Health Canada Santé Canada

Canada

Demystifying Health Product Vigilance in Canada

Canadian Association for Population Therapeutics
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YOUR HEALTH AND SAFETY... OUR PRIORITY.

Presentation Outline

- Provide an overview of health product vigilance in Canada
- Describe post market activities undertaken to monitor safety and effectiveness of health products
- Describe the current state of adverse drug and medical device incident reporting and what is being undertaken to improve reporting
- Provide an overview of advertising monitoring

Definition

Pharmacovigilance or Health Product Vigilance:

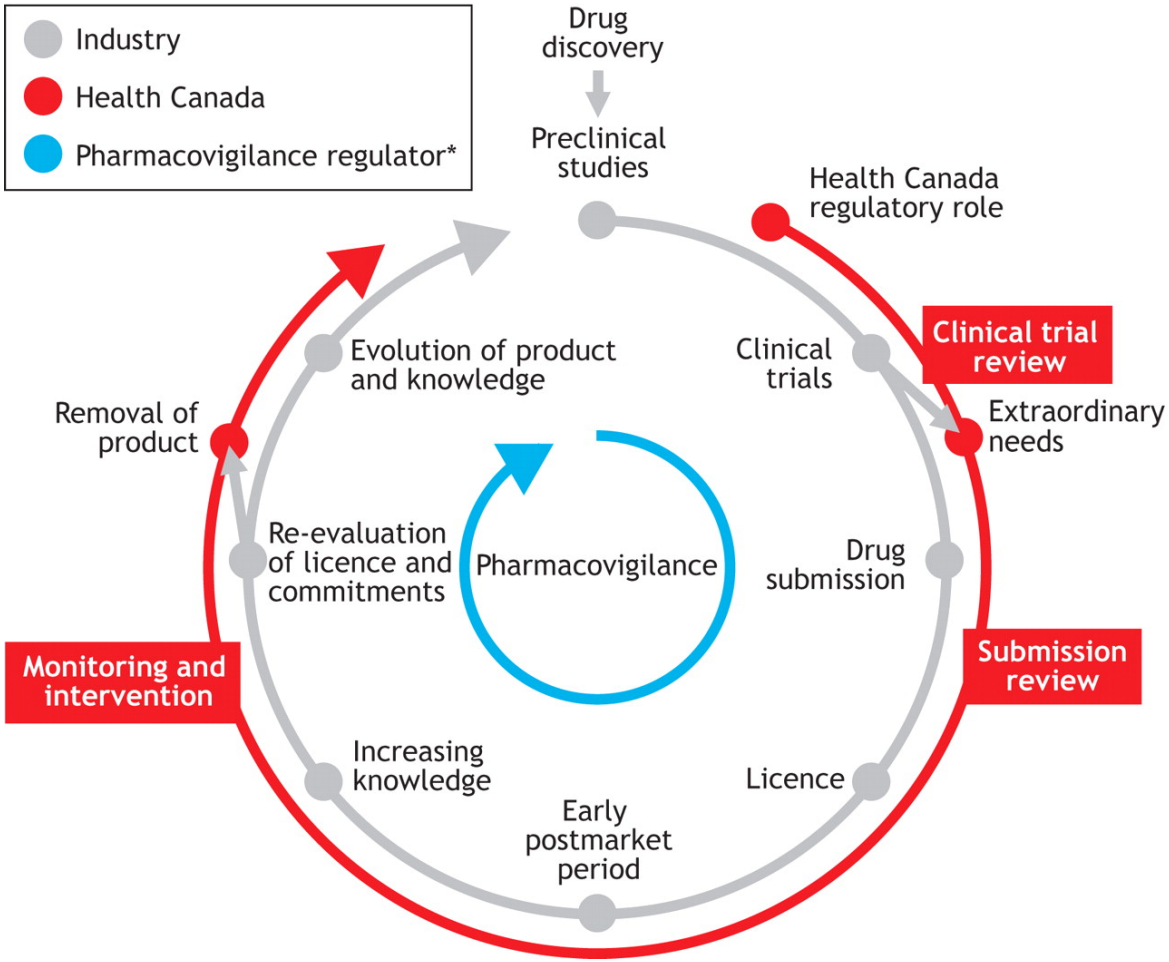
The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other health product related problem.

What does this ‘look like’ in real life….

Health Product Vigilance

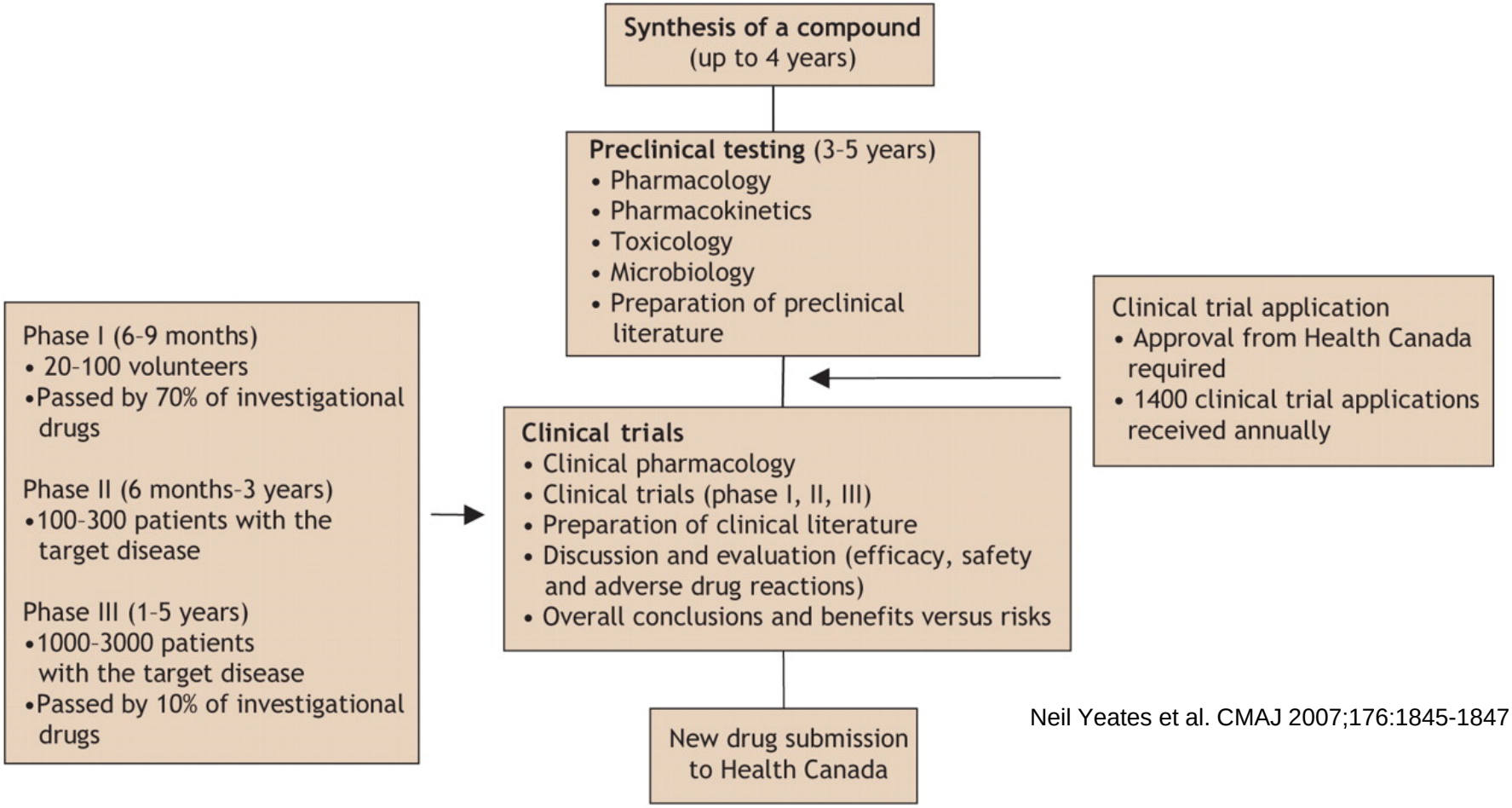
Before a drug comes on to the market, it is assessed for…..

- **Safety**
- **Efficacy**
- **Quality**



Neil Yeates et al. CMAJ 2007;176:1845-1847

Drug Development and Regulatory Process



Neil Yeates et al. CMAJ 2007;176:1845-1847

Even once the safety, efficacy and quality of a potential product is assessed, with all products there are residual risks…..

The Bridges Between Pre and Post Market Vigilance

Risk Management Plans

- When health products are coming onto the market, their residual risk is assessed and **risk management plans (RMPs)** are developed between Health Canada and the Market Authorization Holder (MAH) to mitigate the risks
  - Such plans can include controlled distribution programs, required studies, etc..
  - Progress against these plans is monitored and assessed annually, however, HC does not have regulatory levers to require RMP updates to be submitted, **except for opioid products**

Product Name Labeling

- The proposed name and label from the manufacturer is assessed against Health Canada guidance on good labeling practices and against other products on the market to ensure any confusion is minimized

Once pre market safety, efficacy and quality are assessed, the RMP is in place, the product name and label have been assessed, and the overall benefit to risk ratio is determined to be positive, the product is approved for the Canadian market

Post market surveillance is then launched….

Clinical Trial vs. ‘Real World’

Clinical Trial	Post-Market
• Highly controlled environment • Short trial duration • Highly selected patients • Limited number of patients • Healthy patients • Selected cases and diseases	• Varied and large population • Chronic use • Off-label use • Patients with multiple co-morbidities • Rare events

Given this, what does Health Canada do to monitor the safety and effectiveness of products on the Canadian market…

Health Canada's Post-Market Surveillance: What Do We Do?

- Responsible to monitor the post market safety and effectiveness of all Marketed Health Products in Canada:

  11000 pharmaceutical drugs

  35000 medical devices

- Involves gathering data and information, undertaking risk/benefit assessments, and developing recommendations for….
  - prescription and over the counter (OTC) pharmaceuticals
  - medical devices
  - cells, tissues, and organs
  - blood and blood products
  - radiopharmaceuticals and vaccines
  - natural health products
  - disinfectants and sanitizers with disinfectant claims

How do we do this……

How Do We Do It?

Three Key Activities:

1. Environmental Scanning to Identify and Assess Potential Signals

- In 2017, MHPD completed 166 safety reviews and published 44 Summary Safety Reviews (SSRs)

2. Coordinate or Require Studies to Address Specific Concerns

- Health Canada has a number of regulatory and non regulatory levers to gather data and evidence related to safety and effectiveness of products on the market
- Where there is a demonstrated safety concern with a product, can require Market Authorization Holder to undertake tests and studies (for therapeutic drugs, not natural health products or medical devices)
- A key lever is the Drug Safety and Effectiveness Network (DSEN)

3. Monitoring of ADRs and MDIs

- **Program for Pharmaceuticals**
  - Canada Vigilance Program (CVP): Captures ADRs

- **Program for Medical Devices**
  - Canada Vigilance Medical Device Problem Reporting System (CV-MDS): MDIs
  - Canadian Medical Devices Sentinel Network (CMDSNet): MDIs from participating hospitals

What happens if we find something…

Life Cycle of a Signal

- Through the combined efforts of the key activities, potential issues are identified
- Potential ‘signals’ are reviewed by an internal committee of scientists and physicians to determine if they will undergo a signal assessment
- Depending on the issue, they will either undergo a normal or an expedited review
- Following the completion of the assessment, recommendations are made:
  - Action needed: can include pulling a product from market, changing indications, changing label, etc….
- The approved changes are communicated to the market authorization holder and their progress in implementing the changes are monitored

Communicating on Signal Reviews

- Health Canada communication on safety reviews depends on the nature of the findings:
  - Lower risk
    - Website posting
    - Publishing all reviews in the Health Product InfoWatch e-newsletter
  - Higher risk
    - Dear Health Care Provider letters (from HC or the MAH)
    - Information Updates
    - News release
    - Direct communication
    - Website posting
    - Publishing all reviews in the Health Product InfoWatch e-newsletter
- Findings are also communicated to international regulatory partners as their findings are communicated with us

Process is Dependant on Timely, Quality Information

- The process described is dependant on the quantity, quality and timeliness of data and information Health Canada receives

- What is working well?
  - Approval of drugs amenable to clinical trials for the populations under study
  - Quantity and quality of published data in post market
  - Information sharing between regulators

- What can improve?
  - Use of real world evidence to support indications for populations often excluded from clinical trials (ex. children, seniors, pregnant women) and for rare diseases where clinical trials may be unethical
  - Quality and quantity of ADRs and MDIs

Let’s take a look at both of these issues……

Optimizing the Use of Real World Evidence (RWE)

- RWE refers in general to the intelligence gathered from data developed outside of traditional clinical trial studies, and rather, in ‘real world’ scenarios

- Under Health Canada’s Regulatory Review of Drugs and Devices initiative (R2D2), there is a commitment to:
  - Optimize the use of RWE across the drug life cycle
  - Optimize the use of RWE across the medical device life cycle

- Health Canada already uses RWE across the product life cycle; however, by expanding the use of high quality real world evidence (RWE), Canada can improve timely and evidence based access for Canadians

- There has been great collaborative progress on this front in Canada already:
- A joint workshop hosted by CADTH, HC, the Canadian Association for Population Therapeutics and Institute of Health Economics (AB) was hosted at the end of 2018 with great success.
  - Key outcome were:
    - desire to proceed with a joint action plan and where possible joint guidance between the regulator and the HTAs
    - need for a coordinating body to share information and collectively address the key issues hindering the use of RWE in Canada
    - agreement from participants to ‘build the plane as we fly it’, in essence, expand our learning of the use of RWE across the life cycle while we do it rather than wait til we have detailed guidance for each product line.

RWE: What has happened since the Oct RWE meeting?

- Things are moving!!!!

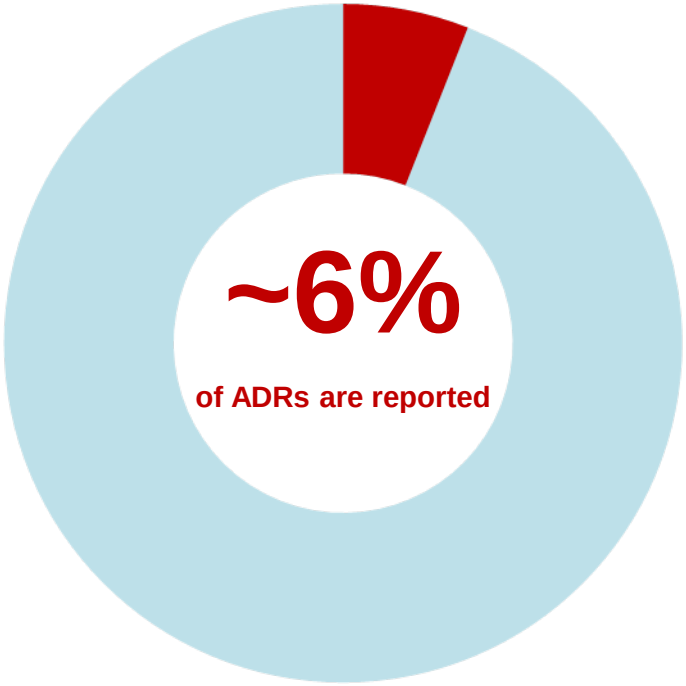
- To address the recommendations stemming from the workshop:
  - HC, CADTH and INESS are developing a joint action plan for release in summer 2019 and similar approach has been launched for medical devices
  - HC and CADTH developed a Core Action Team on RWE that includes regulators, HTAs, payers, academia, industry, and data holders/generators.
    - The Team has met twice and is chaired by HC
    - Terms of Reference have been approved and working groups are being developed to address the highest priority issues.

- Announcement on RWE expected from HC in the coming months on this……stay tuned!

What about reporting of ADRs and MDIs in Canada? How are we doing….

ADR and MDI Reporting in Canada and Abroad: Current Status

- Under-reporting and poor quality of reports is an issue shared by all international regulators
- Under-reporting of ADRs estimated at **94%**[1]
- Health Canada's ability to utilize ADR and MDI data is limited by the quantity and quality of reports we receive



[1] Hazell, *et al*. *Drug Safety* 2006

Quantity and Quality of Reports

- Currently, Health Canada receives
  - ~ **1 M ADR and MDI reports a year**
  - 720 K foreign
  - 150 K domestically

- Voluntary reporting **forms a very small proportion** of reports received annually
  - ~ 1% of ADR reports and 4% of MDI reports

- Reports received through mandatory reporting, by market authorization holders, are generally of high quality

- Most reports received through voluntary reporting are often of a quality that makes them difficult, or impossible, to use because of missing key information useful for report assessment

Domestic Reports

Suspected ADR – Reporter Type	2015	2016	2017
All sources (direct and industry)	93,637	125,561	132,355
All HCPs	7,425	6,167	6,532
Public	1,257	1,276	1,743

Voluntary Reports

HCP	2015	2016	2017
Physician	2,255	2,046	1,909
Pharmacist	3,069	2,589	2,373
Nurse	358	376	637
Other Health Professional	1,743	1,156	1,613

https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/annual-trends-adverse-reaction-case-reports-health-products-medical-device-problem-incidents.html

What's Being Done to Address Issues with Reporting? International Efforts

- While global information sharing of ADR and MDI information between foreign regulators provides the vast majority of information used to detect emerging safety issues, **under-reporting of, and poor quality of, reports is an issue shared by all international regulators.**

- Of 28 European Member States, **22 countries have mandatory reporting of ADRs for healthcare professionals**

- In 2001 and 2005, Health Canada surveyed international regulators with mandatory reporting requirements **for healthcare professionals**, and found that:
  - Reporting requirement for healthcare professionals **had only a small impact**
  - **Most effective approaches** to enhance reporting were determined to be:
    - **education and awareness**
    - **making the reporting process user-friendly** with less reliance on individual practitioners

Given this…

- What will we do in Canada to improve the quantity and quality of ADR and MDI reports we receive, and

- What will we do to optimize the timely and appropriate use of that information by Health Canada and other key health system stakeholders?

Action Plan to Improve Reporting of ADRs and MDIs in Canada

Health Canada will proceed with a three part Action Plan to improve the reporting of ADRs and MDIs in Canada, with the aim to more rapidly identify safety issues for Canadians and to better share safety information with decision makers for action.

- Part 1. Implement Mandatory Reporting of ADRs and MDIs from Hospitals
- Part 2. Improve Reporting of ADRs and MDIs from Other Health Care Settings
- Part 3. Optimize the Timely Analysis and Sharing of Information with Health System Partners

Part 1. *Protecting Canadians from Unsafe Drugs Act* (Vanessa's Law)

- Vanessa Young died in 2000 of a cardiac arrhythmia after being prescribed cisapride (Prepulsid®)
- Her father, Terrance Young, embarked on a campaign for increased regulation of therapeutic products which has resulted in greater powers for Health Canada to request data from hospitals and industry about medications and devices
- Amends the *Food and Drugs Act* to improve Health Canada's ability to:
  - Collect post-market safety information;
  - Take appropriate action when a serious risk to health is identified;
  - Promote greater confidence in the oversight of therapeutic products by increasing transparency
- The amendments to the *Food and Drugs Act* include:
  1. Power to compel information, tests/studies and reassessments
  2. Power to compel a label change
  3. Power to recall unsafe therapeutic products
  4. Tougher measures for those that do not comply
  5. Ability to incorporate by reference
  6. **Mandatory reporting by healthcare institutions**

Part 1. Proposed Regulations for Mandatory Reporting: Details

WHO: All hospitals, as defined by PT legislation

WHAT: Serious ADRs and MDIs where the information is **within the control of the hospital**.

- ***Serious ADR:*** a noxious and unintended response to a drug that occurs at any dose and that:
  - requires in-patient hospitalization
  - prolongation of existing hospitalization
  - causes congenital malformation
  - results in persistent or significant disability or incapacity, or
  - is life- threatening or results in death

- ***Medical device incident*** means an incident related to a failure of a medical device or a deterioration in its effectiveness, or any inadequacy in its labelling or in its directions for use that has led to the death or a serious deterioration in the state of health of a patient, user, or other person, or could do so were it to recur.

WHEN: Hospitals are required to report serious ADRs and MDIs to Health Canada in writing **within 30 calendar days** of first documentation of the reaction or incident within the hospital.

- Does NOT mean the full investigation needs to be done in the 30 days

Part 1. Supporting Implementation of the Regulations: Outreach and Education

- Health Canada has engaged a contractor, the Institute for Safe Medication Practices Canada (ISMP) in a Joint Venture with the Health Standards Organization (HSO) and the Canadian Patient Safety Institute (CPSI) to:
  - assess the needs of impacted hospitals in implementing the regulations
  - develop training materials to support hospitals in their identification and reporting of serious ADRs and MDIs

- Health Canada is carrying out engagement activities to raise awareness about mandatory reporting and developing knowledge translation products to provide reporter specific feedback

Part 2. Improve Reporting of ADRs and MDIs from Other Health Care Settings

- While most serious ADRs and MDIs will be transferred and treated in hospital, some will not. Given this, Health Canada will undertake two activities to improve reporting from non hospital based health care settings.

- Expand Existing Canadian Medical Devices Sentinel Network (CMDSNet)
  - Since 2009, Health Canada has supported the creation of, and sought medical device incident reports through the Canadian Medical Devices Sentinel Network (CMDSNet).
    - This network currently covers 17 healthcare organizations, representing more than 260 hospitals and facilities across the country.
  - Health Canada will aim to expand the scope of the CMDSNet to include facilities outside the hospital setting including long term care facilities and private clinics.

- Outreach and Education:
  - Health Canada will develop outreach and education aimed at non-hospital settings such as private clinics and long term care facilities. This program will aim to:
    - Improve the understanding of Canada's health product safety regime and the critical role non hospital settings and their health care providers play in this regime by reporting reactions and incidents
    - Outline how information gathered through this reporting system is and will be shared back to Canada's healthcare community.
  - Baseline data will help to determine if this education approach is sufficient to improve non hospital reporting. If not, consideration will be given to expanding the mandatory reporting regulations to sites other than hospitals.

Part 3. Optimize the Timely Analysis and Sharing of Information with Health System Partners

- In addition to increasing reporting of ADRs & MDIs, Health Canada will optimize the use of this data.
  - The quantity and quality of ADR and MDI reports received by Health Canada will be influenced by our ability to demonstrate the benefits of reporting to Canadians, reporting institutions and health care providers.
- Currently, Health Canada makes all ADR data available online, produces an annual report and publishes risk communications to providers through a number of forums.
- Health Canada will improve its analysis and knowledge translation (KT) related to ADR and MDI, ensuring health system partners have timely access to key information by undertaking two activities:
  - Optimize Data Analytics
    - Health Canada is investing in IT tools that will better support the timely, appropriate analysis of the ADR and MDI data, streamlining the identification of potential safety signals
    - Health Canada will invest in development of a searchable database for MDIs
  - Optimize Sharing of Information with Partners
    - Through consultation with key stakeholders, Health Canada will identify the content, frequency and format of ADR and MDI products that will be of most use for health system partners thereby getting the right information to the right people in the right formats for uptake; a KT Plan for ADR and MDI information will be developed and implemented as a result
    - Part of the Health Canada KT Plan will include optimizing our Annual ADR and MDI Report to better meet the needs of clients, and the launch of a webinar series
    - The webinar series will aim to provide a quarterly and as needed venue for timely discussions on specific ADR and/or MDI issue with target audiences

That summarizes our health product vigilance cycle….but what if a safe and effective product is on the market, but there is dishonest advertising associated with it?

Advertising Compliance and Enforcement

- Health Canada is responsible to monitor for any health product advertisement that is non compliant with the rules outlined in their associated regulations, and to take appropriate enforcement action. Traditionally, HC had a complaints based system but significant improvements have been made:

1. **June 2018:** Minister of Health announced a new program to address compliance & enforcement of opioid advertising as part of the federal government's efforts to address the opioid crisis
   - This program is up and running, proactively monitoring for non compliant opioid advertisements, and was recently expanded to include proactive monitoring of non compliant advertising for all health products

2. **Fall 2018:** Health Canada put new Terms and Conditions on all opioid manufacturers to get their advertising material pre-cleared by an approved pre-clearance agency and to submit proof of pre clearance with their annual RMP.

3. **March 11, 2019**: Health Canada announced:
   - Additional proposed restrictions on the marketing and advertising of prescription opioid drugs, requiring industry to limit all advertising materials of Class B opioid products provided to health care professionals to include **only statements that have been authorized by Health Canada in the Product Monograph, verbatim.**
   - The Launch of the Stop Illegal Marketing of Drugs and Devices program (SIMDD)
     - SIMDD is a web-based platform designed to raise awareness among health care professionals about the rules governing the marketing of drugs and devices. It consists of educational web content and an easy reporting tool for health care professionals who encounter suspected inappropriate advertising
     - https://www.canada.ca/en/health-canada/services/drugs-health-products/marketing-drugs-devices/illegal-marketing/stop.html

In Conclusion

- Health Canada has one of the strongest health product vigilance programs in the world

- Like any responsible regulator, we are constantly striving to improve; many initiatives are currently underway which aim to enhance our health product vigilance system

- This presentation aimed to provide not only an overview of the current system but a focus on the improvements and evolution being made in the post market space

Questions?