CADTH Common Drug Review

CDR INFORMATION SESSION

TORONTO, ON
OCTOBER 8, 2014

CADTH

CADTH Participants

- Brian O'Rourke – President and CEO
- Peter Chinneck – Special Assistant to the President and CEO
- Chander Sehgal – Director, CDR and Optimal Use of Drugs
- Karen Lee – Director, Health Economics
- Julie Blouin – Manager, Health Economics
- Lili Loorand-Stiver – CDR Submissions and Procedures Officer
- Jessica Birrell – Formulary Review Submissions Coordinator
- Sanja Milanovic – Formulary Review Submissions Coordinator
- Shireen Ghanbari – Administrative Coordinator
- Dale Calder – Events Planning Officer
- Glenna Gosewich - Events Planning Officer

Please note:

- CDR statistics presented in these slides are preliminary in nature, providing only a snapshot in time
- For complete context on any CDR procedure or submission guidelines-related slides, please consult the following documents as appropriate:
  - Procedure for the CADTH Common Drug Review (http://www.cadth.ca/media/cdr/process/CDR_Procedure.pdf)
  - Submission Guidelines for the CADTH Common Drug Review (http://www.cadth.ca/media/cdr/process/CDR_Submission_Guidelines.pdf
  - Guidelines for the Economic Evaluation of Health Technologies: Canada (http://www.cadth.ca/media/pdf/186_EconomicGuidelines_e.pdf)

Overview

- Clearing the backlog of CDR submissions
  - CADTH's plan to eliminate the backlog
  - Status update
- CDR industry application fees
  - Performance metrics
- CDR revised priority review procedure – update
- CDR submitted price – update
- Highlights of 2014 versions:
  - Procedure for the CADTH Common Drug Review
  - Submission Guidelines for the CADTH Common Drug Review
- Pharmacoeconomic update
- Q&A
- Open Forum

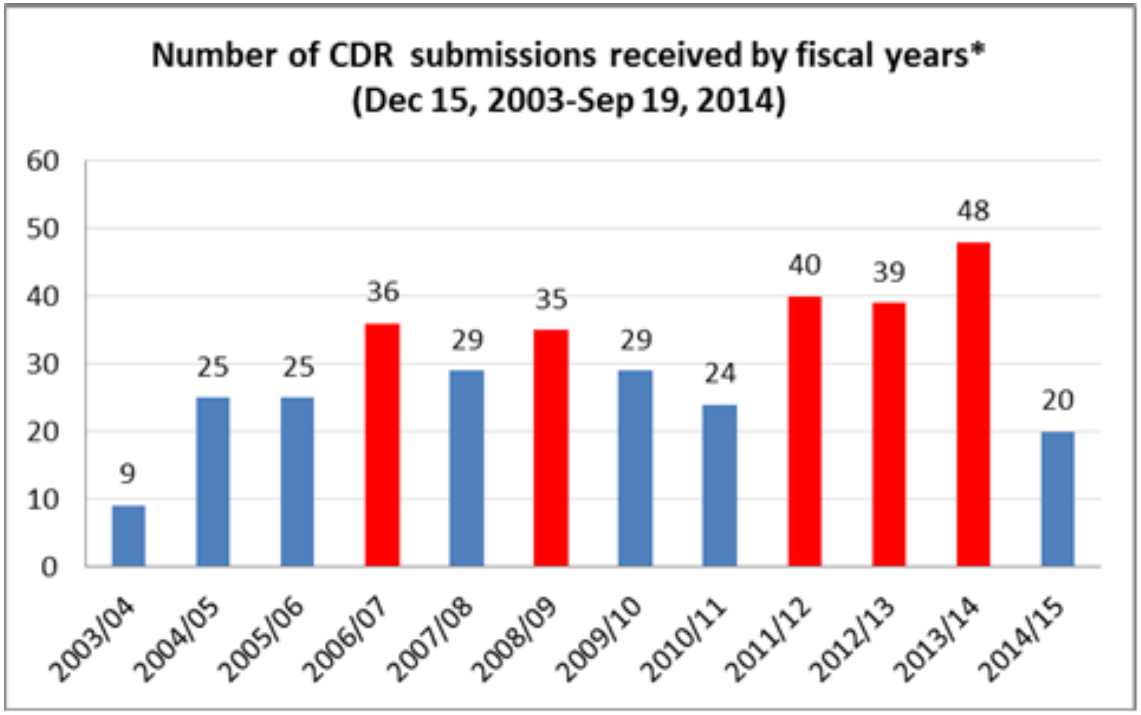
CLEARING THE BACKLOG OF CDR SUBMISSIONS
CDR INDUSTRY APPLICATION FEES
CDR REVISED PRIORITY REVIEW PROCEDURE – UPDATE
CDR SUBMITTED PRICE – UPDATE

CADTH

Reason for the CDR Backlog

- **Fixed Budget:** CDR has a fixed budget (30-35 reviews/year)
- **High Volume:** the number of reviews has exceeded targets

Number of Submissions Received Annually



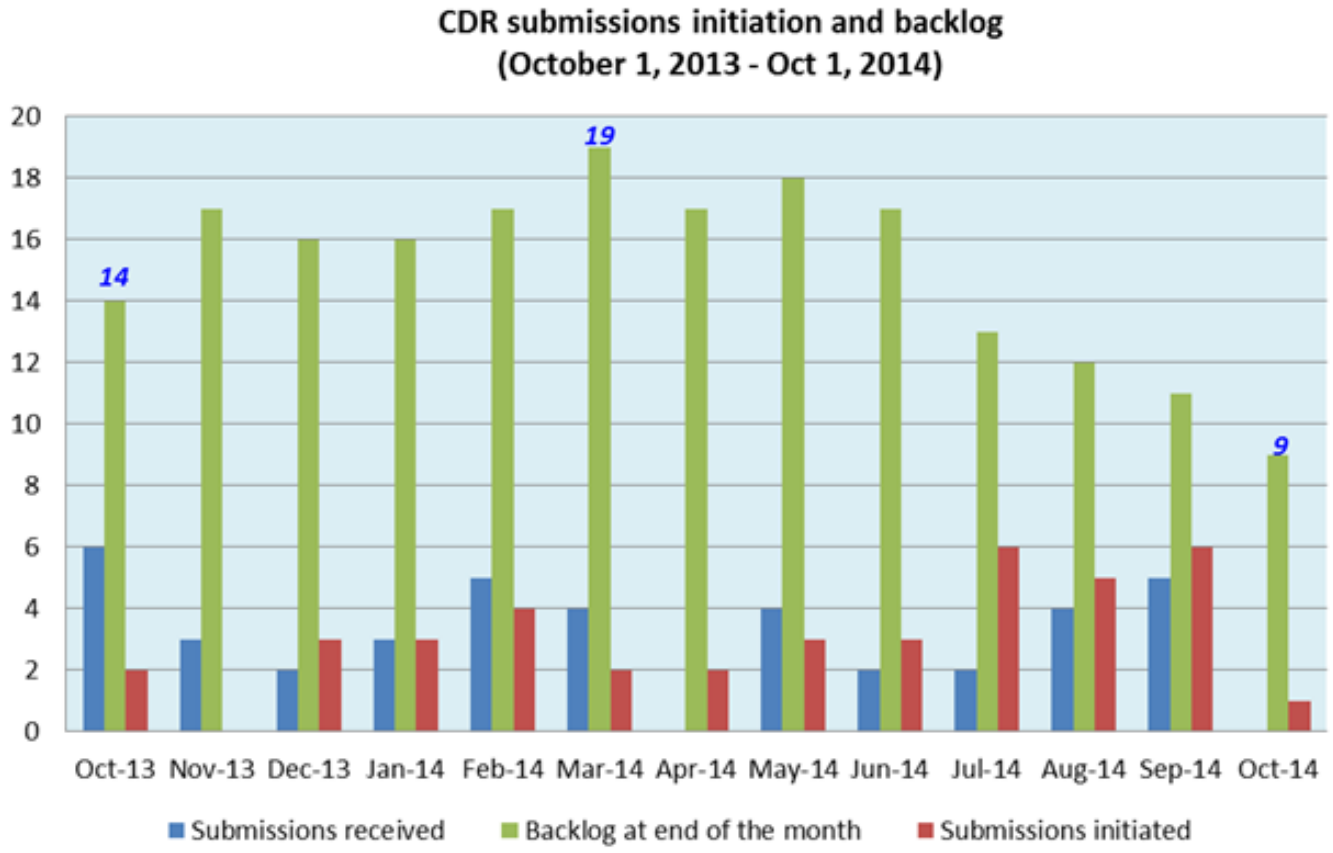
Red = years where submissions ≥30; Blue = years with <30 submissions

CADTH

CADTH's Plan to Eliminate the Backlog

- Special transfer of money from CADTH reserves
- Increasing the number of drug reviews initiated each month and reviewed at each CDEC meeting
- Scheduling an extra meeting of CDEC in December 2014
- Assigning experienced staff from other CADTH programs to CDR on an interim basis
- Recruiting additional staff and contractors

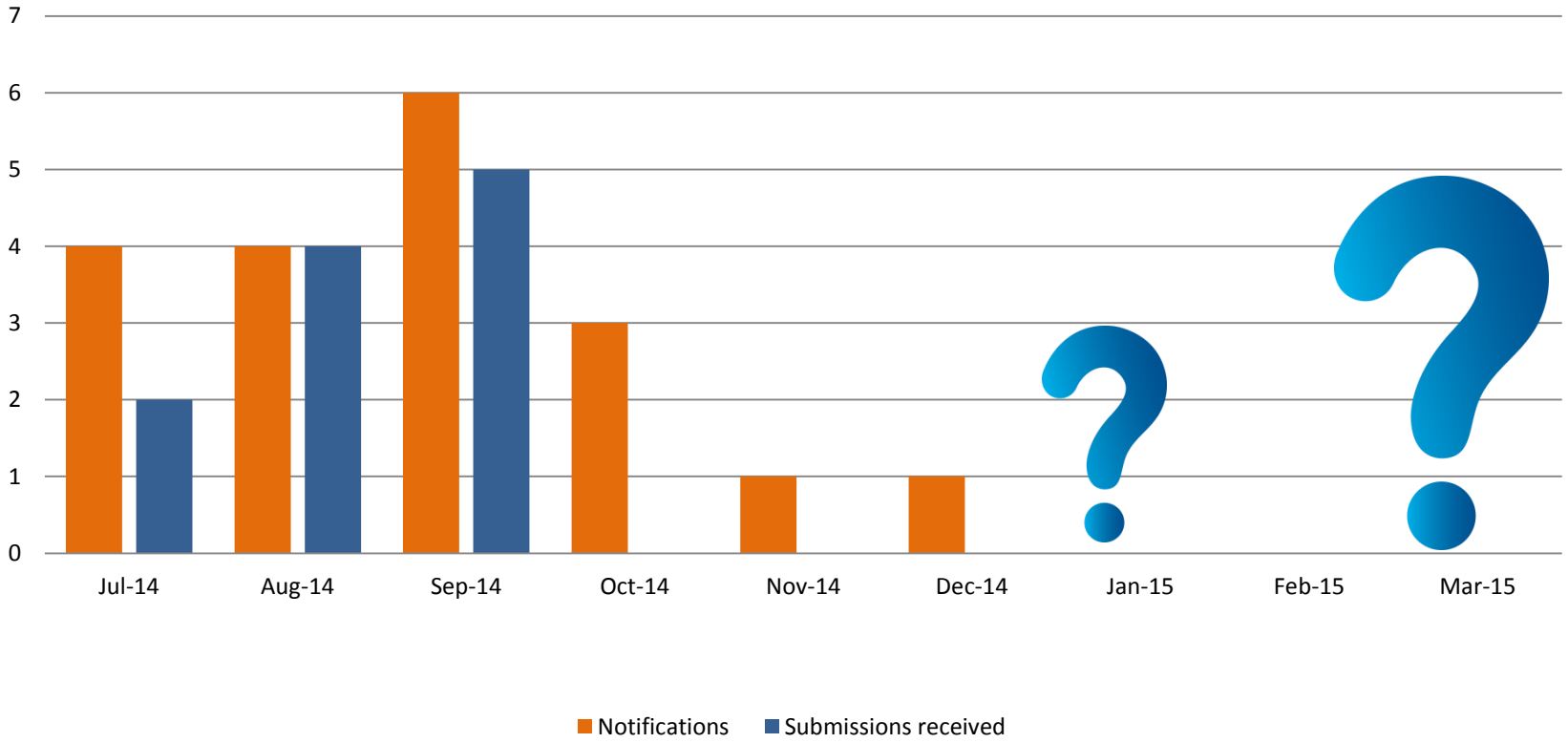
Backlog of CDR Submissions



Backlog numbers reflect aggregate numbers at the end of each month

CADTH

Mandatory Advanced Notification

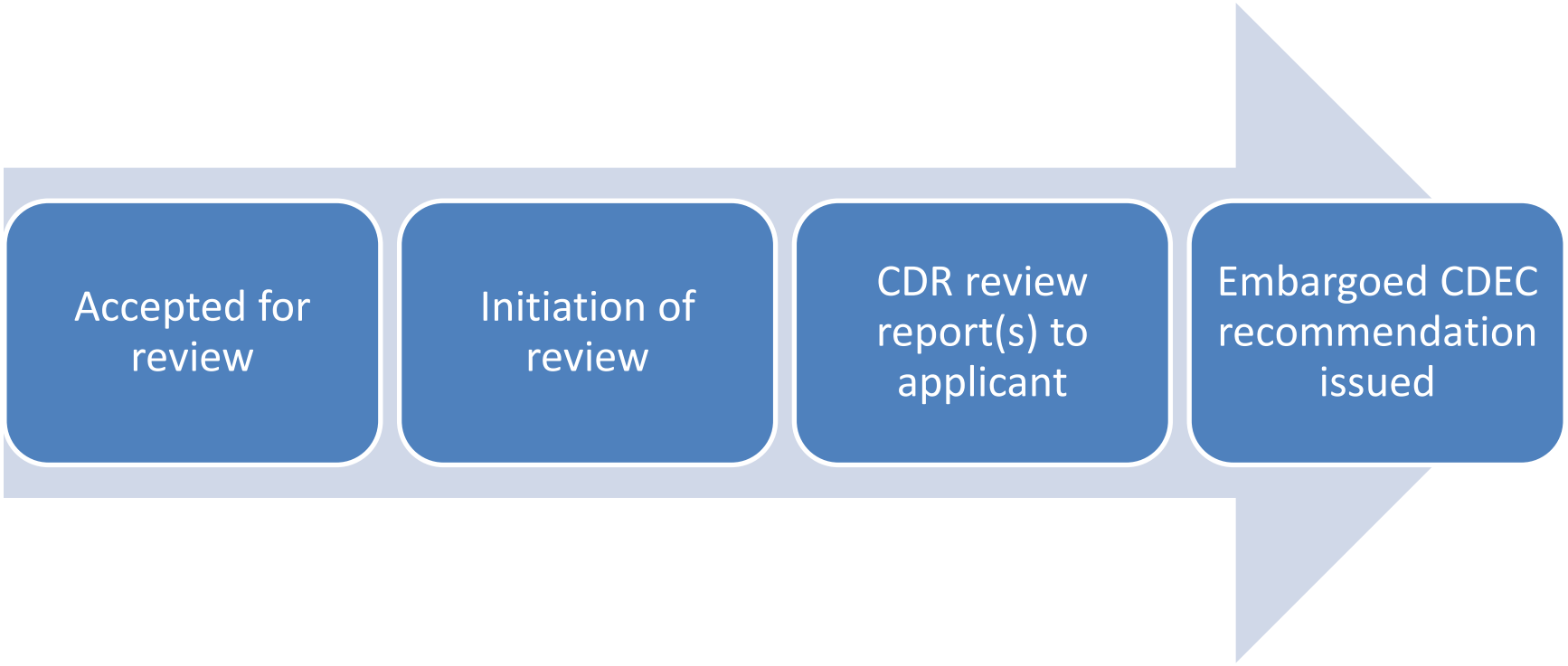


CDR Industry Application Fees

Schedule	Application Type[a]	Fee
A	Submission for a new drug for review of a single indication	$72,000
	Submission for an existing drug for the review of a new indication	
	Submission for a new combination product for review of a single indication	
B	Each subsequent new indication[b] filed at the same time or sequentially for the three application types listed in schedule A	$57,600
	Resubmission based on new clinical information with or without new cost information	
C	Submission for a new combination product (funded components or CADTH designated tailored reviews)	$36,000
	Submission for a subsequent entry biologic	
D	Resubmission based on new cost information only	$7,000
	Request for a resubmission based on a reduced price during the embargo period	
	Request for reconsideration of an embargoed CDEC recommendation	

[a] Application types under schedules A and B would typically undergo a standard CDR review. Application types under schedule C would typically undergo a tailored CDR review. The various application fee schedules reflect the relative difference in estimated effort for the review of the various application types.
[b] When application is filed for the review of multiple indications at the same time and CADTH decides to conduct a standard CDR review for each indication, an application fee of $72,000 will apply to only one of these indications and an application fee of $57,600 (20% discount) will apply to each of the other indication(s) to be reviewed. In addition, for each subsequent indication for a drug filed sequentially at a later date, an application fee of $57,600 will apply.

Performance Metrics



Performance metric of 180 calendar days

Performance Metrics

Milestones for Payment of CADTH Common Drug Review Application Fees							
Schedule	Milestone 1			Milestone 2			Total Fee
	Description	Per Cent Due	Amount Due	Description	Per Cent Due	Amount Due	
A	Initiation of review	70%	$50,400	Sending reports to applicant	30%	$21,600	$72,000
B		70%	$40,320		30%	$17,280	$57,600
C		70%	$25,200		30%	$10,800	$36,000
D	Request accepted	100%	$7,000	NA	0%	$0	$7,000

Compliance with Performance Metrics

Submissions	Performance Metric	Compliance Target	Refund for Non-Compliance
Screening of submission or resubmission and "Acceptance for Review"	10 business days	100%	NA
Date of "Acceptance for Review" to date of issuance of embargoed CDEC recommendation	180 calendar days	95%	25% of the application fee payable back to the manufacturer

Revised Priority Review Criteria

Clinical criteria:

All of the following criteria must be demonstrated:

- The drug is indicated or anticipated to be indicated for an immediately life-threatening or other serious disease.
- The drug addresses an unmet medical need.
- The drug offers substantial improvement in clinically important outcome measures of efficacy and effectiveness, when compared with other appropriate comparators.

Economic criterion:

- For the drug under review, the projected combined cost savings for the participating drug plans is an average of at least $7.5 million per year for the first three years the product is marketed in Canada, when compared with appropriate comparators.

Priority Review Status

Brand Name	Non-proprietary	Indication
Priority Review Granted		
Ultibro Breezhaler	indacaterol/glycopyrronium	COPD
Kalydeco	ivacaftor	CFTR gating mutations
Firazyr	icatibant	Hereditary angioedema
Remsima	infliximab	RA, AS, PA, psoriasis
Inflectra	infliximab	RA, AS, PA, psoriasis
Vimizim	elosulfase alfa	Mucopolysaccharidosis IVA
Zaxine	rifaximin	Hepatic encephalopathy
Esbriet	pirfenidone	idiopathic pulmonary fibrosis
TBC	Sofosbuvir/Ledipasvir	Hepatitis C infection
Priority Review NOT Granted		
Invokana	canagliflozin	Type 2 diabetes
Signifor	pasireotide	Cushing's disease
Afinitor	everolimus	SEGA-TSC
Xeljanz	tofacitinib	RA
Juxtapid	lomitapide	Familial hypercholesterolemia
Pending and Ongoing assessments		
Xolair	omalizumab	Chronic idiopathic urticaria

AS = ankylosing spondylitis, **COPD** = chronic obstructive pulmonary disease; **PA** = psoriatic arthritis, **RA** = Rheumatoid arthritis; **SEGA** = subependymal giant cell astrocytoma; **TBC** = to be confirmed; **TSC** = tuberous sclerosis complex

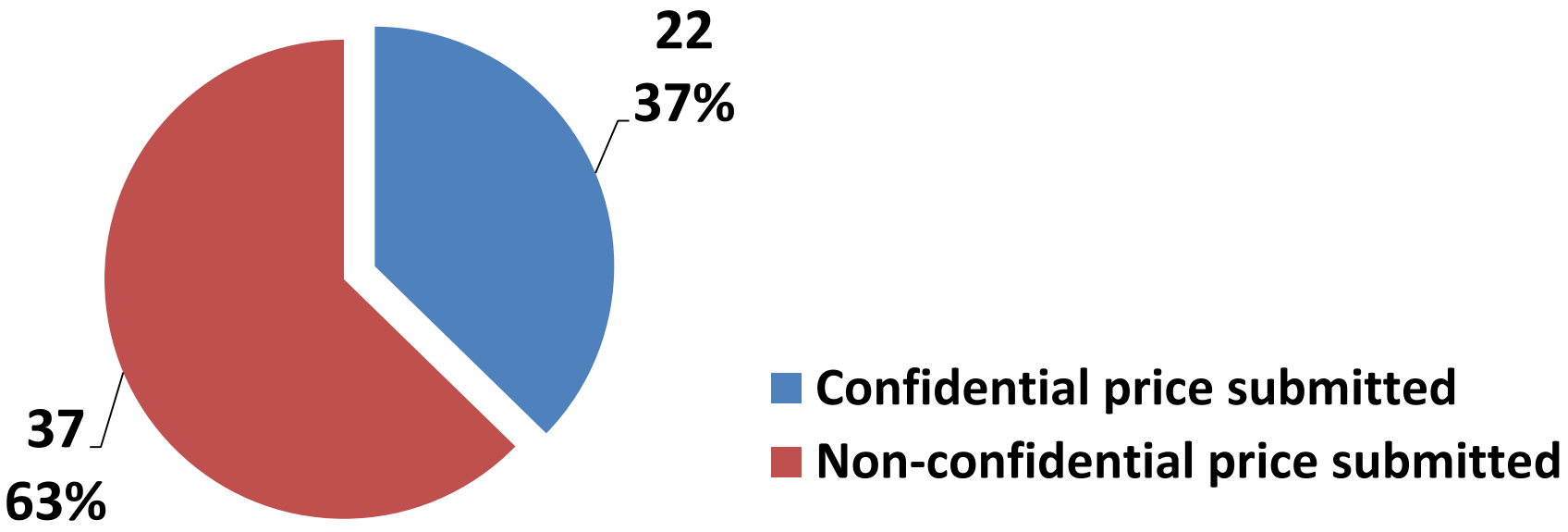
CDR - Price considerations

- Confidential price permitted through the CDR process

Revised Definitions (September 2014 version)	
Submitted price	The price per unit that is submitted to CDR and that must not be exceeded for any of the drug plans following release of a CDEC Final Recommendation, irrespective of the type of recommendation made and whether or not the Canadian Drug Expert Committee criteria for listing are the same as the criteria requested by the manufacturer.
Confidential Price	A price per unit that is submitted in confidence, as part of the CDR submission requirements and to which the provisions of the CADTH Common Drug Review Confidentiality Guidelines apply.

Key Issue: should the confidential price become public if a drug plan decides to list the drug for the indication reviewed through the CDR process

Confidential versus Non-confidential Prices

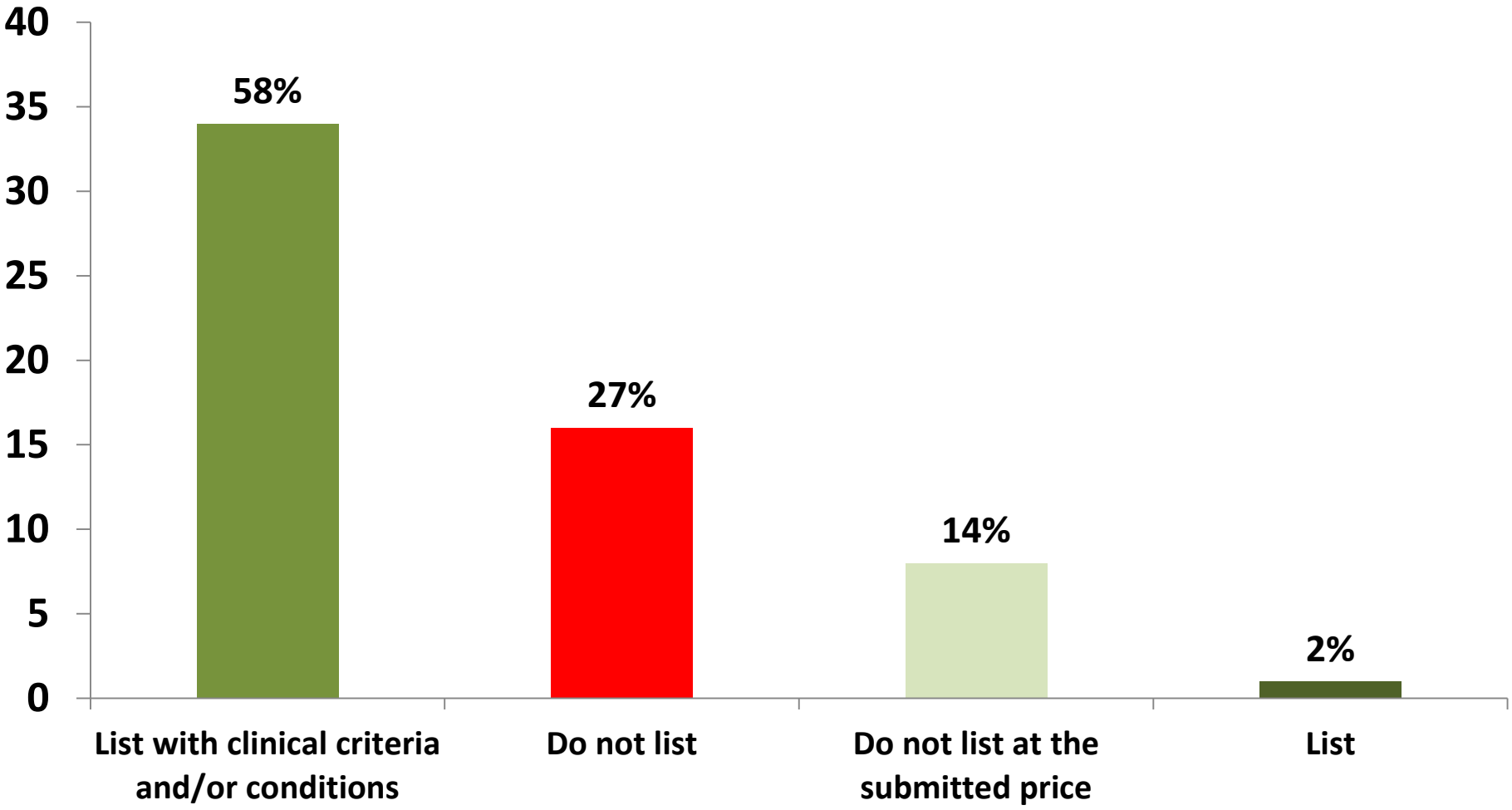


- 59 CDEC recommendations were issued from November 2012 to August 2014.
- Approximately 1/3 of submissions/resubmissions were filed with a confidential submitted price.

CDEC Recommendation Options

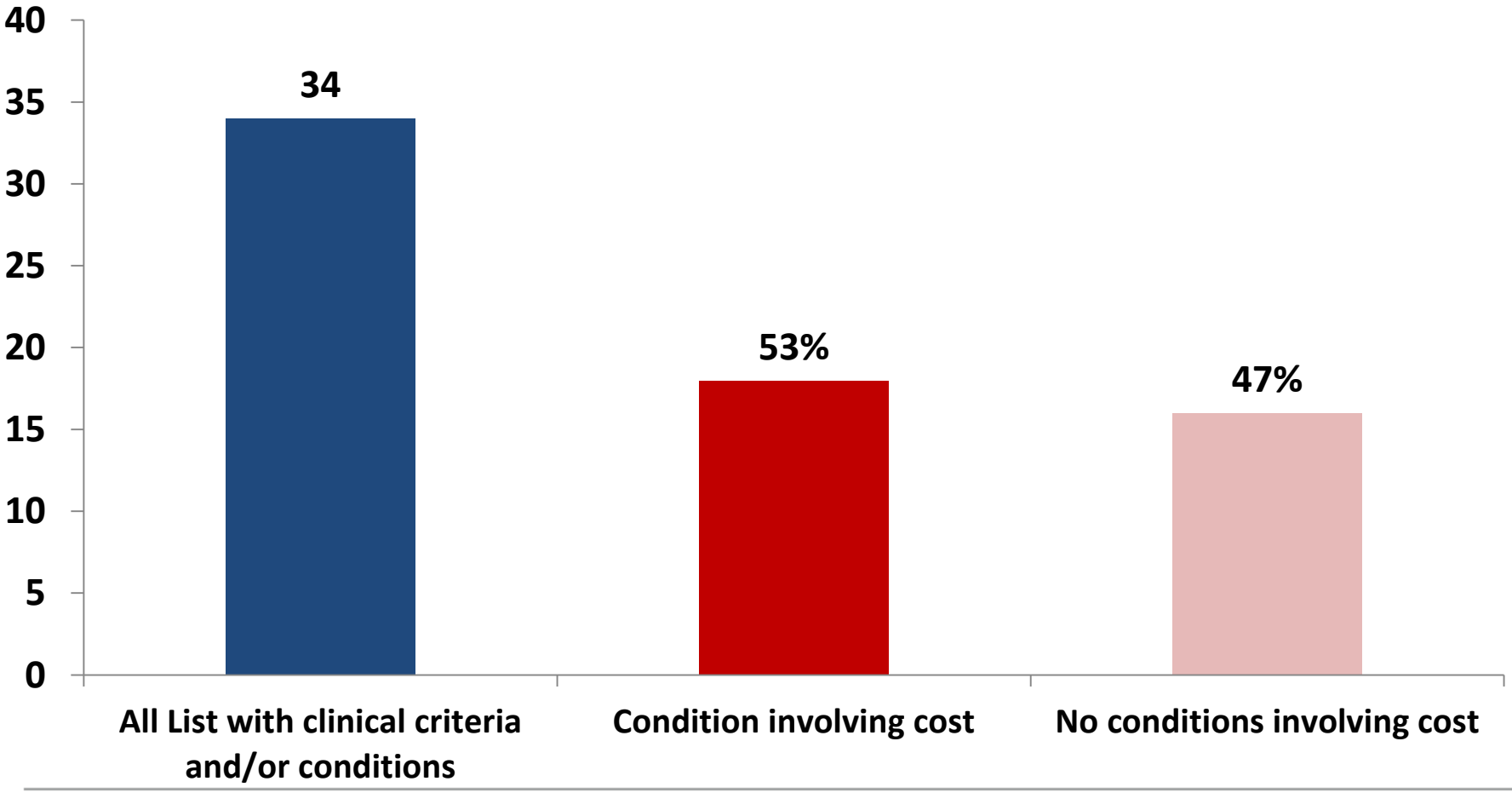
Options	Description and Considerations
List	• Drug demonstrates comparable or added clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators.
List with clinical criteria and/or conditions	• Drug demonstrates comparable or added clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators in a subgroup of patients within the approved indication. • Drug demonstrates added clinical benefit, but the cost/cost-effectiveness relative to one or more appropriate comparators is unacceptable. In such cases, a condition may include a reduced price. • Drug demonstrates comparable clinical benefit and acceptable cost/cost-effectiveness relative to one or more appropriate comparators.
Do not list at the submitted price	• Drug demonstrates no added clinical benefit and the cost/cost-effectiveness relative to one or more appropriate comparators is unacceptable. • Drug demonstrates added clinical benefit, but the cost/incremental cost-effectiveness ratio far exceeds that of existing treatment options and precludes a recommendation to list with clinical criteria and/or conditions.
Do not list	• Drug does not demonstrate comparable clinical benefit relative to one or more appropriate comparators.

CDEC Recommendations Since November 2012



CADTH

Conditions Involving Price or Cost



CADTH

Key initiatives

Transparency

- CDEC deliberative framework
- Recommendations options
- Posting CDR review reports
- Posting patient group input
- Feedback to patient groups

Efficiency

- Elimination of hard copy submissions
- Pre-submission meetings
- New templates to assist manufacturers
- Advanced notification to improve forecast

HIGHLIGHTS OF 2014 VERSIONS:

PROCEDURE FOR THE CADTH COMMON DRUG REVIEW

SUBMISSION GUIDELINES FOR THE CADTH COMMON DRUG REVIEW

CADTH

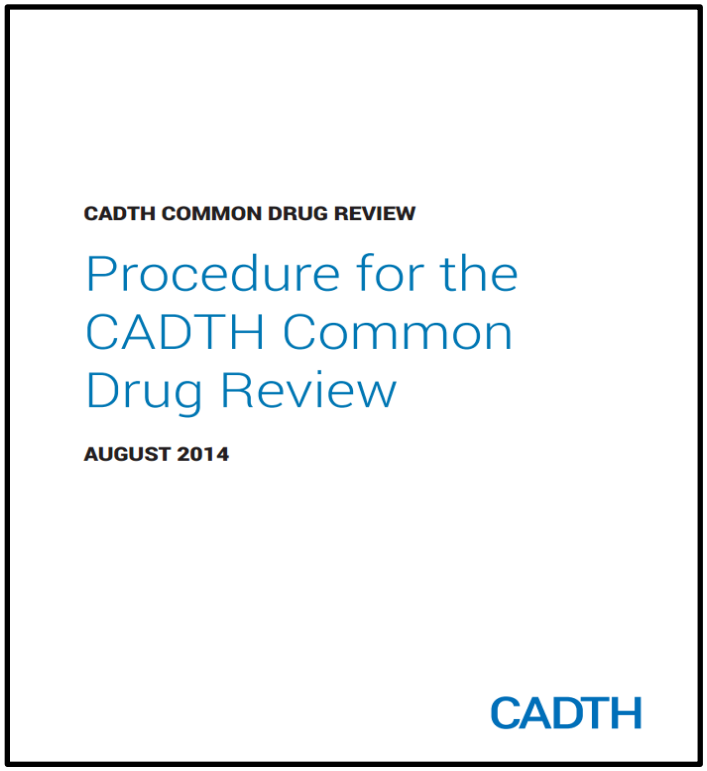
Overview

1. CDR Procedure and CDR Submission Guidelines
    - Introduction to these documents and the *CDR Update*
    - Highlights of the revised 2014 versions

2. CDR Application and Screening
    - Pre-submission meetings
    - Notification of pending submissions or resubmissions
    - Overview of select submission and resubmission requirements
        - Category 1 requirements
        - Category 2 requirements
        - Resubmissions – supporting information
        - Application screening – timelines
    - Key contact information …

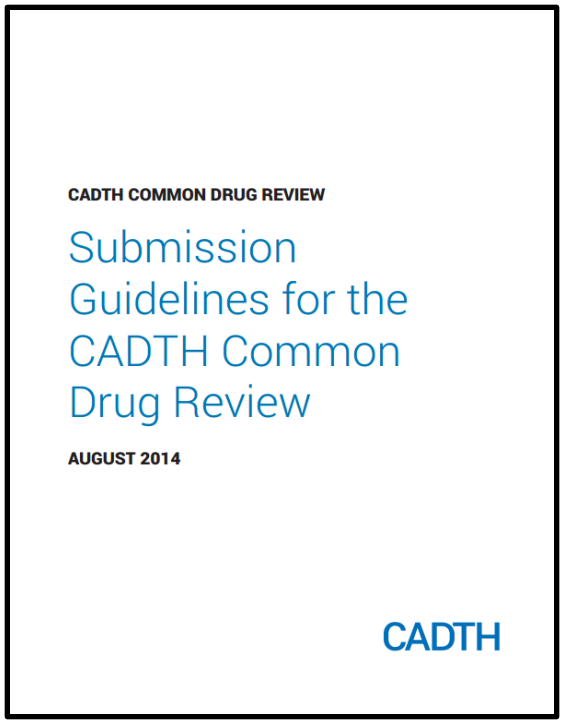
CDR Procedure

Procedure for the CADTH Common Drug Review outlines the procedures to be followed by all participants involved in the CDR process



CDR Submission Guidelines

- Consolidates the requirements of CADTH and the drug plans.
- Detailed guidance for preparing CDR submissions and resubmissions:
  - Application process
  - Type and format of information that is required by CDR
- Application screening and assessment is based on this document.



CDR Update

- Search All Products
- Optimal Use
- Therapeutic Reviews
- Health Technology Assessment
- Common Drug Review
  - About the Common Drug Review
  - Recommendations and Status of Drug Submissions
  - Filing a Submission
  - Patient Input
  - Advisory Committees
  - CDR Update
  - CDR Links
- Rapid Response
- Environmental Scanning
- Methods and Guidelines
- Projects in Progress

CADTH » Search All Products » Common Drug Review » CDR Update

CDR Update

CDR Update provides detailed information on initiatives and activities relating to CADTH's Common Drug Review process.

To receive *CDR Update*, subscribe to *CADTH-Alert*. If you previously received *CDR Update* notifications via the *CADTH Communiqué*, you must subscribe to CADTH E-Alert to continue receiving the notifications.

2014 | 2013 | 2012 | 2011 | 2010 | 2009 | 2008 | 2007 | 2006 | 2005 | 2004 | 2003

CDRUpdate - newsletter

CDR Update — Issue 99

January 9, 2014

In This Issue

Highlights of August 2014 Revisions: Submission Guidelines & Procedure

- 17 new or revised templates to assist applicants in preparing to file a CDR submission or resubmission
- Templates include detailed instructions and/or FAQ sections to assist in completion.
- Consistency of category 1 requirements across different submission types
  - e.g., less variation between submissions filed on a pre-NOC basis versus post-NOC basis
- Improved structure and formatting of CDR documents
  - Extensive cross-referencing added throughout documents
  - Central location for all CDR templates

New or Revised Templates

Pre-submission Phase	Voluntary pipeline notification template
	Pre-submission meeting request form
	Mandatory notification submission/resubmission templates
	New combination product considerations form
Category 1 Requirements	Application overview template
	Executive summary templates submissions/resubmissions
	Table of studies template
	Number of patients accessing new drug
	Commitment to honour submitted price letter
	Unrestricted sharing of information letter
	Letter for sending NOC or NOC/c to CADTH
	Letter for finalized category 1 requirements
Tailored Review Templates	Subsequent entry biologic submission template
	New combination product submission template
Priority Review	Priority review application template

Filing a CDR Submission or Resubmission

Pre-submission Procedure

- Pre-submission meetings
- Notification of pending submission

CDR Application and Screening

- Category 1 requirements
- Category 2 requirements
- Resubmission requirements – supporting information
- Application screening – timelines

Other Key Information

- Contact information
- E-Alerts

Pre-submission Meetings

Purpose

- Opportunity for the applicant to introduce a drug to CADTH and discuss submission requirements
- Opportunity for dialogue between CADTH staff and manufacturers and are not meant to be consultative in nature, outside of clarifying submission requirements

Pre-submission meetings

Standard Pre-submission Meetings

- For submissions or resubmissions to be filed within 6 months

Early Pre-submission Meetings* **NEW**

- For submissions or resubmissions to be filed within 6-12 months
- For drug submissions with all of the following characteristics:
  - indicated for a relatively small patient population
  - clinical data are limited to surrogate end points
  - natural history of the disease is poorly characterized
  - limited number of clinical trials with small sample sizes
  - treatment has a high cost relative to appropriate comparators
  - the manufacturer has questions regarding the appropriate type of economic analysis to submit

* Please note that this is not related to CADTH's Scientific Advice program

Pre-submission Meetings

Format

- Maximum of 1 hour and limited to 1 meeting per pending drug submission

Requesting a Meeting

- Manufacturers are required to complete the pre-submission meeting request form template provided and submit it to CADTH (meetingrequests@cadth.ca)

Preparation for Pre-Submission Meetings

- Scheduled in the order that pre-submission meeting requests are received by CADTH
- The completed agenda and slide deck must be received by CADTH 2 weeks prior to the pre-submission meeting
- Manufacturers are asked to arrive 15 minutes prior to the meeting and sign in with reception
- Follow-up questions from the meeting should be submitted to requests@cadth.ca

Pre-submission Meetings

Common Drug review Pre-submission Meeting Request Form

Section 1: All Requests for Pre-submission Meetings	
Background	**Details**
Drug name	State the brand name and the non-proprietary name
Route of administration	State the route of administration (e.g., oral, intravenous, subcutaneous, inhalation, etc.)
Dosage form and strength(s)	Provide a list of all the dosage forms and strengths of the drug.
Location of administration/use	Indicate if the drug is used in the community and/or hospital setting.
Indication, as per NOC or anticipated NOC	Provide the exact wording of the indication(s) approved by Health Canada or the anticipation indication(s).
Anticipated or actual date of NOC or NOC/c	Provide the actual or anticipated date for issuance of the NOC or NOC/c.
Trial information	Provide a brief high-level overview of pivotal trials (i.e., study design, sample size, population description, intervention & comparator details, primary and key secondary endpoints)
Comparator(s)	Provide a list of the other treatments and/or procedures used for the condition.
How is/are the comparator(s) funded	Please indicate if and how the comparator(s) is/are currently funded by the drug plans in Canada.

Notification of Pending Submissions

Voluntary Pipeline Notification (~12 months) **NEW**

- Applicants encouraged to voluntarily provide advanced notification of a pending submission at the time of regulatory filing
- Those willing to participate are asked to complete and submit the advanced notification template to requests@cadth.ca

Mandatory Notification (~1 month) **NEW**

- Applicants required to provide notification of a pending submission or resubmission ≥20 business days prior to filing.
- Complete and submit the advanced notification template for a submission or resubmission by email to requests@cadth.ca.
- Failure to provide notification at least 20 business days in advance of filing may result in a delay in the processing and review of the submission or resubmission by CADTH.

Submission/Resubmission Requirement Categories

Category	Function in the CDR Process	Due
Category 1	Used by the CDR review team and CDEC for the review and recommendation process	When application is filed
Category 2	Used by the drug plans and are not considered as part of the CDR review process	≥ 20 days before CDEC meeting
Priority review request	Used by CADTH, CDEC, and the drug plans for determining whether or not priority review status should be granted	At the time of filing the application
Additional information	Additional information that may be required for completion of the review (e.g., CSRs)	ASAP following a request by CADTH

Category 1 Requirements

General Information
• Application overview template **NEW** • Signed cover letter • Executive summary template **NEW template** • Product monograph
Health Canada Documentation
• NOC or NOC/c • Health Canada clinical reviewers report **NEW** • Table of Clarifaxes **REVISED**

Category 1 Requirements

Efficacy, Effectiveness, and Safety Information
• CTD sections 2.5, 2.7.1, 2.7.3, 2.7.4, 5.2 **REVISED**
• Copies of key clinical studies and errata*
• Table of studies **REVISED**
• Copies of editorial articles*
• Literature search strategies
• Signed declaration that all known studies disclosed
• CONSORT diagrams
• Copies of new data*
• Copies of articles for validity of outcomes*

* **NEW** reference lists now required for these requirements

Category 1 Requirements

Economic and Epidemiologic Information
• Pharmacoeconomic evaluation • Economic model • Number of patients accessing a new drug **NEW template** • Disease prevalence and incidence data
Pricing and Distribution Information
• Submitted price to 4 decimal places • Method of distribution • Commitment to honour submitted price **REVISED**
Sharing of information
• Letter authorizing unrestricted sharing of information

Category 2 Requirements

Category 2 Requirements	Notes
Certified Product Information Document	Required
Budget Impact Analyses	Required
Letter Confirming Ability to Supply	Discontinued
Drug Notification Form	Discontinued
Product Patent Expiration Date	Discontinued
CPS listing and PAAB-approved materials	Discontinued
Number of patients accessing new drugs	Discontinued
Disease prevalence and incidence	Discontinued

- Majority of requirements discontinued **NEW**
- Target date for filing: at least 20 business days before CDEC meeting
- CDEC Final Recommendation not issued until complete

Resubmission Requirements – Supporting Information

Basis	Required Supporting Information
New clinical information supporting efficacy	• New randomized controlled trial(s) • New pharmacoeconomic evaluation • New BIAs
New clinical information supporting safety	• New case-control or cohort studies • New RCT(s), if available • New pharmacoeconomic evaluation • New BIAs
New cost information	• New pharmacoeconomic evaluation • New BIAs

Application Screening Timelines

- Screening for category 1 requirements for submissions and resubmissions is completed within 10 business days
  - This has been increased in 2014 from 5 business days to ensure that adequate time is available for screening (particularly for situations with more complex PE models)
- CADTH makes an effort to communicate any deficiencies to manufacturer's within the allotted 10-day screening period
  - In the past 18 months only four submissions have been deemed incomplete
- Category 2 requirements are screened within 5 business days

Contact Information

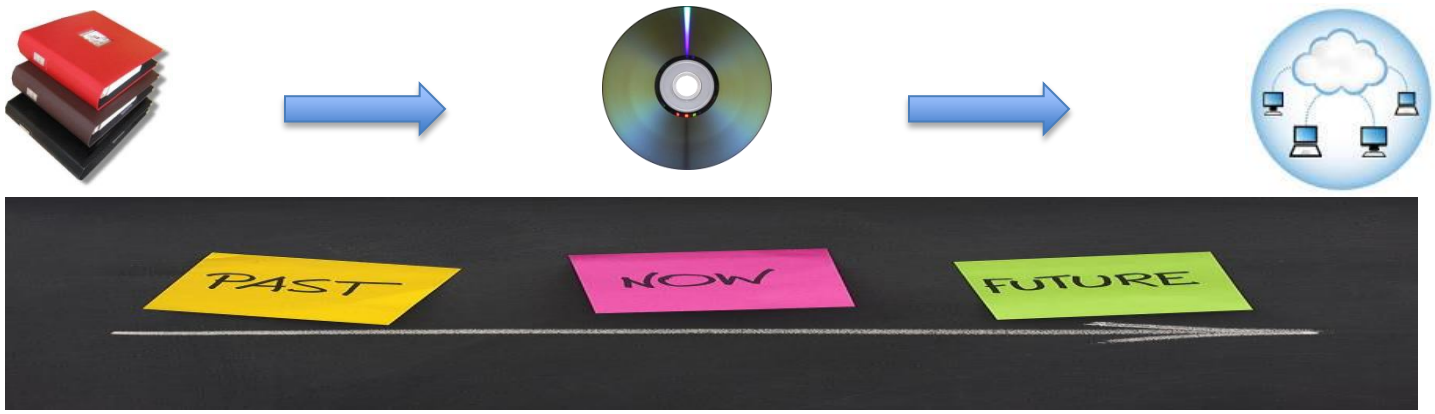
Type of Inquiry	Contact Information
• CDR submission requirements • CDR process • CDR procedure	Email to requests@cadth.ca *
• Filing CDR applications	Registered mail, courier, or in person: Central Intake, CADTH 600-865 Carling Avenue Ottawa, ON, K1S 5S8
• Inquiries regarding a CDR application for which the review has been initiated	Email to the designated coordinator contact provided by CADTH

* Always direct these inquiries to requests@cadth.ca to ensure appropriate tracking and timely responses

CADTH E-Alerts

- CADTH E-Alert notifies subscribers to time-sensitive news, such as opportunities to provide feedback on CADTH products and other opportunities.
- Subscribe at: www.cadth.ca/en/media-centre/e-alert/about-e-alert

Continuous Improvement in Efficiencies for both Applicants and CADTH



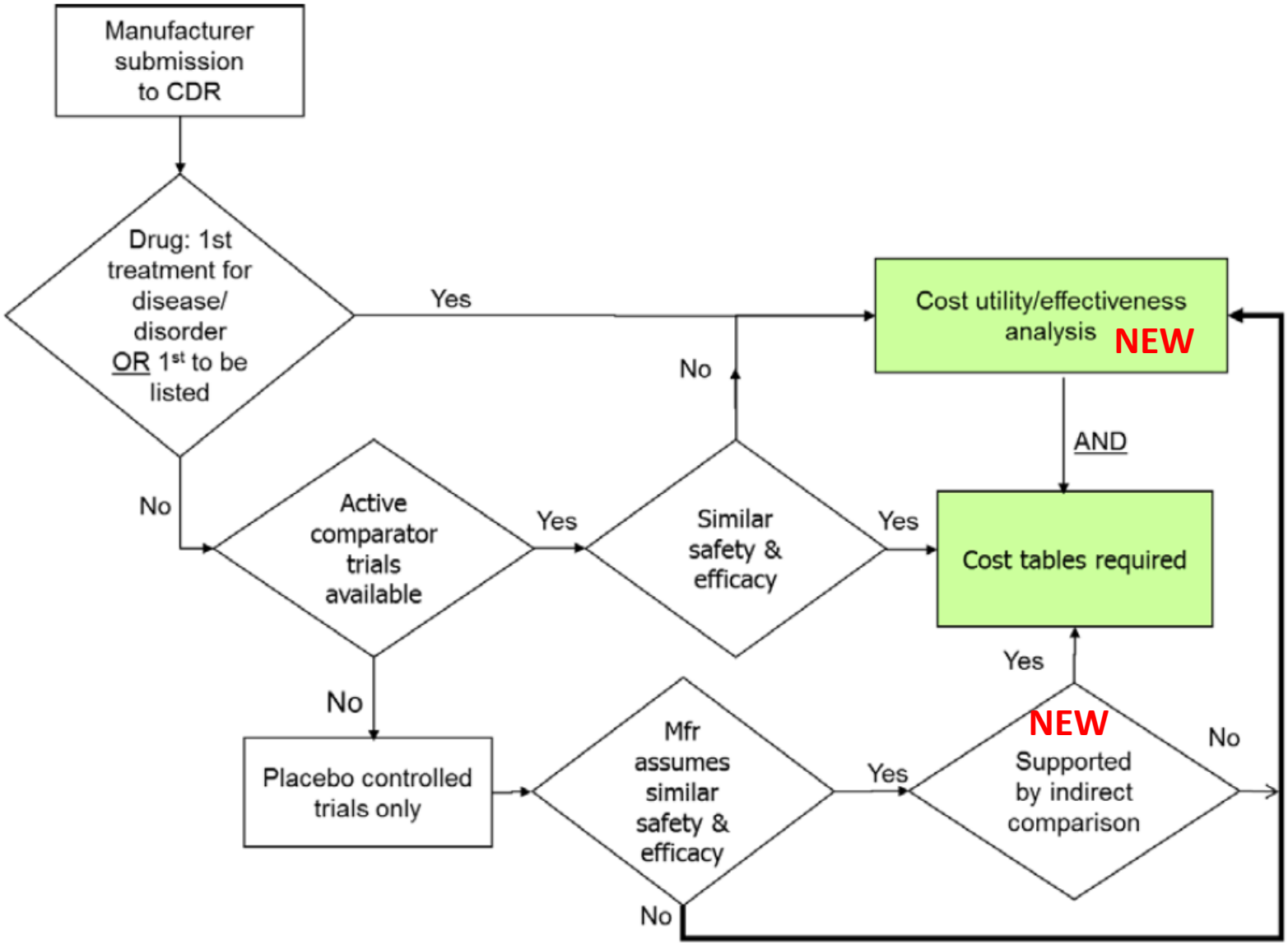
PHARMACOECONOMIC UPDATE

CADTH

Category 1 - What's New?

- Only one type of pharmacoeconomic analysis to be submitted
- Where the clinical inputs are based on an indirect treatment comparison (ITC), the full technical report of the ITC must be provided as part of the filed material
- Copies of any supporting materials that are used as part of the modelling exercise must be provided
- Clarification on type of analysis to be submitted

Figure 1: Summary of the Guidelines for the Type of Economic Analysis to Submit



CDR = CADTH Common Drug Review; Mfr = manufacturer.

Frequently Asked Questions

- Target population
  - Base Case : Full population identified in the approved Health Canada indication(s) to be reviewed by CDR
  - Listing request for a subpopulation: Additional analysis
- Comparators
  - The new therapy should be compared with the accepted therapy (existing practice)
- Software
  - The preferred economic model software platforms are Excel, TreeAge, or Arena

Frequently Asked Questions

- Drugs for small patient populations:
  - Pharmacoeconomic analyses are critical for all drugs reviewed through the CDR process
- Redaction/ confidential information
  - The type of analysis performed, the methodology, comparators, assumptions and outputs from the economic model (results) are not redacted.
  - Confidential price is redacted
  - Pharmacoeconomic model (program) is confidential

Common Issues

- Locked version of the economic model, not fully unlocked or executable
- Insufficient information on methods
- Price used in the model differs from price submitted
- Insufficient sensitivity analyses performed and/or model does not allow the reviewers to run relevant sensitivity analyses
- Appropriate comparators not included in the analyses

REQUESTS@CADTH.CA

CADTH