



Health  
Canada

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Canada



# Inspectorate Program

## Annual Inspection Summary Report 2015–2016

## MESSAGE FROM THE ASSISTANT DEPUTY MINISTER

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I am pleased to present Health Canada's 2015–2016 *Annual Inspection Summary Report* for the Inspectorate Program, now part of the Regulatory Operations and Regions Branch which was launched on April 4<sup>th</sup>, 2016. The Branch's mission is the national delivery of front-line compliance, enforcement and complementary scientific-programs. Through this work, Canadians are better informed and protected from health risks associated with products, substances and their environment. This fourth annual report highlights our inspection work that helps ensure drugs and health products sold in Canada comply with the *Food and Drugs Act* and Regulations and are safe for Canadians to use.

In 2015–2016, the Inspectorate Program conducted 1,091 on-site inspections in Canada, 16 on-site foreign inspections, 45 foreign remote paper-based inspections and 1,525 paper reviews of inspections conducted by our international regulatory partners. This report provides details about the types of inspections conducted for drugs, medical devices, blood, donor semen, and cells, tissues and organs. It presents summaries of inspection results, the common issues observed and the overall compliance ratings of the establishments.

The context in which Health Canada conducts its regulatory compliance and enforcement continues to change, with growing reliance on global manufacturing, distribution and increasing consumer demand for access and transparency. Regulatory oversight is challenged by increasingly complex and fragmented global supply chains, which may introduce risks to Canadian consumers.

From a consumer perspective, consumers are increasingly making use of ubiquitous health information online and actively seeking out new therapies to maintain or improve their health, which is facilitated by e-commerce, where unauthorized, sub-standard, or counterfeit products are more commonplace. In response, Health Canada is enhancing its foreign inspection approach, particularly for drugs, and is finding more opportunities to collaborate and share information with international regulatory partners. Health Canada does this by increasing the number of foreign on-site inspections it conducts of higher-risk sites to verify the safety of health products imported into Canada.

Developing this report allows us to take stock of our inspection work to identify key priorities, and announce the progress being made and areas that need greater focus. It helps identify changing business conditions and new challenges. Most importantly, this report helps set a course for the future.

Four key areas are currently impacting all facets of our inspection work and will remain top priorities moving forward.

- *Transparency* – Embracing the global trend for transparency by putting more information in the hands of Canadians to help them make informed decisions.

- *Risk-based approach* – Developing new tools to help assess the risks for the facilities and activities we regulate. This risk-based approach allows us to target our regulatory oversight of establishments deemed to be higher risk.
- *Foreign inspection approach* – Enhancing our foreign inspection approach in response to the increase in issues with foreign sites and the volume of health products imported into Canada. We are looking at ways to increase on-site inspections of high-risk foreign sites and to further increase collaboration with trusted international regulatory partners, as no one agency in the world has the resources to inspect all establishments in the global supply chain.
- *Emerging issues* – Continue to monitor the environment to identify emerging issues for the facilities and activities we regulate in order to be able to take steps to address them. For example, addressing the issue of data integrity by enhancing the training of inspectors to identify data integrity issues and working with trusted international regulatory partners to align approaches.

We have work ahead of us but are confident that with our expert team from across the country, we will continue to meet the challenges of today as well as the ones of tomorrow. We believe that our work will continue to have a positive impact on the safety and quality of health products in Canada and, ultimately, on the health of Canadians.

Anne Lamar  
Assistant Deputy Minister  
Regulatory Operations and Regions Branch  
Health Canada

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## EXECUTIVE SUMMARY

Health Canada’s Inspectorate Program conducted a wide range of compliance and enforcement activities in 2015–2016. These activities help ensure the health products sold in Canada comply with the *Food and Drugs Act and Regulations*, and are safe for Canadians to use.

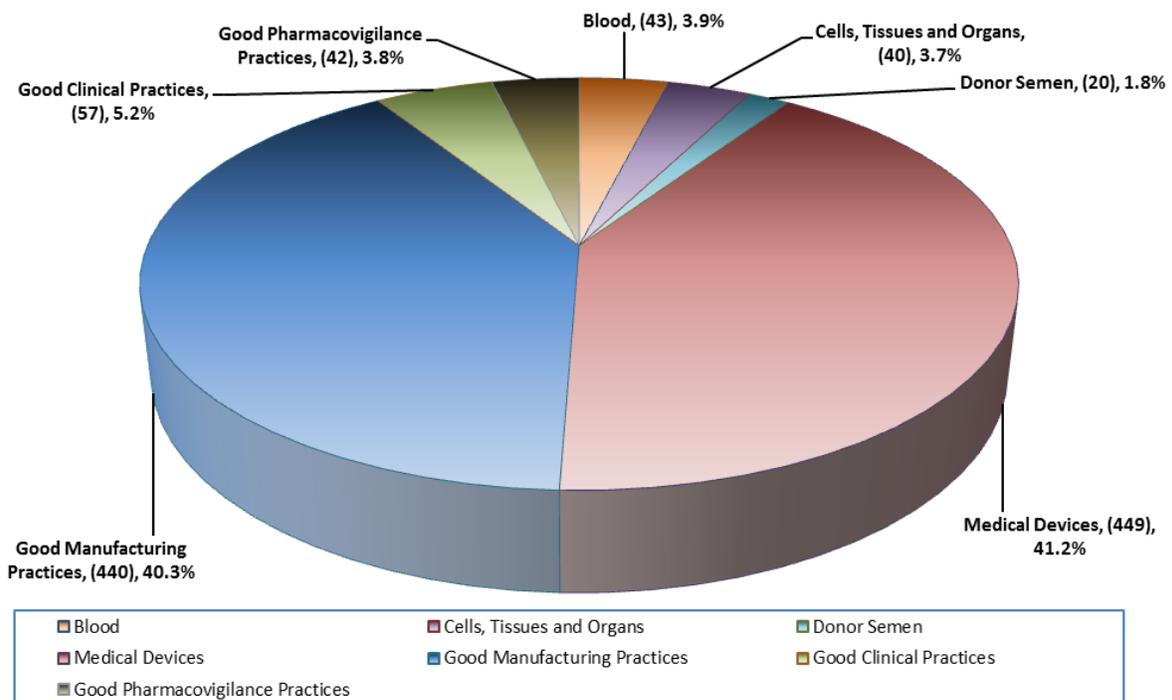
For the 2015–2016 fiscal year (from April 1, 2015 to March 31, 2016), 97 inspectors conducted 1,091 on-site inspections in Canada, made thousands of observations that required establishments to take corrective actions, and issued 37 non-compliant ratings.

Inspectors also conducted 16 on-site foreign inspections, 45 foreign remote paper-based inspections and performed 1,525 paper reviews of inspections conducted by foreign regulatory partners.

**Inspectors conducted 1,091 on-site inspections in Canada for:**

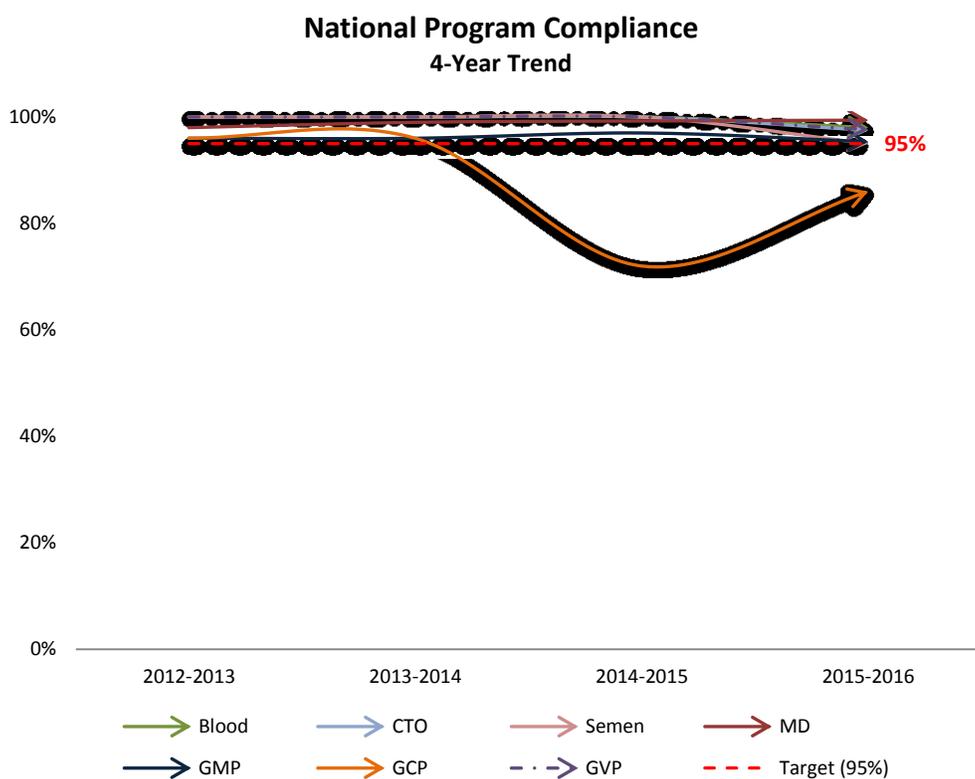
1. Blood
2. Cells, Tissues and Organs
3. Donor Semen
4. Drugs – Good Clinical Practices
5. Drugs – Good Manufacturing Practices
6. Drugs – Good Pharmacovigilance Practices
7. Medical Devices

### National Inspections by Program



**Figure A** – National inspections by health product for 2015–2016. The number of inspections for each product type depends on several factors including: the number of regulated establishments, inspection cycles and inspection complexity.

The health product establishments inspected in Canada in 2015–2016 had a very high level of compliance with the *Food and Drugs Act and Regulations*, with an overall compliance of 97 percent. The graph below shows overall compliance over the last four years. While Good Clinical Practices showed a downward trend prior to 2015–2016, which is partly attributed to its relatively small program size, the complexity of the clinical trial process and data integrity issues, its compliance rate has risen to 86%.



**Figure B** – National compliance by program from 2012–2013 to 2015–2016.

While this high overall compliance rate is a positive outcome, it does not capture the varying degrees of compliance. Some establishments, for example, were highly compliant with very few observations (activities that deviate from the regulations). Other establishments had many observations that required immediate corrective action. The Inspectorate will continue to focus its efforts on addressing poor compliance and serious risk issues.

The chapters in this report provide more detailed findings for the Inspectorate’s seven key inspection programs. Along with the overall compliance rate for each program, the information presented includes:

- overview and background for each type of inspection
- frequency of inspections
- summary of inspection results and statistics
- top observations and risk ratings
- four-year inspection trends

## Key priorities

For the 2015–2016 fiscal year, four key priorities impacted all programs and areas within the Inspectorate. They will continue to be top priorities for the Inspection Program for the 2016–2017 fiscal year and beyond:

- Transparency
- Risk-based approach
- Foreign inspection approach
- Data integrity

### Transparency

Citizens around the world are demanding access to more information to help them make informed decisions about their health. In 2014–2015, the Inspectorate launched two key online transparency initiatives related to inspections:

- [The Inspection Tracker](#)
- [The Drug and Health Product Inspections Database](#)

The Inspection Tracker provides information on foreign sites for which Health Canada received non-compliance information from its trusted partners, the nature of the non-compliance and actions taken by Health Canada.

The Drug and Health Product Inspections Database allows Canadians to search the results of inspections conducted by Health Canada and read detailed report cards for individual inspections of drug establishments, clinical trials, medical devices, good pharmacovigilance practices, blood, donor semen, and cells, tissues and organs.

### 2015–2016 Key priorities

#### Transparency

Putting more information in the hands of Canadians

#### Risk-based approach

Targeting the highest-risk activities

#### Foreign inspection approach

Increasing our collaboration with regulators around the world

#### Data integrity

Enhanced training of inspectors and continued engagement with regulated parties to identify data integrity issues

Transparency will continue to be a priority for the Inspectorate in the future. It increases awareness and helps Canadians understand how and why decisions are made. It encourages industry to comply with the regulations. It helps Canada collaborate with international regulatory partners through the sharing of information. See the Health Canada website ([www.healthycanadians.gc.ca](http://www.healthycanadians.gc.ca)) for other transparency initiatives like recalls and safety alerts, and the drug and health product register.

### **Risk-based inspection approach**

The environment in which Health Canada regulates health products has become increasingly global, complex, fast-paced and innovative, with new products rapidly coming to market. In response, Health Canada is developing a suite of new tools to help identify risks and shift from regular inspection cycles to a more flexible risk-based approach.

This flexible approach will be updated on an ongoing basis as new information comes to light, such as non-compliant ratings from international regulators. Health Canada can then prioritize sites to be inspected in Canada and abroad, the frequency of inspections, and scope of inspections.

### **Foreign inspection approach**

Over the past decade, the volume of health products imported into Canada has significantly outpaced Canada's own domestic production. The majority of health products are now imported into Canada, with many products containing ingredients from other countries.

As the global supply chain continues to expand with companies producing more products around the world, Canadians may be exposed to greater risks from new technologies, counterfeit or contaminated products, and products manufactured in countries with little regulatory oversight.

In response, Health Canada is enhancing its foreign inspection approach particularly for drugs by finding more opportunities to collaborate and share information with international regulatory partners. Health Canada is also increasing the number of foreign on-site inspections it conducts and identifying the higher-risk sites to verify the safety of health products imported into Canada.

Health Canada will work collaboratively with international regulatory partners to plan and conduct foreign on-site inspections of the higher risk facilities.

### **Data integrity**

In 2015–2016, data integrity issues were observed during inspections in Canada and globally.

Problems included:

- failure to record activities
- back-dating of records
- presenting existing data as new information
- re-running of samples to obtain better results

### **Data integrity**

Companies are required to perform testing at various stages of manufacturing to verify the quality of the health products they produce.

Reliable and accurate data is critical to making decisions about the quality of a health product.

Data integrity will continue to be a key priority for Health Canada given its potential negative impact on the safety, quality and efficacy of health products. The Inspectorate is enhancing its training of inspectors to better detect data problems. In addition, Health Canada is taking several measures to communicate the importance and requirement to maintain data integrity to regulated parties through stakeholder engagement discussions and through publication of guidance to industry.

## Summary of inspection results by health product

The following summaries provide a high-level overview of the inspections conducted for each type of health product. The full details are provided in each chapter of this report. The frequency and type of inspection varies by product type and is based on regulations, risk level, activities conducted by the establishment and other factors.

During an inspection, an inspector assesses the activities of a regulated establishment and records all observations (areas that deviate from the regulatory requirements). The inspector then assigns each observation a level of risk. The risks are generally described as follows:

- **Risk 1 – Critical:** Could cause an immediate or potentially serious health risk. Also includes fraud, or falsification of products or data.
- **Risk 2 – Major:** Could pose a potential health risk and affect the safety of the health product.
- **Risk 3 – Minor:** Low impact on risk to health and the safety of the health product.

Based on the number and type of risks involved, and taking into account the nature and extent of the deviations with the category of health products evaluated, the inspector issues an overall rating of compliant or non-compliant with the *Food and Drugs Act* at the time of the inspection.

A compliant rating means that an establishment is complying with the *Food and Drugs Act*. It is common for an establishment to receive a compliant rating even if a number of observations have been identified. However, all observations noted during an inspection must be addressed by the establishment. A non-compliant rating means that an establishment is not complying with the *Food and Drugs Act*. It also means observations have been made that could lead to immediate or potentially serious health risks to Canadians. Establishments are required to take corrective measures, as well as address all observations. Regardless of whether establishments are compliant or non-compliant, they must address all observations by implementing a corrective action plan.

Non-compliant ratings could result in:

- suspension or cancellation of the establishment licence, authorizations and/or registration
- amendment of the licence with terms and conditions
- more frequent inspections
- product recalls and public advisories
- criminal investigation

### Blood inspections

Health Canada inspects establishments that collect human blood for transfusions or for use in human drugs. For 2015–2016:

- 10 inspectors (shared with CTO and Semen inspection programs)
- 43 inspections conducted
- 202 observations made
  - 0% critical risks
  - 11% major risks
  - 89% minor risks
- Top observations:
  - records
  - operating procedures
  - equipment
- 98% compliance rate

### Cells, tissues & organs inspections (CTO)

Health Canada inspects cell, tissue and organ (such as kidneys, livers, lungs) establishments to minimize health risks to Canadians receiving transplants. For 2015–2016:

- 10 inspectors (shared with Blood and Semen inspection programs)
- 40 inspections conducted
- 185 observations made
  - 0% critical risks
  - 4% major risks
  - 96% minor risks
- Top observations:
  - quality assurance
  - personnel, facilities, equipment, supplies
- 98% compliance rate

### Donor semen inspections

Health Canada inspects establishments that process, import, or distribute donor semen for use in assisted conception in Canada to reduce the potential risk of transmitting infectious agents and diseases. For 2015–2016:

- 10 inspectors (shared with Blood and CTO inspection programs)
- 20 inspections conducted
- 24 observations made
  - 4% critical risks
  - 25% major risks
  - 71% minor risks
- Top observations:
  - records
  - prohibition
- 95% compliance rate

### Drugs – Good clinical practices inspections

Health Canada regulates clinical drug trials to protect the safety of human subjects. Clinical trial results are also inspected to help ensure the integrity of the data. For 2015–2016:

- 9 inspectors
- 57 inspections conducted
- 488 observations made
  - 2% critical risks
  - 51% major risks
  - 47% minor risks
- Top observations:
  - records
  - systems and procedures
  - training
- 86% compliance rate

### Drugs – Good manufacturing practices inspections

Health Canada inspects drug establishments against good manufacturing practices requirements to help ensure safety and quality standards are met before drugs are sold to Canadians. For 2015–2016:

- 38 inspectors
- 440 inspections conducted
- 16 foreign on-site inspections conducted
- 1,525 foreign site paper assessments conducted
- 2,353 observations made
  - 1% critical risks
  - 57% major risks
  - 42% minor risks
- Top observations:
  - quality control
  - manufacturing control
- 95% compliance rate for domestic inspections

### Drugs – Good pharmacovigilance practices inspections

Health Canada inspects drug manufacturers to help ensure drugs remain safe and effective after they are on the market. Drug manufacturers must report adverse drug reactions. For 2015–2016:

- 9 inspectors
- 42 inspections conducted
- 172 observations made
  - 0% critical risks
  - 51% major risks
  - 49% minor risks
- Top observations:
  - serious adverse drug reaction reporting
  - annual summary report and case report
- 98% compliance rate

### Medical devices inspections

Health Canada inspects medical device establishments to verify their compliance with the *Food and Drugs Act* and *Medical Devices Regulations* to help ensure that medical devices are safe and effective before they are sold to Canadians. Medical devices range from pacemakers, hip implants, and synthetic skin to lab diagnostic instruments. For 2015–2016:

- 31 inspectors
- 494 inspections conducted
- 45 foreign remote paper-based inspections
- 2,296 observations made
  - 0.3% critical risks
  - 59.9% major risks
  - 39.7% minor risks
- Top observations:
  - recall procedure
  - investigation procedure
  - distribution, complaints and recalls
- 99% compliance rate

## ABOUT THE INSPECTORATE

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### Inspectorate activities

The primary role of Health Canada's Inspectorate Program is to deliver a national compliance monitoring and enforcement program for health products including drugs (human, OTCs, NHPs and veterinary), medical devices, natural health products, blood, donor semen, and cells, tissues and organs.

The Inspectorate achieves its mandate through a number of core activities:

- establishment licensing and registration
- inspections of facilities
- compliance verifications and investigations (including recalls and public advisories)
- working with the Canada Border Services Agency (CBSA) to control imports of health products
- laboratory analyses of health products
- international activities

In Canada, the importation, sale and advertising of health products is regulated under the *Food and Drugs Act*, *Food and Drug Regulations*, and other related regulations. Health Canada inspects fabricators, processors, testers, packagers/labellers, distributors, wholesalers, and importers of health products to verify compliance.

This report focuses solely on the Inspectorate's inspection activities and does not include all Inspectorate compliance and enforcement activities. Recalls and public advisories can be found on the Health Canada website ([www.healthycanadians.gc.ca](http://www.healthycanadians.gc.ca)).

Health Canada cooperates and collaborates with international regulatory partners through, for example, Mutual Recognition Agreements to facilitate the exchange of inspection information for sites located in other countries. Health Canada reviews this inspection information through paper reviews and, at times, performs foreign on-site inspections to verify that the good manufacturing practices standard is met. Actions may be taken at the border in partnership with the Canada Border Services Agency to verify compliance via an admissibility assessment. If determined to be non-compliant, the health product is recommended to be refused entry or seized.

## CHAPTER 1

### BLOOD INSPECTION PROGRAM (BLOOD)

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#### Overview

The Inspectorate conducted **43 blood inspections** in 2015–2016. Inspectors made **202 observations** under the *Blood Regulations*. Most observations were cited against requirements for either Records (s.117) or Operating Procedures (s.95). Of these observations, 22 were major and 180 were minor. No critical observations were made.

#### Background

Health Canada monitors human blood that is collected for transfusion or for further manufacture into a drug for human use. Since the *Blood Regulations* came into force, blood establishments must secure an establishment licence before they can process allogeneic blood or import blood. Similarly, blood establishments must register with Health Canada if they process autologous blood, have a pre-assessed donor program, or transform blood.

#### Inspection cycles

The goal of an inspection is to assess whether blood establishments comply with all requirements of the *Food and Drugs Act* and the *Blood Regulations*. The *Inspection Strategy for Blood Establishments (POL-0039)* outlines how often blood establishments are inspected:

- main centres and testing laboratories – every year
- sub-centers – every two years
- fixed sites – every three years

Registered establishments are also subject to inspection. Establishments that conduct activities regulated under the *Blood Regulations* that do not require an establishment licence or registration may also be inspected.

#### **Allogeneic blood:**

Blood that is collected from one individual, either for transfusion into another individual or for use in the manufacture of a drug for human use.

#### **Autologous blood:**

Blood that is collected from an individual for transfusion into the *same* individual at a later time.

#### **Establishment licence:**

Allows establishments that process allogeneic (donor) blood or import blood to operate in Canada. These establishments undergo regular inspections to assess their continued compliance with the Regulations so they may keep their licence.

#### **Registration:**

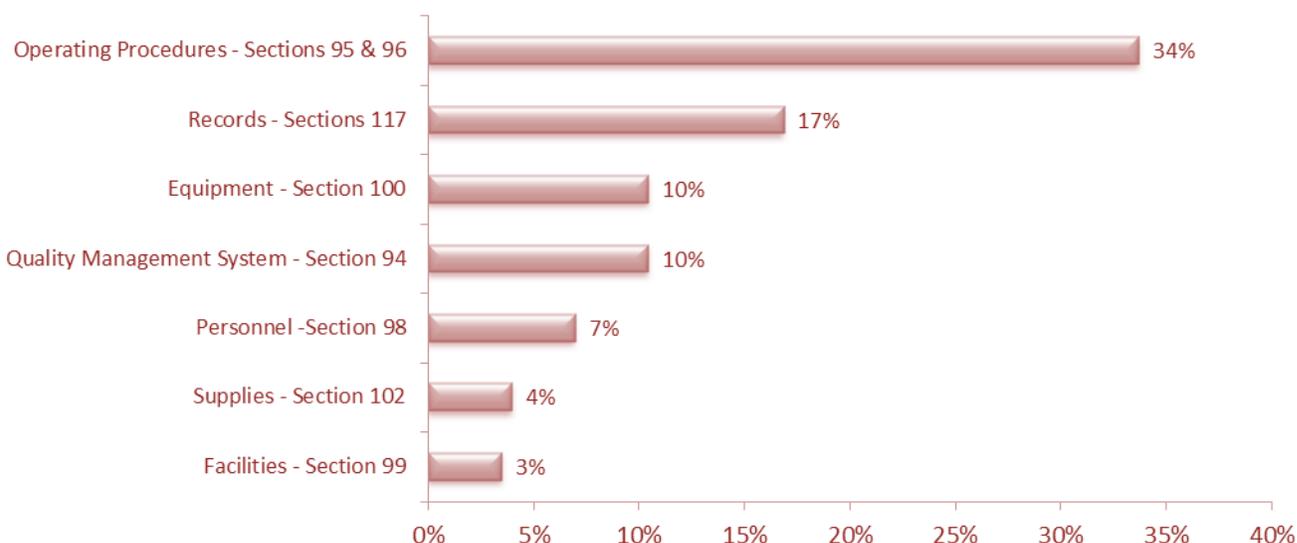
Establishments that process autologous (recipient's) blood, that transform blood, or have a pre-assessed donor program must register with Health Canada to conduct these activities.

## Inspection results and statistics

In 2015–2016, there were 4 licensed blood establishments with a total of 55 sites across Canada in addition to 48 registered hospitals. Forty-three blood inspections were conducted. All but one establishment was found to be in compliance with the Regulations at the time of inspection.

### Most common observations

Inspectors noted 202 observations during 43 blood inspections in 2015–2016. Twenty-two observations were major and 180 were minor. **Figure 1.1** shows which sections of the *Blood Regulations* were most often cited. Most observations were cited against requirements for Operating Procedures (Section 95) and Records (Section 117) under the *Blood Regulations*. Example observations under the *Blood Regulations* are listed in **Table 1.1**.



**Figure 1.1** Sections of the *Blood Regulations* most often cited, as a percentage of the total number of observations cited during blood inspections in 2015–2016.

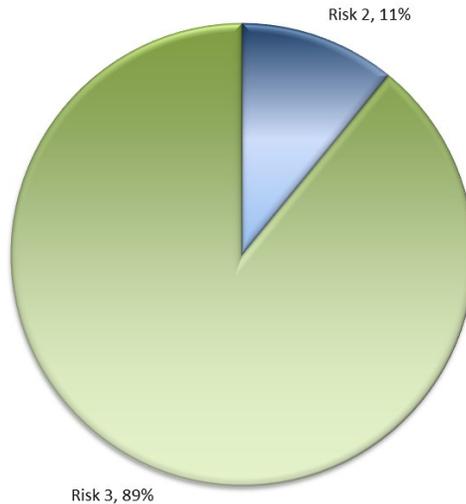
**Table 1.1 – Examples of common observations cited**

<i>Blood Regulations</i>	Example of observations
<b>Operating Procedures s. 95 and 96</b>	<ul style="list-style-type: none"> <li>Some operating procedures were not always followed.</li> <li>Some operating procedures were not kept up-to-date.</li> </ul>
<b>Records s.117</b>	<ul style="list-style-type: none"> <li>Records kept by an establishment were not always accurate, complete, legible, indelible and/or readily retrievable.</li> </ul>
<b>Equipment s. 100</b>	<ul style="list-style-type: none"> <li>The validation, calibration, cleaning, or maintenance of critical equipment were not sufficient.</li> </ul>
<b>Quality Management System - Section 94</b>	<ul style="list-style-type: none"> <li>The document control or records management system was not sufficient.</li> </ul>

**Table 1.1** Examples of blood inspection observations, from the sections of the *Blood Regulations* most often cited in 2015–2016.

## Observation risk ratings

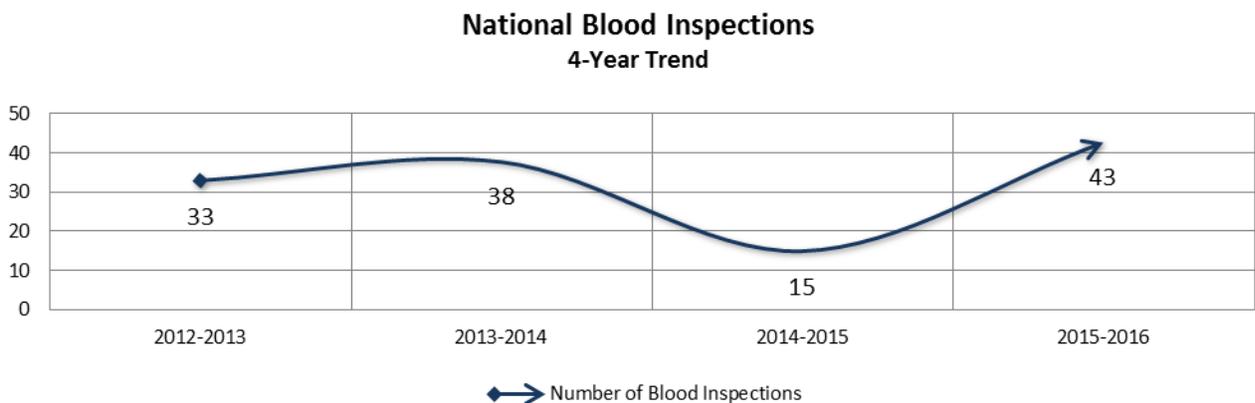
In 2015–2016, 202 observations were noted during 43 inspections. As shown in **Figure 1.2**, 89% (180) were given a Risk 3 (minor) rating, and 11% (22) were given a Risk 2 (major) rating. No Risk 1 (critical) observations were noted.



**Figure 1.2** Distribution of risk ratings for observations noted during blood inspections across Canada in 2015–2016.

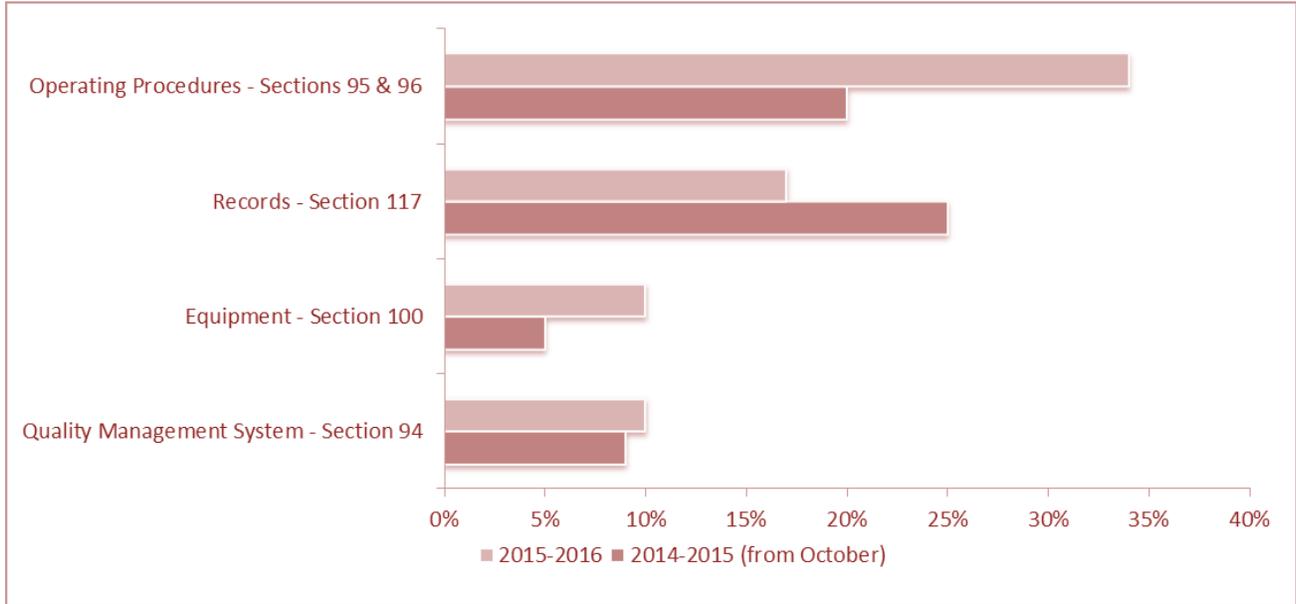
## Four-year inspection trend

**Figure 1.3** shows the four-year trend for blood inspections. This past year, the number of inspections have increased to 43, from a low of 15 in 2014–2015 when the new *Blood Regulations* were introduced which led to a decrease in inspections as efforts focused on promoting the new regulations.



**Figure 1.3** Number of blood inspections across Canada over the last four years (2012–2016).

**Figures 1.4** shows a two-year trend for Blood observations. To keep the comparison on the same legal framework, the 2014-15 data only includes observations from the switch to the new Blood Regulations in October 2014 to the end of the 2014-2015 fiscal year. Operating Procedures were the most commonly cited sections of the regulations in 2015-2016, while deficiencies with Records was the most common section cited in 2014-2015.



**Figure 1.4** Most common observations in 2015-2016 compared to previous year

Note – Numbers for 2014-2015 will differ from those published in last year’s 2014-2015 Annual Inspection Summary Report as Sections 95 and 96 of Operating Procedures in the Blood Regulations were combined for this year’s report. Figures included in last year’s report differ as they include Blood observations under the *Food and Drug Regulations* and the new *Blood Regulations* separately.

## CHAPTER 2 CELLS, TISSUES AND ORGANS INSPECTION PROGRAM (CTO)

### Overview

The Inspectorate conducted **40 cells, tissues and organs (CTO) inspections** in 2015–2016 and made **185 observations**. Most observations were cited against requirements for Quality Assurance Systems and Personnel, Facilities, Equipment and Supplies. Of these observations, 7 were major and 178 were minor. No critical observations were made.

### Background

In Canada, organs and “minimally manipulated” cells and tissues are regulated under the *Food and Drugs Act* and the *Safety of Human Cells, Tissues and Organs for Transplantation Regulations*. Health Canada regulates cells, tissues and organs (such as kidneys, livers, lungs) to minimize potential health risks to Canadians receiving transplants.

#### Source establishment:

An establishment that processes cells, tissues and organs (CTO)—either directly or through another establishment—and determines whether CTO are safe for transportation.

Source establishments that distribute CTO within Canada or import CTO for further distribution must register with Health Canada and attest that they comply with the *CTO Regulations*. **Figure 2.1** shows the number of CTO programs in Canada by type.

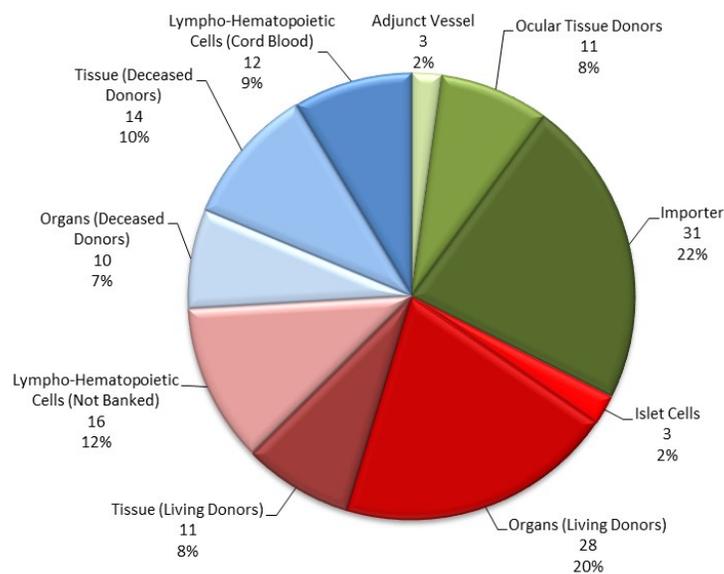


Figure 2.1 Proportion of CTO programs by type in 2015–2016.

As of March 31, 2016, 165 CTO establishments were registered with Health Canada. Some establishments registered each program as a separate entity (for example: kidney program, liver program, lung program). The total number of registered CTO programs is therefore higher than the total number of registered CTO establishments. All data presented are based on 139 registered Canadian CTO programs.

## Inspection cycles

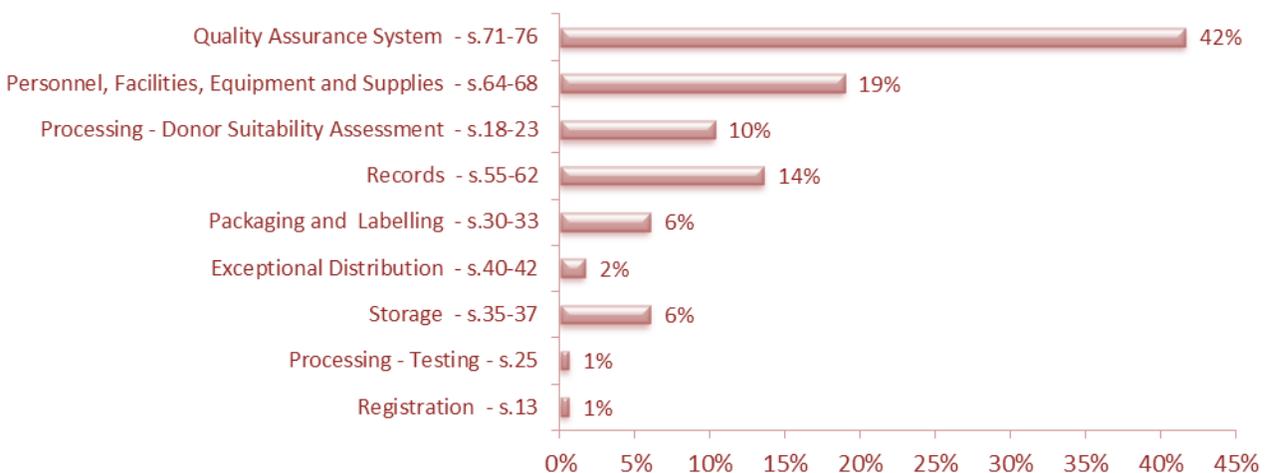
The *Inspection Strategy for Cells, Tissues and Organs Establishments (POL-0057)* outlines how often CTO establishments are inspected. Inspection frequency is based on the level of risk of the activity and the overall ratings of the previous two inspections.

## Inspection results and statistics

A total of 40 of the 139 registered Canadian CTO programs were inspected. All but one of the programs inspected were found to be in compliance at the time of inspection.

## Most common observations

Inspectors noted 185 observations during 40 inspections in 2015–2016. **Figure 2.2** shows which sections of the *CTO Regulations* were most often cited in observations. The most cited groups of observations are Quality Assurance System and Personnel, Facilities, Equipment and Supplies. Examples of these observations are listed in **Table 2.1**.



**Figure 2.2** Sections of the *Safety of Human Cells, Tissues and Organs for Transplantation Regulations* most often cited, as a percentage of the total number of observations cited during CTO inspections across Canada in 2015–2016.

Note – Due to rounding, percentages add to greater than 100%.

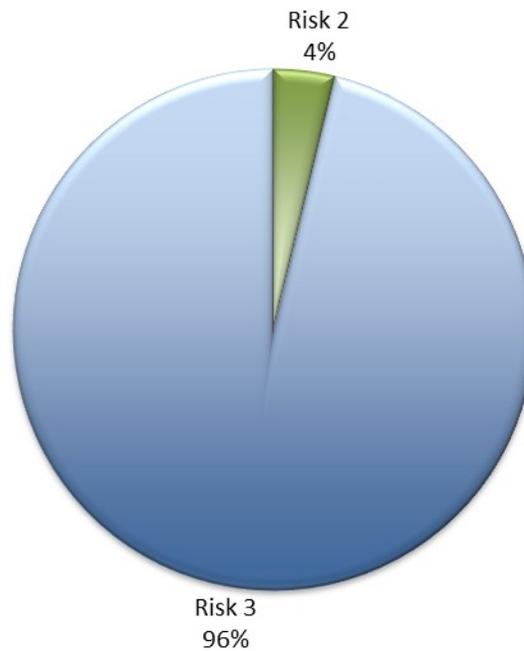
**Table 2.1 – Examples of common observations cited**

<i>CTO Regulations</i>	<b>Example of observations</b>
<b>Quality Assurance System – Standard Operating Procedures s. 73</b>	<ul style="list-style-type: none"> <li>The standard operating procedures were not kept up to date.</li> </ul>
<b>Quality Assurance System – Standard Operating Procedures s. 72</b>	<ul style="list-style-type: none"> <li>The establishment did not follow the standard operating procedures as written.</li> </ul>
<b>Records s. 55</b>	<ul style="list-style-type: none"> <li>The establishment’s records were not accurate, complete, legible and/or indelible.</li> </ul>

**Table 2.1** Examples of cells, tissues and organs observations, from the sections of the *Safety of Human Cells, Tissues and Organs for Transplantation Regulations* most often cited in 2015–2016.

### Observation risk ratings

In 2015–2016, 185 observations were noted during 40 inspections. As shown in **Figure 2.3**, 96% (178) were Risk 3 (minor), while 4% (7) were Risk 2 (major). No Risk 1 (critical) observations were noted.



**Figure 2.3** Distribution of risk ratings for observations noted during CTO inspections across Canada in 2015–2016.

## Four-year inspection trend

Figure 2.4 shows the four-year trend for CTO inspections. There was a small variation in the number of inspections year-over-year due to the criteria used to determine inspection frequency of establishments (as outlined in the *Inspection Strategy for Cells, Tissues and Organs Establishments (POL-0057)*).



Figure 2.4 Number of CTO inspections across Canada over the last four years (2012–2016).

Figure 2.5 shows the four-year trend for CTO observations, which are relatively constant. Quality Assurance Systems – Standard Operating Procedures was the most commonly cited section of the regulations each year. From 2014–2015 to 2015–2016, deficiencies with Personnel, Facilities, Equipment and Supplies increased by approximately 6% of overall observations.

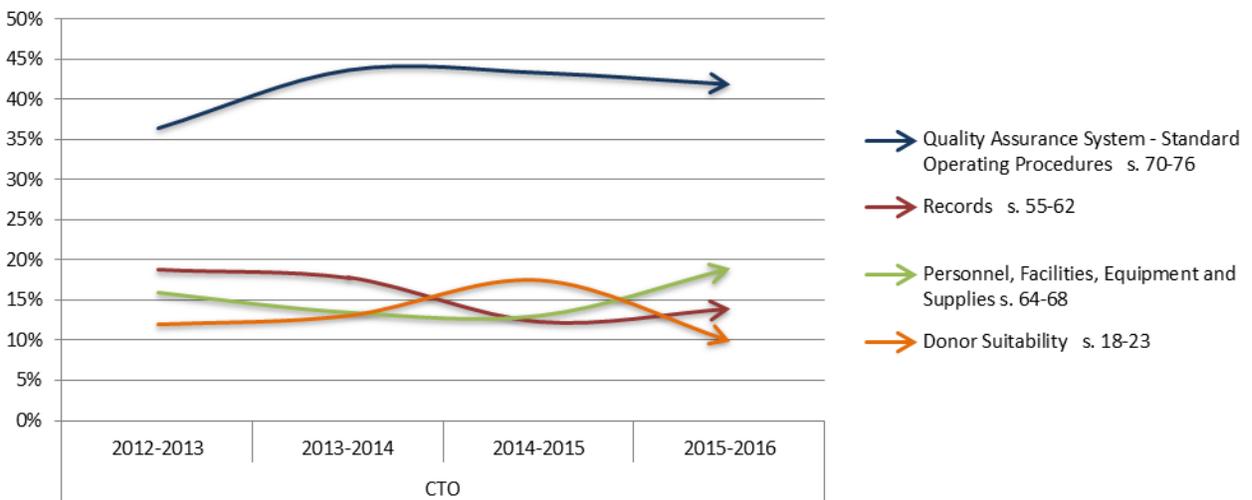


Figure 2.5 Most common observations over the last four years (2012–2016).

## CHAPTER 3

### DONOR SEMEN INSPECTION PROGRAM (SEMEN)

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#### Overview

The Inspectorate conducted **20 semen inspections** in 2015–2016 and made **24 observations**. Most observations were cited against requirements for Records (s. 13 and 12(1)) and Prohibition (s.5). Of these observations, 1 was critical, 6 were major and 17 were minor.

#### Background

In Canada, donor semen for assisted conception is regulated as a drug under the *Food and Drugs Act* and the *Processing and Distribution of Semen for Assisted Conception Regulations*. The purpose of these regulations is to reduce the potential risk of transmitting infectious agents through use of donor semen in assisted conception.

Health Canada inspects processors, importers and distributors of donor semen intended for use in assisted conception in Canada, to verify they comply with the *Processing and Distribution of Semen for Assisted Conception Regulations*.

#### Inspection cycles

The *Inspection Strategy for Semen Establishments (POL-0023)* outlines how often semen establishments are inspected. Semen processors and importers are inspected every year. Distributors that further distribute donor semen are inspected every 2 years. Final distributors (including doctors) are inspected every 5 years.

Other types of inspections or compliance verification activities may be conducted at the discretion of Health Canada, and may be unannounced.

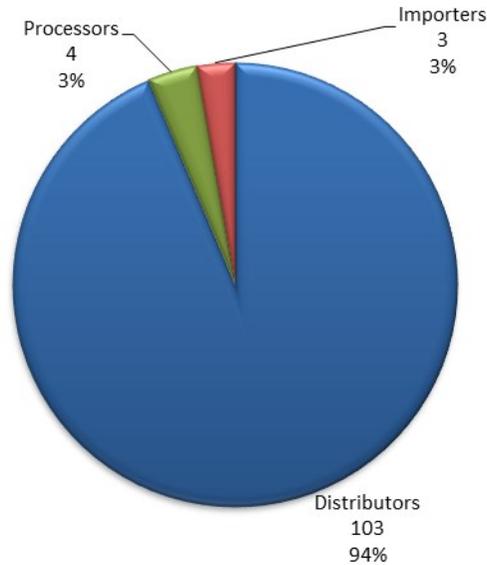
#### Inspection results and statistics

In 2015–2016, 20 out of 103 active processors, importers and distributors of donor semen were inspected. All but one was deemed to be compliant.

In Canada, processors and importers of donor semen must give written notice to Health Canada at least 10 days before the date they begin processing or importing donor semen, and within 90 days of stopping these activities. Distributors of donor semen (including doctors) do not have to provide Health Canada with such notices. The number of donor semen distributors can therefore fluctuate throughout the year, since they are not required to notify Health Canada of their intent to start or stop distributing donor semen.

Some donor semen establishments conduct more than one activity. For the purpose of this report, the number of establishments counted was based on activities conducted. For example, an establishment that processes and imports donor semen is counted twice, as both a processor and an importer.

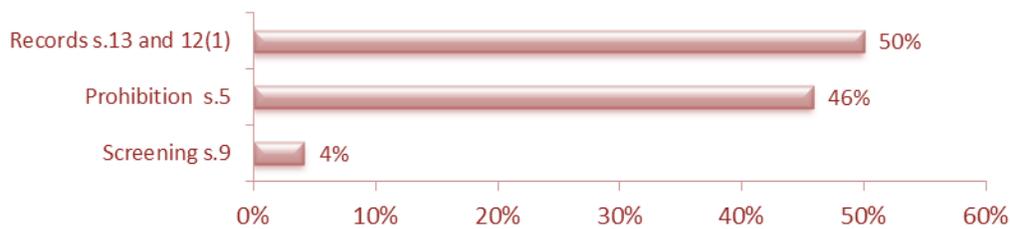
An establishment that conducts more than one activity will be inspected depending on the status of those activities. For example, if an establishment imports and processes donor semen, but has not imported any donor semen since the last inspection by Health Canada, the establishment will only be inspected for its processing activities.



**Figure 3.1** Distribution of the three types of semen establishments in Canada, 2015-2016

### Most common observations

Inspectors noted 24 observations during the 20 semen inspections in 2015–2016. Most of these observations were cited against Records (s.13 and 12(1)) and Prohibition (s.5), as shown in **Figure 3.2**. Examples of these observations are shown in **Table 3.1**.



**Figure 3.2** Sections of the *Processing and Distribution of Semen for Assisted Conception Regulations* most often cited, as a percentage of the total number of observations cited during semen inspections across Canada in 2015–2016.

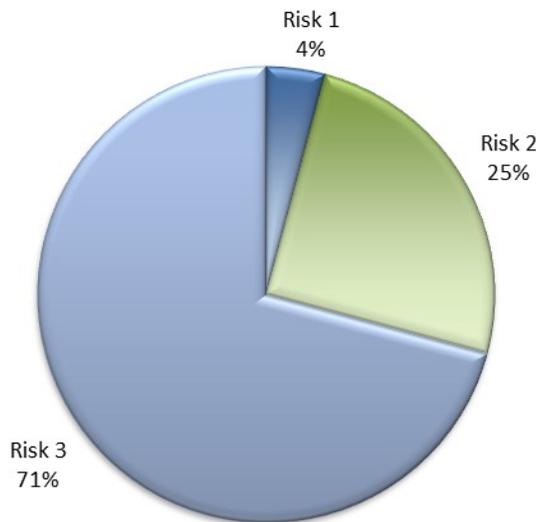
**Table 3.1 – Examples of common observations cited**

<i>Processing and Distribution of Semen for Assisted Conception Regulations</i>	Example of observations
<b>Records s.13</b>	<ul style="list-style-type: none"> <li>The distributor did not keep all required records for each container of semen.</li> </ul>
<b>Prohibition s.5</b>	<ul style="list-style-type: none"> <li>The establishment imported semen for distribution that was not processed according to requirements.</li> </ul>

**Table 3.1** Examples of semen inspection observations, from the sections of the *Processing and Distribution of Semen for Assisted Conception Regulations* most often cited in 2015–2016.

### Observation risk ratings

In 2015–2016, 24 observations were noted during 20 inspections. As shown in **Figure 3.3**, 4% (1) of observations were Risk 1 (critical), while 25% (6) were Risk 2 (major) and 71% (17) were Risk 3 (minor). The one Risk 1 observation was cited against Prohibition (s.5).



**Figure 3.3** Distribution of risk ratings for observations noted during semen establishment inspections across Canada in 2015–2016.

## Four-year inspection trend

Figure 3.4 shows the four-year trend for semen inspections. Overall inspection numbers show a downward trend over the four-year interval.

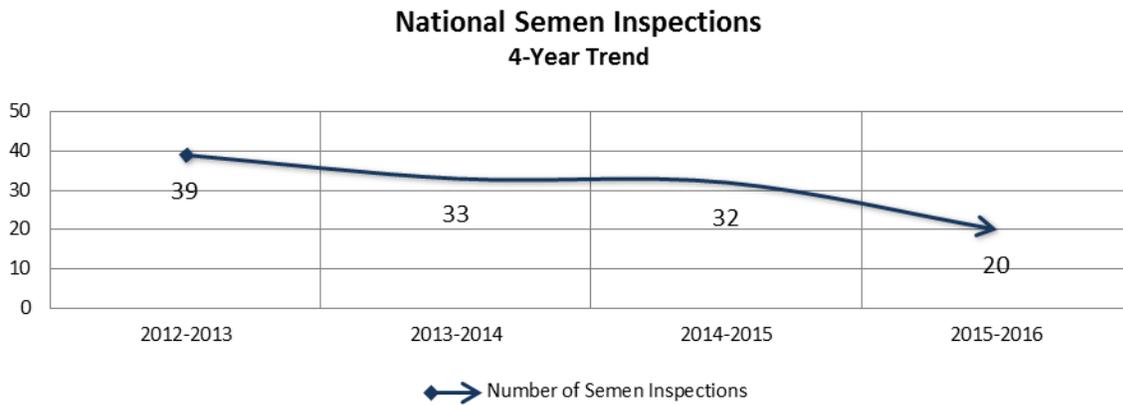


Figure 3.4 Number of semen inspections across Canada over the last four years (2012–2016).

Figure 3.5 shows the four-year trend for semen observations. Although Records (s.13) is the most common observation every year it has trended downward, while Prohibition (s. 5) has increased since 2014-2015. The changes from 2014-2015 to 2015-2016 in observations cited against Distributor Records (s.13) and Prohibition (s.5) is due to the type of semen establishments inspected, and the state of compliance of the individual sites.

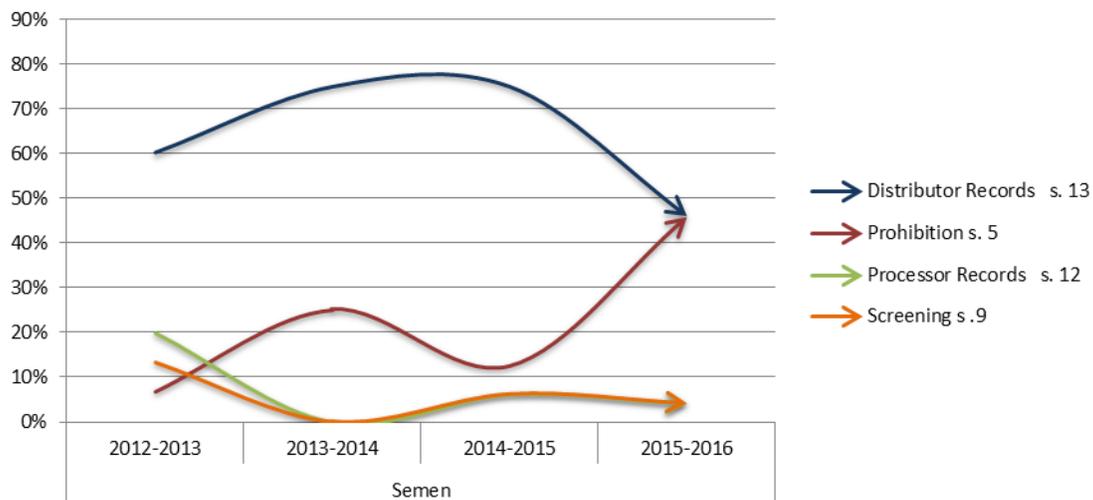


Figure 3.5 Most common observations over the last four years (2012–2016)

## CHAPTER 4

### DRUG GOOD CLINICAL PRACTICES INSPECTION PROGRAM (GCP)

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#### Overview

The Inspectorate conducted **57 good clinical practices (GCP) inspections** in 2015–2016, and made **488 observations**. Most observations were cited against requirements for Records (C.05.012) and System and Procedures (C.05.010(c)). Of these observations, 10 were critical, 248 were major, and 230 were minor.

#### Background

In Canada, clinical trials of drugs are regulated by Health Canada under the *Food and Drugs Act* and Part C, Division 5 of the *Food and Drug Regulations: Drugs for Clinical Trials Involving Human Subjects*. These laws allow Health Canada to regulate the sale and importation of drugs used in clinical trials, and to enforce good clinical practices. Good clinical practices are also described in the *International Conference on Harmonization (ICH) Guidance*, Topic E6.

Inspectors assess whether sites comply with legal requirements. The main goal of these inspections is to protect the rights, safety and well-being of the human subjects enrolled in clinical trials. Inspections are also conducted to verify the integrity of data collected in clinical trials.

#### Clinical trial:

An investigation into the safety and effectiveness of a drug that involves human subjects.

#### Good clinical practices:

Generally accepted practices that are designed to help ensure the protection of the rights, safety and well-being of clinical trial subjects and other people.

#### Inspection process

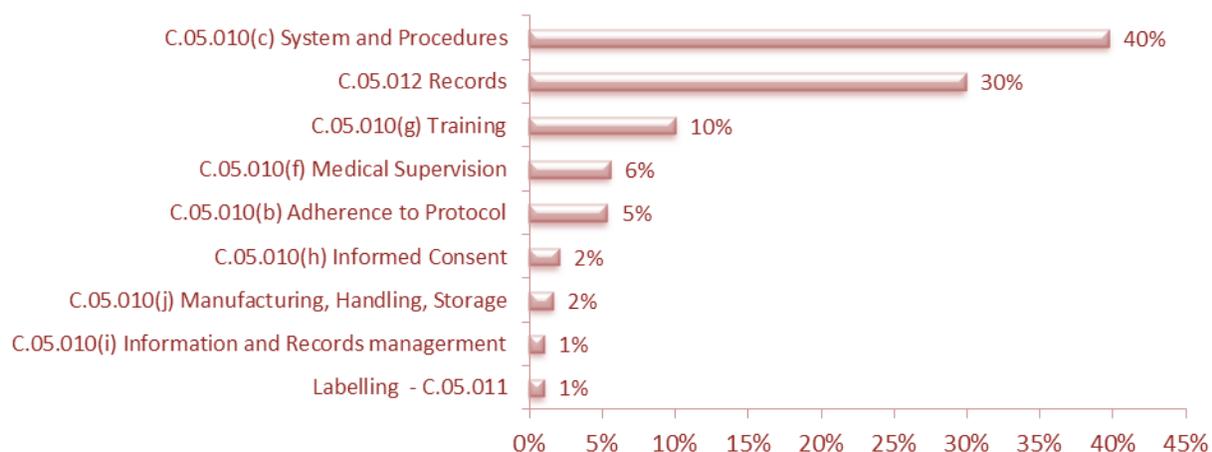
The Inspectorate applies a risk-based approach to selecting sites to be inspected through input from the scientific review bureau (Therapeutic Products Directorate (TPD) and the Biologics and Genetic Therapies Directorate (BGTD)) in the site selection process and focusing on those studies that may present a greater risk to the study population, including clinical trials for new therapies or those conducted in vulnerable populations, such as children, or women who are pregnant. The average length of an inspection is 5 days (at the clinical trial site).

#### Inspection results and statistics

In 2015–2016, 57 clinical trial sites were inspected, and 49 were compliant. Clinical studies conducted at these sites involved biological and pharmaceutical investigational drugs. For sites that were non-compliant, the Inspectorate took action to protect the health and safety of Canadians. This included requiring the inspected parties to immediately correct the deficiencies identified and recommending that Health Canada's authorization to conduct the study be suspended or cancelled.

## Most common observations

Inspectors noted 488 observations in 2015–2016. **Figure 4.1** shows which sections of the *Food and Drug Regulations* were most often cited. All of the observations cited were against Division 5 of Part C of the Regulations. Most observations were cited against requirements for Records (C.05.012) and System and Procedures (C.05.010(c)). Examples of these observations are listed in **Table 4.1**.



**Figure 4.1** Sections of the *Food and Drug Regulations* (Part C, Division 5) most often cited, as a percentage of the total number of observations cited during GCP inspections across Canada in 2015–2016.

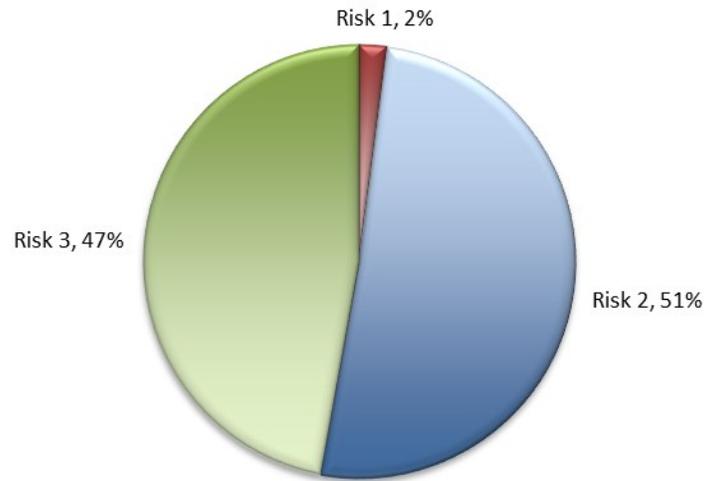
**Table 4.1 – Examples of common observations cited**

<i>Food and Drug Regulations</i>	Example of observations
<b>C.05.010(c) Systems and Procedures</b>	<ul style="list-style-type: none"> <li>Systems and procedures were not implemented to ensure the quality of the clinical trial.</li> <li>Systems and procedures were not implemented to ensure that staff members were adequately trained on Good Clinical Practices and the appropriate <i>Canadian Food and Drug Regulations</i>.</li> <li>Systems and procedures were not implemented to ensure that electronic systems were validated.</li> </ul>
<b>C.05.012 Records</b>	<ul style="list-style-type: none"> <li>The clinical trial records had errors and/or missing information that did not allow for complete and accurate reporting, interpretation and verification of the data.</li> <li>The sponsor did not keep complete and accurate records regarding the use of the drug in a clinical trial, as required by law.</li> </ul>
<b>C.05.010(g) Training</b>	<ul style="list-style-type: none"> <li>Not all individuals conducting the clinical trial had the education, training and experience to perform their respective tasks.</li> </ul>
<b>C.05.010(f) Medical Supervision</b>	<ul style="list-style-type: none"> <li>Medical care and/or medical decisions for the clinical trial were not under the supervision of the qualified investigator at the clinical trial site.</li> </ul>

**Table 4.1** Examples of GCP inspection observations, from the sections of the *Food and Drug Regulations* (Part C, Division 5) most often cited in 2015–2016.

## Observation risk ratings

In 2015–2016, 488 observations were noted in 57 inspections. As shown in Figure 4.2, 2% (10) were given a Risk 1 (critical) rating, 51% (248) were given a Risk 2 (major) rating, and 47% (230) were given a Risk 3 (minor) rating.

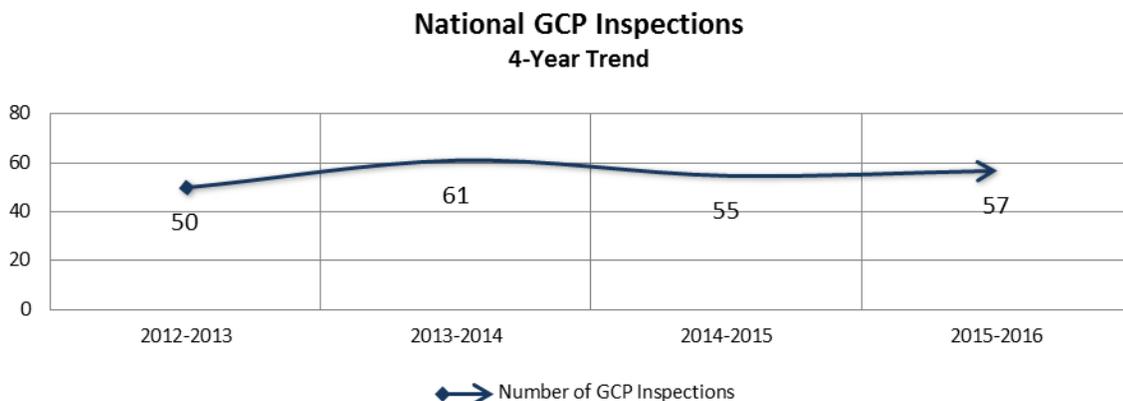


**Figure 4.2** Distribution of risk ratings for observations noted during GCP inspections across Canada in 2015–2016.

All Risk 1 observations were cited against section C.05.010. This requires the sponsor to ensure, at each clinical trial site, that medical care and medical decisions are under the supervision of a qualified investigator, and that systems and procedures are in place to ensure the quality of every aspect of the clinical trial.

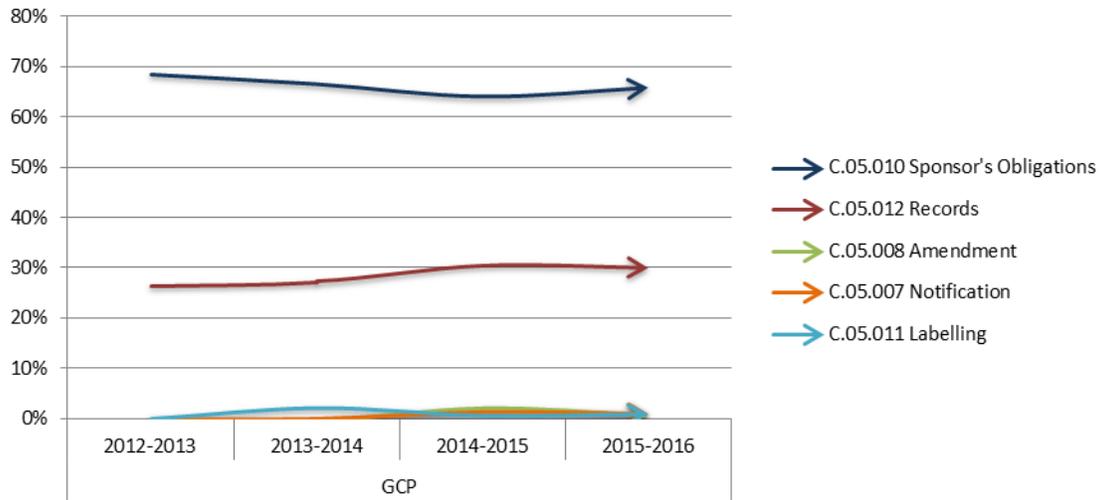
## Four-year inspection trend

**Figure 4.3** shows the four-year trend for GCP inspections. The number of GCP inspections has been relatively constant.



**Figure 4.3** Number of GCP inspections across Canada over the last four years (2012–2016).

**Figure 4.4** shows the four-year trend for GCP observations. The trends do not vary greatly. Sponsor Obligations and Records continue to be the areas where most observations are cited.



**Figure 4.4** Most common observations over the last four years (2012–2016)

## CHAPTER 5

### DRUG GOOD MANUFACTURING PRACTICES INSPECTION PROGRAM (GMP)

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#### Overview

The Inspectorate conducted **440 domestic good manufacturing practices (GMP) inspections** in 2015–2016, and made **2,353 observations**. Most observations were cited against requirements for Quality Control (C.02.015) and Manufacturing Control (C.02.011-12). Of these observations, 23 were critical, 1,336 were major and 994 were minor. The Inspectorate also conducted **1,525 drug foreign site paper assessments** and **16 foreign on-site GMP inspections**.

#### Background

Health Canada inspects drug establishments against GMP requirements to verify that safety and quality standards are met before drugs are sold to Canadians. In Canada, GMP is regulated under Part C, Division 2 of the *Food and Drug Regulations*. Establishments must comply with GMP requirements outlined in these regulations to obtain an establishment licence.

#### Inspection cycles

The Inspectorate aims to perform an initial on-site inspection of a domestic establishment within three months of receiving a complete Drug Establishment Licence Application. It then conducts a regular inspection within 12 months of the initial inspection.

After that, the date of further inspections depends on the activities being conducted by the establishment. Generally, fabricators, packagers/labelers, and testing labs are inspected on a two to three-year cycle. Importers, wholesalers and distributors are inspected on a three to four-year cycle. If an establishment is conducting multiple activities at the same time, the higher risk activity dictates the inspection cycle.

#### Active pharmaceutical ingredients

In 2014–2015, Health Canada implemented an inspection program for active pharmaceutical ingredients (APIs) to verify whether establishments were complying with the new API regulations. Regulating active pharmaceutical ingredients in Canada helps increase the quality and safety of drugs for consumers. It also strengthens the pharmaceutical drug supply system in Canada and will bring Canada in line with international regulatory partners.

Health Canada conducted a number of compliance promotion visits with industry to inform them about the amended regulatory framework and provide guidance on GMP inspections.

Recognizing the complexity and interconnectedness of API global supply chains, Health Canada continues to collaborate with

#### Active pharmaceutical ingredients:

Active ingredients are the substances in drugs that are responsible for the beneficial health effects experienced by consumers. The active ingredient in a pharmaceutical drug is called an active pharmaceutical ingredient (API).

regulatory partners on different initiatives to harmonize strategies, share best practices and conduct joint inspections.

## Foreign reviews and inspections

Given the global nature of the drug manufacturing business, many drug products available on the Canadian market are manufactured outside of Canada.

Health Canada establishes Mutual Recognition Agreements (MRA) with many countries from around the world. A MRA is a legal agreement that recognizes the equivalency of the drug GMP program between regulatory authorities. Once MRA agreements are in place, the import of drugs from MRA countries is made easier by exchanging certificates of compliance instead of conducting full paper reviews or on-site inspections.

Health Canada is also a member in the Pharmaceutical Inspection Cooperation Scheme (PIC/S). PIC/S is another important international forum for like-minded regulators to discuss and share information and advance issues of mutual interest with respect to the application of GMP.

For non-MRA countries, Health Canada reviews the inspection reports of trusted regulatory partners to verify that foreign sites comply with GMP when they fabricate, package/label or test drugs to be imported into Canada. If inspection reports are not available for a foreign site, or if an importer requests it, Health Canada may conduct a foreign on-site inspection.

Foreign establishments must comply with GMP requirements in order to be added to a Canadian importer's establishment licence so their product may be sold in Canada. The Inspectorate conducted 1,525 paper assessments and 16 on-site inspections of foreign establishments involved in the fabrication, packaging/labelling and testing of drugs in 2015–2016. Of the 16 foreign on-site inspections, all received a compliant rating except for 4 sites (2 received a non-compliant rating and 2 were not rated because the inspections were to verify corrective and preventive actions).

Health Canada expects to increase the total number of foreign on-site inspections over the coming years. Health Canada will work with international regulatory partners to plan using site risk profiles and conduct foreign on-site inspections of the higher risk facilities. This risk-based approach will help promote an appropriate level of regulatory oversight, efficient and effective use of resources, and a collaborative global approach for compliance and enforcement actions.

## Data integrity

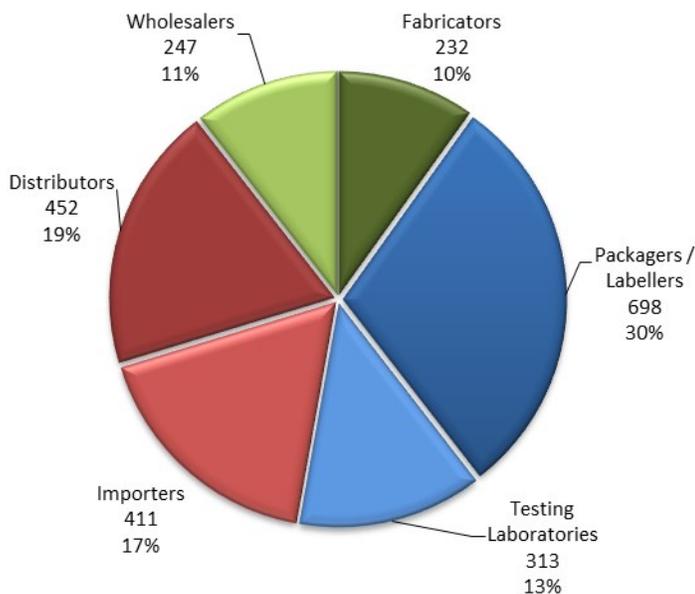
In 2015–2016, data integrity issues were noted during inspections of establishments both domestically and globally. Data integrity confirms that the data and records produced during manufacturing are accurate, complete and intact. In other words, data integrity acts as evidence that drugs are safe, effective and of high quality. Regulated parties are required to demonstrate that data integrity is intact at their establishments as well as those they are linked through contractual agreements. An ongoing focus on data integrity signal detection and analysis allows the Inspectorate to take appropriate regulatory action in situations where data integrity may be an issue. Any potential for compromising the

reliability of data is a risk that should be identified and understood by companies in order for them to take appropriate corrective and preventative actions. These actions are reviewed and assessed by Health Canada. It is important to note that data integrity issues do not necessarily mean that there is a risk to the health of Canadians. If such a risk is identified, Health Canada will take immediate action.

## Inspection results and statistics

In 2015–2016, the Inspectorate conducted 440 domestic inspections of establishments involved in fabricating, packaging/labelling, testing, importing, distributing and wholesaling drugs listed in Table II, Section C.01A.008 of the *Food and Drug Regulations*. Of these inspections, 411 resulted in a compliant rating, 20 were rated non-compliant and 9 were not rated. These were initial inspections that were not rated because it was determined on-site that the company was not ready to conduct licensable activities and a full inspection could not be completed.

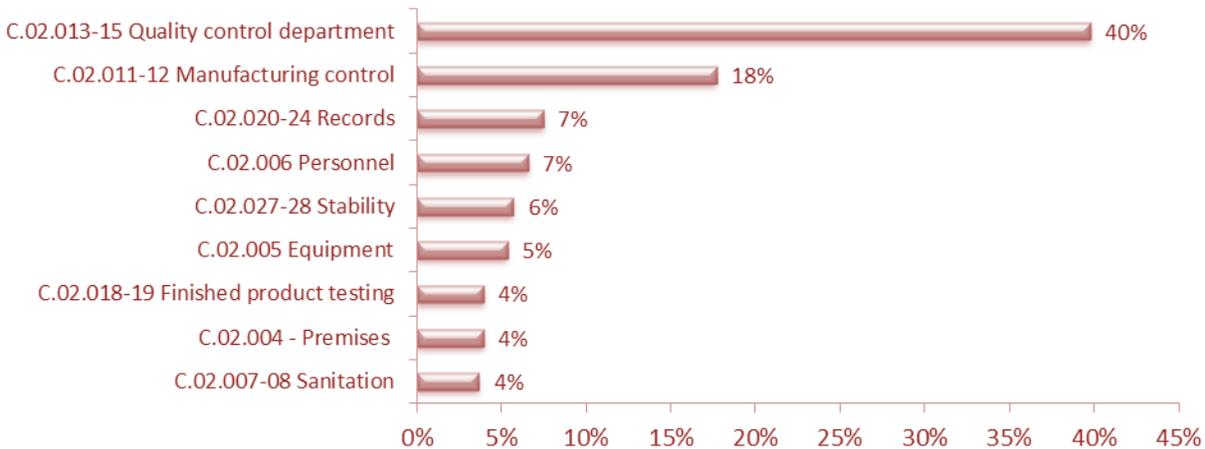
Since one establishment may be licensed for multiple activities, the total number of domestic licence holders for each activity in **Figure 5.1** is higher than the total number of establishments.



**Figure 5.1** Proportion of domestic Drug Establishment Licence holders by activity.

## Most common observations

Inspectors noted 2,353 observations during 440 GMP inspections in 2015–2016. Most observations were cited against requirements for the Quality Control Department (C.02.013-15) and Manufacturing Control (C.02.011-12), as shown in **Figure 5.2**. Examples of these observations are listed in **Table 5.1**.



**Figure 5.2** Sections of the *Food and Drug Regulations* most often cited, as a percentage of the total number of observations cited during GMP inspections across Canada in 2015–2016.

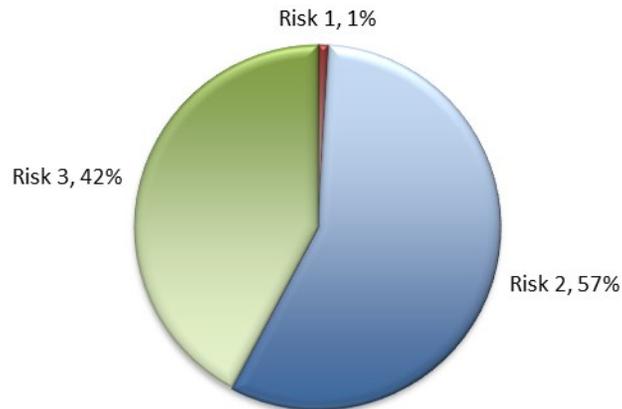
**Table 5.1 – Examples of common observations cited**

<i>Food and Drug Regulations</i>	Example of observations
<b>C.02.013–15 Quality control department</b>	<ul style="list-style-type: none"> <li>Segregation and identification of quarantined and released drug products at the warehouse offered potential for mix-up as both quarantined and released product were stored in the same location, and not all skids of product were identified as to their shipment (sublot) or quarantine/release status.</li> <li>A written change control procedure is required that describes the action to be taken if a change is proposed to facilities, materials, equipment and processes used in fabrication, packaging and testing of drugs or any change that may affect quality or support system operation noting that any significant change may necessitate re-validation.</li> </ul>
<b>C.02.011–12 Manufacturing control</b>	<ul style="list-style-type: none"> <li>A written and comprehensive self-inspection program had not been devised, nor were any of the personnel suitably trained or qualified in GMP, to carry-out regular periodic self-inspections.</li> <li>The computer system inventory adjustment “transfer” did not indicate the transaction /rationale e.g. returned to manufacturer, outdated/ short dated stock or inventory deviation. There was no written procedure for inventory counts including a requirement to document and investigate discrepancies between physical and computer inventory.</li> </ul>
<b>C.02.020–24 Records</b>	<ul style="list-style-type: none"> <li>Records of product re-packaging performed at the warehouse were available but were incomplete in that they did not always include packaging orders, document the quantity and lots of the product that were packaged, and were not signed by the warehouse supervisor or reviewed by quality assurance.</li> <li>Deficiencies were noted with the demonstration of consistent results for all critical production processes. There was no evidence that the critical manufacturing and packaging processes produced consistent results for each product. An evaluation was presented for only one formulation produced by manufacturer/packager site.</li> </ul>

**Table 5.1** Examples of GMP inspection observations, from the sections of the *Food and Drug Regulations* most often cited in 2015–2016.

## Observation risk ratings

In 2015–2016, 2,353 observations were noted during the 440 domestic inspections conducted. As shown in **Figure 5.3**, 1% (23 observations) were classified as Risk 1 (critical), 57% (1,336) were classified as Risk 2 (major) and 42% (994) were classified as Risk 3 (minor).

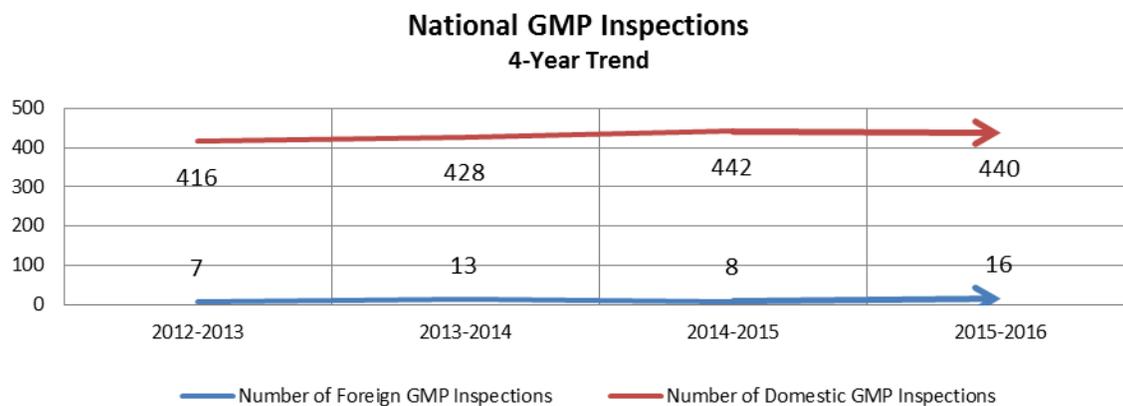


**Figure 5.3** Distribution of risk ratings for observations noted during GMP inspections across Canada in 2015–2016.

The highest number of Risk 1 (critical) observations—nineteen (19)—was recorded under Quality Control (C.02.013-013, C.02.013-014 and C.02.013-015).

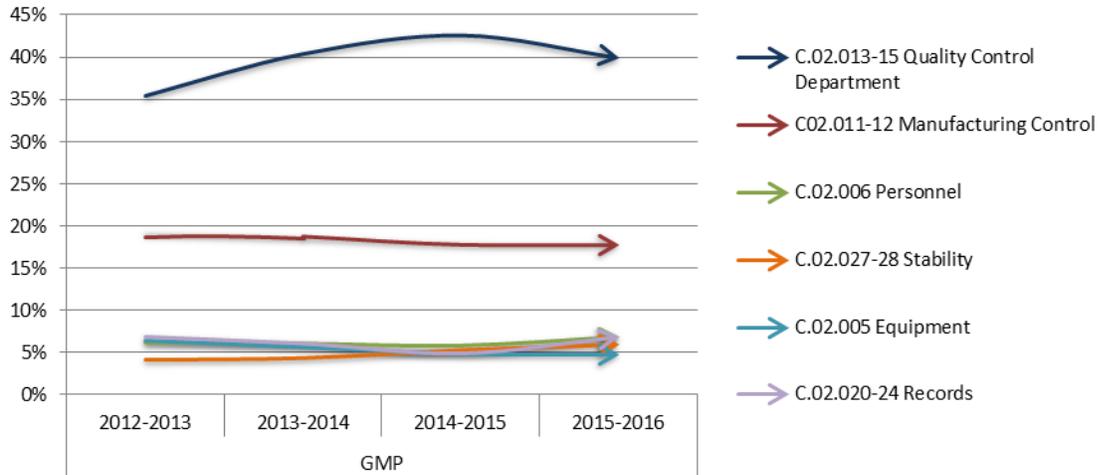
## Four-year inspection trend

**Figure 5.4** shows the four-year trend for both domestic and foreign GMP inspections. Domestic inspections have increased over the prior three years and levelled off in 2015-2016 as there has been no net increase in the number of establishments. Foreign inspections have remained steady, with a slight increase in 2013–2014 and again in 2015-2016.



**Figure 5.4** The four-year trend for GMP inspections.

**Figure 5.5** shows the four-year trend of *Food and Drug Regulations* sections against which observations were cited. Most GMP observations were cited against Quality Control (C.02.013-015) and Manufacturing Control (C.02.011 and C.02.012). The next four categories total 25% of all observations. Overall, GMP observations are trending down, indicating that compliance with previously problematic areas of GMP is improving.



**Figure 5.5** Most common observations over the last four years (2012–2016)

## CHAPTER 6

### DRUG GOOD PHARMACOVIGILANCE PRACTICES INSPECTION PROGRAM (GVP)

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#### Overview

The Inspectorate conducted **42 good pharmacovigilance practices (GVP) inspections** in 2015–2016, and made **172 observations**. Most observations were cited against requirements for Serious Adverse Drug Reaction Reporting (C.01.017) and Annual Summary Report and Case Reports (C.01.018). Of these observations, 88 were major and 84 were minor. No critical observations were made.

#### Background

The GVP inspection program verifies that manufacturers comply with sections C.01.016 to C.01.020, C.08.007(h) and C.08.008(c) of the *Food and Drug Regulations*.

As part of these requirements, manufacturers must report adverse drug reactions (ADR) and unusual failure in the efficacy of new drugs. Manufacturers must also have and maintain a rigorous ADR management program. This includes issuing annual summary reports to analyze whether there has been a significant change in what is known about the risks and benefits of a marketed drug.

Domestic market authorization holders and importers of drug products are both subject to GVP inspections. Since the names of market authorization holders and importers appear on product labels, they may receive ADR reports from other companies, healthcare practitioners or consumers.

The following health products marketed in Canada for human use are subject to GVP inspections:

- pharmaceuticals
- biologics (including biotechnology products)
- vaccines and fractionated blood products
- medical gases
- radiopharmaceuticals

#### **Adverse drug reaction (ADR):**

An unexpected or dangerous reaction to a health product. An unwanted effect caused by the administration of a health product.

#### **Pharmacovigilance:**

The practice of monitoring the effects of health products after they have been licensed for use, to identify and evaluate adverse reactions.

#### **Unusual failure in efficacy:**

When a health product fails to produce the expected intended effect, and there may be an adverse outcome for the patient (including a worsening of the condition the health product is intended to treat).

## Inspection cycles

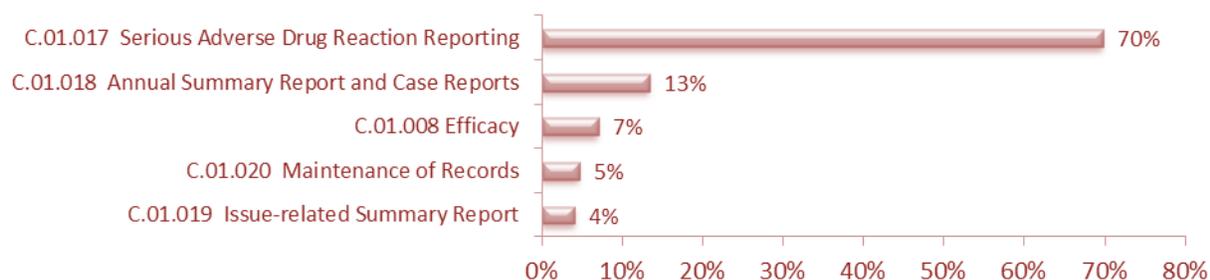
The Inspectorate selects establishments for GVP inspection based on several criteria, including the compliance history of the establishment, information about the health product, and reported adverse drug reactions. The length of these inspections varies depending on the type of activities, the number of health products and the number of reported ADRs.

## Inspection results and statistics

In 2015–2016, 42 GVP inspections were conducted. All but one of the establishments was found to be in compliance at the time of inspection.

### Most common observations

Inspectors noted 172 observations during 42 GVP inspections in 2015–2016. Most observations were cited against requirements for Serious Adverse Drug Reaction Reporting (C.01.017), Annual Summary Report and Case Reports (C.01.018), and Efficacy (C.01.008), as shown in **Figure 6.1**.



**Figure 6.1** Sections of the *Food and Drug Regulations* most often cited, as a percentage of the total number of observations cited during GVP inspections across Canada in 2015–2016.

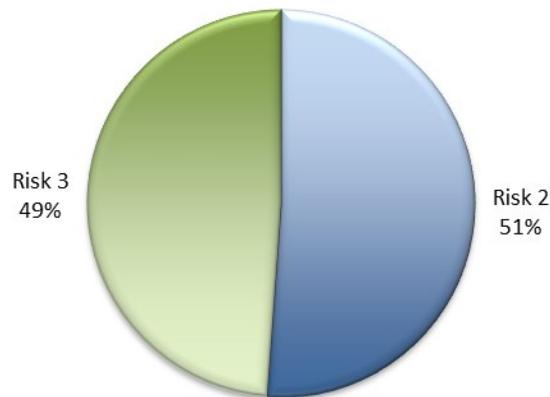
**Table 6.1 – Examples of common observations cited**

<i>Food and Drug Regulations</i>	Example of observations
<b>C.01.017 Serious Adverse Drug Reaction Reporting</b>	<ul style="list-style-type: none"> <li>The systems and processes for receiving, handling, evaluating, and reporting adverse drug reactions were inadequate.</li> <li>The company's processes for inspecting its own pharmacovigilance system were inadequate.</li> <li>The company lacked systems and processes for conducting literature searches.</li> </ul>
<b>C.01.018 Annual Summary Report and Case Reports</b>	<ul style="list-style-type: none"> <li>The annual summary reports were incomplete.</li> <li>The company did not always prepare an annual summary report each year for each drug marketed in Canada.</li> <li>The systems and processes for preparing annual summary reports were inadequate.</li> </ul>

**Table 6.1** Examples of GVP inspection observations, from the sections of the *Food and Drug Regulations* most often cited in 2015–2016.

## Observation risk ratings

In 2015–2016, 172 observations were noted during 42 inspections. As shown in **Figure 6.2**, 51% (88) were given a Risk 2 (major) rating. The other 49% (84) were given a Risk 3 (minor) rating. No Risk 1 (critical) observations were noted. Corrective actions proposed in response to the observations were found to be acceptable in all cases.



**Figure 6.2** Distribution of risk ratings for observations noted during GVP inspections across Canada in 2015–2016.

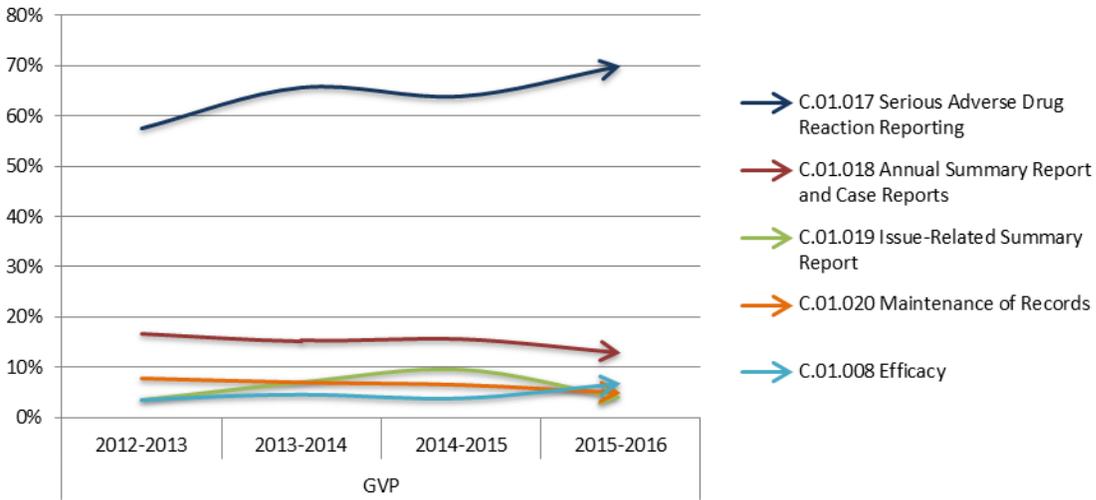
## Four-year inspection trend

**Figure 6.3** shows the four-year trend for GVP. Over the past two years, inspection numbers have dropped due to a new approach being taken for GVP inspections. As of 2014–2015, inspections have become more in-depth and now include the review of more systems (such as the establishment’s self-inspection program and validation of computerized systems). Also, site selection is conducted using a risk-based approach where higher-risk establishments are prioritized for inspection, which can lead to longer inspection timeframes.



**Figure 6.3** Number of GVP inspections across Canada over the last four years (2012–2016).

**Figure 6.4** shows the four-year trend for GVP observations. Most GVP observations were made against Serious Adverse Drug Reaction Reporting. The trends are fairly static with the exception of observations related to Serious Adverse Drug Reaction Reporting trending upwards.



**Figure 6.4** Most common observations over the last four years (2012–2016).

## CHAPTER 7

### MEDICAL DEVICES INSPECTION PROGRAM (MD)

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#### Overview

The Inspectorate conducted a total of **494 medical device inspections** of which **449 were domestic inspections** and **45 foreign remote paper-based inspections** in 2015–2016, and made **2,297 observations**. Most observations were cited against requirements for Recall Procedure (MDR s. 58(b)) and Investigation Procedure (MDR s.58(a)). Of these observations, 8 were critical, 1,377 were major and 912 were minor.

#### Background

In Canada, the importation, sale and advertising of medical devices is regulated under the *Food and Drugs Act* and the *Medical Devices Regulations* (MDR). Health Canada inspects medical device establishments to verify their compliance with the *Food and Drugs Act* and MDR. This helps to ensure that medical devices are safe and effective before they are sold to Canadians.

Before selling a device in Canada, manufacturers of Class II, III and IV devices must get a medical device licence from Health Canada. Although Class I devices do not require a device licence, their manufacturers are subject to medical device establishment licensing (MDEL) requirements. Importers and distributors of all classes of device are also subject to MDEL requirements.

#### Inspections

MDEL holders are inspected by Health Canada inspectors. The inspection cycle for MDEL holders is as follows: every 3 years for manufacturers, every 4 years for importers and every 5 years for distributors. Companies conducting multiple activities are inspected according to their highest risk activity.

#### Inspection results and statistics

In 2015–2016, 494 inspections were conducted. Of these, 491 resulted in an overall compliant rating for the establishment and 3 resulted in a non-compliant rating.

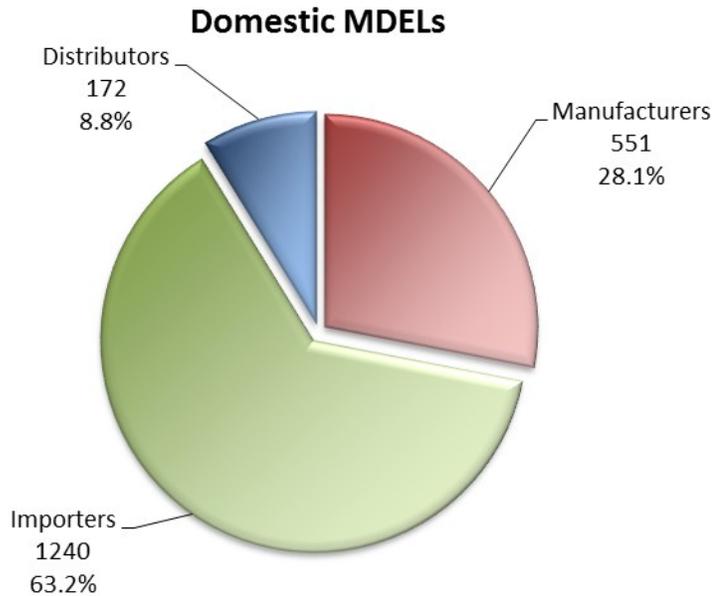
#### Medical device:

Products used in the treatment, diagnosis or prevention of a disease or abnormal physical condition. Examples include pacemakers, hip implants, dentures, test kits for diagnosis, and condoms.

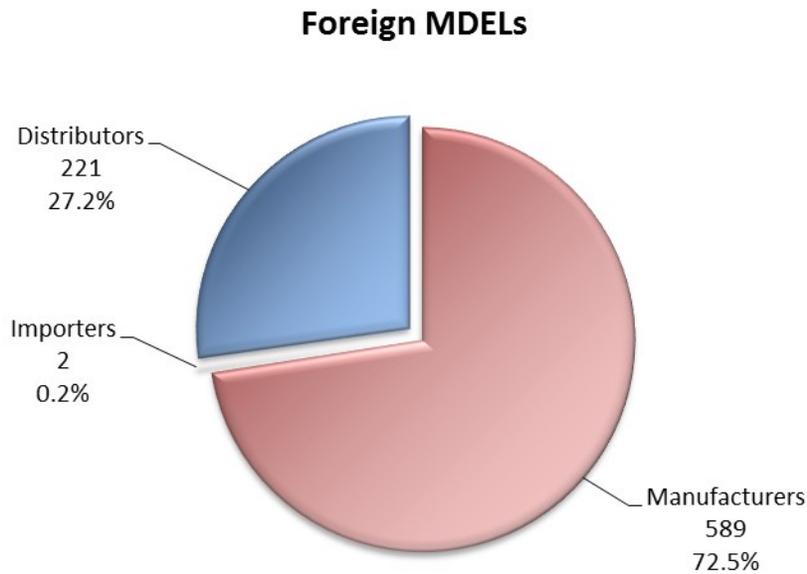
#### Medical device classes:

Medical devices are categorized into four classes by the level of health risk related to their use. Class I devices present the lowest potential risk (e.g. a thermometer). Classes II and III present mid-level risks. Class IV devices present the greatest potential health risk (e.g. pacemakers).

As of September 2016, there were 2,775 MDEL holders: 1,963 domestic and 812 foreign. The number of MDEL holders continually fluctuates because of licence withdrawals/cancellations and the issuance of MDELS to new applicants. **Figure 7.1** shows the proportion of domestic licence holders identified as manufacturers, importers and distributors. **Figure 7.2** shows the proportion of foreign licence holders identified as distributors, manufacturers and importers.



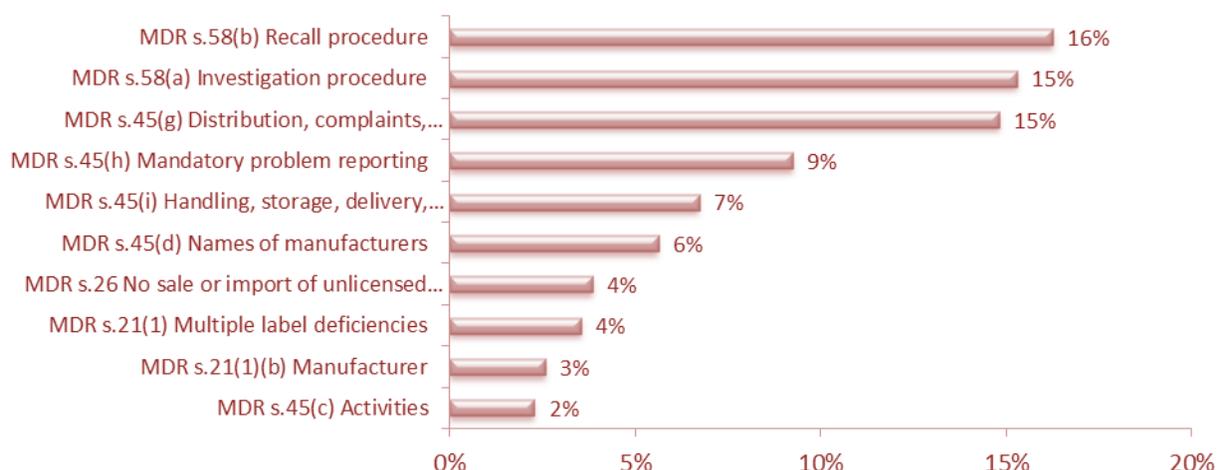
**Figure 7.1** Proportion of domestic MDEL holders who are manufacturers, importers and distributors.



**Figure 7.2** Proportion of foreign MDEL holders who are manufacturers, importers and distributors.

## Most common observations

Inspectors noted 2,297 observations during 494 medical device inspections in 2015–2016. About half (55%) of these observations were cited against four sections of the *Medical Devices Regulations*. As shown in **Figure 7.3**, most observations were related to deficiencies in documentation relating to recall procedures (MDR s. 58(b)), the investigation of complaints (MDR s.58(a)), complaint handling and recalls (MDR s.45(g)), and mandatory problem reporting (MDR s. 45(h)). Examples of these observations are shown in **Table 7.1**.



**Figure 7.3** Sections of the *Medical Devices Regulations* most often cited, as a percentage of the total number of observations cited during medical device inspections in 2015–2016.

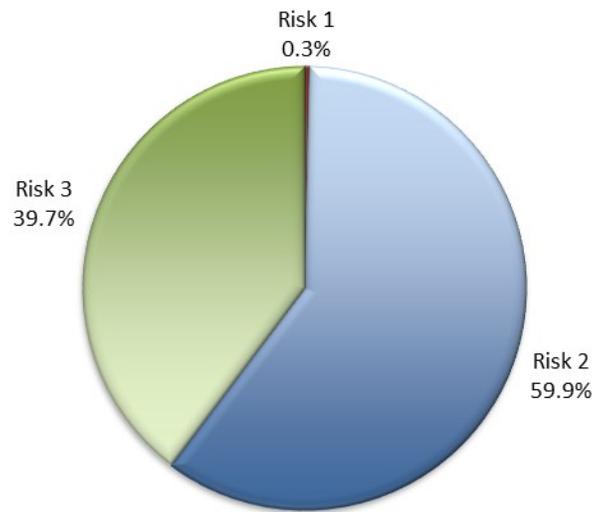
**Table 7.1 – Examples of common observations cited**

<i>Medical Devices Regulations</i>	Example of observations
<b>MDR s. 58(b) Recall procedure for the effective and timely recall of device</b>	<ul style="list-style-type: none"> <li>The documented procedure, "Recall", does not contain sufficient information to ensure effective and timely recall of devices.</li> </ul>
<b>MDR s. 45(g) Documented procedures for distribution records, complaint handling and recalls</b>	<ul style="list-style-type: none"> <li>The procedure titled "Distribution Records" is inadequate.</li> <li>The company's procedure for maintenance of distribution records, does not adequately address the requirements of the following sections of the <i>Medical Devices Regulations</i>:               <ul style="list-style-type: none"> <li>- s.53 Record shall contain sufficient information to permit complete and rapid withdrawal</li> <li>- s.56 Timely retrieval</li> </ul> </li> </ul>
<b>MDR s. 58(a) Investigation procedure</b>	<ul style="list-style-type: none"> <li>The complaint handling procedure is inadequate. The following information is not included: a time frame, based on risk for the investigation of the problems referred to in Section 57(1)(b) and corrective actions in relation to device safety and efficacy.</li> </ul>

**Table 7.1** Examples of medical device observations, from the sections of the *Medical Devices Regulations* most often cited in 2015–2016.

## Observation risk ratings

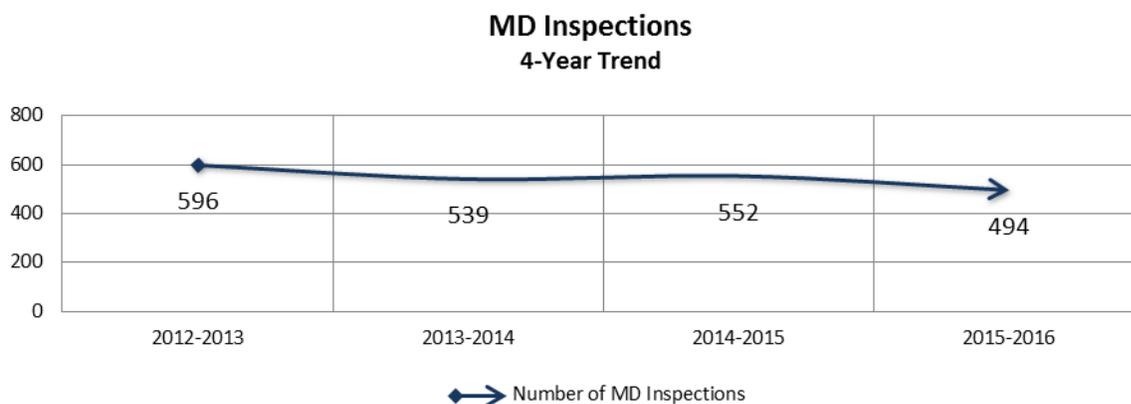
As shown in **Figure 7.4**, 59.9% (1,377) observations were Risk 2 (major) and 39.7% (912) were Risk 3 (minor). Only 0.3% (8) were Risk 1 (critical). The eight Risk 1 observations were cited for deficiencies in prohibition of misrepresentation (Act s.20(1)), manufacturer labels (MDR 2.21(1)(b)), no sale or import of an unlicensed device (MDR s.26), distribution records (MDR s.52(1)) and sufficient product withdrawal (MDR s.53).



**Figure 7.4** Distribution of observations noted during medical device establishment inspections in 2015–2016, classified by their risk rating.

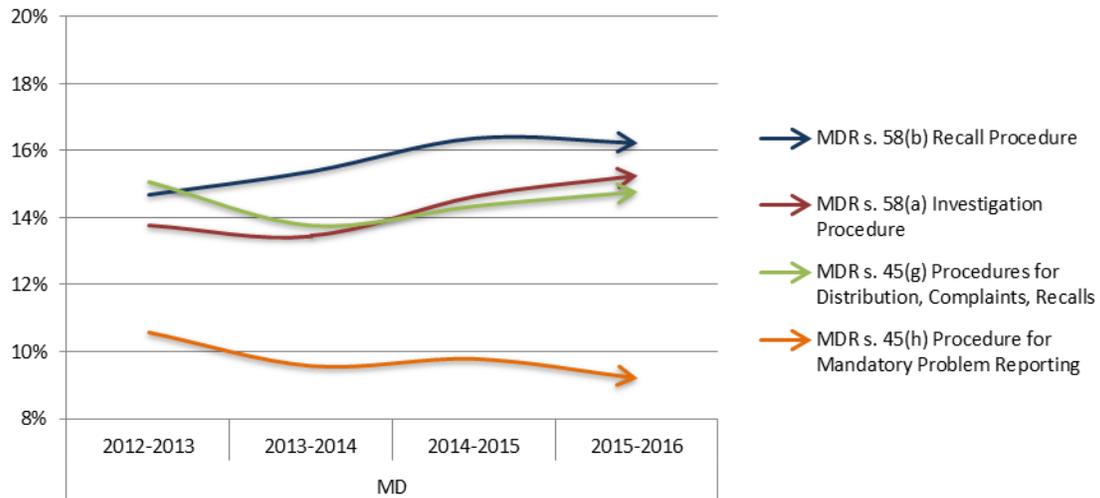
## Four-year inspection trend

**Figure 7.5** shows the four-year trend for medical device inspections. The number of inspections over the previous three years (2012 – 2015) did not change significantly, and the decline in inspection numbers in 2015-2016 compared to 2014-2015 does not show a discernable downtrend trend.



**Figure 7.5** Number of medical device establishment inspections over the last four years (2012–2016).

**Figure 7.6** shows the four-year trend for medical device observations. The three most-observed categories have remained the same over three years. In 2013–2014, 2014–2015 and 2015–2016, the dominant observation is Recall Procedures (MDR s.58(b)). Procedures for Mandatory Problem Reporting (MDR s. 45(h)) has steadily declined.



**Figure 7.6** Most common observations over the last four years (2012–2016).

Note that MDR s.58(b) requires that a procedure be established to ensure a timely and effective recall. MDR s.45(g) is a more general observation that deals with the recall procedure itself.

## APPENDIX 1 – CONTACT INFORMATION

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<p><b>Health Product Compliance</b></p> <p>200 Eglantine Driveway AL 1913B Ottawa ON K1A 0K9 Tel: (613) 957-6836 Email: <a href="mailto:HPC-CPSCorrespondence@hc-sc.gc.ca">HPC-CPSCorrespondence@hc-sc.gc.ca</a></p>	<p><b>Medical Devices and Clinical Compliance</b></p> <p>200 Eglantine Driveway AL 1914A Ottawa ON K1A 0K9 Tel: (613) 941-3387 Email: <a href="mailto:MDCCD-DCMMMCCorrespondence@hc-sc.gc.ca">MDCCD-DCMMMCCorrespondence@hc-sc.gc.ca</a></p>
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## APPENDIX 2 – REFERENCES

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Drug and Health Product Inspection Database - <http://www.healthycanadians.gc.ca/drugs-products-medicaments-produits/inspecting-monitoring-inspection-controle/inspections/index-eng.php>

### Chapter 1 – Blood Inspection Program

#### *Blood Regulations*

*Blood Regulations* Guidance Document (GUI-0113)

Compliance and Enforcement Policy (POL-0001)

#### *Food and Drugs Act*

Inspection Strategy for Blood and Source Plasma Establishments (POL-0039)

Risk Classification of Observations made during Inspections of Blood Establishments (GUI-0061)

### Chapter 2 – Cells, Tissues and Organs Inspection Program

Compliance and Enforcement Policy (POL-0001)

#### *Food and Drugs Act*

Guidance Document for Cells, Tissues and Organs Establishments – Safety of Human Cells, Tissues and Organs for Transplantation

Guidance on Classification of Observations for Inspection of Cells, Tissues and Organs Establishments (GUI-0101)

Inspection Strategy for Cells, Tissues and Organs Establishments (POL-0057)

*Safety of Human Cells, Tissues and Organs for Transplantation Regulations*

### Chapter 3 – Donor Semen Inspection Program

Compliance and Enforcement Policy (POL-0001)

#### *Food and Drugs Act*

Guidance on Donor Semen Special Access Programme: Donor Semen Eligible for Special Access

Guidance on the Processing and Distribution of Semen for Assisted Conception Regulations (GUI-0041)

Health Canada Directive: Technical Requirements for Therapeutic Donor Insemination

Inspection Strategy for Semen Establishments (POL-0023)

*Processing and Distribution of Semen for Assisted Conception Regulations*

Risk Classification of Observations to Donor Semen Establishments (GUI-0053)

### Chapter 4 – Drug Good Clinical Practices Inspection Program

Drugs Used in Clinical Trials (GUI-0036)

#### *Food and Drug Regulations*

#### *Food and Drugs Act*

Guidance Document – Annex 13 to the Current Edition of the Good Manufacturing Practices Guidelines

Guidance on the Retention of Records for Clinical Trials (GUI-0068)

International Conference on Harmonization (ICH) Guidance, Topic E6 (ICH E6)

Inspection Strategy for Clinical Trials (POL-0030)

Risk Classification of Observations in Clinical Trials (GUI-0043)

## **Chapter 5 – Drug Good Manufacturing Practices Inspection Program**

Compliance and Enforcement Policy (POL-0001)

Drug Establishment Good Manufacturing Practices Pre-Application Package (Importers, Distributors and Wholesalers)

GMP and Establishment Licencing Enforcement Directive (POL-0004)

GMP Inspection Policy for Canadian Drug Establishments (POL-0011)

Good Manufacturing Practices (GMP) for Active Pharmaceutical Ingredients (APIs) (GUI-0104)

Good Manufacturing Practices (GMP) Guidelines (GUI-0001)

Risk Classification of GMP Observations (GUI-0023)

## **Chapter 6 – Drug Good Pharmacovigilance Practices Inspection Program**

Good Pharmacovigilance Practices (GVP) Guidelines (GUI-0102)

Guidance Document for Industry Reporting Adverse Reactions to Marketed Health Products

ICH Harmonised Tripartite Guideline, Clinical Safety Data Management: Periodic Benefit-Risk Evaluation Report E2C (R2) (2012)

Inspection Strategy for Good Pharmacovigilance Practices (GVP) for Drugs (POL-0041)

International Conference on Harmonisation, Post-Approval Safety Data Management: Definitions and Standards for Expedited Report (ICH E2D) 2003

Risk Classification of GVP Observations (GUI-0063)

## **Chapter 7 – Medical Devices Inspection Program**

*Food and Drugs Act*

Guidance on the Medical Devices Inspection Program (GUI-0064)

*Medical Devices Regulations*

Summary of the Results of the Medical Devices Inspections Program from 2004–2009