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CHAPTER 4, REGULATING PHARMACEUTICAL DRUGS – HEALTH CANADA, OF THE FALL 2011 REPORT OF THE AUDITOR GENERAL OF CANADA

Report of the Standing Committee on Public Accounts

David Christopherson, MP
Chair

FEBRUARY 2013

41st PARLIAMENT, 1st SESSION

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has the honour to present its

ELEVENTH REPORT

Pursuant to its mandate under Standing Order 108(3)(*g*), the Committee has studied Chapter 4, Regulating Pharmaceutical Drugs – Health Canada, of the Fall 2011 Report of the Auditor General of Canada and has agreed to report the following:

INTRODUCTION

Health Canada, through the *Food and Drugs Act*, regulates the safety, efficacy, and quality of all pharmaceutical drugs for use by humans in Canada before and after the products enter the Canadian marketplace. The Department does this through a combination of scientific review, monitoring, compliance, and enforcement activities. It aims to ensure that the public has timely access to safe and effective pharmaceutical drugs and that those who need to know of safety concerns are informed.

The Office of the Auditor General of Canada (OAG) conducted an audit covering the period of January 1, 2009 to December 31, 2010 to determine if Health Canada fulfilled its four main responsibilities related to drug regulation.[1] These responsibilities are:

- **regulating clinical trials** of new pharmaceutical drugs being conducted in Canada;
- **reviewing submissions** from manufacturers seeking approval of new drugs for sale in Canada or of changes to drugs already on the market;
- **monitoring product safety** of drugs and ensuring that potential safety concerns are communicated to health care professionals and the public; and
- **enforcing compliance** of the pharmaceutical industry with regulations, including those related to clinical trials, drug manufacturing, and the reporting of adverse reactions to drugs.[2]

On March 29, 2012 the House of Commons Standing Committee on Public Accounts (the Committee) heard from witnesses regarding Chapter 4 of the *Fall 2011 Report* of the Auditor General of Canada. From the OAG, the Committee heard from Neil Maxwell, Assistant Auditor General, and Louise Dubé, Principal. From Health Canada (HC), the witnesses were Glenda Yeates, Deputy Minister; Paul Glover,

[1] Auditor General of Canada, *Fall 2011 Report*, Chapter 4, "Regulating Pharmaceutical Drugs—Health Canada," Ottawa, 2011.
[2] Ibid, paragraph 4.11.

Assistant Deputy Minister, Health Products and Food Branch; and Marc Berthiaume, Director, Marketed Pharmaceuticals and Medical Devices Bureau, Marketed Health Products Directorate, Health Products and Food Branch.

AUDIT FINDINGS

During this hearing, the Committee asked Health Canada officials to provide details on how the department regulates prescription drugs to ensure that it is putting the health and safety of Canadians first. Deputy Minister Glenda Yeates responded that "this is done in a variety of ways. It's done before the drugs ever come to market by looking at the clinical trials. It's done as the drugs are submitted for approval. It's done as we put them on the market and continue to have surveillance mechanisms to ensure that we understand all the possible consequences of these drugs."[3] Some examples provided by Ms Yeates included:

- Canada is the only drug regulator in the world that has established performance standards on the post-market side for completing safety assessments when a drug is already on the market – a practice international partners may be interested in adopting.
- Strengthening the implementation of user fees under the *User Fees Act*, which now supplies a substantially enhanced resource base to the department and rebalances the fees paid by industry in accordance with the support given by the public tax base, allowing Health Canada to increase the number of chemists who are able to work on drug files.
- Health Canada has enhanced the MedEffect database to allow physicians or consumers who have experienced an adverse drug event to report the event to Health Canada with greater ease, making more information available to Canadians.[4]

[3] House of Commons, Standing Committee on Public Accounts, *Evidence*, 1st Session, 41st Parliament, March 29, 2012, Meeting 36, 900.
[4] Meeting 36, 900.

In addition to this, Ms. Yeates stated that the findings of the OAG were helpful, and that the department was using these as a foundation for improving services to Canadians.[5]

The Committee was encouraged to see the commitment of Health Canada officials to improving services. However, some concerns remained and witnesses were questioned at length about the recommendations of the OAG, with Committee members asking for more detail about the problems identified by the OAG and how these would be dealt with by the department. The OAG made ten separate recommendations to Health Canada.

To summarize the audit's findings, the OAG stated in its report: "we examined key Health Canada responsibilities involving timeliness, consistency, transparency, conflict of interest, and risk-based post-market activities. We found that the Department has not adequately fulfilled most of these key responsibilities related to clinical trials, submission reviews, and post-market activities for pharmaceutical drugs."[6]

In response to the OAG's findings, Health Canada created an action plan to address of each of the OAG's recommendations within certain timeframes. This was shared with the Committee before the hearing and was updated on June 1, 2012 (see Appendix B).

CLINICAL TRIALS

Clinical trials are experiments involving volunteer participants that are used to determine whether a drug is safe and effective and what side effects are associated with its use. In order to conduct a clinical trial in Canada, parties must submit a clinical trial application to Health Canada, except for clinical trials on drugs that are already on the market and are being tested to treat conditions for which they were authorized.[7]

[5] Ibid, 905.
[6] Chapter 4, paragraph 4.115.
[7] Ibid, paragraph 4.16.

At the time of the audit, the OAG stated that there was no definitive, publicly accessible source of information on clinical trial results authorized by the department. In the audit, the OAG recommended that, "Health Canada should fulfill longstanding commitments to enhance public access to information on authorized clinical trials, including the summary results of its clinical trial inspections."[8] Neil Maxwell, Assistant Auditor General, commented on the progress of Health Canada in this area, stating that "I'm encouraged by the action Health Canada is taking, but a gap still exists today in the information Canadians have."[9]

When asked if Health Canada was committed to the establishment of a Health Canada administered database on authorized clinical trials in progress, Glenda Yeates responded that Health Canada was in consultations and exploring possibilities on creating this database because "we want to build something here. We want to go down the path that is most useful to Canadians."[10] The Committee recognizes that Health Canada did in fact take steps to address Parliament's 2004 recommendation, but strongly encourages Health Canada to complete work in this area.

REVIEW OF NEW DRUG SUBMISSIONS

Health Canada reviews pre-market submissions to determine whether claims made by industry regarding a drug's safety, efficacy, and quality were supported by sufficient evidence. The Department received about 4,400 drug submissions in 2009 and 2010.

In this area, Neil Maxwell, from the OAG, told the Committee that Health Canada was "not meeting its service standards for the timely review of most of the drug submissions it receives, thus delaying Canadians' access to the health benefits of new drugs. It is also delaying access to more affordable treatments."[11] In 2009 and 2010, Health Canada's four review bureaus:

[8] Ibid, paragraph 4.41.
[9] Meeting 36, 1030.
[10] Ibid, 1035.
[11] Ibid, 850.

- did not review most drug submissions within its established time frame for service standards,[12] with none of its four review bureaus fully meeting established targets;[13]
- had a quality assurance framework in place, but Health Canada did not assess whether its four review bureaus consistently interpreted and applied procedures designed to support timely, consistent, and high-quality reviews of drug submissions;[14]
- increased the amount of information publicly available on approved drugs and on its rationale for approving these drugs, but could have released information in a more timely fashion;[15] and did not disclose information on drug submissions that were rejected or withdrawn even though other jurisdictions were following this practice.[16]

When members questioned Health Canada witnesses about these matters, Glenda Yeates responded that "With regard to evaluating drug submissions, I am pleased to report that we are making progress. The backlog for new drug submissions was eliminated in December 2011. We do still have a challenge in meeting our performance targets for generic drug reviews and we have devoted significant new resources to tackle this area."[17]

She also said:

> We've strengthened the user fee proposal that was put through Parliament under the User Fees Act, which now supplies a substantially enhanced resource base to the department and rebalances the fees paid by industry in accordance with the support given by the public tax base, thus providing us with new resources. For example, we have virtually doubled the number of chemists who are able to work on the generic drug files. While we are up to date in meeting our performance standards and have eliminated the backlog for brand-name or new drugs, we are not yet

[12] Chapter 4, paragraph 4.48.
[13] Drug review responsibilities are divided among four review bureaus based on the type of review required – 1) new drugs, 2) generic drugs, 3) over-the-counter drugs and 4) post-market changes.
[14] Chapter 4, paragraph 4.56.
[15] Ibid, paragraph 4.59.
[16] Ibid, paragraph 4.62.
[17] Meeting 36, 900.

> meeting our performance standards for generic entities. That's why we've put these new resources in—to improve our performance in that area.[18]

As adequate service standards and meeting performance objectives are essential for efficient and effective regulation, the Committee encourages Health Canada to resolve these issues identified by the OAG as early as possible.

POST MARKET SAFETY ASSESSMENTS

Health Canada monitors the safety of post marketed drugs by collecting, analyzing, and assessing domestic adverse drug reaction reports that are submitted by the pharmaceutical industry, health professionals, and consumers.[19] Ms. Yeates stated that:

> We are the only drug regulator in the world that has established performance standards on the post-market side for completing safety assessments when a drug is already on the market. Our international partners are very interested in talking to us to see if they can adopt this practice. Most drug regulators have only timelines and benchmarks for the review of drugs.[20]

Some members questioned Health Canada officials on the issue of the response time of the department when safety issues are identified for drugs that are already on the market. In 2009 and 2010, the OAG found that Health Canada took at least one year to complete 34 of its 54 safety assessments.[21] In some cases, it took significantly longer, and the department missed meeting its own established performance measures by a significant margin. For example, five medium-priority assessments required more than two years to complete, and one of these five required more than three years to complete, even though Health Canada's targets dictated that these were to be completed in 130 or 200 days.[22]

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[18] Ibid, 900.
[19] Chapter 4, paragraph 4.71.
[20] Meeting 36, 900.
[21] Chapter 4, paragraph 4.83.
[22] Ibid, paragraph 4.84.

Expressing concern over the potential dangers of not completing safety assessments in a timely manner, Committee members asked Health Canada officials if they could explain why the process took as long as it did, and whether it would be important for improvements to be made in this area. Dr. Marc Berthiaume of Health Canada, as part of his response, stated that:

> [W]hat's important is dealt with as a priority. Of course, we always want to do things as quickly as possible. However, when there is a significant risk for Canadians, we act as quickly as we can. I think that, in the past few years, the department has made considerable progress with respect to its ability to tackle the drug safety issues that arise. The department has increased its ability to respond; it has improved its response time; it has increased the number of issues that are analyzed. There are more resources. Everything has been done to be more and more efficient with respect to the department's response time to health issues that emerge when products are put on the market.[23]

The Committee notes that while Health Canada's response showed a desire to improve, the department should act quickly and actually demonstrate measureable efficiency improvements. The OAG found that "delays in approving new drug submissions mean that access to the potential health benefits of these drugs is delayed."[24]

CONFLICT OF INTEREST

Members of the Committee, hearing that the OAG had encountered issues with transparency in the pharmaceutical regulation system, queried the department on issues of conflict of interest. The OAG reported that Health Canada's conflict-of-interest guidelines are generally consistent with the government's Values and Ethics Code for the Public Service. However, in 2010, the Department did not comply with the Code's requirement to issue an annual reminder to employees of their conflict-of-interest obligations.[25] Also, at the time of the audit's completion, the department had not yet issued this reminder for 2011, nor had it determined the necessary measures to

[23] Meeting 36, 910.
[24] Chapter 4, paragraph 4.52.
[25] Ibid, paragraph 4.66.

address the conflict-of-interest risks specific to its pharmaceutical review activities.[26] Mr. Maxwell stated to the Committee that "Our main concern was really the fact that we thought the department hadn't really assessed where the risks lie in terms of managing conflict of interest for its reviewers of drug submissions. And really, its processes were meeting Treasury Board requirements, but nothing more."[27] In its audit, the OAG stated:

> The government's Values and Ethics Code for the Public Service requires that departments establish measures to manage conflicts of interest. To determine whether Health Canada had systems to manage conflict-of-interest risks to the drug submission review process, we examined its Code of Conduct and its conflict-of-interest guidelines, and interviewed key entity officials. The audit was not designed to find cases of officials being in a conflict of interest, and we did not find any such cases.[28]

The OAG pointed out in the audit that some federal government departments (as well as a different international regulator of pharmaceuticals) have developed additional measures to manage conflict-of-interest possibilities for particular activities that employees undertake in their area of work that may not be covered under the general government-wide application of the Values and Ethics Code for the Public Service.[29] For example, this may include developing conflict-of-interest measures for Health Canada employees working closely with publicly traded pharmaceutical companies on new drug approval matters who would be in a position to profit from knowledge gained in their work. As such, the Committee agrees that Health Canada should develop specific conflict-of-interest guidelines that apply to pharmaceutical regulation work at Health Canada. Guidance could be drawn from the OAG's *Fall 2010 Report* on "Managing Conflict of Interest."

RECOMMENDATION

The Committee has reviewed the ten separate OAG recommendations that touch on varied areas of pharmaceutical regulation at Health Canada. Based on the OAG's findings, the Committee feels that Canadians, while generally well-served, should

[26] Ibid, paragraph 4.67.
[27] Meeting 36, 925.
[28] Chapter 4, paragraph 4.65.
[29] Ibid, paragraphs 4.67-4.69.

receive improved services from Health Canada. The Committee is encouraged to see that Health Canada has created an action plan that addresses each of the OAG's recommendations separately, and that includes timelines for completion. The Committee intends to monitor the progress of Health Canada in implementing the action plan that was provided to the Committee one day prior to the hearing and updated on June 1, 2012, and recommends:

RECOMMENDATION:

That Health Canada provide to the Public Accounts Committee by March 31, 2013 a detailed progress report on its June 1, 2012 action plan items so the Committee may appraise the progress of Health Canada regarding its commitments to address the OAG's recommendations. This update should provide evidence of substantive, measurable progress, especially for action items that are to be completed by March 31, 2013.

CONCLUSION

During the hearing, the Committee expressed its satisfaction with the work of the OAG noting that:

> The Auditor General examined many important areas of regulating pharmaceutical drugs, including transparency and timeliness in communicating information about clinical drug trials, conflicts of interest, timeliness of safety assessment recommendations for marketed drugs, and how Health Canada applies risk-based standard operating procedures. Along with Health Canada's other drug regulation activities, these are all important areas to Canadians and to Canadian drug manufacturers and suppliers.[30]

The Committee reaffirms that effective pharmaceutical regulation is key to ensuring the safety of the many Canadians who rely on these drugs, and notes that Health Canada has shown progress in its regulatory program.

However, the Committee also notes the findings of the OAG, and asks that Health Canada respond without delay to the recommendations of the OAG and to work

[30] Meeting 36, 900.

toward meeting the commitments made within the timelines set in the action plan that was provided to the Committee on June 1, 2012.

APPENDIX A
LIST OF WITNESSES

Organizations and Individuals	Date	Meeting
Department of Health	2012/03/29	36
Marc Berthiaume, Director, Marketed Pharmaceuticals and Medical Devices Bureau, Marketed Health Products Directorate, Health Products and Food Branch		
Paul Glover, Assistant Deputy Minister, Health Products and Food Branch		
Glenda Yeates, Deputy Minister		
Office of the Auditor General of Canada		
Louise Dubé, Principal		
Neil Maxwell, Assistant Auditor General		

APPENDIX B

Update and Response to OAG Recommendations for the Regulation of Pharmaceutical Drugs in Fall 2011 Health Canada's Action Plan as of: June 1, 2012

The Findings of the Auditor General: In 2011, the Office of the Auditor General conducted an audit on the Regulation of Pharmaceuticals, which was tabled in the House of Commons in the Fall Report, on November 22nd, 2011. The audit covered a period of two years, from January 1, 2009 to December 31, 2010. The Auditor General did not question the safety or effectiveness of drugs authorized by Health Canada, but made 10 (ten) recommendations to strengthen and improve processes that are already in place. This action plan describes actions taken to date to address the recommendations and the specific timelines that have been adopted to measure and report progress. Short term deliverables scheduled to be completed in 2011 have been finalized and medium and long term deliverables (in fiscal years 2012-2013 and 2013-2014) are on target. The Department plans on sharing this report with the public and periodically releasing updates on progress made to address the recommendations.

The 10 recommendations can be grouped under three themes: Safety, Timeliness and Transparency:

<u>Safety:</u> Canada has one of the safest and most rigorous drug safety systems in the world. In 2010-2011, Health Canada identified over 1,500 potential safety issues with varying degrees of urgency and severity. For 1,350 of these a health risk was either ruled out or the available evidence was not sufficient to warrant action; while 150 underwent more in-depth safety assessments. To identify health and safety risks as quickly as possible, Health Canada promotes adverse reaction reporting by Canadian consumers and health professionals. Health Canada also maintains the Canada Vigilance adverse reaction database; receives domestic adverse reaction reports from consumers and health professionals; receives domestic and foreign adverse reaction reports on a mandatory basis from companies; and uses automated and scientific professional review methods to detect new safety risks. In 2010-2011, Health Canada received approximately 33,000 domestic adverse reaction reports and more than 350,000 foreign adverse reaction reports for health products. Electronic reporting that will capture both foreign and Canadian adverse drug reaction reports will be implemented incrementally and Health Canada will start receiving data electronically in the summer of 2012. This will make it quicker and easier to identify potential drug safety concerns.

<u>Timeliness:</u> Cost recovery is a federal government policy intended to promote more business-like and equitable management of government programs. The Cost Recovery Initiative goal was to develop and implement a framework to provide a long-term stable funding source for regulatory activities. This has resulted in Health Canada increasing its revenue for the first time in approximately 15 years in April 2011. The

updated fees provide the Department with stable funding for the delivery of regulatory services; specifically these revenues have been invested in hiring and training new scientific experts, and improving business processes and systems. The OAG audit covered the two years prior to the implementation of the updated fees on April 1, 2011 and as a result, benefits of increased resources were not captured in the OAG report.

Through the Canada-US Regulatory Cooperation Council and in other key international fora, the Department is increasing cooperation with trusted regulators in other countries to share information on inspection and adverse drugs reactions so that domestic timely actions can be taken to protect Canadians. In addition, Health Canada is making authorizations more efficient by making increased use of outside expertise and information from other regulators. Recognising that the use of foreign regulatory information contributes to the marketing authorisation process, Health Canada is moving into formal implementation of the use of foreign regulatory information to allow Health Canada to make effective regulatory decisions with the best information available. A pilot for the use of foreign reviews was initiated in October 2011 and an evaluation of the pilot will be completed by March 2014.

<u>Transparency:</u> Health Canada is enhancing public access to information on authorized clinical trials. The Department encourages sponsors to register their clinical trials, within 21 days of the onset, using publicly available registries recognised by the World Health Organization. Health Canada has recently added new text in the No Objection Letter, issued when a trial is authorized, to encourage sponsors to register their clinical trials within this 21 day period. In 2011 Health Canada completed a review of the current risk-based approach to clinical trial site selection for inspection which will inform the development of a documented, enhanced site selection process. Health Canada also maintains a national inspection program that examines the operations of drug makers to verify that they are complying with internationally accepted Good Clinical Practices. In March 2012 the Department published a summary report of Health Canada's clinical trial inspections and has committed to publishing inspection summary reports annually. The report noted that 92% of the 329 inspections conducted in the time period of the report were assigned an overall compliant rating. Health Canada is exploring how to publish inspection reports of individual inspections for compliance with Good Clinical Practices and Good Manufacturing Practices.

Health Canada initiated a process to require employees to declare that they understand and are in compliance with their Conflict Of Interest (COI) obligations. To date, 99% of drug reviewers have complied with this requirement. In parallel, Health Canada commissioned an

assessment of the risks of conflict of interest, including the drug review process. Although no unreported or emerging COI was found, the report recommended areas for management action to mitigate COI risks. Health Canada is in the process of building COI measures that respond to the recommendations and ensure continued COI compliance in HPFB to maintain the integrity of the drug regulatory process.

The first phase of the Summary Basis of Decision Project has made information on new drug approval decisions available to Canadians since 2005. The Department is improving the transparency of marketed health products to the Canadian public with the launch in June 2012 of the second phase of this project which will incorporate information on post-approval decisions including approvals with conditions, rejections and withdrawals into documents made available to the public via the Health Canada web-site. It is also working to make labels, including the Product Monograph, easier to read and understand through the Plain Language Labelling Initiative. A draft updated Consumer information section of the Product Monograph was posted for consultation in 2011, and is currently being finalised.

Given the growing number of drugs products available, the rapid pace of innovation, and the worldwide nature of production and supply; Health Canada is constantly looking for ways to strengthen its drug authorization and safety systems. Implementing the Auditor General's recommendations builds on Health Canada's commitments to achieve a modern system that delivers more timely approval of needed medications, strengthens drug safety and is more transparent and understandable to Canadians.

Update and Response to OAG Recommendations for the Regulation of Pharmaceutical Drugs in Fall 2011

Theme	*Audit Recommendations*	*Health Canada's Overview of Audit Findings*	*Actions to address recommendations*	*Current Status*
Safety	***1. The OAG recommended (4.35) that Health Canada strengthen its risk-based approach for monitoring and assessing clinical trial adverse drug reaction reports and for inspecting clinical trial sites, so potential safety issues are mitigated.***	• The Auditor General found that Health Canada had a risk-based inspection strategy that included criteria to help inspectors consider a number of potential risk factors, such as the type of drug being tested, or the study's intended patient population. However, the report found that this process could be strengthened. • The Auditor General also found that the manual process used by Health Canada to receive Adverse Drug Reaction reports was labour intensive and could be made more efficient. • Health Canada has responded to this recommendation by strengthening its risk-based approaches for monitoring and assessing clinical trial adverse drug reaction reports and selecting clinical trial sites for inspection. • It is also pursuing electronic reporting initiatives to expedite the reporting of both foreign and Canadian adverse drug reactions. Enabling electronic submissions will speed the process and make it quicker and easier to identify potential drug safety concerns in clinical trials.	• Health Canada implemented a process detailing a risk-based approach to monitor and assess clinical trial adverse drug reaction reports, such that the safety information received for drugs in early development and/or being studied in high risk populations is being evaluated first. A strategy guide was developed as part of this process to help assessment officers constantly prioritize the highest risk safety signals. This will allow Health Canada to identify risks and notify appropriate parties in a timely manner. • Health Canada completed a review of the current risk-based approach to clinical trial site selection for inspection which will inform the development of a documented, enhanced site selection process. • Clinical trials have been included in the Canada Vigilance database since October 2011 and are also part of the scope of the electronic reporting initiative. This will make it quicker and easier to: identify potential drug safety concerns; synthesize this information; and make decisions. There are two electronic reporting initiatives underway, including a gateway for large manufacturers and a web-based system for small to medium sized manufacturers. Pilots for the gateway will	***Completed July 2011*** ***Completed December 2011*** ***Gateway Pilot to be completed Summer, 2012***

Update and Response to OAG Recommendations for the Regulation of Pharmaceutical Drugs in Fall 2011

Theme	*Audit Recommendations*	*Health Canada's Overview of Audit Findings*	*Actions to address recommendations*	*Current Status*
			take place in the summer of 2012, and a web-based system is currently under development.	
Timeliness	***2. The OAG recommended (4.36) that Health Canada should establish timelines for officially notifying clinical trial sites of non-compliant ratings and for reviewing proposed corrective measures to verify compliance with the Food and Drug Regulations.***	• In its review of six inspection reports with non-compliance ratings, the Auditor General noted that Health Canada took up to 142 days to notify entities of their rating. Furthermore, Health Canada took approximately 110 days to review corrective actions proposed by inspection entities. • Health Canada has risk-based processes in place for inspecting clinical trials and taking compliance action, including set timelines for companies to propose corrective actions. Health Canada is strengthening its Standard Operating Procedures (SOP) to include timelines for non-compliance rating notification and the review of proposed corrective actions. As a result, the Department has developed Standard Operating Procedures (SOP) that includes timelines for non-compliance rating notification and the review of proposed corrective actions.	• Health Canada is currently revising the Department's existing SOP for conducting clinical trial inspections. This revised SOP will establish timelines for key steps in the inspection process, including notification of non-compliant ratings and the review of proposed corrective measures. The revised SOP is targeted for completion by June 2012. • Training activities will be undertaken in July 2012 to support the consistent adherence to the SOP, in particular, to the newly established timelines for notification to clinical trial sites of non-compliant ratings and review of proposed corrective measures. Training and implementation will be completed by March 2013.	***On target* (June 2012)** ***On target (July 2012 and next fiscal year)***
Transparency	***3. The OAG recommended (4.41) that Health Canada should fulfill longstanding***	• The Auditor General found that, despite commitments to increase the transparency of authorized clinical trials (such as in the 2007Blueprint for Renewal II), the amount of information	• Since 2007, Health Canada has been encouraging clinical trial registration and disclosure of information in publicly accessible registries recognised by the World Health Organisation (WHO). Health Canada has	***Completed November 2011***

Update and Response to OAG Recommendations for the Regulation of Pharmaceutical Drugs in Fall 2011

Theme	*Audit Recommendations*	*Health Canada's Overview of Audit Findings*	*Actions to address recommendations*	*Current Status*
	commitments to enhance public access to information on authorized clinical trials, including the summary results of its clinical trial inspections.	that Health Canada has made available to Canadians has not changed. • Health Canada is taking action by implementing measures that encourage sponsors to register their clinical trials within a recommended time period. Health Canada will also, subject to feasibility publish an administrative list of clinical trials that have been authorised. It has also started publishing a summary report of HC's clinical trial inspection findings on the HC website annually to make this information more accessible to Canadians. • Health Canada is also taking action to publish more information regarding inspection reports.	recently added new text in the No Objection Letter, issued when a trial is authorized, to encourage sponsors to register their clinical trials within 21 days of the trial's onset. This will promote sponsors' voluntary registration in publicly accessible registries recognised by the World Health Organisation. • Health Canada is considering how it will publish an administrative list of clinical trials that have been authorised by Health Canada. The objective of this initiative is to publish in a timely manner high-level key information about each trial that has been authorised, providing sufficient information so that prospective clinical trial participants can make a more informed decision about participating in a clinical trial. With information about clinical trial authorisations, individuals can search other more comprehensive databases such as clinicaltrials.gov for additional details. It is expected that this project will be completed in 2 phases: 1) scoping &feasibility; 2) implementation. Phase 1 began May 2012 and is targeted to be completed by the end of September 2012. The timelines for Phase 2 will depend on the strategy chosen and the need for stakeholder consultation. • Health Canada is also exploring how it will publish inspection reports of individual inspections for compliance with Good Clinical	***Initiated May 2012 (scoping & feasibility to be completed by September 2012. Implementation timeline dependant on option chosen (i.e. need for consultation)*** ***Targeted for December 2012*** ***Completed 2010/2011***

Update and Response to OAG Recommendations for the Regulation of Pharmaceutical Drugs in Fall 2011

Theme	*Audit Recommendations*	*Health Canada's Overview of Audit Findings*	*Actions to address recommendations*	*Current Status*
			Practices and Good Manufacturing Practices. It is expected that the project will be completed in two phases: 1) scoping and feasibility; 2) implementation. The timelines will depend on the outcome of the scoping exercise. • Health Canada held Technical Discussions with stakeholders on regulatory modernization to explore options for including new information in product submissions to Health Canada, including a comprehensive list of all clinical trials and documentation that all clinical trials performed by the applicant or sponsor would be publicly registered in accordance with international accepted practice. • In March 2012, the Department published a summary report of HC's clinical trial inspections and has committed to update and publish updated reports on the HC website annually. This report will: improve transparency by making public a summary of HC's clinical trial inspection findings; promote greater regulatory compliance; and provide a better understanding of regulatory oversight to stakeholders and the public. The March report provides the results of clinical trial inspections conducted by HC's Inspectorate Program between April 1, 2004 and March 31, 2011. The report found that 92% of the 329 inspections conducted during that time period were assigned an overall compliant rating.	***Completed March 2012***

Update and Response to OAG Recommendations for the Regulation of Pharmaceutical Drugs in Fall 2011

Theme	*Audit Recommendations*	*Health Canada's Overview of Audit Findings*	*Actions to address recommendations*	*Current Status*
			Further details are available in the online report found at:http://hc-sc.gc.ca/dhp-mps/compli-conform/clini-pract-prat/report-rapport/2004-2011-eng.php	
Timeliness	***4. The OAG recommended (4.53) that Health Canada should ensure that it meets service standards for the review of all drug submission types by giving due consideration to the appropriate allocation of additional resources from increased user fees charged to industry, to the use of foreign regulatory information, and to streamlining its review processes.***	The OAG findings have identified three areas where Health Canada should meet its service standards for all the review of all drug submission types. These include: <u>Cost Recovery Initiative</u> • The Cost Recovery Initiative was implemented on April 1, 2011, after the period of the audit (Jan 2009-Dec 2010). As a result, benefits of increased resources were not captured in the OAG report. • In the first year with updated user fees, Health Canada has been meeting most performance standards and has been decreasing drug approval backlogs through the implementation of HR, IT and financial plans. • New resources have assisted in reducing and eliminating the backlog on new drug submissions and will continue to assist in decreasing the generic drug submissions backlog.	• Since June 2011, Health Canada has been closely monitoring its ability to meet performance standards, through monthly dashboards, as well as quarterly and annual reports. <u>Cost Recovery Initiative</u> • In 2011, revenue collected for drug submission reviews allowed Health Canada to augment our human resources : scientific experts, drug inspectors and from other Branches, or government departments. • Cost Recovery revenues have contributed to eliminating the backlog for innovative new drug submissions, as of December 2011, and meeting 100% of annual inspection targets and post-market drug surveillance standards. • In addition, the pharmaceutical program continues to address the large volume of applications for generic drugs. The Department has nearly doubled its chemistry review capacity for generic drugs review in the past year in order to address this backlog. • Fees will be reviewed by 2014 in accordance	***On target*** ***Completed*** ***Pilot was initiated in October 2011***

Update and Response to OAG Recommendations for the Regulation of Pharmaceutical Drugs in Fall 2011

Theme	*Audit Recommendations*	*Health Canada's Overview of Audit Findings*	*Actions to address recommendations*	*Current Status*
		<u>Foreign Regulatory Information</u> • Health Canada has increased its focus on international collaboration, including improved sharing of best practices and greater alignment with partners. • This increased use of outside expertise and information from other regulators is resulting in more efficient drug reviews and authorizations. <u>Improving Processes and Systems</u> • Health Canada is looking at its business processes to find further efficiencies.	with the commitment made to Parliament. <u>Foreign Regulatory Information</u> • A pilot for the use of foreign reviews was initiated in October 2011.Work has been initiated for the use of foreign reviews in the generic drugs area where industry has been encouraged to submit information about the generic approvals from other jurisdictions. Often, the generic drugs sold in the different jurisdictions are slightly different, so companies are asked to provide a comparison of the differences as part of the review process. • The results of the pilot have been encouraging and are being reviewed to explore the expansion of the pilot to include submission reviews of other products. • Full evaluation of the pilot will be completed by March 2014. <u>Improving Processes and Systems</u> • The pharmaceutical program continues to strive to address the large number of applications for generic drugs through continuous process improvements and pilot projects to determine potential operational efficiencies. Addressing the generic backlog is	***Generics Pilot to be assessed in Fall 2012*** ***In progress*** ***Evaluation will be completed by March 2014.*** ***Completed May 2011*** ***On target***

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			an operational priority in 2012-2013. • Health Canada has developed a mechanism to better obtain information from drug companies about anticipated submission volumes to allow for better forward planning. • In the past year, CRI revenues were invested in projects to improve information management and information technology capacity. Strategic investments include improvements to the Canada vigilance system to continue strengthening Health Canada's ability to address drug safety concerns across the drug product life cycle; leveraging the US FDA Gateway to exchange drug submission information with industry in a secure electronic environment; and improving internal performance measurement systems.	
Timeliness	***5. The OAG recommended (4.57) that Health Canada should regularly assess whether the procedures and guidelines, which were established to ensure timely, consistent and high quality review decisions, are***	The audit highlighted that although the Department had in place a quality assurance system, it had not assessed whether its review bureaus interpret and apply review procedures and guidelines consistently. The audit found no evidence indicating that inconsistencies arose in the drug review process from the lack of regular assessment of employee adherence to quality documents. • Health Canada has good review practices, reviewer training, and regular evaluations of operating procedures in	• Health Canada has examined internal audit systems and has met with the European Medicines Agency to discuss both their review training program as well as their audit functions as it relates to standard operating procedure and guidance compliance to further align international best practices. • Health Canada is assessing whether the procedures and guidelines, that ensure timely, consistent and high quality review decisions, are being interpreted and applied consistently. Health Canada is taking two specific actions: • Developing a system, by December	***Completed March 2012*** ***On target (December 2012 and 2013)***

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	interpreted and applied consistently by all four review bureaus.	order to adapt to the changing regulatory environment and support reviewers' current knowledge on procedures.	2012, to assess and measure compliance with procedures and consistency of interpretation. • Implementing the system, including assessment of compliance with and consistent interpretation of procedures; and corrective actions, by December 2013.	
Transparency	***6. The OAG recommended (4.63) that Health Canada disclose information related to new drug approvals in a timely manner and improve the transparency of "approvals with conditions", rejections, and withdrawals of new drugs so that Canadians and health care professionals can access information about these drugs.***	• To determine whether the Department had fulfilled its commitments for increasing the transparency of review decisions, the Auditor General examined the availability and the timeliness of the public disclosure of key documents to its website. The timelines were met for posting product monographs, but timelines were not met consistently for posting information about the reasons products had been approved. • Since 2005, Health Canada has disclosed information about new drug approvals (for novel therapies) which included safety, efficacy and quality (chemistry and manufacturing) considerations. However, the Auditor General found that information is not being disclosed on	• The Department is improving transparency in the process of drug reviews. Public consultations were completed in December, 2011 on the Summary Basis of Decision (SBD) project, which aims to expand public access to information about marketed drugs. The final report of the SBD project was posted in May 2012. SBD made public positive decisions about new drugs. • Phase II of the SBD is being launched in June 2012 with the publication of a Notice to advise stakeholders that as of September 1, 2012, the SBD will be expanded to include a broader	***Consultation completed (December 2011) Final report completed May 2012*** ***Launch on target for June 2012***

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		drugs that are rejected by the Department or on drugs that the manufacturer withdraws from the review process. • Transparency is a key strategic goal for the health products and food Branch. The Branch's Transparency and Openness Agenda focuses on making relevant, timely and useful information available to the public. Part of the commitments under this agenda includes increasing the amount of information publicly available on approved drugs for Canadians and health care professionals to make informed choices.	range of both positive and negative decisions.	
Transparency	***7. The OAG recommended (4.70) that Health Canada assess the risks posed by conflicts of interest to the drug review process, determine what measures are necessary to manage these risks and implement those measures.***	• The Auditor General found that while the Health Products and Food Branch's Conflict of Interest guidelines and Code of Conduct comply with government policy, the Department could benefit from developing risk-mitigation measures to address potential conflict of interest risks specific to the drug review process. • The Auditor General did not find any cases of Conflict of Interest (COI) at Health Canada during its review.	• In November of 2011, Health Products and Food Branch employees were asked to complete a new COI Declaration requirement to actively confirm that they have reviewed their conflict of interest obligations and have taken the necessary steps to address them, including by filing a Confidential Report to the department, if required. To date, 99% of active drug reviewers in the Branch have submitted their declarations, and the Branch is striving for 100%. • A new HC Values and Ethics Code came into force on April 2, which includes Health Canada policy on COI and is in-line with the new TBS	***Completed November 2011*** ***Completed April 2012*** ***On target (Report completed***

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			Code and COI policy. • In parallel, Health Canada commissioned an assessment of the risks of conflict of interest including the drug review process by a third-party advisor. Although no unreported or emerging COI was found, the report recommended areas for management action to mitigate COI risks. • Health Canada is in the process of building COI measures that respond to the recommendations and ensure continued COI compliance in HPFB to maintain the integrity of the drug regulatory process. Planned activities to reinforce the code include: distribution of hard copies of the Code to employees, communications to all staff, pop up to confirm compliance with values and ethics, and values and ethics training.	***April 2012)*** ~~***Spring 2013***~~ ***Fall 2012***
Safety	***8. The OAG recommended (4.96) that Health Canada should improve the timeliness of safety assessments and the implementation of related recommendations to***	• The Auditor General Report did not question the quality of safety assessments conducted in Canada, but made recommendations towards strengthening the systems that Health Canada already has in place for monitoring drug safety. • The report included two case studies as examples of where the management of	• In October, 2011, MHPD implemented performance standards for several Post-Market Surveillance Activities including Signal Assessments, Risk Management Plan Reviews, and Periodic Safety Update Report Reviews for Pharmaceuticals. The new standards will help to identify and provide Canadians with new safety information in a timelier manner. In 2011-2012, 91% of post market surveillance activities have been completed on time.	***Completed October 2011*** ***On target for September***

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	update labels and to issue risk communications thereby ensuring that Canadians and health care professionals are informed of new drug information in a timely fashion.	safety assessment recommendations could have been improved. • Health Canada has established new performance measurement standards for safety assessments and is assessing options for a notification system that would make new drug information accessible to Canadians in a timely manner.	• Health Canada is currently assessing options to implement a stakeholder notification system to inform generic drug manufacturers of new drug labelling information in a timely manner. • The implementation of the new notification system is expected to be completed by the end of the third quarter in 2012.	***2012***
Safety	***9. The OAG recommended (4.97) that Health Canada establish a systematic process to implement safety assessment recommendations for marketed drugs, to ensure that the recommendations are handled appropriately and in a timely manner.***	• The Auditor General Report did not assess the safety or effectiveness of drugs authorized by Health Canada. However, it did identify ways that Health Canada could strengthen and improve internal processes that were already in place. • Health Canada is establishing a systematic process to ensure that safety assessment recommendations for marketed drugs are handled in a more timely and appropriate manner.	• Since December 2010, new coordinator positions to track and follow up on MHPD safety assessment recommendations were created (staffing completed for 3 of 3 TPD review bureaus). • A tracking tool for innovator pharmaceuticals was developed and first used in July 2011 by one pre-market review bureau. The tool is now in use by MHPD and the 3 pre-market review Bureaus. • A tracking tool for safety recommendations for all pharmaceuticals is being finalised. The projected date to begin implementing this tool for all pharmaceuticals, including generic products is March 2013.	***Completed 2011-2012*** ***Tracking tool implemented July 2011*** ***On track to be completed March 2013***

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Timeliness	*10.* ***It was recommended (4.109) by the OAG that Health Canada should consistently apply its risk-based standard operating procedures, so the priority of the drug complaints it receives is properly addressed and documented in a timely manner.***	• The audit concluded that although Health Canada had risk-based standard operating procedures for prioritizing cases of non-compliance, it could not demonstrate that these procedures were consistently applied.	• Health Canada is improving on its risk-based standard operating procedures, so that high priority drug complaints received are addressed and documented in a timely manner. Specifically;
			  • Procedures relating to handling drug incidents have been updated.
			  • Staff will be trained on the revised procedures by December 2012.
			• The Department will review incident files by March 2013 to ensure that decisions and prioritization have been documented in accordance with the procedures. This will allow for consistency in the prioritization of drug complaints.
				Completed March 2012)
				On target (December 2012)
				On target (March 2013)

List of Acronyms:

COI-Conflict of interest
CRI-Cost Recovery Initiative
HC-Health Canada
HPFB-Health Products and Food Branch
MHPD-Marketed Health Products Directorate
OAG-Office of the Auditor General of Canada
SBD-Summary Basis of Decision
SOP-Standard operating procedures

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TPD-Therapeutic Products Directorate
TBS-Treasury Board of Canada Secretariat
US FDA-United States Food and Drug Administration
WHO-World Health Organization

REQUEST FOR GOVERNMENT RESPONSE

Pursuant to Standing Order 109, the Committee requests that the government table a comprehensive response to this Report.

A copy of the relevant Minutes of Proceedings (41st Parliament, 1st Session: Meetings Nos. 36, 46, 65, 68, 72 and 73) is tabled.

Respectfully submitted,

David Christopherson, M.P.

Chair