to help those living with rare diseases. At their meeting in December 2004, Deputy Ministers of Health approved the initiation of work to develop a comprehensive long-term national drug benefit framework to address expensive drugs for rare diseases.[62] During the early years numerous discussions took place, but the process remained unchanged.

The Criticisms

CDR was scrutinized and criticized during its formation and throughout the early years. The criticisms came largely from the pharmaceutical industry, but also from some patient and professional organizations.

An ongoing criticism was that CDR was a vehicle for simply controlling costs. While it was always understood that publicly funded drug plans expected formulary recommendations that considered both clinical effectiveness and cost-effectiveness, there were calls to be clear about the definition of cost-effectiveness. What was the threshold for cost-effectiveness below which a recommendation would be "to list" a drug and above which it would be "do not list"? Some countries publicly posted their cost-effectiveness thresholds, some did not. After much deliberation a decision was made that each drug should be considered in the context of its effectiveness and safety (first and foremost) and its costs compared with available alternatives. There would be no hard threshold. Some of the rationale for this decision was to provide latitude for the experts to recommend a drug for coverage that was costly, but that they believed should be covered because it provided some benefit despite its cost.

Among other areas, criticisms were also heard about a lack of transparency and about a potential exclusion of clinical experts because of the rigid COI Guidelines.[39]

National and International Recognition

During the early years, CDR's national and international reputation was growing. Nationally, CDR had the support of drug plans, as evidenced in the EKOS evaluation and during the HESA hearings. CDR considered the concurrence of drug plans listing decisions with CEDAC recommendations (about 90% concurrence) as a strong indicator of drug plan agreement with the process and results. While Quebec was not a participant in CDR, personnel from the Quebec drug plan met periodically with CDR staff to exchange ideas and to learn from CDR's experiences. Nonetheless, Quebec's participation was missed.

"Not having Quebec as a participant meant it could be held up by detractors that CDR wasn't a truly national program."

— Mike Tierney, former Vice-President, CDR (2006-2008)

Countries planning to set up processes for reviewing and reimbursing drugs, similar to Canada's, were contacting CCOHTA for information and advice. Personnel from established national and international HTA agencies included CDR and CEDAC members in discussions about mutual issues and efforts to find potential solutions. A quote from Steve Morgan, Assistant Professor, UBC Centre for Health Services and Policy Research in the CADTH Annual Report 2006-2007 noted that, "The CDR has rapidly become an internationally recognized and respected peer among the review agencies internationally."[63]

The First Five Years

During the first five years of CDR, the participating drug plans and CCOHTA collaborated and worked effectively to maintain and enhance CDR.

"It is hard to think about drug reimbursement in Canada without CDR. During times when there were challenges, all the plans worked together and still do — and as a result, we have a pan-Canadian process for drug reviews."

— Leanne Jardine, Executive Director, Pharmaceutical Services, NB

CHAPTER 06

Chapter 06

The Common Drug Review is Firmly Established

CDR is not the only success story in F/P/T collaboration, but it is a shining example of cooperation. It is a story where a common need, willing and committed governments, teams and individuals, and a receptive host agency combined to make it so.

We know now that the collaboration did work, the program was established and continues to effectively operate (as of 2017). There were many contributing factors at the time of CDR's development: rising drug costs, growing public advocacy, calls for consistency, recognition of needed efficiencies, and a climate conducive to F/P/T governments working together toward this common goal.

Interesting as it would be, it's not possible to quantify the number of issues that had to be addressed, the number of people with various roles and responsibilities and expertise who were involved, the hours spent, and the degree of effort it took to bring about CDR.

"There was (I think) a zeitgeist phenomenon — the mood of the times toward accords and common approaches created an atmosphere conducive to the development of the CDR."

— Anne MacFarlane, Assistant Deputy Minister Pharmacare and Intergovernmental Affairs, BC (1997)

There is a cliché in flying. "Helicopters are really a bunch of parts flying in relatively close formation; all rotating around a different axis." Delivery of health care in Canada is similar. The F/P/T governments have different roles and responsibilities in the delivery of health care and, in a way, rotate around their own axis. When all parts work together and maintain a close formation, there is successful lift off.

CDR did successfully "lift off." The early years during its development, design, and operation are the foundation for its current operation. It took a great deal of effort, collaboration, and the single mindedness of governments, teams and many individuals across the country for CDR to become a reality.

Appendix 01

Interim Common Drug Review Committee (2002)

Members			
Marnie Mitchell, Chair	BC	**Patrick Crawford**	PEI
David Bougher, Vice-Chair	Alta	**John Downton**	Nfld
Suzanne Solven	BC	**Joe MacGillivray**	YK
Margaret Baker	Sask	**Barb Ouellet**	HC
Jack Rosentreter	Man	**Debra Tattrie**	NIHB
Scott Gavura	Ont	**Andre Corriveau**	NWT
Leanne Jardine	NB	**Regis Vaillancourt**	DND
Emily Somers	NS	**Mike Duffy**	VAC
Observers			
Dr. Jill M. Sanders	CCOHTA	**Ginette Tognet**	PMPRB
Brenda Czich	HC	**Vicky Hogan**	MHPD
Secretariat			
Elaine MacPhail	CCOHTA		

Alta = Alberta; BC = British Columbia; CCOHTA = Canadian Coordinating Office for Health Technology Assessment; DND = Department of National Defence; HC = Health Canada; Man = Manitoba; MHPD = Marketed Health Products Directorate (HC); NB = New Brunswick; Nfld = Newfoundland and Labrador; NIHB = Non-Insured Health Benefits; NS = Nova Scotia; NWT = Northwest Territories; Ont = Ontario; PEI = Prince Edward Island; PMPRB = Patented Medicine Prices Review Board; Sask = Saskatchewan; VAC = Veterans Affairs Canada; YK = Yukon.

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Appendix 02

Inaugural Canadian Expert Drug Advisory Committee (2003)

Dr. Andreas Laupacis Chair	President and chief executive officer of the Institute for Clinical Evaluative Sciences in Toronto
Dr. John Conly Vice-Chair	Head of the Department of Medicine, University of Calgary and Calgary Health Region
Dr. Ken Bassett	Senior medical consultant, University of British Columbia Centre for Health Services and Policy Research
Dr. Margot J. Burnell	Medical oncologist, Department of Oncology and Department of Internal Medicine, Atlantic Health Sciences Corporation
Dr. Bruce Carleton	Associate professor and chair, Division of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, University of British Columbia
Dr. Michael Evans	Family physician, Toronto Western Hospital
Dr. Anne Holbrook	Clinical pharmacologist and internal medicine specialist, Centre for Evaluation of Medicines, St. Joseph's Hospital and Hamilton Health Sciences Corporation
Dr. Laurie Mallery	Acting head, Division of Geriatric Medicine, Dalhousie University and acting director, Centre for Health Care of the Elderly, Queen Elizabeth II Health Science Centre
Dr. Braden Manns	Nephrologist, Faculty of Medicine, University of Calgary
Dr. Tom Paton	Director, Department of Pharmacy, Sunnybrook and Women's College Health Sciences Centre
Dr. Dale Quest	Associate member, College of Medicine/Pharmacology and the College of Dentistry/Biological, Diagnostic and Surgical Sciences; and associate professor, College of Nursing, University of Saskatchewan

Note: Names, titles, and places of work accurate to *CDR Update* in 2003.

Appendix 03

Common Drug Review Internal Management (2003 to Present)

Directors

2003
Barb Shea

2004 to 2005
Elaine MacPhail

2006
Mike Tierney

2007 to 2010
Sandy Pagotto

2010 to 2011
Denis Belanger

2011 to 2016
Chander Sehgal

2016 to Present
Trevor Richter

Vice-Presidents

2004 to 2006
Barb Shea

2006 to 2008
Mike Tierney

2009
Brian O'Rourke

2009 to 2011
Barb Shea

2011 to 2014
Matthew Brougham

2015 to Present
Brent Fraser

CADTH

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