Coding of suspect products in FDA AERS adverse event reports

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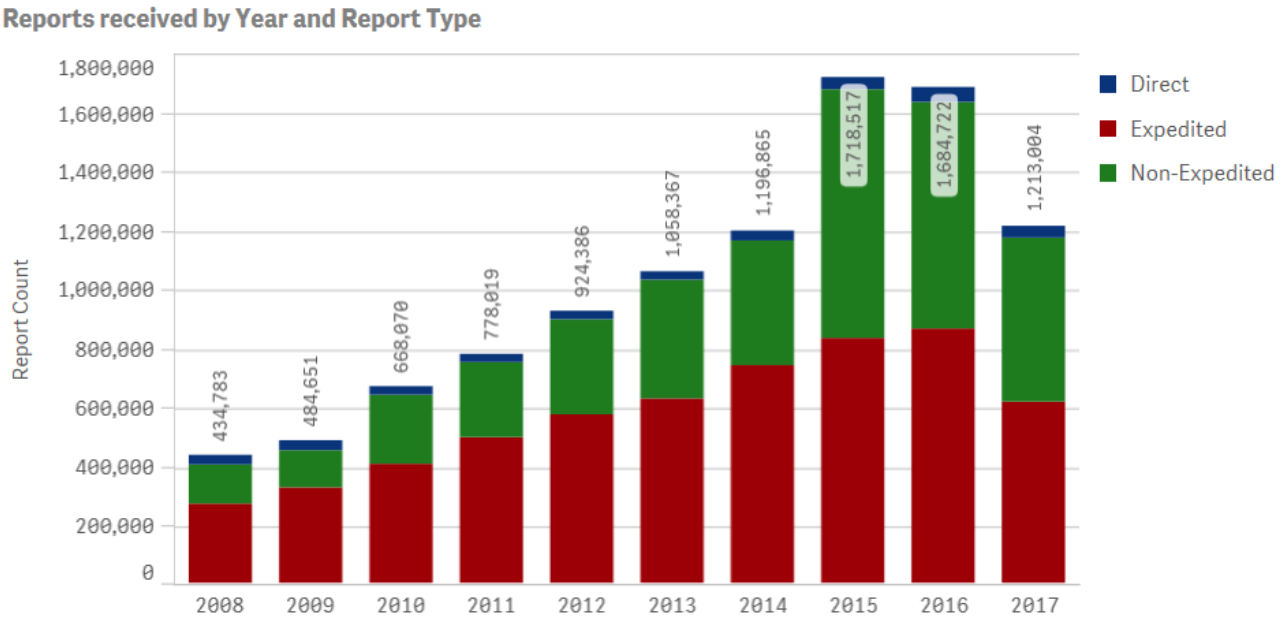
Outline

- FDA Guidance / specifications for submission of suspect product(s) name(s) in FAERS adverse event reports
- FAERS Product Dictionary (FPD)
  - Data sources
  - Structure
  - Coding process
- FAERS Quarterly data extract /Public dashboard
- Examples of issues in coding suspect product-name submissions

FAERS Background

The FDA Adverse Event Reporting System (FAERS) is a database that contains spontaneous adverse event reports that are submitted to FDA from the product manufacturers or directly from the consumer, healthcare professional, or other reporter. The database supports the FDA's post marketing safety surveillance program for drug (Rx and OTC) and therapeutic biologic products.

The database consists of more than fourteen (14) million reports since 1969 to August 2017. Each year, FDA receives over one (1) million adverse events and medication error reports associated with the use of drug or biologic products. Existence of a report does not establish causation.



Guidance / specifications

Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments

Technical Specifications Document

Associated Guidance Document(s):

Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Postmarketing Individual Case Safety Reports (June 2008)

June 2013

https://www.fda.gov/downloads/drugs/developmentapprovalprocess/formssubmissionrequirements/electronicsubmissions/ucm153588.pdf

Future: IDMP standard

Guidance for Industry

E2B(R3) Electronic Transmission of Individual Case Safety Reports (ICSRs) Implementation Guide – Data Elements and Message Specification

February 2014, ICH

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM275638.pdf

Specifications for ICSRs*: Drug description

Table 5: Detailed Description of Drug(s) and Narrative Elements*†

Element	DTD Descriptor 2.1	Length	Element Values for DTD 2.1
B.4.k.1	<drugcharacterization>	1N	1=Suspect 2=Concomitant 3=Interacting
B.4.k.2.1	<medicinalproduct>	70AN	Proprietary medicinal product name
B.4.k.2.2	<activesubstancename>	100AN	Drug substance name
B.5.1	<narrativeincludeclinical>	20000AN	Case narrative

* Include <medicinalproduct> and/or <activesubstancename >. FDA cannot process the ICSR without at least one of these drug elements.

***Specifications for Preparing and Submitting Electronic ICSRs and ICSR Attachments** *Technical Specifications Document*

Specifications for ICSRs: Drug description (2)

Medicinal Product Names (B.4.k.2.1) and Active Substance Name (B.4.k.2.2)

FDA validates medicinal product names to the available Structured Product Labeling (SPL)[5], the submitted label (as ICSR attachment), and the Substance Registration System (SRS).

a) When the product has an SPL, use the same naming convention as it appears in the SPL when submitting the ICSR.

b) When submitting a product label as an attachment to an ICSR, use the name as it appears on the submitted product label.

c) If no medicinal product is named and only the active substance is named, use the name of the active substance as it appears in the SRS[6].

5 The Structured Product Labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product and facility information.

http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

6 Substance Registration System:

https://www.fda.gov/forindustry/datastandards/substanceregistrationsystem-uniqueingredientidentifierunii/default.htm

Main Data Sources for FPD

- Active ingredient for all products
  - G-SRS: 'Preferred name' for an ingredient

  http://gsrs.fda.gov/ginas/app

- US Marketed products
  - SPL: Structured Product Labeling
  - Product name with Active Ingredient and moiety

  http://dailymed.nlm.nih.gov/dailymed/drugList.cfm?startswith=A

- Foreign product names
  - WHODrug Global for the Product name
  - G-SRS for the active ingredient name

G-SRS

Daily Med

Drugs@FDA
FDA Approved Drug Products

the UPPSALA MONITORING CENTRE
WHODrug Insight

pmda 独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

ClinicalTrials.gov

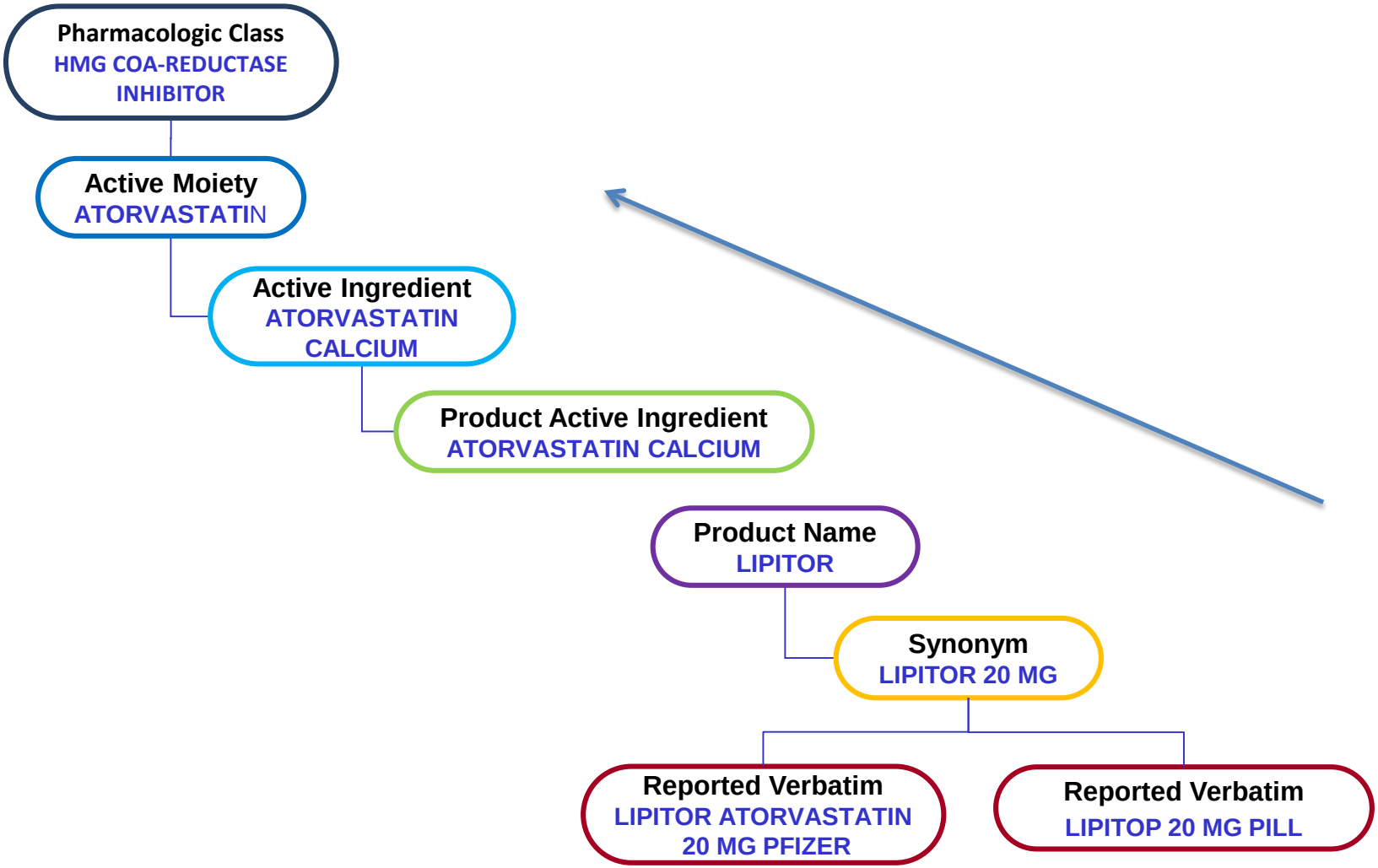
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Health Canada
www.hc-sc.gc.ca

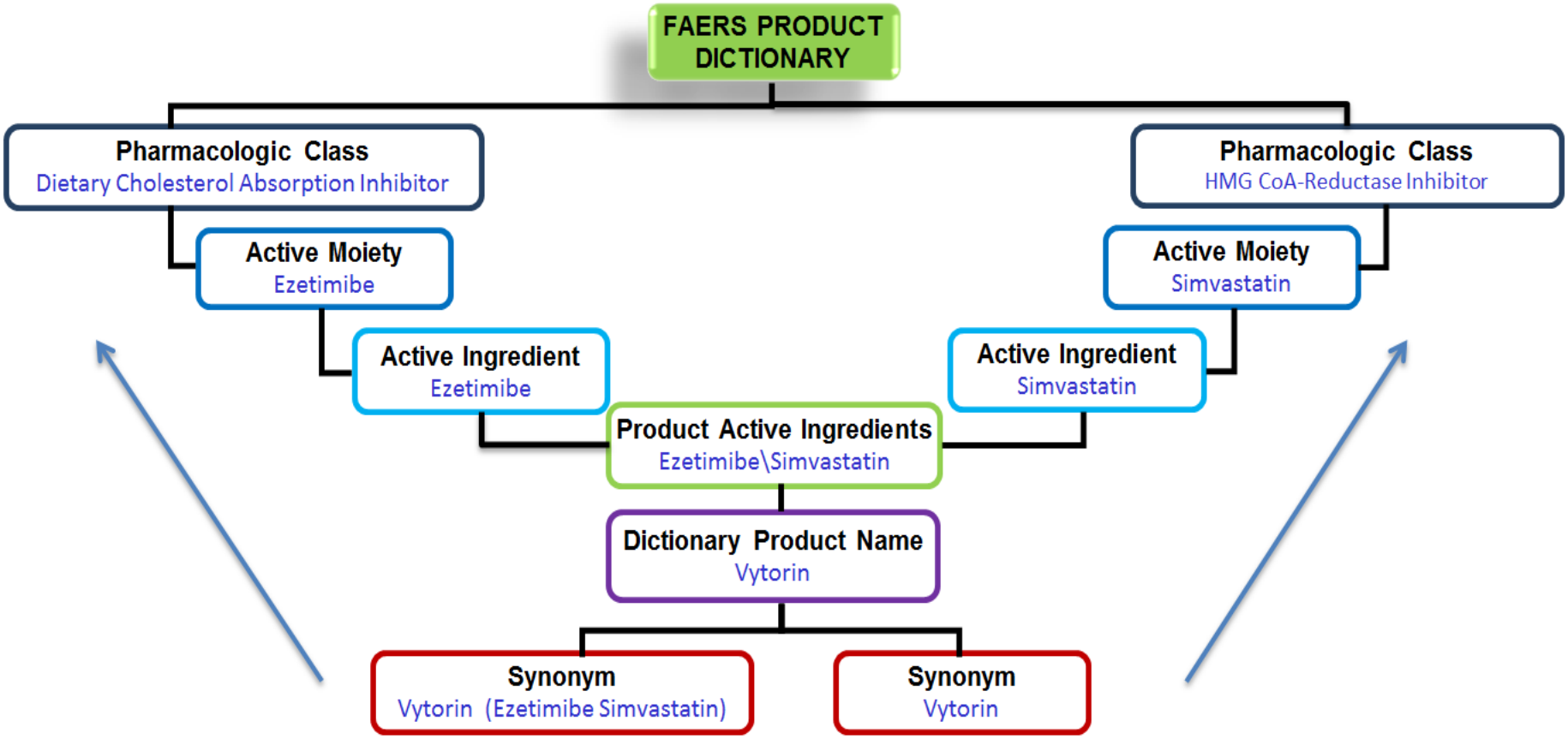
Dietary Supplement Label Database
A Joint Effort of the Office of Dietary Supplements and the U.S. National Library of Medicine

Natural Standard
The Authority on Integrative Medicine

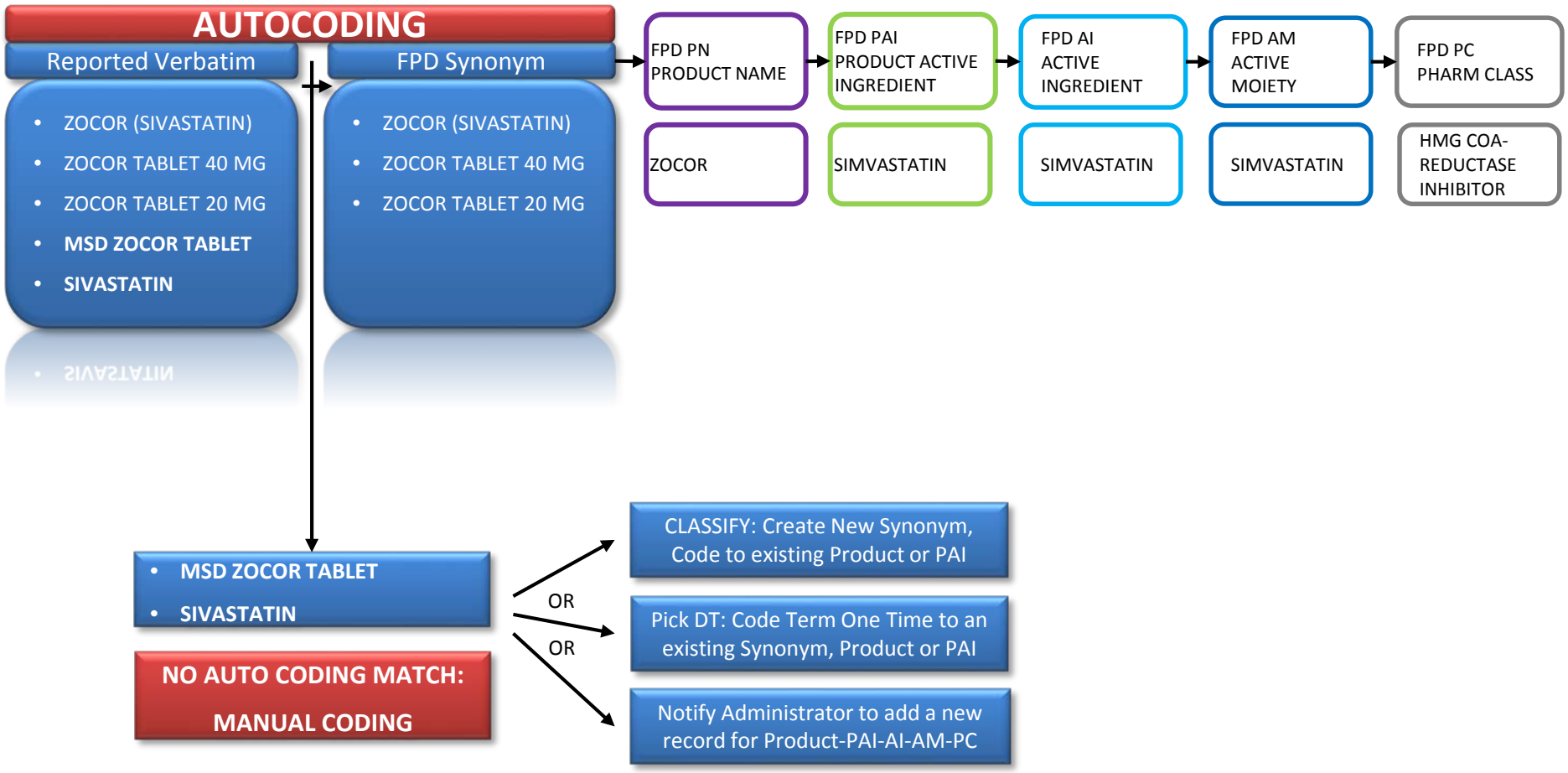
FPD Example: Single Ingredient Product



FPD Example: Multi-Ingredient Product



Suspect product coding



Product Coding Conventions

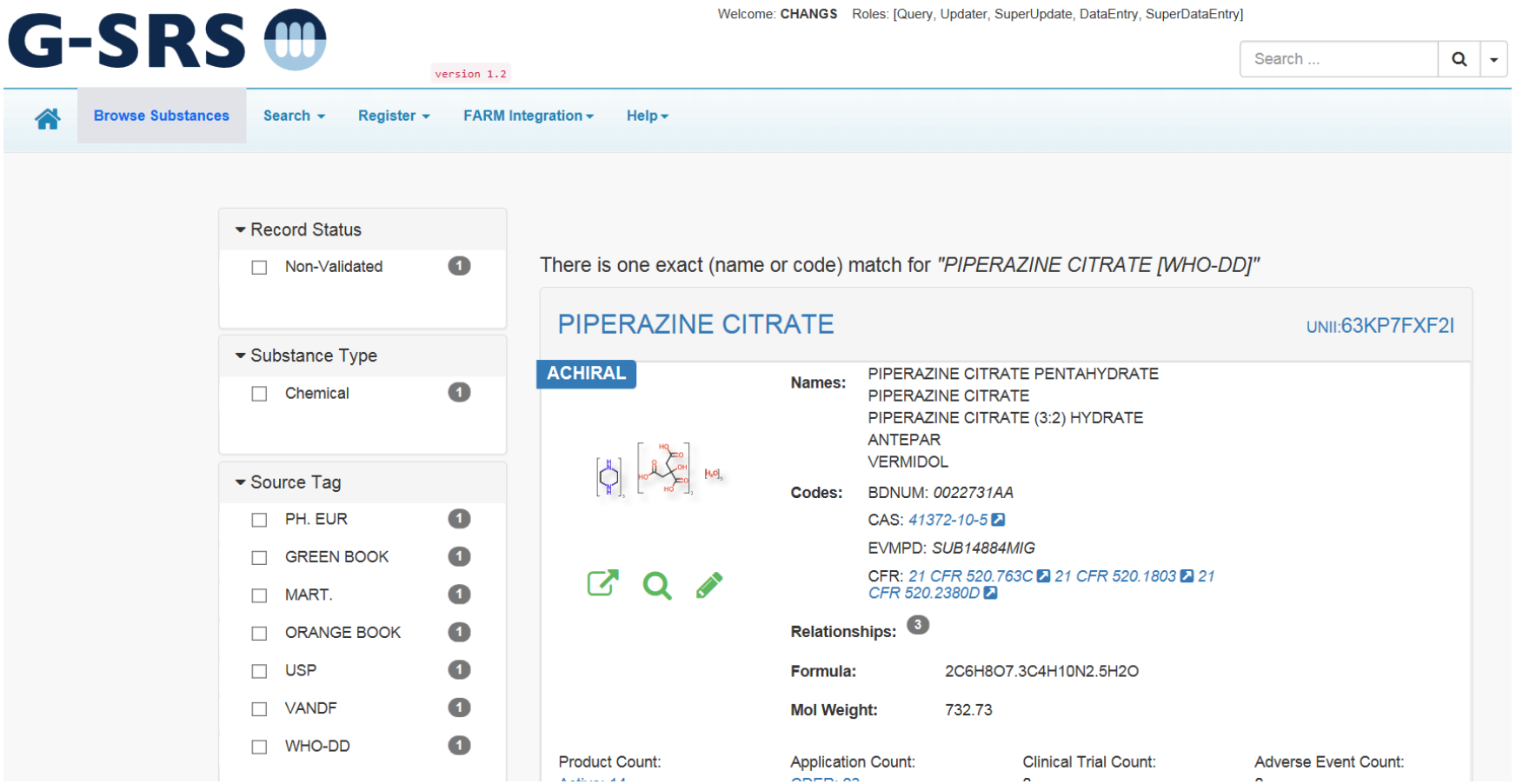
- If the Product name is not unique, and same name exists with one ingredient as well as with another ingredient, then the Product name is amended to include the ingredient in parenthesis, to make it unique.

  Example: DULCOLAX can contain Bisacodyl or Docusate Sodium

Reported Product Verbatim	Dulcolax	Dulcolax
Reported Active Ingredient	BISACODYL	DOCUSATE SODIUM
Product Coded to	DULCOLAX (BISACODYL)	DULCOLAX (DOCUSATE SODIUM)
Product Name	DULCOLAX (BISACODYL)	DULCOLAX (DOCUSATE SODIUM)
Product Active Ingredient (PAI)	BISACODYL	DOCUSATE SODIUM

Global Substance Registration System

http://gsrs.fda.gov/ginas/app



SPL: Structured Product Labeling

Available on DailyMed (National Library of Medicine, NLM, provides this as a public service) http://dailymed.nlm.nih.gov/dailymed/drugList.cfm?startswith=A

40,000 Units/mL

10 x 40,000 Units/mL Single Use Vials NDC 55513-823-10

AMGEN®

EPOGEN®

EPOETIN ALFA

recombinant

40,000 Units/mL

Single Use Vials (containing 1 mL)

For Intravenous or Subcutaneous Use Only

Sterile Solution - No Preservative

Store at 2° to 8°C (36° to 46°F). Do Not Freeze or Shake.

Manufactured by Amgen Manufacturing, Limited, a subsidiary of Amgen Inc.
Thousand Oaks, CA 91320-1799 U.S.A.
U.S. License No. 1080 ©2010 Amgen Inc.

℞ Only

EPOGEN
epoetin alfa solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	Item Code (Source)	NDC:55513-126
Route of Administration	INTRAVENOUS, SUBCUTANEOUS	DEA Schedule	

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
ERYTHROPOIETIN (ERYTHROPOIETIN)	ERYTHROPOIETIN	2000 [IU] in 1 mL

Inactive Ingredients	
Ingredient Name	Strength
SODIUM CHLORIDE	5.9 mg in 1 mL

UMC: WHODrug Global

WHODrug Global Dictionary, Uppsala Monitoring Centre

Browser: WHODrug Insight

Public output: FAERS Quarterly data extract

"XML_NTS.DOC" File

B.4.k.1	drugcharacterization	Reported role of drug in adverse event. Possible Codes are: 1= suspect 2=concomitant 3= interacting NOTE: This set of fields may repeat for each drug where k=1,2,3...
B.4.k.2.1	medicinalproduct	Valid Trade Name if populated; otherwise, verbatim name used by reporter.
B.4.k.2.2	activesubstancename	Product Active Ingredient, when available. + New tag added in 2014Q3 extract.

"ASC_NTS.DOC" File

ROLE_COD	Code for drug's reported role in event(See table below) CODE MEANING_TEXT ---- ------------ PS Primary Suspect Drug SS Secondary Suspect Drug C Concomitant I Interacting
DRUGNAME	Name of medicinal product. If a "Valid Trade Name" is populated for this Case, then DRUGNAME = Valid Trade Name; if not, then DRUGNAME = "Verbatim" name, exactly as entered on the report.
PROD_AI	Product Active Ingredient, when available. + New tag added in 2014Q3 extract.
VAL_VBM	Code for source of DRUGNAME (See table below) CODE MEANING_TEXT ---- ------------ 1 Validated trade name used 2 Verbatim name used
ROUTE	The route of drug administration
DOSE_VBM	Verbatim text for dose, frequency, and route, exactly as entered on report.

As of 2014Q3 extract:

Added new field for Product Active Ingredient (PROD_AI) in ASCII Drug file and new tag (<activesubstancename>) added to XML extract populated with Product Active Ingredient, when available.

FAERS Public dashboard

https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070093.htm

https://fis.fda.gov/sense/app/777e9f4d-0cf8-448e-8068-f564c31baa25/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis

The FAERS Public Dashboard is a highly interactive web-based tool that will allow for the querying of FAERS data in a user friendly fashion. The intention of this tool is to expand access of FAERS data to the general public to search for information related to human adverse events to drug and biologic products reported to the FDA by the pharmaceutical industry, healthcare providers and consumers.

Issues with reported suspect products

- Suspect product: one of minimum data elements for a reportable ICSR
  - ICSR submitted with an invalid suspect product:
    - "unspecified ingredient" or "drug not known"
    - "antihypertensive", "beta-blocker", etc.
    - "unspecified study drug"
    - "code not broken" or "blinded X"
- Primary suspect <medicinal product> name reported as an internal company code in post-market ICSR

Issues with reported suspect products (2)

Two products reported as a single product:

- Repoted VT: Clopidogrel,Triflusal
- Reported VT:

  CEFTAZIDIME+VANCOMYCIN
- Repoted VT: Tavor (fluconazole)

  the narrative states: Tavor

  (lorazepam) and Fluconazole

Single ingredient reported as all-available-salts-multi-ingredient:

- PROPRANOLOL/PROPRANOLOL HYDROCHLORIDE/PROPRANOLOL PHENOBARBITAL
- DOCUSATE/DOCUSATE CALCIUM/DOCUSATE POTASSIUM/ DOCUSATE SODIUM
- HYDROXYZINE/HYDROXYZINE EMBONATE/HYDROXYZINE HYDROCHLORIDE
- METFORMIN/METFORMIN CHLOROPHENOXYACETATE/METFORMIN EMBONATE/METFORMIN HYDROCHLORIDE

Issues with reported suspect products (3)

- Difficult-to-decipher reported suspect product:
  - "XC DAY PE-NITE FREE LIQGL COMB 090"
  - "ASP SEV SIN CONG LG"
  - "LONG-ACTING IM"
  - "MTAB"

Summary

- <*Medicinal product*> and <*active substance name*> data submitted in FAERS ICSRs are reviewed for data quality and auto- or manually coded
- G-SRS Preferred name active ingredient is the standard for the <*active substance name*> data
- Standardization of drug data through accurate and consistent coding enables data aggregation and analysis
- FAERS uses ICH E2B(R2) format but is moving towards incorporating ICH E2B(R3) and the IDMP standard