

PHARMACOVIGILANCE WORKSHOP SUMMARY

McLaughlin Centre for Population Health Risk Assessment
University of Ottawa, Senate Room (083)
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This Summary is based on presentations and discussions held at the 2007 'Pharmacovigilance Workshop', and represents the collective views and key messages of speakers, panel members and workshop participants including the U.S. Institute of Medicine of the National Academies committee member, governmental organizations, academics, non-governmental organizations and industry representatives from Canada and the United States. The objective of the Workshop was to 'Understand the sources of data and risk assessment tools currently available to assess the safety of marketed health products and to explore the role of academia in pharmacovigilance in Canada'. The organizing committee for the Workshop included representatives from the University of Ottawa, Risk Sciences International (RSI), Cerner Corporation and Health Canada¹.

This Summary represents the main messages of the speakers' and panel members' presentations and the afternoon group discussion session. Additional information including the final report of the Workshop, the PowerPoint presentations from the speakers and panel members and the Pharmacovigilance Workshop participants are available for reference. http://www.mclaughlincentre.ca/events/pharmaco_WS.shtml. The summary was prepared by the Workshop organizing committee.

¹ Comments made at the Pharmacovigilance workshop are not necessarily those of HC but reflect the comments of the individual attendees.

Key Concepts in Understanding Pharmacovigilance

Workshop Summary

What is Pharmacovigilance?

- Pharmacovigilance is the science and activities relating to the detection assessment, understanding and prevention of adverse effects or any other drug-related problems. (WHO 2002)
- Pharmacovigilance is an umbrella term used to describe the processes for monitoring and evaluating adverse drug reactions (ADRs) following the introducing of new drugs into the marketplace, and is a key component of effective drug regulation systems.

Role of Pharmacovigilance

- To monitor the effectiveness and safety of new and medically evolving treatments under real-life conditions post release.
- To gather information about use in specific population groups notably children, pregnant women and the elderly.
- To gather information on the efficacy and safety of chronic use of drugs in combination with other medicines.

How is Pharmacovigilance done?

- Most countries monitor Adverse Drug Reaction (ADR) via passive pharmacovigilance.
- Individual case safety reports (ICSRs) are submitted to a regulatory agency by manufacturers, health professionals, consumers and hospitals.
- WHO's Drug Monitoring Program consolidates data from a number of National Centres.
- Each report represents a suspicion, opinion or observation of the individual making the report
- Since not all ADRs are reported, pharmacovigilance data cannot be generally used to estimate the incidence of adverse reactions on a population basis.

Pharmacovigilance at Health Canada

- The Marketed Health Products Directorate (MHPD) is responsible for adverse drug reaction reporting and signal detection in Canada.
- The Canadian Adverse Drug Reaction Monitoring Program (CADRMP) was established in 1965, and the current Canadian Adverse Reaction Information System (CADRIS) now contains about 170,000 ADR reports. A subset of the CADRIS with personal identifiers removed is available on the Health Canada website at the MedEffect page (see further information).
- Data is collected primarily by a spontaneous surveillance system in which adverse reactions to marketed health products are reported to Health Canada; reporting is mandatory for Market Authorization Holders, but voluntary for others like health professionals and consumers.
- ADR information is available through CADRMP on-line query and data extracts; the Canadian Adverse Reaction Newsletter; and through MedEffect a website portal providing information on the latest advisories, warnings and recalls.
- Market authorization holders (MAHs) are responsible for monitoring the safety and effectiveness of their products on the market and for continually assessing the risk-benefit profile of products marketed in Canada as well as keeping consumer/health professional information on their products updated and truthful.

WHO's Vigibase for Adverse Drug Reactions (ADRs)

- Vigibase is the data repository that has accumulated about 4 million ICSRs since 1968.
- This international repository not only facilitates the pooling of data from different countries, but also permits comparisons among countries.
- A number of methods for analysis like the Bayesian approach are used for signal detection in Vigibase.

Interpretation of Pharmacovigilance Data

- Pharmacovigilance data require careful interpretation, taking into account its strengths and weaknesses.
- Pharmacovigilance is particularly important in identifying potential adverse drug reactions that may have been missed in pre-market tests.
- Pharmacovigilance data is also important in identifying potential risks to pregnant women and children, who are not included in clinical trials conducted prior to market authorization.
- Pharmacovigilance data requires careful interpretation. Because reporting of adverse drug reactions is not mandatory (with the exception of market authorization holders), the number of ADRs occurring in the general population will be underestimated. Data is primarily collected by MAH's into their own databases and by a spontaneous surveillance system at Health Canada in which adverse reactions to marketed health products are reported by market authorization holders and others to Health Canada on a voluntary basis.
- ICSRs are limited by lack of information on the health status of the individual making the report, lack of information on other medications that the patient may also be taking, possible bias by the reporter, complexity of product(s) used versus underlying disease(s) and incomplete outcome information.
- Potential signals of adverse drug reactions detected using passive pharmacovigilance may need to be followed up through active surveillance and more detailed pharmacoepidemiology studies.
- Health Canada*, FDA*, and WHO* have all provided guidance on ways in which pharmacovigilance data can be used in assessing potential adverse drug reactions.

* See further information

Datamining Tools for Signal Detections

- There are a number of statistical datamining algorithms available for assessing when there is sufficient evidence of a signal of adverse reactions associated with a specific product.
- These include Bayesian methods and other recognized, which take into account prior information about the possibility of occurrence of adverse reactions.

Communicating Information about Potential Risks of Marketed Health Products

- It is important that information on potential risks of marketed health products be clearly communicated to health professionals and the general public in a timely fashion and in an understandable language level.
- It is important to increase public awareness that new drugs carry some uncertainty, and that all drugs have risks and benefits.
- Risk communication challenges include translating technical information into terminology that can be understood by the lay person.
- Communication by the market authorization holders is often discussed in advance with the federal regulatory authority (Health Canada).
- At Health Canada, there are multiple health professional and public risk communication vehicles to distribute messages, including Health Canada products such as Public Warnings, Public Advisories, Information Updates, Foreign Product Alerts. (see Health Canada Fact Sheet on web for details)

The Future of Drug Safety

- The Institute of Medicine (IOM) in the United States recently completed a comprehensive report on:
"The Future of Drug Safety: Promoting and Protecting the Health of the Public"
- A fundamental message of the IOM report was the need for more resources for the Food & Drug Administration to fulfill its mandate in this area.
- The IOM report also recommended a lifecycle approach to the evaluation of drug risks and benefits.

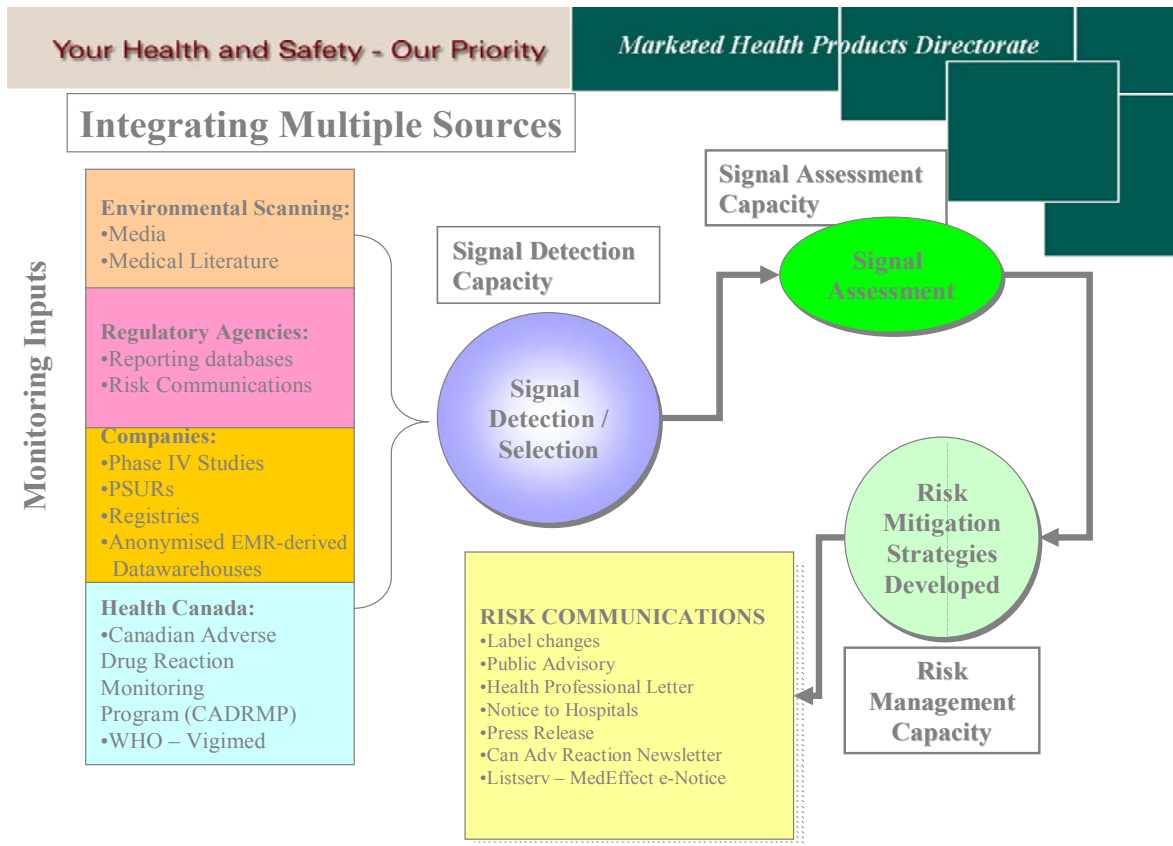
Conclusions

- Pharmacovigilance is an important tool for monitoring drug risks following market authorization in a "real world setting".
- International collaboration is essential for successful post-market surveillance program, providing the sample sizes needed to evaluate small risks, and dissemination information to countries without established post-market surveillance programs.
- The management of the risks associated with the use of medicines requires close and effective collaboration between the key stakeholders in the field of pharmacovigilance, including:
 - Academia
 - Health professionals
 - Hospitals
 - International conference on Harmonization (ICH) for drugs and Global Harmonization Task Force (GHTF) for medical devices
 - Manufacturers
 - Medical and pharmaceutical associations
 - National Regulatory agencies
 - Patients and consumers
 - World Health Organization Program for Drug Safety

Pharmacovigilance! What Happens Next?

- Continued work on improving quality in ADR reporting and development of data standards and uniform data definitions and practice will enhance the value of pharmacovigilance databases.
- Health Canada's new ADR Database replacing CADRIS will meet all of the international requirements (ICH, CIOMS) and will include electronic reporting and electronic data exchange.
- Health Canada is currently reviewing the IOM report as well as conducting work on a Progressive Licensing Framework as part of its Blueprint for renewal project.
- Academia can play a role in helping develop methodological approaches; providing basic research that links to population-based studies; conducting industry-independent studies on risk perception in risk management; and developing capacity for education, certification and review of drug safety analyses.
- A move to active pharmacovigilance using data resources such as the Cerner HealthFacts™ Datawarehouse will enhance pharmacovigilance providing information on polypharmacy and co-morbidity.
- Internationally, pharmacovigilance data, such as that collected by federal regulatory authorities and by the WHO will be valuable in helping to develop standards and uniform data definitions and practice.
- Successful detection of potential signals should be through a combination of spontaneous ADR reporting and rich database with effective data mining tools.
(Figure 1)

Figure 1: Health Canada's Approach to Integrating Multiple Sources



Further Information

Health Canada

Guidance documents

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/index_e.html

MedEffect Website

http://www.hc-sc.gc.ca/dhp-mps/medeff/index_e.html

Food and Drug Administration guidance documents

<http://www.fda.gov/cder/guidance/6359OCC.htm>

World Health Organization

WHO (October 2004). 'Pharmacovigilance: ensuring the safe use of medicines'

<http://www.who-umc.org/DynPage.aspx?id=13136#19>

Institute of Medicine Drug Safety report

http://www.nap.edu/catalog.php?record_id=11750