Content of Health Canada Regulatory Databases

February, 2013

Prepared by Health Products and Food Branch
Health Canada
Overview

• Background on Health Canada
• Health Canada Systems Context
• Database Synopsis – TPD, VDD, and BGTD
• Database Synopsis – NHPD
• Database Synopsis – HECSB and FD
• Database Synopsis – MHPD
• Moving Forward
BACKGROUND
HPFB is a trusted regulatory authority…

The Branch’s over 2000 employees work to:

- minimize health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food

- promote conditions that enable Canadians to make healthy choices

- provide information so that Canadians can make informed decisions about their health

…committed to protecting the health and safety of Canadians
HPFB’s regulated health products

• Pharmaceuticals and Medical Devices
  - includes over 13,000 pharmaceutical drugs (prescription and non-prescription, brands and generics, and disinfectants) on the market
  - over 120,000 medical devices
  - some non-marketed drugs for serious or life threatening conditions authorized through the Special Access Program

• Biologics and Genetic Therapies
  - includes over 400 biologics and biotechnology products (e.g., vaccines, blood, cells, tissues and organs, gene therapies)
  - transitioning the regulation of Assisted Human Reproduction to HPFB in September 2012

• Veterinary Drugs
  - includes over 1,300 veterinary drugs administered to food-producing and companion animals

• Natural Health Products (NHPs)
  - includes over 56,000 NHPs, which are regulated proportional to risk, while respecting the diversity of Canadians choices
Our role in the regulation of health products

- Review health products (drugs, medical devices, natural health products) to **assess the risks and benefits** prior to market authorization

- Review **clinical trial applications** for drugs and natural health products, as well as investigational testing applications for medical devices, to ensure the studies are properly designed and that participants will not be exposed to undue health risks

- Manage a national **compliance and enforcement** program for all products under the mandate of the Branch, except food (for which CFIA performs compliance and enforcement activities)

- Coordinate **post-market surveillance** of health products and assessment of safety signals and trends

- Share **new safety information** about health products with Canadians
Health Canada: Regulatory Business Reference Model

**RE-EVALUATION**
- Continuous research
- Structured evaluations
- Adhoc or unstructured evaluations
- Continuous research

**SURVEILLANCE AND MONITORING**
- Incident reporting
- Problem Reporting
- Post-market studies/trials
- Risk communications if necessary
- Product safety update reports (PSUR’s)

**COMPLIANCE & ENFORCEMENT**
- Inspections
- Investigations
- Enforcement
- Active prevention
- Border integrity

**PRODUCT AND SUBSTANCE DISCOVERY**
- Evolution of product and knowledge
- Decision Rendering
- Information Gathering
- Risk Management and Reporting

**PRODUCT REMOVAL**
- Re-evaluation
- Re-evaluation
- Inspections
- Pre-submission meeting
- Submission
- License
- Submission Review
- Evaluation

**MARKET REGISTRATION**
- Market Authorization for drugs, Med Devices, Foods, NHPs
- Market Authorization for registration, Pesticides, Pesticide devices
- Product Labelling updates

**EMERGENCY ACCESS AUTHORIZATION**
- Emergency access to human drugs/medical devices/vet drug
- Special access to medical marijuana or methadone
- Emergency Access Pesticide and pesticide devices

**RESEARCH TRIAL AUTHORIZATION**
- Clinical trials
- Investigational Testing
- Field trials

**RESEARCH & PRODUCT DEVELOPMENT**
- Research
- Pre-submission meeting
- Submission
- Submission Review
- Evaluation

**ESTABLISHMENT LICENSING**
- Establishment licensing
- Import licenses/permits for controlled substances
- International trade certificates
Current Strategic Drivers and Operational Goals

Strategic Drivers
- Global Supply Chain Management
- Product Safety
- Cost Recovery
- International Regulatory Practices
- Transparency & Accountability

Operational Goals
- Risk-based regulatory framework
- Improved regulation of Health Products
- Better informed of scientific innovations
- Business Intelligence support for better decision making
- Improved Transparency
- Improved Operational Excellence
- Domestic and foreign partnerships
- Data standards, control vocabularies, and regulatory harmonisation
- International Work sharing
IT Modernization in Support of Transparency and International Cooperation
HEALTH CANADA
SYSTEMS CONTEXT
Substance and Data Management Owners

**Health Products and Food Branch**
- Marketed Health Products Directorate
- Natural Health Products Directorate
- Biologics and Genetic Therapies Directorate
- Therapeutic Products Directorate
- Veterinary Drugs Directorate
- Food Directorate
- Inspectorate

**Healthy Environments and Consumer Safety Branch**
- Consumer Product Safety Directorate
- Controlled Substances and Tobacco Directorate
- Environmental and Radiation Health Sciences Directorate
- Safe Environments Directorate
- Workplace Hazardous Materials Directorate
Current Relationship Diagram

- Canadians
- Health Care Practitioners
- Hospitals Pharmacies
- Industry
- Regulatory Partners
- Drug Establishments

- Approved regulatory product information (Monographs, Labels, PCI etc.) are silo specific, difficult to understand.
- Transparency of process and line of accountability are based on web structure not organizational structure – increases difficulty of management.
- Confusing web of communication channels for similar types of product information and safety reports.
- Silo approach to information handling leads to silos and institutional barriers, where organizational knowledge sharing is constrained within Health Canada.
- Duplication of Product Information
- Growth in Health Products will compound current system limitations.
- Health Product innovation is increasingly cutting across silos.
- Inconsistency of data standards and regulatory practices.

- Lack of ability to share regulatory information across programs / directorates.
REGULATORY DATABASES
TPD, VDD, BGTD
TPD, BGTD, VDD Database

• **Drug Product Database (DPD)**
  - An internal master drug dictionary for marketed domestic health products which is maintained by Health Canada systems. The DPD is updated regularly and is the preferred source for the latest health product information for domestic marketed products relevant to HC.

• **Drug Submission Tracking System (DSTS)**
  - An internal database to capture submission and product-related meta-data that is used to track submission workflow. It includes information on substances, routes of administration and dosage forms.
Benefits and Limitations to Health Canada

- One substance list for TPD, BGTD and VDD
- This list has been carefully and meticulously managed in its current format since 1996 (Single Table)
- It includes a preferred name as well as synonyms for each substance
- Validation may reference several dictionaries including INN, USAN, Martindale, Merck Index however these references are not maintained as part of the database
DPD System Relationship
REGULATORY DATABASES
NHPD
NHP Substance Data Model – High Level

- Complex Schema based on cross reference of ingredient information combined with essential meta-data that more fully and accurately describes the chemical, protein, or organism substance.
- Captures relationships to regulatory Pre-Cleared Information used for publication and complex form validations for market authorization requests.
- Preferred (Approved Names) linked to product information
NHPD Dictionaries

- NHP – Data Maintained and managed by Health Canada and supplemented via standard databases
- Three groups of NHP ingredients
  - Chemical Substances
  - Protein Substances
  - Organism Substances (i.e. a plant or a plant material, an alga, a bacterium, a fungus or a non-human animal material, an extract of the preceding or a probiotic).
Naming Standard: Approach

**Chemical/Protein Substances:**

- Approved Name
- Reference

<table>
<thead>
<tr>
<th>Ref. Code</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>British Pharmacopoeia</td>
</tr>
<tr>
<td>USP</td>
<td>United States Pharmacopoeia</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>MI</td>
<td>Merck Index</td>
</tr>
</tbody>
</table>

Conceptual: NHP Ingredients Database

CODED
Chemical Substance: an example (web-view)

Chemical Substance

Approved Name: Calcium Carbonate
Proper Name: Calcium
Category: Approved Chemical Name
Monographs: Antacid
Schedule 1: Mineral
Synonyms:
  • Calcium carbonate
  • Carbonic acid calcium salt (1:1)
SubIngredients: Calcium
CAS Registry Number: 471-34-1
Reference: BP

Unique identifier

Additional information
Protein Substance: an example (web-view)

Protein Substance

Approved Name: whey protein
Proper Name: whey protein
Category: Approved Protein Name
Schedule 1: Isolate
CAS Registry Number: 84082-51-9
Source Organism Parts: • Bos taurus
   (Parts: Milk)
Reference: ICID

Roles

Medicinal

Rationale: Classified as an NHP under Schedule 1, item 2 (an isolate) of the Natural Health Products Regulations
Reference: NHPD
Naming Standard: Approach

**Organism Substances:**

1. **Predefined Organism Substance**
   - Approved Name
   - Reference
   - Authorized List
   - Approved Species Name + Org. Part + Org. Prep

2. **Custom Organism Substance**
   - Approved Species Name
   - Org. Part
   - Org. Preparation
   - Latin binomial
   - Organism part list
   - Preparation list & details
   - E.g. Extract liquid standardized
   - Ext. Ratio + Solvent(s) (strength) + Equiv. dry/fresh + Equiv Component

Conceptual: NHP Ingredients Database
**Organism Substance : an example (web-view)**

### Defined Organism Substance

<table>
<thead>
<tr>
<th>Approved Name:</th>
<th>Orange Oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proper Name:</td>
<td>Citrus sinensis</td>
</tr>
<tr>
<td>Category:</td>
<td>Approved Herbal Substance Name</td>
</tr>
<tr>
<td>Schedule 1:</td>
<td>Extract</td>
</tr>
</tbody>
</table>
| Synonyms:     | - *Citrus Aurantium Dulcis (Orange) Peel Oil*  
                - *sweet orange*  |
| Organism(s):  | - *Citrus sinensis*  
                (Parts: *Fruit peel*) |
| Preparations: | Oil essential |
| Reference:    | BP |

**Roles**

#### Medicinal

**Rationale:** Considered NHP under Schedule 1 item 2, extract, of the NHP Regulations.  
**Reference:** NHPD

#### Non-medicinal

**Purposes:** Flavor enhancer, Fragrance ingredient, Skin-conditioning agent - miscellaneous

**Restrictions:** General
Organism Substance: source organism

<table>
<thead>
<tr>
<th>Organism</th>
<th>Synonymous Taxa</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family:</strong> Rutaceae</td>
<td><strong>Citrus aurantium var. sinensis</strong>, <strong>Citrus macracantha</strong></td>
</tr>
<tr>
<td><strong>Genus:</strong> Citrus</td>
<td></td>
</tr>
<tr>
<td><strong>Species:</strong> sinensis</td>
<td></td>
</tr>
<tr>
<td><strong>Organism:</strong> Citrus sinensis</td>
<td></td>
</tr>
<tr>
<td><strong>Type:</strong> Plant</td>
<td></td>
</tr>
<tr>
<td><strong>Taxa:</strong></td>
<td></td>
</tr>
<tr>
<td>Common Name(s):</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>blood orange</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Immature orange</strong></td>
</tr>
<tr>
<td></td>
<td><strong>navel orange</strong></td>
</tr>
<tr>
<td></td>
<td><strong>orange</strong></td>
</tr>
<tr>
<td></td>
<td><strong>sweet orange</strong></td>
</tr>
<tr>
<td></td>
<td><strong>tian cheng</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Valencia orange</strong></td>
</tr>
<tr>
<td>Reference: GRIN</td>
<td></td>
</tr>
</tbody>
</table>

| Organism Part Constituent(s):                |                                          |
|                                               | **Flower**                               |
|                                               | **Flower bud**                           |
|                                               | **Fruit**                                |
|                                               | **Fruit peel**                           |
|                                               | **Fruit pericarp**                       |
|                                               | **Leaf**                                 |
|                                               | **Leaf bud**                             |
Benefits to Health Canada

- Specific to HC NHP (Regional) requirements
- Allows for validation of ingredients and pre-cleared information against e-Form submissions (smart-forms)
- Reduction of substance and licence application errors in submissions
REGULATORY DATABASES
HPFB – MHPD
MHPD Dictionaries

- **Drug Product Dictionary (DPD)**
  - An internal master drug dictionary for marketed domestic health products which is maintained by other Health Canada systems. The DPD is updated regularly and is the preferred source for the latest health product information for domestic marketed products relevant to HC.

- **Canadian Product Dictionary (CPD)**
  - The CPD is the main drug dictionary that is part of the current ARISg safety system. It is used to code the health product information for all suspect products and most concomitant products. The dictionary stores all the domestic health products and is primarily populated by the DPD.

- **WHO DDE (DRL Drug Dictionary)**
  - WHO DRL Drug dictionary is the world’s most comprehensive dictionary of medicinal product information. The WHO drug dictionary contains all types of drugs from all the countries including the ones that are domestic to Health Canada. The majority of entries in WHO refer to prescription-only products, but also includes over-the-counter (OTC), biotech and blood products, diagnostic substances and contrast media.
HC HPID (Health Product Identification Database)

- HPID will be used by Health Canada for Electronic Adverse Event Reporting
- HPID is populated with Product and Ingredient information from:
  - DPD (domestic product information),
  - WHO DDE (foreign product information)

- HPID validates information in the `<drug>` Field of the electronic adverse reaction message and matches the information to a record in the Canada Vigilance Product Dictionary (CPD)
- Ingredient terms
  - `<activesubstancename>` must match exactly CPD (Suspect/Interacting)
Benefits and Limitations to Health Canada

- DPD / CPD focus on Canadian Drugs only

- HPID driven by necessity to address lack of common product standard required in order effectively process foreign ICSR reports (e.g. US Domestic).

- HPID Facilitates statistical analysis on both foreign and domestic data.
REGULATORY DATABASES
FD, HECSB
Food Directorate and HECS Branch

- **Food Directorate** is the federal health authority responsible for establishing policies, setting standards and providing advice and information on the safety and nutritional value of food. Focus is in the following areas:
  - chemical and microbiological contaminants of foods, such as heavy metals or E. coli
  - food additives, novel foods, food processes, and nutrition

- HECSB’s Programmes touches on many aspects of day-to-day living in Canada; issues like drinking water, air quality, alcohol and drug use, toy safety, smoke detectors, the safety of cosmetics and personal care products, and second-hand smoke, as well as how new products of biotechnology and new chemicals may affect Canadians
Dictionaries and COTS Substance Management

- **IUCLID = International Uniform Chemical Information Database**
- A free database application managed by the Organisation for Economic Co-operation and Development (OECD) and the European Chemicals Agency (ECHA)
- Facilitates capture, maintenance and exchange of health and environmental data in a standard format (OECD Harmonized Templates).
- Provides a standardized “database and interface” to maintain data, but you capture “your” data (which can be shared because of common data and file format).
- Used by companies and regulatory authorities around the world.
- Benefits include: ease of use, rich data capture capacity, structured data capture, standardized picklists, cost (free), built in audit, access control interface, stand-alone and distributed versions, built in querying and reporting functionality, proven track record, regular software update cycle.
How HC is managing data within IUCLID

- Substance records
  - Legal entity to indicate ownership; also relying on business rules & training
  - Managing information for several HECSB programs in a common database, maintaining ownership using business rules and training

- Data entry
  - Detailed written instructions for some endpoints, more in development
  - In-class, hands-on training for users

- Confidential information
  - Information on identity, structure, and endpoints can be flagged as confidential; users select if reports include or exclude CBI

- Reporting
  - Repurposing an ECHA plug-in for tabular summary reports
  - Pushing for greater flexibility in dossier reports in later version
  - Intend to use Cognos to create custom reports from back-end
Benefits and Limitations to Health Canada

- IUCLID has extensive metadata structure for substance definition
- Limited “Single Substance” Data model to Chemicals
- Does not handle complex substance combinations
- HC has implemented a “products” data structure layered over IUCLID
- Maintains the integrity of the IUCLID model while addressing HC Regional / Regulatory specific requirements.
Moving forward … Changes in HC IT Investment Management

• Prior to 2011
  ➢ Software developed as a series of *silos*
  ➢ Data architecture has been driven by specific scientific and policy requirements
  ➢ Very narrow definitions
  ➢ No holistic approach to data management
  ➢ No common infrastructure or tools

• Since 2011
  ➢ Move towards a unified model of business architecture IT Investment portfolio management
  ➢ Development of common infrastructure, common tools, and standards
  ➢ Increased stakeholder engagement – industry cooperation. e.g. Group on Electronic Regulatory Activities (GERA)
  ➢ Movement towards international cooperation
To Be System Relationship Diagram

Health Products Register

Data Exchange, Format, Terminology Standards and Regulatory Harmonization
- eCTD
- RPS
- ICSR
- IDMP

- Patent Register
- HECSB Submission Tracking
- docuBridge
- Drug Submission Tracking System
- Drug Product Database
- Natural Health Product Database
- Canada Vigilance Database
Next Steps

• Develop a communication plan for management, working staff and impacted stakeholders.

• Conduct a “Fit analysis”, on systems, data sources, and standards which manage product and substance information in priority sequence

• Develop a plan for the implementation of an HC environment which supports the adoption of 11238.
For more information

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How HC is managing data within IUCLID

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