Canada Vigilance Database Project and eReporting

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Canada Vigilance Project

- Implementation of a pharmacovigilance database to manage both **Clinical Trial and Post-Market Adverse Reaction (AR) Reports** to enhance the overall efficiency of processing and managing adverse reaction reports over the life cycle of a product
- Implementation of **Electronic Reporting of all ARs (domestic and foreign) coded with MedDRA** for small, medium & large Industry/Sponsors to account for varying technological capability
- Includes data analysis capabilities including a data mining and signal detection tool
- Incorporates **international standards** as recommended by the International Conference on Harmonization (ICH)
- Bring Health Canada in-line with other Regulators (FDA, EMA, etc.) who have eReporting
- Engagement of External Stakeholders

Health Product Types

- Adverse reaction information collection, management, data entry and assessment across the product life cycle from clinical trials to post-market for:
  - Pharmaceutical Drugs (prescription and non-prescription)
  - Biologics (includes biotechnology products, vaccines and fractionated blood products)
  - Radiopharmaceutical Drugs
  - Natural Health Products

Reporting Obligations Unchanged

Adverse Reaction Reporting Obligations:

- "**What**" to report as per existing Regulations and Health Canada guidance:
  - Food and Drug Regulations (C.R.C., c. 870) sections C.01.016, C.01.017, and C.05.014
  - Guidance Document for Industry - Reporting Adverse Reactions to Marketed Health Products
  - Guidance for Clinical Trial Sponsors - Clinical Trial Applications (Section 12.3)

Why Electronic Reporting?

- Recognized as a faster, more efficient method to exchange information than paper
- Enhance pharmacovigilance activities
- Mandatory in European Union since November 2005
- Cost savings for sponsors
- No more paper jams and fax machine problems

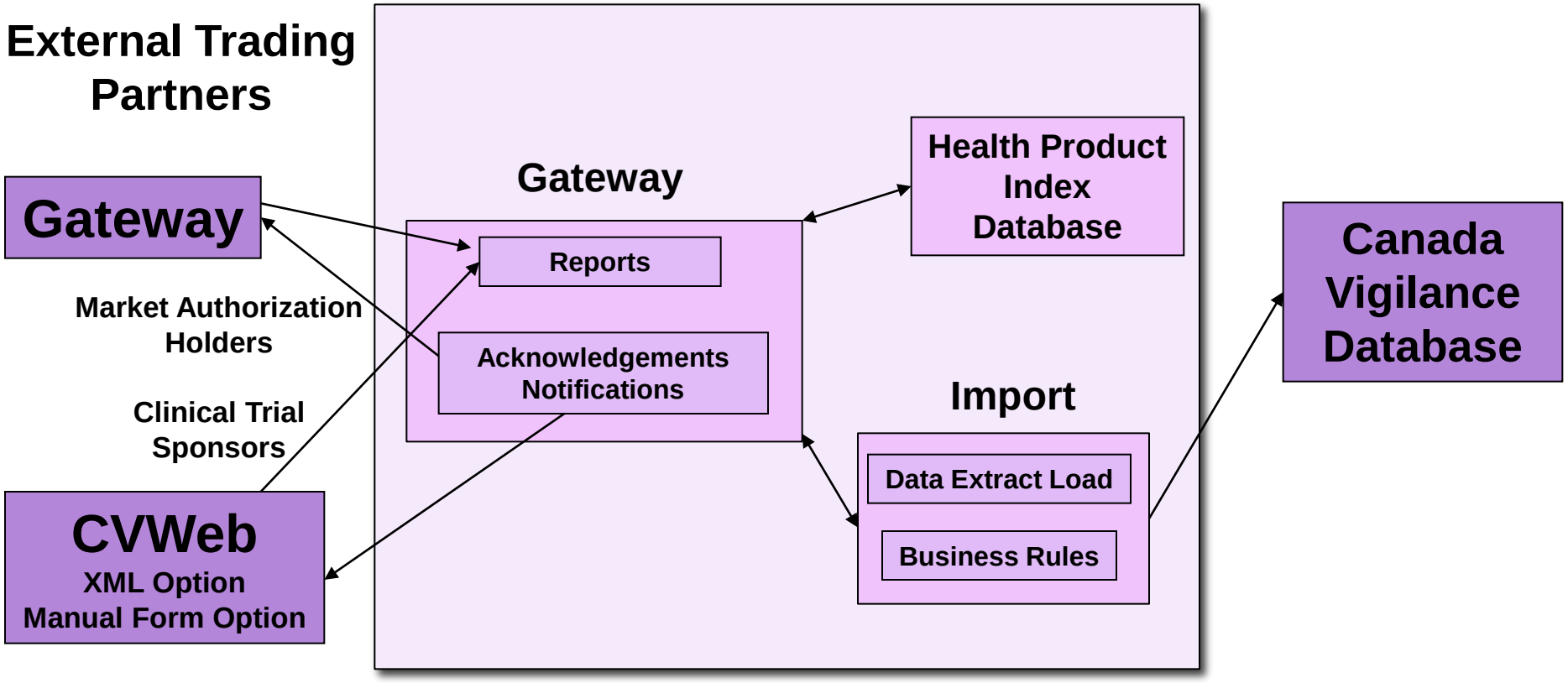
Approach taken for eReporting

- MAH / Sponsors file adverse reaction reports as individual case safety reports (ICSRs) into an electronic file (XML) and transmit it securely **by one of three methods**
  - Gateway to Gateway
    - Fully automatic 2-way communication
    - A gateway is required
  - Transmit/Post XML to CVWeb using the internet
    - Without a gateway
  - Manual entry
    - Sponsors enter and transmit each ICSR individually to the CVWeb using the internet

Canada Vigilance eReporting

- Standardized electronic messages according to international standards (ICH)
- Validation of content of each data element against Canada Vigilance Business Rules
- Extracts data elements from XML and uploads into Canada Vigilance
- Each message sent electronically is ‘acknowledged’
- English and French User Interfaces

Canada Vigilance eReporting



Business Rules – Examples

- Authenticate sender
- Mandatory E2B(R2) fields are populated
- Four minimum criteria are met:
  - Patient
  - Suspect health product
  - Adverse reaction
  - Reporter

Business Rules – Examples

- Current MedDRA version is used for medical terminology
  - Adverse reaction
  - Indication (suspect health product)
  - Medical history
  - Lab tests, etc.
- Sufficient *Suspect* health product information for Signal detection
  - Active ingredient term submitted match to Canada Vigilance Dictionary

Canada Vigilance Health Product Index (HPID)

Combines 2 available sources of information

1. Canada Vigilance (Health Canada) Product Dictionary
   - Domestic regulatory information (DIN,NPN,HDIN)
   - Available on Health Canada website

2. WHO DDE
   - Foreign product information
   - Includes information from several recognized sources
     - INN
     - USAN
     - Martindale
     - Merck Index

Canada Vigilance eReporting Messages

- OK!
- Errors:
  - An error is generated when a business rule is not met and the report is sent back to the sender for corrections
  - Compliance clock keeps ticking
- Warnings:
  - The ICSR is accepted and uploaded into Canada Vigilance
  - Compliance clock stops ticking
- Acknowledgement highlights the data element(s) that need correction or clarification

Canada Vigilance Gateway Pilots

- eReporting partners brought on in a phased approach
- Undergo a pilot process designed to assist and validate ICSR messages
- Frequent communication between Health Canada database team and the external partner
- Kick off meeting followed by weekly teleconferences until the external partner moves to eReporting
- Gateway pilots started in the Summer 2012 and several partners with gateways are currently working through the pilot process

Pilot Process

- Step 1 – MAH or Sponsor familiar with reporting obligations and process
- Step 2 – Trading Partner Agreement and Profile
- Step 3 – Register with Canada Vigilance
- Step 4 – Obtain Canada Vigilance Gateway Certification (for internet communication)

Pilot Process

- Step 5 – Communication test (to assure successful communication)
- Step 6 – Development and validation testing
- Step 7 – XML validation phase with submission of sample cases
- Step 8 – Production pilot validation
- Step 9 – Production

Trading Partner Management Office (TPMO)

Clinical Trial Sponsors and Market Authorization Holders who eReport to Canada Vigilance are called trading partners

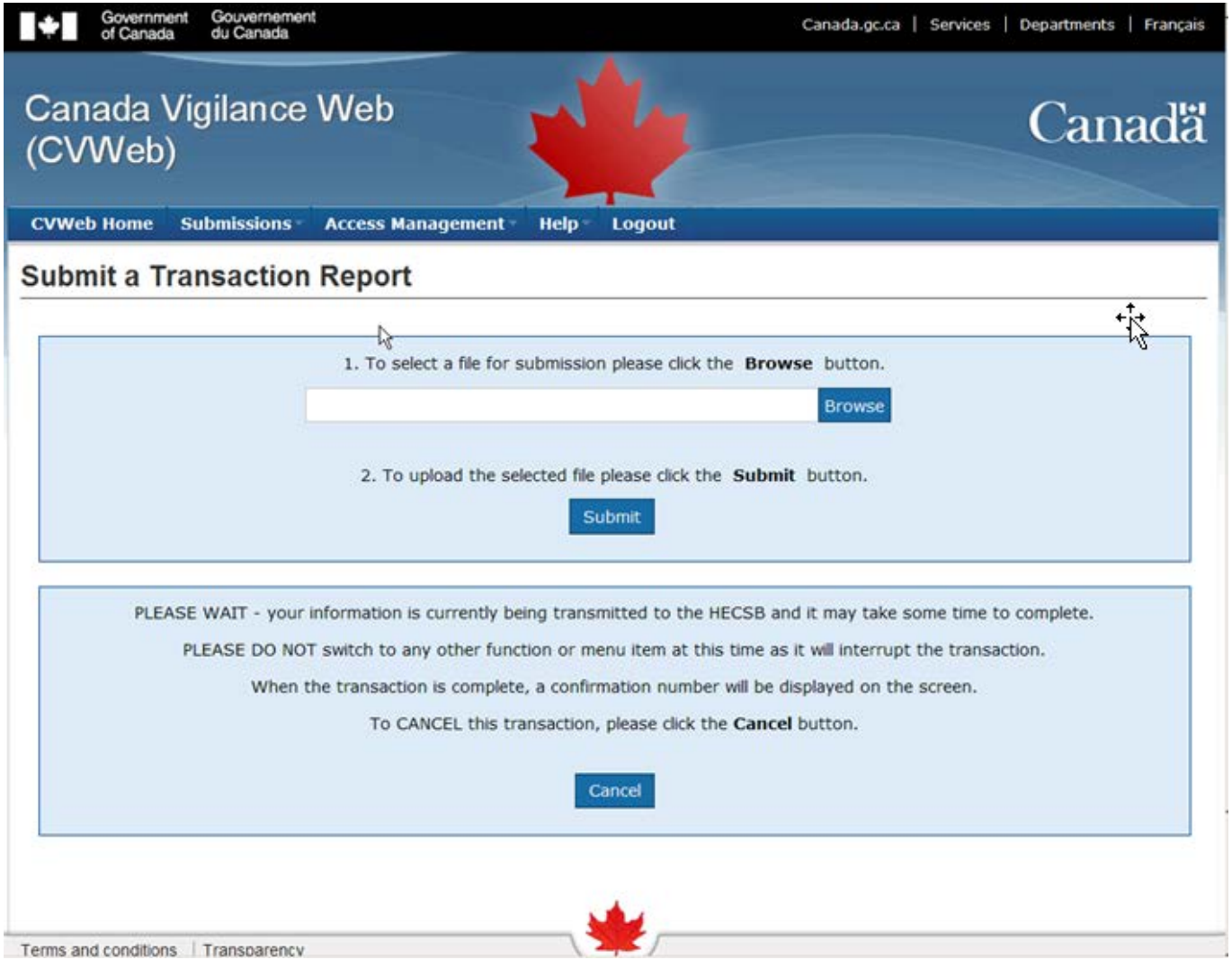
TPMO

- Provides a single identification and repository for all trading partners
- Administers the Registration and Enrolment of trading partners
- Supports the trading partner during the pilot process
- Provides ongoing liaison with trading partners
- Single point of contact

Distribution Rules for ICSRs

Report type	Message type	Receiving Directorate(s)	Case Characteristics
Clinical Trial, Phase 1,2, or 3	cticsr	Pre-Market (TPD or BGTD)	• Patient is part of a Clinical Trial Phase 1, 2, or 3. • Excludes cases already reported under Scenario 3 or 4.
Spontaneous and Solicited reports	ichicsr	MHPD	• Patient is NOT part of an interventional clinical trial, Phase 1, 2 or 3. • Includes solicited reports, e.g. from a Phase IV study, Post-market surveillance program, Registries, etc. • Excludes cases already reported under Scenario 3 or 4.
Health Canada Special Access Programme (SAP)	sapicsr	Pre-Market (TPD and BGTD)	• Patient was authorised to use at least one Suspect product under SAP.
Canada's Access to Medicines Regime (CAMR)	camricsr	MHPD	• Patient received at least one Suspect product because it was authorised under CAMR.

CVWeb XML Transaction Report Option



CVWeb Manual Form Option

Secure access to CVWeb

- Encrypted delivery of data and communication over the internet using GoC standard online “Cyber Authentication” program
- TPMO performs authentication and identification of users via registration and enrollment process
- Secure web portal account users access a unique web address (URL) in order to log in using access credential services

CVWeb Pilots

- Phased approach similar to gateway pilots
- Pilot process designed to assist partners
- Validation of ICSR messages
- Frequent communications (kick off teleconference, weekly teleconference, ad hoc meetings)
- Work through any issues during pilot process
- Expected early 2014

MedDRA (Medical Dictionary for Regulatory Activities)

- A single terminology for use through all phases of life cycle *(both pre- and post-marketing)*
- Support for electronic submissions
- Applicable for a range of medicinal products
  - Drugs, Biologics, Vaccines, Radiopharmaceuticals, Herbal/Natural Health Products, Medicine/devices combination products
- Available in 11 languages
  - Chinese, Czech, Dutch, English, French, German, Hungarian, Italian, Japanese, Portuguese, Spanish

MedDRA Training & Guidance for Users

- Two Points to Consider (PTC) documents
  - PTC: MedDRA Term Selection
  - PTC: MedDRA Data Retrieval and Presentation
- Promotes the standard use of MedDRA for term selection/retrieval/presentation
- Free Training Courses available to all MedDRA Subscribers
- Health Canada hosted free Training Sessions for Subscribers in 2013.
- Courses:
  - May 7th, 2013, Coding with MedDRA, Ottawa, ON
  - May 8th, 2013, Safety Data Analysis and SMQs, Ottawa, ON
- Additional training information, as well as registration information can be found on the MSSO website:

  http://www.meddramsso.com/public_training.asp

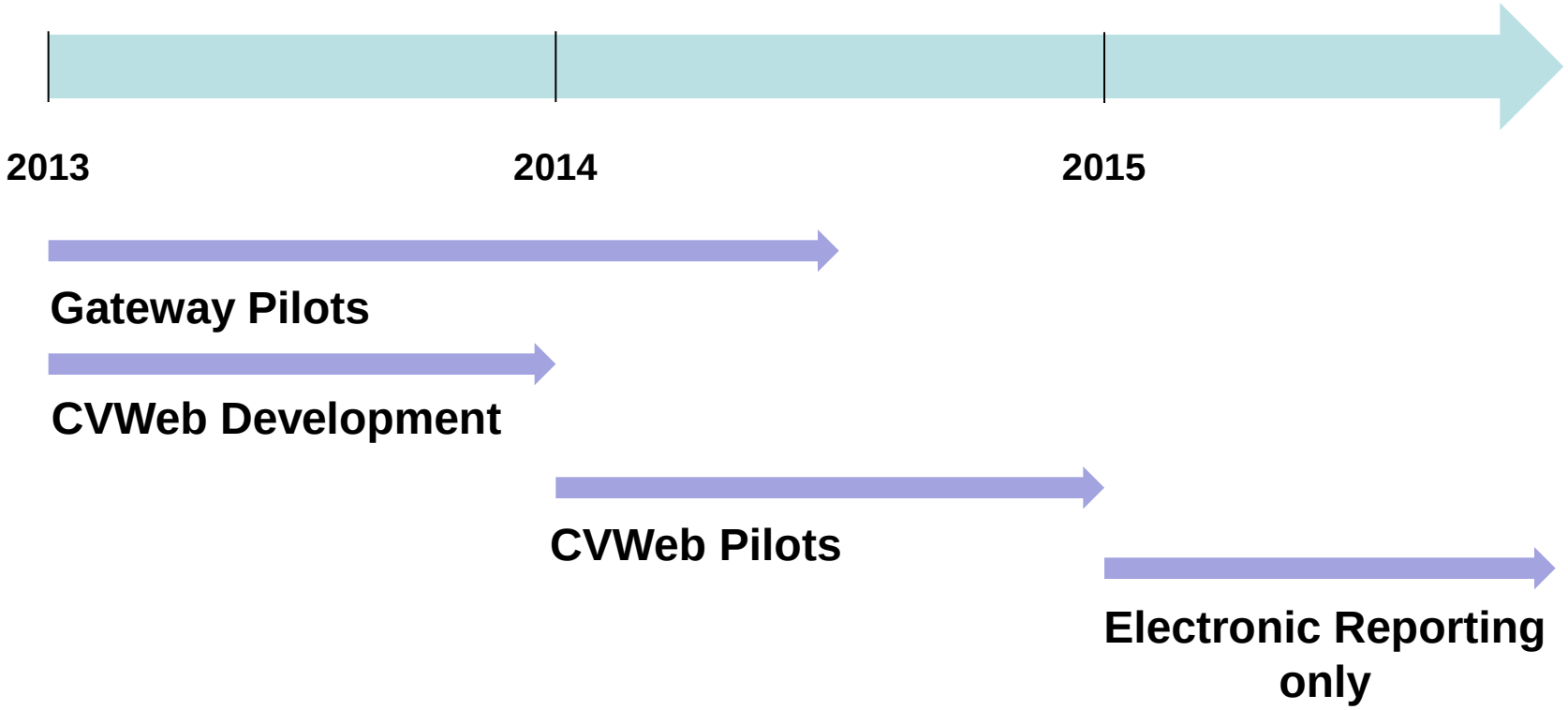
MedDRA Licences/Special Licences

- Free for all Healthcare Providers, Academics and Regulators
- Sliding scale subscription rates for commercial organizations
- For eReporting, MedDRA terminology coding in the current version will be required for adverse reaction data being submitted to Canada Vigilance
- MedDRA Special Licenses will be offered to small businesses for eReporting to CVWeb, at no cost to the small business

Communication – External Stakeholders

- Guidance Document – Electronic Reporting of Adverse Reactions coded with MedDRA by MAHs and Clinical Trial Sponsors
- Trading Partner Guidance
- HC Industry Bilateral Meetings
- DIA Canada, CAPRA, Pharmacovigilance Network etc.
- Inclusion in Industry mailings
- Academic Research Community
- Information regarding eReporting on website (in progress)

Canada Vigilance eReporting Project Timelines



Next Steps – Canada Vigilance eReporting

- Progressing through Gateway Pilots with Trading Partners
- Further communication with Stakeholders
- Calling for additional Trading Partners for Gateway Pilots
- Notice of Interest for CVWeb Pilots

Contact: CanadaVigilance@HC-SC.GC.CA to join Canada Vigilance Gateway Pilots or express interest in CVWeb Pilots