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Canada

Evaluation of the Pharmaceutical Drugs Program

Prepared by the Office of Audit and Evaluation
Health Canada and the Public Health Agency of Canada

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To obtain additional information, please contact:

Health Canada
Address Locator 0900C2
Ottawa, ON K1A 0K9
Tel.: 613-957-2991
Toll free: 1-866-225-0709
Fax: 613-941-5366
TTY: 1-800-465-7735
E-mail: publications-publications@hc-sc.gc.ca

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List of Acronyms

ADR	Adverse Drug Reaction
API	Active pharmaceutical Ingredients
DIN	Drug Identification Number
DEL	Drug Establishment Licensing
EMA	European Medicines Agency
FTE	Full Time Equivalent
GMP	Good Manufacturing Practices
HC	Health Canada
HPFB	Health Products and Food Branch
HTA	Health Technology Assessment
IO	Interim Order
IT	Information Technology
MHPD	Marketed Health Products Directorate
MRA	Mutual Recognition Agreement
NAS	New Active Substance
NNHPD	Natural and Non-prescription Health Products Directorate
PDD	Pharmaceutical Drugs Directorate
PDP	Pharmaceutical Drugs Program
PIP	Performance Information Profile
PSES	Public Service Employee Survey
RMP	Risk Management Plans
ROEB	Regulatory Operations and Enforcement Branch
VDD	Veterinary Drugs Directorate
UK	United Kingdom
US	United States
US FDA	United States Food and Drug Administration

Executive Summary

Evaluation Purpose and Scope

The evaluation focused on the impact of the Pharmaceutical Drugs Program (PDP) activities and its agility in addressing current and emerging needs regarding human and veterinary drugs. The evaluation also considered how the Program adjusted to the pandemic crisis, including regulatory and operational adjustments, and the extent to which these are being considered moving forward to fulfill its regulatory role.

Covering activities from 2017-18 to 2022-23, the evaluation examined pharmaceutical drugs for human and veterinary use, including both prescription and non-prescription drugs. Activities related to biologics, radiopharmaceuticals, natural health products and medical devices were excluded from this evaluation, as there are separately planned evaluations to assess these other health products.

Findings

Program adaptation to changing context

The pharmaceutical drug landscape has evolved at a fast pace in recent years, with an increasing number and complexity of drugs reviewed in both the innovative and generic categories. To address this changing environment, the PDP has put several changes in place since 2017 to modernize its regulatory processes. These include conducting parallel aligned reviews with Health Technology Assessment (HTA) organizations, aligning with international pre- and post-market practices, addressing challenges posed by the globalization of the supply chain, embracing the real-world evidence approach along the drug life cycle, and addressing unique challenges due to the COVID-19 pandemic. Thus, multiple priorities at both the corporate and branch levels were put in place at the same time as the Program continued to address core delivery objectives. There is now an opportunity for a thorough priority review as the Program moves forward in a post-pandemic landscape where expectations have increased, and faces additional important issues that may impact drug safety, efficacy and quality, such as climate change, global supply chain issues and nitrosamines (based primarily on animal studies, nitrosamine impurities are probable human carcinogens, meaning that long-term exposure to a level above what is considered safe may increase the risk of cancer).

Program achievements and challenges

Over the past five years, the PDP has ensured that Canadians have access to safe, effective, and quality pharmaceutical drugs. This includes maintaining service standards to approve drugs and drug establishment licenses and an expedited approval process under specific circumstances during the pandemic. The Program also worked on implementing the provisions under the *Protecting Canadians from Unsafe Drugs Act* (Vanessa's Law) to strengthen safety oversight, including enhancing the reporting of serious Adverse Drug Reactions (ADRs) by hospitals, as well as facilitating approval in recent years of some categories of innovative drugs, while other types of drugs, such as veterinary, are less accessible.

Nonetheless, due to the number and complexity of submissions, pre-market reviews required more time during the evaluation period than they previously have (greater than 30%). Decisions have been made increasingly closer to the deadlines for generic drug reviews, putting the Program at risk of not meeting its performance standards. Internal stakeholders have also mentioned an extensive use of overtime and extra human resources (including staff and contractors) to review submissions. Moreover, approval rates for new generic drugs in the first cycle of review decreased over the period (from 45% in 2018-19 to 35% in 2022-23) due to a decrease in the quality of evidence provided in submissions, which often led to a second or third cycle of review.

Challenges also remain in raising awareness among practitioners of their role in supporting healthcare institutions reporting requirements under Vanessa's Law. Although communication documents have adequate content and language overall, the communication channels are not optimal because stakeholders are not able to navigate the website to find relevant information, and dissemination lists are not up to date. Moreover, stakeholders indicated that some guidance has not been aligned with recent regulatory changes. Information Technology (IT) systems continue to be siloed and outdated, and this has affected the Program's ability to be efficient throughout the regulatory life cycle and for international collaboration. Enhancements in these areas could lead to greater integration and timelier sharing of surveillance and compliance data, better collaboration with international regulators, and ultimately, support of access to drugs and sharing drug-related risks with Canadians.

Recommendations

Recommendation #1

- Review and update Program priorities to align with its objectives and pressures moving forward, as well as workload and resource capacity.

The increasing workload over the period in scope, for both pre- and post-market activities, is related to many factors, including increased volume and complexity of applications, multiple priorities at the corporate and branch levels being implemented simultaneously, decreased mature data available pre-market, which requires reinforced monitoring post-market, or increased requirements in labeling, Vanessa's Law commitments, as well as increased expectations for more transparency, which may impact the Program's capacity to meet its core objectives in the future. The approach to respond to present and future critical issues, including factors such as nitrosamines and climate change should also be considered in this process.

Recommendation #2

- Review and update the Program's communications approach to ensure stakeholders can access relevant information.

The Health Canada (HC) website and other tools used to disseminate new and existing regulatory requirements to industry, or for practitioners and Canadians to find information on drug safety, are sometimes difficult for stakeholders to navigate. Furthermore, current distribution lists are not comprehensive. Industry associations use this material to relay relevant regulatory information to their members to ensure they are aware of current requirements and amendments that may impact their activities. The Program should review and update its communications approach to facilitate timely and efficient stakeholder access to the relevant information they need.

Recommendation #3

- Enhance information technology systems to support program activities, including integration across the regulatory life cycle.

Despite both branches implementing several initiatives to digitalize the Program to adapt to the new working environment created by the pandemic, internal IT systems have been updated in a piecemeal fashion, leading to legacy issues with outdated systems, including a lack of integration across the various existing systems, with some still being paper based. Fragmented and outdated systems are a barrier for information-sharing and collaboration between teams within and between both the Health Products and Food Branch (HPFB) and the Regulatory Operations and Enforcement Branch (ROEB), as well as with international partners. Both HPFB and ROEB should work together to identify opportunities to update and integrate their IT systems across their various activities to gain efficiency and remain timely in ensuring access to pharmaceutical drugs and protecting Canadians from unsafe products, including by sharing drug-related risks and benefits with Canadians.

Recommendation #4

- Examine the potential causes for the higher rate of negative decisions in the first cycle review of applications for new generic drugs, and communicate them with industry to improve its application submissions moving forward.

The proportion of new generic drugs approved in the first cycle has decreased significantly since 2018, due to limited or low-quality evidence provided in applications. This has led to an increased number of second and third cycle reviews and associated workload for both the Program and industry. The Program should review feedback provided to applicants to identify trends in evidence gaps and share that information with new and potential applicants to improve the quality of new submissions.

Recommendation #5

- Explore the factors leading to the downward trend in veterinary drug availability in Canada.

Access to marketed veterinary drugs has decreased in recent years, though it is not entirely clear what is driving this downward trend. This has become an increasing concern to external stakeholders in the veterinary drugs sector for both food-producing and companion animals. The Program should explore the factors causing this downward trend to better understand whether there are any areas involved within the Program’s control.

Program Description

The PDP is responsible for helping to ensure human and veterinary pharmaceutical drugs sold in Canada are safe, effective, and of high quality. It verifies that regulatory requirements are met through pre-market submission reviews, risk-benefit assessments, monitoring, surveillance, compliance, and enforcement activities, including laboratory analysis. It also provides information to enable informed decision making on pharmaceutical products.

The PDP is led by the Health Products and Food Branch (HPFB) in partnership with the Regulatory Operations and Enforcement Branch (ROEB) at HC. The Program works with industry, including sponsors, market authorization holders, and establishment license holders, as well as health care professionals and practitioners, patient safety groups, academia, Health Technology Assessment (HTA) organizations, and the public to achieve its objectives.

The PDP operates in an environment where improving affordability, accessibility to,[1] and appropriate use of prescription drugs are priorities for the Government of Canada. Other players in this environment include the Patented Medicine Prices Review Board, who regulates the pricing of patented medicines sold in Canada, as well as HTA organizations and provincial jurisdictions that focus on prescription drug use and reimbursement conditions.

Evaluation Scope and Approach

The evaluation focused on the impact of the Pharmaceutical Drugs Program's (PDP) activities and its agility in addressing current and emerging needs regarding human and veterinary drugs. The evaluation also considered how the Program adjusted to the pandemic crisis, including regulatory and operational adjustments, and the extent to which these are being considered moving forward to fulfill its regulatory role.

Covering activities from 2017-18 to 2022-23, the evaluation focused on pharmaceutical drugs for human and veterinary use, including both prescription and non-prescription drugs. Activities related to biologics, radiopharmaceuticals, natural health products and medical devices were excluded from this evaluation as there are separately planned evaluations to assess these other health products. Finally, the evaluation did not examine the issue of drug shortages, as these were covered by the Audit of Drug Shortage Reporting, Monitoring and Compliance Activities.

The evaluation examined the following questions:

1. Within its regulatory mandate, what progress has the Program made towards ensuring Canadians have access to safe, effective, and quality pharmaceutical drugs, including:
    a. Evidence-based regulatory decisions are issued in a timely manner to help ensure new pharmaceutical drugs could be made available to Canadians;
    b. Industry is compliant with pre-market and post-market regulatory requirements; and
    c. Partners, stakeholders, and Canadians are informed of the risks and benefits of pharmaceutical drugs and use that information to inform their decisions?
2. Since the last evaluation, what regulatory measures has the PDP put in place to enhance its agility as a regulator?
    a. What has been the impact of these measures?
    b. Are program resources being used efficiently and effectively?

The evaluation draws on evidence from multiple data sources, including a survey of industry respondents, interviews with both internal and external key informants, document and file review, international comparison with other regulators, as well as a review of performance and financial data. For more information on methodology, refer to Annex A.

Context

Key Takeaways:
The pharmaceutical landscape has evolved at a fast pace in recent years, with an increasing number and complexity of reviewed drugs in both the innovative and generic categories, as well as the continued globalization of the drug supply chain. The focus on innovative drugs for rare diseases has limited the ability to produce robust evidence for drug approvals. Industry and Canadians' expectations have also increased for the Program to be more transparent, efficient, and accountable.

Economic context

Canada is the ninth largest market of pharmaceutical drugs in the world at 2.1% of the global market. From 2011 to 2019, the value of its total sales, including non-patented, over-the-counter medicines, has increased by 35.3% to $29.9 billion, with 86.7% sold to retail drug stores and 13.3% to hospitals. Brand-name products account for 81.3% of sales and 27.1% of prescriptions, while generics account for the rest. The top ten pharmaceutical products sold in Canada accounted for 16% of 2020 industry sales. Leading therapeutic categories include medicines for arthritis, ophthalmology, and autoimmune diseases. The Canadian market's share of expensive drugs for rare diseases rose from 1.4% in 2011 to 10.4% in 2020. From 2011 to 2020, pharmaceutical imports to Canada from the rest of the world increased by 58%. The European Union and the United States accounted for 48% and 29% of imports in 2020, respectively.[2]

In 2020, the manufacturing portion of the sector employed approximately 31,500 people on average, and, over the last five years, employment has grown by 15.5%. Over the past decade, the industry has been able to diversify its research and development (R&D) activities via external partners: 60% of new pharmaceutical drugs, except biologics, have been developed outside of major pharmaceutical companies.[2]

Pharmaceuticals are the second largest component of health care expenditures (15%). Governments account for 37.2% of drug expenditures and private payers, including private coverage and individuals, account for the remaining 62.8%.[3]

Evolving landscape

Prior to COVID-19, the volume of both innovative and generic drugs (copy of a brand name drug) increased due to the multiplication of niche markets and the number of products that reached the expiration of intellectual property rights protection, among other factors. The complexity of files submitted for approval increased as well, due to the focus on rare diseases or the combination of a drug with medical devices, for example. The focus of new drugs on niche or smaller populations has resulted in less robust evidence being available on the safety and effectiveness of drugs presented in pre-market applications due to the difficulty in carrying out clinical trials. This trend has led to a focus on increasing the use of risk mitigation measures, such as reducing and preventing harm to patients, preventing burden to healthcare professionals, stopping barriers for patients, and increasing post-market monitoring. The globalization and increased complexity of the drug supply chain has increased the need for foreign oversight and border controls for active ingredient producers.[4]

Canadians have greatly increased their demand for more transparency and accountability regarding pharmaceutical drugs in recent years. This has included an increased focus on proactive life-cycle risk management, the growing need for efficient post-market surveillance to identify potential safety and quality issues, especially when pre-market evidence is more limited, such as in the case of rare diseases, and rapid responses to safety questions. In addition, following expedited approaches for approving COVID-19 related health products, expectations to maintain the pace of approval deployed for the COVID-19 response have increased.[5] To date, the Program has undertaken various initiatives to improve openness and transparency, including the creation of lists of products and applications authorized for COVID-19 responses, the Regulatory Decision Summary initiative, a Submissions Under Review List for innovative and generic drug submissions, as well as making clinical trial results for approved drug submissions available and other revisions to the website, such as the new Drug and Health Product Portal to improve the quality of information available to program stakeholders.

Several other issues have changed the pharmaceutical landscape within which the Program operates since the last evaluation, and have led to increased attention by the Program to address them. For example, since greater awareness of the presence of nitrosamine impurities in some pharmaceutical drugs emerged in 2018, international regulatory agencies, including Health Canada, and the pharmaceutical industry have been taking actions to mitigate and manage the risks associated with these potentially carcinogenic compounds.

Moreover, consequences of climate change, such as extreme weather events, have become an increasing concern as they have hindered the drug supply chain, with unexpected facility closures and transportation challenges, impacting the

Program's compliance and enforcement activities. Finally, artificial intelligence (AI) is creating opportunities and potential challenges in adapting future work methodologies for inspections and surveillance, among other areas.

In Budget 2019, Canada pledged up to $1 billion over two years to help Canadians access necessary medications to address rare diseases,[6] and develop a national list of effective and cost-efficient drugs to be covered by a national pharmacare program.[7] The Canadian Drug Agency Transition Office was created in 2019 to address high Canadian drug prices and fragmented drug coverage.

Findings

Program adaptation to changing context:

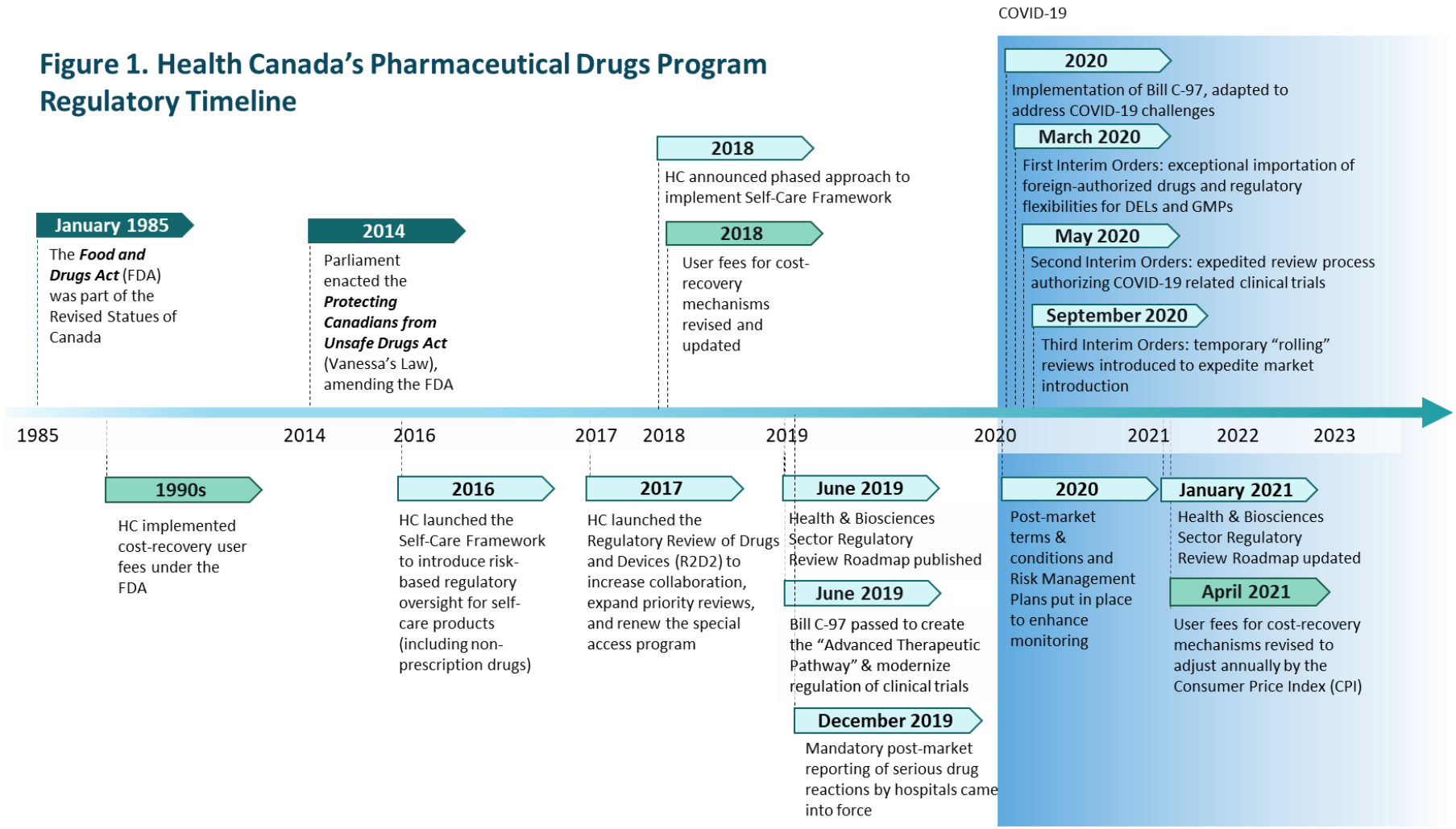
Since the last evaluation, what regulatory measures has the Pharmaceutical Drugs Program put in place to enhance its agility as a regulator?

Regulatory reviews and changes over the evaluation's scoping period

> **Key Takeaways:**
> To address the changing pharmaceutical drug environment, the PDP has put in place several regulatory changes since 2017 to modernize its approval process. These include conducting parallel aligned reviews with HTA organizations, aligning with international pre- and post-market practices, addressing challenges posed by the globalization of the supply chain, embracing the real-world evidence approach along the drug life cycle, and addressing unique challenges due to the COVID-19 pandemic.

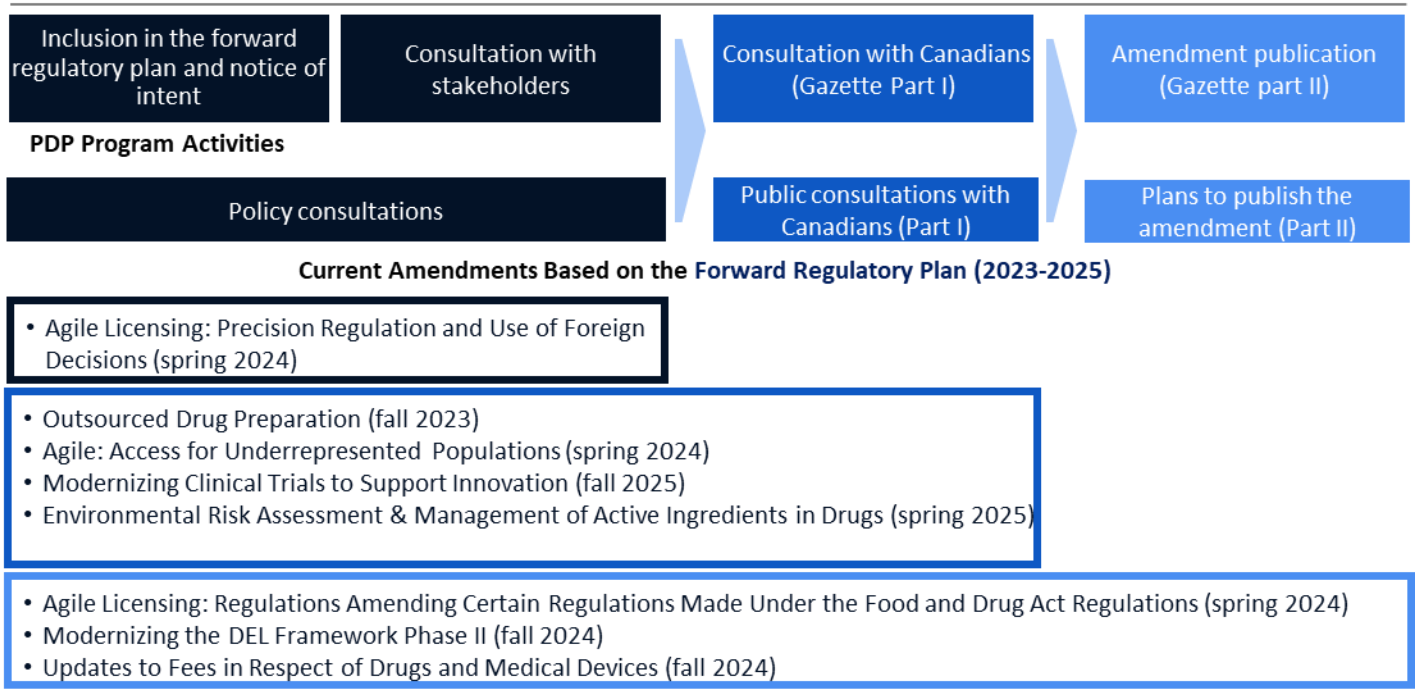
During the evaluation period, the Program put in place several regulatory changes to better protect Canadians' health and safety, by improving regulated product oversight, strengthening international standards alignment, and becoming more agile. These modernization efforts have progressively built on each other, as shown in Figure 1, and covered a broad range of areas including expediting reviews, integrating evidence along the drug life cycle, collaborating with HTAs and international partners, as well as strengthening safety oversight. User fees were also revised twice over the evaluation period, in 2018 and 2021, to cover the larger workload due to increased and more complex submissions. [8]

Figure 1. Health Canada's Pharmaceutical Drugs Program Regulatory Timeline



In the post-pandemic context, the implementation of the 2019 roadmap continues through the forward regulatory plan for 2023 to 2025, as summarized in Figure 2.[9] As part of these regulatory amendments, the Program is also progressively stabilizing temporary measures put in place under the various Interim Orders (IOs).

Figure 2. Ongoing Food and Drug Regulation Amendment Steps



Regulatory changes were enacted to adapt to the sector's changing environment. The impact of most of these changes will be observable and measurable in the future. However, regulatory tools have also been put in place in several areas as described in the rest of this section.

Expedited reviews and approvals to support health care needs

The Program has facilitated approval processes throughout the evaluation's scoping period, starting with the Regulatory Review of Drugs and Devices Initiative, which identified pathways to be explored as of 2017, and initiated the drafting of regulatory changes based on consultations. In 2020, building on this preparatory work, the Program was able to quickly put three IOs in place to address the unique challenges that arose due to the pandemic, in particular to enable access to COVID-19 related products as quickly as possible. These adaptations were completed to help ensure the safety of pharmaceutical drugs and helping to maintain the drug supply or find alternatives in response to drug shortages. Other improvements include the following:

- The Health and Biosciences Sector Regulatory Review Roadmap was introduced in 2019 to accommodate scientific and technological developments in the review process.
- The special access program has also been improved to accelerate access to treatment for patients with life-threatening diseases or serious conditions, or to address outbreaks.[10]
- The Program also introduced rolling reviews in 2020 to support timely access to COVID-19 related products. To expedite the review process for COVID-19 drugs, the Department provided sponsors the ability to file a New Drug Submission (NDS) that are completed as data becomes available. Sponsors can thus choose to file an NDS for a new COVID-19 drug without including certain required information if they include a plan identifying the missing parts of the submission, along with timelines for when the outstanding information will be submitted.
- The Non-Prescription Drug Action Plan was lunched in 2022 to implement non-regulatory measures to simplify market access for non-prescription drugs.

External stakeholders highlighted the need to increase reliance on the work of other regulators, as shown in the collaboration section below, and to shift to a risk-based rather than a precautionary approach, including amount and type of evidence needed, thresholds for permanent substances or on residues in food-producing animals, to improve timeliness and effectiveness.[11]

Similar to other regulatory agencies (including the European Medicines Agency (EMA) and the US Food and Drug Administration (US FDA), Health Canada issued a call for review requiring manufacturers to conduct risk assessments of their marketed pharmaceutical drugs for the potential presence nitrosamine impurities. Depending on the outcomes of these risk assessments, further actions may be required (e.g., testing or changes to the manufacturing or other details to control the levels of nitrosamines to acceptable levels). Health Canada has published and updated a guideline for industry to share its current thinking and recommendations on nitrosamines.

Drug life-cycle integration between pre- and post-market

HC's mandate focuses on drug safety and efficacy, as well as harm mitigation, while HTA organizations are focused on cost-effectiveness and the extent to which the benefits justify the expense of pharmaceutical drugs. Effectiveness, which is the extent to which a drug is improving a medical issue, is at the intersection of these two mandates, and is less of a focus, although recent regulatory changes focus on real-world evidence.

In 2014, Parliament enacted the *Protecting Canadians from Unsafe Drugs Act*, also called Vanessa's Law, to strengthen safety oversight of therapeutic products, which led to the implementation of the mandatory post-market reporting of serious ADRs by hospitals, effective December 2019. The Regulatory Review of Drugs and Devices Initiative (R2D2) initiative introduced in 2017, included as one of its areas of focus the enhancement of the use of real-world evidence. Then, agile licensing tools piloted during the pandemic for COVID-19 related products, such as terms and conditions and Risk Management Plans (RMPs) allowed pharmaceutical drugs to be introduced to the market based on preliminary data. To address limited pre-market evidence, industry had to commit to reporting on post-market effectiveness data once it was available. Industry found these flexibilities useful to address unique challenges of the pandemic. Nonetheless, external interviewees outside of the industry and experts have raised concerns about approving very expensive drugs without sufficient evidence on their actual ability to address a health issue when other effective drugs available have already proven their added value. External interviewees outside of industry highlighted that this practice increases budgetary pressure on the health-care system[12] or raises issues of access and equity. These amendments also considered growth opportunities to facilitate access to the Canadian market.[13]

Fostering collaboration in Canada

Daily collaboration on veterinary drugs has been received very positively by external stakeholders, from both the industry overall, and from other organizations such as Canadian Food Inspection Agency (CFIA) on issues impacting food-producing animals, for example.

Regarding human drugs, collaborative efforts to import needed products during COVID-19 and during the recent pediatric drug shortage were highlighted by many stakeholders. In addition, the R2D2 Initiative enabled the Program to offer the option of parallel aligned reviews with Canadian Health Technology Assessment organizations (HTAs), including the Canadian Agency for Drugs and Technologies in Health (CADTH) and l'Institut National d'Excellence en Santé et en Services Sociaux (INESSS), based on sponsor consent. This mechanism was deemed a great achievement by all parties.[14,15] Nonetheless, downstream players in the pharmaceutical drug access chain (such as pan-Canadian Pharmaceutical Alliance and public drug plans, including those serving Indigenous communities) also play an active role in enabling timely access for Canadians and therefore the benefits of the upstream aligned review initiative may be

limited. According to interview data, they would also benefit from accessing the precise list of drugs under the parallel aligned review process and their review status for timely decision making.

The Program undertook consultations in a systematic manner for each major regulatory change and to develop guidelines. Nonetheless, more than three quarters of survey respondents from industry consider that the Program only seeks feedback to a moderate extent, or not at all, about regulatory requirements and processes. Interviewees from industry explained that, although they provide feedback, they do not think that this information is well integrated into regulatory changes or guidelines.

Fostering collaboration with international partners

To address the increasing challenges of the pharmaceutical landscape, regulators across the globe have increasingly joined forces to share information and efforts. The Program is part of multilateral collaborations, such as the Access consortium that includes Australia, Singapore, Switzerland, and the United Kingdom[16] and Project Orbis on cancer drugs,[17] led by the US that includes the same countries as the Access Consortium, plus Brazil and Israel.[18] These activities can allow for increased synergies, shared review activities and, in some cases, see submissions come to Canada earlier reducing overall approval time of submissions which can improve access to drugs.[19] Canada collaborates with the World Health Organization and is also a member of the International Coalition for Medicines Regulatory Authorities, which includes 38 countries.[20] These collaborations facilitated the pre- and post-market work on COVID-19 vaccines, among many other benefits. The EMA piloted the “Opening our Procedures at EMA to Non-EU authorities” (OPEN) Initiative which makes it possible for trusted regulatory authorities outside of the European Union to collaborate with the EMA. The initiative enabled HC to share expertise, address common challenges, and enhance transparency in evaluating COVID-19 vaccines and treatments.[21]

Pre-market innovative and generic drugs, as well as compounding, which is the preparation of custom medications to fit the unique needs of patients, require specific investigations for the Program to be able to rely on their decisions. Since 2017, the Program has been accepting European Directorate for the Quality of Medicines and Healthcare certificates of suitability to accelerate reviews.[22] Joint reviews for human drugs have increased from 0% in 2017 to 7.1% in 2020, even when considering IT and legal issues.

To align approaches related to Good Manufacturing Practices (GMP) and Good Pharmacovigilance Practices (GVP), the Program actively participates in the Pharmaceutical Inspection Co-operation Scheme (PIC/S), a multilateral forum aimed at harmonizing inspection procedures worldwide. The GMP program maintains and continues to work toward expanding

the scope of established bilateral Mutual Recognition Agreements (MRA) with Australia, Switzerland, the United Kingdom, and multilateral ones with European Economic Area countries, and European Union Member states.[23,24] Some approaches apply to drugs for human use only, while others also include veterinary drugs. The Program is progressively extending the operational scope of MRAs to include APIs, such as the MRA with Australia in 2018, while the Canada-EU Comprehensive Economic and Trade Agreement (CETA) Protocol for pharmaceuticals is in progress.[25,26] The Program also increased its collaboration with other regulators to avoid duplication in inspections of foreign sites, and is planning to explore work-sharing opportunities with other partners. For example, the Program conducts concurrent inspections with the US FDA.[27]

Finally, the Health Products and Food Branch (HPFB) and the Regulatory Operations and Enforcement Branch (ROEB) have also developed confidentiality agreements with countries and international organizations to facilitate information sharing.[28]

Inspections and compliance

Vanessa's Law, which passed in 2014 and gave HC authority to order recalls, imposes tougher penalties for unsafe products, and authorize the regulator to compel drug companies to revise labels and do further testing on products.

Inspections have been adapted to better address the current context. Inspection information has been shared publicly since 2015 in the Drug and Health Products Inspections Database. The Active Pharmaceutical Ingredients (API) framework came into force in 2013 to better control the import of individual drug ingredients. The main objective of the API framework is to protect the health and safety of Canadians by implementing into regulation, internationally accepted and harmonized GMP for API requirements. These GMP requirements help reduce the risk posed by substandard API in pharmaceuticals for human use being on the Canadian market. In addition, this framework enables HC to better track and trace manufacturing sites that handle APIs so cases of non-compliance can be addressed in short order to reduce risk to Canadian consumers.

During COVID-19, regulatory flexibilities and virtual inspections were implemented to protect Canada's drug supply during a time of heightened public health restrictions in Canada and abroad. International collaboration in inspections is especially important to continue to oversee an increasing number of foreign buildings supplying drugs to Canada, where foreign site inspections are resource-intensive. The effects of climate change and geopolitical tensions will continue to affect the global supply chain and impact Canada's ability to maintain a safe and continuous drug supply.

The two ROEB laboratories complement inspection work to verify compliance and address emerging challenges, such as the presence of nitrosamines. Although the Toronto Laboratory is more focused on nitrosamine testing and the laboratory in Longueuil on border-related issues, the two entities are set up to substitute each other in case of disruptions or extra workload. The laboratories provide chemical and microbiological analysis to respond to the diverse needs of the inspection program and lead a proactive, risk-based Drug Quality Sampling Program which is linked to MRA requirements. The internal collaboration between the laboratories and inspection teams is effective according to interviewees. Technical support to inspectors and testing was provided in a timely manner, as labs provided test results within the service standards between 2017 and 2022, 90 to 100% of the time.

Priority setting

Key Takeaways:
In recent years, multiple corporate and branch-level priorities were put in place at the same time the Program continued to address core delivery objectives. There is now an opportunity for a thorough review of priorities as the Program moves forward in a post-COVID landscape where expectations toward it have increased.

The Program put several regulatory changes in place to address the pharmaceutical drug landscape over the last decade as described in the previous section. However, internal and external interviewees highlighted that too many corporate and branch-level priorities have been identified and implemented at the same time. All agreed that there is now an opportunity to determine which are the most important, and should be implemented now, versus those that could be implemented later. Furthermore, interviewees emphasized that these should then be clearly communicated internally and externally.

There were several priorities identified over the past five years:

- Developing openness and transparency approaches in areas such as program communication, legislation modernization, regulation, service delivery, and use of real-world evidence.
- Fostering collaborations in Canada and abroad for more efficiency, and for an optimized use of reliable information, to lower the cost of prescription drugs and to promote timely access to health products.
- Investing in diverse and highly qualified human resources and IT tools and systems.
- Improving responsiveness of the regulatory framework to address health system needs, increase agility of review processes, and modernize compliance and enforcement activities.
- Implementing the Health and Biosciences Sectoral Regulatory Review Roadmap, the forward regulatory plan for 2023 to 2025,[29] including the Self-Care Framework.[30]

Although this list is not meant to be exhaustive, it shows the extent and diversity of the Program's priorities, in addition to addressing increasing and more complex submissions. Moreover, in a post-pandemic landscape, expectations toward the Program have increased because of its work to expedite the authorization of COVID-19 vaccines and treatments in Canada, which has added pressure on the Program to deliver its core work in a similar timeframe, in addition to implementing the identified regulatory changes.

Overall, the Program spent the budgeted amount for each fiscal year. In addition, user fees were collected to recover part or all of the costs incurred to deliver regulatory programs and ensure industry pays their fair share and minimizes the burden on the taxpayer. See Annex B for more details. To support priority setting, resource re-allocation exercises have been done in specific areas of the Program. For example, directorate-specific exercises have suggested increasing reliance on foreign inspections and focusing on domestic inspections that present a higher risk, or to better classify organizational risks to guide monitoring efforts. Nonetheless, there is no evidence that a comprehensive program-wide review was done to prioritize activities and define what the Program's role and responsibilities should be in a post-COVID landscape.

IT infrastructure

> **Key Takeaways:**
> IT systems continue to be siloed and outdated which has affected the Program's ability to be efficient, as they are seen as a barrier throughout the regulatory life cycle and to international collaboration. This has become a bigger concern as Program activities are increasingly digitalized due to the COVID-19 pandemic.

The COVID-19 pandemic resulted in a significant shift to virtual work with the implementation of digital records rather than paper-based ones in 2020. However, interviewees from all Program areas flagged that outdated and inefficient IT systems and tools are an issue. Internal IT systems have been updated in piecemeal fashion without an overarching strategy for digitalizing the existing paper-based process, leading to legacy issues, and lack of integration across various systems. Although international collaboration has been taking place, it was also identified that these IT issues are currently seen as impeding a more comprehensive international collaboration across the entire pharmaceutical drug life cycle, and internal information sharing across teams within the Department.

Interviewees mentioned several specific IT issues. The lack of recording or standardization of a unique identifier is a significant limitation to aligning approvals of the Drug Identification Number (DIN) and Drug Establishment Licensing (DEL), with cases registered in the complaints and recalls databases. This creates challenges in identifying the impact of

an establishment or site going offline, like in an extreme weather event, in terms of affected product and the potential for shortages. Legal constraints on how to store and share information internally, lack of interoperability, restrictions implied by corporate security policies are all challenges to breaking siloes between databases. This creates a challenge to identify all producers of a given drug and thus identify alternative sources in the drug supply chain, especially in case of extreme weather events.

The inspection and enforcement IT systems are digital versions of paper-based processes, such as RADAR or Enterprise Compliance and Enforcement System[31] several workarounds, lack automation and use extra staff time. This also impacts tracking, reporting consistency, data management capacities, interactions with external users and access to pre-market information.

Internal interviewees also highlighted that significant IT challenges apply to laboratory work as well, such as increased need for IT resources and support as instruments are highly technical, greater IT integration and connectivity, and increased use of remote access, to manage, analyse and report data. The Laboratory Information Management System requires more support and greater capability to make changes in a timely manner to serve the needs of the Program and clients. Furthermore, internal interviewees and documents highlighted the reliance on external branches like the Digital Transformation Branch or departments like Shared Services Canada for prioritization and completing these needed supports leaves laboratories vulnerable. Finally, IT issues impact access to labeling information in the veterinary drug sector overall and in the emergency drug release program.

Despite increasing national reporting and more international data being available, surveillance systems lack integration and automation, and require a high volume of human resources, leading to delays and inaccuracies in monitoring. Both internal and external interviewees consider the IT system inadequate for sharing and receiving serious ADR reports from various sources, as shown by sending reports by fax or inadequate online forms that both require manual entry afterward, and surveillance information more broadly, including international signals.

Both HPFB and ROEB have branch-level IT plans in place to address some of these issues. However, these plans are still focused on siloed systems and do not include overall IT architecture integration within and across branches. This integration would help to connect information along the life cycle, better identify safety or drug supply issues across manufacturers, and better inform Canadians of anticipated access issues due to extreme weather events, for example.

It should be noted that IT issues are a general challenge at HC and not specific to this Program. The 2022-23 Management Accountability Framework exercise attributed a low score to HC with regards to metadata, interoperability,

and lack of application-specific IT support among other issues when compared to other departments.[32] Furthermore, the most recent Office of the Auditor General report on IT infrastructure revealed that IT systems are strongly outdated across the federal government. Only 38% of the government's approximately 7,500 information technology applications were considered healthy.[33] \

Program achievements and challenges

Within its regulatory mandate, what progress has the Program made towards ensuring Canadians have access to safe, effective, and quality pharmaceutical drugs?

Key Takeaways
Although drug submissions have increased in volume and complexity and the COVID-19 pandemic has put increasing pressure on the Program, review service standards have been respected overall. However, decisions have been delivered increasingly closer to deadlines, putting the Program at risk. Internal stakeholders have also mentioned an extensive use of overtime and extra human resources, including staff and contractors, to review submissions and deliver on the post-market side.

Overall, during the evaluation period, reviews of submissions for approval and for DEL applications were done within service standards, which determine the expected legal timeframe to deliver decisions.

- Overall, more than 98% of drug submission review decisions for human innovative and generic pharmaceutical drugs were delivered by the target date.
- Decisions related to DEL applications delivered within service standards increased from 93% to 100% between 2016-17 and 2021-22.

Table 1. Service standards for NAS review for regular and priority processes

Country	Regular Process	Priority
Canada	300 calendar days	180 calendar days
U.S.	10 months (for 90%)	6 months
Australia	255 working days	N/A

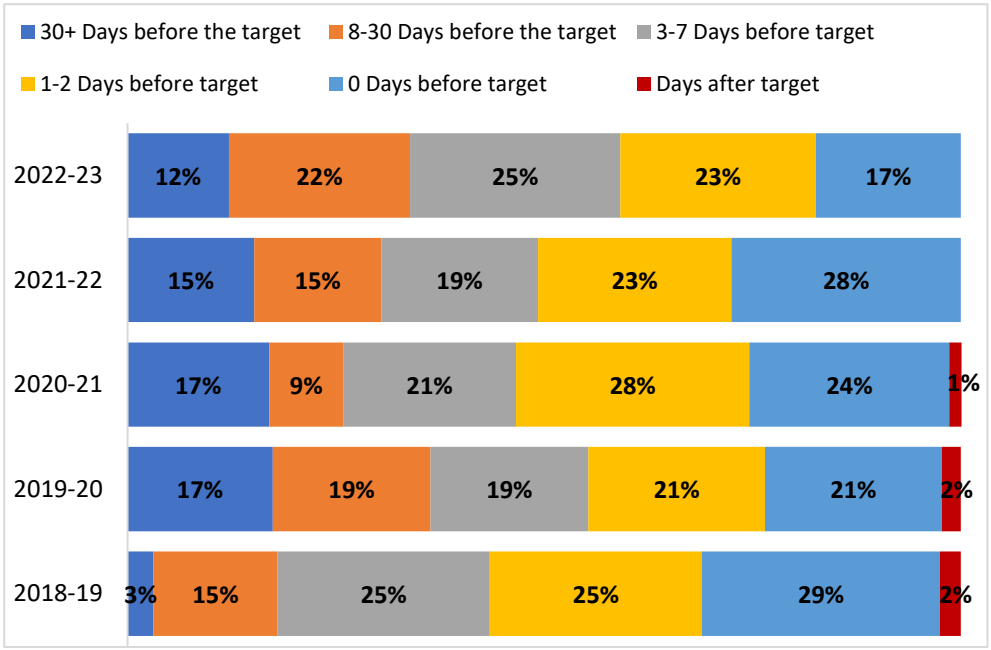
Europe	210 active days	N/A
New Zealand	320 calendar days	N/A
Note: Data excludes clock-stops to answer questions.		

A review of other comparable regulators, including the EU, the US, Japan, Switzerland, and Australia, for the 2018 to 2022 period found that HC service standards and the amount of time needed to review new active substances (NASs) are in line with other regulators. See Table 1 for more details. Moreover, the Program's participation in the Access Consortium and Project Orbis has increased review efficiency through work-sharing and collaboration, respectively. From 2018 to 2022, 34 NASs were approved in Canada through international collaboration pathways, of which 14 were managed through the Access Consortium and completed in 169 fewer days than the Program's average review time, and 20 through the Orbis project, completed in 101 fewer days than the Program's average review time.

However, due to the increasing complexity and number of submissions for prescription human drugs (innovative and generic), reviews required more time, and has led to decisions being made closer to the service standards target date for some categories. Specifically, internal program data shows that between 2018-19 and 2022-23:

- For innovative drugs, decisions made 0 to 2 days before the target date have fluctuated between 40-54% and those made after the target date ranged between 1-2% between 2018-19 and 2020-21 However, it should be noted that no decisions were made after the target date in 2021-22 and 2022-23. See Figure 3a for more details.
- For generic drugs, there has been a significant increase in the volume of submissions, greater than 20%, and the amount of time needed to review submissions, greater than 30%.
- For generic drugs, decisions made 0 to 2 days before the target date have increased from 23%-42% and those made after the target date up to 2% in 2022-23. See Fig. 3b for more details.

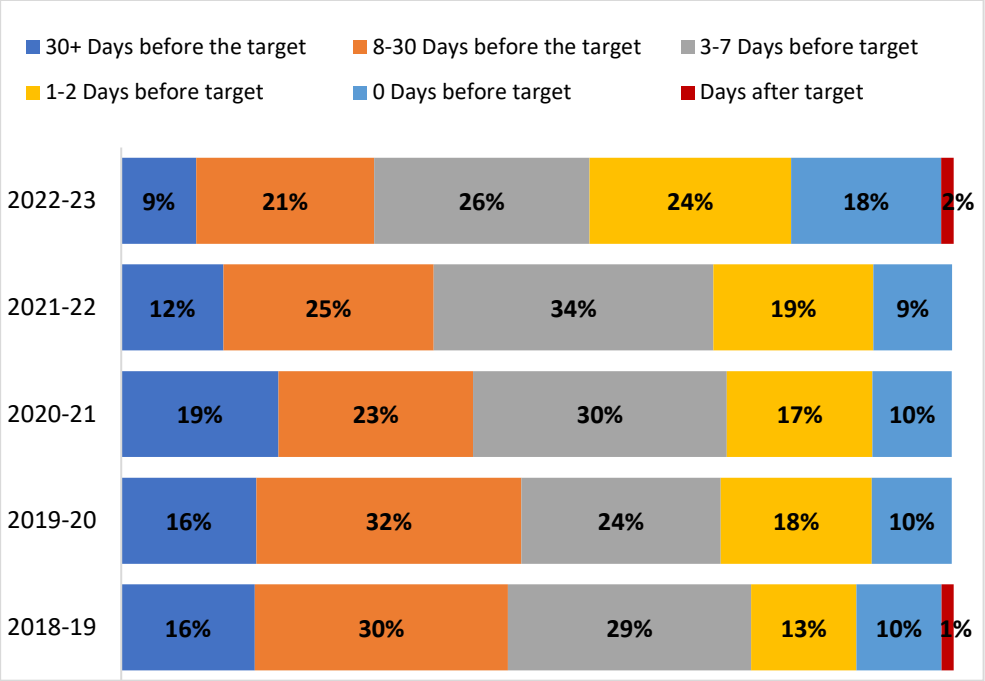
Figure 3a. Average decision time to target date (Innovative drugs)



Note: Includes NAS, Clin/C&M, and Clinical fee lines

Drug submission fees reimbursement for not fulfilling service standards has shifted from an annual overall target to individual targets triggering reimbursement if the target date is not met, which has also increased pressure on the Program.

Figure 3b. Average decision time to target date (Generic drugs)



Note: Includes Comparative and C&M fee lines

Moreover, the approval rate in the first review cycle for new generic drugs submissions (excluding labelling) has decreased from 45% in 2018-19 to 35% in 2022-23. Industry stakeholders mentioned that they lack the time to respond to information requests before the deadline. Meanwhile, the Program observed a decrease in the quality of data being submitted, leading to increased negative responses and more frequent second and sometimes third review cycles. These steps are part of the initial application and do not require additional fees to be charged. For internal interviewees, it is not clear why the data quality in applications is decreasing. Nonetheless, they suggest that the increased detection of nitrosamines, as well as the increased use of foreign manufacturers that do not provide requested data, may be part of the explanation. All cycles included, the final approval rate for new generic drugs was stable over the period at around 93%, but the overall workload has grown due to the increased number of review cycles needed to reach an approval.

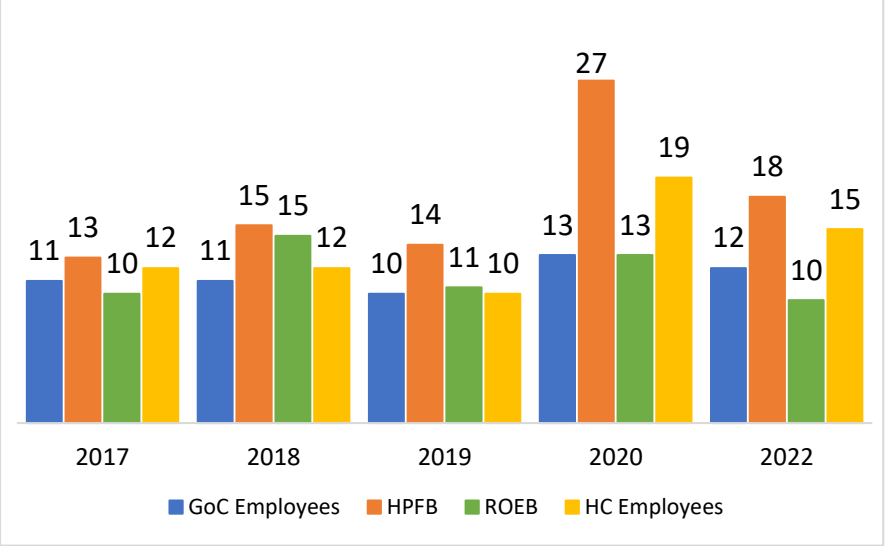
Industry representatives have highlighted that updates about the status of individual reviews and the potential need to provide additional information have not been communicated adequately. They suggested that HC should create a more consistent and transparent approach, whereby any questions or gaps in information are communicated earlier in the process, which would be similar to their experiences with the EMA and the US FDA. They also suggested the Program could review the type of information that is most often missing and share it ahead of time to allow applicants to improve their submission quality and ensure they meet regulatory requirements.[34] More information on the Program's website performance is included in the communication section. For veterinary drugs, there has been an increase in the number of submissions from 2018-19 to 2020-21, though the number dropped back to initial levels in 2022-23.

In addition to Pharmaceutical Drugs Directorate (PDD) reviews, the Marketed Health Products Directorate (MHPD) is also involved in drug submission evaluations through the review of RMPs and consultations on name/product/label considerations. Over the past four years, the time dedicated to these activities increased from 16% to 27% and the workload on RMPs increased by 68%. No additional Full Time Equivalents (FTEs) were allocated to cover this additional workload. As a result, resources allocated to surveillance and monitoring were redirected to address the additional workload.

To maintain decision service standards while the number of submissions received have doubled in the past five years, 463 additional FTEs, or approximately 35% more, have been added across HPFB from 2018-19 to 2022-23, although MHPD has not added any additional FTEs. To further address capacity issues given the increasing number of submissions per evaluator since 2018-19, the Program has also relied more on overtime and contractors, according to internal interviewees.

The 2020[35] and 2022[36] Public Service Employee Surveys (PSES) show a significant increase in stress due to overtime and heavy workload among HPFB staff in directorates involved in PDP only, as compared to HC employees overall and federal employees overall. See Figure 4. The PSES was not administered in 2021.[37,38,39] PDP interviewees have also strongly emphasized this issue and raised concerns on sustainability, staff wellness, and retention.

Figure 4. Share of employees experiencing stress to a large or very large extent due to overtime or long working hours (Source: PSES)



Key Takeaways
Communication documents have adequate content and language overall. Nonetheless, communication channels are not optimal, and guidelines are not always well aligned with recent regulatory changes.

Communication channels and efforts

Expectations towards the Program in terms of transparency and accountability have strongly increased in recent years, as discussed in the Context section of this report. Communication on changes in regulatory processes needs to be shared with parties as efficiently as possible, even more so when the environment or context changes.

Survey respondents (on human and veterinary drug areas) identified that the Program reaches them through a variety of overlapping channels. Respondents indicated that HC shares information through its website (95%), emails, correspondence or bulletins (81%), webinars (52%), and meetings (43%). Other sources of information are mostly industry association events (59%) and international regulators (9%). Interviewees from the industry highlighted industry associations' important contribution in relaying relevant regulatory information to their members.

Despite this broad coverage, HC communication channels might not be optimal tools:

- Although HC's website is the main channel, almost all external interviewees found it difficult to navigate and to access relevant information released by the Program. See more details on the Communication with practitioners and Canadians section.
- Industry representatives felt that the email dissemination list might not be complete and would be willing to help HC update it on a frequent basis. They also felt that communication was not proactive enough regarding each application's review status.[40]

For veterinary drugs, interviewees found the interaction with the Veterinary Drug Directorate (VDD) effective. Direct access to program consultants to understand requirements and adapt to regulatory changes has greatly improved in recent years.

Industry awareness

Industry interviewees who were included in the dissemination list found the information on regulatory changes clear and communicated effectively. This finding is consistent with the 2020 Assessment of HC's Communications to External Stakeholders on Marketed Health Products.[41] Furthermore, industry survey respondents who are also on the

dissemination list are well informed on regulatory processes and can access information on requirements, use it, and find processes easy to understand, for both human and veterinary drugs. Specifically, for:

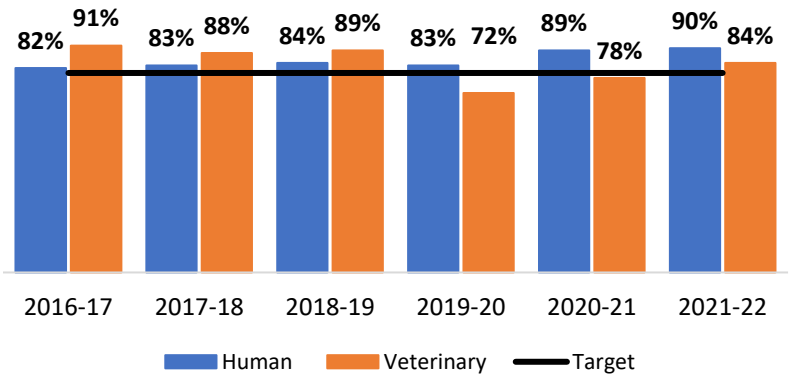
- **Access:** Most survey respondents are relatively well or fully informed of pre- and post-market processes, at around 84%. Most can access useful information from HC about regulatory, policy, and process requirements. Still, 70% need to do additional research, while 24% have the information they need from HC. Most respondents (88%) found HC's information was up-to-date to at least a moderate extent.
- **Use:** Most (88%) respondents use HC's information to inform their pre- and post-market decisions to at least a moderate extent.
- **Clarity:** Many (65%) respondents found processes clear and easy to follow to at least a moderate extent across all areas (i.e., pre-market review, licensing, inspections, packaging, marketing, distribution, compliance and enforcement, laboratory work and surveillance).

There is mixed evidence on the quality and availability of guidelines, as some were updated and more user friendly, including the guidance on Priority Review Pathways in 2019 and step-by-step guidance documents for new applicants in non-prescription health products in 2020. Both internal and external interviewees found that other guidelines are outdated and do not align with new regulatory changes, such as guidelines for rare disease applications, where large clinical trials are not available. Some guidance work was postponed due to an increased workload in surveillance during the pandemic related to COVID-19, for example.

Industry compliance

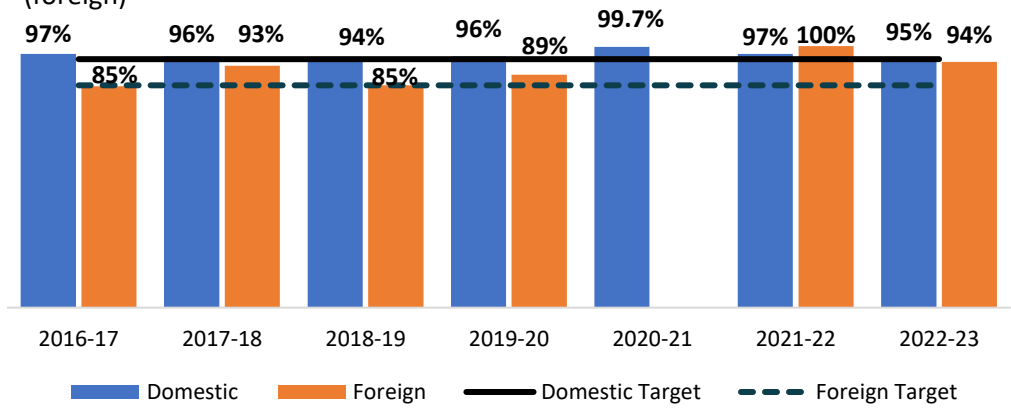
Before a drug product is authorized for sale in Canada the drug manufacturer must submit scientific evidence of the product's safety, efficacy, and quality to Health Canada for review and approval. Overall, human drug companies are compliant with regulatory requirements under the *Food and Drugs Act* and associated regulations as part of their submission for approval, as more than 80% met requirements every year. See Figure 5a for more details. For veterinary drugs, this target was not met in 2019-20 (72%) and 2020-21 (78%). Once a product is on the market, the producer must show that their manufacturing processes comply with requirements for good manufacturing practices. More than 85% of foreign manufacturers and around 97% of domestic ones comply with GMP requirements every year. See Figure 5b for more details. When a manufacturer has been determined to be non-compliant to GMP requirements during an inspection, evidence shows that they have all have either mitigated the risk or addressed the source of non-compliance within specified timelines.

Fig. 5a. Share of submissions that meet regulatory pre-market requirements. Target: 80% for human and veterinary drugs



Note: Approval rate for review 1 iteration 1 only for human drugs. General approval rate for veterinary drugs.

Fig. 5b Share of companies compliant with good manufacturing practices requirements. Target: 85%-95% (domestic), 80%-85% (foreign)



Note: No foreign inspections in 2020-21 due to COVID-19 restrictions.

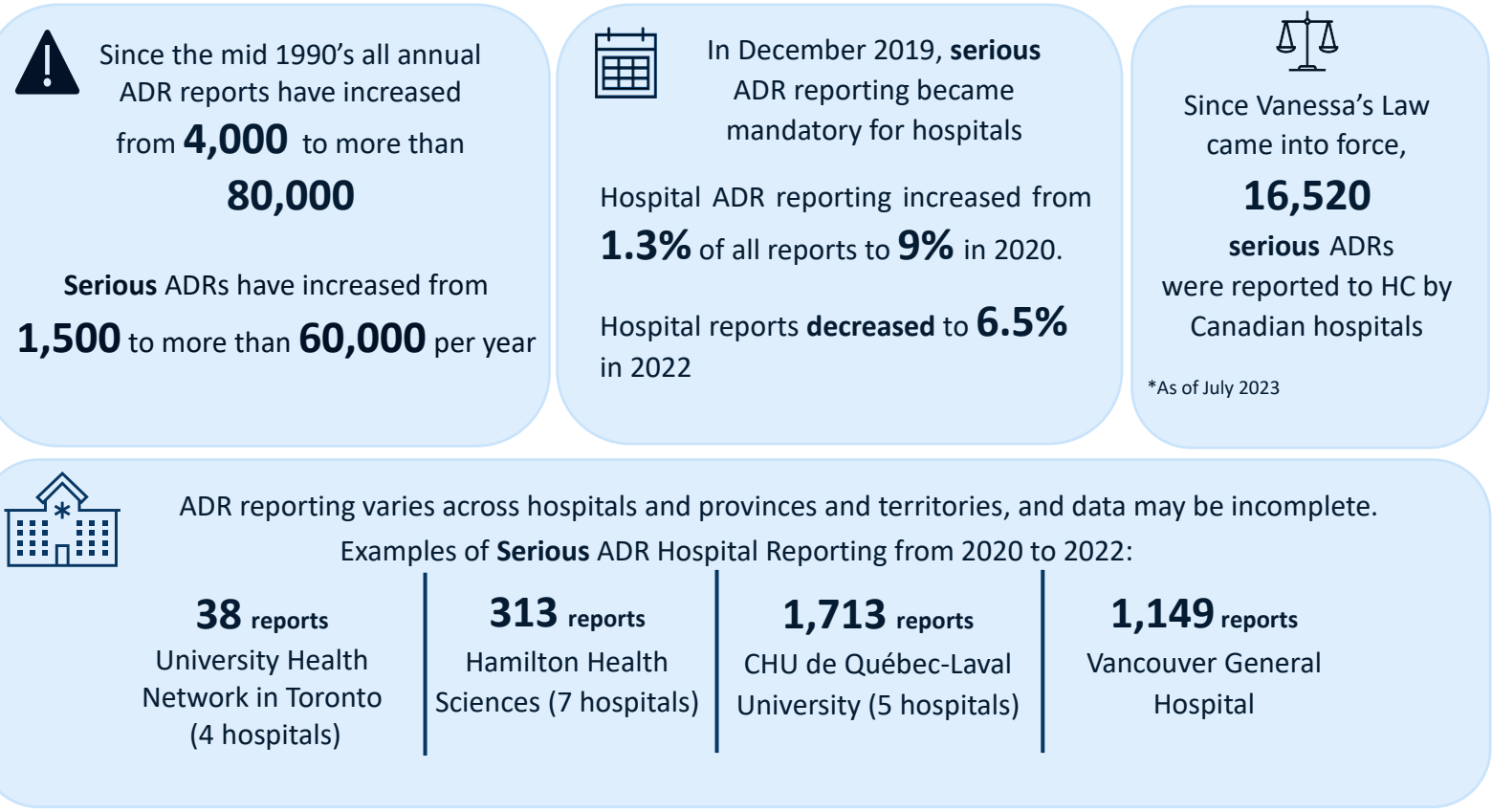
Key Takeaways

The national mandatory reporting of adverse drugs reactions (ADR), implemented just before the COVID-19 pandemic, still requires education and outreach to hospitals to reach its full potential. Communication documents have adequate content and language overall. Nonetheless, communication channels are not optimal, and guidelines are not always well aligned with recent regulatory changes.

Surveillance and reporting

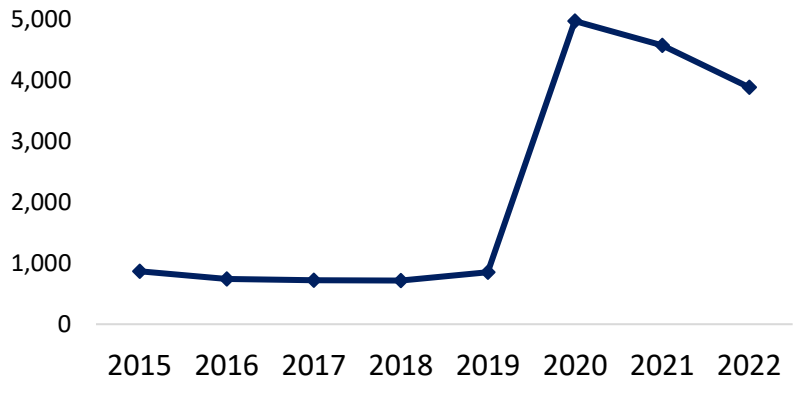
Overall, most survey respondents from industry can easily report issues related to quality, compliance, or ADR at around 95%, changes in the risk-benefit profile, issues related to RMPs, notice of foreign actions, or provide annual summary reports at around 90%. They highlighted reporting issues such as limited phone communication with the Program, lack of sharing of ADR reports with manufacturers, and timelines that are too short to properly develop RMPs.

Figure 6: Historical Canadian ADR Reporting and Trends Following Vanessa's Law



Since the mid 1990's, the number of ADRs reported annually has increased from approximately 4,000 to more than 80,000, and from 1,500 to more than 60,000 for serious ADRs. See Figure 6 for more details. ADRs are mostly reported by industry, including 96.1% of serious ADRs in 2019 with pharmaceutical drug products the most often reported (68.1%).[42] In December 2019, reporting of serious ADRs became mandatory for hospitals. Since Vanessa's Law came into effect, hospitals across the country reported 16,520 serious ADRs to HC, of which 678 were fatal.[43] Serious ADR reporting from hospitals, which was minimal until 2019, increased from 1.3% of all ADR reporting, in 2019 to 9% in 2020, before decreasing to 6.5% in 2022. See Figure 7 for more details).[44] Since December 2019, reports about pediatric cases ranged between 3% and 21% of all reports submitted by provinces, according to internal program data.

Fig. 7 Number of Serious ADR Reports by Canadian Hospitals



Since 2018, the US FDA has received reports of around 2.2 million ADRs annually, and 1.4 million serious ADR reports, mostly from mandatory reporting.[45,46]

To support and encourage reporting by healthcare institutions, the Program has started building awareness through various activities. From December 2019 to August 2023, the Canada Vigilance Program (CVP) completed four national webinars, sent nine newsletter updates on mandatory reporting, completed 348 regional outreach activities, as well as responding to more than 1,500 communications on interpretation of regulation, electronic reporting onboarding, ID provision, and guidance document requests. The impact of these communication efforts is not clear as reporting trends have not shown an increase after the initial jump in 2020. Unfortunately, mandatory reporting was implemented just before the pandemic, and impact the CVP's ability to fully build reporting capacity. Health care and practitioner group representatives feel that more education among healthcare institutions, including healthcare practitioners working there, is needed to better understand their obligations on mandatory reporting. Some interviewees also highlighted local initiatives to support practitioners, such as the use of specifically trained administrative staff to detect and report ADRs found in medical files.

Once issues are detected, the Program can make safety-related recommendations including labelling changes, risk communications, reinforced monitoring, requests for information, additional studies or license cancellations. Issues are detected through the CVP, as well as the literature and media, foreign agencies, PDD requests, other reviews, and marketing authorization holders. An average of 15 recommendations are made per year, with only 10% triggered by the CVP as the primary source, including 0.5% by hospitals reports. See Figure 8 for more details. Although 15 recommendations a year might seem low compared to about 200 deaths a year due to serious ADRs, available evidence does not show if recommendations and deaths are related to the same drugs.

Communication with practitioners and Canadians

Expectations to improve transparency and accountability have increased on the post-market side, leading to the Program significantly increasing its outward communication activities. See the Context section for more details. For instance, the Program is answering about a thousand data or media requests each year from the public and from health professionals. Moreover, since the last evaluation, the Program has undertaken work to improve openness and transparency, including the addition of two central sections to the HC website dedicated to COVID-19 and to drug shortages.[47,48] The former contains information for health care professionals, industry, and consumers, and includes information on IOs, updates on product authorizations, and import and export requirements. The latter includes frequent updates on drug shortages to inform Canadians. HC also introduced a new centralized portal with information on drugs and health products authorized by HC.[49] The Recalls and Safety Alerts Database was also revised to improve access to information about drug safety and quality based on user research.[50] Finally, MHPD continued to offer Health Product InfoWatch to provide health product safety information for Canadians.[51]

During the period covered by the evaluation, all targeted risk communications on human drugs were tailored for specific health care professionals and completed within service standards,[52] except in 2019-20 where only 67% were disseminated on time due to the need to focus attention on the COVID-19 pandemic. Interviewed practitioners and patient representatives found documents produced by the Program about drug safety to be of excellent quality and using appropriate language.

According to most interviewees, HC website searchability is an issue for all types of users, including industry, practitioners and Canadians, and for distinct types of information communicated, including regulatory changes, guidance and drug safety. This was also identified as an issue in the 2020 Assessment of HC's Communications to External Stakeholders on Marketed Health Products. The current website includes a sizable number of pages that users must navigate. Moreover, as content is updated and added to existing information, there is little guidance on how to navigate based on the user's

profile, including for new applicants, returning ones, practitioners, and patients. For example, the US FDA website offers a page dedicated to navigating the drug section[53] and the UK has a welcome page to help users find the section they are searching.[54]

Moreover, while practitioners are key players in relaying safety information to patients, they need to be aware of it beforehand. Roles and responsibilities between HC and practitioner colleges to disseminate this information are not clear, nor broadly communicated. These issues were also noted in the 2020 Assessment of HC's Communications to External Stakeholders on Marketed Health Products.

The Program is also expected to provide Canadians with information on drug safety. Nonetheless, direct engagement with patient groups is limited, according to internal and external interviewees. Although several active external advisory bodies at HC related to PDP exist, it is not clear what role they play or could play in disseminating information to patient groups. These bodies include the Paediatric Expert Advisory Committee, the Scientific Advisory Committee on Health Products for Women, the Scientific Advisory Committee on Oncology Therapies, and the Scientific Advisory Committee on Respiratory and Allergy Therapies.[55,56]

Finally, beyond needed website improvement, communication with Indigenous communities might require other channels, such as partnering with Indigenous-led organizations to disseminate relevant drug safety information. This might overcome the lack of trust some communities might have toward government sources.

Equity

With the increased focus on personalized medicine, Canadians are expecting to have access to disaggregated data about the impact of pharmaceutical drugs on them, rather than on the overall population. To address this expectation and implement the Government of Canada's commitment to using GBA+, and in line with the Health Portfolio SGBA Plus policy, a review of SGBA Plus activities was done for the PDP in 2023.

On the pre-market side, around half of applicants submitted disaggregated trial data that was not easy to identify in the current internal database. As part of the SGBA Plus action plan, a clinical trial portal was proposed to allow the industry to declare more systematically against which dimension their data can be disaggregated, including sex, age, and ethnicity. This information will allow the Program to identify more easily available pre-market data that could be submitted, but is not currently a mandatory requirement. Better access to disaggregated data would allow for group-specific labeling and guidance on dosage. Nonetheless, requesting disaggregated data is also a challenge while working with international regulators for application reviews, as equity considerations might be less of a priority elsewhere. See the Fostering

collaboration with international partners section. Clinical trials are more likely to exclude those with co-morbidity or may not be able to reach those living far from research centres or living in remote areas, immigrants for whom language may be a barrier to participation, or those facing other barriers to participation.

Since 2019, a Scientific Advisory Committee on Health Products for Women has provided advice opinion on health products and pharmaceutical drugs specific to women, including representation of women in clinical trials.

On the post-market side, surveillance data includes some disaggregation along sex, but not gender, and age, but excludes ethnicity or Indigenous status. Internal interviewees highlighted that data sources and reporting mechanisms might also be an equity challenge as ADR reporting is mainly from industry, foreign sources, and hospitals. While individuals living in Canada are also able to report through the website, equity groups excluded from clinical trials might also be under-reporting due to the additional barriers they may face, including language, IT literacy, and trust in the government. Finally, patient reporting is also influenced by awareness of reporting systems even when adequate reporting mechanisms are in place.**Error! Bookmark not defined.** Levels of awareness may vary across equity groups.

Ensuring access to pharmaceutical drugs

> **Key Takeaways**
> Overall, the Program has facilitated approval in recent years for innovative and generic drugs. Due to several factors, certain types of drugs are becoming less accessible.

Although regulatory changes have allowed for prioritizing certain categories of innovative drugs that are more in demand, in other specific areas, access has deteriorated over the evaluation period due to several factors in several areas:

- Access to drugs for pediatric use is more limited due to the lack of clinical trials, including children and youth. Recent shortages have revealed access vulnerability for drugs that are no longer protected by intellectual property. In recent years, compounding without prescription has been temporarily authorized for a restricted category of pediatric drugs to address the shortage.
- Since 2005, the number of marketed veterinary products decreased from 1,162 to 672 in 2022. In addition, cancelled post-market drugs have increased from 857 to 1,535. Finally, dormant drugs have increased since 2017 from 1 to 384 in 2022.[57] The number of veterinary drugs available in Canada is also lower compared to the US and Europe. In addition, while the Emergency Drug Release Program (EDR) exists to provide access to unapproved drugs,[58] external interviewees do not feel it is adequate to meet the needs of food-producing and companion animal industries. Although there has been a decrease in drug availability, it is not entirely clear what is driving

these trends. External interviewees mentioned regulatory changes may be one contributing factor, although it is not clear to what extent.[59]

Pharmaceutical Industry in Canada

Since 2014, new drugs are being submitted less often for approval in Canada than the US or the EU.[60] Several factors may contribute to this, including that Canada is seen as a small market, fees have increased more in Canada than in comparable countries, except the US (see Table 2); and Canada's perceived lower risk tolerance, amongst others. Given that service standards and actual time needed to review submissions are similar to comparable regulators, interviewees mentioned that it is more advantageous for the pharmaceutical industry to first target bigger and more profitable markets such as the US and EU. This might be influenced by both user fees and drug prices. See the Drug approval section for more details.

Table 2. Increase in NAS fees for 2017 and 2023 by country

Country	2017 Fee – NAS[61.62]	2023 Fee – NAS	Change from 2017 to 2023
Canada	**Can$341,770**	**Can$565,465**	+65%
U.S.	**Can$2,669,678**	**Can$4,400,726**	+65%
U.K.	**Can$165,065**	**Can$173,213**	+5%
Australia	**Can$234,894**	**Can$247,321**	+1%
Europe	**Can$401,266**	**Can$504,176**	+26%

Switzerland	**Can$84,977**	**Can$121,904**	+43%
New Zealand	**Can$78,576**	**Can$85,490**	+9%

User fees were revised and updated in 2018 and 2020 to better reflect HC's actual costs incurred throughout the drugs life cycle. Canada's fee for the review of a New Active Substance (NAS) has increased from $355,579 in 2019-20 to $437,009 on April 1, 2021, and then $565,465 on April 1, 2023.[63] Table 1 presents the fees applied for NAS by comparable regulators. Canada and the US have increased their fee the most over the period shown. Of note, different fee categories apply depending on drug categories.

People living in Canada pay more for prescription drugs than other countries with universal health care[64] and the implementation of a national pharmacare program is currently in the planning phase.7 Nonetheless, ongoing price negotiations might also make the Canadian market less profitable and thus less attractive,[65,66] given its size, although this aspect is beyond the Program's mandate. The actual contribution of these factors to the trend of decreasing applications remains to be established and might be investigated by the Program.

Conclusions and Recommendations

Conclusions

Program adaptation to changing context

The pharmaceutical drug landscape has evolved at a fast pace in recent years, with an increasing number and complexity of drugs reviewed in both the innovative and generic categories. To address this changing environment, the PDP has put several changes in place since 2017 to modernize its regulatory processes. These include conducting parallel aligned reviews with Health Technology Assessment (HTA) organizations, aligning with international pre- and post-market practices, addressing challenges posed by the globalization of the supply chain, embracing the real-world evidence approach along the drug life cycle, and addressing unique challenges due to the COVID-19 pandemic. Thus, multiple priorities at both the corporate and branch levels were put in place at the same time as the Program continued to address core delivery objectives. There is now an opportunity for a thorough priority review as the Program moves forward in a post-pandemic landscape where expectations have increased, and faces additional important issues that may impact drug safety, efficacy and quality, such as climate change, global supply chain issues and nitrosamines (based primarily on animal studies, nitrosamine impurities are probable human carcinogens, meaning that long-term exposure to a level above what is considered safe may increase the risk of cancer).

Program achievements and challenges

Over the past five years, the PDP has ensured that Canadians have access to safe, effective, and quality pharmaceutical drugs. This includes maintaining service standards to approve drugs and drug establishment licenses and an expedited approval process under specific circumstances during the pandemic. The Program also worked on implementing the provisions under the *Protecting Canadians from Unsafe Drugs Act* (Vanessa's Law) to strengthen safety oversight, including enhancing the reporting of serious Adverse Drug Reactions (ADRs) by hospitals, as well as facilitating approval in recent years of some categories of innovative drugs, while other types of drugs, such as veterinary, are less accessible.

Nonetheless, due to the number and complexity of submissions, pre-market reviews required more time during the evaluation period than they previously have (greater than 30%). Decisions have been made increasingly closer to the deadlines for generic drug reviews, putting the Program at risk of not meeting its performance standards. Internal stakeholders have also mentioned an extensive use of overtime and extra human resources (including staff and contractors) to review submissions. Moreover, approval rates for new generic drugs in the first cycle of review decreased over the period due (from 45% in 2018-19 to 35% in 2022-23) to a decrease in the quality of evidence provided in submissions, which often led to a second or third cycle of review.

Challenges also remain in raising awareness among practitioners of their role in supporting healthcare institutions reporting requirements under Vanessa's Law. Although communication documents have adequate content and language overall, the communication channels are not optimal because stakeholders are not able to navigate the website to find relevant information, and dissemination lists are not up to date. Moreover, stakeholders indicated that some guidance has not been aligned with recent regulatory changes. Information Technology (IT) systems continue to be siloed and outdated, and this has affected the Program's ability to be efficient throughout the regulatory life cycle and for international collaboration. Enhancements in these areas could lead to greater integration and timelier sharing of surveillance and compliance data, better collaboration with international regulators, and ultimately, support of access to drugs and sharing drug-related risks with Canadians.

Recommendations

Recommendation #1

Review and update Program priorities to align with its objectives and pressures moving forward, as well as workload and resource capacity.

The increasing workload over the period in scope, for both pre- and post-market activities, is related to many factors, including increased volume and complexity of applications, multiple priorities at the corporate and branch levels being implemented simultaneously, decreased mature data available pre-market, which requires reinforced monitoring post-market, or increased requirements in labeling, Vanessa's Law commitments, as well as increased expectations for more transparency, which may impact the Program's capacity to meet its core objectives in the future. The approach to respond to present and future critical issues, including factors such as nitrosamines and climate change should also be considered in this process.

Recommendation #2
Review and update the Program's communications approach to ensure stakeholders can access relevant information.

The Health Canada (HC) website and other tools used to disseminate new and existing regulatory requirements to industry, or for practitioners and Canadians to find information on drug safety, are sometimes difficult for stakeholders to navigate. Furthermore, current distribution lists are not comprehensive. Industry associations use this material to relay relevant regulatory information to their members to ensure they are aware of current requirements and amendments that may impact their activities. The Program should review and update its communications approach to facilitate timely and efficient stakeholder access to the relevant information they need.

Recommendation #3
Enhance information technology systems to support program activities, including integration across the regulatory life cycle.

Despite both branches implementing several initiatives to digitalize the Program to adapt to the new working environment created by the pandemic, internal information technology (IT) systems have been updated in a piecemeal fashion, leading to legacy issues with outdated systems, including a lack of integration across the various existing systems, with some still being paper based. Fragmented and outdated systems are a barrier for information-sharing and collaboration between teams within and between both the Health Products and Food Branch (HPFB) and the Regulatory Operations and Enforcement Branch (ROEB), as well as with international partners. Both HPFB and ROEB should work together to identify opportunities to update and integrate their IT systems across their various activities to gain efficiency and remain

timely in ensuring access to pharmaceutical drugs and protecting Canadians from unsafe products, including by sharing drug-related risks and benefits with Canadians.

Recommendation #4
Examine the potential causes for the higher rate of negative decisions in the first cycle review of applications for new generic drugs, and communicate them with industries to improve their application submissions moving forward.

The proportion of new generic drugs approved in the first cycle has decreased significantly since 2018, due to limited or low-quality evidence provided in applications. This has led to an increased number of second and third cycle reviews and associated workload for both the Program and industry. The Program should review feedback provided to applicants to identify trends in evidence gaps and share that information with new and potential applicants to improve the quality of new submissions.

Recommendation #5
Explore the factors leading to the downward trend in veterinary drug availability in Canada.

Access to marketed veterinary drugs has decreased in recent years, though it is not entirely clear what is driving this downward trend. This has become an increasing concern to external stakeholders in the veterinary drugs sector for both food-producing and companion animals. The Program should explore the factors causing this downward trend to better understand whether there are any areas involved within the Program’s control.

Management Response and Action Plan: Evaluation of the Pharmaceutical Drugs Program 2018-19 to 2022-23

Recommendation 1				
Review and update Program priorities to align with its objectives and pressures moving forward, as well as workload and resource capacity.				
Management response				
HC agrees with the recommendation. Over the past five years, the Pharmaceutical Drugs Program (PDP) played an active role to help ensure that Canadians have access to safe, effective, and quality pharmaceutical drugs. Since 2020, the Program faced an unprecedent strain on workload and resources. The PDP was required to be agile and reallocate resources where needed. As the Program looks ahead, it is undergoing a number of priority-setting exercises for workload and resource management.				
Action Plan	**Deliverables**	**Expected Completion Date**	**Accountability**	**Resources**
The PDP has clear priorities and has resources in place to complete the work.	Confirmation of program objectives by reviewing and updating the PDP logic model.	August 2024	HPFB in collaboration with ROEB	Existing resources
	Identification of program priorities as they align with the program objectives.	November 2024		
	Confirmation of resources to deliver on priorities that align with objectives.	December 2024		

	Program objectives and priorities approved by senior management and disseminated to HPFB and ROEB PDP staff.	June 2025		
Recommendation 2				
Review and update the Program's communications approach to ensure stakeholders can access relevant information.				
Management response				
HC agrees with the recommendation. The Department works to provide transparent communication documents in adequate content and language in an efficient manner. However, communication channels could be made clearer through the website. The PDP recognizes that changes in regulatory processes need to be communicated to` parties as efficiently as possible, even more so when the environment or context changes.				
Action Plan	**Deliverables**	**Expected Completion Date**	**Accountability**	**Resources**
That stakeholders have easier access to relevant and current information.	Inventory and analysis of existing PDP communications products and the related distribution approaches.	November 2024	HPFB in collaboration with ROEB.	Existing resources
	Analysis of web traffic of PDP communications products.	November 2024		
	Inventory of existing PDP stakeholder lists.	August 2024		
	Report on options for improvements to the communications approach to senior management.	January 2025		

Recommendation 3				
Enhance information technology systems to support program activities, including integration across the regulatory life cycle.				
Management response				
HC agrees with the recommendation. The Department uses a variety of information technology systems in their activities to gain timely efficiency in ensuring access to pharmaceutical drugs and protecting Canadians from unsafe products, including sharing drug-related risks and benefits with Canadians. Currently, within Health Canada, branches are implementing several initiatives to digitize the program to adapt to the new working environment created by the pandemic. The PDP recognizes that an integrated, internal system would reach maximum efficiency.				
Action Plan	**Deliverables**	**Expected Completion Date**	**Accountability**	**Resources**
The information technology systems are reviewed and plans in place to consider best way to support program activities across the regulatory life cycle.	Review the Data Governance Network (HPFB led) and build on the data scorecard exercise to help inform a life cycle approach to IT, which in turn will support efforts to review and update the Business Innovation Plan.	June 2024	HPFB and ROEB co-lead.	Existing resources
	Complete report of ROEB Laboratories' evaluation of laboratory IT governance and support in federal organizations.	June 2024		
	Complete exploration phase for an enterprise compliance and enforcement system at ROEB.	June 2025		

	Identify internal data sharing necessary for life cycle integration across existing HPFB business activities and prioritize for metadata harmonization.	June 2025		

Recommendation 4				
Examine the potential causes for the higher rate of negative decisions in the first cycle review of applications for new generic drugs, and communicate them with industry to improve its application submissions moving forward.				
Management response				
HC agrees with the recommendation. Health Canada has an open collaboration with stakeholders concerning submissions. Health Canada works within service standards to review submissions. In this regard, the PDP completed an analysis of the number and reasons for negative decisions in 2021-22, which has been shared with generic industry stakeholders and associations and presented at the Pharmaceutical Sciences Group (2023). Subsequently, PDP led an education session aimed at generic industry representatives in September 2023. The aim was to educate stakeholders on the reasons for these common negative decisions and provide information and guidance to enable them to avoid these issues in the future.				
Action Plan	**Deliverables**	**Expected Completion Date**	**Accountability**	**Resources**
The generic industry has a better understanding of submission requirements, thereby leading to improved submission quality and an anticipated increase in the rate of first cycle review approvals.	Expand the analysis of negative decisions to 2022-23 to permit for further trending.	December 2024	HPFB lead (PDD with support from NNHPD)	Existing resources
	Present the findings and guidance for improvements to an industry event (Fall 2024).	December 2024		

<table>
<tr><th colspan="5">Recommendation 5</th></tr>
<tr><td colspan="5">Explore the factors leading to the downward trend in veterinary drug availability in Canada.</td></tr>
<tr><th colspan="5">Management Response</th></tr>
<tr><td colspan="5">HC agrees with the recommendation. Throughout the past five years, the Department has worked on implementing Vanessa’s Law to strengthen safety oversight, including enhancing the reporting of serious Adverse Drug Reactions (ADRs), as well as facilitating approval in recent years for some categories of innovative drugs, while other types of drugs (veterinary and generics) are less accessible. The PDP recognizes that the ability to bring products to market rests with a number of areas (drug industry, agricultural industry, veterinarian associations, government, etc.). Through stakeholder discussion, staff engagement, and examining submission trends, an analysis will be done to examine the current situation with veterinary drug availability in Canada.</td></tr>
<tr><th>Action Plan</th><th>Deliverables</th><th>Expected Completion Date</th><th>Accountability</th><th>Resources</th></tr>
<tr><td rowspan="2">The Department is working with stakeholders to improve veterinary drug availability.</td><td>Conduct analysis to link to work already underway on which priority products are needed in Canada and the factors contributing to their availability.

Draft report is produced.

The report is Director General approved.</td><td>

September 2024

December 2024</td><td rowspan="2">HPFB (VDD) lead</td><td rowspan="2">Existing resources</td></tr>
<tr><td>Share information with stakeholders with the expectation that it will help inform business decisions and bring more products to market.</td><td>March 2025</td></tr>
</table>

Annex A: Methodology

The evaluation focused on the impact of the PDP's activities related to human and veterinary drugs and program agility to address current and emerging needs from 2017-18 to 2022-23. Multiple lines of evidence were analyzed from the Program and external sources and triangulated to improve the reliability and credibility of evaluation findings and conclusions.

Document and File Review

OAE reviewed over 330 internal and public documents related to program delivery, including administrative files, guiding policy and regulatory documents, records of decisions, briefing materials, summary reports, examples of public education and communications materials, and internal work plans.

Interviews

Interviews were conducted with 60 representatives from the following groups:

Internal:

- HC Program Staff and Management: 19

External Stakeholders and Partners:

- Industry Stakeholders: 18
- Patient Interest Groups: 3
- Practitioners: 9
- Hospitals: 4
- HTA organizations: 3
- Other Federal Department Staff: 1
- International Partners: 3

International Comparison

Information from comparable regulators was collected to serve as a benchmark for HC's achievements. Data collected includes service standards and average decision times for New Active Substances, user fees, and nitrosamine threshold policies.

Performance Measurement Data

Performance indicators were specified in HPFB and ROEB performance information profiles (PIP). Annual updates to performance indicators were collated and compared to established targets. Additionally, results from internal performance data were analyzed to complement the performance data from the PIP.

Financial Analysis

A breakdown of annual planned versus actual expenditures for PDP activities was provided by HPFB and ROEB for the period under review. Evaluators analyzed this data for variance and key trends.

Industry Survey

A survey targeting industry was distributed to collect feedback on program impact from 2017-18 to 2022-23. The survey was distributed to all subscribers to the DIN and DEL distribution lists (1559). The survey received 163 completed responses from eligible respondents during the period of June 15, 2023, to July 24, 2023.

OAE analyzed quantitative survey results in Excel by grouping survey responses by evaluation sub-question and summarizing the results in tables and charts. The analysis also involved calculating proportions and response patterns based on the

affiliation or type of survey respondent. Responses to open-ended questions were analyzed by theme.

Limitations and Mitigation Strategies

OAE identified evaluation findings by comparing and combining information gathered from the various sources listed above. The use of multiple sources of information is meant to increase the accuracy and authority of any conclusions made in this report. Still, many evaluations face conditions that limit their accuracy and may be important to consider. The following table lists the limitations for this evaluation and actions taken to address them.

Limitation	Impact on the evaluation	How OAE addressed the limitation
Survey respondents were identified through the contact list provided by the Program.	There is likely a bias in terms of access to the relevant information released by HC due to pre-existing relationships, as survey respondents are those currently on HC's distribution lists which are not complete (e.g., patient interest groups).	Findings from the survey were triangulated with evidence from complementary lines of evidence, including performance data collected by the PDP, internal documents, and feedback from key informants.
There were limitations with the performance data analysis collected as part of the Performance Information Profile (PIP) process, as there were inconsistencies, gaps, and overall issues with the quality of the data provided.	Data inconsistencies make it challenging to assess overall impact of activities.	Performance data was triangulated with other lines of evidence to fill in any gaps and provide context on methodological challenges and updates to indicators throughout the evaluation period.
Key informant interviews are retrospective in nature, providing only a recent perspective on past events.	This could influence the validity of respondents' assessment of activities or results that may have changed over time.	The other lines of evidence were triangulated with the data received from interviews to substantiate or provide further information. Document review also provided corporate knowledge.
The Program has limited contact with patient groups. Those contacted for an interview were often unsure about why they had been selected and how they could contribute to the current	It was not possible to build a user list for a survey on the access to and use of the Program documents targeting Canadians and patients.	Once clarifications were provided, interviewees were able to provide valuable information on the quality and dissemination of the documents.

evaluation given the limited interaction with the Program.	A limited number of interviews were undertaken with patient groups by using a snowball method.	Additional information on patients' needs were gathered through the literature.

The evaluation considered the *SGBA Plus Lens for Evaluation* in its assessment of the Pharmaceutical Drug Program, including issues of equity related to access to safety information and access to pharmaceutical drugs. Although Official Languages were not specifically examined, it was not raised naturally as a challenge for PDP activities. Furthermore, an examination of the Sustainable Development Goals was not applicable for this evaluation.

In conducting the evaluation, a single window was identified at each branch (HPFB and ROEB), with whom the Office of Audit and Evaluation worked closely throughout the evaluation. The scope for this evaluation was presented at the Performance Measurement, Evaluation and Results Committee (PMERC) meeting in April 2023. The preliminary findings were presented at PMERC on October 19, 2023, and the final report was presented at PMERC in January 2024.

Program performance data

PIP indicators clearly articulate critical elements of the Program’s performance, but related data was not consistently measured and documented to analyze time trends. Moreover, indicators are sometimes too narrow, and other information is available to the Program which may demonstrate performance more thoroughly. For instance, time to target date for approval decision is a key indicator for measuring Program exposure to fee reimbursement and reputational risks. Data comparing drugs submissions made in Canada with other countries as well as disaggregated data on priority review performance would complement information on drug access.

Annex B: Financial Tables – Planned vs Actual Spending

The financial analysis in Table 3 shows that overall, the Program is spending its allocated resources every year. Specifically, the PDP had a total planned budget of approximately $960 million over the period from 2017-18 to 2022-23, including approximately $690 million for HPFB activities and $270 million for ROEB activities. As shown in Table 3 below, both branches spent their planned budget. Between In 2018-19, 2019-20, and 2022-23, HPFB spent over its budget and then slightly under its budget in 2017-18, 2020-21 and 2021-22, averaging out to 100%. ROEB spent slightly over its budget in 2018-2019 to 2020-2021, and then slightly under the following years, averaging out just over 100%.

Table 4 presents the planned and actual cost recovery fees collected. Specifically, the PDP expected to recover approximately $497 million over the period from 2017-18 to 2022-23, including approximately $342 million for HPFB activities and $155 million for ROEB activities. In total, the Program recovered approximately $480 million, averaging 96%.

Table 3: Total planned and actual expenditures and FTEs for the Pharmaceutical Drugs Program, 2017-18 to 2022-23.

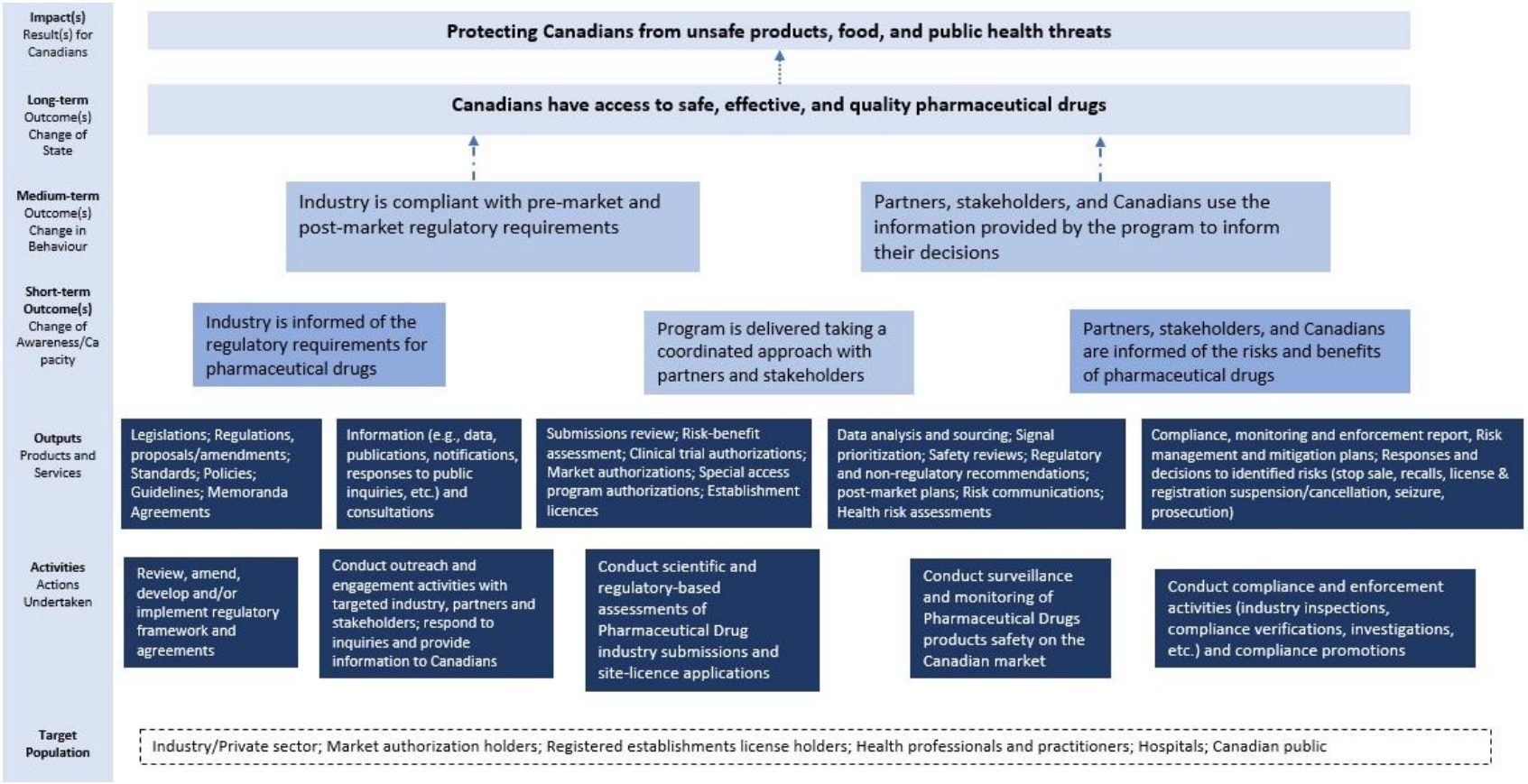
Fiscal Year	Planned Spending					Actual Spending					Variance Analysis	
	FTE	Total salary	O&M	Capital	Total	FTE	Total salary	O&M	Capital	Total	$ Variance	% Variance
HPFB - overall												
2017-18	712	88,869,259	9,996,097	2,087,066	100,952,422	674	84,788,087	10,057,160	1,360,910	96,206,157	4,746,265	95.30%
2018-19	844	87,767,989	7,771,234	1,230,987	96,770,210	747	86,780,197	9,933,716	843,020	97,556,933	-786,723	100.81%
2019-20	798	89,590,367	9,043,873	1,293,047	99,927,287	762	94,734,353	14,064,978	895,971	109,695,302	-9,768,015	109.78%
2020-21	811	112,584,578	10,891,684	300,000	123,776,262	848	106,442,993	12,354,383	300,000	119,097,376	4,678,887	96.22%
2021-22	816	120,228,335	15,794,436	-	136,022,771	926	117,713,056	17,063,829	-	134,776,885	1,245,886	99.08%
2022-23	983	109,888,188	23,148,280	-	133,036,468	897	114,759,700	21,993,987	-	136,753,687	-3,717,219	102.79%
TOTAL	**4,963**	**608,928,716**	**76,645,604**	**4,911,100**	**690,485,420**	**4,854**	**605,218,385**	**85,468,053**	**3,399,901**	**694,086,339**	**-3,600,918**	**100.52%**
ROEB - overall												
2017-18	316	35,975,921	4,978,624	-	40,954,545	259	31,342,955	3,230,453	1,029,107	35,602,515	5,352,030	86.93%
2018-19	316	36,592,417	4,440,357	-	41,032,774	283	34,824,617	6,135,210	622,095	41,581,922	-549,148	101.34%
2019-20	315	36,518,116	4,406,157	-	40,924,273	366	40,688,899	5,145,017	723,153	46,557,069	-5,632,796	113.76%
2020-21	318	37,549,886	4,688,304	-	42,238,190	374	42,915,317	3,438,445	921,833	47,275,595	-5,037,405	111.93%

2021-22	371	45,956,322	5,401,364	-	51,357,686	416	44,072,829	4,359,150	1,004,507	49,436,486	1,921,200	96.26%
2022-23	391	53,436,919	- 310,864	-	53,126,055	393	47,083,003	5,030,309	590,579	52,703,891	422,164	99.21%
TOTAL	**2,027**	**246,029,581**	**23,603,942**	**-**	**269,633,523**	**2,091**	**240,927,620**	**27,338,584**	**4,891,274**	**273,157,478**	**-3,523,955**	**101.31%**

Table 4: Total planned and actual recovery of fees for the Pharmaceutical Drugs Program, 2017-18 to 2022-23.

Fiscal Year	Planned					Actual					Variance Analysis	
	FTE	Total salary	O&M	Capital	Total	FTE	Total salary	O&M	Capital	Total	$ Variance	% Variance
HPFB - overall												
2017-18	261	31,359,209	7,259,447	-	38,618,656	253	30,320,983	7,018,707	-	37,339,690	1,278,966	96.69%
2018-19	281	33,775,392	7,036,541	-	40,811,933	267	32,094,185	6,686,285	-	38,780,470	2,031,463	95.02%
2019-20	274	32,883,733	6,850,778	-	39,734,511	290	34,744,075	7,238,345	-	41,982,420	-2,247,909	105.66%
2020-21	488	58,617,595	12,211,999	-	70,829,594	450	53,992,632	11,248,459	-	65,241,091	5,588,503	92.11%
2021-22	497	59,678,456	12,433,012	-	72,111,468	461	55,346,623	11,530,540	-	66,877,163	5,234,305	92.74%
2022-23	611	73,360,795	6,792,666	-	80,153,461	580	69,569,218	6,441,603	-	76,010,821	4,142,641	94.83%
TOTAL	**2,414**	**289,675,181**	**52,584,443**	**-**	**342,259,624**	**2,301**	**276,067,716**	**50,163,939**	**-**	**326,231,655**	**16,027,969**	**95.32%**
ROEB - overall												
2017-18	143	17,117,850	3,566,219	-	20,684,069	142	16,992,111	3,540,023	-	20,532,135	151,934	99.27%
2018-19	148	17,780,890	3,704,352	-	21,485,242	143	17,184,448	3,580,093	-	20,764,542	720,700	96.65%
2019-20	154	18,485,949	3,851,239	-	22,337,189	151	18,157,888	3,782,893	-	21,940,782	396,407	98.23%
2020-21	145	17,399,257	3,624,845	-	21,024,102	147	17,695,065	3,686,472	-	21,381,537	-357,434	101.70%
2021-22	234	28,156,169	5,865,869	-	34,022,038	236	28,288,054	5,893,345	-	34,181,398	-159,361	100.47%
2022-23	261	31,402,137	4,259,980	-	35,662,116	255	30,545,264	4,143,737	-	34,689,002	973,115	97.27%
TOTAL	**1,085**	**130,342,253**	**24,872,503**	**-**	**155,214,756**	**1,074**	**128,862,831**	**24,626,564**	**-**	**153,489,395**	**1,725,361**	**98.89%**

Annex C: Intended Outcomes – Logic Model



End Notes

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