



Health
Canada

Santé
Canada

*Your health and
safety...our priority.*

*Votre santé et votre
sécurité...notre priorité.*

Canada Vigilance

Adverse Reaction Monitoring Program and Database

Pharmacovigilance Transformation Workshop
University of Ottawa
Friday May 29, 2009

Heather Sutcliffe
Director
Marketed Health Products Safety and Effectiveness Information Bureau
Marketed Health Products Directorate
Health Canada



MedEffect Canada

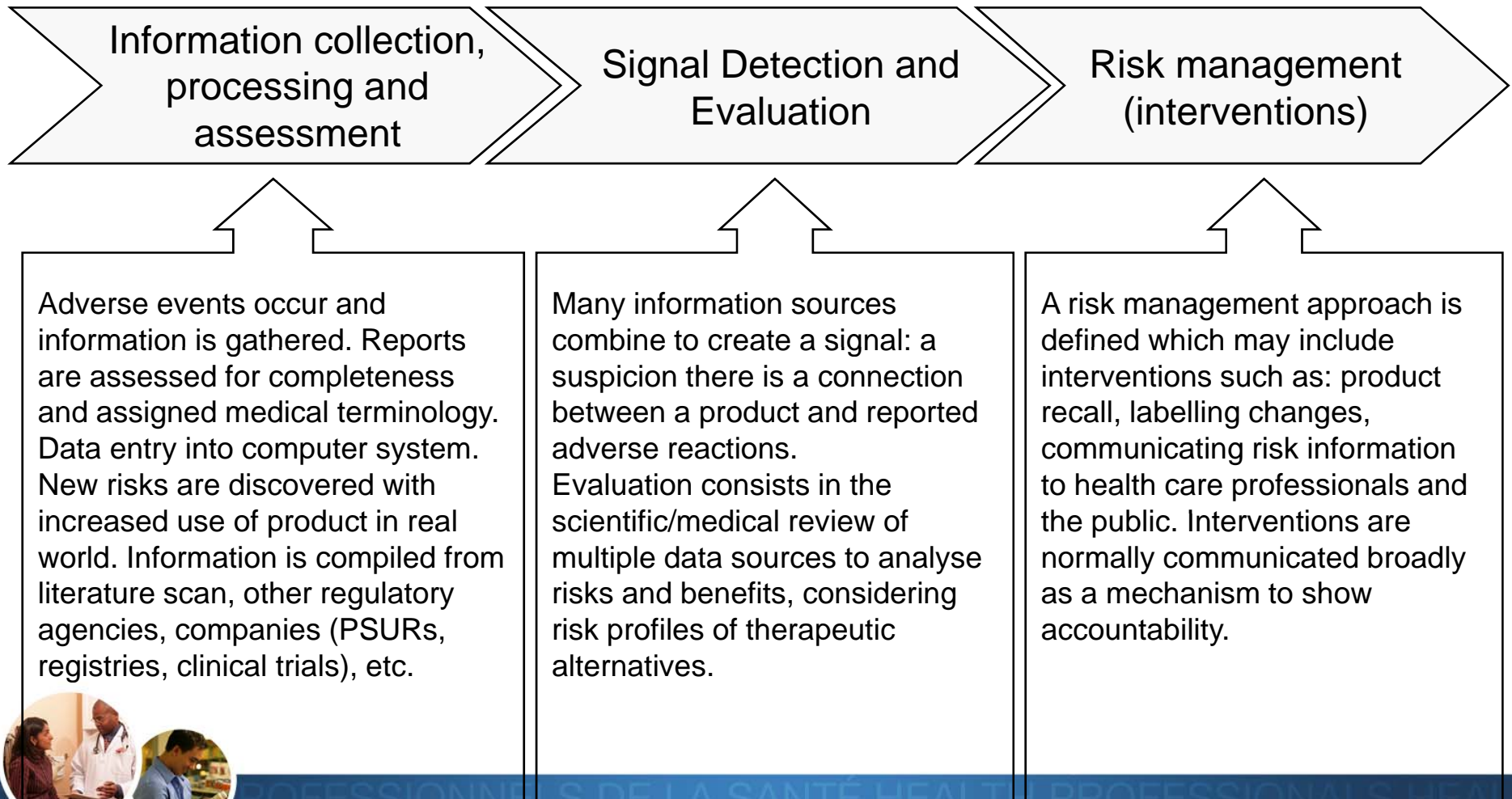
*Together we can improve
health product safety*

MedEffet Canada

*Ensemble nous pouvons améliorer
l'innocuité des produits de santé*

Canada 

Post-market surveillance is composed of three major activities:



Canada Vigilance Program

- Spontaneous Adverse Reaction Reporting Program exists since 1965
- Canada Vigilance Program (name change 2007)
- Mandatory reporting for Market Authorization Holders (i.e. manufacturers)
- Voluntary reporting for Health Professionals and Consumers
- Legislative Framework (e.g. *Food and Drugs Act and Regulations* (C.01.016), Access to Information and Privacy Act etc.)



Purpose of Adverse Reaction Reporting Program

- Detection, prioritization, confirmation and risk management of signals
- SIGNAL – reported information on a possible causal relationship between an adverse event and a health product the relationship being unknown or incompletely documented previously



Mandatory Reporting Market Authorization Holders (MAH)

- AR reports submitted by MAHs are collected by the Canada Vigilance National Office located in Ottawa
- MAHs are responsible as per the *Food and Drug Regulations* for the reporting of ARs to Health Canada
- Domestic AR report information is entered into the Canada Vigilance Database



Adverse Reaction Reports

- Domestic Adverse Reaction Reports
 - Reports concerning reactions occurring in Canada to a product that is marketed in Canada
 - Market Authorization Holder reporting within 15 calendar days of receiving the information (expedited reporting)
 - Serious Adverse Reactions
 - Unusual failure in efficacy reports for new drugs
- Foreign Adverse Reaction Reports
 - Reports concerning reactions occurring outside Canada to a product with the same combination of active ingredients that is marketed in Canada
 - Market Authorization Holder reporting within 15 calendar days of receiving the information (expedited reporting)
 - Serious Unexpected Adverse Reactions



Canada Vigilance Regional Offices

- Collection of reports, review for completeness, follow-up with reporters
- Initial Data Entry into Canada Vigilance Workflow
- Provide acknowledgement letters to the reporters
- Increase health professional and consumer awareness of Canada Vigilance
- Provide guidance, in order to maximize the quality of reports
- Direct Canadians to Health Canada sources of new safety information
- Consumer Reporting Form/Guidelines Project for reporting of adverse reactions



Reporting to Canada Vigilance

- Adverse reaction reporting form
 - Available Regional/National Offices, MedEffect website, CPS
- Submit by fax or mail
- On-Line submission
- Toll Free Telephone and Fax
- Verbal reports accepted
- Postage paid mail

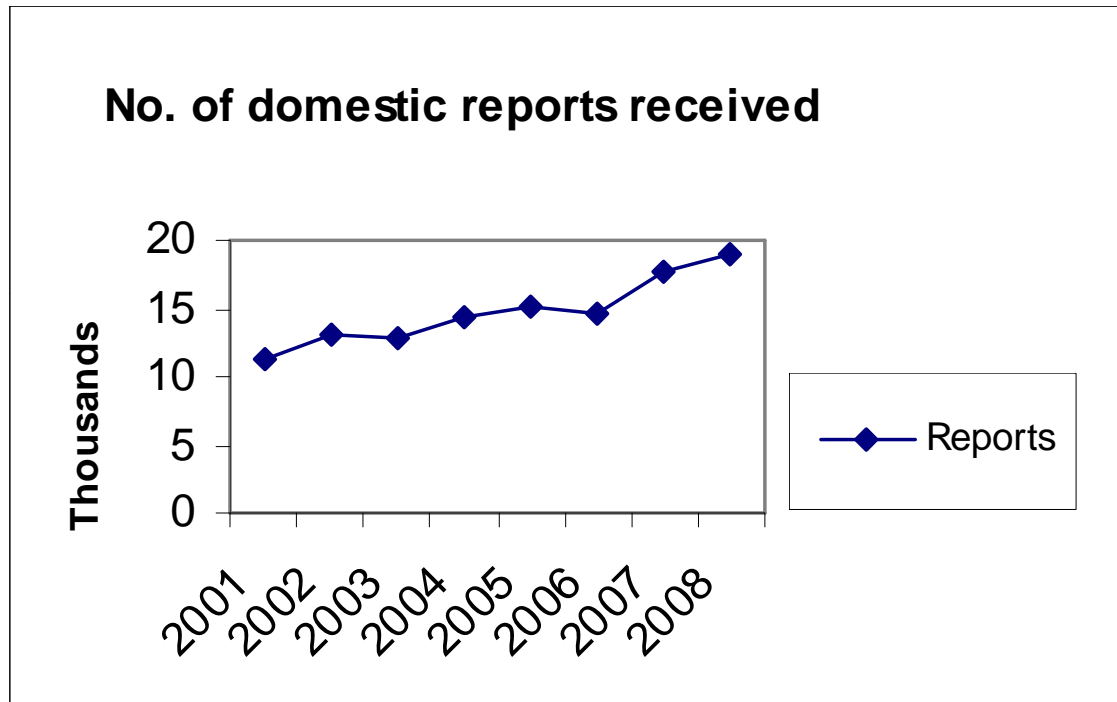


Scope

- The Canada Vigilance Program collects adverse reaction reports for the following marketed health products approved for use in humans:
 - Pharmaceutical drugs (prescription and non-prescription)
 - Biologics (Schedule D, biotechnology products, therapeutic and diagnostic vaccines and fractionated blood products)
 - Radiopharmaceuticals drugs
 - Natural health products
 - Cells, Tissues and Organs (CTOs)



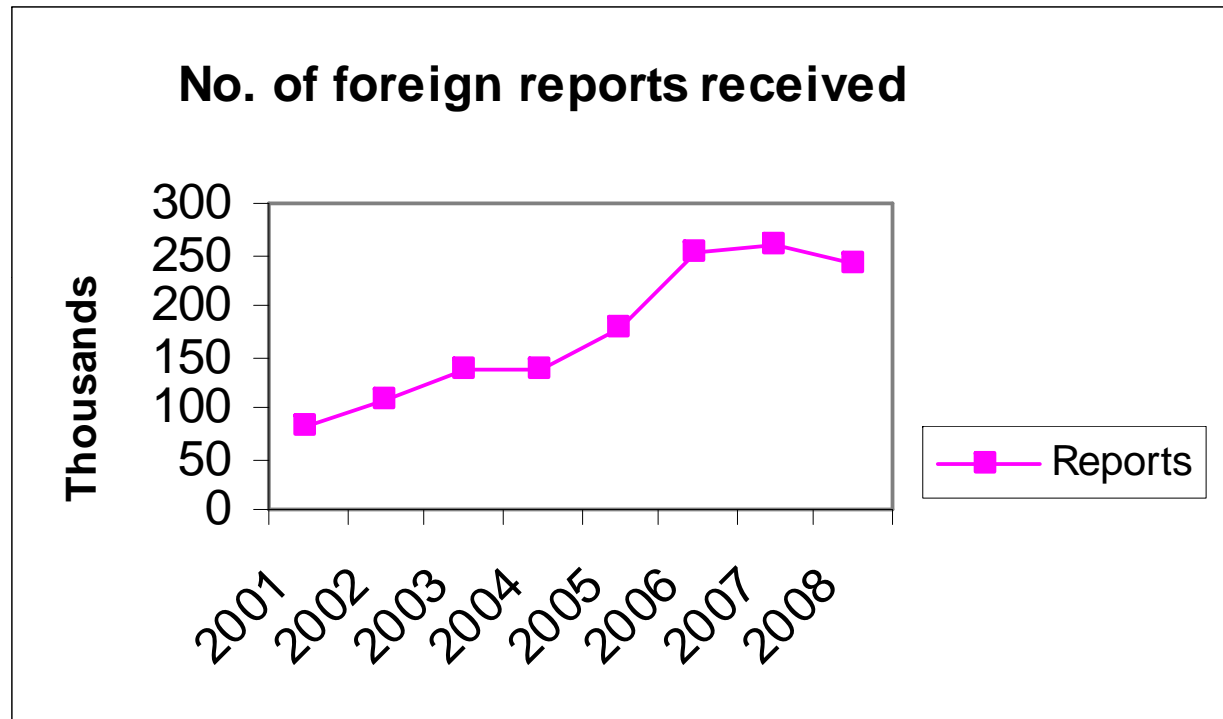
Canada Vigilance Program Domestic Reports



20,360 Domestic Reports Received in 2008



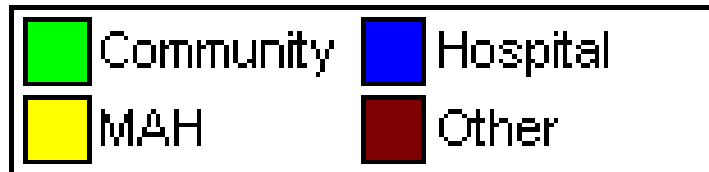
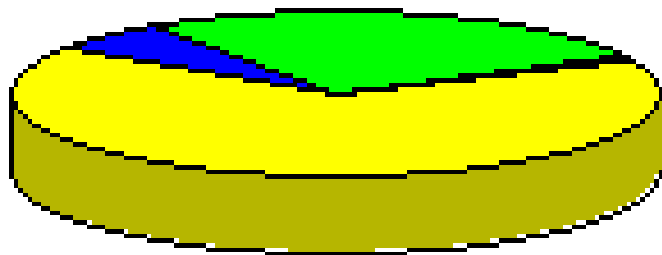
Canada Vigilance Program Foreign Reports



241,417 Foreign Reports Received in 2008



Source of Domestic Reports - 2008



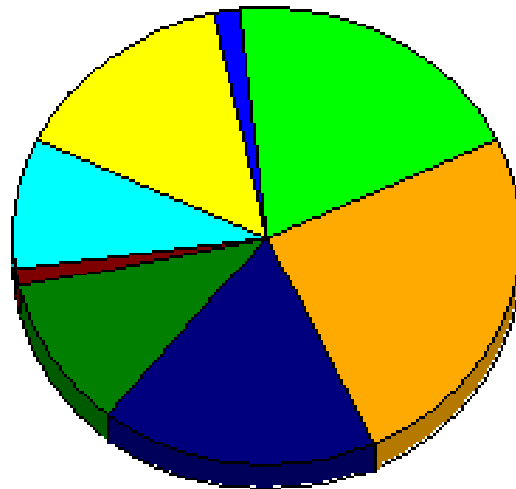
Source	Percentage
Community *	27.57 %
Hospital	6.04 %
MAH **	65.58 %
Other	0.80 %
Total:	100.00%













* Community – Consumer, patient and non-hospital based health care professionals

** MAH – Market Authorization Holder (MAH)



Reporter Type – Domestic Reports - 2008



 Consumer	 Coroner/Medical Examiner
 Dentist	 Health Professional
 Lawyer	 Naturopath
 Nurse	 Other
 Patient	 Pharmacist
 Physician	 Physician, specialized

Reporter Type	Percentage
Consumer	19.63 %
Coroner/Medical Examiner	1.54 %
Dentist	0.02 %
Health Professional	14.85 %
Lawyer	0.15 %
Naturopath	0.01 %
Nurse	9.05 %
Other	1.50 %
Patient	10.55 %
Pharmacist	17.81 %
Physician	24.85 %
Physician, specialized	0.04 %
Total:	100.00%



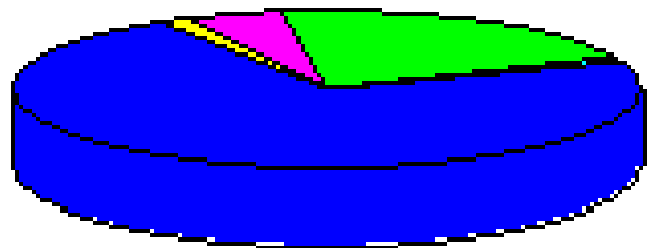
Serious Domestic Reports - 2008



Serious	Percentage
No	30.75 %
Yes	69.25 %
Total:	100.00%



Product Type – Domestic Reports - 2008

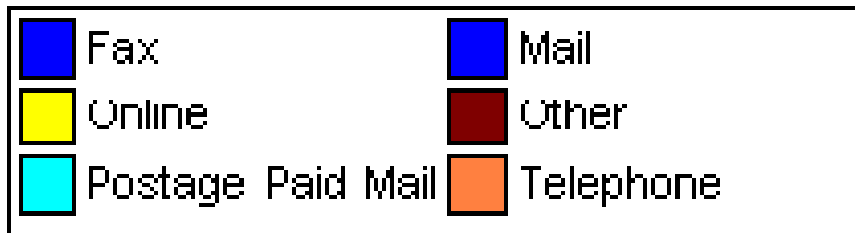
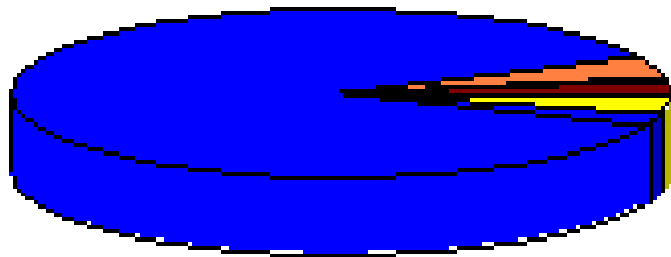


	Biotechnology Products
	Blood Products and Biologics
	Natural Health Products
	Pharmaceuticals
	Radiopharmaceuticals

Product Type	Percentage
Biotechnology Products	20.21 %
Blood Products and Biologics	4.97 %
Natural Health Products	1.72 %
Pharmaceuticals	71.32 %
Radiopharmaceuticals	1.78 %
TOTAL:	100.00%



Reporting Method – Domestic Reports - 2008



Initial Reporting Method	Percentage
Fax	86.80 %
Mail	1.91 %
Online	3.59 %
Other	2.44 %
Postage Paid Mail	0.30 %
Telephone	4.96 %
Total:	100.00%

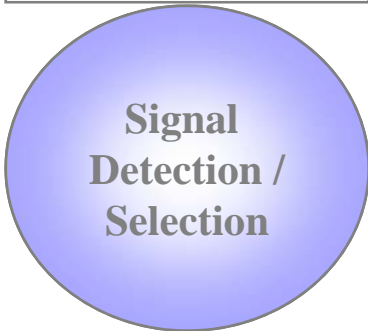


Integrating Multiple Sources

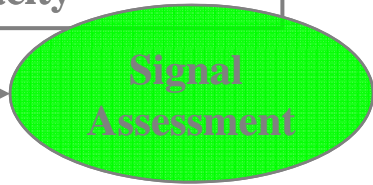
Monitoring Inputs

- Environmental Scanning:**
 - Media
 - Medical Literature
- Regulatory Agencies:**
 - Reporting databases
 - Risk Communications
- Companies:**
 - Phase IV Studies
 - PSURs
 - Registries
- Health Canada:**
 - Canada Vigilance Program
 - WHO – Vigimed

Signal Detection Capacity



Signal Assessment Capacity



Risk Management Capacity

- RISK COMMUNICATIONS**
- Label changes
 - Public Advisory
 - Health Professional Letter
 - Notice to Hospitals
 - Press Release
 - Can Adv Reaction Newsletter
 - Listserv – MedEffect e-Notice



Adverse Reaction Data

- Each report represents the suspicion, opinion or observation of the individual reporter
 - Cause and effect relationships have not been established in the vast majority of reports submitted
 - Only a small proportion of suspected adverse reactions are reported to the program, consequently this information must not be used to estimate the incidence of adverse reactions



MedEffect™ Canada Initiative

- Launched in August 2005 to better communicate health product safety information and increase awareness of AR reporting
- Centralized access to :
 - Reliable & relevant health product safety information
 - Advisories & CARN
 - Information on how to report ARs & other reporting initiatives
 - Industry Guidance & Templates for Issuance of Health Professional & Public Communications



MedEffect Canada
Together we can improve health product safety

Adverse Reactions to Drugs and Other Health Products

*Get Informed!
 Keep Informed!
 Report Adverse Reactions.*

www.healthcanada.gc.ca/medeffect

Advisories, Warnings and Recalls	Guidance Documents
Adverse Reaction Reporting	Adverse Reaction Database
Sign-up for MedEffect e-Notice	



MedDRA Terminology

Medical Dictionary for Regulatory Activities

- MedDRA Implemented with Canada Vigilance
- Standardized terminology for classification, retrieval, presentation and communication of medical information (ICH standard)
- Scope: symptoms, signs, diseases and diagnoses, investigations and tests, therapeutic indications, surgical and medical procedures, & medical, social and family history
- Includes medication error related terms
- Sharing of data requires consistency of data coding and assessment
- Facilitates standardized electronic transmission of medical information
- Terminology and MedDRA training provided free of charge to academic researchers



Canada Vigilance Online Reporting Form

The Canada Vigilance Adverse Reaction (AR) Monitoring Program offers health professionals and the public the ability to complete and submit an AR report online through the MedEffect™ Canada website.

The screenshot shows the top navigation bar with the Health Canada logo and the text 'Health Canada / Santé Canada'. To the right is the 'Canada' logo. Below this is a menu with links: 'Français', 'Contact Us', 'Help', 'Search', and 'Canada Site'. A secondary menu contains 'Just For You', 'It's Your Health', 'Media Room', 'A-Z Index', and 'Home'. A banner for 'Drugs & Health Products' is visible, along with a breadcrumb trail: 'Home > Drugs & Health Products > MedEffect > Adverse Reaction Reporting'. The main heading reads 'Canadian Adverse Drug Reaction Monitoring Program Form HC/SC 4016' with a 'PROTECTED B (when completed)' label. The section is identified as 'Section 1 of 5'. Navigation buttons include 'View', 'Reset', 'Guide', and 'Next >'. The form content includes a question: 'Is this a followup report to a previously submitted AR report? If so, please enter the tracking number assigned by Health Canada to your previous AR report here.' Below this is a 'Tracking number:' field with a 'MED -' prefix and a text input box. The form is divided into five numbered sections: 1. Identifier (for privacy purpose do not use the patient's name) with a text input; 2. Age at time of reaction with a 'Year(s)' dropdown; 3. Sex with radio buttons for 'Male' and 'Female'; 4. Height with input fields for feet, inches, and centimeters; 5. Weight with input fields for pounds and kilograms. At the bottom, there are 'View', 'Reset', 'Guide', and 'Next >' buttons, a 'Last Update: 2006-06-28' timestamp, and a link to 'Important Notices'.



Canada Vigilance Online Database

This database is available on the MedEffect™ Canada website and enables users to query AR report-related information extracted from the Canada Vigilance AR database. This site will be undergoing a re-design to improve the search capabilities.

Health Canada Santé Canada

Français Contact us Help Search Canada Site

Drugs & Health Products

Health Canada Home

CADRMP Online Query

1. Report Search Criteria

Date Received at MHPD:

From Date: 1965 - 01 (YYYY-MM)

To Date: 2008 - 12 (YYYY-MM)

Data will be updated quarterly.

2. Health Product Search Criteria

Health Product Name: [Health Product Name Search *](#) - OR - [Active Ingredient Search *](#)

Health Product Involvement: Suspected

3. Patient Search Criteria

Age From: 0 Year(s) Old To: ALL Year(s) Old

Gender: ALL

Outcome: ALL

Submit

[Search Assistance Notes](#)
[Glossary of Database Fields](#)

*Mandatory Search Criteria

Last Updated - 2007-05-15 [Important Notices](#)



Canada Vigilance Database Status

- Feb 2006 – Request for Proposal posted on Public Works and Government Services Canada website
- Oct 2006 – Contract signed with ArisGlobal
- March 2008 – Initial Implementation of Post Market Module
- ArisGlobal products/services are used mainly by industry but also by the French and Irish Regulatory Agencies
- MedDRA terminology implemented with Canada Vigilance



Business Requirements

- Clinical trial AR requirements
- Post market AR requirements
- Signal Detection & powerful query tools
- ICH compliant (E2B, MedDRA, ESTRI-Gateway)
- Management & ICSR reporting
- Scanning and Imaging
- Capability for future integration document management solution, small manufacturer reporting interface



Canada Vigilance Database

- The Canada Vigilance database is comprised of an integrated and complementary suite of 3 applications which include:
 - Core application
 - Signal detection tool
 - ESTRI gateway module



Canada Vigilance Database: Core Application

- For the collection, coding, assessment and reporting of adverse reaction data
- Workflow module routes AR cases to Specialists/Assessors automatically, based on pre-defined criteria such as drug class, seriousness, etc.
- Enables full compliance with the ICH international AR reporting requirements, such as ICH E2B, MedDRA coding, etc.
- Configurable and will offer English and French user interfaces
- Scanned images of AR reports



Canada Vigilance Database: Signal Detection

- Data mining and signal detection tool
- Facilitates safety data analysis
- Facilitates the identification of patterns in the data and identify possible associations underlying signals
- Users can build, save and share ad-hoc queries
- Provides access to the FDA (FOI) data, a larger pool of data for analysis and signal detection
- Statistical module includes algorithmic analyses, such as PRR, Bayesian, Chi-Square, Log-Likelihood



Signal Detection: Standard Reports

The screenshot displays the SafetyMart web application interface. At the top, the browser title is "SafetyMart - Microsoft Internet Explorer". The application header includes the "SafetyMart" logo and navigation tabs for "Analysis Modules", "Reports", and "Admin". Below the header, the "Universe" is set to "SafeMart" and a "Report Designer" button is visible. The main content area is divided into two panels: "Report Groups" on the left and "Report Names" on the right. The "Report Groups" panel lists: 1. StandardReports, 2. EUCTD, 2. Line Listing, and 3. SMQS. The "Report Names" panel lists several reports, each with a folder icon: Adverse Event Count Per Month, Adverse Event Count Per Year, Dechallenge Rechallenge Case Count, Number of Serious Adverse Events and Cumulative Total Over Time, Number of Serious and Non-Serious Cases by SOC Level, Serious Adverse Events - Labeled vs Outcomes by Drug, Serious Adverse Events by Age Grouping and Gender by Drug, Serious Count Per Month, and Serious Count Per Year. A mouse cursor is positioned over the bottom of the "Report Names" list.



Signal Detection: Statistical Analysis

Statistical Analysis Output - Microsoft Internet Explorer

SafetyMart

Analysis Modules | Reports | Admin

Statistical Analysis Output

SafetyMart

Back Home Selection Criteria Save

Refresh Print Preview Export to Excel Statistical Analysis Tool

Reaction Level Refresh Include All Clear Clear All

Graphical View Drilldown Hierarchy

Select	Drug	Reaction	N	FRR	ROR	EBOS	EBOM	χ^2	χ^2 is significant at a significance level of \leq @	LogLikelihood Ratio (G)	G is significant at a significance level of \leq @	BCPNN
<input type="checkbox"/>	CHAMPIX	SUICIDAL IDEATION	43	30.21	35.329	4.477	30.802	1320.71 ^{a,b}	0.001	212.81 ^b	0.001	4.917

a - Yates correction for continuity used. (Yates, 1934)
 b - The contingency table for χ^2 analysis has expected values greater than the absolute difference between observed and expected values
 Log-likelihood ratio analysis (G) should be used. (Williams, 1976)
 @ - if blank, the significance is greater than 0.100



Signal Detection: Trend Analysis



Canada Vigilance Database: Trend Analysis Outputs

SafetyMart

Analysis Modules | Reports | Admin

Output

SafetyMart

◀ Back | 📄 Selection Criteria | 🖨️ Print Preview | 📄 Export to Excel

PRR Code

	>10
	>5 to <=10
	>3 to <=5
	<=3

Drug : CHAMPIX

Event	Q1, 2007	Q1, 2007 - Q2, 2007	Q1, 2007 - Q3, 2007	Q1, 2007 - Q4, 2007
Suicidal ideation	0	0	5	10
Syncope	0	0	1	1
Syncope vasovagal	0	0	0	1
Tachycardia	0	0	0	1
Thinking abnormal	0	0	0	2
Throat tightness	0	0	1	2
Thrombophlebitis superficial	0	0	0	1
Tinnitus	0	0	0	1
Tremor	0	0	1	3
Urinary incontinence	0	1	1	2

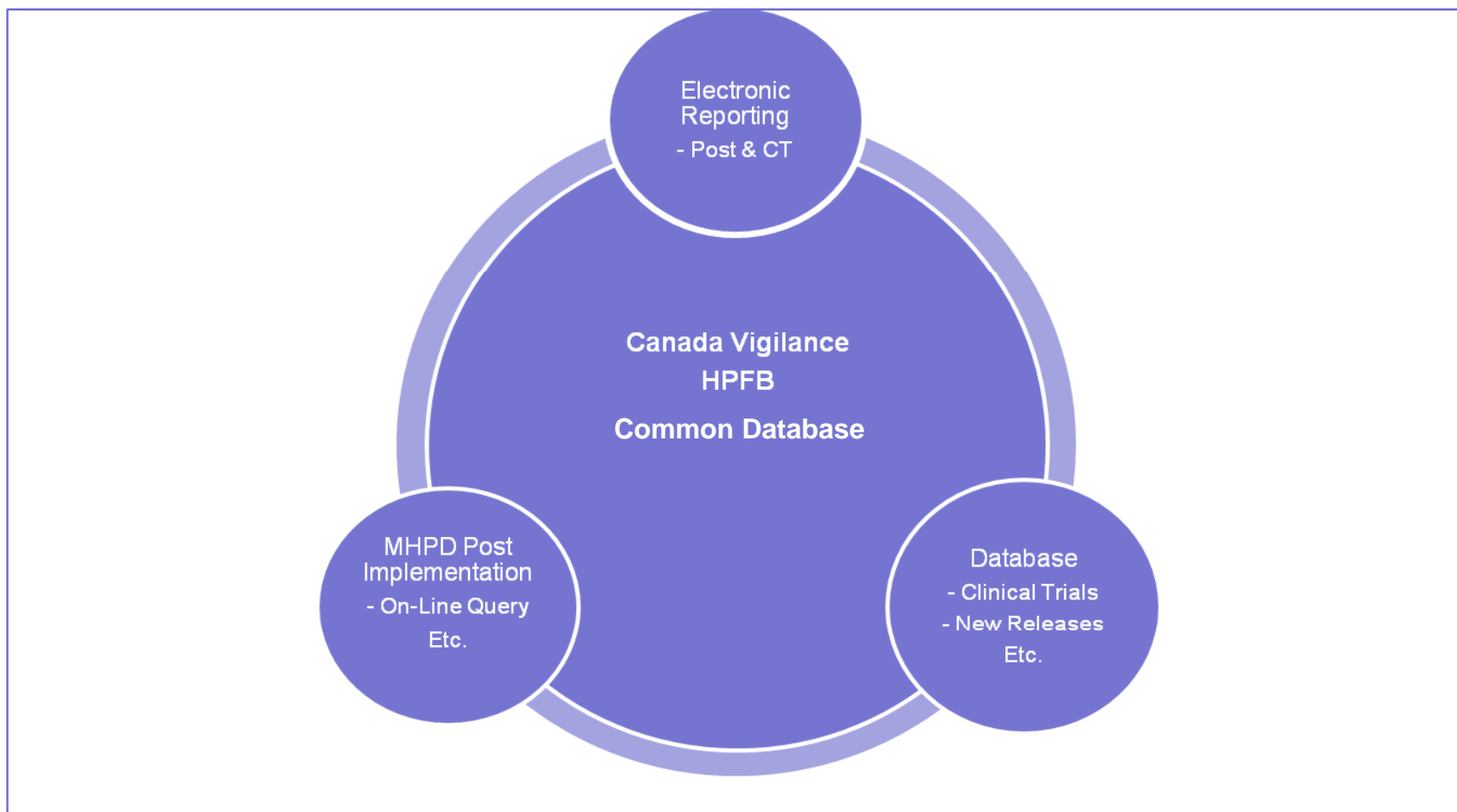


Canada Vigilance Database: Electronic Exchange

- ESTRI Gateway module
- Enables the secure electronic exchange and management of safety information in the ICH E2B and M2 standards
- Planned implementation for Phase 2 of this project



Canada Vigilance – Health Products & Food Branch

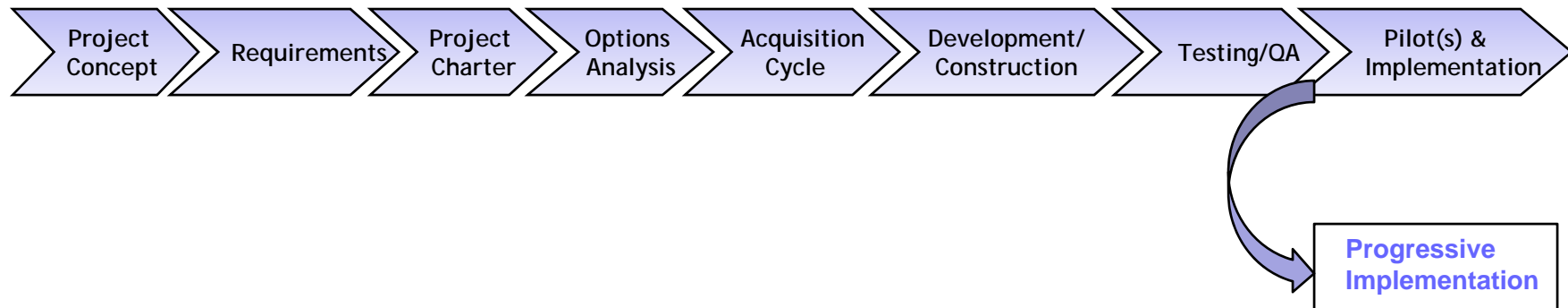


Canada Vigilance Database Sub-Projects

- Post-Market Implementation (MHPD)
- Sustainability and On-Going Maintenance
- Post-Market On-Line Database
- Clinical Trials Implementation (BGTD, NHPD, TPD)
- Electronic Reporting by Small/Medium/Large MAH/Sponsors
- Signal detection business transformation project underway



Electronic Reporting by Small/Medium/Large MAHs/Sponsors



Proposed Timeline

- Acquisition Cycle Fall 2009
- Electronic Reporting Pilots starting Fall 2010
- Staggered implementation by small/medium/large MAHs




 Health Canada / Santé Canada

Your health and safety... our priority. / Votre santé et votre sécurité... notre priorité.



Canada Vigilance

Adverse Reaction Monitoring Program and Database

Suspect an adverse reaction?
Report it...

Phone: 1-866-234-2345
Fax: 1-866-678-6789
Online: www.healthcanada.gc.ca/medeffect
Postage Paid Mail

A Program of
MedEffect Canada
Together we can improve health product safety






Questions?

