Canada Vigilance

Adverse Reaction Monitoring Program and Database

Pharmacovigilance Transformation Workshop
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Post-market surveillance is composed of three major activities:

Information collection, processing and assessment

Adverse events occur and information is gathered. Reports are assessed for completeness and assigned medical terminology. Data entry into computer system. New risks are discovered with increased use of product in real world. Information is compiled from literature scan, other regulatory agencies, companies (PSURs, registries, clinical trials), etc.

Signal Detection and Evaluation

Many information sources combine to create a signal: a suspicion there is a connection between a product and reported adverse reactions.
Evaluation consists in the scientific/medical review of multiple data sources to analyse risks and benefits, considering risk profiles of therapeutic alternatives.

Risk management (interventions)

A risk management approach is defined which may include interventions such as: product recall, labelling changes, communicating risk information to health care professionals and the public. Interventions are normally communicated broadly as a mechanism to show accountability.

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

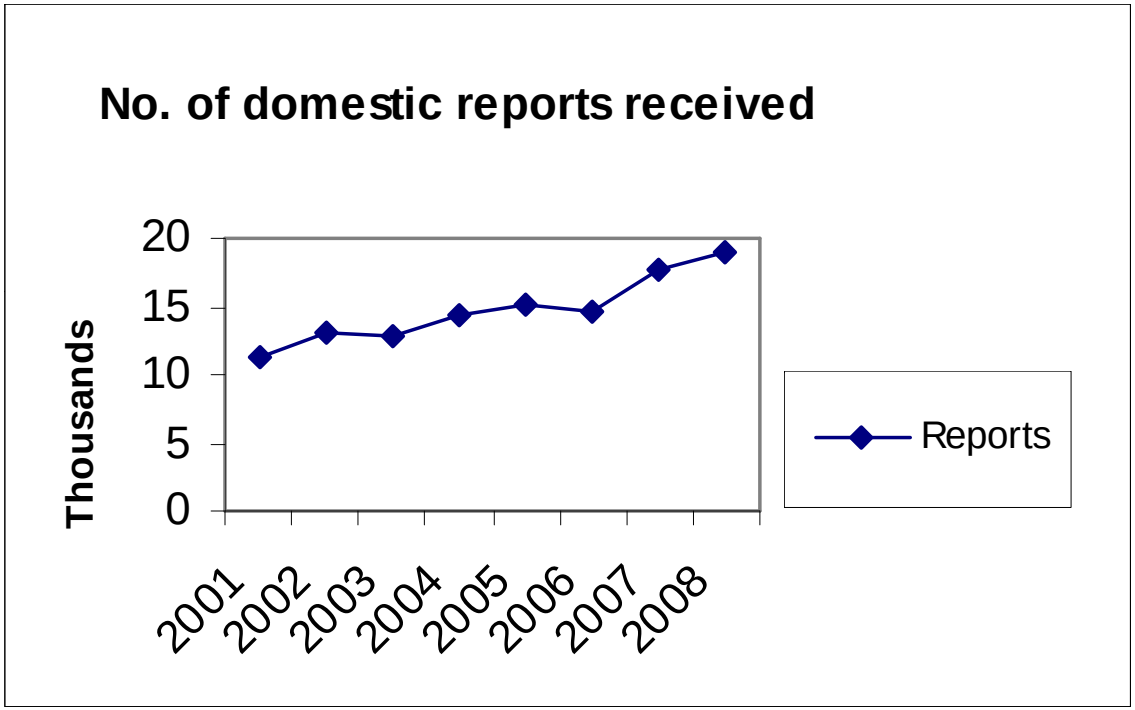
Reporting to Canada Vigilance

- 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

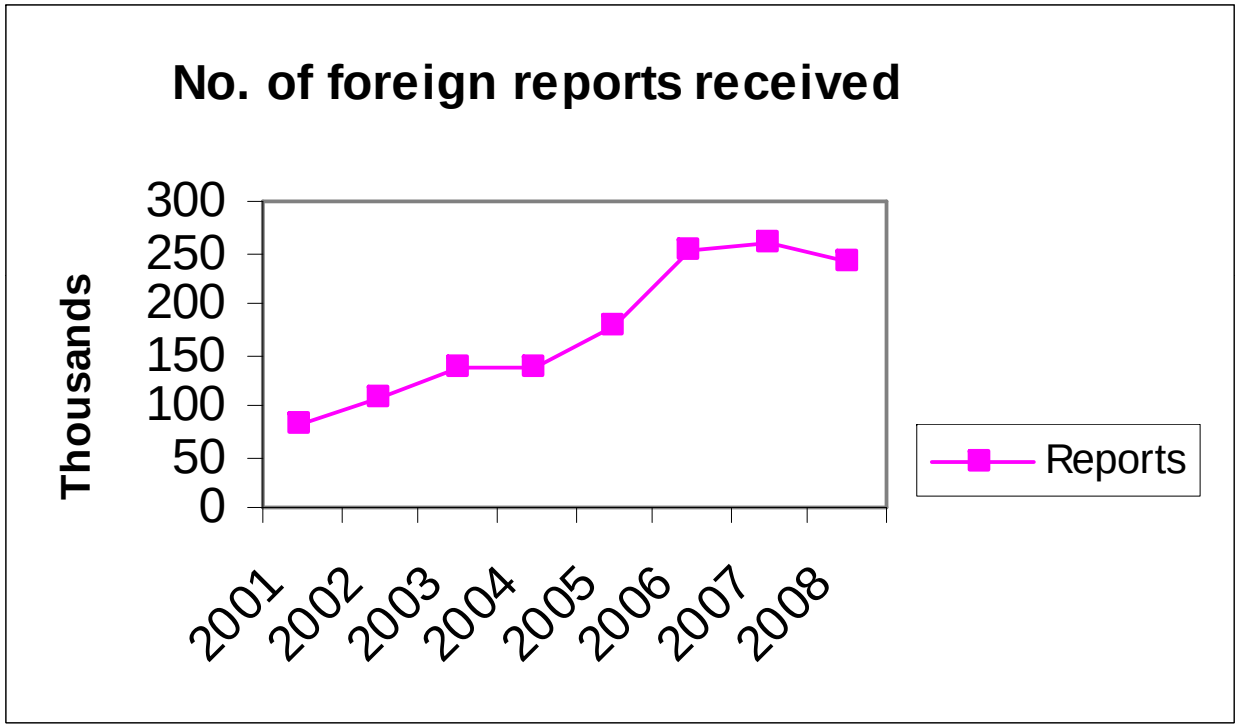
- The Canada Vigilance Program collects adverse reaction reports for the following marketed health products approved for use in humans:
  - Pharmaceutical drugs (prescription and non-prescription)
  - Biologics (Schedule D, biotechnology products, therapeutic and diagnostic vaccines and fractionated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

Canada Vigilance Program Domestic Reports



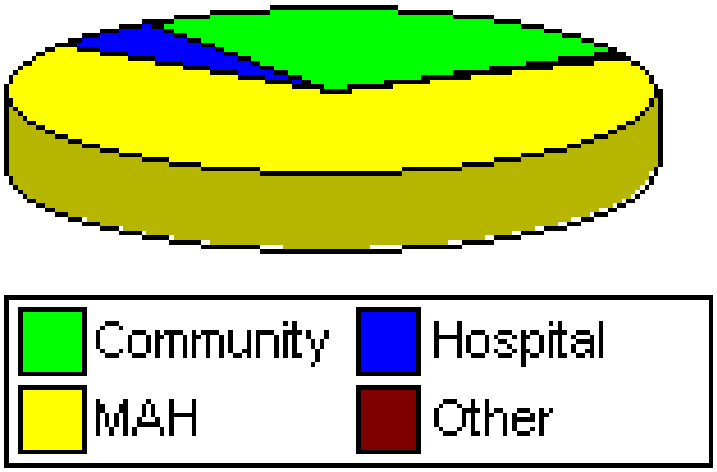
20,360 Domestic Reports Received in 2008

Canada Vigilance Program Foreign Reports



241,417 Foreign Reports Received in 2008

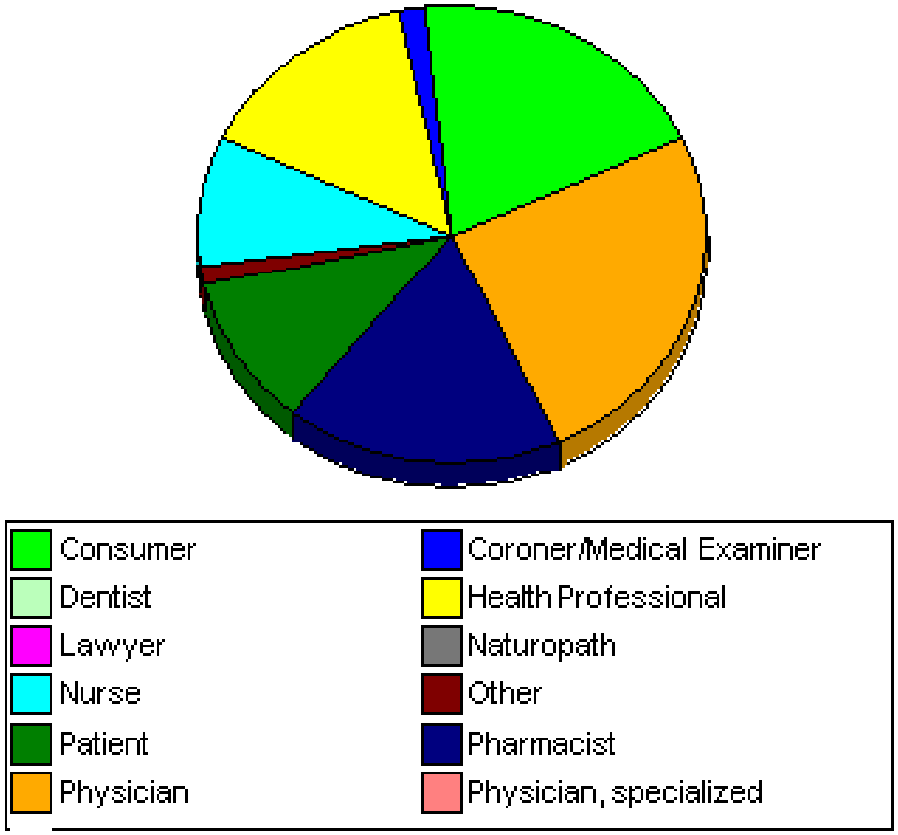
Source of Domestic Reports - 2008



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

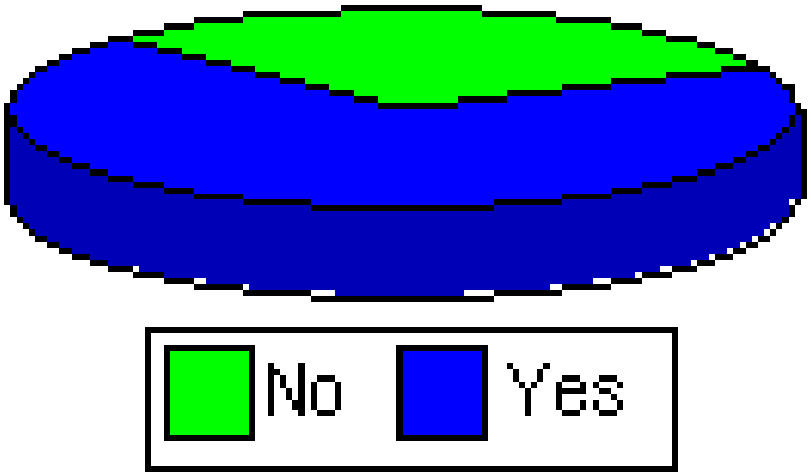
*** Community – Consumer, patient and non-hospital based health care professionals**
**** MAH – Market Authorization Holder (MAH)**

Reporter Type – Domestic Reports - 2008



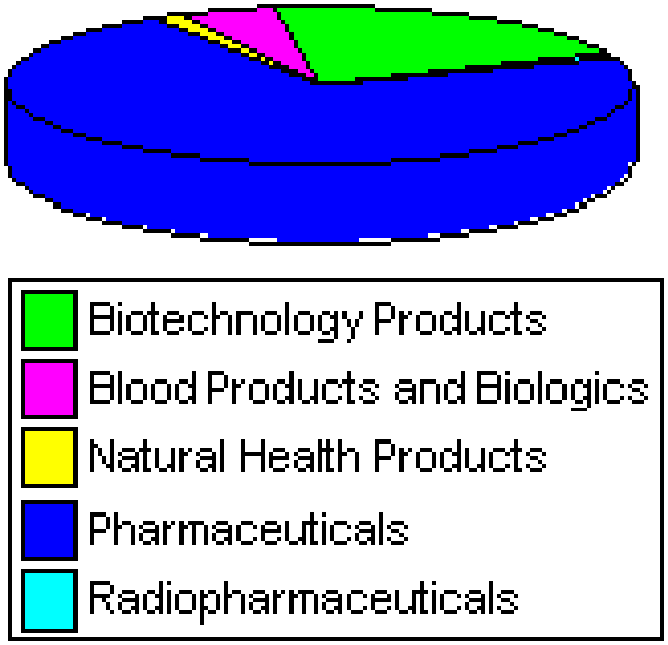
Reporter Type	Percentage
Consumer	19.63 %
Coroner/Medical Examiner	1.54 %
Dentist	0.02 %
Health Professional	14.85 %
Lawyer	0.15 %
Naturopath	0.01 %
Nurse	9.05 %
Other	1.50 %
Patient	10.55 %
Pharmacist	17.81 %
Physician	24.85 %
Physician, specialized	0.04 %
Total:	**100.00%**

Serious Domestic Reports - 2008



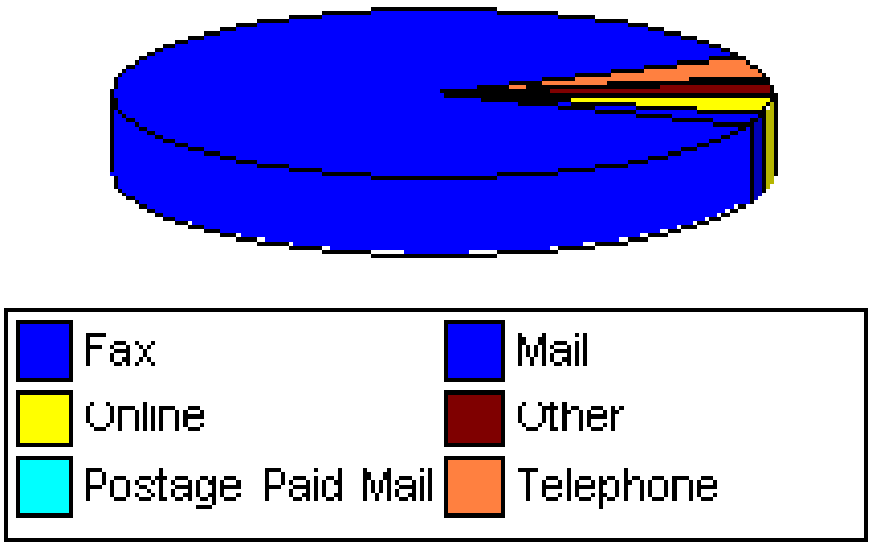
Serious	Percentage
No	30.75 %
Yes	69.25 %
Total:	**100.00%**

Product Type – Domestic Reports - 2008



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 Detection / Selection

Signal Assessment Capacity

Signal Assessment

Risk Mitigation Strategies Developed

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

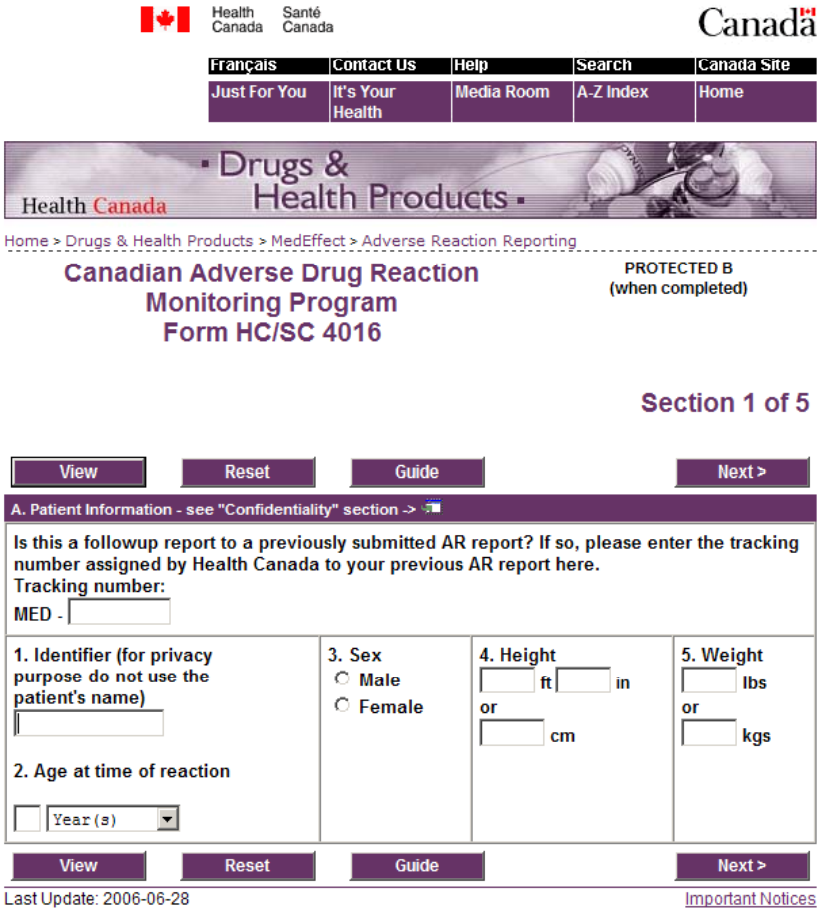
MedDRA Terminology

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

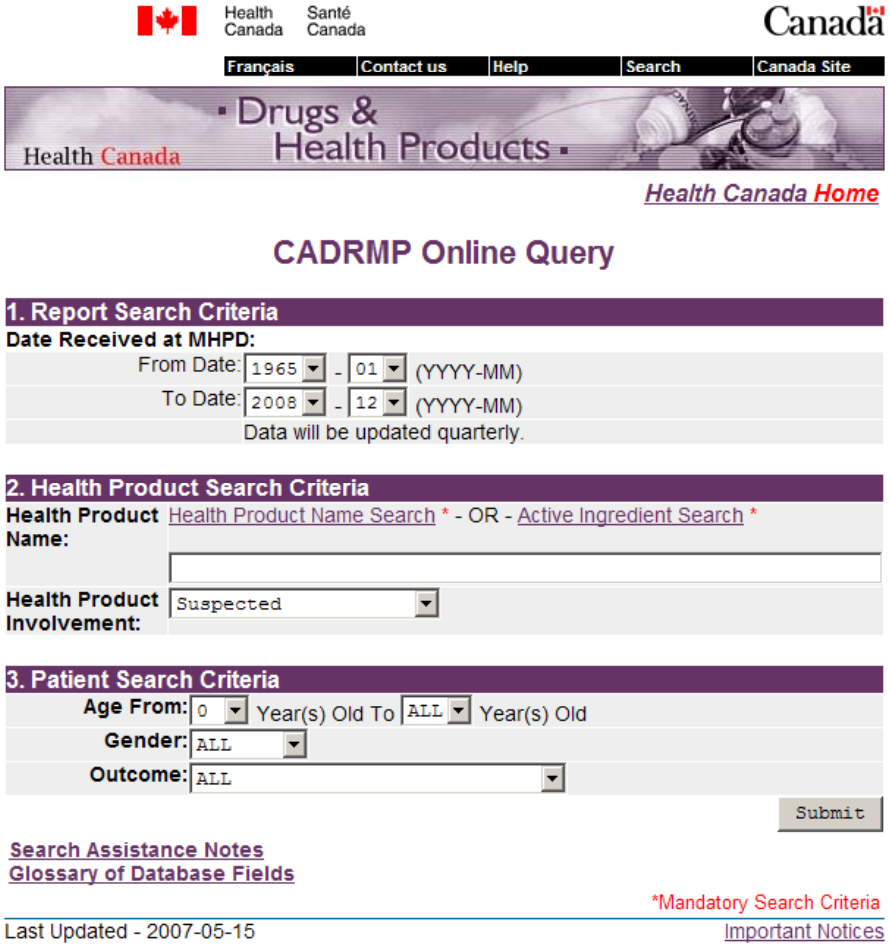
Canada Vigilance Online Reporting Form

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.



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.



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

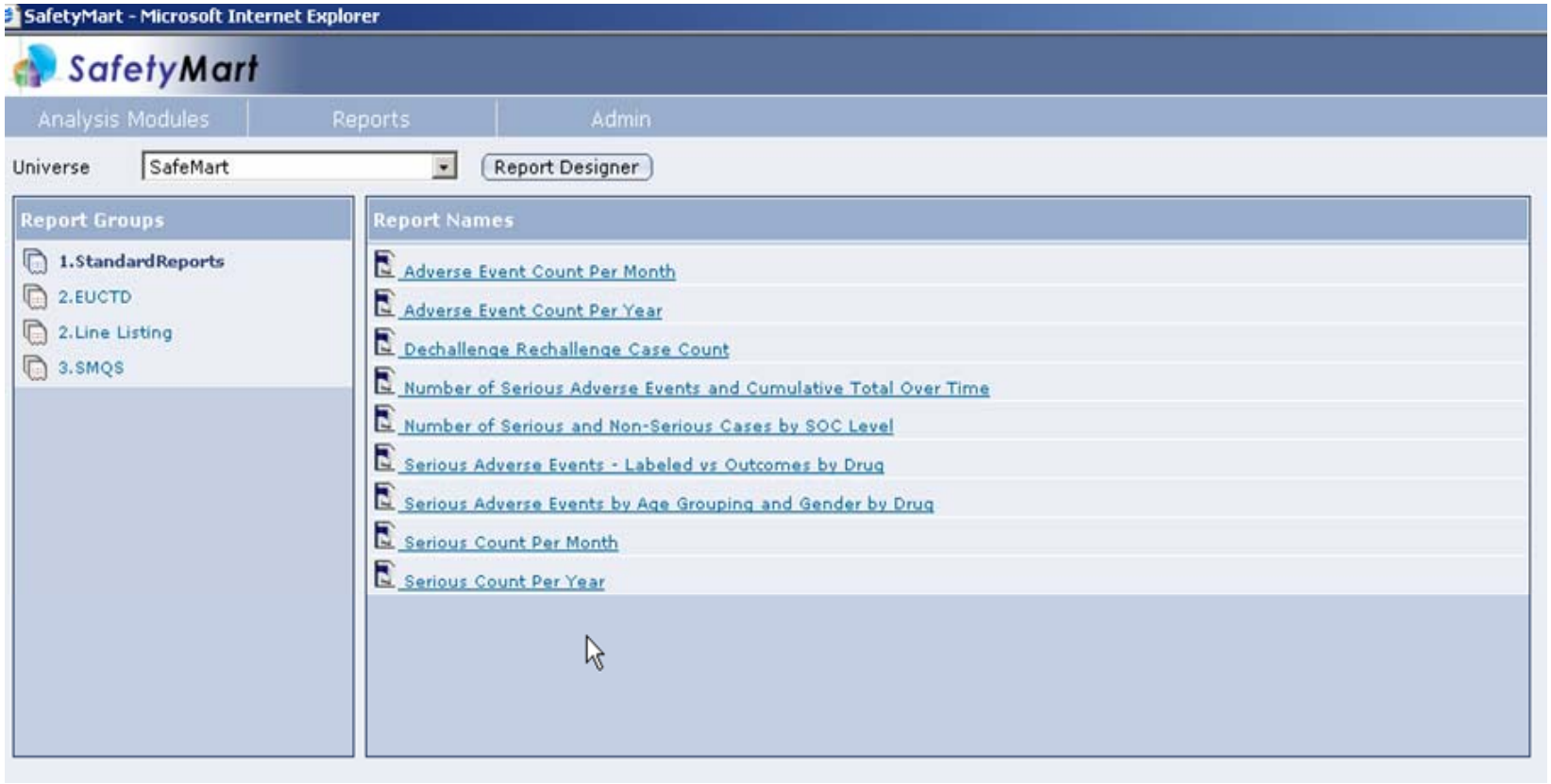
Canada Vigilance Database: Core Application

- 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

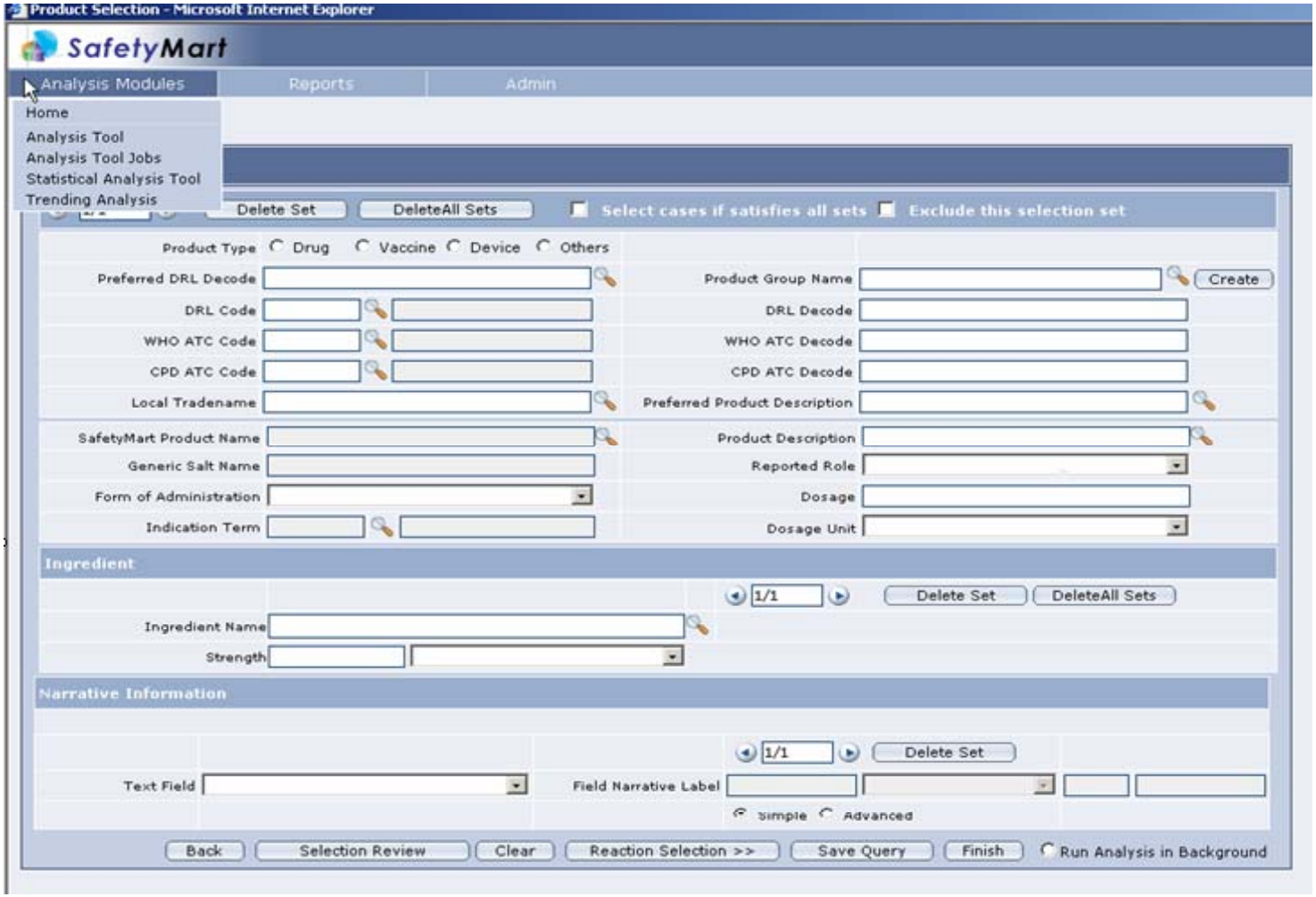
Canada Vigilance Database: Signal Detection

- 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



Signal Detection: Analysis Tool



Signal Detection: Statistical Analysis

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

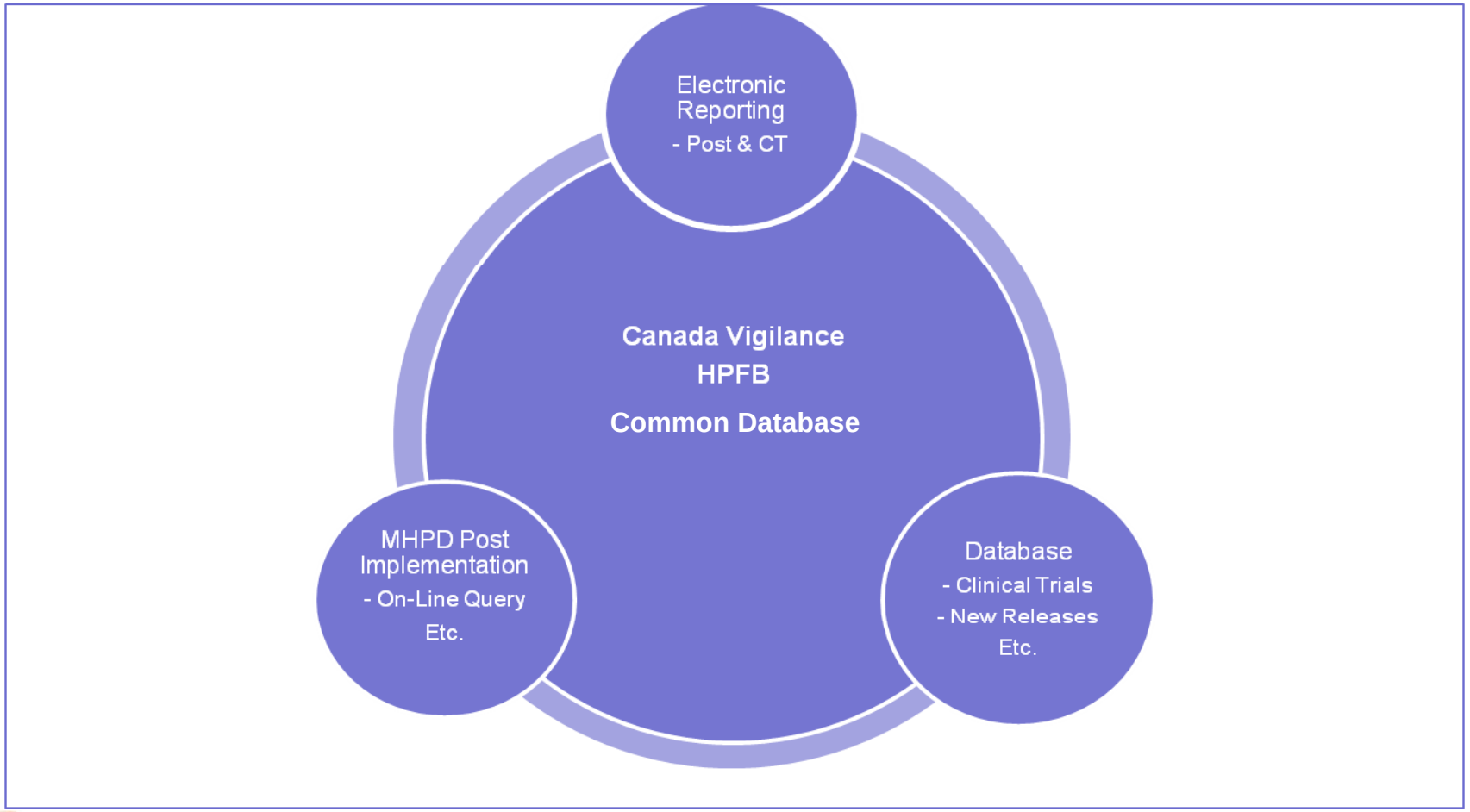
<< < 16 17 18 19 20 > >>

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

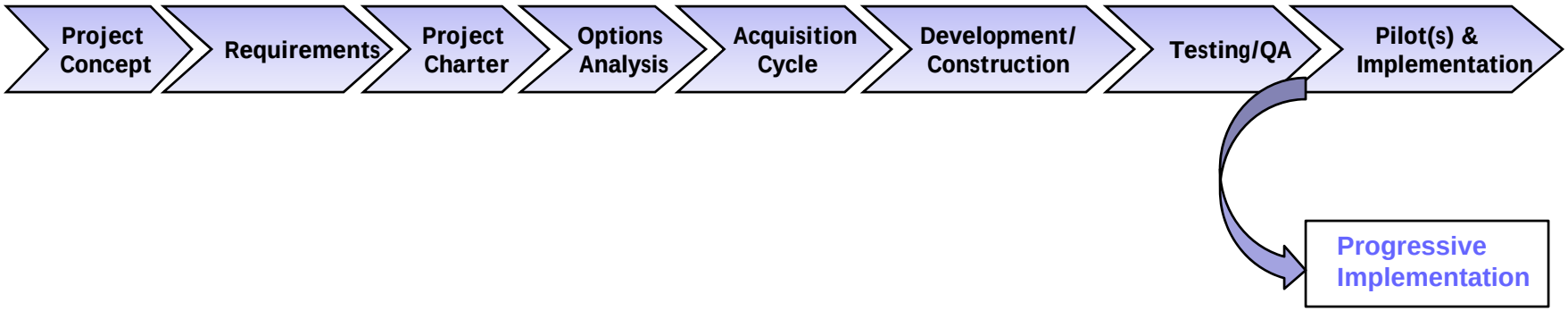
Canada Vigilance – Health Products & Food Branch



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
Canada

Questions?