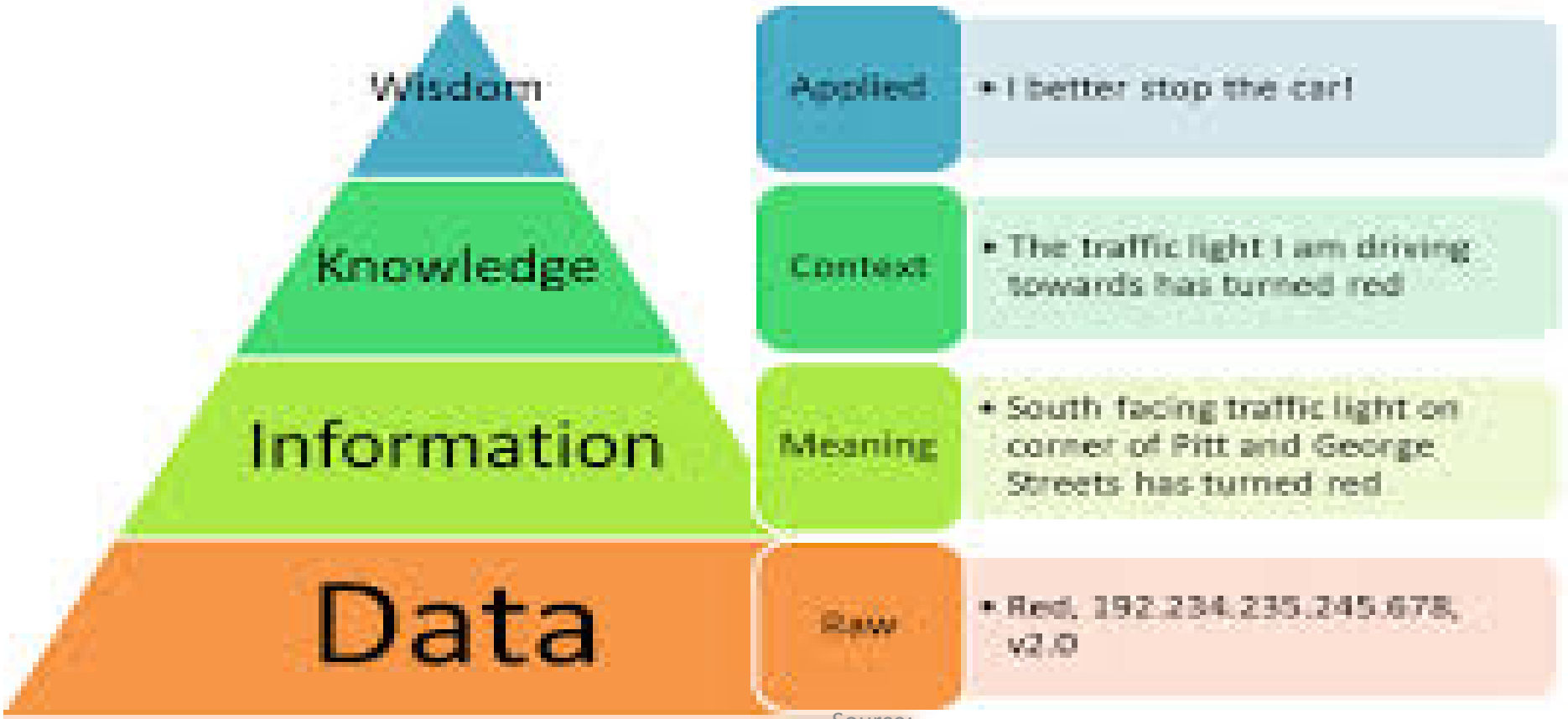
U.S. FDA Activities: ISO IDMP

Vada A. Perkins
Dep. Assoc. Director (Acting)
U.S. Food and Drug Administration
Center for Biologics Evaluation and Research
Review Management

DIKW or "WKID" Method



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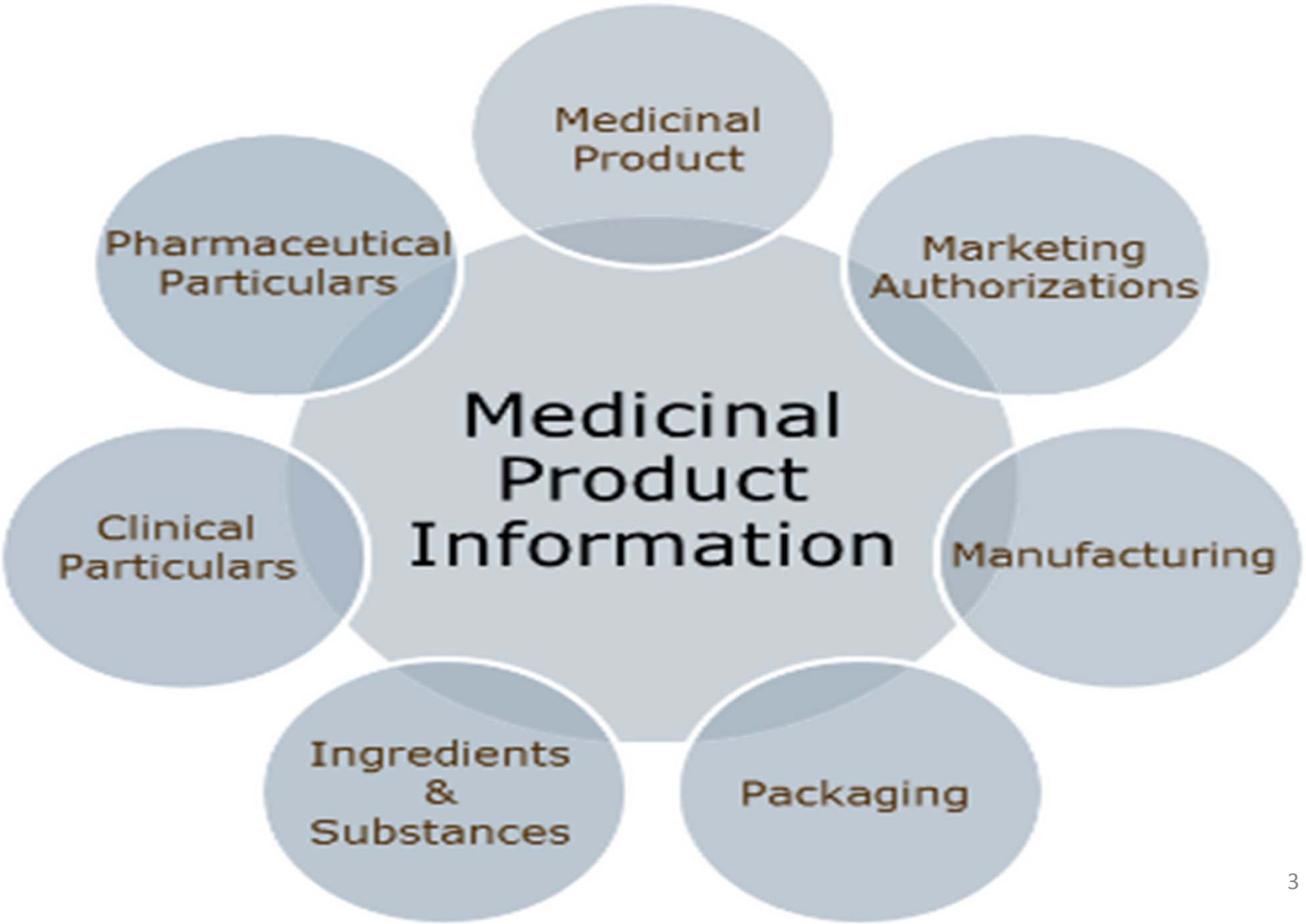
https://www.google.com/search?q=wkid+knowledge+wisdom&biw=1093&bih=520&source=lnms&tbm=isch&sa=X&ved=0CAYQ_AUoAWoVChMI9Iqvx9TkxwIVyFYeCh24sghr#imgrc=xyyD7GiyvBmRaM%3A


Medicinal Product
Pharmaceutical Particulars
Marketing Authorizations
Medicinal Product Information
Clinical Particulars
Manufacturing
Ingredients & Substances
Packaging

Regulatory Use Cases Throughout the Product Lifecycle (1)

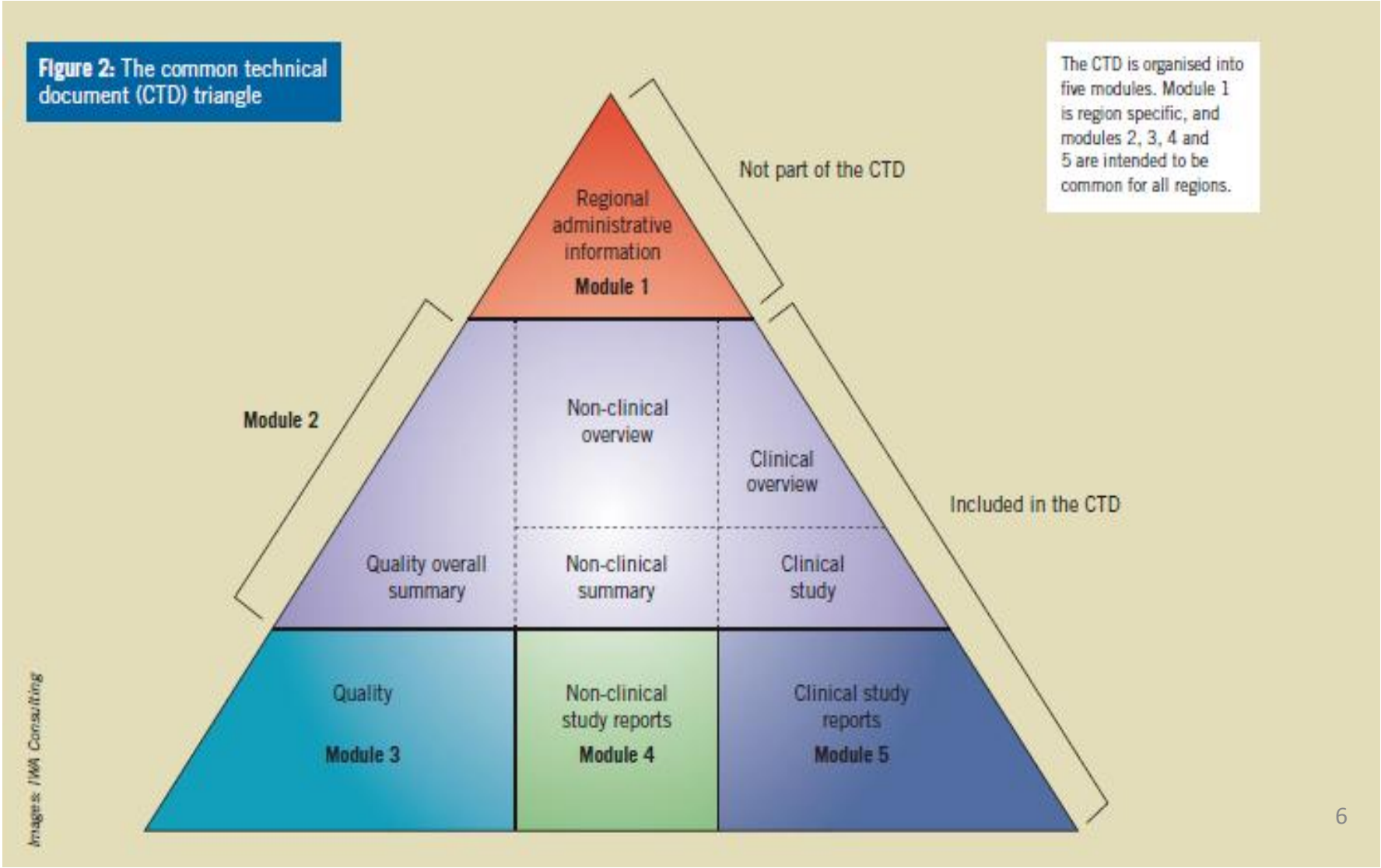
- **Investigational**
  - Clinical trials
    - Tracking formulation/dose changes throughout the investigational process
  - Clinical trial registration requirements (Industry)

- **Pre-Market**
  - New drug/biologics review
  - Pre-approval inspections

Regulatory Use Cases Throughout the Product Lifecycle (2)

- **Post-Market**
  - Pharmacovigilance
    - Adverse events/adverse drug reaction reporting
  - Compliance
    - Product-Establishment relationship
      - Supply chain
      - Counterfeiting
    - Import/export
    - Recalls

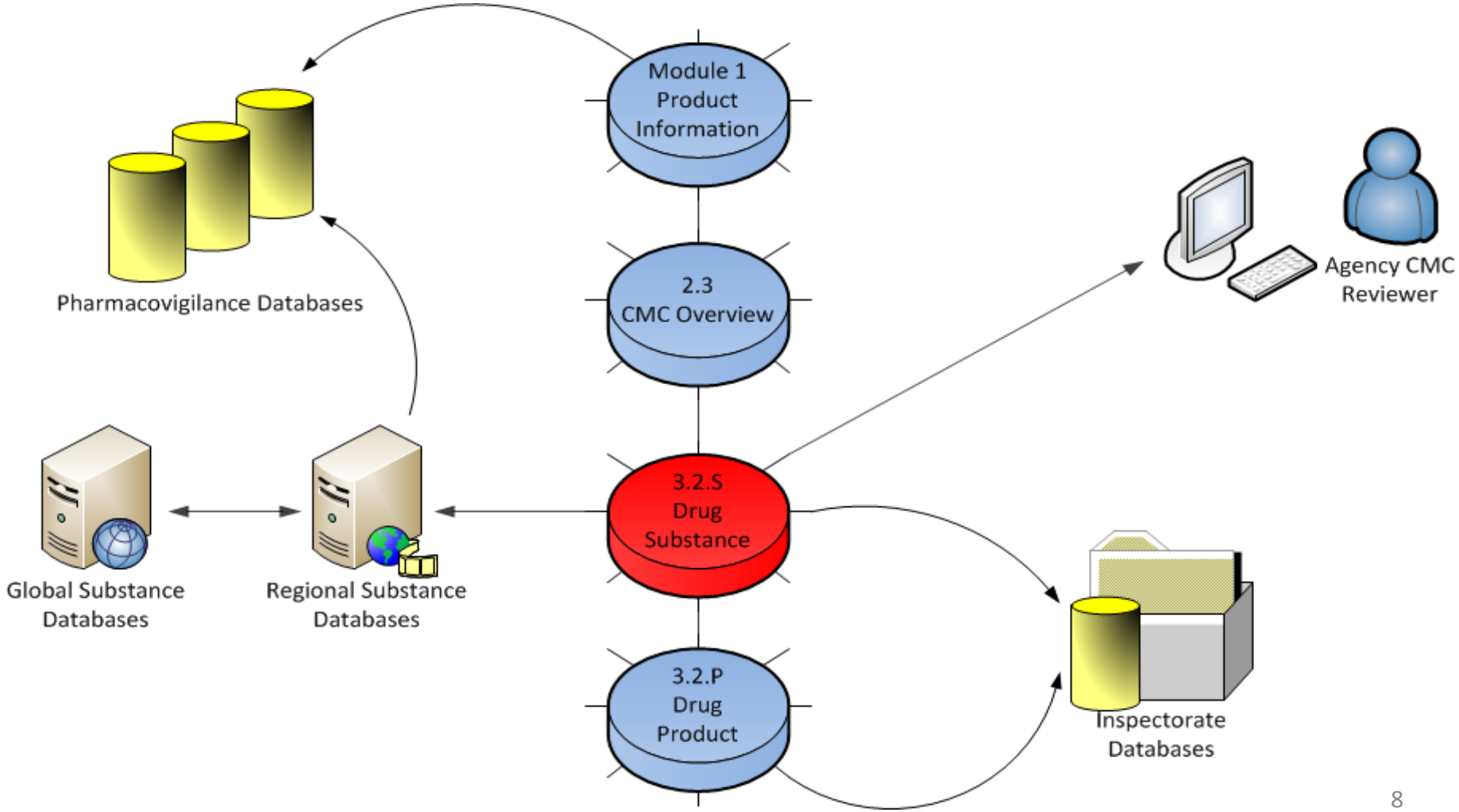
Common Technical Document (CTD)



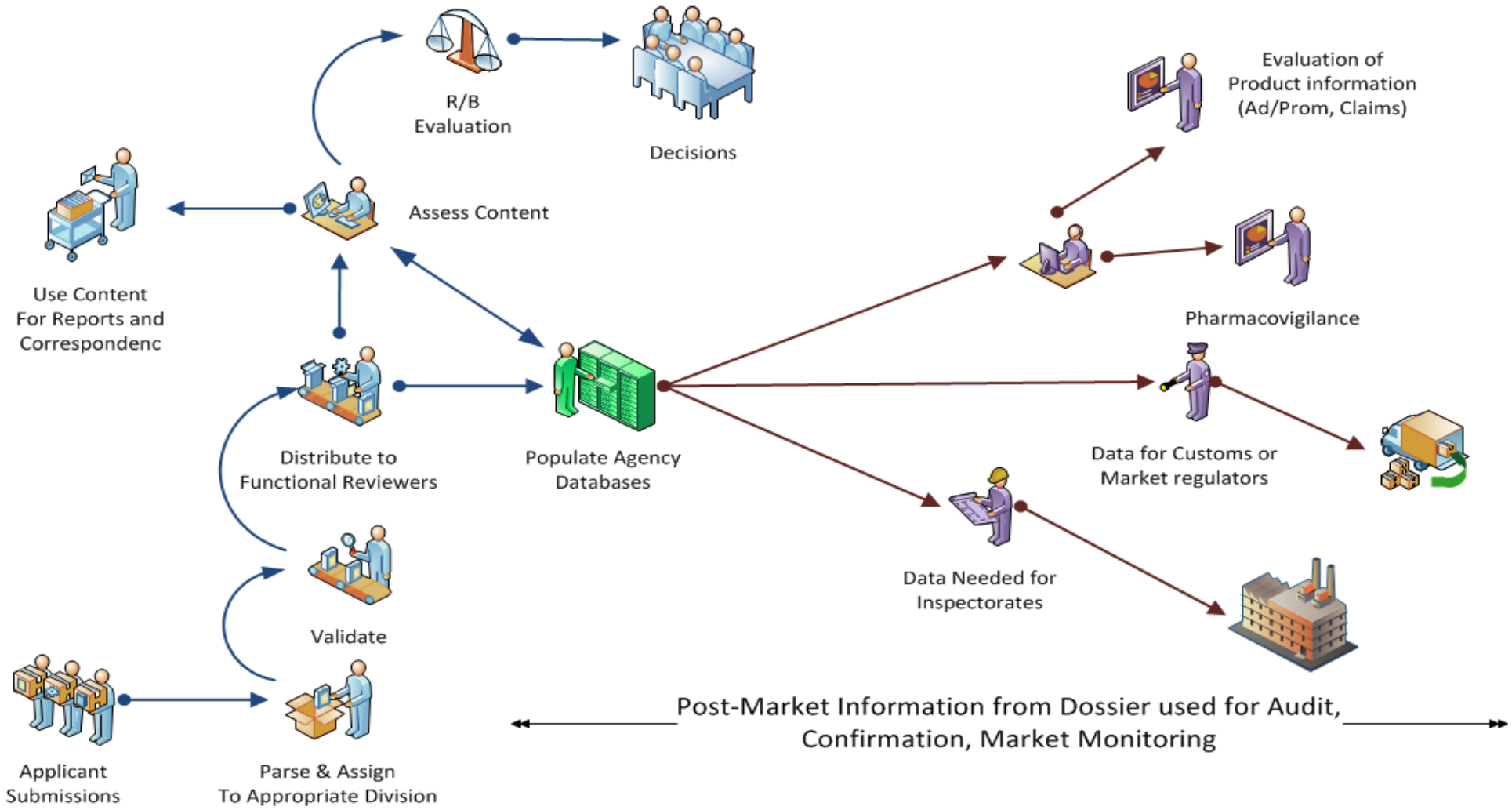
Module 3: Chemistry, Manufacturing, Controls (CMC)

- Analytical Methods
- Degradation Products
- Specifications
- In-process controls
- Methods Validation
- Process Validation
- (DP/DS) Characterization
- Container / Closure System
- Characterization
- Stability

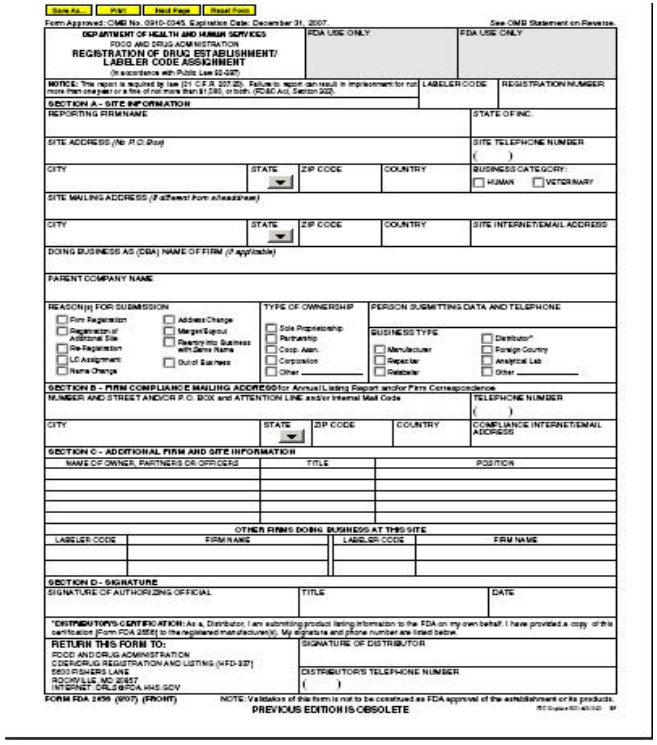
Use of Regulated Medicinal Product Information



Regulatory Data Flow



Paper Forms (obsolete)


Form Approved: OMB No. 0910-0045. Expiration Date: December 31, 2007. See OMB Statement on Reverse.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

REGISTRATION OF DRUG ESTABLISHMENT/ LABELER CODE ASSIGNMENT

(In accordance with Public Law 92-387)

FDA USE ONLY | FDA USE ONLY

NOTICE: The report is required by law (21 C.F.R. 207.20). Failure to report can result in imprisonment for not more than one year or a fine of not more than $1,000, or both. (FD&C Act, Section 302).

LABELER CODE | REGISTRATION NUMBER

SECTION A - SITE INFORMATION

REPORTING FIRM NAME | STATE OF INC.

SITE ADDRESS (No P.O.Box) | SITE TELEPHONE NUMBER

CITY | STATE | ZIP CODE | COUNTRY | BUSINESS CATEGORY: ☐ HUMAN ☐ VETERINARY

SITE MAILING ADDRESS (If different from addressee)

CITY | STATE | ZIP CODE | COUNTRY | SITE INTERNET/EMAIL ADDRESS

DOING BUSINESS AS (DBA) NAME OF FIRM (If Applicable)

PARENT COMPANY NAME

REASON(s) FOR SUBMISSION
- ☐ Firm Registration
- ☐ Registration of Additional Site
- ☐ Re-Registration
- ☐ LC Assignment
- ☐ Name Change
- ☐ Address Change
- ☐ Merger/Buyout
- ☐ Reentry into Business with Same Name
- ☐ Out of Business

TYPE OF OWNERSHIP
- ☐ Sole Proprietorship
- ☐ Partnership
- ☐ Coop. Assn.
- ☐ Corporation
- ☐ Other

PERSON SUBMITTING DATA AND TELEPHONE

BUSINESS TYPE
- ☐ Manufacturer
- ☐ Repacker
- ☐ Relabeler
- ☐ Distributor*
- ☐ Foreign Country
- ☐ Analytical Lab
- ☐ Other

SECTION B - FIRM COMPLIANCE MAILING ADDRESS for Annual Listing Report and/or Firm Correspondence

NUMBER AND STREET AND/OR P.O. BOX and ATTENTION LINE and/or Internal Mail Code | TELEPHONE NUMBER

CITY | STATE | ZIP CODE | COUNTRY | COMPLIANCE INTERNET/EMAIL ADDRESS

SECTION C - ADDITIONAL FIRM AND SITE INFORMATION

NAME OF OWNER, PARTNERS OR OFFICERS	TITLE	POSITION

OTHER FIRMS DOING BUSINESS AT THIS SITE

LABELER CODE	FIRM NAME	LABELER CODE	FIRM NAME

SECTION D - SIGNATURE

SIGNATURE OF AUTHORIZING OFFICIAL | TITLE | DATE

*DISTRIBUTOR'S CERTIFICATION: As a Distributor, I am submitting product listing information to the FDA on my own behalf. I have provided a copy of this certification (Form FDA 2656) to the registered manufacturer(s). My signature and phone number are listed below.

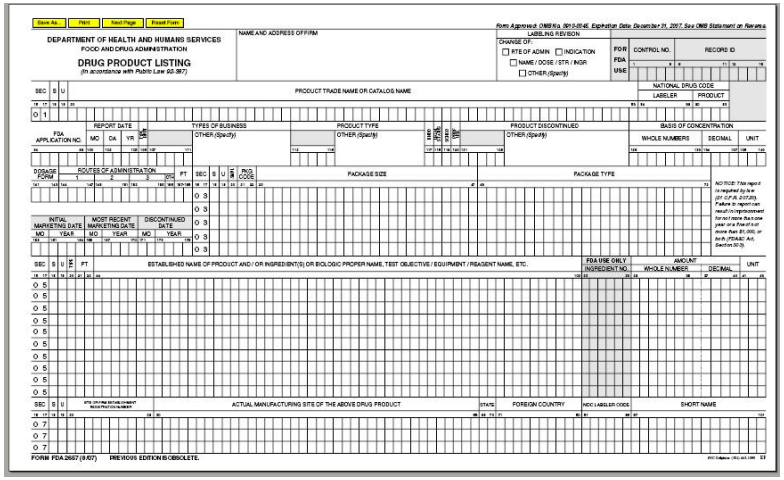
RETURN THIS FORM TO:
FOOD AND DRUG ADMINISTRATION
CDER/DRUG REGISTRATION AND LISTING (HFD-327)
5600 FISHERS LANE
ROCKVILLE, MD 20857
INTERNET: CRLS@FDA.HHS.GOV

SIGNATURE OF DISTRIBUTOR

DISTRIBUTOR'S TELEPHONE NUMBER

FORM FDA 2656 (9/07) (FRONT) NOTE: Validation of this form is not to be construed as FDA approval of the establishment or its products.

PREVIOUS EDITION IS OBSOLETE


Form Approved: OMB No. 0910-0045. Expiration Date: December 31, 2007. See OMB Statement on Reverse.

DEPARTMENT OF HEALTH AND HUMANS SERVICES
FOOD AND DRUG ADMINISTRATION

DRUG PRODUCT LISTING

(In accordance with Public Law 92-387)

NAME AND ADDRESS OF FIRM

LABELING REVISION
CHANGE OF:
☐ RTE OF ADMIN ☐ INDICATION
☐ NAME / DOSE / STR / INGR
☐ OTHER (Specify)

FOR FDA USE | CONTROL NO. | RECORD ID

PRODUCT TRADE NAME OR CATALOG NAME | NATIONAL DRUG CODE: LABELER | PRODUCT

REPORT DATE | TYPES OF BUSINESS | PRODUCT TYPE | PRODUCT DISCONTINUED | BASIS OF CONCENTRATION

FDA APPLICATION NO. | MO | DA | YR | OTHER (Specify) | OTHER (Specify) | OTHER (Specify) | WHOLE NUMBERS | DECIMAL | UNIT

DOSAGE FORM | ROUTE OF ADMINISTRATION 1 2 3 | PACKAGE SIZE | PACKAGE TYPE

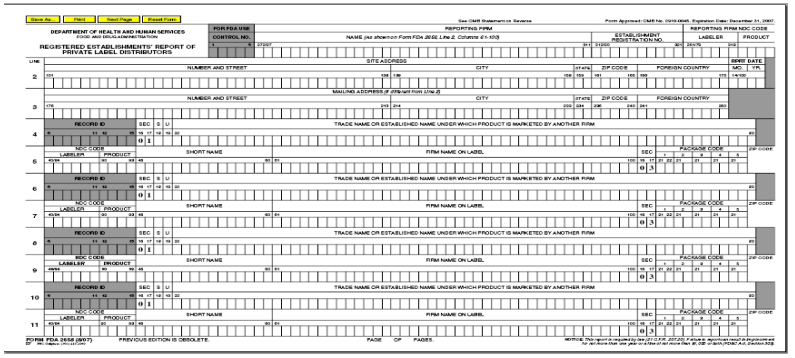
NO FDA: This report is required by law (21 C.F.R. 207.20). Failure to report can result in imprisonment for not more than one year or a fine of not more than $1,000, or both (FD&C Act, Section 303).

INITIAL MARKETING DATE: MO YEAR | MOST RECENT MARKETING DATE: MO YEAR | DISCONTINUED DATE: MO YEAR

ESTABLISHED NAME OF PRODUCT AND / OR INGREDIENT(S) OR BIOLOGIC PROPER NAME, TEST OBJECTIVE / EQUIPMENT / REAGENT NAME, ETC. | FDA USE ONLY INGREDIENT NO. | AMOUNT: WHOLE NUMBERS | DECIMAL | UNIT

ACTUAL MANUFACTURING SITE OF THE ABOVE DRUG PRODUCT | STATE | FOREIGN COUNTRY | NDC LABELER CODE | SHORT NAME

FORM FDA 2657 (9/07) PREVIOUS EDITION IS OBSOLETE.


DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

REGISTERED ESTABLISHMENTS' REPORT OF PRIVATE LABEL DISTRIBUTORS

FOR FDA USE | CONTROL NO. | REPORTING FIRM | NAME (As shown on Form FDA 2656 Line 2, Column 61-100) | ESTABLISHMENT REGISTRATION NO. | REPORTING FIRM NDC CODE: LABELER | PRODUCT

SITE ADDRESS | NUMBER AND STREET | CITY | ZIP CODE | FOREIGN COUNTRY | MAILING ADDRESS (If Different from Line 2)

RECORD ID | SEC | S | U | TRADE NAME OR ESTABLISHED NAME UNDER WHICH PRODUCT IS MARKETED BY ANOTHER FIRM

NDC CODE: LABELER | PRODUCT | SHORT NAME | FIRM NAME ON LABEL | PACKAGE CODE

FORM FDA 2658 (9/07) PREVIOUS EDITION IS OBSOLETE. PAGE OF PAGES.

Image: http://rllukitvexd0gj49.zippykid.netdna-cdn.com/wp-content/uploads/2013/12/Messy_storage_room_with_boxes2.jpg

Style Sheet View/Source Code (XML)

CONTRAINDICATIONS

Miracle Drug Injection is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

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<code code="34070-3" codeSystem="2.16.840.1.113883.6.1" displayName="CONTRAINDICATIONS SECTION" />
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<text><paragraph>Miracle Drug Injection is contraindicated in severe toxic central nervous system depression or comatose states from
any cause and in individuals who are hypersensitive to this drug or have Parkinson&amp;#8217;s disease.</paragraph></text>
<effectiveTime value="20070813" />
</section>
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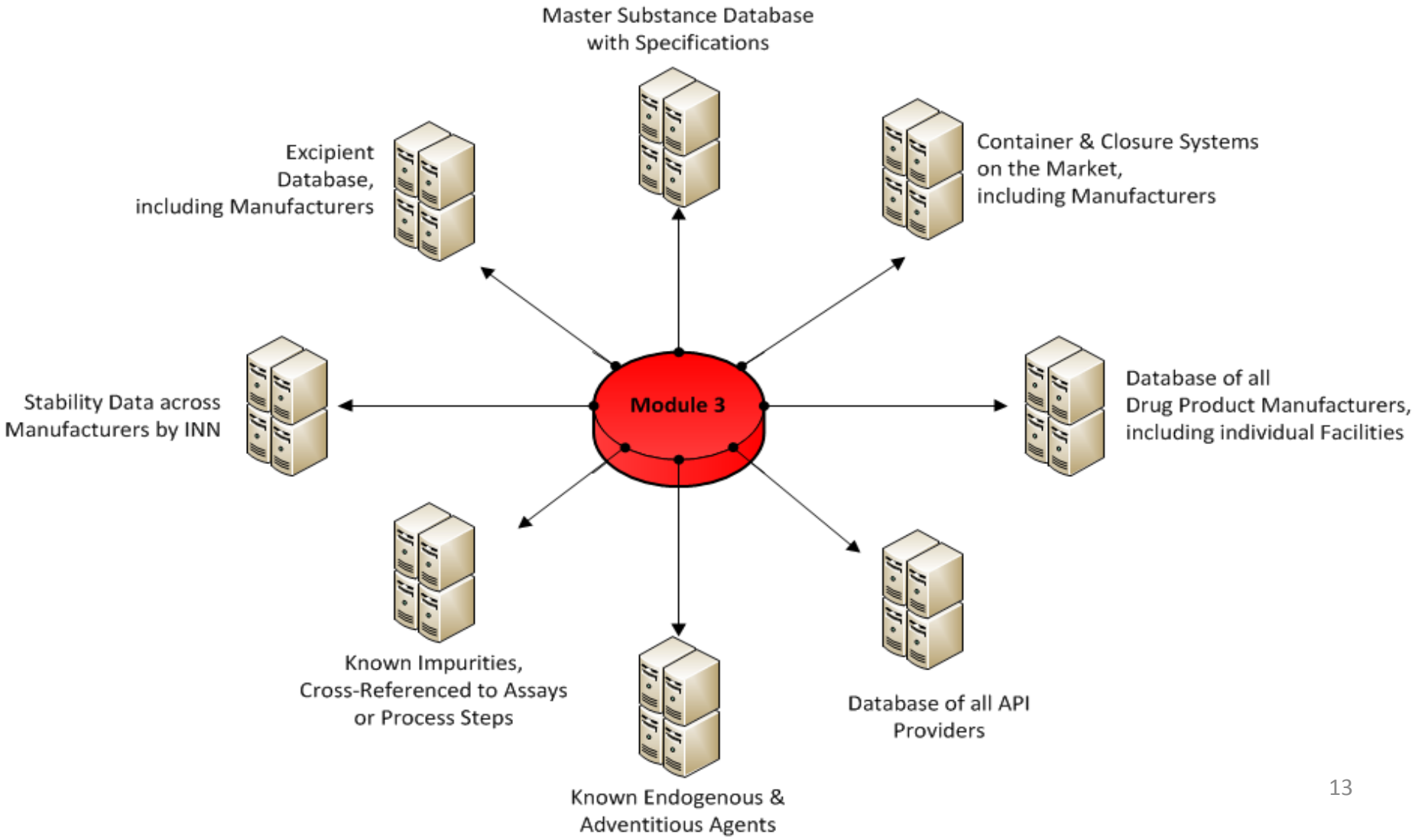
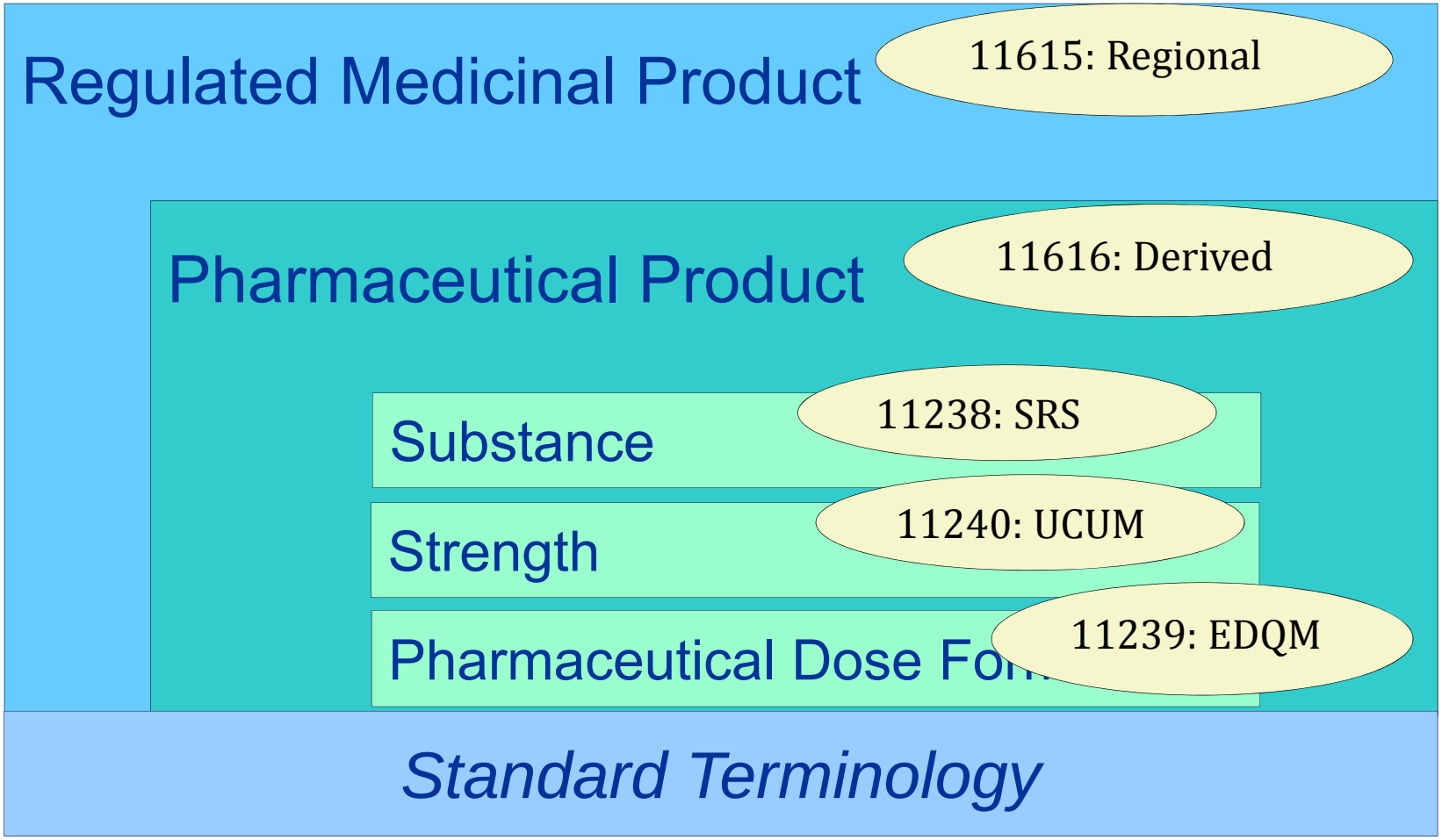
Benefit to Regulators/Industry



ISO IDMP Standards



ISO 11238: Substances/Specified Substances

- Substance:
  - Is defined based on its main, general characteristics
  - Can have different roles e.g. active, adjuvant, basis of strength, excipient
- Specified Substance:
  - More granular, specific description of a substance e.g. including manufacturing information, purity, grade
  - Allows for the specification of multiple substances ("Intermediate Products" e.g. AS03 - adjuvant composed of squalene (10.69 milligrams), DL-α-tocopherol (11.86 milligrams) and polysorbate 80 (4.86 milligrams))

ISO 11616: Pharmaceutical Product Identification

- Pharmaceutical Product Identification (PhPID) based on the following subset of elements that describe the pharmaceutical product:
  - Substance(s)/Specified Substance(s)
  - Strength(s) - Strength units (units of measurement and/or unit of presentation)
  - Reference Strengths
  - Administrable Dose Form
  - **Medical device: when it is a component of a medicinal product**

ISO 11615: Medicinal Product Identification

- Defines, characterizes and uniquely identifies regulated medicinal products for human use during their entire life cycle
  - Development, authorization, post-marketing and renewal or withdrawal from the market
- Establishes definitions and concepts
- Use of other normative standards for messaging purposes (e.g., HL7)

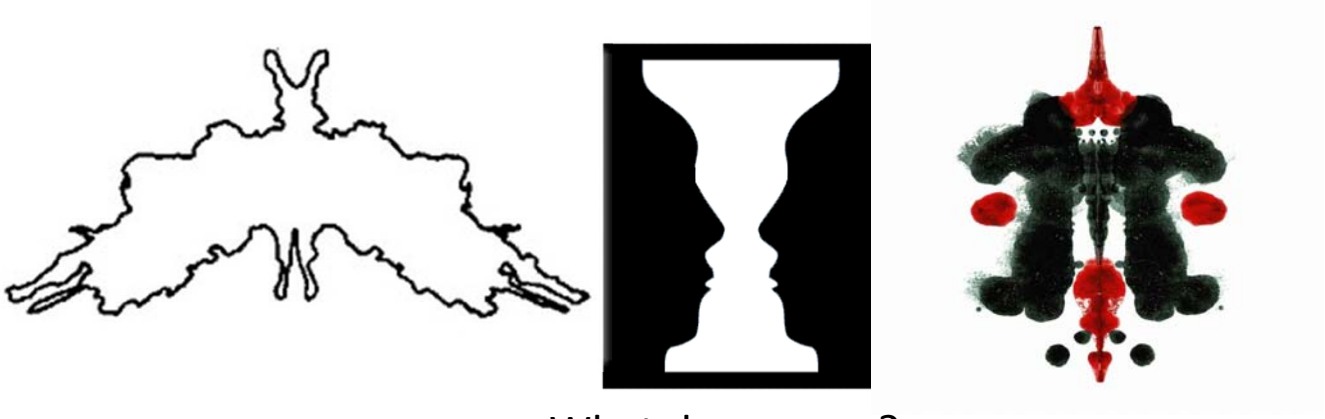
ISO IDMP: International Harmonization

Image: https://www.aacc.org/~/media/images/cln/articles/2012/expo-issue/globewithinternationalflags.jpg?h=259&w=300&la=en

Adoption and Implementation

Consistent adoption and implementation is dependent upon how different implementers *interpret* data:

- ✓ISO IDMP Technical Specifications
- ✓ISO IDMP Terminology Maintenance Report



What do you see?

Incompatibility

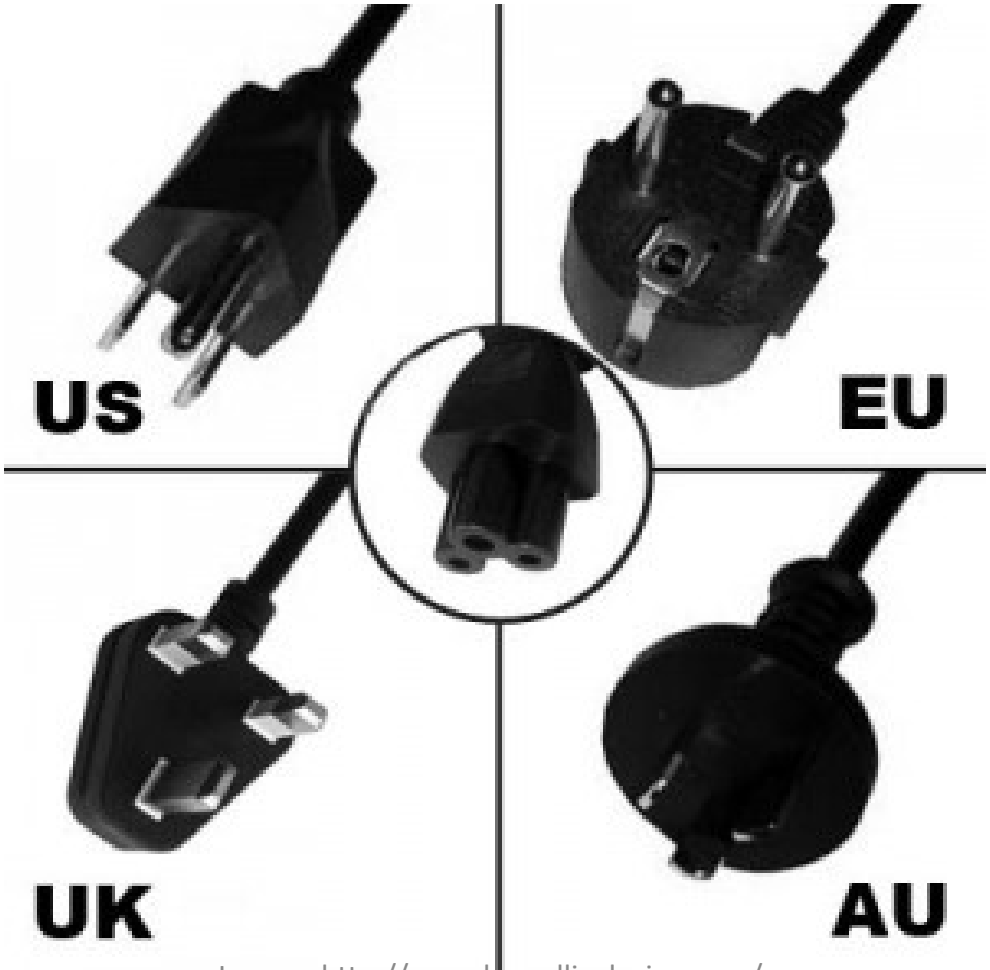
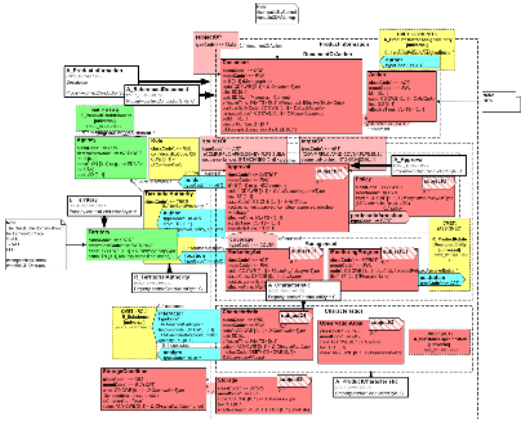


Image: http://www.hassellinclusion.com/wp-content/uploads/2012/12/plugs-300x300.jpg

Standard e-Message for Data Exchange: Common Product Model (CPM)

- The Health Level Seven (HL7) Common Product Model (CPM) provides:



✓ **Overarching information model**

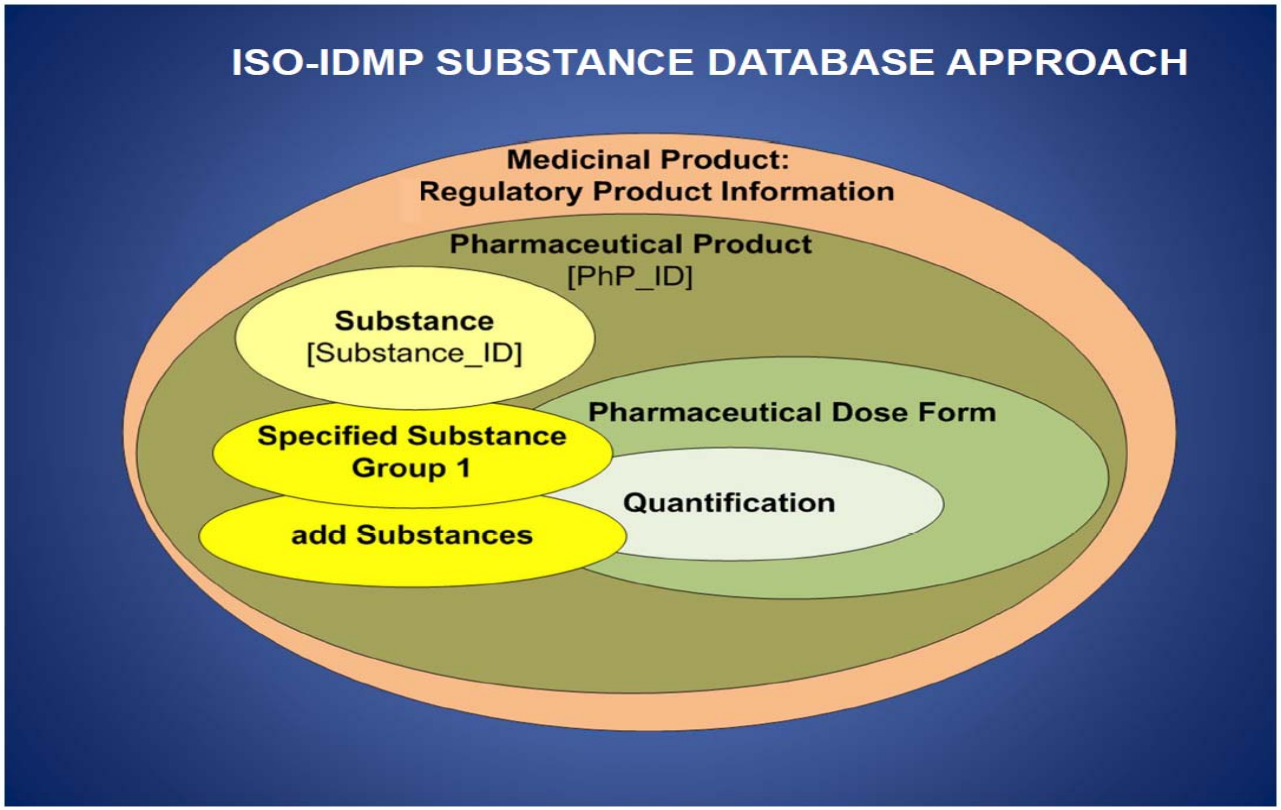
✓ **Reusable Common Message Element Types (CMETs)**

✓ **Consistent data types and conformance rules**

✓ **Vocabulary domains**

✓ **Schemas for data exchange**

ISO 11238/I9844 (GiNAS/G-SRS)
Business Case:
ISO IDMP Maintenance-Substances



Conclusion

- Pre-defined structure makes it possible to perform more complex *business* actions faster using *IT* systems.

- *Common* structure enables systems to exchange information within and across company and global boundaries.

IDMP
Governance and Maintenance

Understanding the Internal/External Interface: Current Practice

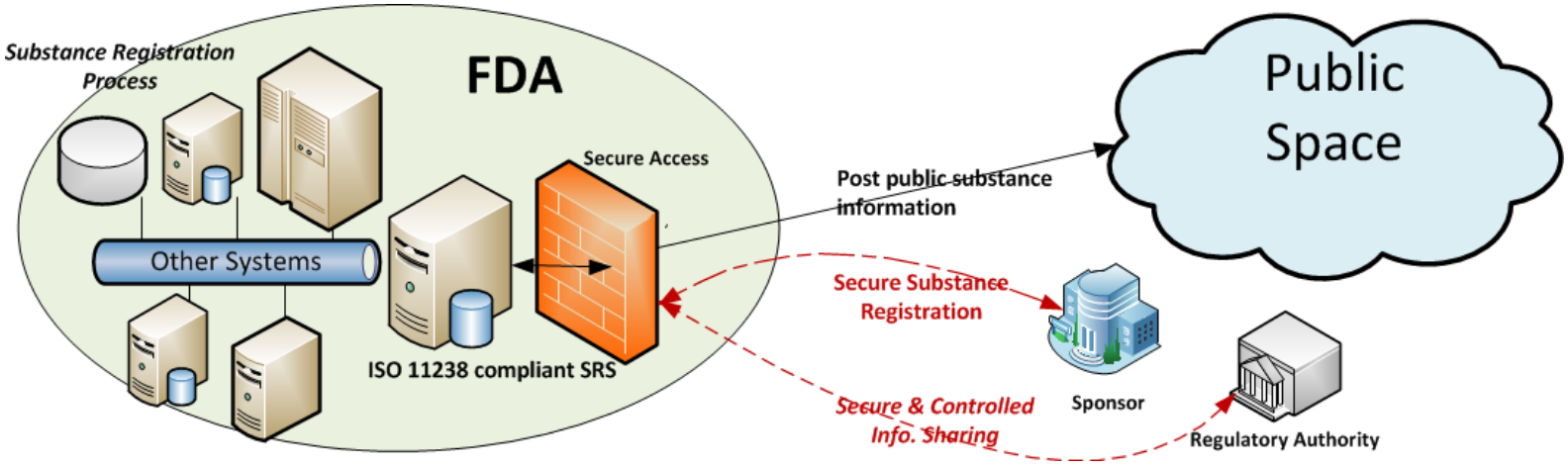
- Substance registration and use maintained internally
  - Within the FDA firewall
  - Protection of confidential/trade secret information
- Two way communication/updates from internal to external sources (public information) based on internationally accepted “sources of truth” and confidentiality/trade secret requirements
- To the extent it is public, regulators with legal requirements can push to GInAS once information is publicly available

Fundamental Maintenance Organization (MO) Criteria

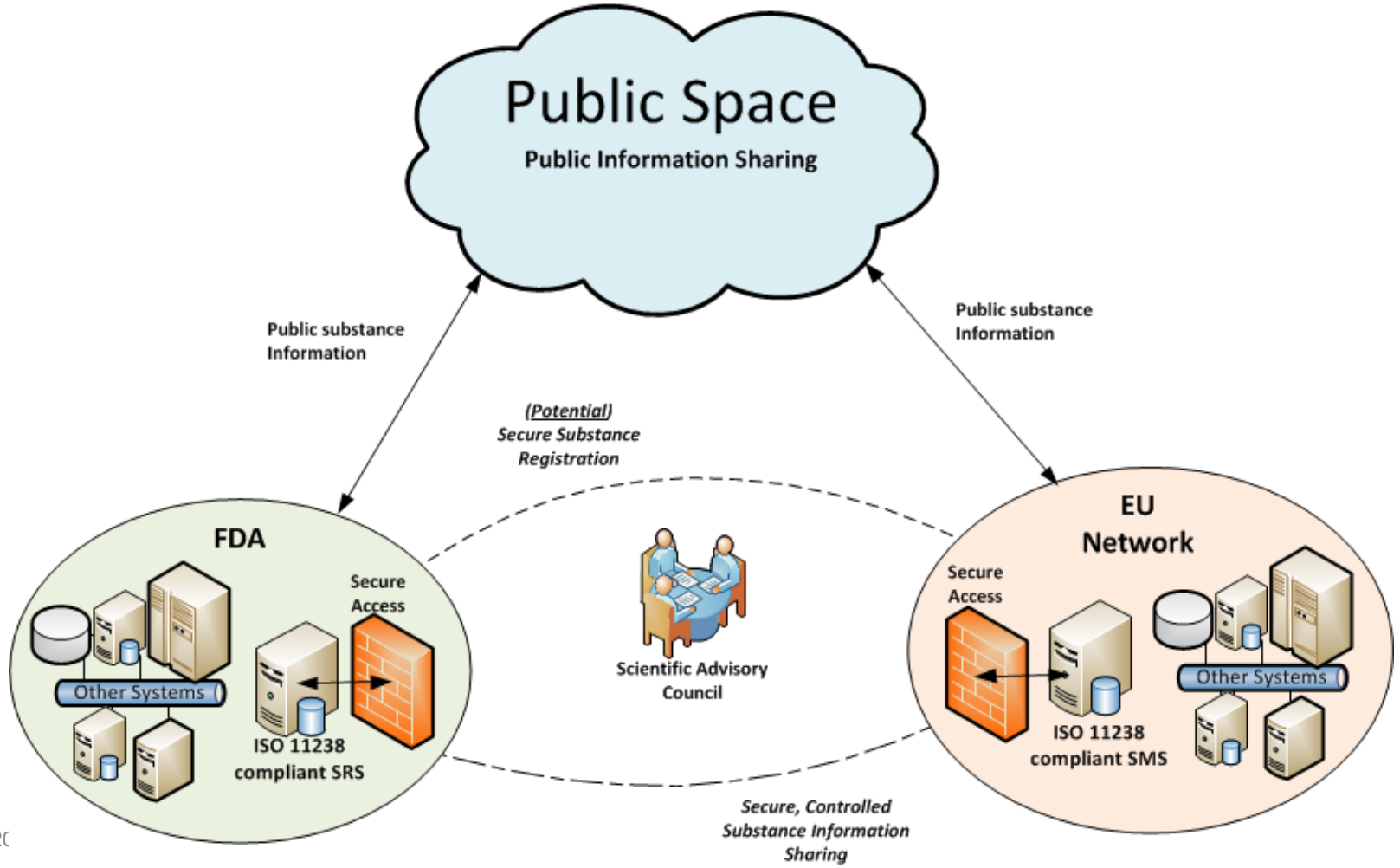
- ***Initial creation*** of the controlled vocabulary, including associated controlled sub-vocabularies;
- Change requests for both ***new and existing terms, non-preferred terms and synonyms***
- Process/procedure for handling multiple ***translations***
- Change requests for both ***new and existing underlying definitions***
- ***Up-to-date publication*** of change release documentation reflecting significant updates and additions
- Maintenance of the ***technical implementation of the structures*** in response to changes

US FDA Requirements for Substance ID Maintenance

- Must Maintain Substance ID For Pre And Post Market Substances
- Must Support Confidential/Trade Secret Information
  - Safeguard against unauthorized access
  - Post online only after information is publicly available
  - Not ALL defining elements that describe a substance may be in the Public Domain
- Authoritative Source
  - Safeguard data integrity
  - Safeguard against improper/inappropriate data
    - No automatic acceptance of substance information
    - Information must be verified and validated before acceptance



Example EU/EMA-FDA Substance Registration and Data Sharing Model



ISO Draft Technical Report (DTR) 14872

- ISO is developing a draft technical report that describes the maintenance model and core principles for implementation and use of the suite of ISO Identification of Medicinal Products (IDMP) standards.

- ISO TR 14872 identifies fundamental requirements that an ISO IDMP MO should address:
  - Receiving requests for change
  - Categorization of changes
  - Authorization of changes
  - Producing change schedules
  - Planning/testing changes
  - Implementing changes
  - Reviewing the changes to ensure successful adoption/integration

What Would These Roles Require? What Is Possible?

- Repository of publicly available substance information and IDs
  This requires:
  –Availability (24x7 ?)
  –Accessibility (Web, Mobile ?)
  –Data Integrity (Trusted source or resource only?)
  –Repository maintenance
  –Funding model

- Resource for Global Substance ID that maps to Regional IDs (Harmonization)
  All of the above requirements, plus:
  –Authoritative (trusted) source
  –Governance body
  –Governance processes
  –Handling substance IDs with partial information (FDA's confidential information issue)

- Registration & Maintenance Organization for Unique Substance IDs
  All of the above requirements, plus:
  –Additional level of governance
  –Ensure data confidentiality and controlled access
  –Service level agreement

FDA IDMP 11238/19844 G-SRS Update

Substance Registration Policy/Process and Governance – FDA Maintenance Organization – Internal

FDA/EMA-EU Substance Registration Governance and Maintenance Organization – External

IDMP SDO Implementation Guide

- First version of ISO DTS 19844 was submitted to Secretariat.
- First edition of the technical specifications guide (ISO TS 19844) contains proteins, chemicals, and nucleic acids.

FDA IDMP 11238/19844 G-SRS Update

- **GSRS Implementation/Governance-FDA/Internal**
  - Goal: Install system to support ISO compliance substance registration.
  - Update:
    - First planned production release ***2nd QTR 2016***.
      - FDA: Larry Callahan/Frank Switzer
      - NCATS: Noel Southall/Tyler Peryea

Thank You

vada.perkins@fda.hhs.gov

Acknowledgments to all GInAS, ISO, HL7, ICH Colleagues

Very Special Thanks to our Hosts:

WHO-UMC

Back Up Slides

Definition of "Drug"

- The term "new drug" means …any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof (except drugs so recognized subject to the Food and Drugs Act of June 30, 1906) ["Old Drug"]

Drug Substance (cont.)

- An active ingredient intended to furnish pharmacologic activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the body; it does not include intermediates used in the synthesis of such an ingredient

Drug Product

- A dosage form that contains an active drug ingredient or placebo.
- A finished dosage form of a therapeutic agent as described in regulations.
- A medication in its marketed form, including its fillers, coloring agents, and other active or inactive agents.