CADTH

Industry Application Fees:
An Administrative Review, September 26, 2016

Background

In recent years, the number of drug submissions to CADTH has surpassed CADTH's funded capacity to conduct the reviews. CADTH began collecting fees for applications to the Common Drug Review (CDR) on September 1, 2014, and for the pan-Canadian Oncology Drug Review (pCODR) on April 1, 2015. Revenues from the application fees help to finance an increase in the number of drugs that CADTH reviews annually. The fees supplement existing federal, provincial, and territorial (F/P/T) funding.

CADTH committed to conducting an administrative review of the industry application fees after one full year of implementation.

Scope and Objectives

The scope of this administrative review covers:

- Activities and results pertaining to the collection of industry application fees for CDR from September 1, 2014 to March 31, 2016
- Activities and results pertaining to the collection of industry application fees for pCODR from April 1, 2015 to March 31, 2016.

The objectives of this administrative review are to explore:

1. **Capacity:** whether collecting application fees has enabled CADTH to increase the number of drug reviews conducted annually

2. **Performance:**
   a) whether CADTH has met program-specific performance targets
   b) whether applicants have submitted payments on time.

3. **Revenue:** whether the value of application fees collected has remained at or below 40% of the overall cost of the CDR and pCODR programs (inclusive of overhead).

Findings

Capacity

1. Since the implementation of industry application fees, has the annual volume of reviews conducted by CDR and pCODR changed?

CDR

The CDR program is operating at or above its planned capacity. The number of reviews delivered in both 2014-2015 and 2015-2016 was greater than the number of reviews projected to be delivered for those years in the CADTH Annual Business Plan.

The number of CDR reviews that CADTH has been able to deliver annually has increased substantially since the introduction of the application fees. Table 1 demonstrates that the number of reviews delivered in 2015-2016, the first complete fiscal year following the implementation of industry application fees for CDR, represents a 63% increase over 2013-2014, the last fiscal year prior to implementation of the fees for CDR.

Table 1: CDR Reviews Conducted and Percentage Increase Over Previous Year

Fiscal Year	Number of Reviews Projected in Annual Business Plan	Number of Reviews Conducted	Percentage Increase in Reviews Conducted Over Previous ear
2011-2012	30 to 35	27	NA
2012-2013	30 to 35	25	–7%
2013-2014	30 to 35	30	20%
2014-2015	30 to 35	37	23%
2015-2016	40 to 45	49	32%

NA = not applicable

pCODR

The number of pCODR reviews that CADTH has been able to deliver has increased since the introduction of the application fees, as demonstrated in Table 2. The annual number of reviews completed has been uneven, with a substantial increase of 144% in 2015-2016 over the previous fiscal year. The number of reviews completed in 2015-2016 fell within the range projected in the CADTH Annual Business Plan.

Table 2: pCODR Reviews Conducted and Percentage Increase Over Previous Year

Fiscal Year	Number of Reviews Projected in Annual Business Plan	Number of Reviews Conducted	Percentage Increase in Reviews Conducted Over Previous Year
2011-2012	NA	1	NA
2012-2013	NA	12	1,100%
2013-2014	NA	19	58%
2014-2015	15 to 20	9	–53%
2015-2016	20 to 25	22	144%

NA = not applicable.

Performance

2. What have been the CDR and pCODR compliance rates for meeting key performance metrics?

Table 3 presents the performance metrics and targets for both CDR and pCODR.

Table 3: CDR and pCODR Performance Metrics

	Performance Metric	Compliance Target
CDR		
Screening of submission or resubmission and “Acceptance for Review”	10 business days	100%
Date of “Acceptance for Review” to date of issuance of Embargoed CDEC Recommendation	180 calendar days	95%
pCODR		
Screening of submission and “Submission Deemed Complete”	5 business days	100%

	Performance Metric	Compliance Target
Screening of resubmission and "Resubmission Deemed Complete"	10 business days	100%
Date of "Submission Deemed Complete" to date of issuance of a pERC Initial Recommendation	180 calendar days	95%

CDEC = CADTH Canadian Drug Expert Review Committee; CDR = CADTH Common Drug Review; pCODR = CADTH pan-Canadian Oncology Drug Review; pERC = pCODR Expert Review Committee.

CDR

Following the introduction of application fees, CDR committed to reporting against two key performance metrics: a 10-business-day screening metric for submissions and a 180-calendar-day review metric. The first metric measures the percentage of submissions and resubmissions that are screened for completeness within 10 business days of receipt by CDR to determine whether they can be accepted for review. The screening for completeness entails assessing whether a submission includes all of the information requirements stipulated in the CDR guidelines. Since CADTH introduced this measure of performance (as of the date of the introduction of application fees), CDR has complied with its screening metric 100% of the time.

The second metric is measured from the time a submission is accepted for review until an Embargoed Recommendation is issued. Over the first seven months that application fees were collected — from September 1, 2014 to March 31, 2015 — CDR met the performance target 67% of the time, due to a backlog in submissions. Five of 15 submissions were not completed within the 180-day time frame. A backlog was created because the annual volume of submissions exceeded the annual funded capacity of CDR to conduct reviews. Following the resolution of the backlog in February 2015, after fees were introduced, all reviews have met the target of 180 calendar days. Over the 2015-2016 fiscal year, CDR complied with the 180-calendar-day review metric 100% of the time, exceeding the target of 95%.

pCODR

Following the introduction of application fees, pCODR committed to reporting against three key performance metrics: a five-business-day screening metric for submissions; a 10-business-day screening metric for resubmissions; and a 180-calendar-day review metric.

The first metric measures the percentage of submissions screened for completeness within five business days of receipt by pCODR, to determine if they can be accepted for review. The screening for completeness entails assessing whether a submission includes all of the information requirements stipulated in the pCODR guidelines. Since CADTH introduced this measure of performance (as of the date of the introduction of application fees), pCODR has complied with its screening metric 100% of the time.

The second metric measures the percentage of resubmissions screened for completeness within 10 business days, to determine whether they can be accepted for review. The screening for completeness entails assessing whether a submission includes all of the information requirements stipulated in the pCODR guidelines. No resubmissions were received within the time period being examined.

The final metric is measured from the time that a submission is accepted for review until an Initial Recommendation is issued. Over the 2015-2016 fiscal year, pCODR complied with the 180-calendar-day review metric 100% of the time, exceeding the target of 95%.

3. To what extent have circumstances beyond the reasonable control of CADTH prevented CADTH from achieving the key performance metrics described in question 2?

Since CADTH started collecting CDR application fees (September 1, 2014), five CDR application fee refunds (of 25% each) have been issued due to non-compliance with the 180-business-day review performance metric (i.e., from acceptance for review to the issuing of an Embargoed Recommendation). The compliance target was not met in these five cases because of the backlog of submissions. Since the backlog was resolved, CADTH has met its compliance target for reviewing submissions 100% of the time.

The names of the drugs submitted and the number of days required in excess of the 180-day-review metric are shown in Table 4.

Table 4: Number of CADTH Common Drug Review Application Fee Refunds Issued Due to Non-Compliance With the 180-Business-Day Performance Metric From September 1, 2014 to March 31, 2016.

Submission	Manufacturer/Applicant	Number of Days in Excess of the 180-Day Metric
Triumeq (abacavir/dolutegravir/ lamivudine)	ViiV Healthcare	50
Eylea (aflibercept)	Bayer Inc.	18
Eliquis VTE (apixaban)	Bristol-Myers Squibb Canada and Pfizer Canada Inc.	16
Simbrinza (brinzolamide/brimonidine)	Alcon Canada Inc.	11
Trintellix (vortioxetine)	Lundbeck Canada	15

4. What proportion of applicants has complied with the payment procedures (e.g., paid within 45 days of the date of issue of the invoice)?

For the period within the scope of this assessment, CADTH issued 155 invoices (for some review types, two invoices are issued). Of those invoices, 143, or 92%, were paid on time (within 45 days of being issued). On average, late payments were received nine days after the 45-day threshold.

The CADTH Guidelines for Manufacturers on Application Fees indicate that in cases where payment is outstanding after 45 calendar days, all work on the review will be temporarily suspended and there is no assurance that the review can be completed as originally scheduled. CADTH has issued warning letters where payment is late to indicate that the review will be suspended. In these cases, payment was soon received, and no reviews were temporarily suspended as a result.

Revenue

5. What percentage of the total cost of the CDR and pCODR programs (inclusive of overhead) do the industry application fees represent?

As per Table 5, for the 2015-2016 fiscal year — the first full year for the collection of application fees for CDR — application fees represented 31% of program costs.
For pCODR, the percentage of total program costs that application fees represented in 2015-2016 is 30.2%.

Revenue from application fees was intended to account for no more than 40% of the total cost of operating the programs; both program areas are operating at approximately 25% below this threshold.

Table 5: Percentage of Total Program Cost Represented by Application Fees

	CDR	pCODR	TOTAL
April 1, 2015 to March 31, 2016			
Revenue from application fees	2,302,400	1,045,200	3,347,600
Cost of program	7,424,632	3,455,429	10,880,061
FY 2016	**31.0%**	**30.2%**	**30.8%**

CDR = CADTH Common Drug Review; FY = financial year; pCODR = CADTH pan-Canadian Oncology Drug Review.

6. What has been the mix of application types (as defined by the application fee schedule) since the implementation of industry application fees?

The application fees charged for CDR and pCODR submissions depend upon the application type. The number of each application type for reviews initiated by CDR and pCODR (in response to industry applications) in 2015-2016 is presented in Table 6. For both CDR and pCODR, the largest proportion of reviews initiated (in response to industry applications) was for Schedule A applications. In 2015-2016, Schedule B applications represented 28% of CDR reviews initiated (in response to industry applications) and 42% of pCODR reviews initiated (in response to industry applications). Schedule B applications are subject to a lower fee, as they are for products being submitted for review of a subsequent indication or for resubmissions with new clinical information. Based on pipeline intelligence, it is anticipated that the proportion of Schedule B applications will increase over the next few years.

Table 6: Application Fee Schedule

Schedule	Application Type				Fee
	Description (CDR)	Number of CDR Reviews Initiated 2015-2016[a]	Description (pCODR)	Number of pCODR Reviews Initiated 2015-2016[a]	
A	Submission for a new drug for review of a single indication Submission for an existing drug for the review of a new indication Submission for a new combination product for review of a single indication	22	*Standard pCODR reviews* Submission for a new drug for review of a single indication or multiple drug products to be used in combination (e.g., new chemotherapy protocol)	11	$72,000
B	Each subsequent new indication filed at the same time or sequentially for the 3 application types listed in	13	Each subsequent submission for an indication, including in a new line of therapy (e.g., first-line,	8	$57,600

Schedule	Application Type				Fee
	Description (CDR)	Number of CDR Reviews Initiated 2015-2016[a]	Description (pCODR)	Number of pCODR Reviews Initiated 2015-2016[a]	
	Schedule A Resubmission based on new clinical information with or without new cost information		relapsed refractory, adjuvant, neoadjuvant), filed at the same time or sequentially for the application types listed in Schedule A		
C	Submission for a new combination product (funded components or CADTH-designated tailored reviews) Submission for a subsequent entry biologic	6	*Additional pCODR Reviews:* Submission for a subsequent entry biologic	0	$36,000
D	Resubmission based on new cost information only Request for a submission based on a reduced price during the embargo period Request for reconsideration of an embargoed CDEC recommendation	6	NA	NA	$7,000

CDEC = CADTH Canadian Drug Expert Committee; CDR = CADTH Common Drug Review; NA = not applicable; pCODR = CADTH pan-Canadian Oncology Drug Review.
[a]Does not include Formulary Working Group or tumour group–initiated submissions (see question 8 for details).

7. **What is the value of refunds issued to industry for CADTH's lack of compliance with the stated performance metrics for pCODR and CDR submissions? What proportion of the total application fee revenue does this represent?**

As of March 31, 2016, the total revenue earned from application fees is $3,849,800. Since the introduction of application fees, the total amount of refunds for non-compliance that CADTH has paid to industry is $64,800. This represents 1.7% of total (CDR plus pCODR) revenue from fees collected to March 31, 2016. All of the fees refunded were associated with submissions to the CDR program that were placed in a backlog. The backlog has since been resolved and no additional refunds have been issued.

8. **Have the number of Formulary Working Group–initiated submissions to CDR and the number of tumour group–initiated submissions to pCODR (i.e., those not subject to an application fee) changed since the introduction of application fees?**

Five Formulary Working Group submissions (not including Requests for Advice) have been received since the implementation of the industry application fees. In comparison, no Formulary Working Group submissions were received from April 1, 2011 up to the date of implementation of the fees for CDR (April 1, 2014).

No tumour group submissions have been received since the implementation of the industry application fees. From the inception of pCODR, there has been no consistent pattern in the number of tumour group–initiated submissions received. A total of three tumour group submissions have been received over the past five years, for a total of 4.1% of the overall number of submissions.

Conclusions

Capacity

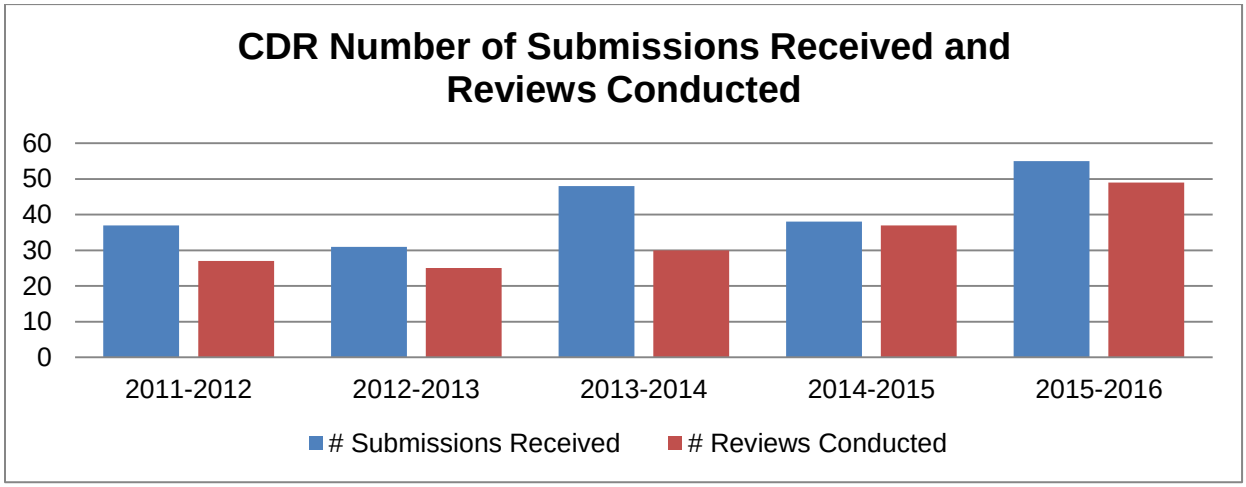
The introduction of industry fees has contributed to both CDR's and pCODR's respective capacities to conduct reviews.

The number of reviews CADTH has been able to conduct annually has increased substantially for both programs since the introduction of the application fees.

CADTH Common Drug Review

The collection of application fees has better positioned CDR to meet the increasing demand for drug reviews. However, at the same time that the number of reviews conducted has increased, the number of submissions to CDR has also increased (by 45% in 2015-2016), which is consistent with a general trend over the past several fiscal years toward increasing annual volumes of CDR submissions. Chart 1 contrasts the number of reviews conducted by CDR with the number of submissions received. Some of the discrepancy between the number of submissions and reviews can be attributed to submission withdrawals and the point in the year at which submissions are received. Despite this, it appears that the increase in CDR capacity may still be outpaced by future increases in submission volume.

Chart 1: CDR Submissions Received and the Number of Reviews Conducted

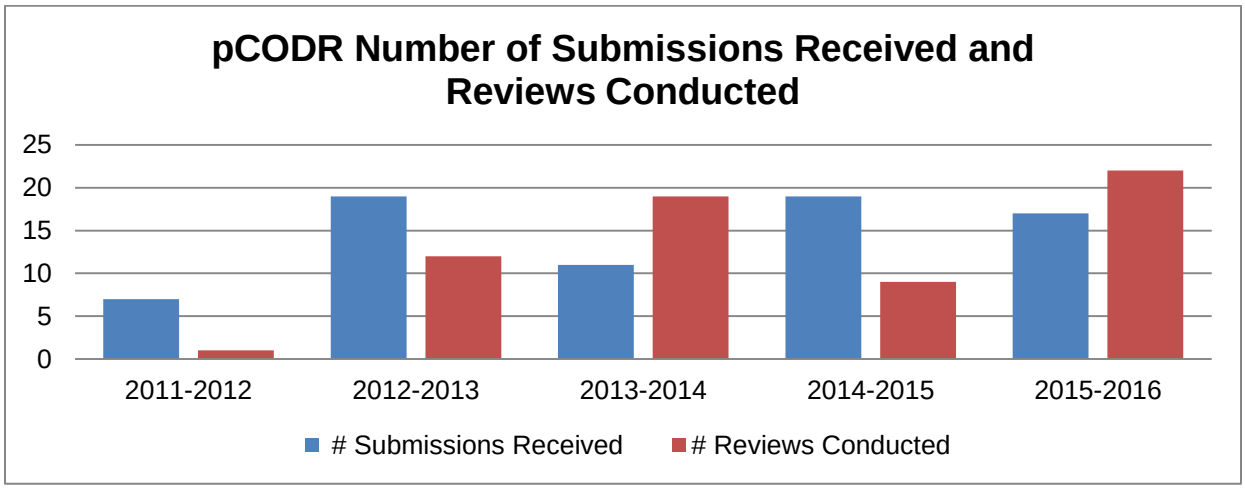


CDR = CADTH Common Drug Review.

CADTH pan-Canadian Oncology Drug Review

The collection of application fees has enabled pCODR to conduct a greater volume of reviews than it has in any previous year. Chart 2 contrasts the number of reviews conducted by pCODR with the number of submissions received. So far, the increase in capacity has allowed pCODR to keep pace with the annual volume of submissions and has better positioned pCODR to respond to the anticipated influx of pCODR submissions in the near future.

Chart 2: pCODR Submissions Received and Number of pCODR Reviews Conducted



pCODR = CADTH pan-Canadian Oncology Drug Review.

Ultimately, there is a limit to the demand that can be met by the increase in capacity financed by application fees.

Performance

Since resolution of the CDR backlog in February 2015, CDR and pCODR have met or exceeded their performance targets.

The introduction of application fees has not negatively affected the performance of either program. Since the introduction of industry fees, the overall performance of both programs can be considered excellent, with both programs meeting their compliance targets for screening submissions.

For CDR, initial performance shortfalls with respect to meeting its 180-day performance target for reviewing submissions can be attributed to historical factors that were the cause of the backlog of submissions. Since this backlog was resolved, CDR has complied with the 180-calendar-day review metric 100% of the time.

With respect to the timely paying of invoices, industry applicants have been compliant 92% of the time with the 45-day standard that was established. This implies that the standard is a reasonable one to maintain.

Revenue

The value of application fees collected has remained below 40% of the overall cost of the CDR and pCODR programs.

At the outset of the collection of industry application fees, the intention was for the fees to account for not more than 40% of the total costs of operating the CDR and pCODR programs, inclusive of overhead, to help finance an increase in the number of drugs reviewed annually. In the first full year of fee collection for each program, the total cost recovered is 31.0% for CDR, and 30.2% for pCODR. With a 40% threshold for program-specific revenues from application fees, both program areas are operating at approximately 25% below this threshold.