Health Canada Santé Canada





Inspectorate Program

Annual Inspection Summary Report 2014–2015

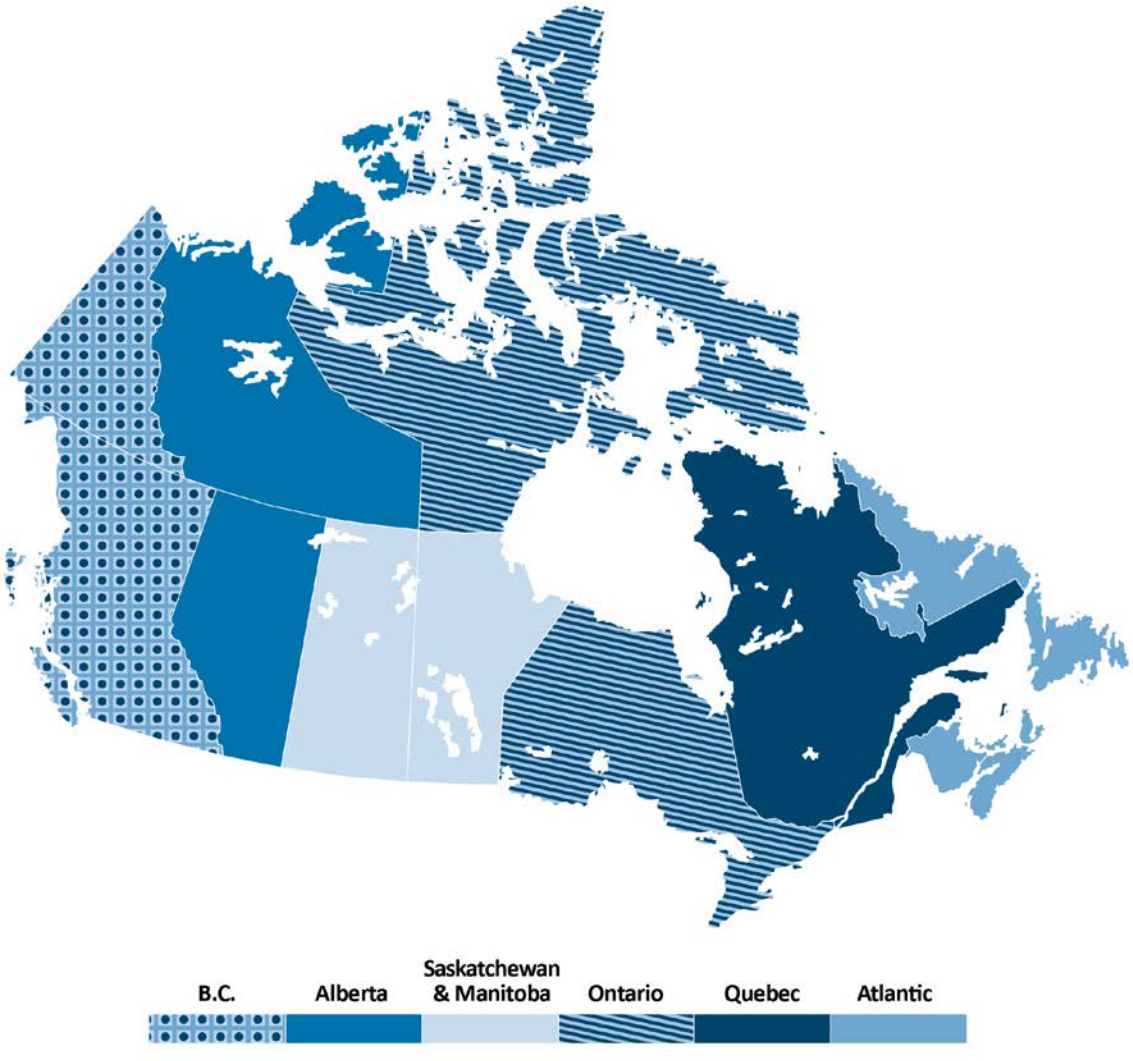
Canada

OUR VISION

To be a trusted national organization committed to regulatory compliance and enforcement activities of health products based on modern risk management decision-making strategies that will effectively contribute to the safety of health products and positively impact the health of Canadians.

OUR MISSION

The primary role of the Inspectorate Program is to deliver a national compliance and enforcement program for health products under the mandate of the Health Products and Food Branch (HPFB), in collaboration with the Regions and Programs Bureau (RAPB).



MESSAGE FROM THE DIRECTORS GENERAL

We are pleased to present Health Canada's 2014–2015 *Annual Inspection Summary Report* for the Inspectorate Program. This third 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 2014–2015, the Inspectorate Program conducted 1,184 on-site inspections in Canada, 8 on-site foreign inspections and 1,563 paper reviews of inspections conducted by our international regulatory partners. Our inspectors made thousands of observations that required companies to take corrective actions.

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.

Developing this report allows the Inspectorate Program to stop and take stock of our inspection work over the past year, to identify key priorities, 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 next year and the years beyond.

Four key areas are currently impacting all facets of the Inspectorate Program's work and will remain top priorities moving forward. For each area, the Inspectorate Program is:

- *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 oversight of establishments deemed to be high risk.

- *Foreign inspection approach* – Enhancing our foreign inspection program in response to the significant 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 international regulatory partners, as no one agency in the world has the resources to inspect all establishments in the global supply chain.

- *Data integrity* – Addressing the emerging issue of data integrity by enhancing the training of inspectors to spot data integrity issues and working with our regulatory partners to align approaches.

We have much 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.

Steven Schwendt
Acting Director General
Health Products and Food Branch Inspectorate
Health Canada

Lucy Butts
Regional Director General
Regions and Programs Bureau
Health Canada

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EXECUTIVE SUMMARY

Health Canada's Inspectorate Program conducted a wide range of compliance and enforcement activities in 2014–2015. 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 2014–2015 fiscal year (from April 1, 2014 to March 31, 2015), 121 inspectors conducted 1,184 on-site inspections in Canada, made thousands of observations that required companies to take corrective actions, and issued 30 non-compliant ratings.

Inspectors also conducted 8 on-site foreign inspections and performed 1,563 paper reviews of inspections conducted by foreign regulatory partners.

Inspectors conducted 1,184 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

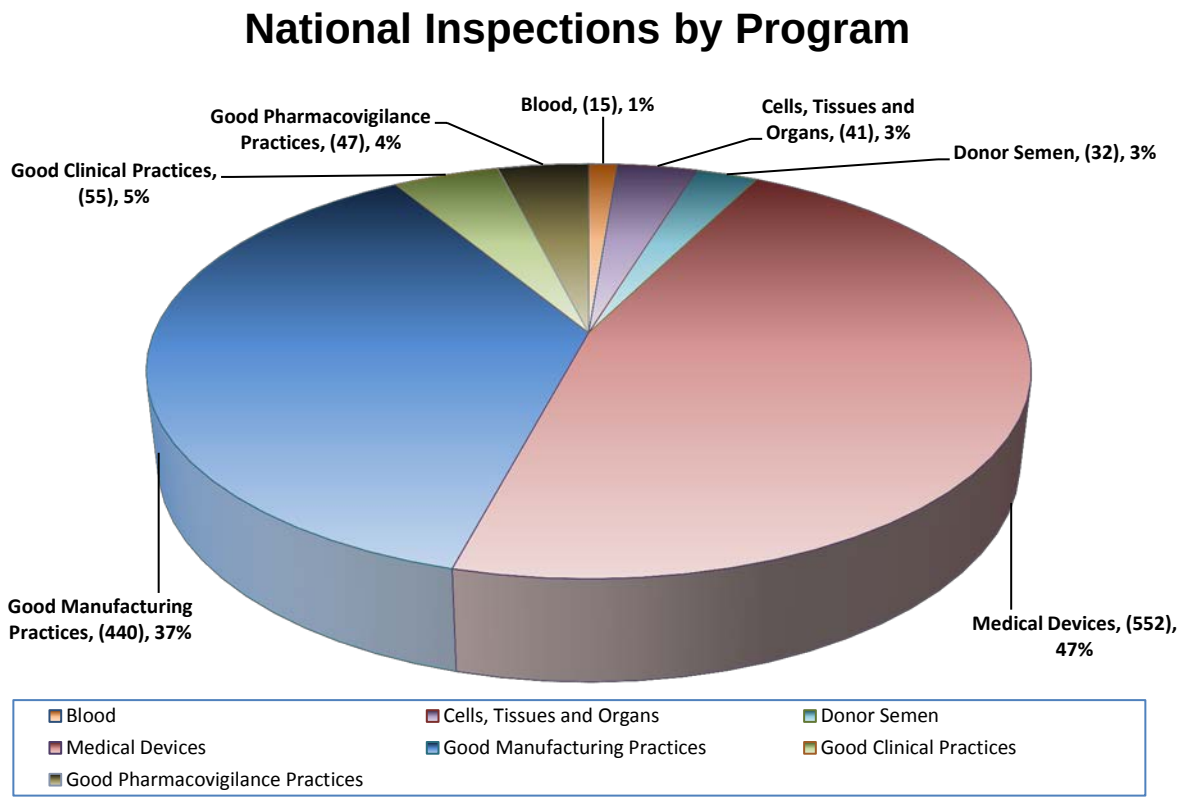

Figure A – National inspections by health product for 2014–2015. The number of inspections for each product type depends on several factors including: the number of regulated establishments, inspection cycles and inspection complexity.

The health product establishments inspected in Canada in 2014–2015 had a very high level of compliance with the *Food and Drugs Act* and Regulations, with an overall rating of 97 percent. The graph below shows overall compliance over the last three years. While Good Clinical Practices shows a downward trend, this is partly attributed to its relatively small program size, the complexity of the clinical trial process and data integrity issues found at a few sites in 2015 (41/55 sites received a compliant rating, which is a 75% compliance rate).

Over the same timeframe, all other programs reached their highest recorded levels of compliance.

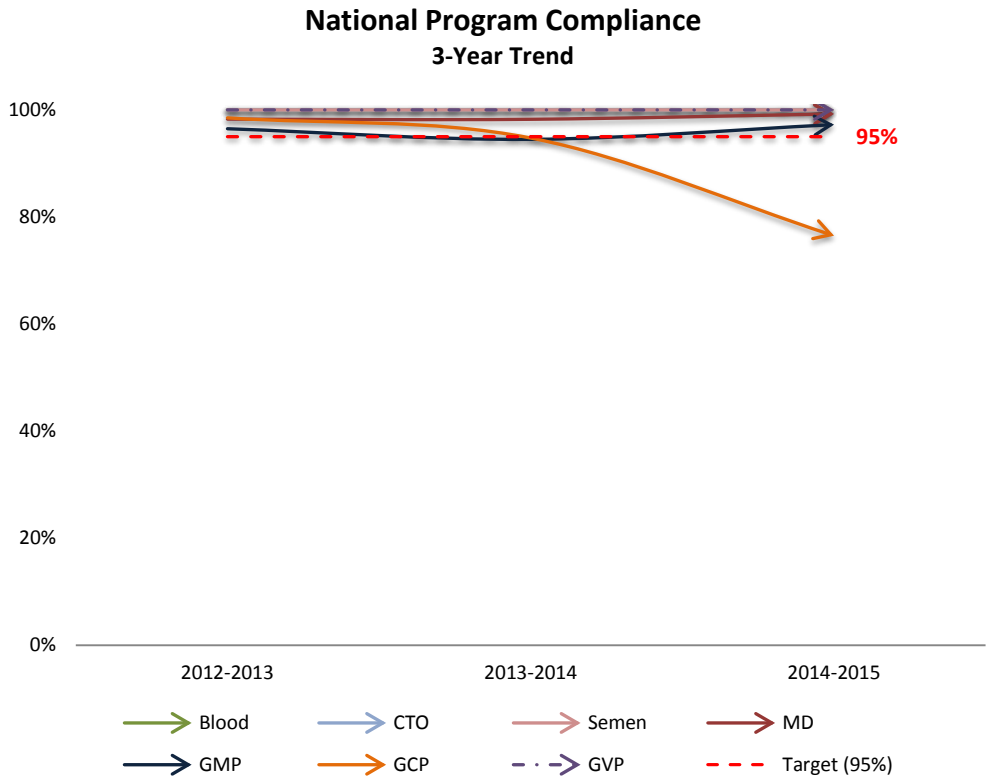

Figure B – National compliance by program from 2012–2013 to 2014–2015.

While this high overall compliance rate is a positive outcome, it does not capture the varying degrees of compliance. Some companies, for example, were highly compliant with very few observations (activities that deviate from the regulations). Other companies 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
- three-year inspection trends

Key priorities

For the 2014–2015 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 2015–2016 fiscal year and beyond:

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

2014–2015 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
Training inspectors to spot data integrity issues

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 advises Canadians of key emerging issues Health Canada has identified during its inspections, and the immediate actions Health Canada is taking (recalls and safety alerts).

The Drug and Health Product Inspections Database allows Canadians for the first time to search the results of inspections and read detailed report cards for over a thousand individual inspections of drug establishments. In the coming year, this database will be expanded to include more types of inspections including clinical trials, medical devices, good pharmacovigilance practices, blood, donor semen, and cells, tissues and organs.

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.hc-sc.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. Over 80 percent 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 are 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 program 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 targeting the highest-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 highest risk facilities. It is expected that the total number of foreign on-site inspections will multiply in the coming years.

Data integrity

In 2014–2015, 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.

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. While risk is defined differently for each type of health product, 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 types of observations, the inspector issues an overall rating of compliant or non-compliant 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, given Canada's high regulatory standards. 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, border restrictions, public advisories
- criminal investigation

Blood inspections

Health Canada inspects establishments that collect human blood for transfusions or for use in human drugs. In 2014–2015, new *Blood Regulations* were introduced leading to a decrease in inspections as efforts focused on promoting the new regulations. For 2014–2015:

- 9 inspectors
- 15 inspections conducted
- 60 observations made
  - 0% critical risks
  - 2% major risks
  - 98% minor risks
- Top observations:
  - records
  - operating procedures
  - facilities
- 100% compliance rate

Cells, tissues & organs inspections

Health Canada inspects cell, tissue and organ (such as kidneys, livers, lungs) establishments to minimize health risks to Canadians receiving transplants. For 2014–2015:

- 9 inspectors
- 41 inspections conducted
- 277 observations made
  - 0% critical risks
  - 10% major risks
  - 90% minor risks
- Top observations:
  - operating procedures
  - records
- 100% 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 2014–2015:

- 9 inspectors
- 32 inspections conducted
- 16 observations made
  - 0% critical risks
  - 25% major risks
  - 75% minor risks
- Top observations:
  - records
  - prohibition
- 100% 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 2014–2015:

- 10 inspectors
- 55 inspections conducted
- 457 observations made
  - 2% critical risks
  - 64% major risks
  - 34% minor risks
- Top observations:
  - records
  - systems and procedures
  - training
- 75% 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. In 2014–2015, Health Canada also launched a new inspection program for active pharmaceutical ingredients. For 2014–2015:

- 49 inspectors
- 442 inspections conducted
- 8 foreign on-site inspections conducted
- 1,507 foreign site paper assessments conducted
- 3,096 observations made
  - 0.6% critical risks
  - 48.4% major risks
  - 51% minor risks
- Top observations:
  - quality control
  - manufacturing control
- 97% compliance rate

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. In 2014–2015, inspections became more in-depth, leading to a decrease in the overall number of inspections. For 2014–2015:

- 10 inspectors
- 47 inspections conducted
- 8 foreign on-site inspections conducted
- 201 observations made
  - 0% critical risks
  - 57.2% major risks
  - 42.8% minor risks
- Top observations:
  - serious adverse drug reaction reporting
  - annual summary report and case report
- 100% compliance rate

Medical devices inspections

Medical devices range from pacemakers, hip implants, and synthetic skin to lab diagnostic instruments. For 2014–2015:

- 49 inspectors
- 552 inspections conducted
- 2,691 observations made
  - 0.1% critical risks
  - 62.6% major risks
  - 37.3% minor risks
- Top observations:
  - recall procedure
  - investigation procedure
  - distribution, complaints and recalls
- 99% compliance rate

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 and veterinary), medical devices, natural health products, blood, donor semen, and cells, tissues and organs.

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

- establishment licensing and registration
- inspections of facilities
- compliance verifications and investigations (including recalls and public advisories)
- work 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.hc-sc.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-based assessments and, at times, performs foreign on-site inspections to verify safety and quality standards are met before health products are sold in Canada. Actions may be taken at the border in partnership with the Canada Border Services Agency to refuse entry or seize non-compliant products.

CHAPTER 1
BLOOD INSPECTION PROGRAM (BLOOD)

Overview

The Inspectorate conducted **15 blood inspections** in 2014–2015. Inspectors made **60 observations** under either the *Food and Drug Regulations* or the new *Blood Regulations* (which came into force on October 23, 2014 and superseded the *Food and Drug Regulations* for the products that fall within its scope). Most observations were cited against requirements for either Records (s.117) or Operating Procedures (s.95). Of these observations, 1 was major and 59 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 centers 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 2014–2015, there were 4 licensed blood establishments with a total of 55 sites across Canada. Fifteen blood inspections were conducted. All establishments were found to be in compliance with the Regulations at the time of inspection.

Most common observations

Inspectors noted 60 observations during 15 blood inspections in 2014–2015. One observation was major and 59 were minor. **Figure 1.1** shows which sections of the *Food and Drug Regulations* were most often cited in observations before the transition to the new regulations. **Figure 1.2** shows which sections of the *Blood Regulations* were most often cited after the transition to these regulations. Most observations were cited against requirements for Records (Section 117) and Operating Procedures (Section 95) under the new *Blood Regulations*. Under the previous regulations, most observations were cited against Manufacturing Control. Example observations under the *Blood Regulations* are listed in **Table 1.1**.

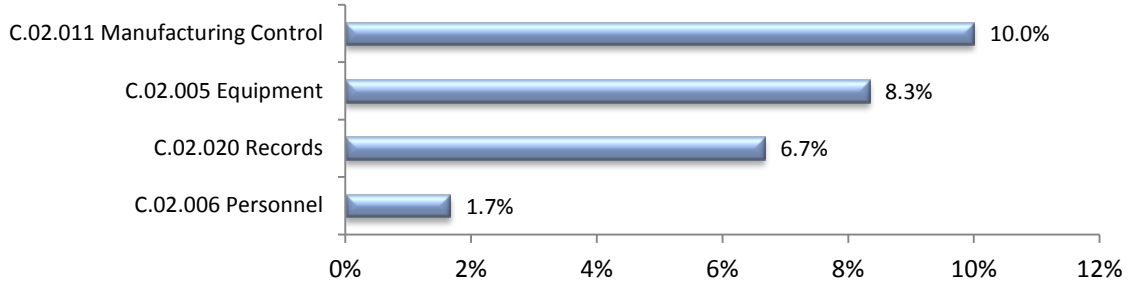

Figure 1.1 Sections of the *Food and Drug Regulations* most often cited, as a percentage of the total number of observations cited during blood inspections in 2014–2015.

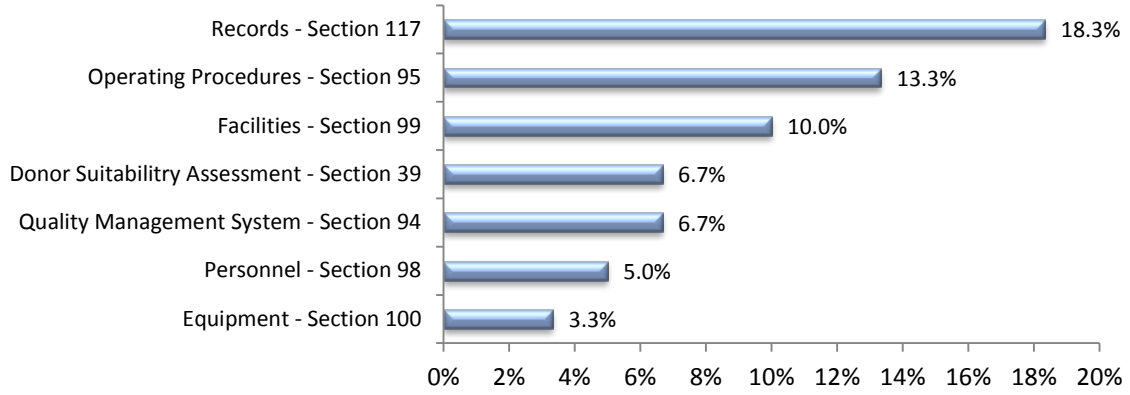

Figure 1.2 Sections of the *Blood Regulations* most often cited, as a percentage of the total number of observations cited during blood inspections in 2014–2015.

Table 1.1 – Examples of common observations cited

Blood Regulations	Example of observations
Records s.117	• Records kept by an establishment were not always accurate, complete, legible, indelible and/or readily retrievable.
Operating Procedures s. 95	• Certain operating procedures were not always followed.
Facilities s. 99	• The establishment's facilities did not have controlled access to some/all areas where its activities were conducted.
Equipment s. 100	• Deficiencies were noted in the validation, calibration, cleaning, and/or maintenance of critical equipment.

Table 1.1 Examples of blood inspection observations, from the sections of the *Blood Regulations* most often cited in 2014–2015.

Observation risk ratings

In 2014–2015, 60 observations were noted during 15 inspections. As shown in **Figure 1.3**, 98.3% (59) were given a Risk 3 (minor) rating, and 1.7% (1) was given a Risk 2 (major) rating. No Risk 1 (critical) observations were noted.

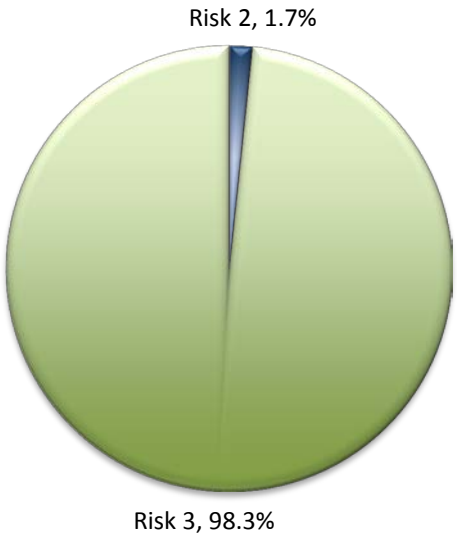

Figure 1.3 Distribution of risk ratings for observations noted during blood inspections across Canada in 2014–2015.

Three-year inspection trend

Figure 1.4 shows the three-year trend for blood inspections. This past year, this program focused on stakeholder engagement and compliance promotion activities to prepare for the implementation of the *Blood Regulations*. Activities included conducting national web conferences, updating public documents, and developing a guidance document to promote the new regulations. As a result, there was a decrease in the number of inspections conducted in 2014–2015.

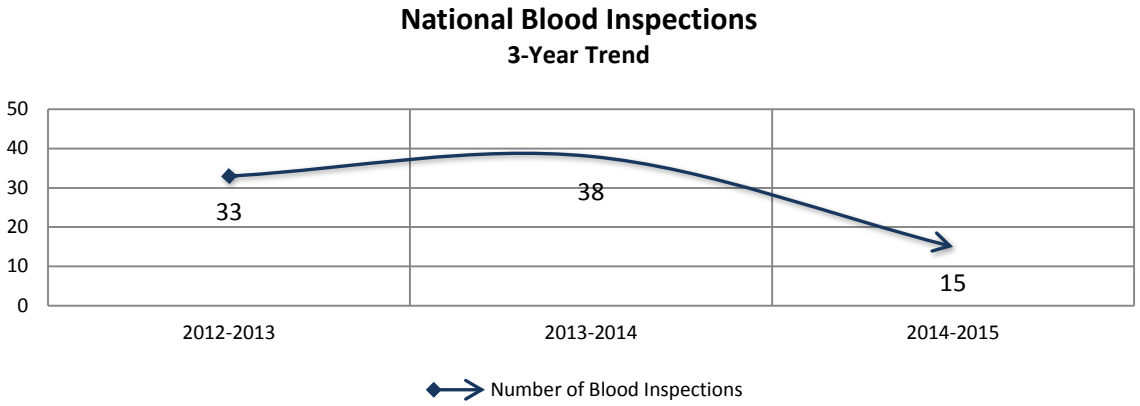

Figure 1.4 Number of blood inspections across Canada over the last three years (2012–2015).

Figures 1.5 and 1.6 show the three-year trend for Blood observations. The switch to the new Blood Regulations in October 2014 requires the inclusion of two graphs to cover the last three years of trending data. **Figure 1.5** captures the first two years and shows a drop in the top observations as the old regulations were phased out and new regulations introduced. **Figure 1.6** covers the third year and captures the top observations under the new regulations.

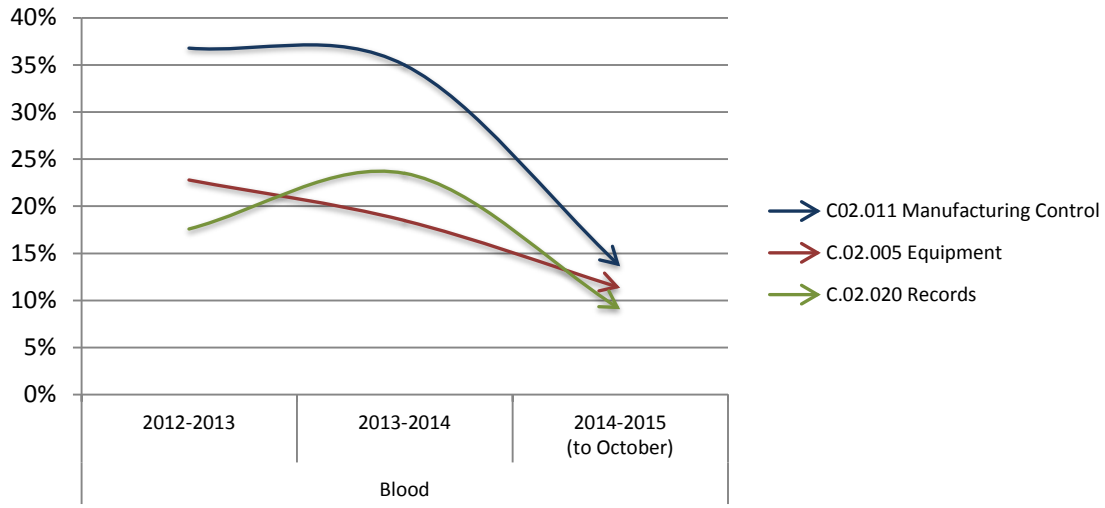

Figure 1.5 Most common observations over the last three years until October 2014, based on the old regulations.

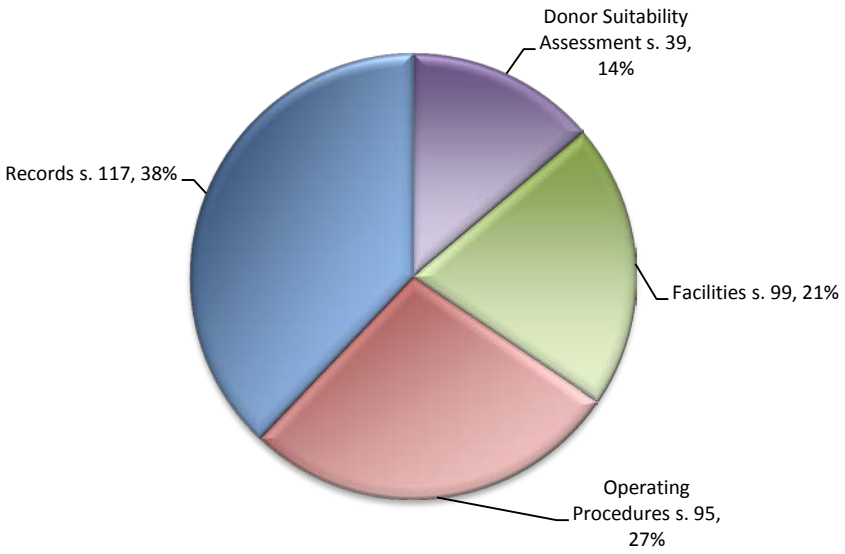

Figure 1.6 Most common observations from October 2014 until March 31, 2015, based on the new regulations.

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

Overview

The Inspectorate conducted **41 cells, tissues and organs (CTO) inspections** in 2014–2015 and made **277 observations**. Most observations were cited against requirements for Quality Assurance Systems and Personnel, Facilities, Equipment and Supplies. Of these observations, 29 were major and 248 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.

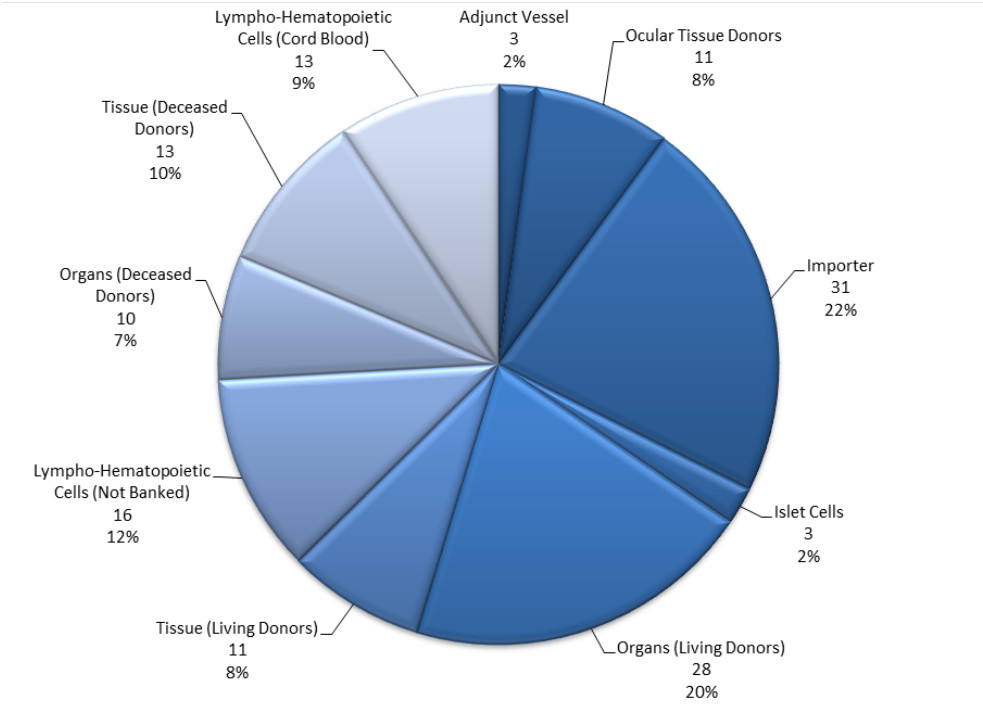

Figure 2.1 Proportion of CTO programs by type in 2014–2015.

As of March 31, 2015, 112 Canadian 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. For consistency in analysis and reporting, 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 41 of the 139 registered Canadian CTO programs were inspected. All programs inspected were found to be in compliance at the time of inspection.

Most common observations

Inspectors noted 277 observations during 41 inspections in 2014–2015. **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**.

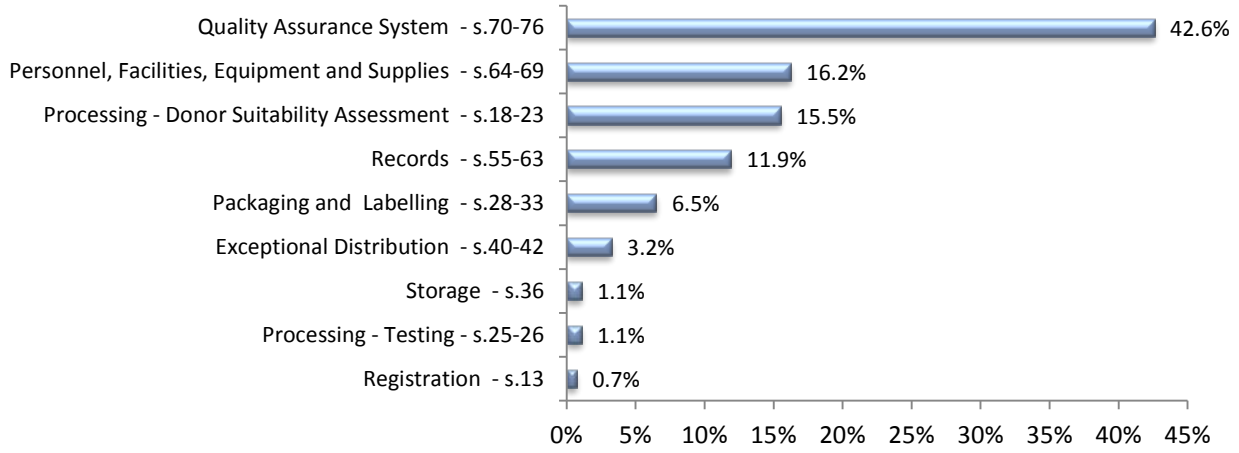

Figure 2.2 Sections of the *Safety of Human Cells, Tissues and Organs for Transplantation Regulations* most often cited, as a percentage of the total number of observations cited during CTO inspections across Canada in 2014–2015.

Table 2.1 – Examples of common observations cited

CTO Regulations	Example of observations
Quality Assurance System – Standard Operating Procedures s. 73	• Standard Operating Procedures were not consistently kept up-to-date.
Records s. 55	• Establishment records were not always complete.
Quality Assurance System – Standard Operating Procedures s. 72	• The establishment did not have Standard Operating Procedures for all regulated activities.

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 2014–2015.

Observation risk ratings

In 2014–2015, 277 observations were noted during 41 inspections. As shown in **Figure 2.3**, 89.5% (248) were Risk 3 (minor), while 10.5% (29) were Risk 2 (major). No Risk 1 (critical) observations were noted.

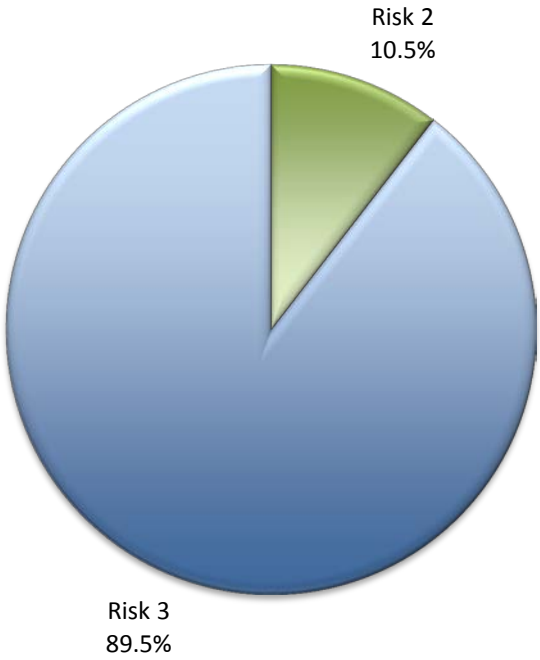

Figure 2.3 Distribution of risk ratings for observations noted during CTO inspections across Canada in 2014–2015.

Three-year inspection trend

Figure 2.4 shows the three-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)*).

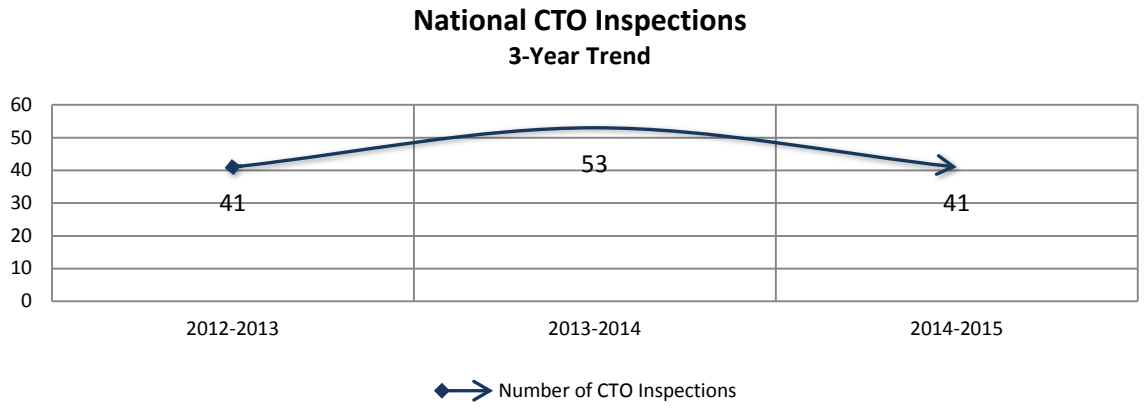

Figure 2.4 Number of CTO inspections across Canada over the last three years (2012–2015).

Figure 2.5 shows the three-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 2012–2013 to 2014–2015, deficiencies with Donor Suitability Assessment increased by 6% of overall observations.

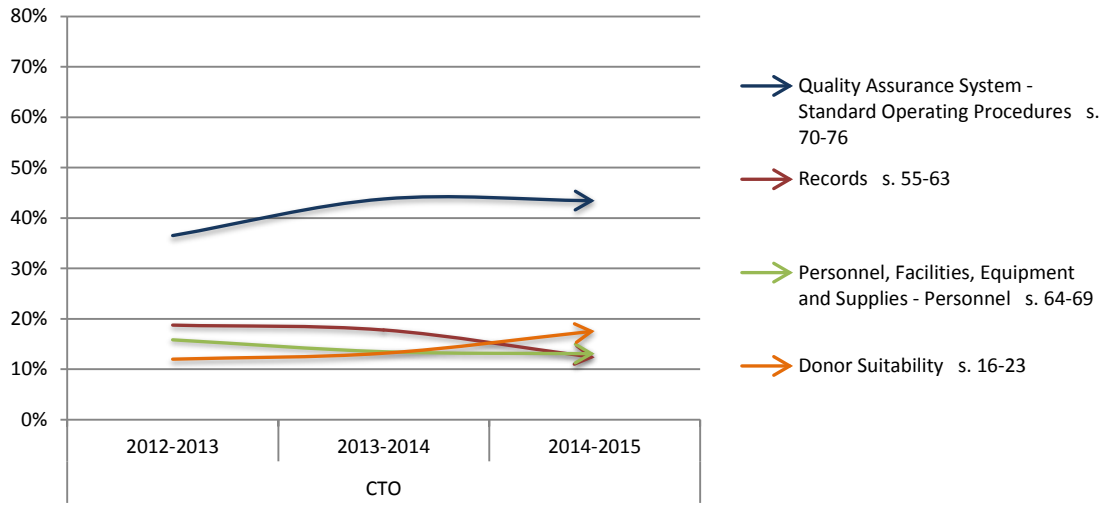

Figure 2.5 Most common observations over the last three years (2012–2015).

CHAPTER 3
DONOR SEMEN INSPECTION PROGRAM (SEMEN)

Overview

The Inspectorate conducted **32 semen inspections** in 2014–2015 and made **16 observations**. Most observations were cited against requirements for Records (s. 13 and 12(1)) and Prohibition (s.5). Of these observations, 4 were major and 12 were minor. No critical observations were made.

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 2014–2015, 32 out of 111 active processors, importers and distributors of donor semen were inspected. All were in compliance with the regulations.

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.

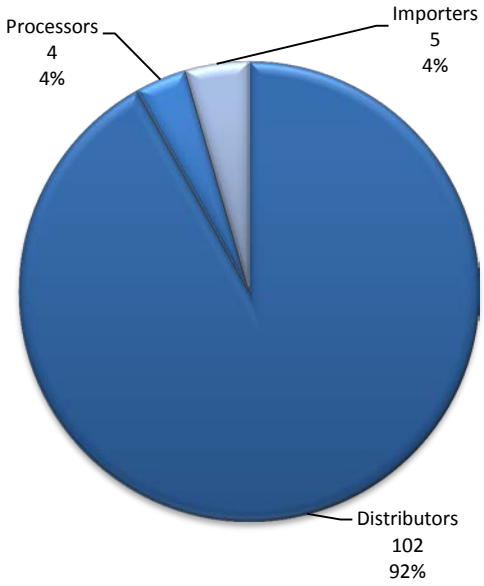

Figure 3.1 Distribution of the three types of semen establishments in Canada, 2014-2015

Most common observations

Inspectors noted 16 observations during the 32 semen inspections in 2014–2015. Most (81%) of these observations were cited against Records (s.13 and 12(1)). The rest were cited against Prohibition (s.5) and Screening (s.9), as shown in **Figure 3.2**. Examples of these observations are shown in **Table 3.1**.

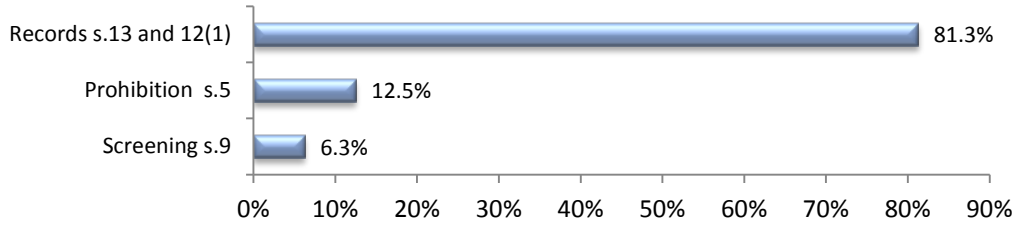

Figure 3.2 Sections of the *Processing and Distribution of Semen for Assisted Conception Regulations* most often cited, as a percentage of the total number of observations cited during semen inspections across Canada in 2014–2015.

Table 3.1 – Examples of common observations cited

Processing and Distribution of Semen for Assisted Conception Regulations	Example of observations
Records s.13	• The establishment that distributed semen processed by another establishment did not always keep the appropriate records with respect to each container of semen.
Prohibition s.5	• The establishment imported semen for distribution that was not processed in accordance with the necessary requirements.
Screening s.9	• The establishment did not screen the donor for all exclusion criteria.

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 2014–2015.

Observation risk ratings

In 2014–2015, 16 observations were noted during 32 inspections. As shown in **Figure 3.3**, no Risk 1 (critical) observations were noted, while 25% (4) were Risk 2 (major) and 75% (12) were Risk 3 (minor).

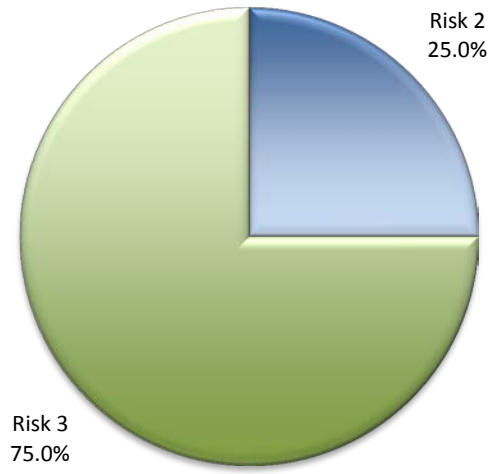

Figure 3.3 Distribution of risk ratings for observations noted during semen establishment inspections across Canada in 2014–2015.

Three-year inspection trend

Figure 3.4 shows the three-year trend for semen inspections. Overall inspection numbers were fairly constant over the three-year interval, with a slight downward trend.

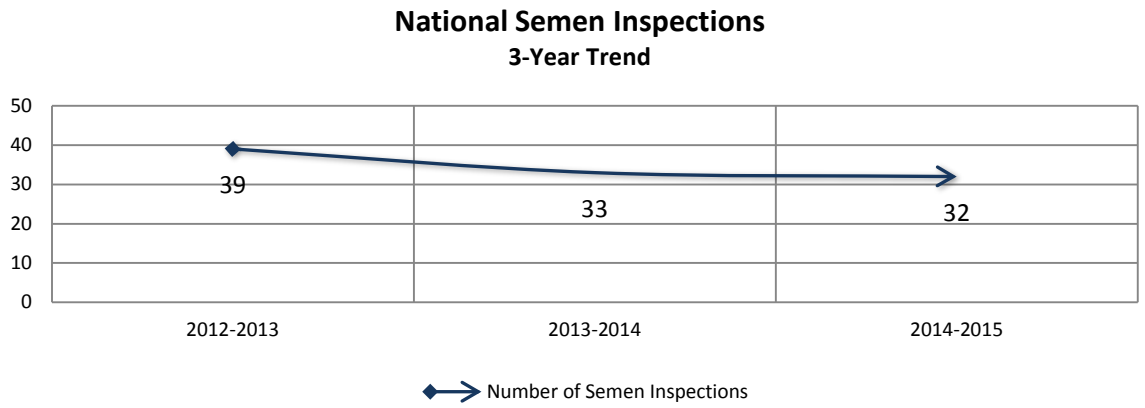

Figure 3.4 Number of semen inspections across Canada over the last three years (2012–2015).

Figure 3.5 shows the three-year trend for semen observations. Records (s.13 and 12(1)) is the most common observation every year by a wide margin. Over the past year, Prohibition (s. 5) has trended downward and Screening (s.9) has returned to levels consistent with those of 2012–2013.

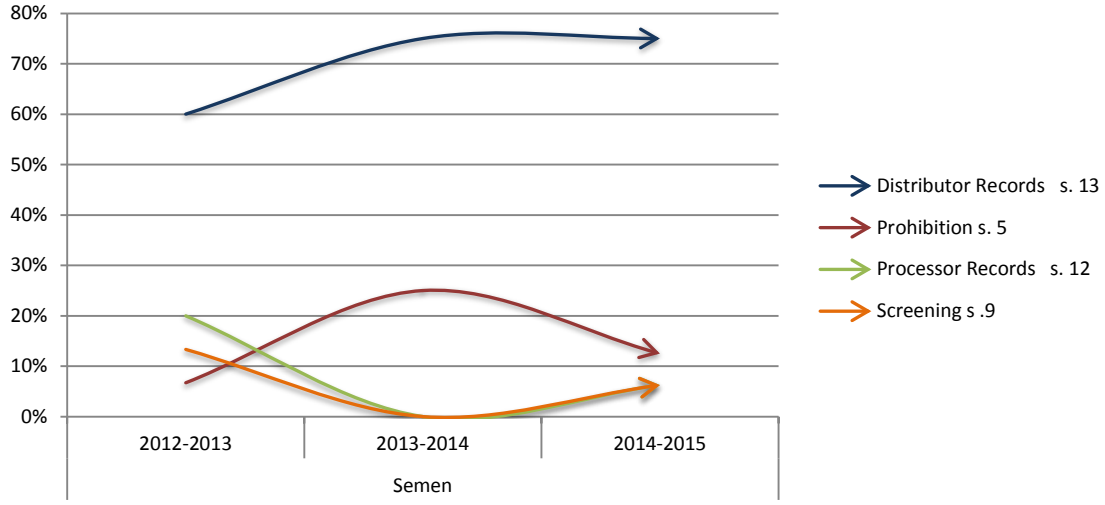

Figure 3.5 Most common observations over the last three years (2012–2015)

CHAPTER 4
DRUG GOOD CLINICAL PRACTICES INSPECTION PROGRAM (GCP)

Overview

The Inspectorate conducted **55 good clinical practices (GCP) inspections** in 2014–2015, and made **457 observations**. Most observations were cited against requirements for Records (C.05.012) and System and Procedures (C.05.010(c)). Of these observations, 11 were critical, 292 were major, and 154 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 results and statistics

In 2014–2015, 55 clinical trial sites were inspected, and 41 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 457 observations in 2014–2015. **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**.

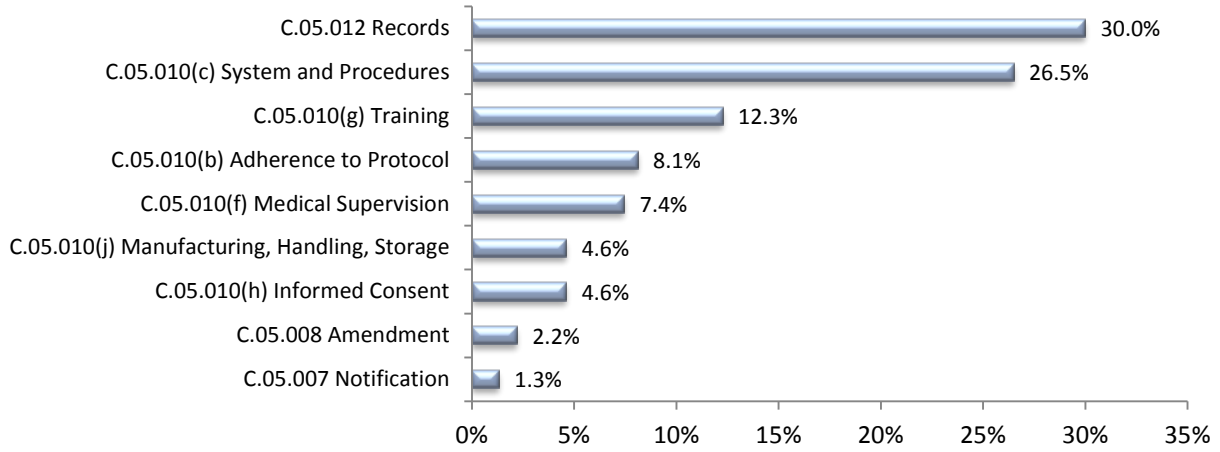

Figure 4.1 Sections of the *Food and Drug Regulations* (Part C, Division 5) most often cited, as a percentage of the total number of observations cited during GCP inspections across Canada in 2014–2015.

Table 4.1 – Examples of common observations cited

Food and Drug Regulations	Example of observations
C.05.012 Records	• 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. • The sponsor did not keep complete and accurate records regarding the use of the drug in a clinical trial, as required by law.
C.05.010(c) Systems and Procedures	• Systems and procedures were not implemented to ensure the quality of the clinical trial. • Systems and procedures were not implemented to ensure that staff members were adequately trained on Good Clinical Practices and the appropriate *Canadian Food and Drug Regulations*. • Systems and procedures were not implemented to ensure that electronic systems were validated.
C.05.010(g) Training	• Not all individuals conducting the clinical trial had the education, training and experience to perform their respective tasks.
C.05.010(b) Adherence to Protocol	• The clinical trial was not conducted according to the protocol. • The clinical trial drug was not used according to the protocol.

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 2014–2015.

Observation risk ratings

In 2014–2015, 457 observations were noted in 55 inspections. As shown in Figure 4.2, 2.4% (11) were given a Risk 1 (critical) rating, 63.9% (292) were given a Risk 2 (major) rating, and 33.7% (154) were given a Risk 3 (minor) rating.

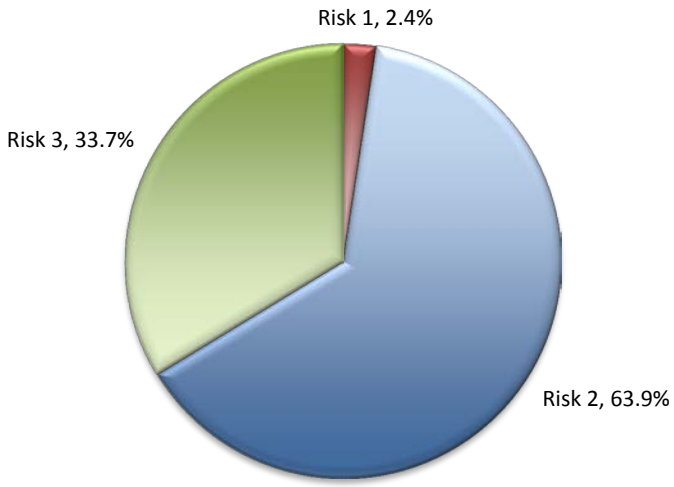

Figure 4.2 Distribution of risk ratings for observations noted during GCP inspections across Canada in 2014–2015.

All Risk 1 observations were cited against sections C.05.010 and C.05.012. Both of these require 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 the records are maintained to ensure complete and accurate reporting, interpretation and verification.

Three-year inspection trend

Figure 4.3 shows the three-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 three years (2012–2015).

Figure 4.4 shows the three-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.

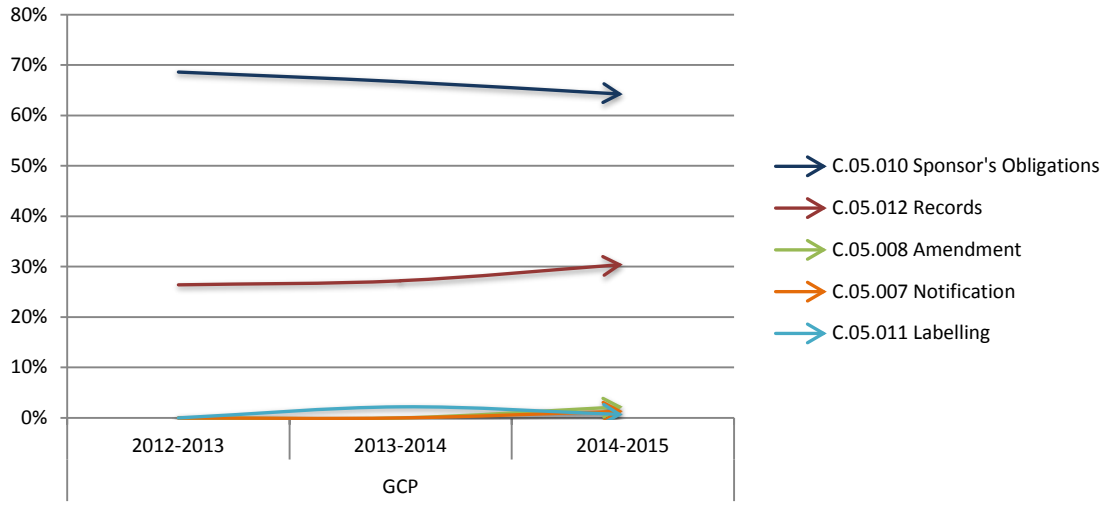

Figure 4.4 Most common observations over the last three years (2012–2015)

CHAPTER 5
DRUG GOOD MANUFACTURING PRACTICES INSPECTION PROGRAM (GMP)

Overview

The Inspectorate conducted **442 domestic good manufacturing practices (GMP) inspections** in 2014–2015, and made **3,096 observations**. Most observations were cited against requirements for Quality Control (C.02.015) and Manufacturing Control (C.02.011-12). Of these observations, 17 were critical, 1,500 were major and 1,579 were minor. The Inspectorate also conducted **1,507 drug foreign site paper assessments** and **8 foreign on-site GMP inspections**.

Background

Health Canada inspects drug establishments against GMP standards 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-year cycle. Importers, wholesalers and distributors are inspected on a three-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 establishments were complying with the new API regulations. Regulating active pharmaceutical ingredients in Canada will help increase the quality and safety of drugs for consumers. It will also strengthen the pharmaceutical drug supply system in Canada and will bring Canada in line with international regulatory partners.

Active pharmaceutical ingredients:
The substances responsible for the beneficial health effects experienced by consumers taking pharmaceuticals.

In 2014–2015, Health Canada participated in 17 stakeholder engagements, providing valuable information and regulatory guidance on APIs. 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 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. The objective under an MRA is to recognize 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.

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 1,507 paper assessments and 8 on-site inspections of foreign establishments involved in the fabrication, packaging/labelling and testing of drugs in 2014–2015. All foreign sites received a compliant rating with the exception of one site, which received a compliant rating for some activities and a non-compliant rating for other activities.

In the next few years, it is expected that the total number of foreign on-site inspections will multiply. Health Canada will work with international regulatory partners to plan using site risk profiles and conduct foreign on-site inspections of the highest 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 2014–2015, data integrity issues were noted during inspections of establishments both domestically and globally. The GMP program has been requiring regulated parties to demonstrate that data integrity is intact at their establishments as well as those they are linked to through contractual agreements. An ongoing focus on data integrity signal detection and analysis allows the Inspectorate to take appropriate regulatory actions in situations where data integrity may be an issue.

Inspection results and statistics

In 2014–2015, the Inspectorate conducted 442 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, 430 resulted in a compliant rating.

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.

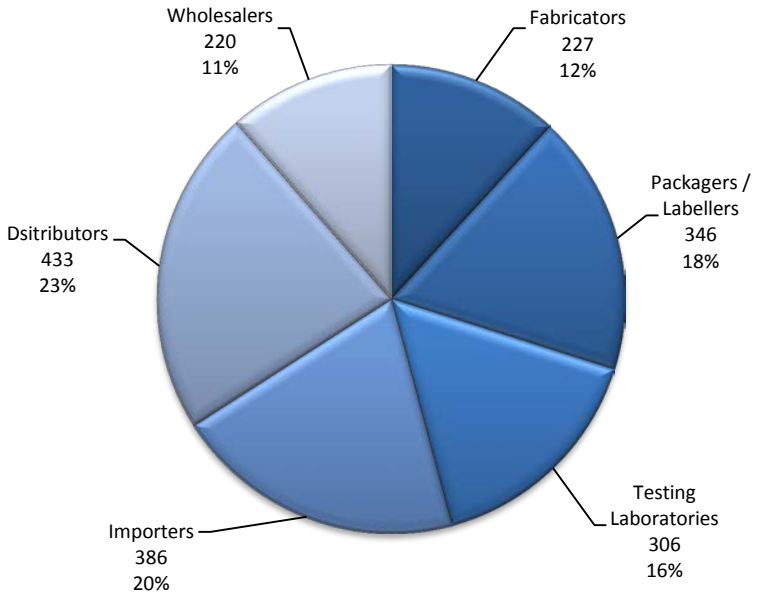

Figure 5.1 Proportion of domestic Drug Establishment Licence holders by activity.

Most common observations

Inspectors noted 3,096 observations during 442 GMP inspections in 2014–2015. Most observations were cited against requirements for the Quality Control Department (C.02.015) and Manufacturing Control (C.02.011-12), as shown in **Figure 5.2**. Examples of these observations are listed in **Table 5.1**.

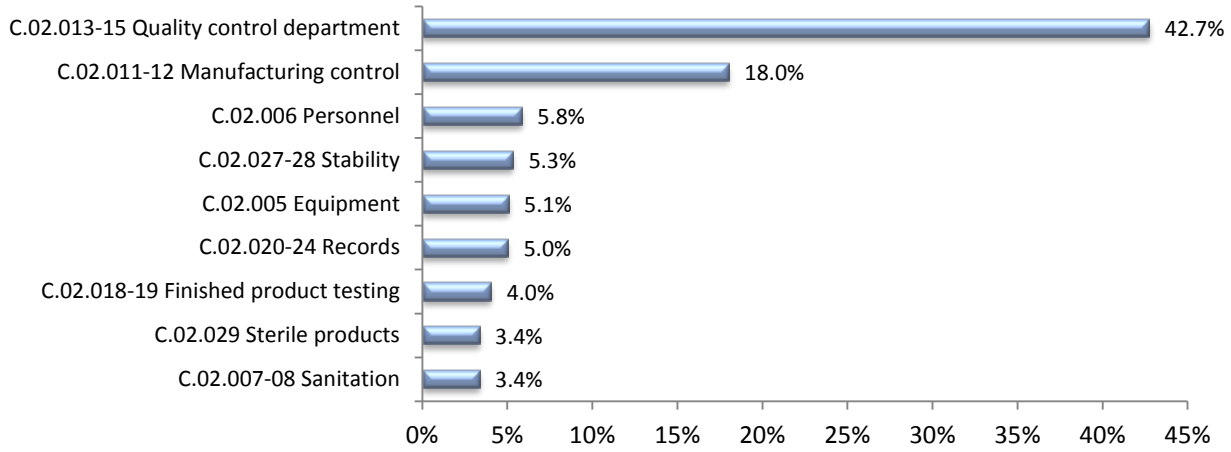

Figure 5.2 Sections of the *Food and Drug Regulations* most often cited, as a percentage of the total number of observations cited during GMP inspections across Canada in 2014–2015.

Table 5.1 – Examples of common observations cited

Food and Drug Regulations	Example of observations
C.02.013–15 Quality control department	• There was no system in place to ensure that the storage conditions during the transportation of products were maintained for API imported from sites X and shipped to clients. • There was no approved shipping packaging configuration for ambient and refrigerated products. • There is no procedure specifying the handling and storage of the ice packs which are used to pack drug products X for outbound shipment to customers.
C.02.011–12 Manufacturing control	• It was not indicated in the recall procedure that Health Canada would be notified within 24 hours of having made the decision to recall, followed by a written report within 3 business days of initiating the action. • Quality agreements between the importer and various distributors did not indicate which party (importer or distributor) was responsible for reviewing and approving validation documentation. • The cleaning of some equipment was not documented in the equipment log as noted in the deviation reports.
C.02.020–24 Records	• The complete process validation evidence of the manufacturing process for product X, manufactured at Company Z were not maintained on the premises. • There were no controls in place to prevent unauthorized access or changes to data and to protect from omission of data. • Completed packaging batch records were stored as loose pages bound by a paper clip, rather than being fixed more securely to prevent lost or mismatched papers. • There was no documented procedure detailing the retention time for evidence and records to be maintained. For example: Distribution records, Complaint records (C.02.023), Self-inspection records (C.02.024).

Table 5.1 Examples of GMP inspection observations, from the sections of the *Food and Drug Regulations* most often cited in 2014–2015.

Observation risk ratings

In 2014–2015, 3,096 observations were noted during the 442 domestic inspections conducted. As shown in **Figure 5.3**, 0.5% (17 observations) were classified as Risk 1 (critical), 50.2% (1,612) were classified as Risk 2 (major) and 49.3% (1,579) were classified as Risk 3 (minor).

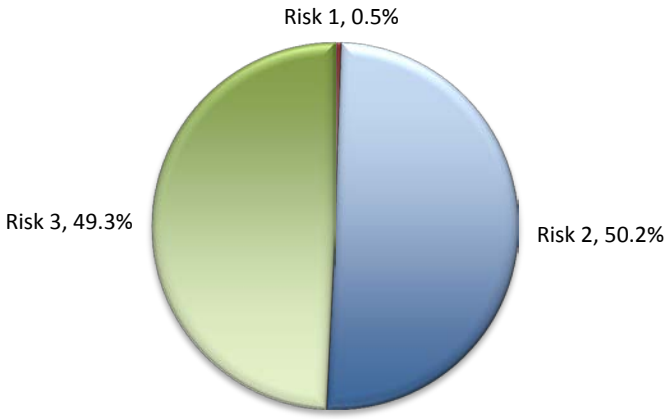

Figure 5.3 Distribution of risk ratings for observations noted during GMP inspections across Canada in 2014–2015.

The highest number of Risk 1 (critical) observations—eight (8)—was recorded under Quality Control (C.02.013-015). This was followed by three (3) Manufacturing Control (C.02.011 and C.02.012) and three (3) Finished Product Testing (C.02.019) Risk 1 (critical) observations.

Three-year inspection trend

Figure 5.4 shows the three-year trend for both domestic and foreign GMP inspections. Domestic inspections have increased by approximately 3% per year over the past three years. Foreign inspections have remained steady, with a slight increase in 2013–2014.

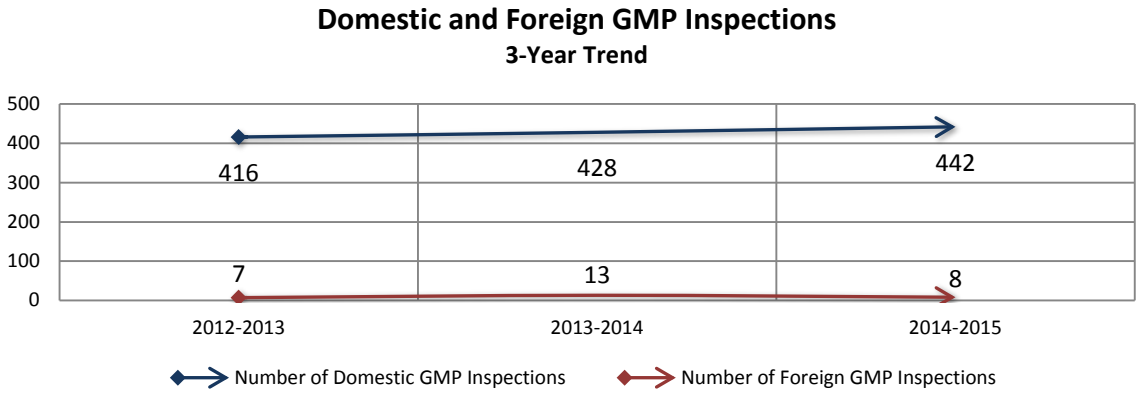

Figure 5.4 The three-year trend for GMP inspections.

Figure 5.5 shows the three-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 just under 25% of all observations. Records and Equipment, which were 3rd and 4th in 2012–2013, have dropped and been replaced by observations against Personnel and Stability (although only Stability-related observations are currently trending upwards). Overall, GMP observations are trending down, indicating that compliance with previously problematic areas of GMP is improving.

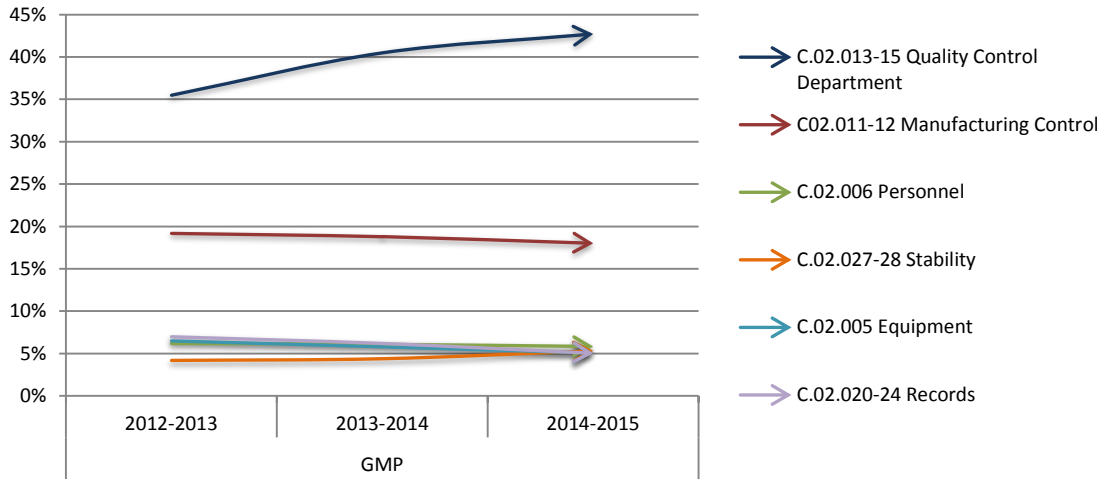

Figure 5.5 Most common observations over the last three years (2012–2015)

CHAPTER 6
DRUG GOOD PHARMACOVIGILANCE PRACTICES INSPECTION PROGRAM (GVP)

Overview

The Inspectorate conducted **47 good pharmacovigilance practices (GVP) inspections** in 2014–2015, and made **201 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, 115 were major and 86 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 2014–2015, 47 GVP inspections were conducted. All establishments were found to be in compliance at the time of inspection.

Most common observations

Inspectors noted 201 observations during 47 GVP inspections in 2014–2015. 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 Issue-related Summary Report (C.01.019), as shown in **Figure 6.1**.

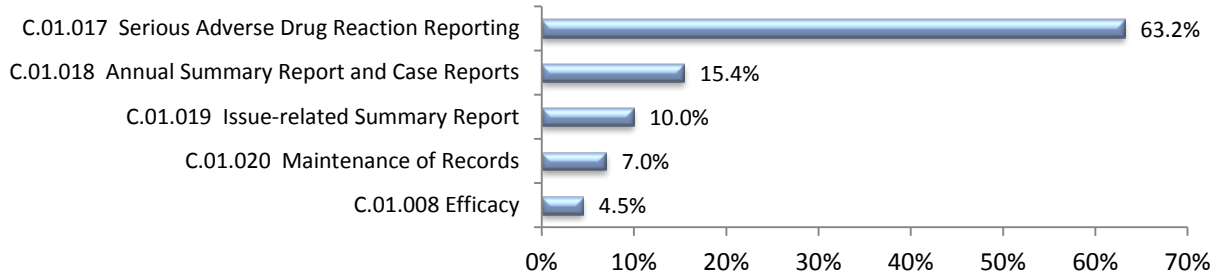

Figure 6.1 Sections of the *Food and Drug Regulations* most often cited, as a percentage of the total number of observations cited during GVP inspections across Canada in 2014–2015.

Table 6.1 – Examples of common observations cited

Food and Drug Regulations	Example of observations
C.01.017 Serious Adverse Drug Reaction Reporting	• Systems and processes for receiving, handling, evaluating and reporting adverse drug reactions did not meet regulatory requirements. • Contractual agreements that defined the responsibilities of all parties involved in pharmacovigilance activities did not meet requirements.
C.01.018 Annual Summary Report and Case Reports	• Systems and processes for preparing Annual Summary Reports were not acceptable. • Annual Summary Reports were not always prepared each year for all drug products marketed in Canada.

Table 6.1 Examples of GVP inspection observations, from the sections of the *Food and Drug Regulations* most often cited in 2014–2015.

Observation risk ratings

In 2014–2015, 201 observations were noted during 47 inspections. As shown in **Figure 6.2**, 57.2% (115) were given a Risk 2 (major) rating. The other 42.8% (86) 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.

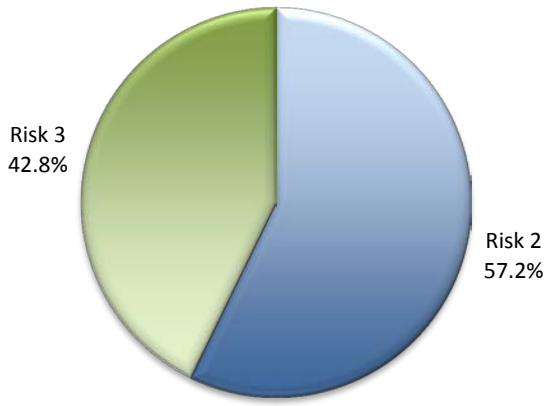

Figure 6.2 Distribution of risk ratings for observations noted during GVP inspections across Canada in 2014–2015.

Three-year inspection trend

Figure 6.3 shows the three-year trend for GVP. This past year, 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.

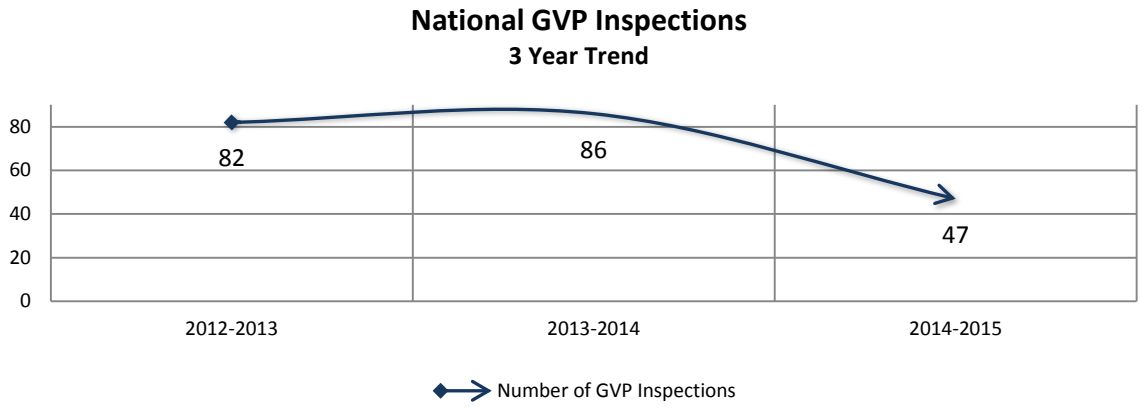

Figure 6.3 Number of GVP inspections across Canada over the last three years (2012–2015).

Figure 6.4 shows the three-year trend for GVP observations. The trends are fairly static. Most GVP observations were made against Serious Adverse Drug Reaction Reporting. Only observations related to the Issue-Related Summary Report are trending upward.

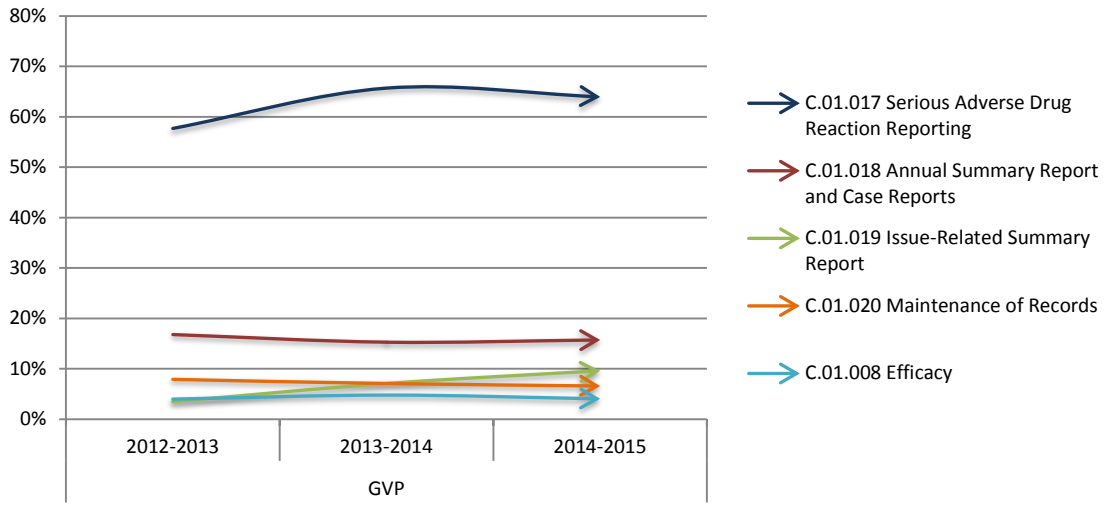

Figure 6.4 Most common observations over the last three years (2012–2015).

CHAPTER 7
MEDICAL DEVICES INSPECTION PROGRAM (MD)

Overview

The Inspectorate conducted **552 medical device inspections** in 2014–2015 and made **2,691 observations**. Most observations were cited against requirements for Recall Procedure (MDR s. 58*(b)*) and Investigation Procedure (MDR s.58*(a)*). Of these observations, 3 were critical, 1,684 were major and 1,004 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.

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).

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 2014–2015, 552 inspections were conducted. Of these, 549 resulted in an overall compliant rating for the establishment and 3 resulted in a non-compliant rating.

As of April 2015, there were 2,627 MDEL holders: 1,880 domestic and 747 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 and manufacturers.

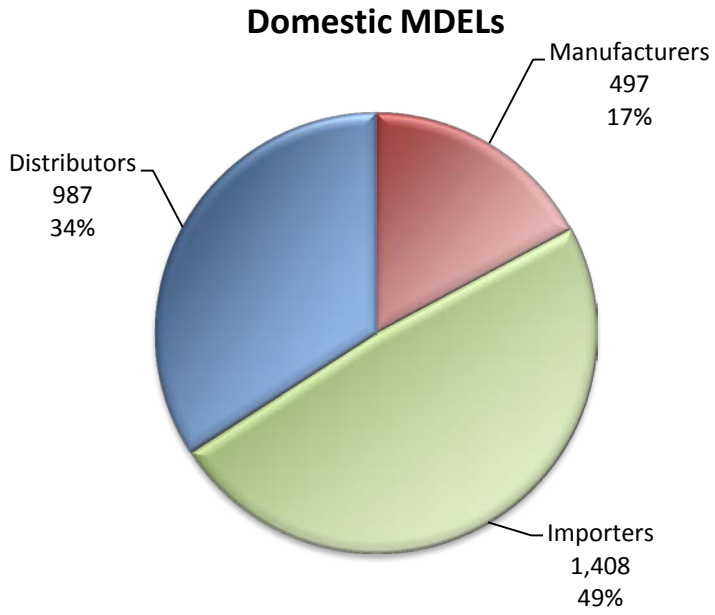

Figure 7.1 Proportion of domestic MDEL holders who are manufacturers, importers and distributors.

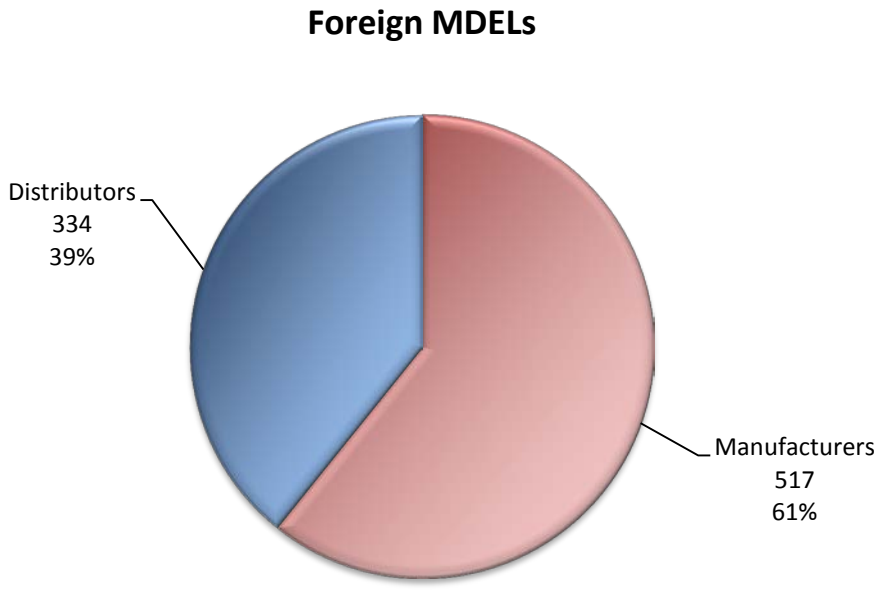

Figure 7.2 Proportion of foreign MDEL holders who are manufacturers and distributors.

Most common observations

Inspectors noted 2,691 observations during 552 medical device inspections in 2014–2015. 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.**

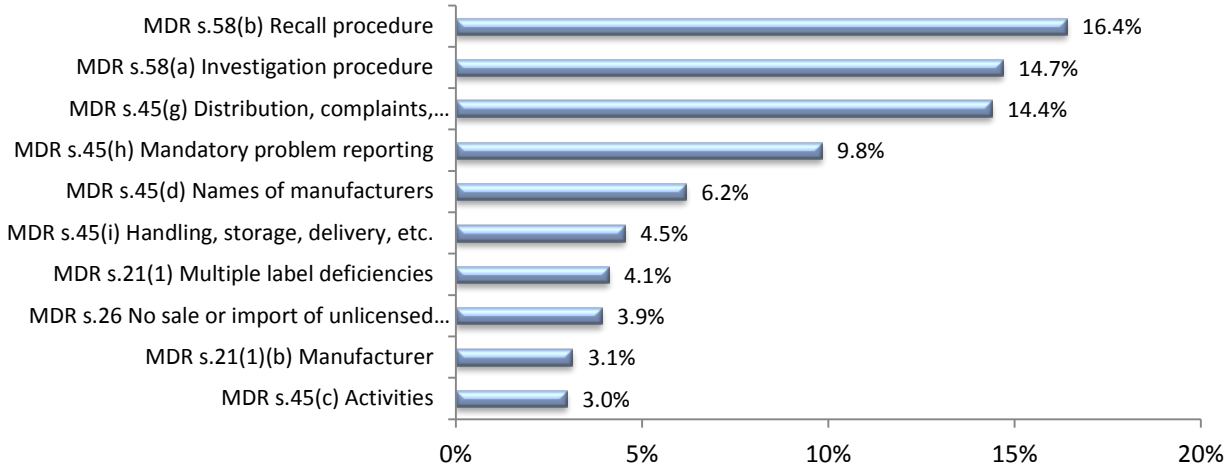

Figure 7.3 Sections of the *Medical Devices Regulations* most often cited, as a percentage of the total number of observations cited during medical device inspections across Canada in 2014–2015.

Table 7.1 – Examples of common observations cited

Medical Devices Regulations	Example of observations
MDR s. 58*(b)* Recall procedure for the effective and timely recall of device	• At the time of the inspection, the company did not have a designated quarantined area for recalled products. • The recall procedure was incomplete in that the procedure for sending recall preliminary and final reports to Health Canada was not specified. • The recall procedure was not adequate to assure that all recalls would be conducted in a timely and effective manner.
MDR s. 45*(g)* Documented procedures for distribution records, complaint handling and recalls	• The company did not have written procedures in place for distribution records, complaint handling, and/or recalls, contrary to what was committed to on its establishment licence application. • The company's distribution record procedure does not address the requirements of the following Regulation(s): s.55 Record Retention and s.56 Timely Retrieval.
MDR s. 58*(a)* Investigation procedure	• The company's documented procedure for complaint handling does not adequately address the requirements of the following Regulations: s.58(a): Timelines for effective and timely investigation, s.57(1)(a): Maintain records of reported problems, and s.57(1)(b): Maintain records of actions taken by the manufacturer, importer or distributor.

Table 7.1 Examples of medical device observations, from the sections of the *Medical Devices Regulations* most often cited in 2014–2015.

Observation risk ratings

As shown in **Figure 7.4**, 62.6% (1,684) observations were Risk 2 (major) and 37.3% (1,004) were Risk 3 (minor). Only 0.1% (3) were Risk 1 (critical). The three Risk 1 observations were cited for deficiencies in documentation relating to recall procedures (MDR s.58*(b)*), submission of initial recall reports (MDR s.64), and records sufficient for product withdrawal (MDR s.53).

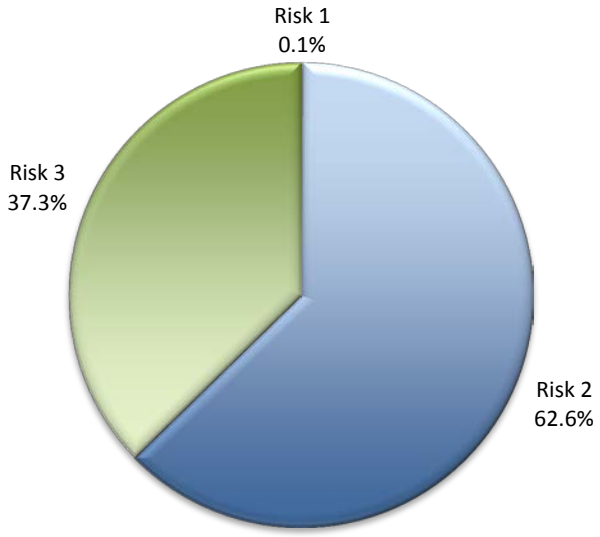

Figure 7.4 Distribution of observations noted during medical device establishment inspections across Canada in 2014–2015, classified by their risk rating.

Three-year inspection trend

Figure 7.5 shows the three-year trend for medical device inspections. The number of inspections over three years did not change significantly, with a slight drop between 2012–2013 and 2013–2014. This constancy is also reflected in the observations and risk trends.

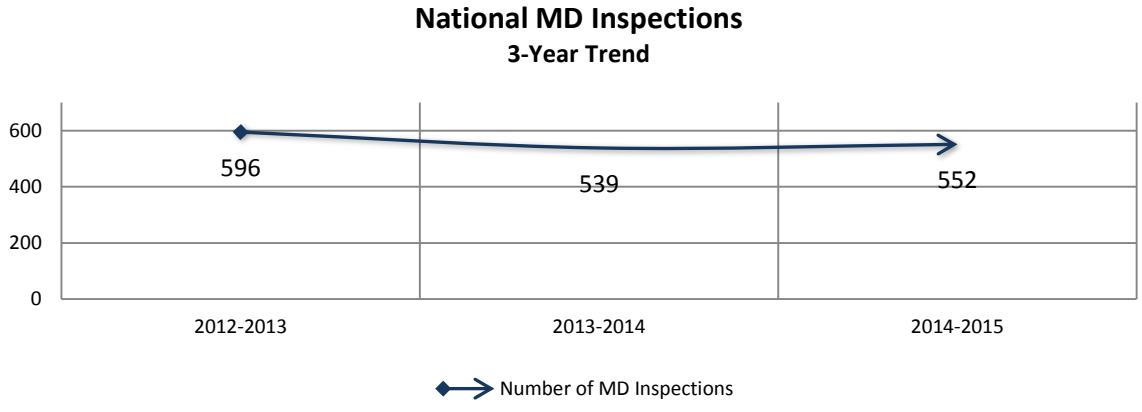

Figure 7.5 Number of medical device establishment inspections across Canada over the last three years (2012–2015).

Figure 7.6 shows the three-year trend for medical device observations. The three most-observed categories have remained the same over three years. However, Procedures for Distribution, Complaints, Recalls (MDR ss. 45*(g)*) has dropped from the most observed in 2012–2013 to second most observed in 2013–2014, and then to third most observed in 2014–2015. No observation is clearly dominant in medical devices in 2012–2013. In 2013–2014 and 2014–2015, the dominant observation is Recall Procedures (MDR s.58*(b)*).

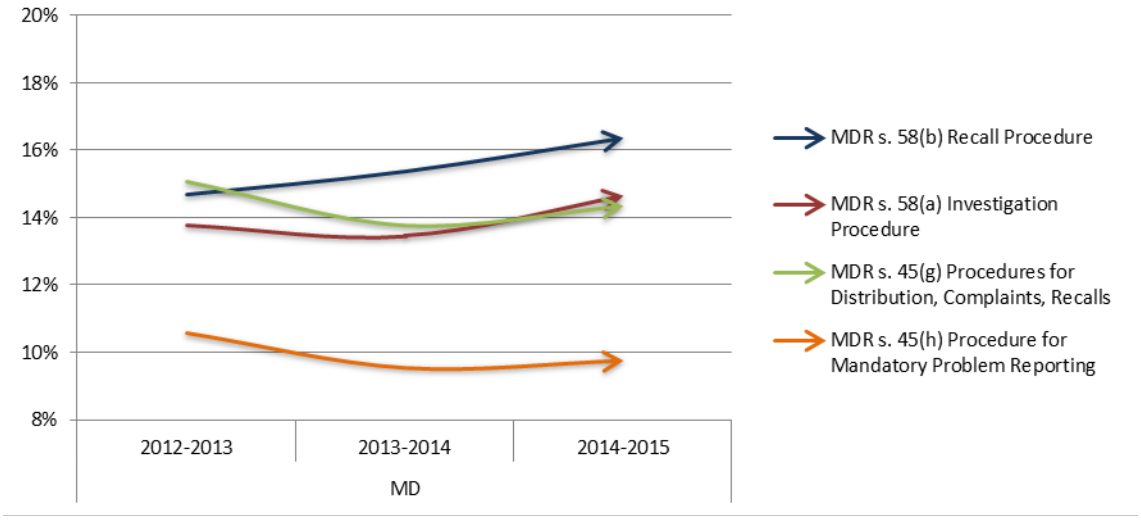

Figure 7.6 Most common observations over the last three years (2012–2015).

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

Director General's Office

Graham Spry Building
3rd Floor, 250 Lanark Avenue
Ottawa, ON
K1A 0K9
Tel: (613) 946-5095
Fax: (613) 952-9805
Email: insp-dgo_bdg-insp@hc-sc.gc.ca

Atlantic Region

16th Floor, 1605 Barrington St.
Halifax, NS
B3J 3Y6
Tel: (902) 426-2160
Fax: (902) 426-6676
Email: insp_aoc-coa@hc-sc.gc.ca

Québec Region

1001 St-Laurent St. W
Longueuil, QC
J4K 1C7
Tel: (450) 646-1353
Fax: (450) 928-4184
Email: qoc-coq@hc-sc.gc.ca

Ontario Region

2301 Midland Ave.
Scarborough, ON
M1P 4R7
Tel: (416) 973-1600
Fax: (416) 973-1954
Email: insp.onoc-coon@hc-sc.gc.ca

Prairie Region (Manitoba/Saskatchewan)

300-391 York Ave.
Winnipeg, MB
R3C 4W1
Tel: (204) 594-8061
Fax: (204) 594-8153
Email: insp_msoc_coms@hc-sc.gc.ca

Prairie Region (Alberta)

730-9700 Jasper Ave.
Edmonton, AB
T5J 4C3
Tel: (780) 495-0490
Fax: (780) 495-2624
Email: insp_aboc-coa@hc-sc.gc.ca

B.C. Region

4th Floor, 4595 Canada Way
Burnaby, BC
V5G 1J9
Tel: (604) 666-3350
Fax: (604) 666-3149
Email: insp_woc-coo @hc-sc.gc.ca

APPENDIX 2 – REFERENCES

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