



CADTH and Common Drug Review in Canada

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2007-12-7



CCOHTA

- In August of 1990, the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) opened its doors on a three-year trial basis.
- Its mandate was to provide Canadian health care policy managers with evidence-based information on emerging and existing medical devices.
- In 1993, the Conference of the Deputy Ministers of Health declared CCOHTA a permanent entity.
- Pharmaceutical reviews were added to the organization's mandate



Common Drug Review, CDR

- In early 2002, the Conference of Deputy Ministers asked CCOHTA to undertake the **Common Drug Review (CDR)**, a single process for reviewing new drugs and providing listing recommendations to participating publicly-funded federal, provincial and territorial drug benefit plans in Canada.
- CDR became a permanent entity at CCOHTA in **2003**

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COMPUS

- In **March 2004**, CCOHTA continued to expand with the creation of the Canadian Optimal Medication Prescribing and Utilization Service (COMPUS).
- It identifies and promotes optimal drug prescribing and use among health care providers and consumers.
- CCOHTA received an initial five-year funding agreement from Health Canada to deliver the COMPUS program.

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HTIS

- In 2005, CCOHTA's HTA program introduced the Health Technology Inquiry Service (HTIS).
- The service was established to provide Canadian health care decision makers with access to available health technology information in a quick and efficient manner.
- HTIS responds to inquiries about drugs, devices, and procedures.
- Depending on the urgency and/or complexity of the request, information is provided from 24 hours to 30 business days.



Rebrand of CCOHTA

- Over the years, CCOHTA has transformed from an organization whose mandate related strictly to evidence-based information on emerging and existing medical devices. With the addition of CDR and COMPUS and further responsibilities spelled out for the organization in HTS 1.0, it was felt the organization needed to rebrand to reflect those changes.



- On **April 3, 2006**, the Canadian Coordinating Office for Health Technology Assessment was reborn as the **Canadian Agency for Drugs and Technologies in Health** (CADTH), a name that better reflects the breadth of services the organization now provides to Canadian health care decision makers.



Vision

To facilitate the appropriate and effective utilization of health technologies within health care systems across Canada.

Mission

To provide timely, relevant, rigorously derived, evidence-based information to decision makers and support for the decision-making processes.



Common Drug Review Submission Guidelines for Manufacturers

February 2007

- The CDR is an initiative undertaken by all publicly funded F/P/T (聯邦/省份/地區) Drug Plans (藥品保險計畫) in Canada, with the exception of Québec
- The CDR Drug reviews reflect an evidence-based approach.
- The CDR is managed and overseen by the CDR Directorate of the CADTH in Ottawa.



The goals of the CDR process

- To reduce duplication in the performance of reviews,
- To maximize the use of limited resources and expertise, and
- To provide consistent and rigorous Drug reviews.



CDR reviews consist of

- An evidence-based review of the available clinical evidence, and
- A critique of Manufacturer-submitted pharmacoeconomic studies and Budget Impact Analyses (BIAs).



The Canadian Expert Drug Advisory Committee (CEDAC)

- an appointed, national independent body of physicians, pharmacists and other professionals, uses the CDR reviews to **make common listing recommendations** to participating F/P/T Drug Plans.



CEDAC Membership

- composed of thirteen (13) Members.
- Two of them should be **lay persons**.
- Remaining members must hold qualifications as a physician, a pharmacist, an economist or other professional designation with expertise



Expertise of CEDAC Members

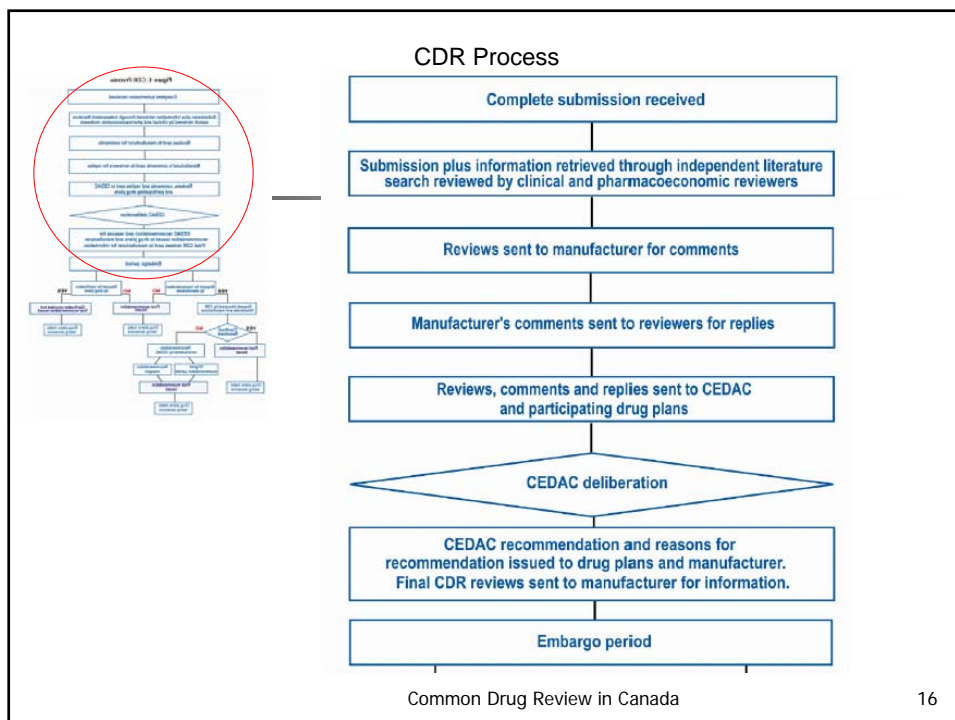
- a) general practice
- b) internal medicine
- c) geriatrics
- d) hospital or community pharmacy
- e) clinical pharmacology
- f) pharmacoeconomics
- g) clinical epidemiology
- h) health services research

Listing(収載) Decisions

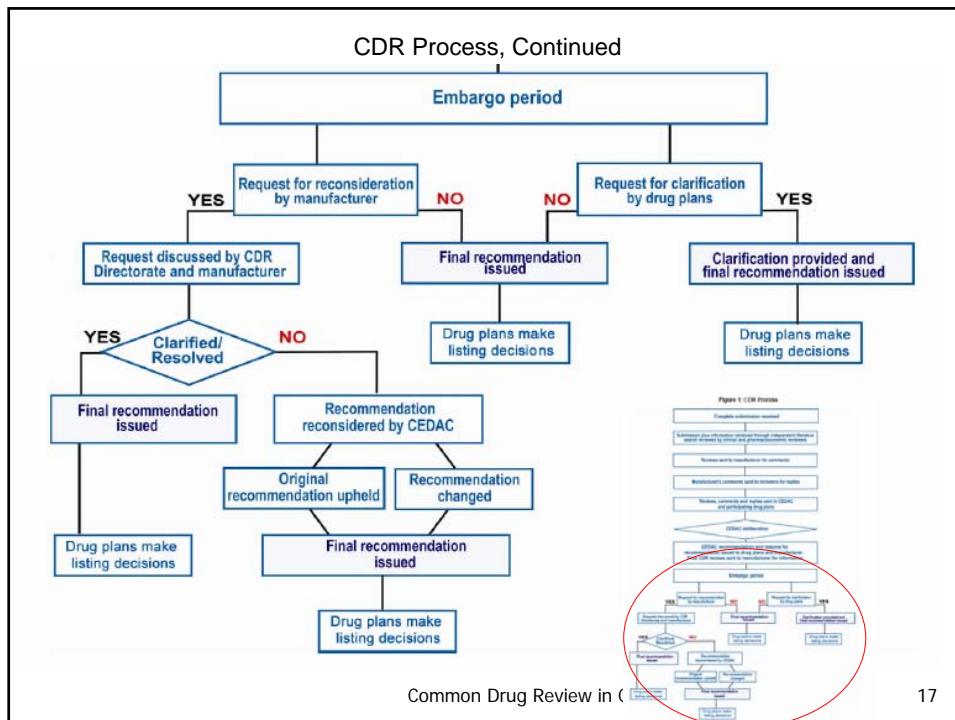
- Each of the participating F/P/T Drug Plans makes its own listing decisions based on CEDAC recommendations plus other factors, including the plan's mandate, priorities and resources.
- Each plan is responsible for **independently advising** the Manufacturer of its listing decision and the coverage status of the Drug.

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The CDR process is initiated

- either:
 - By the Manufacturer, the Advisory Committee for Pharmaceuticals (ACP), or one or more Drug Plans filing a **Submission** with the CDR Directorate; or
 - by the ACP, or one or more Drug Plans, filing a **Request for Advice** with the CDR Directorate; or
 - by the Manufacturer, the ACP, or one or more Drug Plans filing a **Resubmission** with the CDR Directorate

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Eligible Submissions from Manufacturers

- Submissions from Manufacturers are limited to New Drugs and New Combinations that have received, from Health Canada,
 - a Notice of Compliance (NOC) or
 - a Notice of Compliance with Conditions (NOC/c)



New Drugs and New Combinations

- New Drugs
 - are New Active Substances that have not been marketed in Canada, regardless of when the NOC or NOC/c was issued.
- New Combinations
 - consist of two or more Drugs that have not been marketed in Canada in that combination.



- All New Drugs or New Combinations, including new HIV/AIDS agents and “hospital” Drugs that may be potentially funded by one or more of the participating Drug Plans **should be** submitted by Manufacturers to the CDR for review to be **eligible for consideration for coverage** by participating Drug Plans



- The ACP may request that the CDR Directorate undertake the review of Submissions, including Drugs that are **not** New Drugs or New Combinations.
- In these cases, the CDR Directorate will contact the Manufacturers for clinical and pharmacoeconomic data.



review queue is as follows

- Submissions or Resubmissions assigned a Priority Review status
 - Reconsiderations
 - Regular Submissions
 - ACP or Drug Plan initiated reviews
 - Requests for Advice
 - Resubmissions



Submissions may be considered for Priority Review if the Drug is

- A New Drug that is effective for the treatment of an immediately life-threatening disease or other serious disease for which no comparable drug is marketed in Canada; or
- A New Drug that will have a significant impact in reducing the drug expenditures of the Drug Plans. The total combined annual savings to the CDR Drug Plans must be projected to be at least \$2.5 million dollars.



The Submission Requirements

- Category 1 information must all be included when the Submission is filed
- Category 2 information must be provided as a single package within 20 Business Days of filing the initial Submission. They must be satisfied before the Drug review is placed on the CEDAC agenda.




Category 1 Requirements

1. Cover Letter
2. Executive Summary
3. Health Canada NOC or NOC/c.
4. Product Monograph
5. Efficacy, Effectiveness and Safety Evidence
6. Economic and Epidemiologic Information
7. Pricing and Availability Information
8. Letter Confirming Ability to Supply
9. Letter Authorizing Unrestricted Sharing of Information
10. Bibliography of Included References Supporting Validity of Outcome Measures



Category 2 Requirements

1. Drug Notification Form
2. Economic and Epidemiologic Information
3. Compendium of Pharmaceuticals and Specialties (CPS) listing
4. Pharmaceutical Advertising Advisory Board (PAAB)-approved promotional
5. materials – or a draft copy of material submitted to PAAB
6. Certified Product Information Document (CPID)
7. Product Patent Expiration Date



Additional information may be requested by the CDR Directorate

1. Harm and Safety Information
2. Health Canada Reviewer's Report
3. Periodic Safety Update Reports (PSURs)
4. Economic Model and Supporting Documentation



Resubmissions

- Manufacturers may file Resubmissions when they have New Information, e.g. new clinical information or new cost information.
- If the New Information is in support of improved **efficacy**, it must be from a randomized controlled trial.
- If the New Information is in support of improved **safety**, case-control or cohort studies will be accepted if randomized controlled trials are not available.



Review of a Manufacturer's Submission ¹

- a) The Review Team develops a protocol for the review of the Submission with input from participating Drug Plans, CEDAC members and other experts as required.
- b) The Review Team designs and conducts an independent systematic literature search to address the protocol and to supplement the data provided by the Manufacturer.
- c) Regular and frequent interactions occur amongst the members of the Review Team regarding the review of the Submission.



Review of a Manufacturer's Submission ₂

- d) A list of studies included in the Systematic Review portion of the Clinical Review Report is sent to the Manufacturer for information.



Review of a Manufacturer's Submission ₃

- e) The Review Team undertakes a review of the relevant information provided by the Manufacturer and identified through the independent literature search and prepares a Clinical Review Report.



Review of a Manufacturer's Submission ⁴

- f) The Review Team reviews and critiques the PE information submitted by the Manufacturer. The results and conclusions reported in the Clinical Review Report are used in the assessment of the PE information submitted by the Manufacturer.



Review of a Manufacturer's Submission ⁵

- g) The Review Team may request an extension of deadlines from the CDR Directorate. The Manufacturer will be notified of any extensions and reasons for the extensions, granted by the CDR Directorate.



Review of a Manufacturer's Submission ⁶

- h) Once the Review Team has completed the Reports, they are forwarded to the Manager of Drug Reviews who has five Business Days to check that the Reports are complete and to finalize the documents for inclusion in the CEDAC Brief.



CIRCULATION OF INFORMATION

- Distribution of Reviewers' Reports for Manufacturer's Comments
- Manufacturer provides Comments
- Reviewers' Replies to Manufacturer's Comments
- Final Versions of CDR Reports
- Compilation of CEDAC Brief



CEDAC

- CEDAC Recommendation
- Reasons for Recommendation
- Releasing Recommendation and Reasons for Recommendation
- Releasing Record of Advice

Drug Name		
Brand name	XXXXX	
Manufacturer	XXXXX Inc.	
Indication	Hepatitis B	
Submission type	Initial	
Date submission received	2006-04-24	
Status	Completed	Submission status report
Date recommendation issued	2006-11-29	
Recommendation	Do not list	Detailed recommendation

Drug Name		
Brand name	XXXXXX	
Manufacturer	XXXXXX	
Indication	HIV infection	
Submission type	Initial	
Date submission received	2003-12-16	
Status	Completed	Submission status report
Date recommendation issued	2004-05-27	
Recommendation	List in a similar manner to other drugs in class	Detailed recommendation

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Drug Plan Decision

- Upon receipt of the Notice of Final Recommendation, each of the Drug Plans may proceed to take steps to make a listing decision in respect of the applicable Drug.

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Withdrawal or suspension

- Withdrawal Process
 - Withdrawal of Market Authorization by Health Canada
 - Voluntary Withdrawal of a Submission or Resubmission
- Temporary Suspension of Review

CDR Timeframe

	Task within Review Process	Timeframe (in Business Days)	Weeks
Administrative Tasks*			
1	Submission deemed complete	5	1
	Resubmission deemed complete	10	2
2	Manufacturer's binders received by CDR	5	1
3	Manufacturer's binders received by CDR Reviewers	3	0.6
Review Process			
4	CDR Reviewers' Reports completed <ul style="list-style-type: none"> • Reviewers selected and contracted • Literature search and selection completed • Systematic review of clinical data completed • Critical appraisal of pharmacoeconomic (PE) data completed • Clinical and PE reports written • Reports edited and finalized • Reviewers' reports sent to manufacturer 	45	9
5	Comments from Manufacturer on Reviewers' Reports received by CDR	7	1.5
6	Reviewers' Reply to Manufacturer's comments completed	7	1.5
7	CEDAC Brief completed and sent to CEDAC Members and Participating Drug Plans	5	1

		Business Days	Weeks
8	CEDAC meeting (placement on CEDAC agenda)	10 to 40	2 to 8
9	CEDAC Recommendation and Reasons for Recommendation sent to Drug Plans, ACP and Manufacturer; Final CDR Reviews sent to Manufacturer for information	5	1
10	Embargo Period† Manufacturers may make Request for Reconsideration, and Drug Plans may make Request for Clarification of Recommendation and Reasons for Recommendation	10	2
11 (a)	Final Recommendation sent to Drug Plans, ACP, and Manufacturer (no Requests for Clarification AND no Request for Reconsideration; or Request for Reconsideration resolved)	5	1
OR			
11 (b)	Clarification and Final Recommendation sent to Drug Plans, ACP, and Manufacturer (Clarification requested, no Request for Reconsideration)	5	1
	Total Review Time for Submissions*	94 to 124 days	19 to 25 weeks
	Total Review Time for Resubmissions*	94 to 124 days	19 to 25 weeks
OR			
11 (c)	Placed on CEDAC agenda for Reconsideration (at Manufacturer's request)	25 Depends on Meeting Dates	5
12	Final Recommendation sent to Drug Plans, ACP, and Manufacturer	5	1
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Challenges Faced by the CDR

(Laupacis, 2006)

- determining the effectiveness of a drug (particularly interpreting the importance of surrogate markers and changes in QOL measures);
- the massive rise in the cost of new drugs, which does not seem to be accompanied by a massive increase in effectiveness;
- interpreting complex pharmacoeconomic evaluations which often do not provide straightforward answers about the cost effectiveness of a drug;

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Challenges Faced by the CDR

(Laupacis, 2006)

- prescription creep. The tendency for drugs in the real world to be used in patients who were not studied in clinical trials, thus raising concerns about a drug's real-world cost effectiveness;
- ethical and societal issues, particularly the reimbursement of expensive drugs for rare diseases.

Andreas Laupacis: Economic Evaluations in the Canadian Common Drug Review.
Pharmacoeconomics 2006; 24 (11): 1157-1162 CONFERENCE PAPER



Patented Medicine Prices Review Board, PMPRB



Patented Medicine Prices Review Board, PMPRB

- The PMPRB was created by Parliament in 1987 under the *Patent Act* as an **independent quasi-judicial tribunal**.
- It has no authority over the prices of non-patented drugs, including generic drugs, and
- does not have jurisdiction over pharmacists' professional fees and any markups that may be applied by wholesalers or retailers.



PMPRB protects consumer interests and contributes to health care by exercising a two-fold mandate

- Regulatory mandate
 - to ensure that the **prices charged** by manufacturers, i.e. the ex-factory price, for patented medicines sold in Canada (whether prescribed or not) are **not excessive**; and
- Reporting mandate
 - to inform Canadians about the **price trends** of patented medicines and of all drugs, and the **research & development performance** as reported by patent-holding drug manufacturers.



Price Guidelines

- The prices of other drugs in the same therapeutic class;
- Prices of drugs in other countries; and
- Changes in the Consumer Price Index.



The Board's Guidelines

- the prices of most new patented drugs cannot exceed the price of **the most expensive drug** that treats the same disease;
- the prices of most breakthrough or substantial improvement drugs cannot exceed **the median of the prices** in other industrialized countries which are set out in the *Patented Medicines Regulations* (Regulations), i.e., France, Germany, Italy, Sweden, Switzerland, United Kingdom, United States;



- on a yearly basis, prices cannot increase more than the Consumer Price Index; and
- the price of patented drugs in Canada can **never be the highest** in the world.



Filing price information

- patentees are required to file price information on each strength of each patented drug on a regular basis with the PMPRB, for **the duration of the patent**.
- The Act authorizes the Board to establish the price guidelines and provides the Board with remedial powers.



Remedial powers against excessive price

- If a price is excessive the PMPRB may **order** the manufacturer to **reduce** the price to a non-excessive level and to **offset** the excess revenues that have been received by way of a payment to the Government.
- In addition, in the event of a policy of excessive pricing, the Board can order the manufacturer offset **double the excess** revenues received.



to improve timely access to necessary medications at non-excessive prices

- In order that improvements in therapeutic access not be offset by delays in the review of prices, the PMPRB has embarked on a major initiative to **better align** the timing of its price review process with the Common Drug Review.



Thank you
for your attention
