The session will begin shortly

Global IDMP Working Group

Day 3

18 October 2023

3d Global IDMP Working Group (GIDWG) Stakeholders Public Meeting

18 October 2023

Housekeeping notes

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#GIDWG

- Join via **QR code** or **slido.com -** *please provide your questions and comments in Slido only*
- **Send or upvote the questions** you want to hear answered – *before raising a question check whether its has been raised already and vote for it*

Q&A Management

- GIDWG colleagues will **verbally address top voted questions** at the end in the live Q&A session.
- Unanswered questions will be reviewed and will be taken into consideration in future GIWG materials.

Presentations

Presentations will be available at GIWG website in due course (GIDWG Working Group | UMC (who-umc.org))

AGENDA

13:00 – 13:20	**GIDWG Public Meeting** Opening Remarks	Hilmar Hamann (EMA) MaryAnn Slack (FDA) Shanthi Pal (WHO)
13:20 – 14:15	**GIDWG Background** IDMP & GIDWG pilots	Malin Fladvad (UMC)/ Ron Fitzmartin (FDA)/ Panagiotis Telonis (EMA)
14:15 – 14:45	Regulators and Industry Perspective	Ron Fitzmartin (FDA)/ Vada Perkins (IFPMA)
15:00 – 15:30	Standards Development Organizations Perspective	Charles Jaffe (HL7 International) Christian Hay (ISO/CEN) Catherine Chronaki (HL7 Europe)
15:30 – 17:00	**GIDWG End-to-End Use Cases** Pharmacovigilance Drug Shortages Cross border healthcare	Malin Fladvad(UMC)/ Ron Fitzmartin (FDA)/ Robert Stegwee (CEN/TC 251)
17:00 – 17:15	**Questions** Closing Remarks **Public Meeting Adjourned**	All Panagiotis Telonis (EMA)/ Isabel Chicharo (EMA)

GIDWG Public Meeting Opening Remarks

Hilmar Hamann (EMA)
MaryAnn Slack (FDA)
Shanthi Pal (WHO)

GIDWG Background
IDMP & GIDWG pilots

Malin Fladvad (UMC)/
Ron Fitzmartin (FDA)/
Panagiotis Telonis (EMA)

Why GIDWG?

- GIDWG was chartered in 2021 as an outcome of a 2019 WHO IDMP Workshop in Geneva, September 2019.
  - **Why was GIDWG established?**
    - There was no organization focused on demonstrating that the standards can be implemented globally.
  - **Membership**
    - Founding members include EU EMA, U.S. FDA, and WHO-UMC. IFPMA has joined as an industry member, as well as other regulators, e.g., Health Canada and Brazil ANVISA, SwissMedic (pending).
  - **What is its focus?**
    - Develop and execute projects to demonstrate that the IDMP standards are “fit” for global implementation.
    - Develop a framework, including business rules, best practices and operating model, for the global IDMP implementation and maintenance of global identifiers for marketed products.

Global IDMP Standards Complement Regional Standards

US FDA Standards

NIH/ NLM
RxNorm-
Unique Product Identifier (RxCUI)

Unified Code for Units of Measure (UCUM)

SPL Terminology

SwissMedic

edqm
European Directorate for the Quality of Medicines & HealthCare

2013

Substances definition

Global IDMP

Global IDMP Working Group

EMA SPOR

Health Canada

IDMP elements integrated into:
Structured Product Labelling (XML PM)
Increasing use of CVs - moving towards EDQM, GSRS, UCUM

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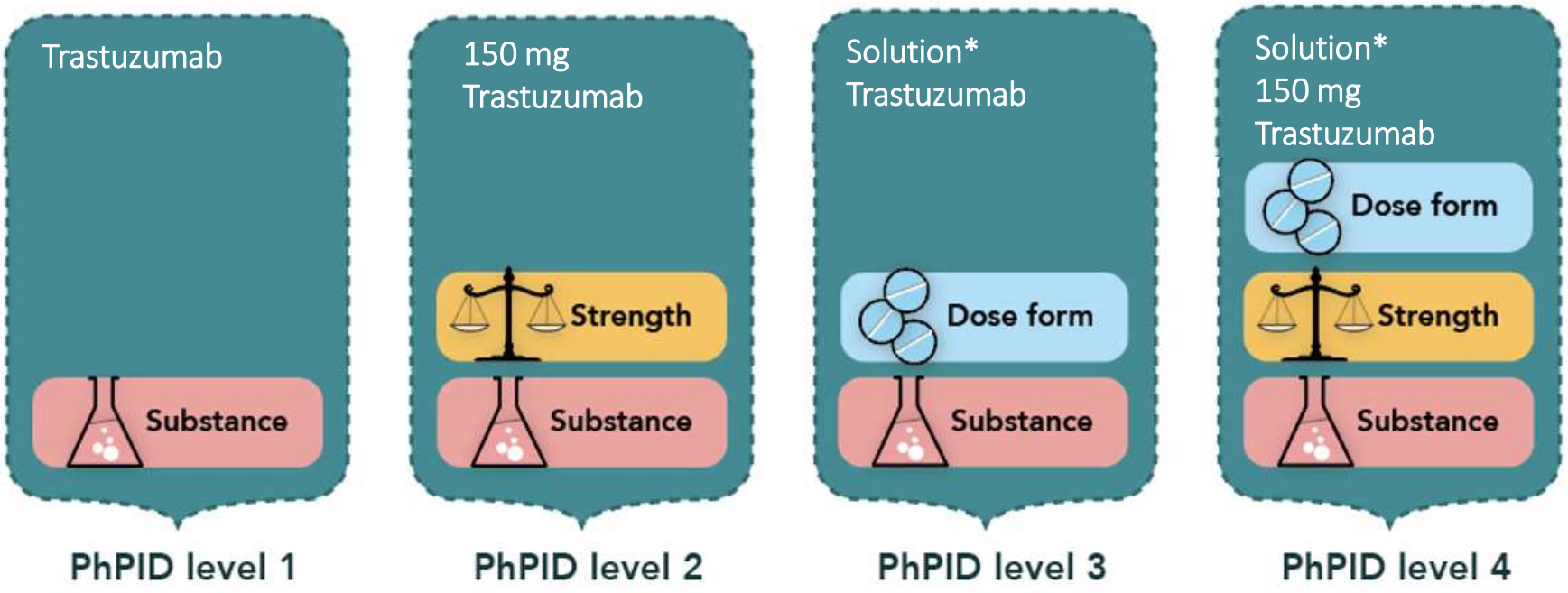
PhPID and its levels



*Dose form characteristics: Solution, Injection, Parenteral, Conventional

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Global PhPIDs – connecting the dots

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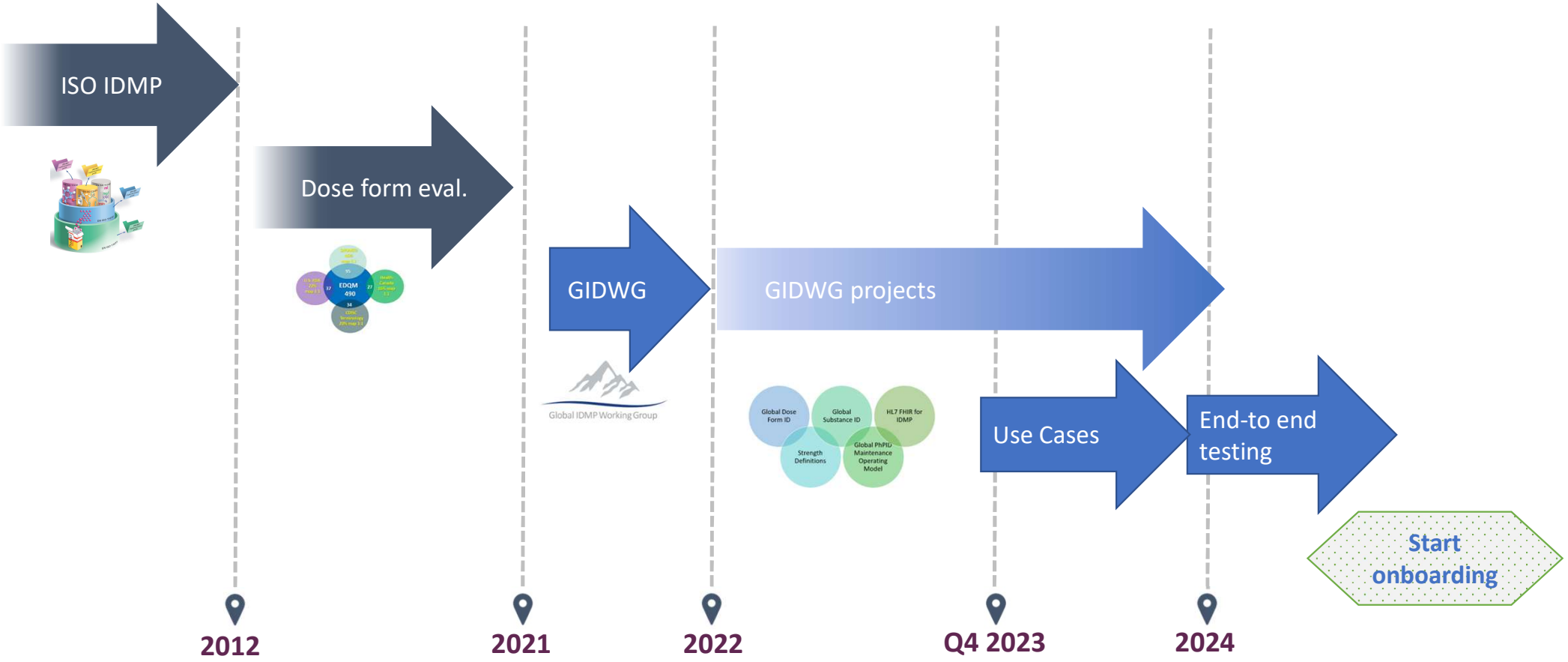
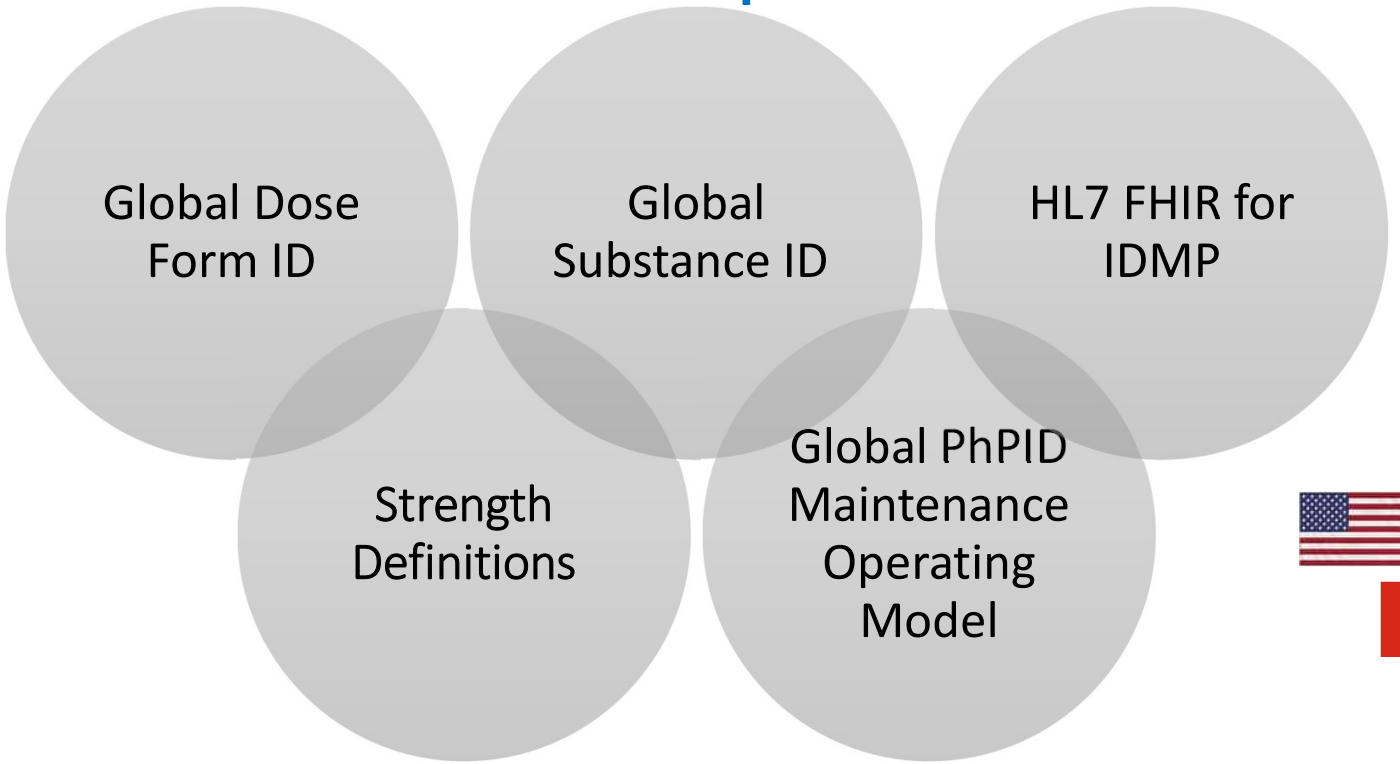
GIDWG is a collaborative project

Our journey – Global PhPIDs



GIDWG projects

Aim to define and reach consensus on processes, best practices and an operating model for maintenance of global identifiers for marketed medicinal products



SME from US FDA, EMA, ANVISA, Health Canada, Swissmedic, WHO-UMC, WHO, EDQM, INN, USP, HL7, HMA-SVG, US-NIH, IFPMA, ISO/CEN, USP

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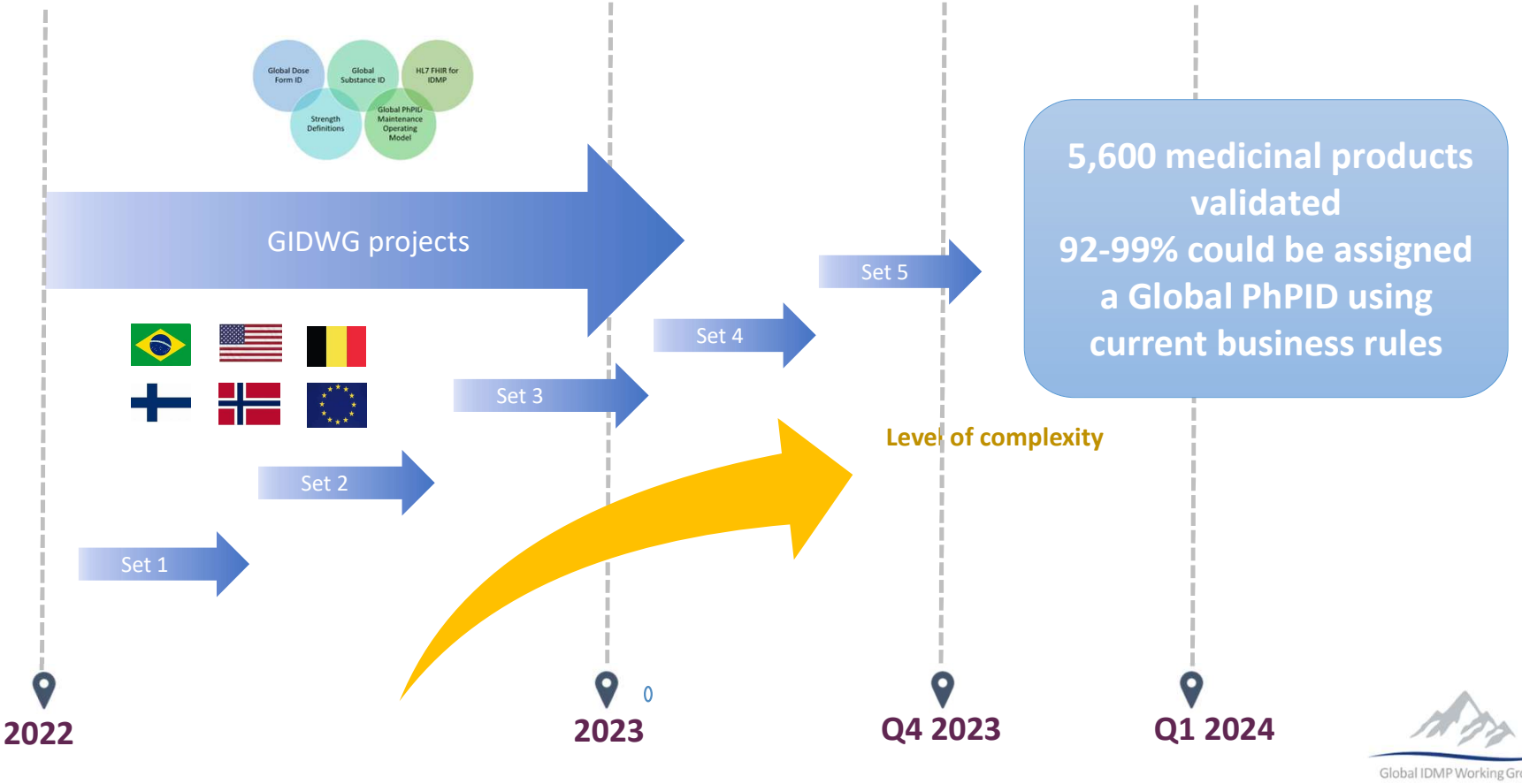
GIDWG validation overview



General business rules for GSID and PhPID

GSID

- The **GSID** assignment is based on **ISO 11238** and **TS 19844**
- The business rules should clarify the standards when needed
- The defining substance information needs to be in the public domain to assign a GSID

PhPID

- **PhPID** assignment is based on **ISO 11616**
- **PhPID is assigned to marketed products**
- Using the appropriate GSID when generating a PhPID in a consistent manner
- All active ingredients and their corresponding GSIDs will be used in PhPID assignment
- Follow the process for PhPID harmonisation/assignment

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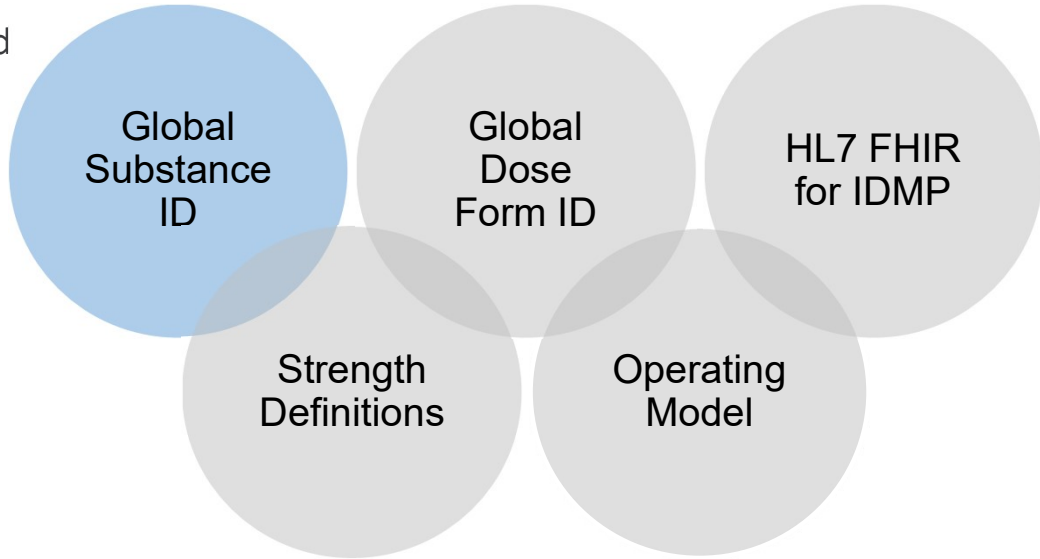
GIDWG Global Substance ID project

Project Scope and Deliverables

Goal: Globally harmonize and define capture of standardized information for global Substance identification and hereby ensure consistent PhPID construction through/by:

- Identifying the core information set via the ISO TC215 WG6 signature field sub-group.
- Adopting a Global substance ID, i.e., GSID
- Establishing business rules regarding which standardized substance data (GSID) to use in the PhPID generation.
- Establishing a mechanism for the use of confidential data in GSID assignment.



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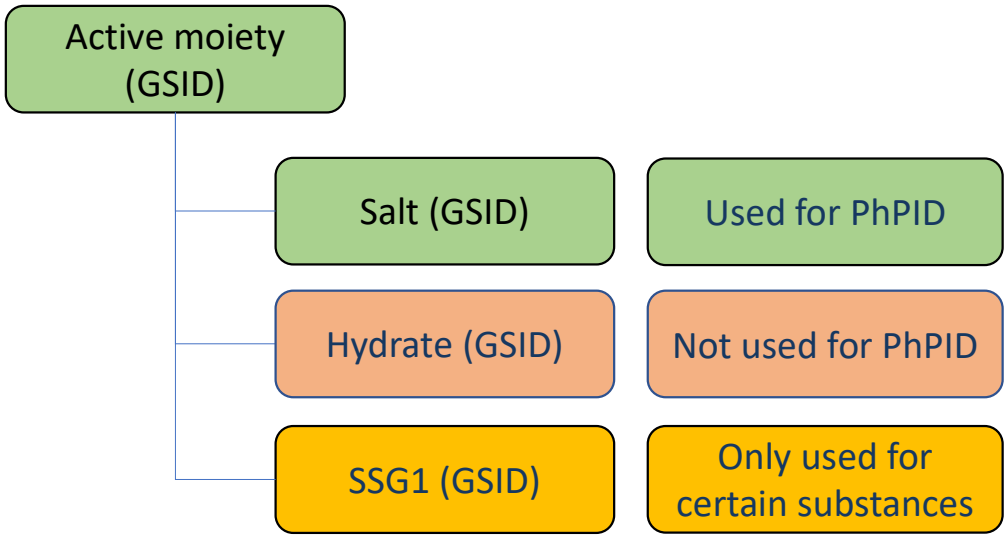
GIDWG pilot – Business rules for GSID in Global PhPID



The active ingredient, disregarding hydrates (replace with the non-hydrated substance), is used

GSID can be assigned at both substance and SSG1 level

SSG1 is only used in certain cases where SSG1 is important to distinguish between different PhPIDs

Input string: GSID; strength; dose form

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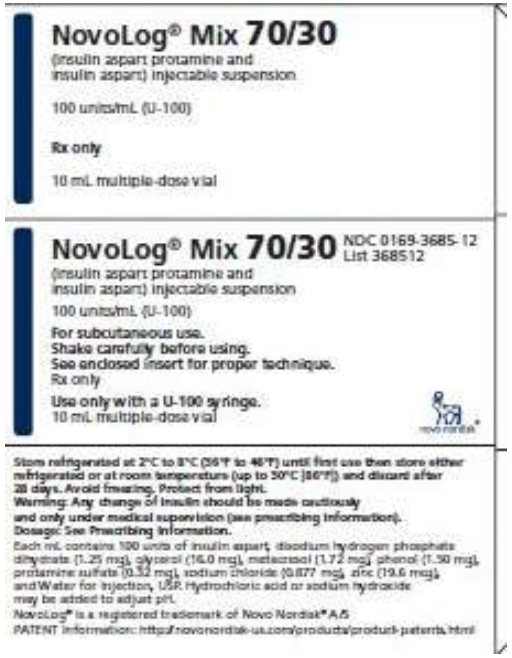
Business rules for GSID for Insulins

Fast acting product

Intermediate acting product



To accurately describe the difference between the two products, the GSID for both substance level and SSG1 level will be used for PhPID generation

Construction of GSID used in the GIDWG pilots

- A unique and consistent code following the ISO/IEC 15459 - Part 3 (Ref ISO/IEC 15459). The code consists of 17 characters long text buildup of a Qualifier, Unique text, and Check character.

GSID**9ST5UC24F36T**N

- The first 4 characters is the qualifier and will always be the text GSID.
- The middle 12 characters are a unique text buildup of random digits and letters.
- The last character is a check character which is used as a redundancy check used for error detection on identification numbers
- The order for how substance combination are expressed in PhPID algorithm is: Order by GSID (not by substance name) where numbers precedes letters i.e. 9 before A.

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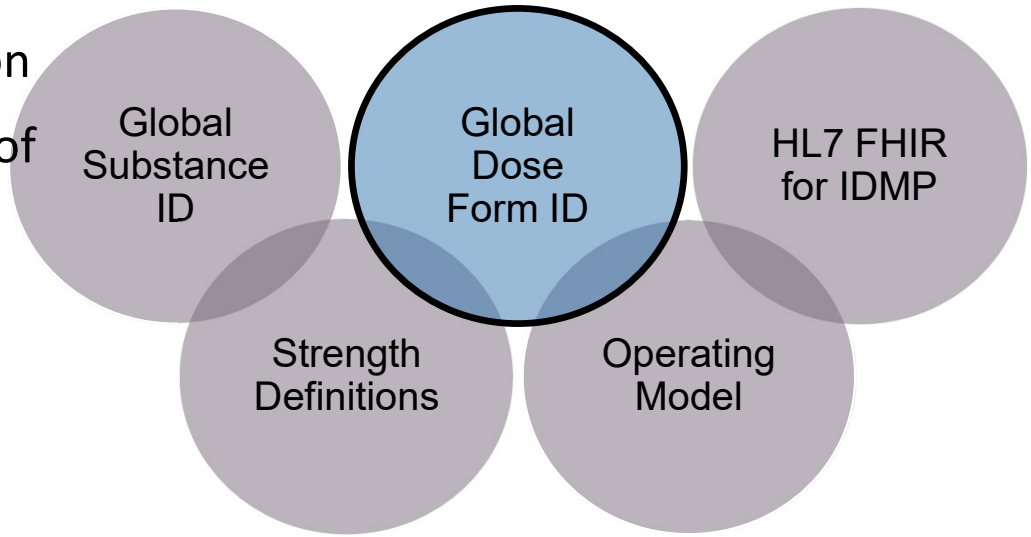
GIDWG Dose Form Identifier project

Project Scope and Deliverables

- Further investigate 4 dose form characteristic approach on larger datasets for at least one another region
- Assert the scalability and automation of the process
- Develop and Formalize Business Rules



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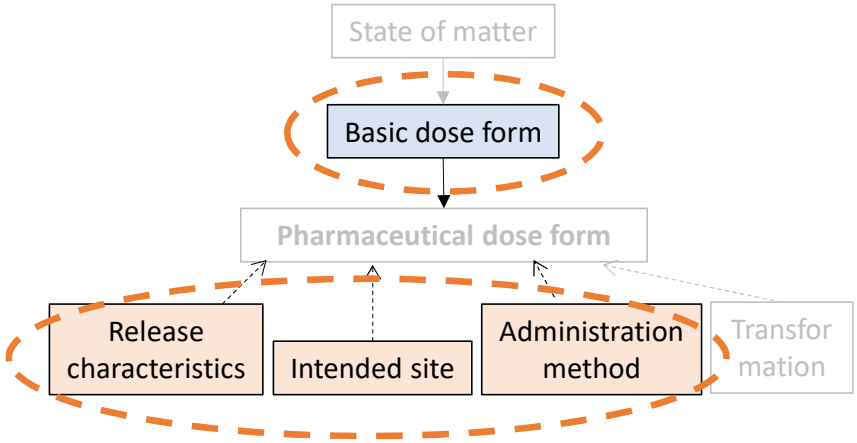
Business rules for dose form identifier

- There is no globally accepted dose form terminology set.
- The basic dose form together with 3 **dose form characteristics** (EDQM) are used to characterize the **administrable dose form** for Global PhPID
- The dose form characteristics are generally assigned based on SmPC information
- Where a medicinal product can be used in more than one way, the focus should be on the **primary use** or the term with the strictest microbiological requirements
- **Administration method** and **Intended site** characteristics can be assigned **more than one term** where it is not possible to identify a primary use

edqm
European Directorate for the Quality of Medicines & HealthCare



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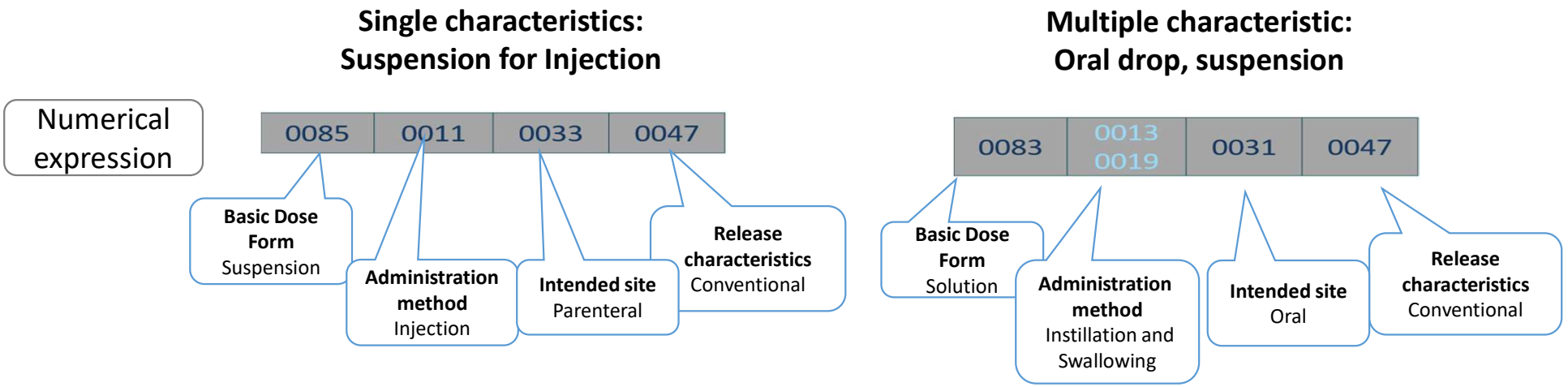
Example of multiple characteristics for Dose Form



Example of multiple characteristics for Release : Extended release oral tablets: assigned one release characteristic according to clinical relevance

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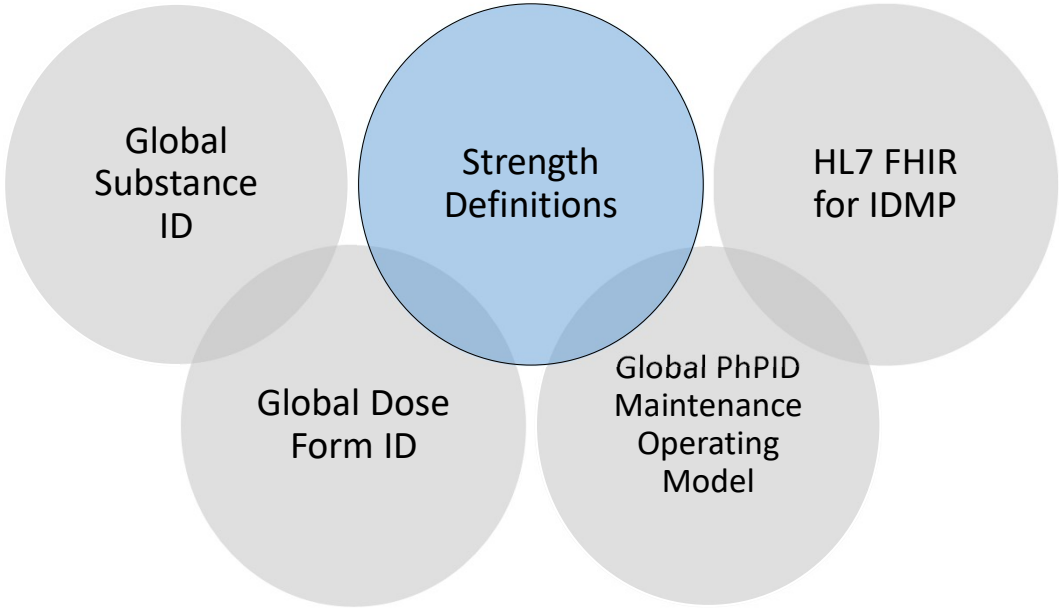
GIDWG Global Strength Definitions ID project

Project scope and deliverables

- Identify and address different representations of strength for products in different regions
- Clarify the use of presentation strength and concentration strength
- Explore the pattern framework further to ensure prioritised dose forms in EDQM and the additional product data set are covered
- Leverage the scalability and automation of the process
- Formalise business rules for each pattern and investigated dose forms



SME from EMA, US FDA, Swissmedic, Health Canada, ANVISA, PMDA, WHO-UMC, WHO, EDQM, INN, USP

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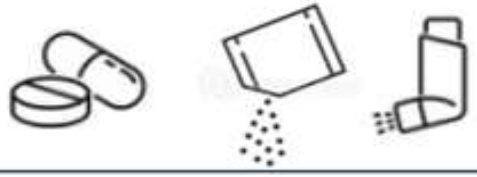
Business rules for Strength and Units

Pattern framework

Pattern	Type of product
A	
B	
C	

Numerical values

2.02 250 $1*10^8$

12,25 1000

Units

mg/ml viral particles

UI Beq

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Example: Pattern A – single-dose liquid and concentrate

----------DOSAGE FORMS AND STRENGTHS----------

100 mg/mL concentration (3.1):

- Prefilled syringes: 30 mg/0.3 mL, 40 mg/0.4 mL
- Graduated prefilled syringes: 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1 mL
- Multiple-dose vial: 300 mg/3 mL

150 mg/mL concentration (3.2):

- Graduated prefilled syringes: 120 mg/0.8 mL, 150 mg/1 mL

Medicinal product	SmPC dose form	Harmonised BDF	SmPC strength	Harmonised strength
Lovenox (enoxaparin sodium)	Prefilled syringe	Solution	40 mg/0.4 mL	**40 mg**

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Example: Pattern B – multi-dose of continuous presentation

For topical use

DESCRIPTION

Locoid® (hydrocortisone butyrate) Cream, 0.1% contains the topical corticosteroid, hydrocortisone butyrate, a non-fluorinated hydrocortisone ester. It has the chemical name: 11β,17,21-Trihydroxypregn-4-ene-3,20-dione 17-butyrate; the molecular formula: $C_{25}H_{36}O_6$; the molecular weight: 432.54; and the CAS registry number: 13609-67-1.

Each gram of Locoid® Cream contains 1 mg of hydrocortisone butyrate in a hydrophilic base consisting of cetostearyl alcohol, ceteth-20, mineral oil, white petrolatum, anhydrous citric acid, sodium citrate, propylparaben and butylparaben (preservatives) and purified water.

Medicinal product	SmPC dose form	Harmonised BDF	SmPC strength	Harmonised strength
Locoid (hydrocortisone butyrate)	Cream	Cream	0.1%	**1 mg/g**

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Example: Pattern C – products enclosed in a ‘presentation’, where the dose has a delivery rate

DESCRIPTION

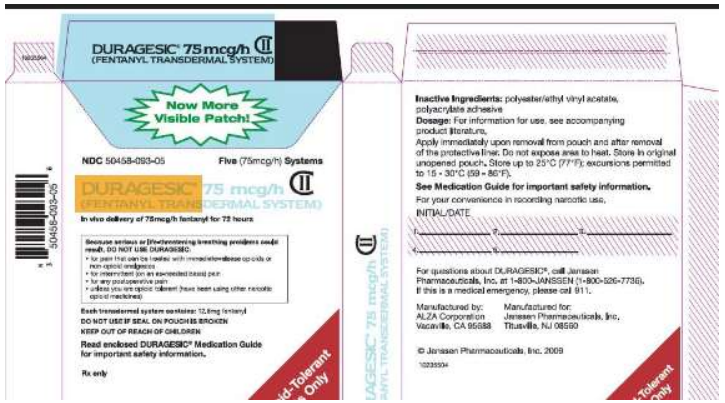
DURAGESIC® (fentanyl transdermal system) is a transdermal system providing continuous systemic delivery of fentanyl, a potent opioid analgesic, for 72 hours. The

System Components and Structure

The amount of fentanyl released from each system per hour is proportional to the surface area (25 mcg/h per 10.5 cm^2). The composition per unit area of all system sizes is identical.

Dose* (mcg/h)	Size (cm^2)	Fentanyl Content (mg)
12**	5.25	2.1
25	10.5	4.2
50	21	8.4
75	31.5	12.6

*Nominal delivery rate per hour
**Nominal delivery rate is 12.5 mcg/hr



Medicinal product	SmPC dose form	Harmonised BDF	SmPC strength	Harmonised strength
Durogesic (fentanyl)	Transdermal system	Patch	25 mcg/h per 10.5 cm2	12.5mcg/h

GIDWG Operating Model

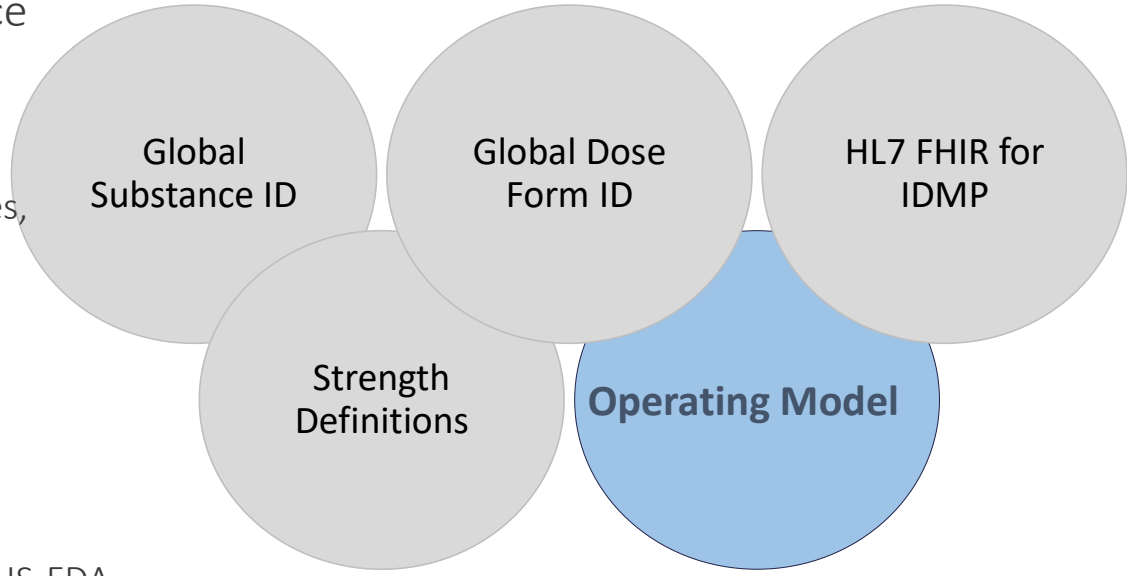
Project Scope and Deliverables

Definition of the consensus-based operating model(s) for WHO-UMC as the international maintenance organization as an end-to-end pilot:

Demonstration of defined operating model(s) for global PhPID on a selection of the following use cases, including product level associations when applicable

- Pharmacovigilance
- Drug shortages
- Drug utilization
- Cross border prescription

- Process definition by three jurisdictions (EMA, US-FDA AND ANVISA)



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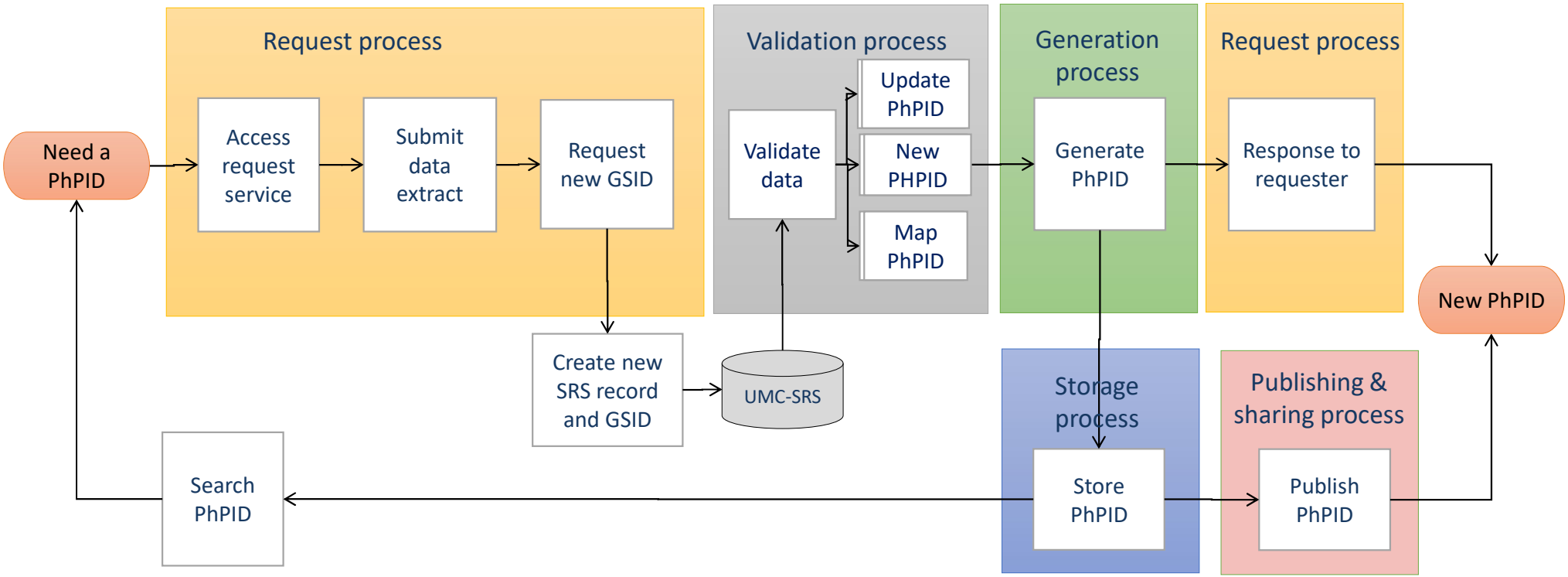
PhPID Operating Model including GSID request technology & solutions



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Business rules for Global PhPID generation input string

General

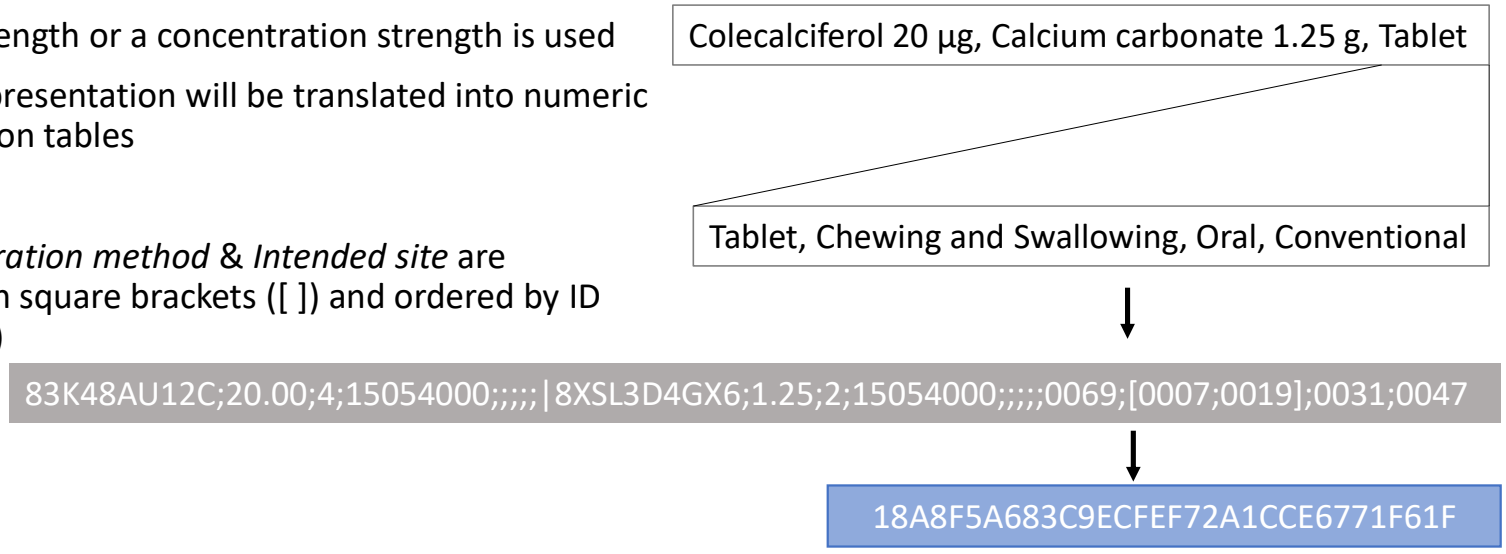
- The identifiers will be separated by a semicolon (;)
- Substances will be separated by a pipe (|) and ordered by GSID

Strength & Units

- Amount is represented with a point (.) and two decimals
- A presentation strength or a concentration strength is used
- Units and unit of presentation will be translated into numeric values by conversion tables

Form

- Multiple *Administration method* & *Intended site* are represented within square brackets ([ ]) and ordered by ID (lowest to highest)



Global PhPID *Request*

Please note that this service is in a development phase and more functionality will be released continuously. Contact IDMP@who-umc.org for any questions.

Welcome to the Global PhPID Request service!

The Pharmaceutical Product Identifier (PhPID) is defined by one of the five ISO standards for Identification of Medicinal Products (IDMP), which aims to increase clarity and efficiency in communications about medicines globally. PhPIDs are created based on the product information for substances, strengths, and dose forms. Some additional information, e.g. country and market authorization holder, are also needed for validation purposes.

In this service you will find two options for requesting PhPIDs for Pharmaceutical Products. Either to complete the form per product via the Single PhPID Request option, or to upload a file with multiple PhPID requests via the PhPID Batch Request option.

You also find an option to request a Global Substance Identifier (GSID). For pharmaceutical products with new substances you need to request a GSID before you can request a PhPID.

Uppsala Monitoring Centre

Global PhPID Publish

marilina.castellano@who-umc.org

Please note that this application is in a development phase and more functionality will be released continuously. The data and assigned PhPIDs may be subject to change at any time. Please contact IDMP@who-umc.org for any questions.

Level	PhPID	GSID	Substance	Strength (Reference Strength)	Basic Dose Form	Administration Method	Intended Site	Release Characteristics
1	B78B712FC26C629344AF2C513DE8E992	GSID-11ZJZ2XD4-U	Amlodipine benzoate					
.2	68CF8B03F8AC9FE6ABF51576BFEA95BE	GSID-11ZJZ2XD4-U	Amlodipine benzoate	1.3 mg/ml (1 mg/ml)				
..3	0E4EE7F1029FB4EF690BD029F7A85CC1	GSID-11ZJZ2XD4-U	Amlodipine benzoate		Suspension	Swallowing	Oral	Conventional
...4	96B0514A1D6F8B361772BDB5D26F39AD	GSID-11ZJZ2XD4-U	Amlodipine benzoate	1.3 mg/ml (1 mg/ml)	Suspension	Swallowing	Oral	Conventional
1	7422765EEE495A837241B2C3620AEF3E	GSID-3YJL6M9Z0-H	Amlodipine besilate					
.2	265D389BFF4C991C7165F8C9BF939DC7	GSID-3YJL6M9Z0-H	Amlodipine besilate	1.39 mg/ml (1 mg/ml)				
.2	4C8AC54E0207ACD9B2994FC3F0E1EB7B	GSID-3YJL6M9Z0-H	Amlodipine besilate	6.93 mg (5 mg) per tablet				
.2	AA39B88AA7D293692BBC235C9F09B5E6	GSID-3YJL6M9Z0-H	Amlodipine besilate	13.87 mg (10 mg) per tablet				
.2	B7769405423433FF1989B348CC143375	GSID-3YJL6M9Z0-H	Amlodipine besilate	3.47 mg (2.5 mg) per tablet				
..3	662A2B95D592B1387A50AB2D9D33465F	GSID-3YJL6M9Z0-H	Amlodipine besilate		Suspension	Swallowing	Oral	Conventional
..3	21E01B86E050659089E8E67A3C6E1363	GSID-3YJL6M9Z0-H	Amlodipine besilate		Tablet	Swallowing	Oral	Conventional
...4	04BAE98EC790205B37298ADB405E3D63	GSID-3YJL6M9Z0-H	Amlodipine besilate	1.39 mg/ml (1 mg/ml)	Suspension	Swallowing	Oral	Conventional
...4	A490DC664C872987E3CEEEFDAC59F034	GSID-3YJL6M9Z0-H	Amlodipine besilate	6.93 mg (5 mg) per tablet	Tablet	Swallowing	Oral	Conventional
...4	5B6880B7763EB0E8D0E127F6C54D26B7	GSID-3YJL6M9Z0-H	Amlodipine besilate	13.87 mg (10 mg) per tablet	Tablet	Swallowing	Oral	Conventional
...4	C92572AA1E2FD469E45C5A7ACD22CA1D	GSID-3YJL6M9Z0-H	Amlodipine besilate	3.47 mg (2.5 mg) per tablet	Tablet	Swallowing	Oral	Conventional
1	B76CF9DC518DF0C0BA42F7E002455F8D	GSID-88APA95ZH-L	Amoxicillin					
.2	20FE199CB0945846A25AEC9C6F41720A	GSID-88APA95ZH-L	Amoxicillin	500 mg per capsule				
.2	2FCEE6E7FA9CA9997DCB6517B2C352F0	GSID-88APA95ZH-L	Amoxicillin	125 mg per tablet				
.2	2FE9D4C41006731128F07CF2C0848EDE	GSID-88APA95ZH-L	Amoxicillin	25 mg/ml				

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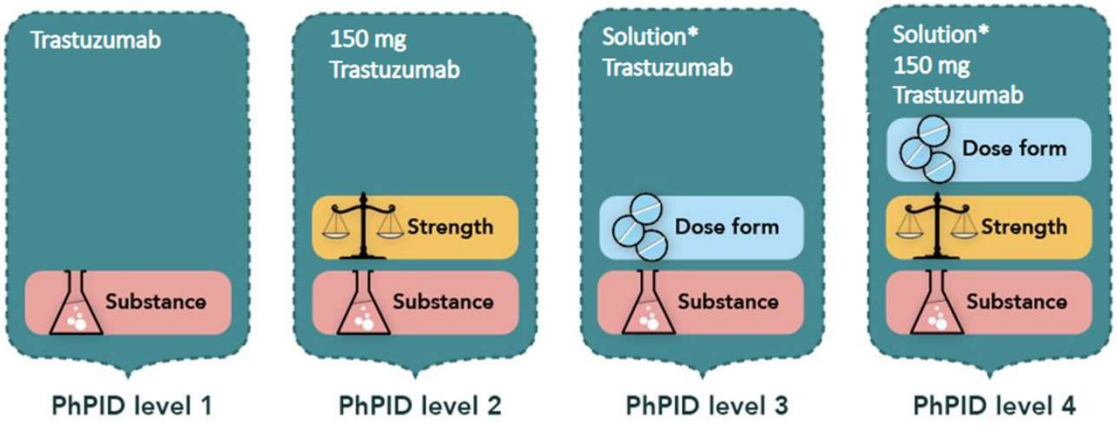
ISO IDMP PhPID and Medicinal Product Dictionary (for example, WHODrug)

Pharmaceutical products

Medicinal products



*Dose form characteristics: Solution, Injection, Parenteral, Conventional

WHODrug

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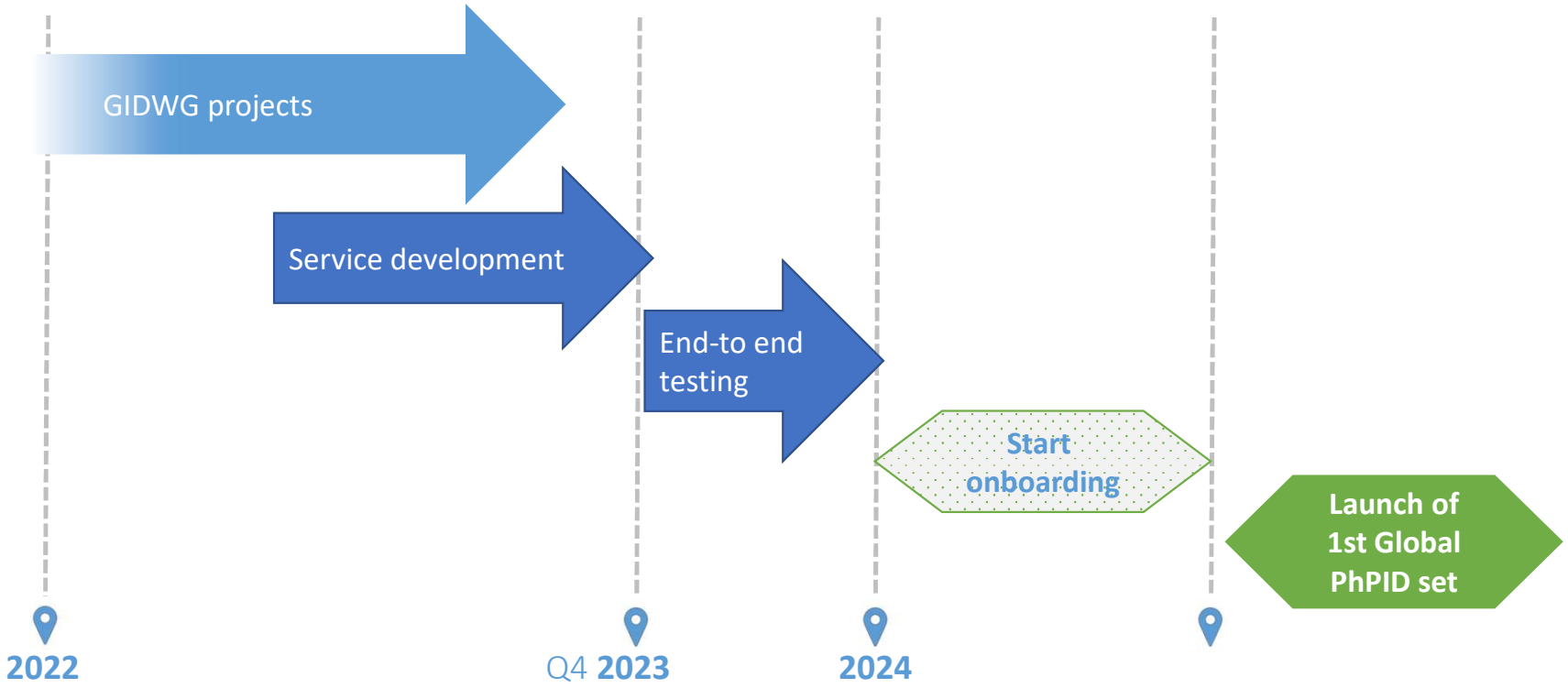
Future plans – Global PhPID



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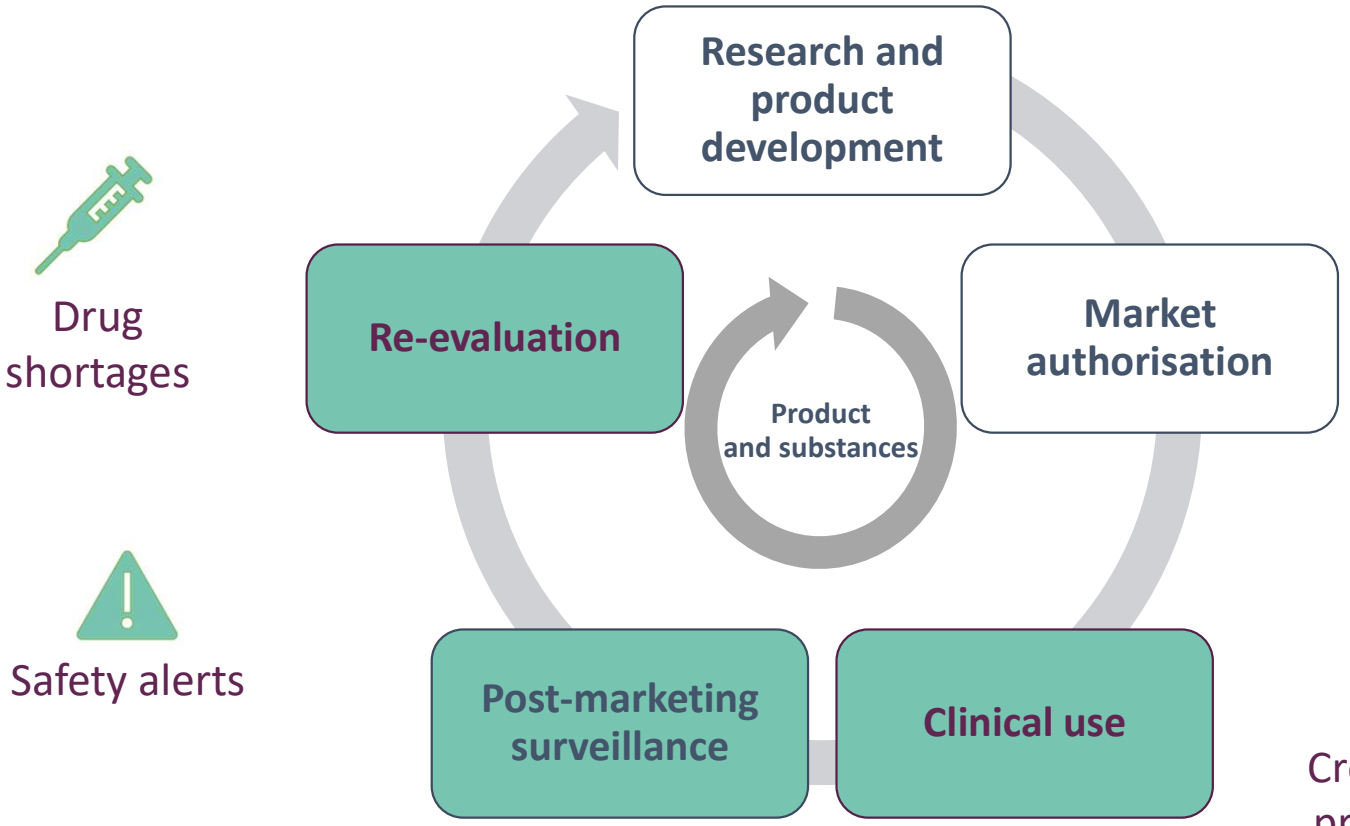
Use cases for global PhPID



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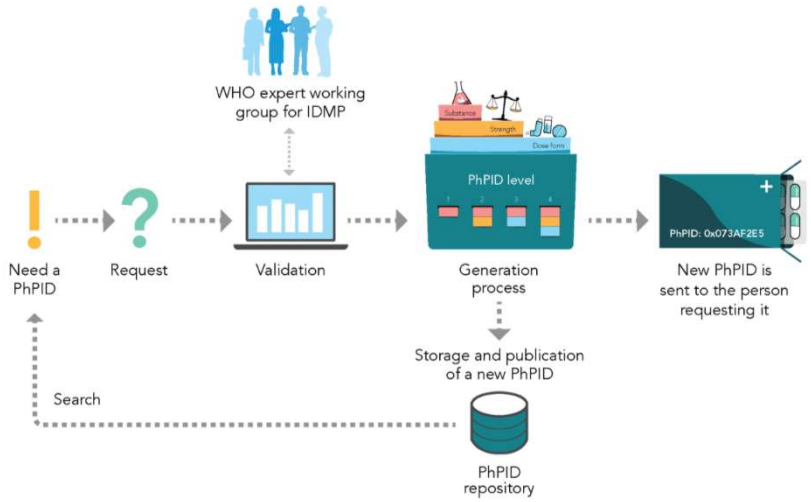
End-to-End Demonstration Q4 2023

Testing of use cases for GSID/PhPID operating model

SCOPE:

- Validate and generate PhPIDs for products based on GIDWG/EWG business rules
- EDQM + non-EDQM countries
- Similar products from different countries
- Larger batches & smaller data sets for regulators
- Validated data sets based on **150 substances**, including chemicals, biosimilars, polymers, nucleic acids, ‘mixtures’



Proposed candidate countries:

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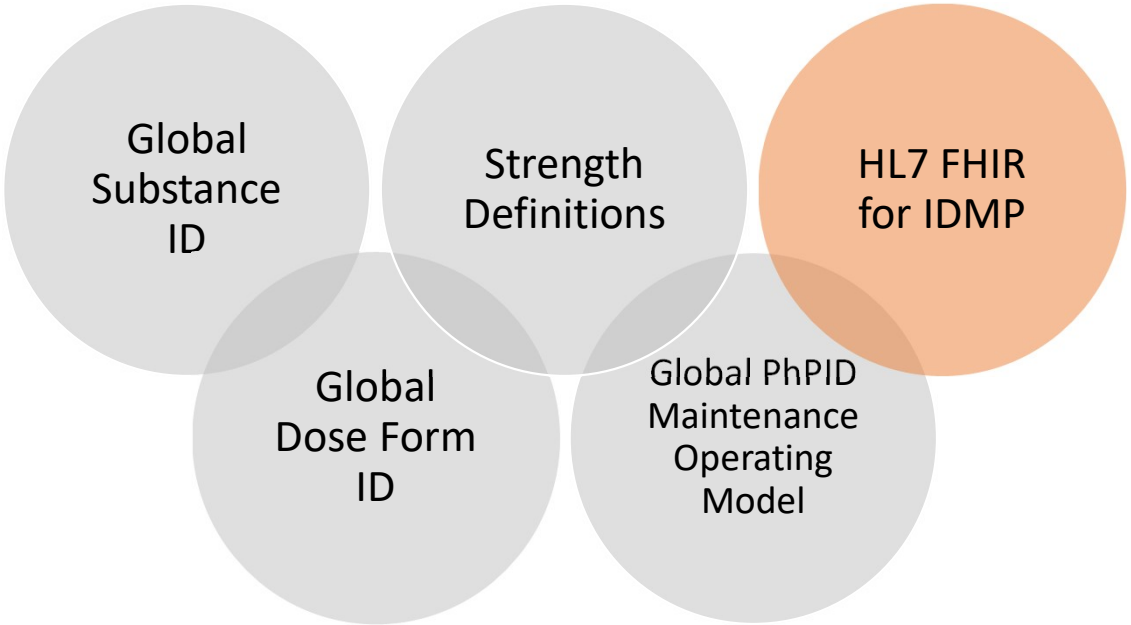
GIDWG IDMP in HL7 FHIR project

Project scope and deliverables

- Challenges regarding automatic exchange of medicinal product and substance information
- Participate in developing, verifying, and balloting HL7 FHIR resources related to IDMP based on the currently identified global use cases (pharmacovigilance, cross-border prescriptions, drug shortages)
- Exchange IDMP/product and substance data between the US, EU and WHO-UMC according to use cases
- Align to common product messages in FHIR
- Demonstrate in HL7 FHIR Connectathons and other stakeholder events



Global IDMP Working Group

Please note that this service is in a development phase and more functionality will be released continuously. Contact IDMP@who-umc.org for any questions.

FHIR

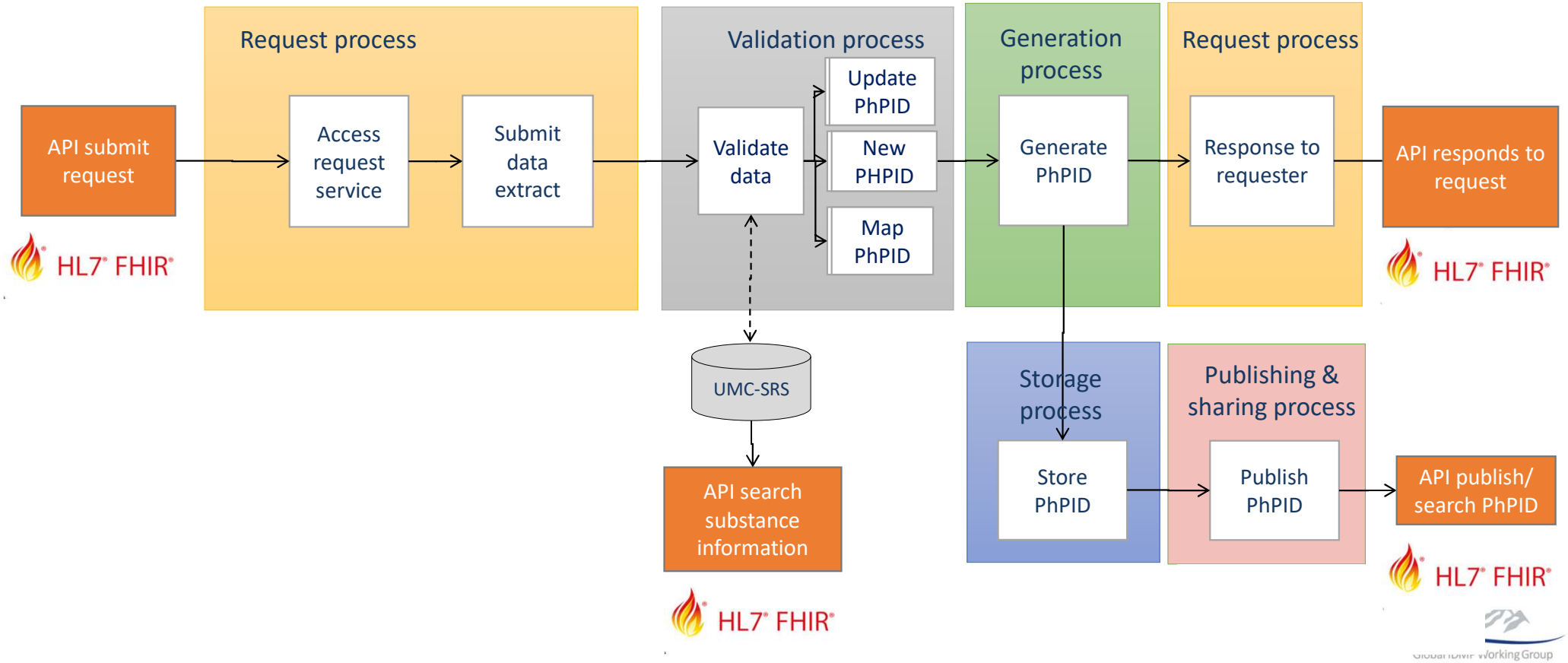
Welcome to the Global PhPID Request service!

The Pharmaceutical Product Identifier (PhPID) is defined by one of the five ISO standards for Identification of Medicinal Products (IDMP), which aims to increase clarity and efficiency in communications about medicines globally. PhPIDs are created based on the product information for substances, strengths, and dose forms. Some additional information, e.g. country and market authorization holder, are also needed for validation purposes.

In this service you will find two options for requesting PhPIDs for Pharmaceutical Products. Either to complete the form per product via the Single PhPID Request option, or to upload a file with multiple PhPID requests via the PhPID Batch Request option.

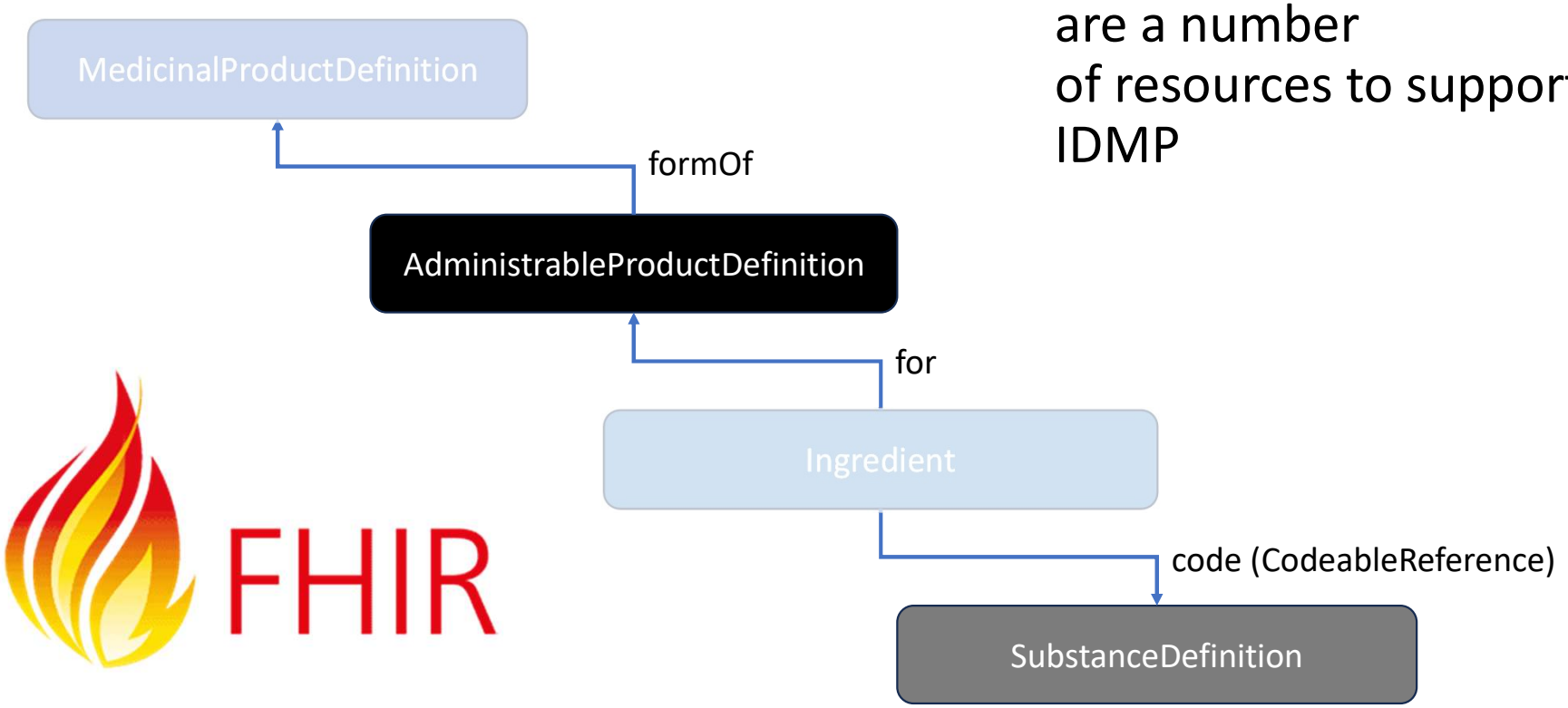
You also find an option to request a Global Substance Identifier (GSID). For pharmaceutical products with new substances you need to request a GSID before you can request a PhPID.

PhPID Operating Model with FHIR



PhPID on FHIR

- As part of HL7 FHIR release 5 there are a number of resources to support IDMP



FHIR

Global IDMP Working Group

HL7 FHIR Connectathon 34 & HL7 WG meeting (9-15 Sep 2023)

Connectathon (What)

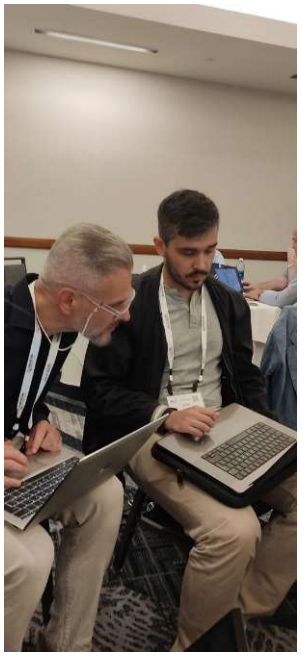
- HL7 FHIR Connectathons feature hands-on FHIR development and testing.
- Implementers and developers come together to hold technical discussions that advance the FHIR specification, develop FHIR-based solutions, and exchange data with other FHIR interfaces.
- Connectathons are a great opportunity to work directly with FHIR developers and senior members of the FHIR standards development team

Track Objective

- Scenarios to Test and gather feedback on the following:
- Test scenario #1: Confirm how to make connections between the Vulcan ePI and SPL-FHIR by manually transforming an ePI to a SPL-FHIR.
- Test scenario #2: A patient travels from Europe to US and has to find the similar US medicinal product to their European prescription.
- Test scenario #3: A patient travels from Japan to US and has to find the similar US medicinal product to their Japanese prescription.
- Test scenario #4: Incorporate ISO IDMP identifiers into the ePIs to facilitate international connections. Focus on the PhPID generation; lookup and usage; and matching identifiers cross-border to support the relevant test scenarios above.

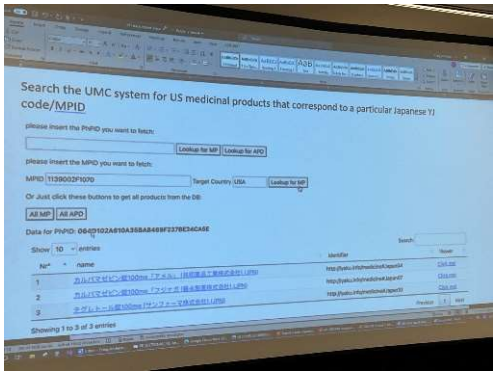
2023 - 09 Connectathon 34 - FHIR - Confluence (hl7.org)

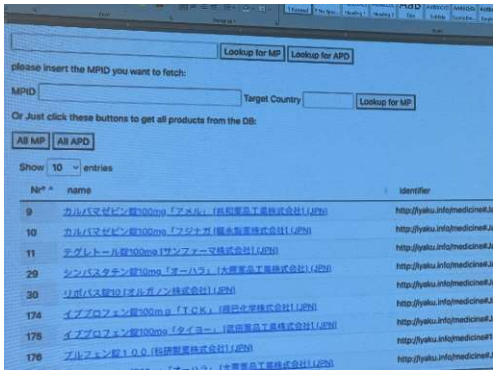
Connectathon 34 Report Out 9.25.23.docx (live.com)

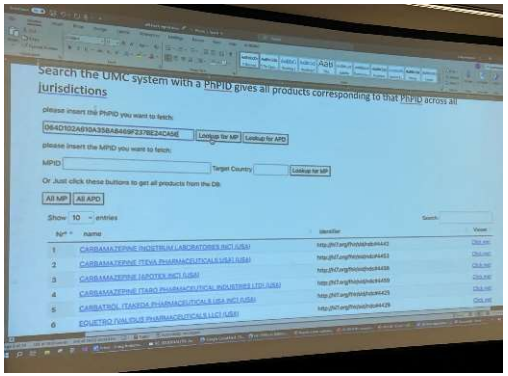


FHIR

Global IDMP Working Group







Use Case

シンバスタチン錠５mg「オーハラ」
2189011F1262

?

Get the PhPID for the Japanese MPID

https://umc-ext-dev-phponfhirdemo-preview-rg01-webapp.azurewebsites.net/AdministrableProductDefinition?form-of.identifier=http://iyaku.info/medicine|2189011F1262

Given the retrieved PhPID we can now retrieve the corresponding MPID in USA

https://umc-ext-dev-phponfhirdemo-preview-rg01-webapp.azurewebsites.net/MedicinalProductDefinition?_has:AdminstrableProductDefinition:form-of:identifier=http://www.who-umc.org/phpid|F92168108C432D63DACDD70444176BB3&name-country=USA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  "type": "searchset"
  "timestamp": "2023
  "total": 11,
  "link": [
    {
      "relation"
      "url": "htt
    },
    {
      "relation"
      "url": "htt
    }
  ],
  "entry": [
```

```
{
  "fullUrl": "https://umc-ext-dev-phponfhirdemo-preview-rg01-webapp.azurewebsite
  "resource": {
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    "id": "4584",
    "identifier": [
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        "value": "00006-0726"
      }
    ],
    "type": {},
    "domain": {},
    "status": {},
    "contact": {},
    "name": [
      {
        "productName": "ZOCOR",
        "usage": [
          {
            "country": {
              "coding": [
                {
                  "system": "urn:iso:std:iso:3166",
                  "code": "USA"
                }
              ]
            },
            "jurisdiction": {},
            "language": {}
          }
        ]
      }
    ]
  }
}
```

```
"resourceType": "AdministrableProductDefinition",
"id": "F92168108C432D63DACDD70444176BB3",
"text": {
  "status": "generated",
  "div": "<div><h1>Pharmaceutical Product (Administrable Product Definition)</h
},
"contained": {},
"extension": {},
"identifier": [
  {
    "type": {
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        {
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          "code": "4"
        }
      ]
    },
    "system": "http://www.who-umc.org/PhPId",
    "value": "F92168108C432D63DACDD70444176BB3"
  }
],
"status": "active",
"formOf": {},
"administrableDoseForm": {
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      "system": "https://standardterms.edqm.eu",
      "code": "10221000",
      "display": "Film-coated tablet"
    }
  ]
},
"routeOfAdministration": {
```


Global IDMP Working Group

Global IDMP Working Group

Thank you

Global IDMP Working Group

Regulators Perspective on IDMP

Ron Fitzmartin, PhD, MBA
Chair, IPRP IDMP Working Group

IDMP Working Group Objectives

- Ensure the awareness and understanding of the standards of the IDMP standards

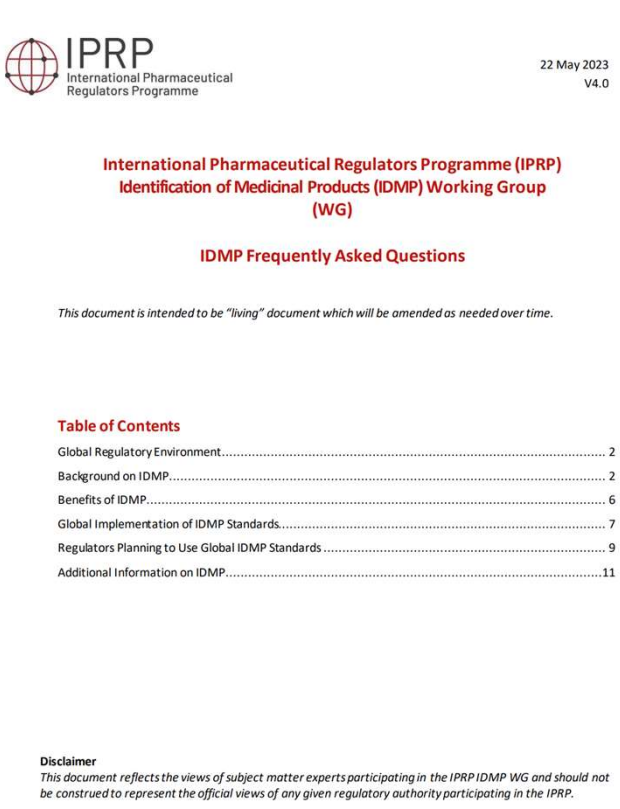
- Clarify how and why these standards can add value to regulator business processes to improve the quality and effectiveness of shared regulatory functions,

- Share strategies and experiences for their successful and consistent implementation.

Members

- Chair: Ron Fitzmartin, US FDA
- Number of experts: **69** experts across **24** organizations
- Parties involved in the Working Group:
  - ANVISA, Brazil
  - APEC
  - ASEAN
  - CECMED, Cuba
  - COFEPRIS, Mexico
  - CPED, Israel
  - EAC
  - EC, Europe
  - EDA, Egypt
  - FDA, United States
  - GHC
  - Health Canada, Canada
  - HSA, Singapore
  - MHLW/PMDA, Japan
  - PAHO/PANDRH
  - Roszdravnadzor, Russia
  - SADC
  - SAHPRA, South Africa
  - SFDA, Saudi Arabia
  - Swissmedic, Switzerland
  - TFDA, Chinese Taipei
  - TGA, Australia
  - TITCK, Turkey
  - WHO

IDMP Frequently Asked Questions Document



IPRP
International Pharmaceutical Regulators Programme

22 May 2023
V4.0

International Pharmaceutical Regulators Programme (IPRP)
Identification of Medicinal Products (IDMP) Working Group (WG)

IDMP Frequently Asked Questions

This document is intended to be "living" document which will be amended as needed over time.

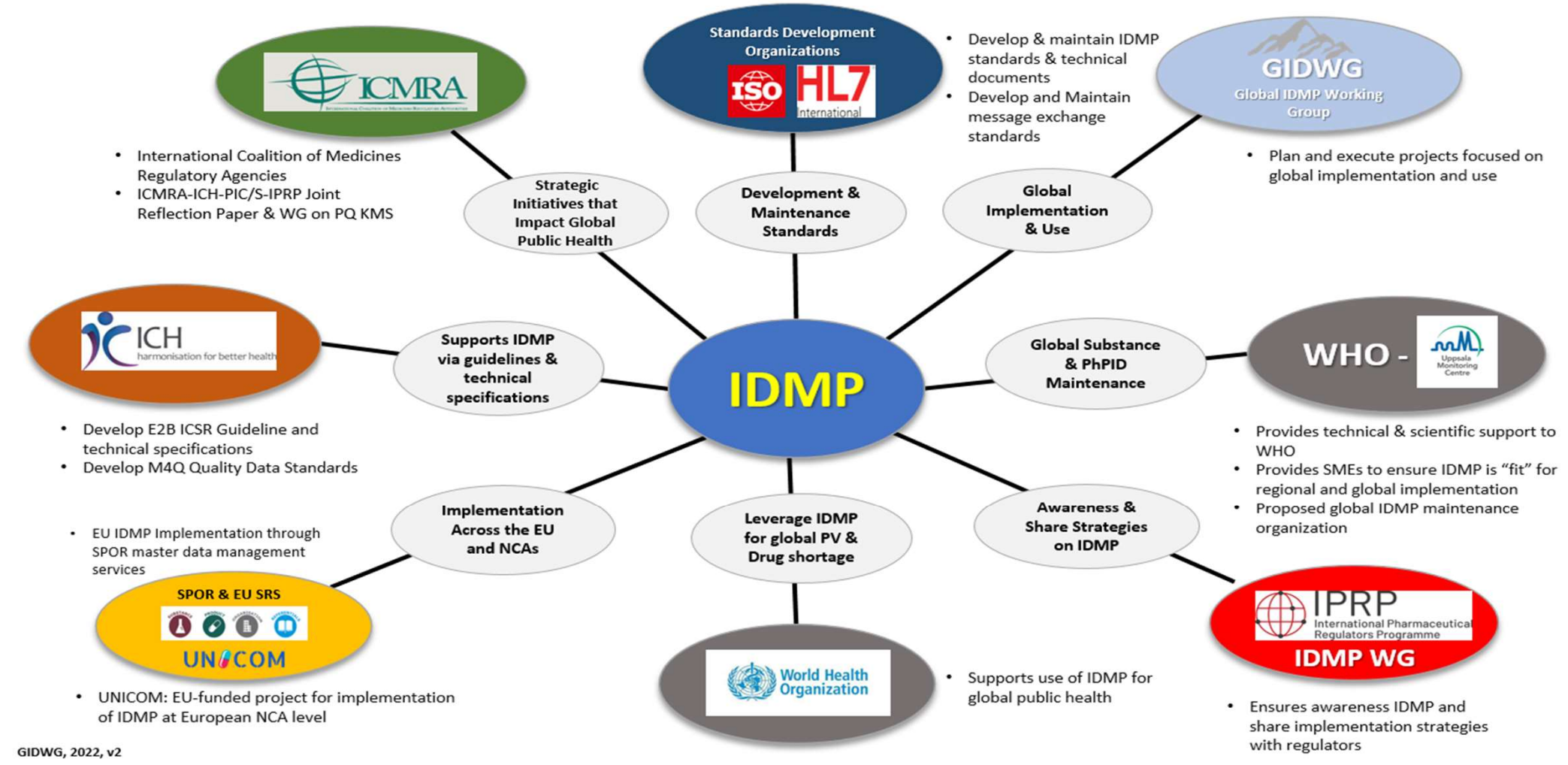
Table of Contents

Disclaimer
This document reflects the views of subject matter experts participating in the IPRP IDMP WG and should not be construed to represent the official views of any given regulatory authority participating in the IPRP.

- Background on IDMP
- Benefits of Global Implementation
- Regulators Planning to use IDMP standards

https://admin.iprp.global/sites/default/files/2023-06/IDMPWG_FAQ_v4_2023_0522.pdf

Where the IPRP IDMP WG Fits with other IDMP Stakeholders



GIDWG, 2022, v2

Going Forward

- IPRP IDMP Working Group will ensure collaboration with:
  - Global IDMP Working Group (GIDWG)
    - To acquire knowledge
    - To gain practical experience on pilots
    - To ensure regulators are aligned / harmonized
  - ISO TC 215 WG6
  - ICMRA PQ KMS WG
  - ICH
- Recommendations for Processes / Procedures / Guidelines at an ICH level

GIDWG Public Meeting
IFPMA Perspective

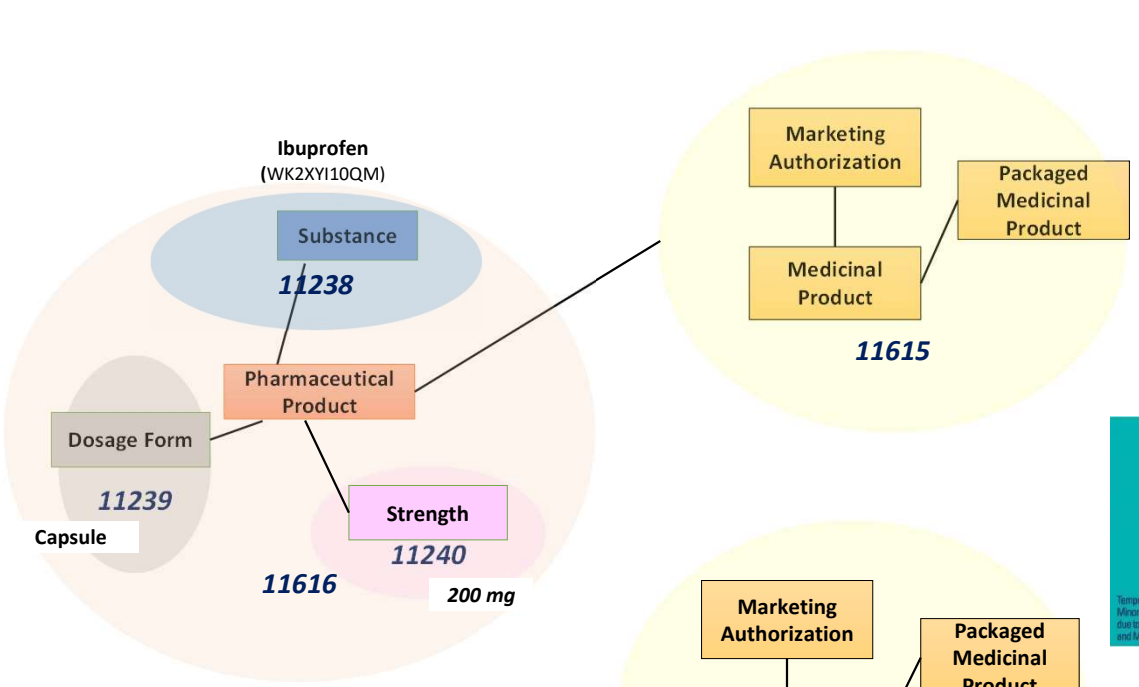
Vada A. Perkins

Executive Director, Regulatory Policy & Innovation

Co-Author: ISO IDMP 11615 & ISO IDMP 11616

10/18/2023

IDMP- Drugs


Ibuprofen
(WK2XYI10QM)
Substance
11238
Pharmaceutical Product
Dosage Form
11239
Capsule
Strength
11240
200 mg
11616
Marketing Authorization
Packaged Medicinal Product
Medicinal Product
11615
Marketing Authorization
Packaged Medicinal Product
Medicinal Product
11615


Easy Open
ARTHRITIS CAP
Advil
LIQUI-GELS
Solubilized Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer (NSAID)
160
Liquid Filled Capsules
Drug Facts


Bayer HealthCare
Midol
Liquid Gels
IBUPROFEN 200mg (NSAID)
PAIN RELIEVER/
FEVER REDUCER
LIQUID FILLED
CAPSULES

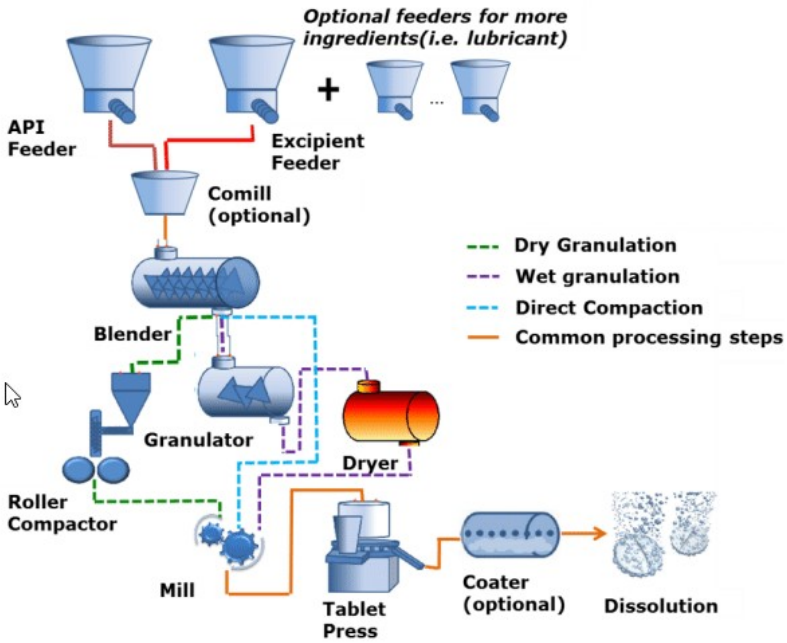

NUROFEN
8HR
PAIN RELIEF
200mg Soft Capsules
Ibuprofen
Lasts Up To 8 Hours
16 Soft Capsules

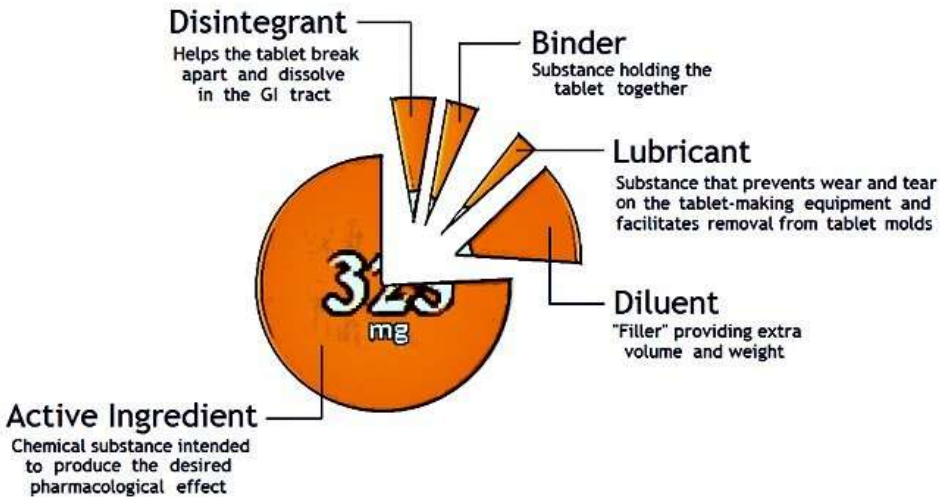

Walgreens
Ibuprofen
IBUPROFEN CAPSULES, 200 mg / PAIN RELIEVER / FEVER REDUCER (NSAID)
SOFTGELS
40 SOFTGELS
SEE NEW WARNINGS INFORMATION


VALUE SIZE
CVS
Ibuprofen
500 COATED CAPLETS


sato
頭痛・歯痛・発熱
生理痛・咽喉痛によく効く
Ringl
リングルアイビー
200
イブプロフェン
1回200mg
液体in
カプセル
24カプセル
24回分

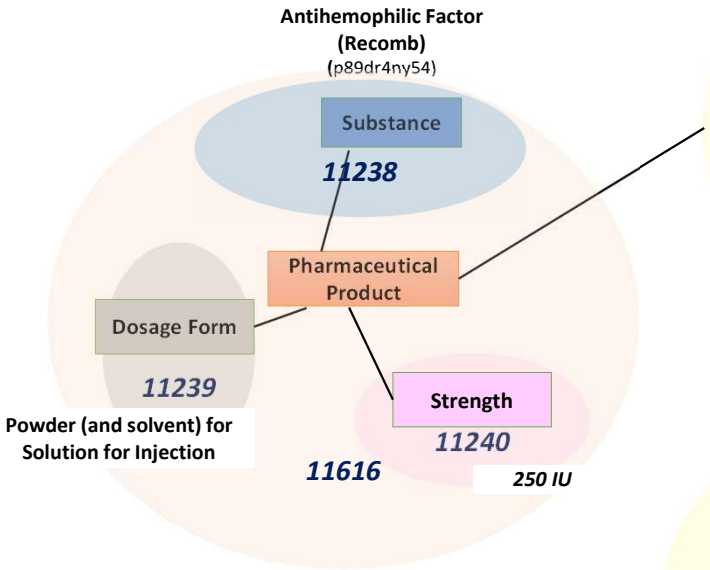
Tablet Manufacturing

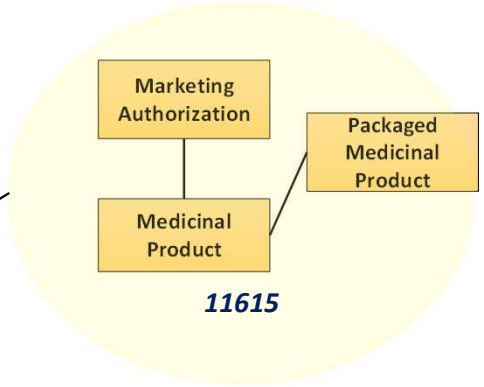


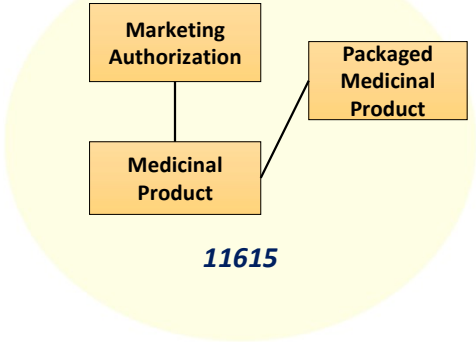


Source: saintytec

IDMP- Biologics

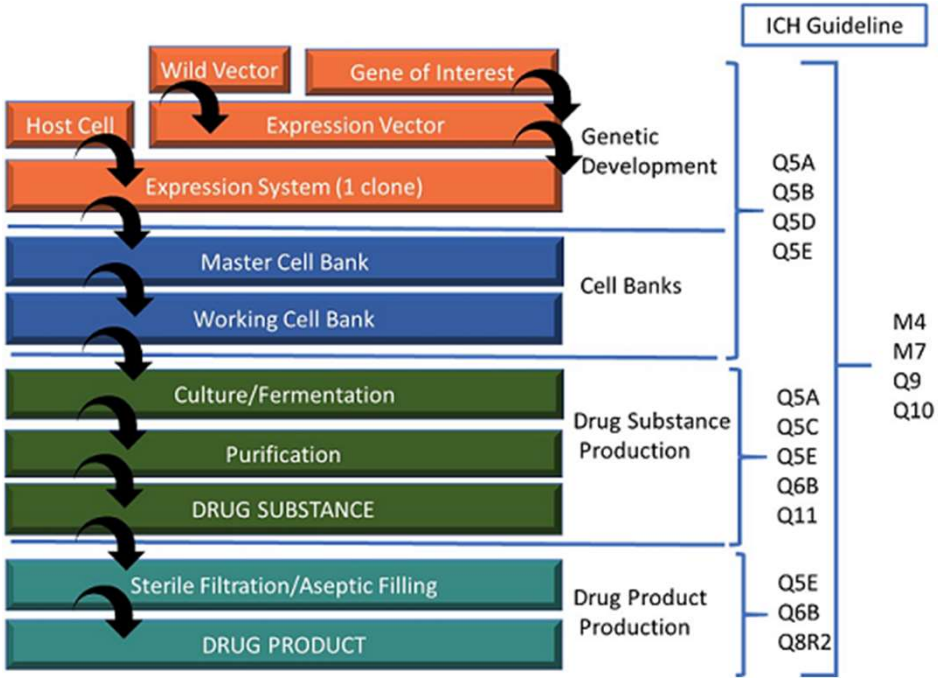


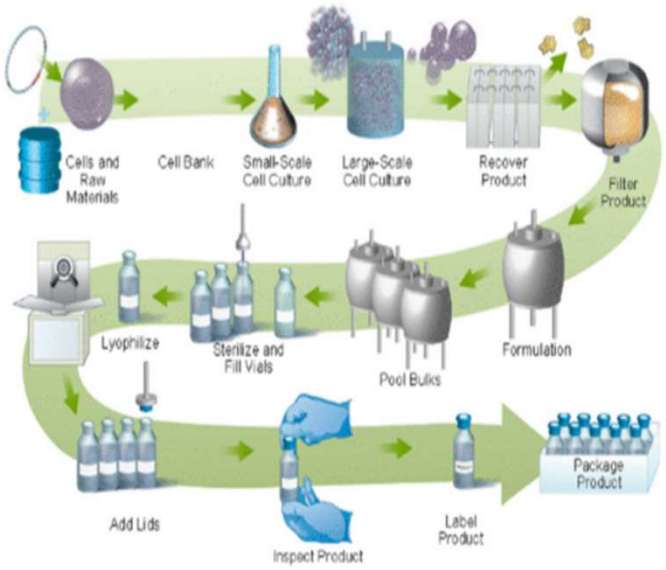




Global IDMP Working Group

Biologics Manufacturing

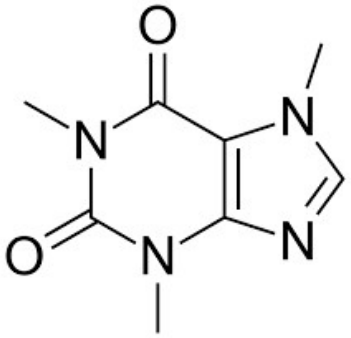




Source: outsourcedpharma

IDMP: Substance Groups and Defining Elements

- **Chemicals**
  - **Defined primarily by molecular structure** (connectivity and stereochemistry)



- **Proteins**
  - **Amino Acid Sequence**, type of **glycosylation**, modifications

- **Nucleic Acids**
  - **Sequence**, type of sugar and linkage, modifications

- **Polymers** (Synthetic or biopolymers)
  - Structural repeating units, type, geometry, type of copolymer (block or random), ratio of monomers, modifications, **molecular weight** or properties related to molecular weight, **biological source** for many biopolymers

- **Structurally Diverse Substances** (viruses, cells, tissues, complex materials)
  - **Taxonomic, anatomical, fractionation, physical properties, modifications**

Unique Identification (Biologics): SARS-CoV-2 (mRNA)

ELASOMERAN

- **UNII:** EPK39PL4R4
- **Preferred Substance Name:** ELASOMERAN
- **2430046-03-8**
- **CX-024414**
- **ELASOMERAN [INN]**
- **ELASOMERAN [WHO-DD]**
- **M-1273**

MODERNA COVID-19 VACCINE RNA

- **MRNA-1273**
- **MRNA-BASED VACCINE**
- **TAK-919**

TOZINAMERAN

- **UNII:** 5085ZFP6SJ
- **Preferred Substance Name:** TOZINAMERAN
- **2417899-77-3**
- **BNT162B2**
- **BNT-162B2**
- **COMIRNATY**

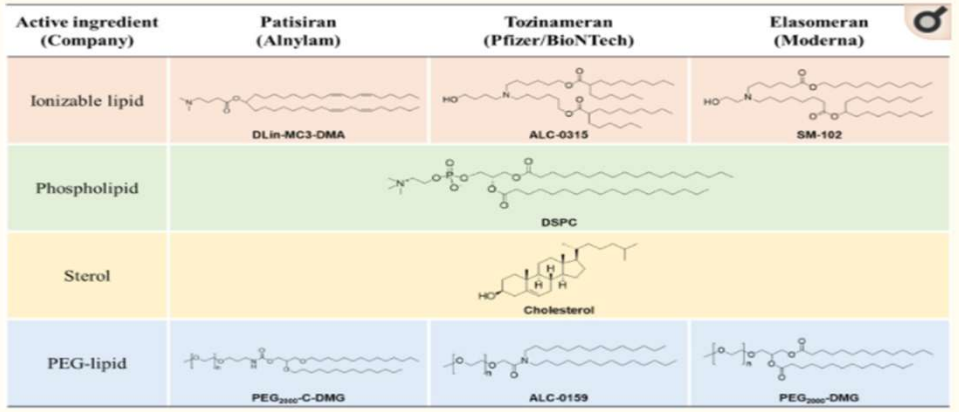
PFIZER COVID-19 VACCINE

- **RNA INGREDIENT BNT-162B2**
- **TOZINAMERAN [INN]**
- **TOZINAMERAN [WHO-DD]**

3. Difference in formulation

Go to:

The three LNP-based drugs share multiple similarities in their formulation, and hence, behave similarly as nanoparticles in vivo. Importantly, all LNPs are composed of four types of lipids; ionizable lipid, phospholipid, cholesterol, and PEG-lipid (Fig. 3). All 3 ionizable lipids have tertiary amine group with pKa 6.0–6.7. These lipids switch its charge from neutral to cationic based on the neutral pH in the blood and the acidic pH in endosomes. The 3 PEG-lipids have dialkyl chains 14-carbon long, which are important for the rapid dissociation from the surface of LNPs once inside the body [43]. The biodegradable design of ALC-0315 [44] and SM-102 [11] is described later.



Open in a separate window

Fig. 3

Chemical structure of lipids in lipid nanoparticles. ALC-0159 has PEG_{2000}. All 3 ionizable lipids have tertiary amine groups, namely Dlin-MC3-DMA (MC3), pKa 6.44 [12] or pKa 6.35 [11]; ALC-0315, pKa 6.09 [44]; and SM-102, pKa 6.68 [11]. The related patents are as follows: Dlin-MC3-DMA, WO/2010/144740; ALC-0315, WO/2017/075531 (Lipid No. 3); and SM-102, WO/2017/049245 (Compound 25).

Drug Metab Pharmacokinet. 2021 Dec; 41: 100424.
Published online 2021 Oct 10. doi: 10.1016/j.dmpk.2021.100424

Global IDMP Working Group

TOZINAMERAN LIPID NANOPARTICLE

FZ4BV6MFB6

GROUP 1 SPECIFIED SUBSTANCE

Names: TOZINAMERAN LIPID NANOPARTICLE ✓
BNT162B2 LIPID NANOPARTICLE

Codes: **BDNUM** : 0137566AB

FDA UNII : FZ4BV6MFB6

Relationships: 1

Constituents: 5

Inxight Drugs

Created: 2/22/21

Created By: CALLAHANL

Status: Validated (UNII)

Validated By: DAMMIKA.AMUGODA-KANK

Validated Date: 2/23/21, 7:20 AM

Last Modified: 3/31/21

Last Modified By: CALLAHANL

Version: 5

Substance Hierarchy

TOZINAMERAN	5085ZFP6SJ *{ACTIVE MOIETY}*
((4-HYDROXYBUTYL)AZANEDIYL)BIS(HEXANE-6,1-DIYL)BIS(2-HEXYLDECANOATE)	AVX8DX713V
CHOLESTEROL	97C5T2UQ7J
1,2-DISTEAROYL-SN-GLYCERO-3-PHOSPHOCHOLINE	043IPI2M0K
2-(MPEG 2000)-N,N-DITETRADECYLACETAMIDE	PJH39UMU6H

Application Count:	Product Count:	Clinical Trial Count:	Adverse Event Count:
0	Active: 0 Inactive: 0	0	0

Reference: G-SRS

CX-024414 LIPID NANOPARTICLE

9NFK69RL7T

GROUP 1 SPECIFIED SUBSTANCE

Names: CX-024414 LIPID NANOPARTICLE ✓
ELASOMERAN LIPID NANOPARTICLE
MRNA-1273 LIPID NANOPARTICLE

Codes: **BDNUM** : 0137125AB

FDA UNII : 9NFK69RL7T

Relationships: 1

Constituents: 5

Created: 1/6/21

Created By: CALLAHANL

Status: Validated (UNII)

Validated By: DAMMIKA.AMUGODA-KANK

Validated Date: 5/5/21, 10:18 AM

Last Modified: 1/19/22

Last Modified By: CALLAHANL

Version: 8

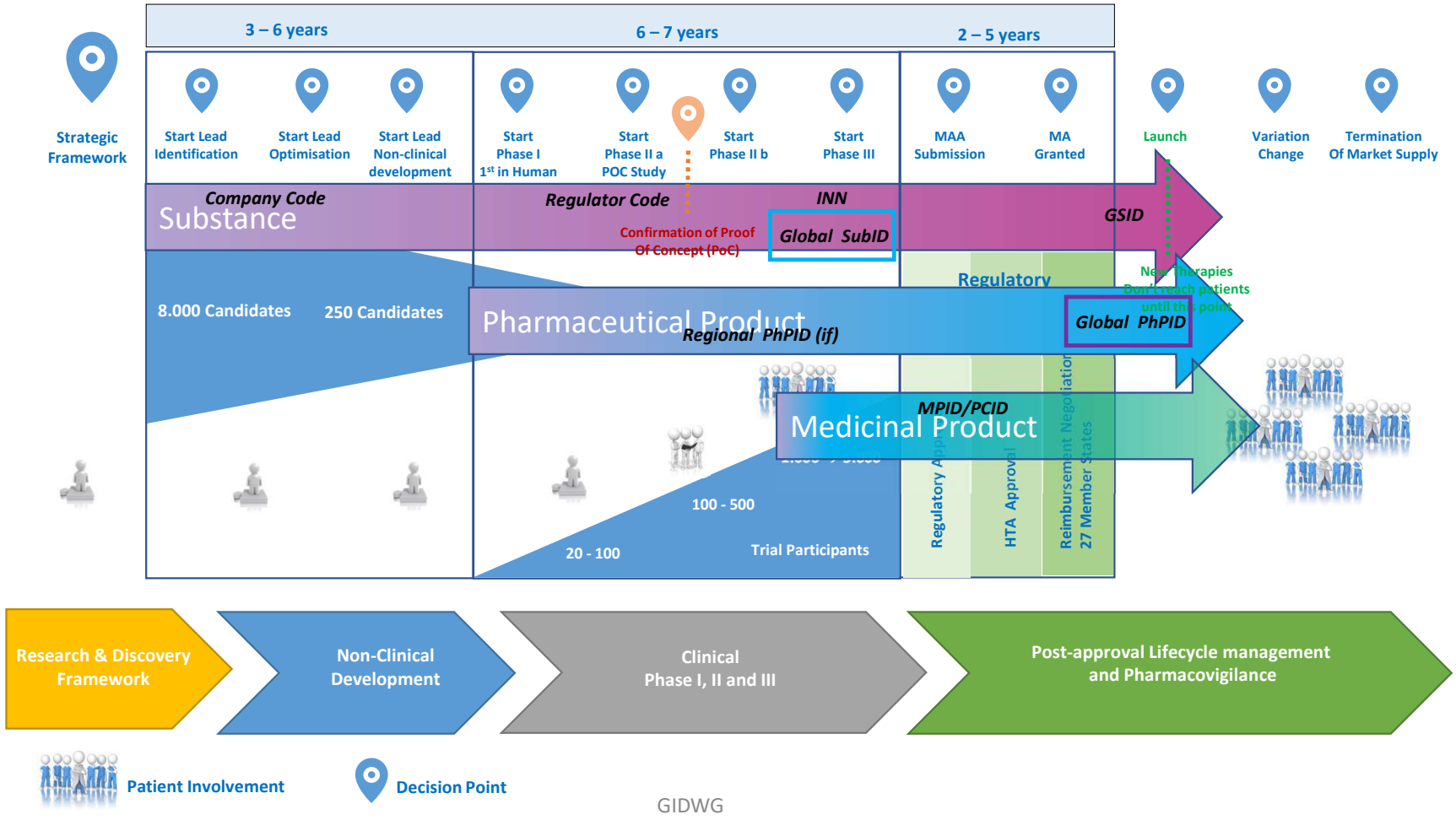
Substance Hierarchy

ELASOMERAN	EPK39PL4R4 *{ACTIVE MOIETY}*
SM-102	T7OBQ65G2I
CHOLESTEROL	97C5T2UQ7J
1,2-DIMYRISTOYL-RAC-GLYCERO-3-METHOXYPOLYETHYLENE GLYCOL 2000	9X2596CIE0
1,2-DISTEAROYL-SN-GLYCERO-3-PHOSPHOCHOLINE	043IPI2M0K

Reference: G-SRS

Recommendation: WHO-UMC MO Assignment: "Global" Substance/PhPID

Global IDMP Working Group



Global Pharmaceutical Market: Shortages

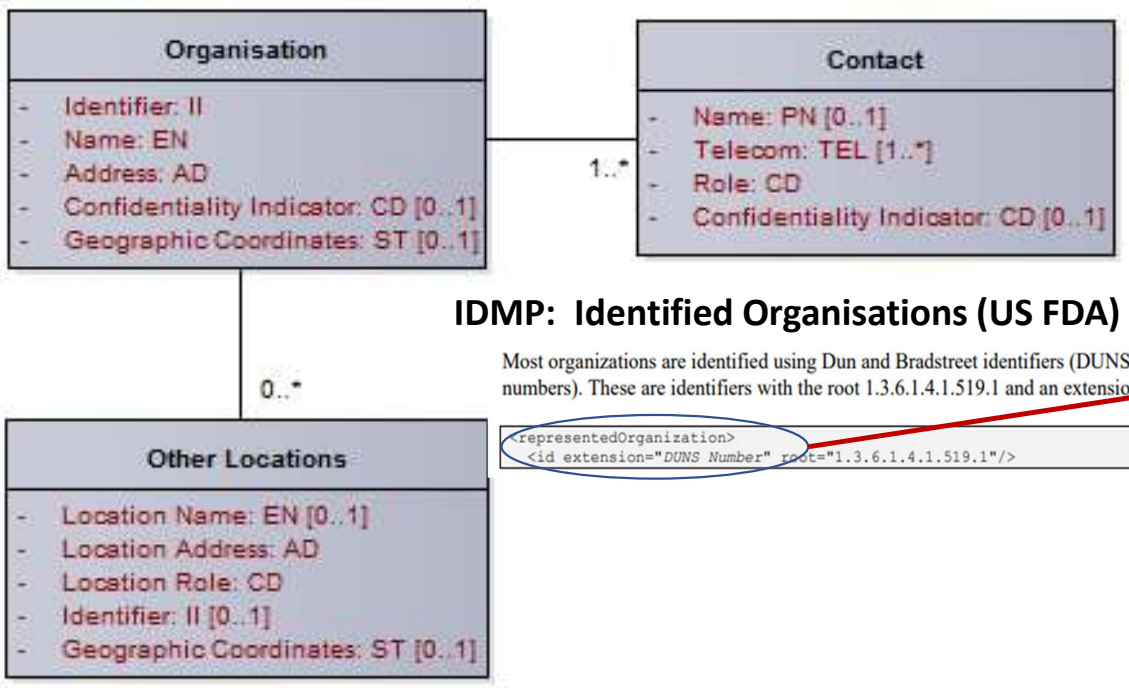
Global IDMP Working Group

- China makes “nearly all” supplies of penicillin G and about 80% of the world’s supply of many antibiotics.
- Indian drug makers rely heavily (about 70%) on China for key starting materials
- Italy was the EU’s largest producer of antibiotics in 2018, accounting for 34% of the total EU consumption. Italy, however, was hit early and hard by COVID-19 cases
- In the US 186 new drug shortages, 82% of which were classified as due to “unknown” reasons largely because of the intentional opacity and secrecy of the upstream supply chain.
- FDA official reported to Congress in 2019 that FDA doesn’t “know whether Chinese facilities are actually producing APIs, how much they are producing, or where the APIs they are producing are being distributed worldwide, including in the United States”
- USP analyzed the labels of 40,178 prescription drug products and found that only 3% reported the API manufacturer, 30% reported the finished product manufacturer, 45% reported only the labeler or packer, and 25% reported no information on the upstream supply chain
- In 2019 vincristine—a pediatric cancer drug—was in severe short supply the drug simply was not available at any price. One of only two US manufacturers of vincristine exited the market, and the second experienced production delays and quality problems.

CIDRAP
Center for Infectious Disease Research and Policy
University of Minnesota

https://www.cidrap.umn.edu/sites/default/files/public/downloads/cidrap-covid19-viewpoint-part6.pdf

IDMP: Unique Organisation (Facility) ID



IDMP: Identified Organisations (US FDA)

Most organizations are identified using Dun and Bradstreet identifiers (DUNS numbers). These are identifiers with the root 1.3.6.1.4.1.519.1 and an extension

```
<representedOrganization>
  <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
```

IDMP: Establishment Information (US FDA)

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization> <!-- Labeler -->
        <assignedEntity>
          <assignedOrganization> <!-- Registrant -->

<assignedEntity>
  <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>

  <assignedOrganization>  <!-- Establishment -->
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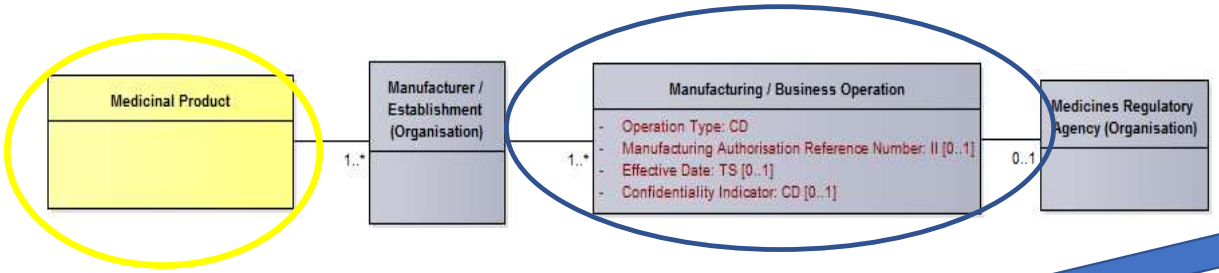
    <name>Middleton Manufacturing company</name>
  </assignedOrganization>

  <performance>
    <actDefinition>
      <code  code="C43360"
             codeSystem="2.16.840.1.113883.3.26.1.1"
             displayName="manufacture"/>
```

IDMP: Manufacturer/Establishment (organisation)

This subclause specifies characteristics about the manufacturing and other associated operations and their authorisations as issued by a Medicines Regulatory Agency, which grants permission to a manufacturer/establishment (organisation) to undertake manufacturing and other associated operations related to an Investigational Medicinal Product in a specific jurisdiction.



IDMP: Business Operation Qualifier

```
<performance>
  <actDefinition>
    ...
    <subjectOf>
      <approval>
        <code code="Qualifier Code" codeSystem="2.16.840.1.113883.3.26.1.1"
              displayName="Qualifier Display Name"/>
      </approval>
    </subjectOf>
```

Business Operation Qualifier Examples:

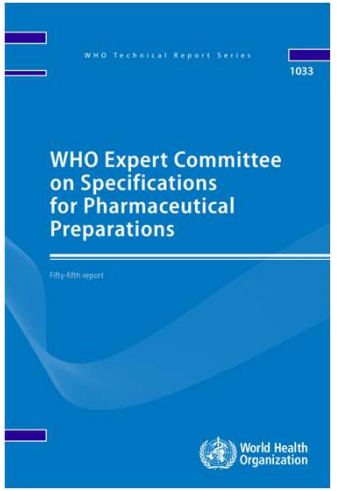
- "Intent to compound 506e (drug shortage) drugs (C112087)
- "unapproved drug for use in drug shortage"(C101533)
- API manufacture (C82401)

IDMP: Business Operation Product

```
<document>
  <author>
    <assignedEntity><representedOrganization>      <!-- Labeler -->
      <assignedEntity><assignedOrganization>       <!-- Registrant -->
        <assignedEntity><assignedOrganization/>    <!-- Establishment -->
<performance><actDefinition>
  <code code="C43360" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="manufacture"/>
  <product><manufacturedProduct classCode="MANU"><manufacturedMaterialKind>
    <code code="0123-12345" codeSystem="2.16.840.1.113883.6.69"/>
  </manufacturedMaterialKind></manufacturedProduct></product>
</actDefinition></performance>
<performance><actDefinition>
  <code code="C43360" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="manufacture"/>
  <product><manufacturedProduct classCode="MANU"><manufacturedMaterialKind>
    <code code="0123-12348" codeSystem="2.16.840.1.113883.6.69"/>
```

WHO Expert Committee on Specifications for Pharmaceutical Preparations: Sameness of a Product

- Two products have identical essential characteristics (i.e. the product being submitted to the relying authority and the product approved by the reference regulatory authority should be essentially the same).
- All relevant aspects of drugs, medical devices and in vitro diagnostics, including those related to the quality of the product and its components, should be considered to confirm that the product is the same or sufficiently similar
  - Same qualitative and quantitative composition
  - Same strength
  - Same pharmaceutical form
  - Same intended use
  - Same manufacturing process
  - Same suppliers of active pharmaceutical ingredients (APIs),
  - Same quality of all excipients).
  - Additionally, the results of supporting studies of safety, efficacy and quality, indications and conditions of use should be the same



IDMP and Unique Medicinal Product Identification

Defining Elements

- purity or grade;
- manufacturer data including information on the manufacturer and processes in manufacturing;
- analytical data in view of the tests and specifications;
- analytical methods used for potency determination;
- constituent substances, including amounts and role when known and relevant;
- specifications for identity, impurities, degradants, related substance limits would be captured using
- constituent substances and potency;
- unitage;
- reference material

To meet the needs of medicinal product identification, the elements of the specified substance shall be divided into **four groups and a specified substance identifier** shall be associated with each group of elements.

ISO IDMP and Manufacturing: Specified Substance Group 4

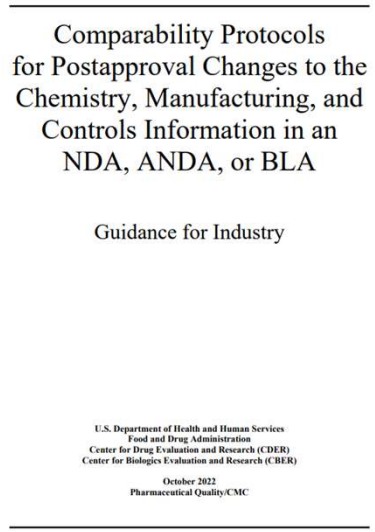
- The 'Manufacturing' element group shall capture information on the manufacturer and critical manufacturing processes that are necessary to distinguish specified substances.
  - Starting materials,
  - Processing materials,
  - Critical process parameters,
  - Equipment used and the resultant material from the manufacturing process

NOTE: The manufacturing group is not intended to capture all the details of manufacturing but only the critical processes that could impact the **quality, safety or efficacy** of a specified substance used in a medicinal product.

Comparability Protocol for the Proposed CMC Change(s)

- The CP for the proposed CMC change(s) should describe the specific tests and studies to be performed, including analytical procedures to be used, and acceptance criteria to be achieved to demonstrate the lack of adverse effect on product quality.

- The level of detail that should be provided in the CP depends on the following (not all-inclusive):
  - Complexity of the product
  - Manufacturing process
  - Comparative assessment of relevant product quality attributes before and after the change(s)
  - Material(s) that may be affected by the proposed CMC change(s) (e.g., in-process material, drug)
  - Substance, intermediate, reagent, product component, drug product, container closure system
  - Raw material or a combination of these, as appropriate
  - Projected number of batches, batch size or scale,
  - Site of manufacture

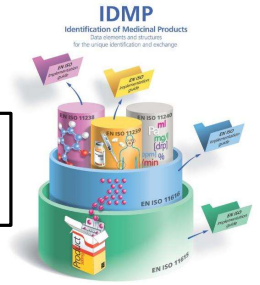

Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA

Guidance for Industry

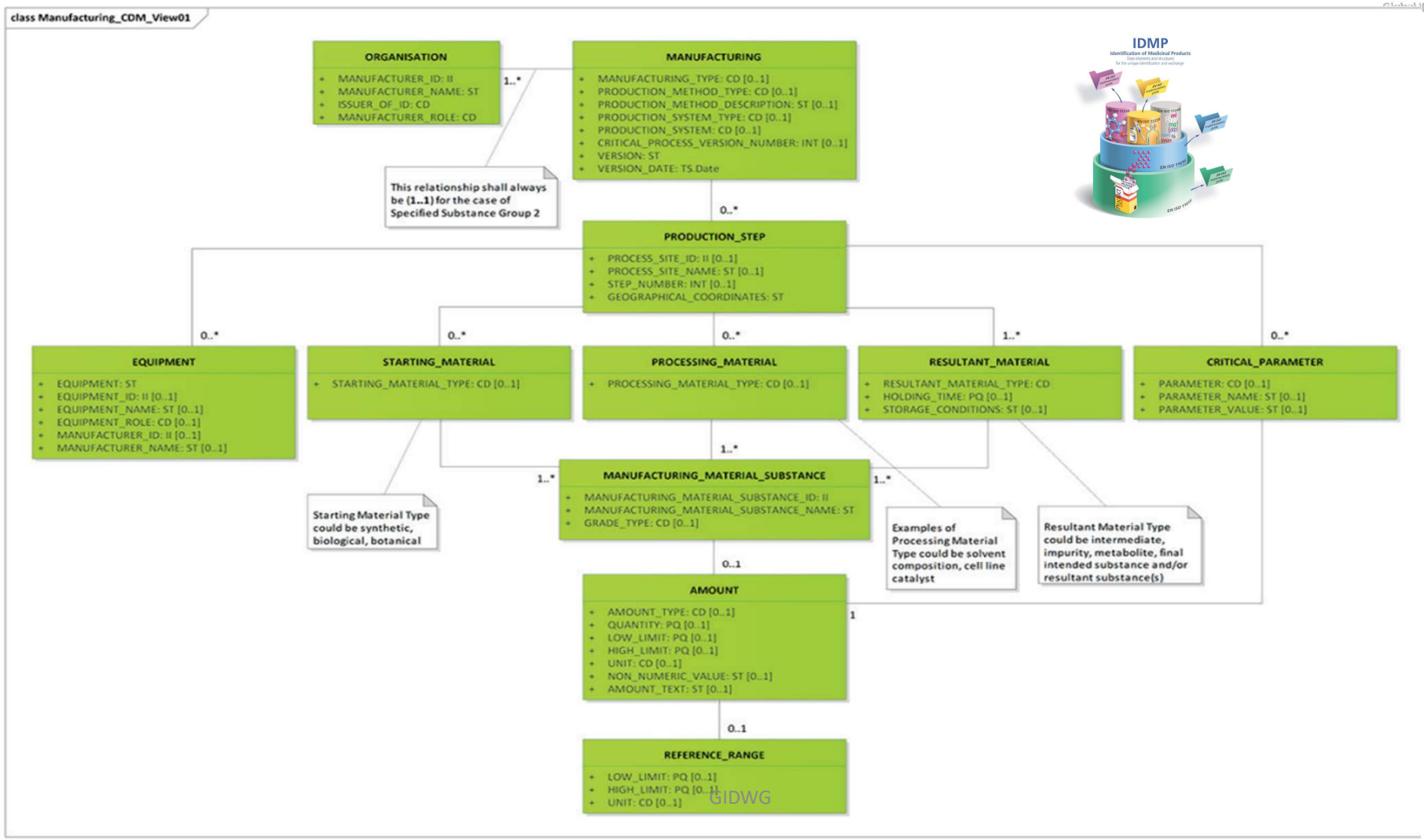
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2022
Pharmaceutical Quality/CMC

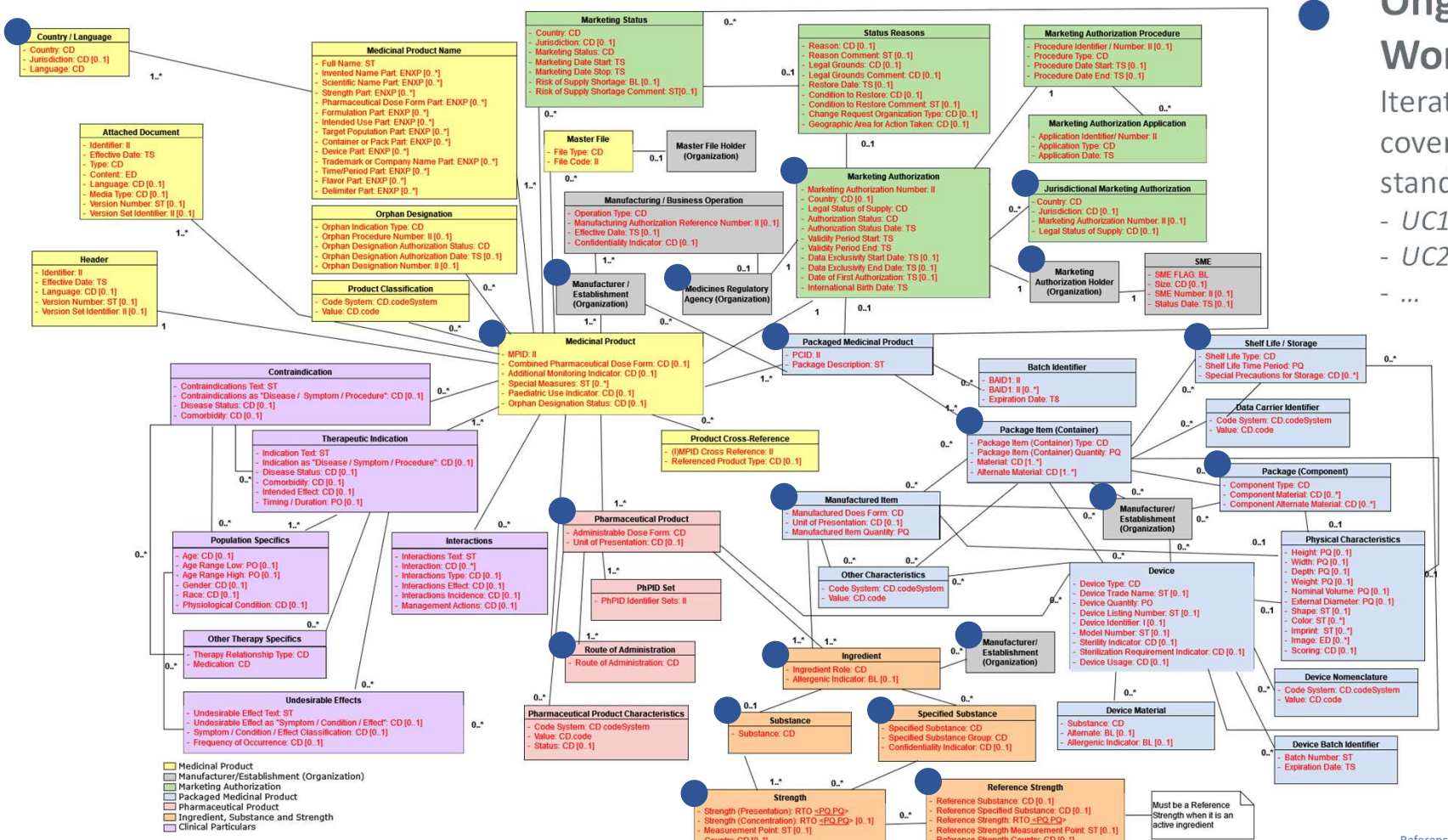
ISO IDMP Specified Substance(s)



IDMP Manufacturing Information Model



IDMP-Ontology Coverage of the ISO IDMP Model



Ongoing Work

Iteratively covering the ISO standards

- *UC1: Substance*
- *UC2: Reg-Manuf.*
- ...

Global IDMP Working Group

Reference: Bayer

Acknowledgments

Industry

Sheila Elz, Bayer

Ciby Abraham, AstraZeneca

Elisabeth Godet, Sanofi

Jean-Gonzague Fontaine, GSK

Christian Hay, GS1

Rodrigo Palacios, Roche

IFPMA

Janis Bernat

Ginny Beakes-Read, J&J

Mumum Gencoglu

Vada A. Perkins

(IFPMA GIDWG Rep)

GIDWG

Lawrence Callahan, FDA

TJ Chen, FDA

Ron Fitzmartin, FDA

Malin Flavdad, WHO-UMC

Panagiotis Telonis, EMA

Global IDMP Working Group

Thank you

Break
(14.40-14:55)

Global IDMP Working Group

Standards Development Organizations Perspective

Charles Jaffe
(HL7 International)
Christian Hay (ISO/CEN)
Catherine Chronaki (HL7 Europe)

Interoperability in Global Healthcare

The Role of the HL7 FHIR Community

Charles Jaffe, MD, PhD

Chief Executive Officer
HL7 International

3rd Global IDMP Working Group

Amsterdam
September 18, 2023


AGENDA
• The Collaborators
• The Implementers
• The Government
• The Innovators
• The Futurists

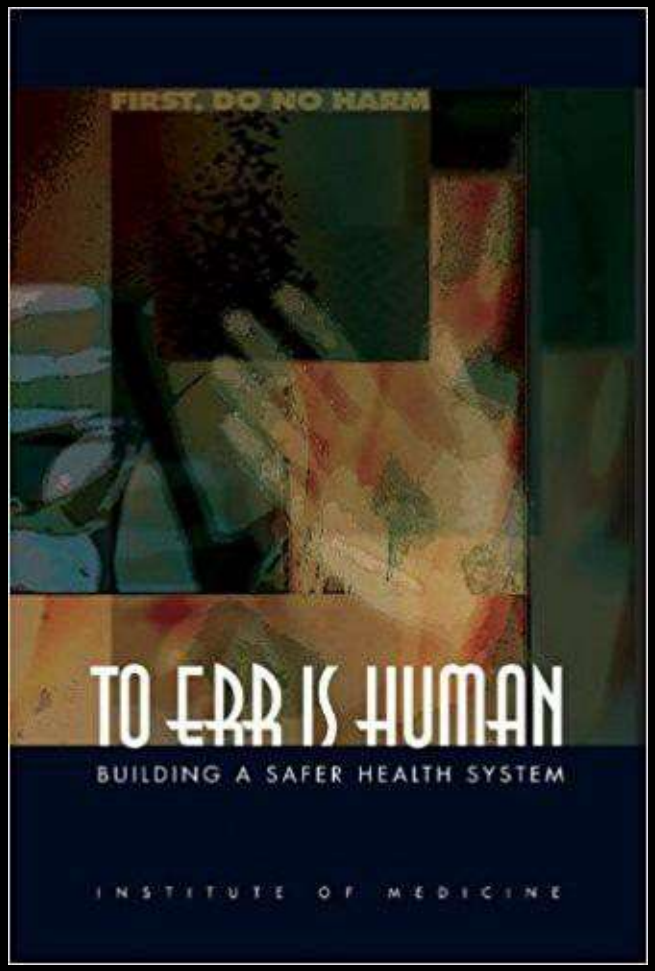
Why me? Why now?

HL7 International

Quality care has always seemed
so difficult to achieve

Two decades ago
the Institute of Medicine
published
To Err is Human

…and we really haven't gotten much better since.



A Johns Hopkins study estimated that 250,000 Americans die each year from *avoidable medical errors*.

It's the third leading cause of death in the US.

*Markey, M & Daniel, M, BMJ 2016 May 3;353

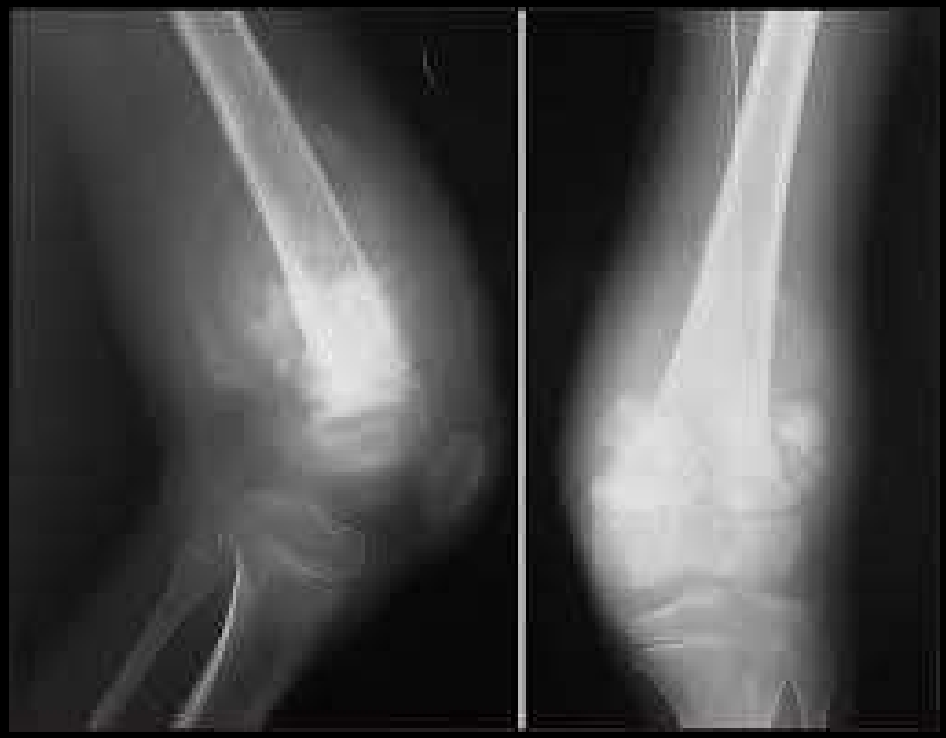
This is Jack’s story

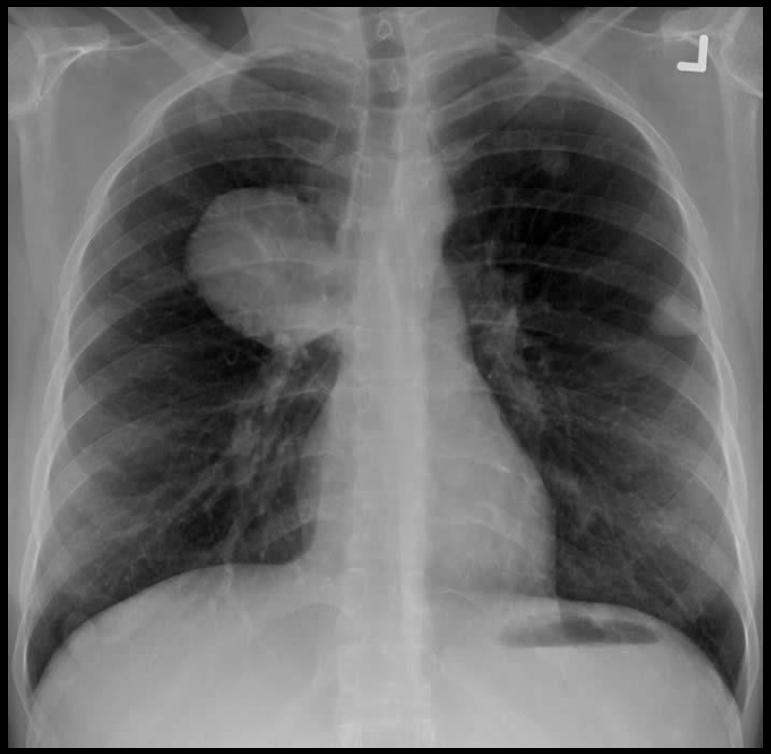
This is Jack

- Honor student
Sports hero
University bound

Jack complained
to his Family Doctor
about knee pain.

This is what Jack's knee looked like, but his doctor never saw the report.





This is Jack’s chest x-ray after I first saw him.

The Pathology Report read metastatic osteosarcoma.

There should be
no more stories
like Jack’s.

Then, there were
Open APIs
and FHIR.

The FHIR Story Line

- What is FHIR?
- Why FHIR?
- How do you crate FHIR?
- When will FHIR be ready?
- Who is transforming the Interoperability Paradigm with FHIR?

Guiding Principle

"How much easier it is to be critical than to be correct."

- Benjamin Disraeli

HL7 FHIR

I have hopes
for tomorrow's healthcare.

Clinicians will have all of the data they require when and where it's needed.

Patients will receive care based upon verifiable evidence.

“The difference between physicians and pilots is that pilots realize that they have to get into the airplane with the people they care for.”

Dr. Lawrence Weed

Clinical decision support
will become a fundamental part
of care delivery.

CDS HOOKS®

HL7 FHIR®

“The plural of anecdote is not data.”

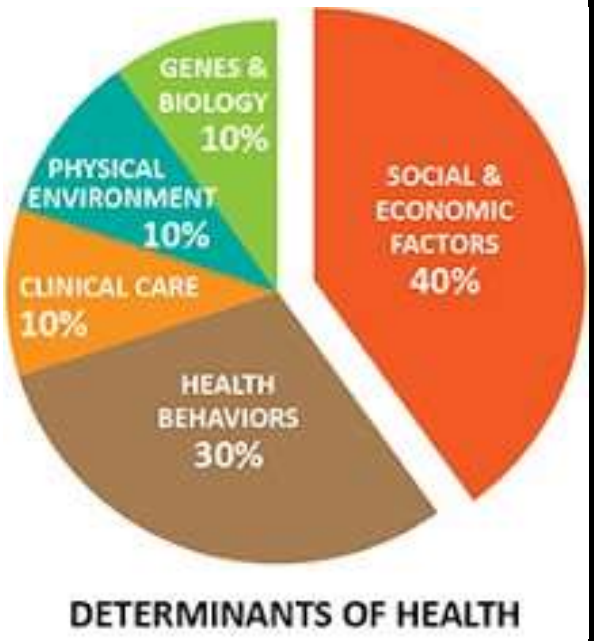
Chris Chute, MD

Regulated clinical research will be based upon *real-world data*.

Drugs in clinical use will be *more than* 50% effective.*

* Huskies, VJB, et al, BMC, 18:5, 2017

The social determinants of health will be seamlessly integrated into patient care decisions.



Physicians will be compensated for outcomes rather than for services.

Value-based Care
will be our legacy.

Goya, The Third of] May
Courtesy: The Prado

HL7 is transforming the ecosystem.

HL7 FHIR is changing the way we view interoperability.

“The best way to predict the future is to invent it.”

Alan Kay
Address to PARC, 1971

Some Questions about Interoperability

- Are we talking about technology, when we should be facing the issues of ambiguous policy?
- Can we ever achieve interoperability without viewing the data in context?
- Will we ever see a convincing business case for interoperability?
- Is the failure to achieve interoperability an ethical issue?

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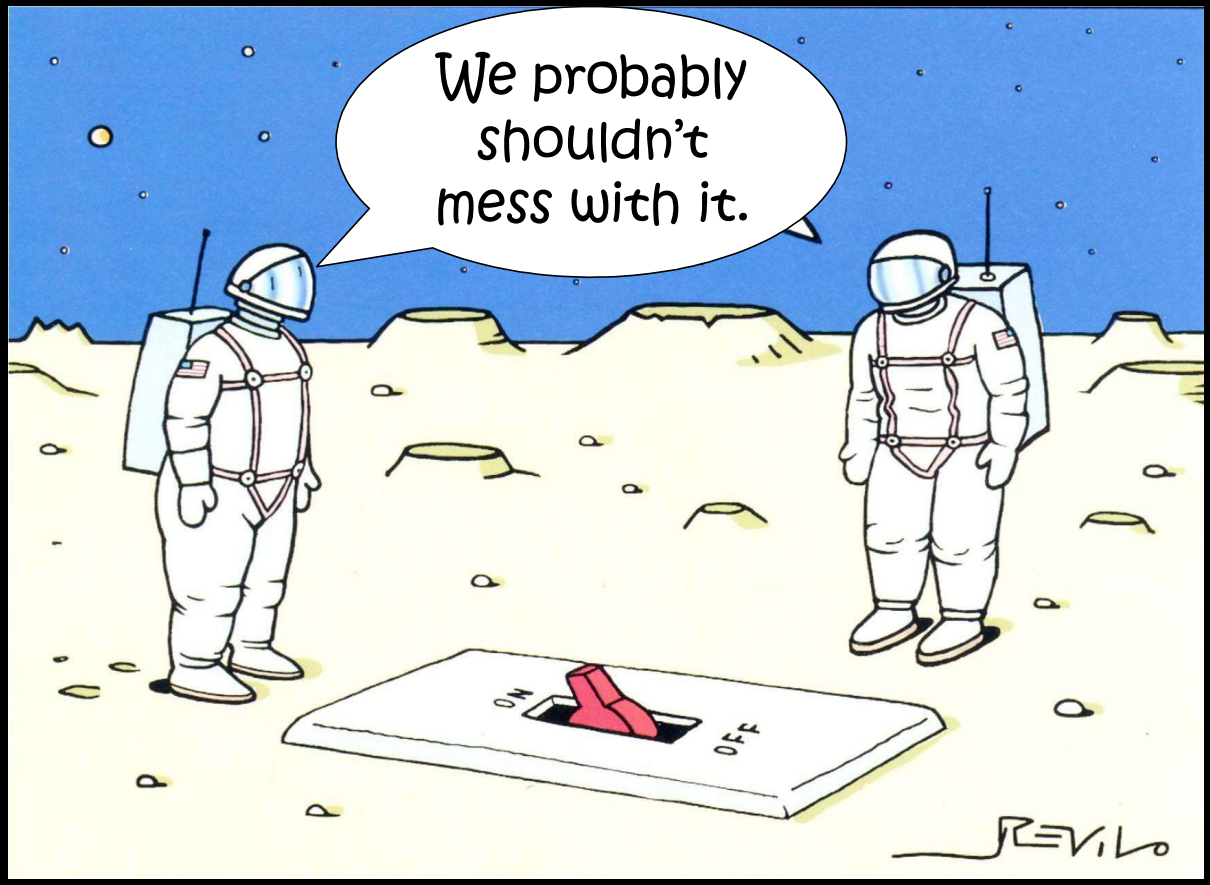
Three Laws of Interoperability

1. Policy supersedes technology.
2. You can hide the complexity, or make it worse, but you can't make it go away.
3. Cheap, flexible, and interoperable: pick two

HL7® FHIR®

Change Management is about taking well-informed chances.



“If you’re doing something the same
way for ten years,
the chances are you are
doing it wrong.”

Charles Kettering

The HL7 Fresh Look asked,
"What would interoperability look like
if only we could start over?"

...and not throw out the good stuff we learned along the way.

HL7 International

"If I had asked my customers what they wanted, they would have asked for a faster horse."

Henry Ford

A little compromise:

FHIR for non-Engineers

In 2 minutes

The magic in the acronym:

FHIR is

Fast Healthcare Interoperability Resources

REST: The Essence of FHIR

- REpresentational State
- Google, Twitter, FaceBook
- Your favorite travel website

HL7 FHIR

FHIR is both the technology and the agreement on the meaning of the data.

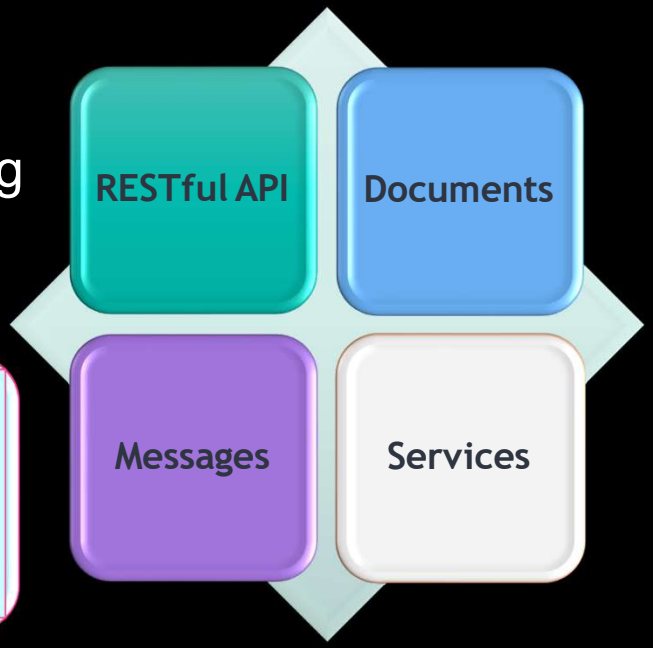
Any system, in any programing language, can read and exchange a FHIR resource…and not lose its meaning.

HL7® FHIR®

Exchanging Resources

FHIR supports 4 exchange mechanisms, or maybe 8.

In the beginning



Transaction Batch

And these emerged (after 2016) because the global community demanded it

Storage

Subscription

Bulk Transfer

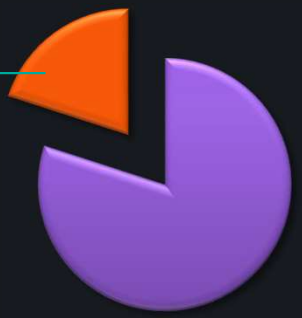
HL7 FHIR

Addressing Unique System Requirements: FHIR Extensions & the 80/20 Rule

FHIR Resources have data elements representing **80%** of existing system requirement

Extensions are the other **20%**

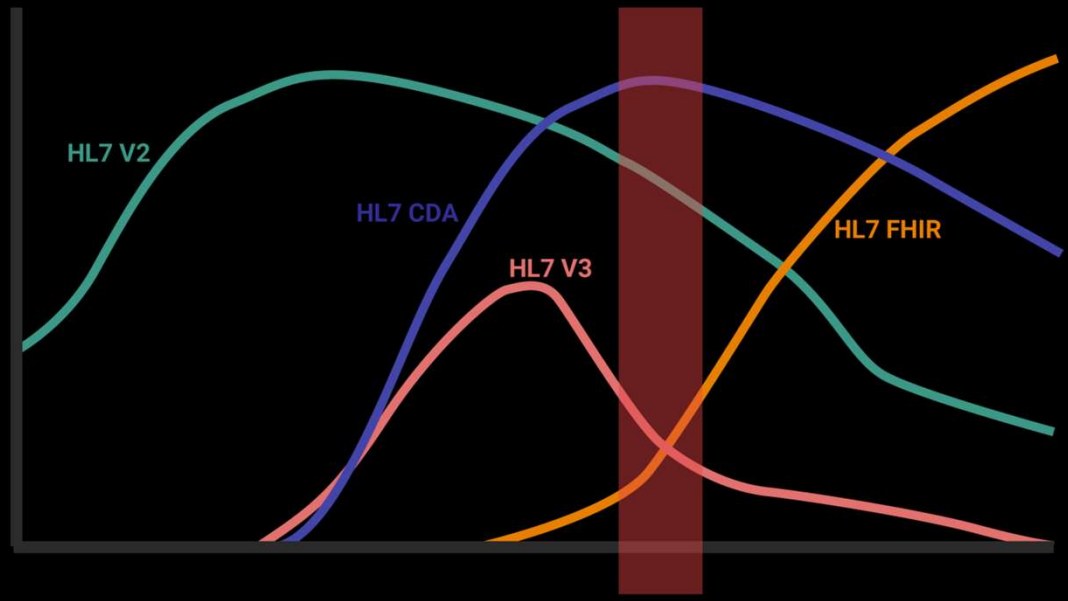
- ISO compliant
- Meet specific use cases
- The encoding looks no different



Extensions solve the problem of
the unique requirements of a health system,
but are interoperable only if shared.

HL7® FHIR®

The Challenge of the Lifecycle of Standards



…is met with a well-defined *Maturity Model*

HL7® FHIR®

HL7 FHIR is more than technology.

HL7 FHIR is about Community.

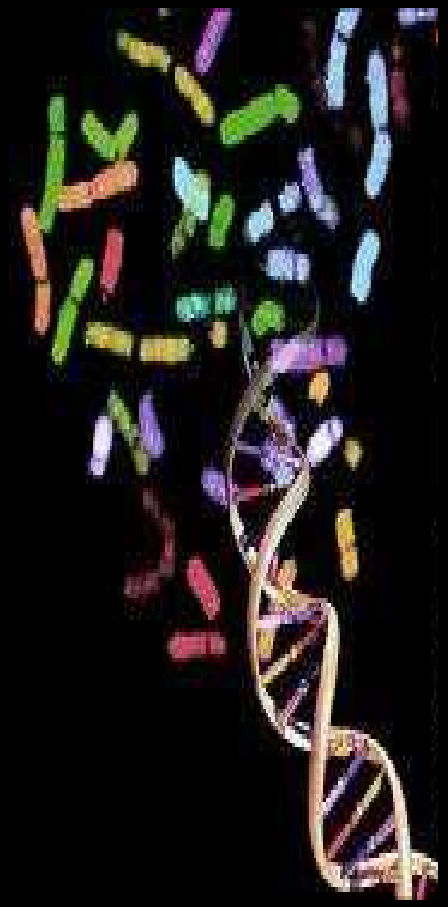
The HL7 FHIR Community of Implementers

“We can’t solve problems with the same kind of thinking when we created them.”

Albert Einstein

International BioPharma
leverages HL7 FHIR
for real-world clinical trials,
post-marketing bio-surveillance,
and genomics integration.

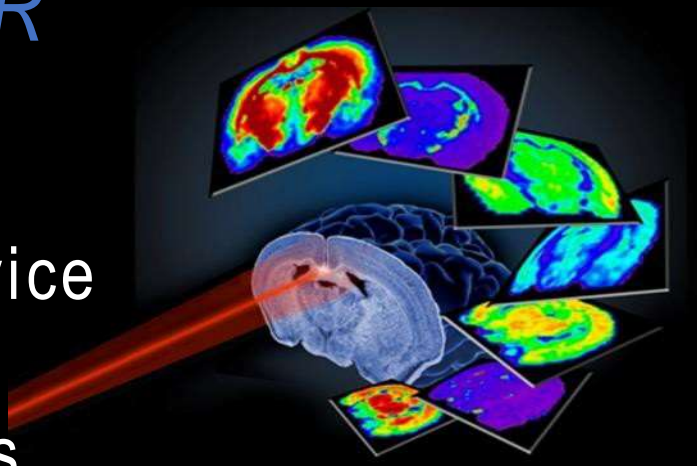
TransCelerate
BIOPHARMA INC.



Sync4Science,
Sync4Genes,
& Sync for Social Needs
use FHIR to enable
Genomic Data for
Precision Medicine,
Translational Science,
& Clinical Decision Support

HL7® FHIR®

Devices on FHIR



A collaboration of device manufacturers & technology vendors committed to seamless exchange of data between clinical devices and health information systems

HL7® FHIR®

The HL7 FHIR Community
of
US Government Agencies

US Federal agencies, including FDA, CDC, NIH, DoD, VAH, and others have active FHIR integration programs

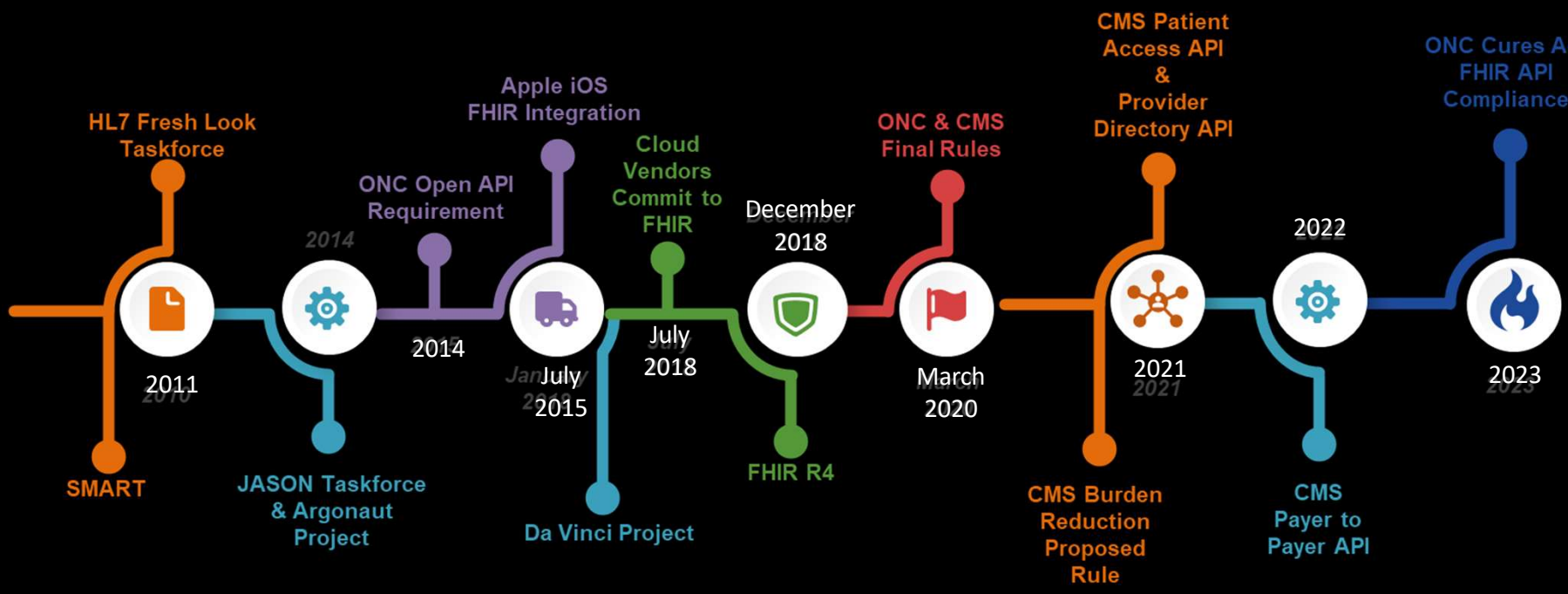
The HL7 FHIR Community
of
Standards Developers

My coach said that I kick like a girl.

I told him that if he tried harder, he could too.

Mia Hamm

HL7 FHIR Timeline



HL7 Collaboration

Nearly 40 collaborations with associations, standards developers, societies, and fellow sojourners in the global community creating public good.

HL7 FHIR Accelerators

HL7 FHIR Accelerator Program

Begun only 4 years ago, the program assists implementers across the healthcare and research spectrum in the creation of FHIR implementation guides and critical public- and private-sector solutions.

Argonaut: Changing the Course of FHIR

Historical Projects

- Apple iOS (Healthkit©)
- Argonaut Data Query
- SMART Web Messaging
- Subscriptions
- Bulk Data
- Questionnaires
- CDS Hooks
- Scheduling

2023 Projects

- Provider Directory
- FHIR for Imaging
- FHIR for Secure Messaging

HL7 FHIR ARGONAUT PROJECT

A private sector coalition of providers and payers that addresses the needs of the Value Based Care Community by leveraging the HL7 FHIR platform.

HL7® FHIR®

https://confluence.hl7.org/display/DVP

Member-driven HL7 FHIR Accelerator, building a community to accelerate interoperable data modeling and applications leading to step-change improvements in Cancer patient care and research.

CodeX has grown to include Cardiology and Genomics.

https://confluence.hl7.org/display/COD/CodeX+Home

The FAST Accelerator will identify FHIR resources, scalability gaps and possible solutions, as well as analyses that will address current barriers and accelerate FHIR adoption at scale.

https://confluence.hl7.org/display/FAST/FHIR+at+Scale+Taskforce+%28FAST%29+Home

HL7 ***FHIR Global Community*** Collaborators

Collaboration
is not what we do when we
run out of ideas or money.

Collaboration
is where we begin.

HL7
30
YEARS OF
STANDARDS
DEVELOPMENT

Standards Development Organization Collaboration

The ANSI-accredited standards development organizations partner with HL7 to support healthcare and research data interoperability. We are aided by other organizations that promote implementation, education, safety, coordination, and play key advisory roles.

HL7 could not aspire to a future of seamless interoperability without their participation.

Gravitate Health

- Community: 40 members from Europe and the US.
- Collaboration:
  - Vulcan FHIR eProduct Info (ePI)
  - Innovative Medicines Initiative (IMI) Gravitate-Health
  - European Medicine Agency (EMA) Electronic product information (ePI) for human medicines
  - EMA ePI API specification v1.0
  - EMA Substance, product, organization and referential (SPOR) master data
  - International Patient Summary (IPS)
- Overview: Creation of a FHIR Implementation Guide demonstrating the methodology for integrating patient health information from the International Patient Summary (IPS) with medicinal product information from regulatory approved electronic Product Information (ePI) documents.

Gravitate Health

HL7 FHIR

OMOP on FHIR

- A collaboration between OHDSI and HL7, begun in 2022, with the objective of harmonizing the FHIR data resources to the OMOP data model.
- An Open-Source FHIR Server built on top of the OMOP Common Data Model.
- A joint project between work groups, supporting both research and patient care.
- Funded by the NCATS (National Center for Advancing Translational Sciences) of the National Institutes of Health.

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

OMOP • ON • FHIR

HL7
international

Professional Society Collaboration

As the members of professional societies are increasingly voicing alarm over escalating clinical burden, they turn to HL7 for solutions to many challenges.

Traditionally, we have relied upon so many of these individuals for domain expertise, for clinical workflow, and for data element definitions.

Now, we witnessing an essential collaboration for standards implementation, for clinical decision support, for research prioritization, and for achieving the quadruple aim.

AMDIS
AMIA INFORMATICS PROFESSIONALS. LEADING THE WAY.
AMA AMERICAN MEDICAL ASSOCIATION
AAFP
AMERICAN COLLEGE of CARDIOLOGY
COLLEGE of AMERICAN PATHOLOGISTS
ACP American College of Physicians® Leading Internal Medicine, Improving Lives
ACS AMERICAN COLLEGE OF SURGEONS
HL7 international

“You can accomplish anything in life,
if you don’t mind who gets
the credit.”

Harry Truman

Technology Vendor Collaboration

To the layman, the technology vendors are the first to mind when advances in healthcare IT are first envisioned.

They are more than the creators of electronic health record innovation. They are both the creators and the adopters of standards.

They build the bridges to the payer organizations, to the clinical community, to the research innovators, and to the patients themselves.

Unique in our collaboration, they stoke the engines and apply the brakes. They are our greatest admirers and most strident critics.

Epic

ORACLE Cerner

MEDITECH

surescripts

veradigm
formerly Allscripts

InterSystems
Creative data technology

eClinicalWorks
"Improving Healthcare Together"

HL7
international

Consultancy Collaboration

From very large global organizations to boutique firms that specialize in standards, these are just a few of the many consultancies that support HL7 through

Implementation

Technical Resources

Education & Training

Development collaboration

Application Development

Policy Support

Government Relations

smile DIGITAL HEALTH

firely

Deloitte.

infor

elimu informatics

cognizant

HL7 International

Non-government Organization (NGO) Collaboration

One of the most difficult to define categories of organizations with which we collaborate are NGOs.

The NGOs are more than non-profits. They provide critical support. They provide policy and help to define the ecosystem. They influence decision makers with their ability to define solutions to challenging problems. They oversee very specific domains and very large communities. And, yes, they help to fund our vision.

These are but a very few examples of our collaborators.

MITRE

KLAS RESEARCH

World Health Organization

PAHO Pan American Health Organization

THE PEW CHARITABLE TRUSTS

Robert Wood Johnson Foundation

HL7 international

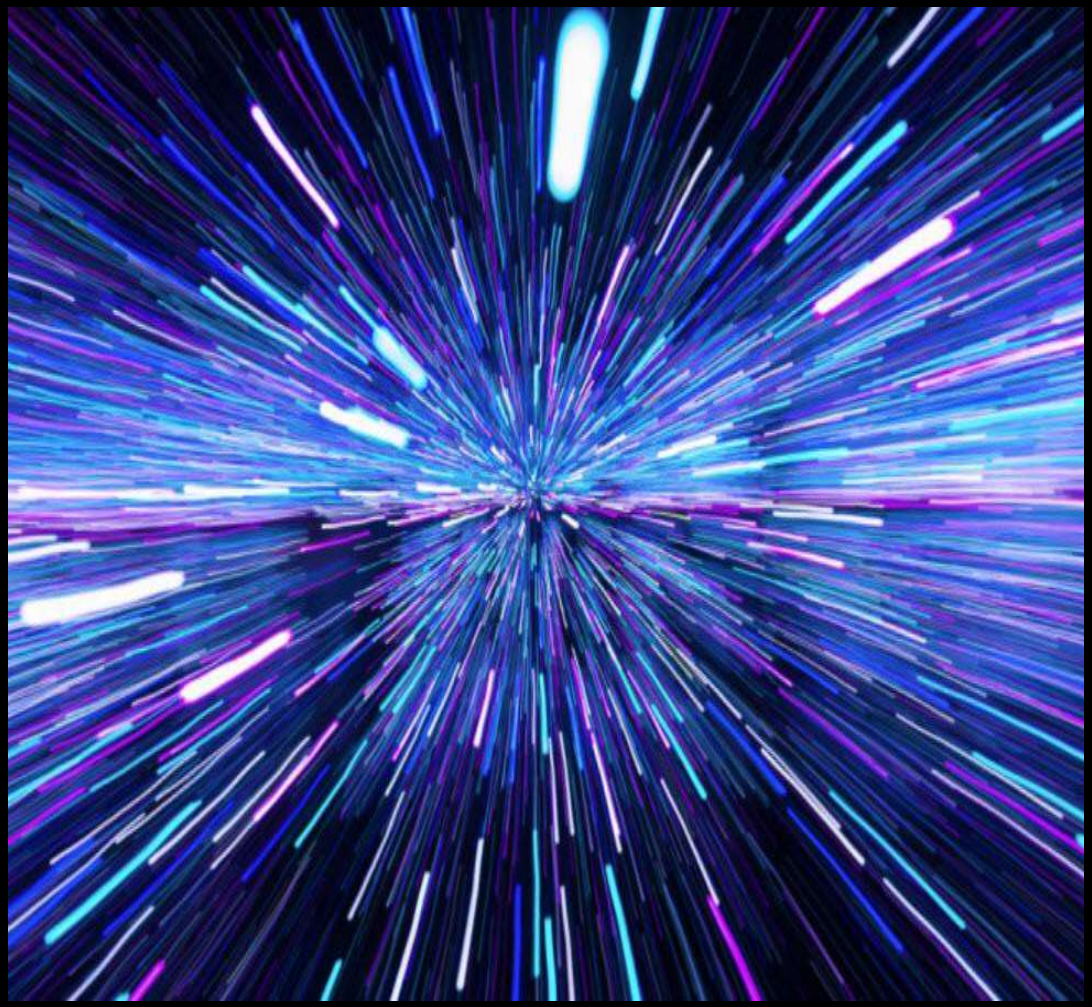
Cloud Vendor Collaboration

In August 2018 in Washington, the six largest cloud vendors announced their collaboration for implementation of the FHIR API.

Less than two years later, they each announced a collaborative initiative for importing large cohorts of data with Bulk FHIR.

HL7 FHIR

University graduates can remember 3 facts in 45 minutes.

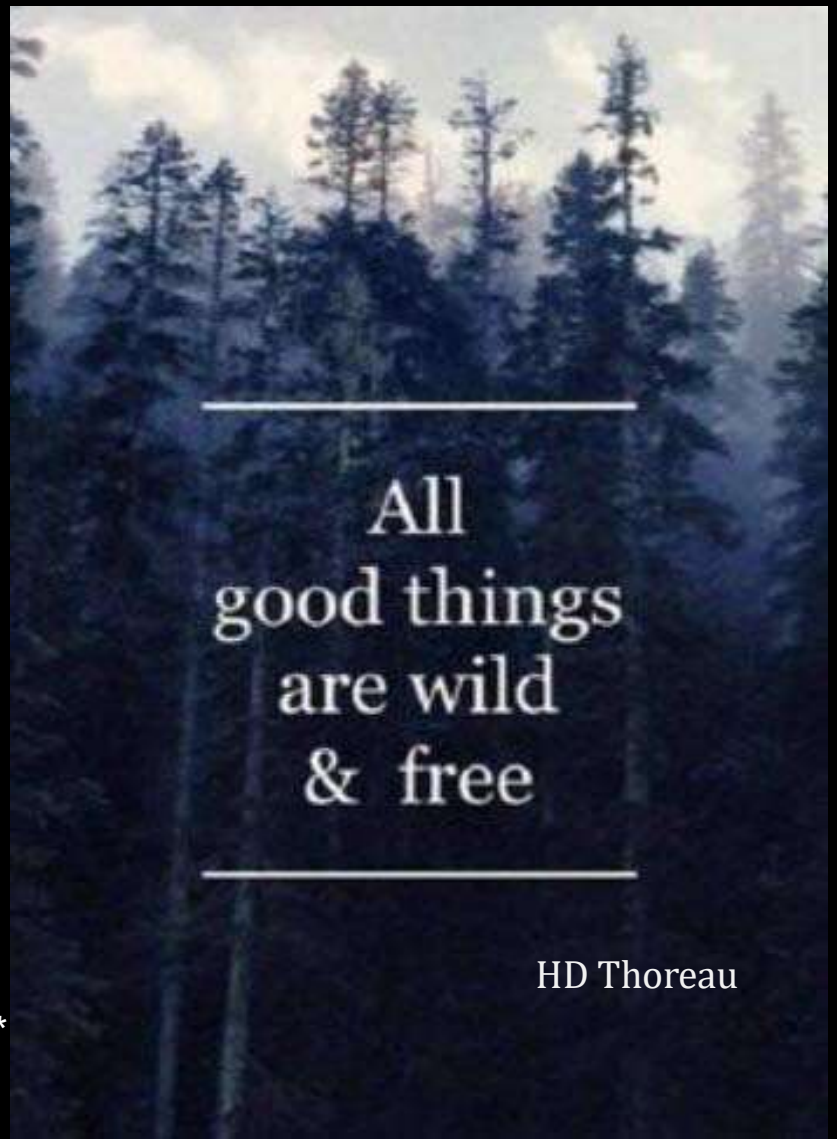


FHIR is Fast

Fast to learn.
Fast to implement.
Fast to innovate.

HL7 FHIR


FHIR is Global



FHIR is FREE

*

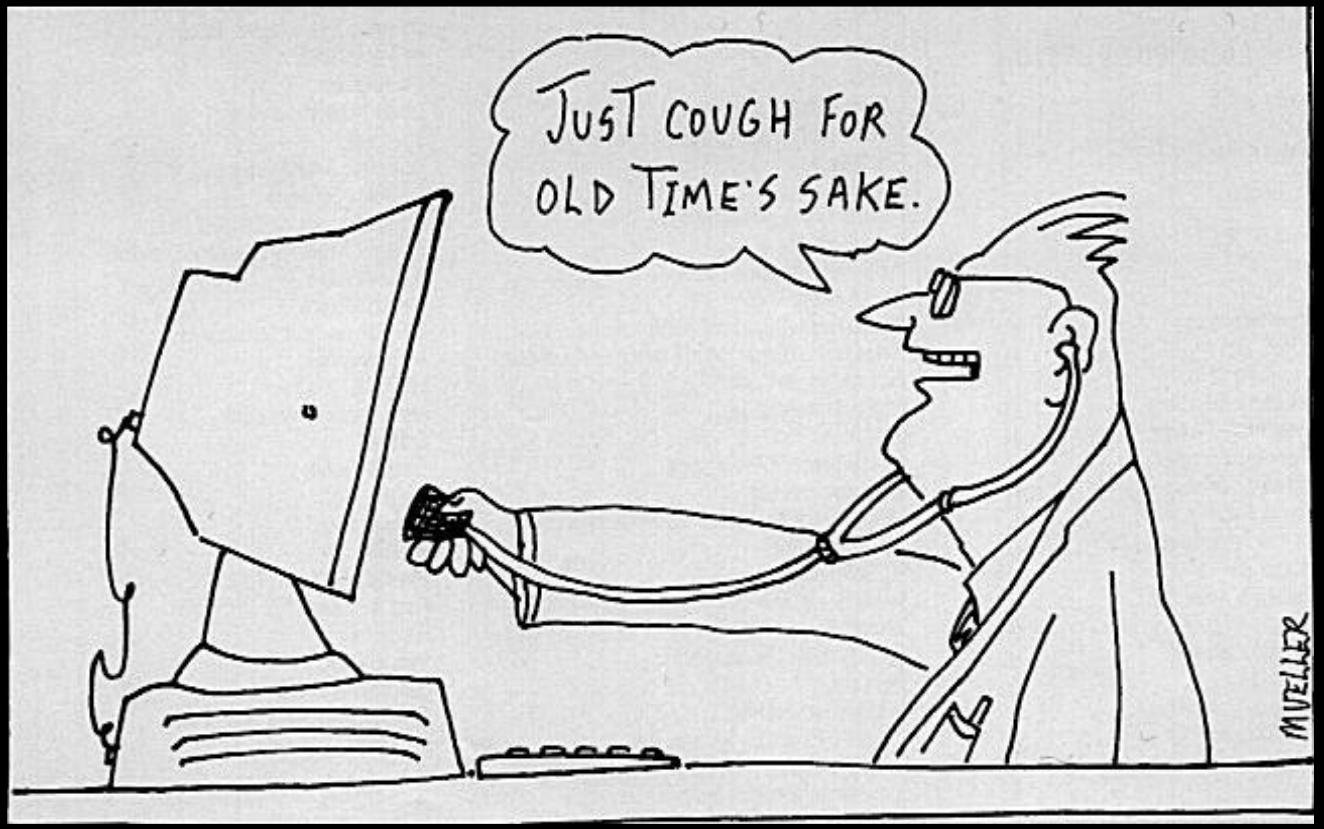
A very special thanks to

Grahame Grieve (Australia) Ewout Kramer (The Netherlands) Dr. Viet Nguyen (US)
Dr. Daniel Vreeman (US) Diego Kaminker (Argentina) Rik Smithies (UK)

without whom this success could not have been achieved.

HL7 FHIR

Thank you.



cjaffe@HL7.org

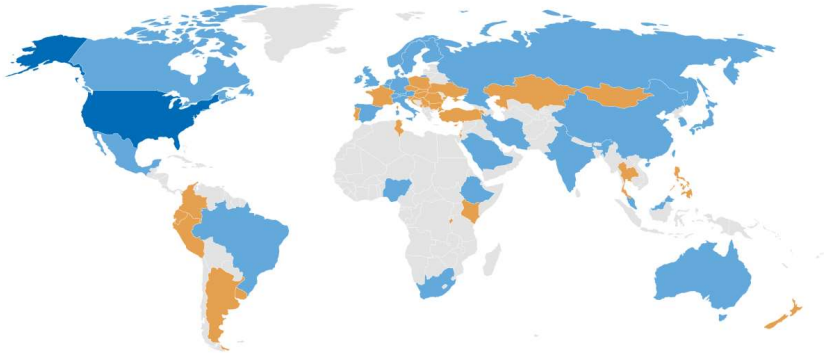
HL7 FHIR

Standards Development Organizations Perspective ISO TC 215 / WG 6

Christian Hay,
Convenor ISO TC 215 WG 6 «pharmacy and medicines business»
18 October 2023

ISO : member driven

- ISO standards are developed because they meet a **need**, are **useful** and are **usable**.
- The rules secure that the “bottom-up” process takes a majority of opinions into consideration.
- Only “participating members” (blue) can express their vote. “Observer member” (orange) and liaisons can cast their comments.



About WG6 and IDMP

- Currently, WG6 counts over 180 members from most of the TC 215 member bodies.
- Most of WG6' products are at conceptual & logical levels
- Journey to develop IDMP has been long, starting 2008 in Goteborg.
- Journey to work on its maintenance is on-going for over 12 years
- With IDMP maturity coming, interdependences have grown

IDMP and IDMP-derived documents

IDMP «core» documents

Reference	Document title
ISO 11615 TS 20443	Regulated Medicinal Product Terms and IDs
ISO 11616 TS 20451	Regulated Pharmaceutical Product Terms and Ids
ISO 11238 TS 19844	Substance Terms and IDs
ISO 11239 TS 20440	Dose forms
ISO 11240	Units of measures
DTS 6476	Logical Model for ISO 11615
ISO 22532	Core vocabulary (terms and definitions) for the IDMP Standards
TS 21405	Methodology & Framework for Development and Representation of IDMP Ontology
DTS 5499	Core Principles for Harmonization of Therapeutic Indications Terms and IDs
TR 14872	Core Principles for Maintenance of IDMP Terms and IDs
ISO 27953-1-2	ICSR

IDMP «derived» documents

DTS 5384	Data Elements and Structures for the Identification and Exchange of Immunization Data
TS 16791	Requirements for international machine-readable coding of medicinal product package identifiers
TS 17251	dose syntax
ISO 17523	ePrescription
DTR 18728	Global medicinal product/subst traceability
DTS 19293	eDispensation
TS 19256	Requirements for medicinal product dictionary systems for health care
TR 20831	Medication management concepts and definitions
TS 22703	Requirements for medication safety alerts
TS 22756	Requirements for a knowledge base for clinical decision support systems to be used in medication-related processes
DTS 23261	digital medicinal product information

Interdependances

		reference listed left, impacts reference listed below										
		ISO 11615 TS 20443	ISO 11616 TS 20451	ISO 11238 TS 19844	ISO 11239 TS 20440	ISO 11240	DTS 6476	ISO 22532	TS 21405	DTS 5499	TR 14872	ISO 27953-1-2
Reference	Document title											
ISO 11615 TS 20443	Regulated Medicinal Product Terms and IDs		X	X	X	X	X	X	X	X	X	X
ISO 11616 TS 20451	Regulated Pharmaceutical Product Terms and Ids	X		X	X	X	X	X			X	X
ISO 11238 TS 19844	Substance Terms and IDs	X	X				X	X	X	X	X	X
ISO 11239 TS 20440	Dose forms	X	X	X		X		X			X	
ISO 11240	Units of measures	X		X	X			X			X	
DTS 6476	Logical Model for ISO 11615	X	X	X	X	X		X	X			
ISO 22532	Core vocabulary (terms and definitions) for the IDMP Standards	X	X	X	X	X	X		X	X	X	X
TS 21405	Methodology & Framework for Development and Representation of IDMP Ontology	X	X	X	X	X	X	X				
DTS 5499	Core Principles for Harmonization of Therapeutic Indications Terms and IDs	X	X	X	X	X		X			X	
TR 14872	Core Principles for Maintenance of IDMP Terms and IDs	X	X	X	X	X		X				
ISO 27953-1-2	ICSR	X	X	X	X	X		X				

Status of the «core» IDMP documents

Reference	Document title	published (stable)	decision to revise	current new work item	revision in process	ballot / pending ballot
ISO 11615 TS 20443	Regulated Medicinal Product Terms and IDs		X			
ISO 11616 TS 20451	Regulated Pharmaceutical Product Terms and Ids		X			
ISO 11238 TS 19844	Substance Terms and IDs		X			
ISO 11239 TS 20440	Dose forms	X				
ISO 11240	Units of measures	X				
DTS 6476	Logical Model for ISO 11615			X		
ISO 22532	Core vocabulary (terms and definitions) for the IDMP Standards			X		
TS 21405	Methodology & Framework for Development and Representation of IDMP Ontology			X		
DTS 5499	Core Principles for Harmonization of Therapeutic Indications Terms and IDs			X		
TR 14872	Core Principles for Maintenance of IDMP Terms and IDs		X			
ISO 27953-1-2	ICSR	X				

Take away from this GIDWG meeting

- GIDWG to develop procedures or business rules for defining IDMP identifiers
  - GSID (Global Substance IDentifier)
  - PhPID (Pharmaceutical Product IDentifier)
- But as well for defining
  - Dose Forms
  - Strengths

- This with the purpose to streemline efforts, encourage convergences by providing piloted, tested, rules

Take away from this GIDWG meeting

ISO TR 14872 - Core principles for maintenance of identifiers and terms

- Technical reports are non-normative, but descriptive documents
- This TR includes presentation of the rules, governance, for defining and maintaining IDMP identifiers
- For example, to state that Dose Form codes are under EDQM's governance
- Could be in due time a good place to state WHO-UMC's role and governance for GSID, PhPID generation, etc.

As a non-normative document, this TR **will not** incorporate the procedures and business rules, but point to where these are to be found.

Questions? Feedback?

Christian Hay

Convenor ISO TC 215, WG6 «pharmacy and medicines business»

Sr consultant GS1

Christian.hay@gs1.org

+41 76 36910524

Global IDMP Working Group

Standards Development Organizations Perspective

Catherine CHRONAKI
Secretary General, HL7 Europe
Past President, EFMI

GIDWG End-to-End testing Plans with HL7 FHIR

with support from Gravitate-Health and UNICOM projects and the HL7 FHIR Vulcan Accelerator Program

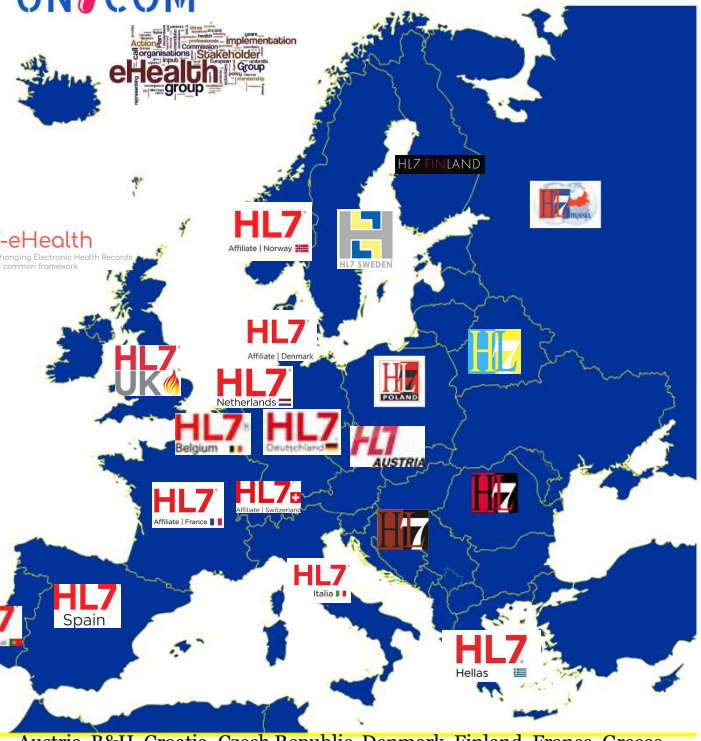
Catherine CHRONAKI
Secretary General, HL7 Europe
Past President, EFMI

chronaki@HL7europe.org

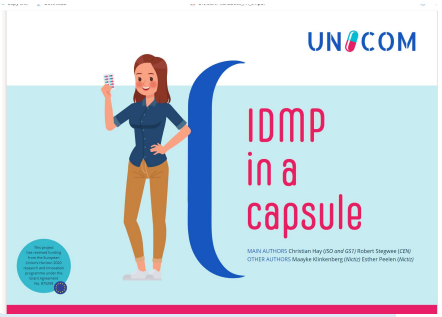
HL7 Vision A world in which everyone can securely access and use the right health data when and where they need it.

HL7 Europe

- HL7 the best and most widely-used eHealth standards since 1986
  - HL7 v2, Clinical Document Architecture, HL7 FHIR
  - 22 National Affiliates in Europe (~35 wordwide)
  - European HL7 foundation established in 2010
- European Funded Research Projects
  - Past: eHGI, Antilope, Semantic Healthnet, Trillium Bridge, Expand, ASSESS CT, OpenMedicine, eStandards,Trillium-II
  - Current: Gatekeeper, FAIR4Health; mHealthHub, UNICOM,
  - Annual HL7 in Europe Newsletter
  - Website: www.HL7.eu
- eHealth policy & Research
  - EU eHealth stakeholders (2012-ENISA expert grp
  - EFMI council (2012-): EFMI Board (2016-)
  - HIMSS Europe – PIE, CEN/TC251
  - Digital Health Society
- SDO Joint Initiative Council



Austria, B&H, Croatia, Czech Republic, Denmark, Finland, France, Greece, Germany, Italy, Netherlands, Norway, Poland, Portugal, Slovakia, Romania, Russia, Slovenia, Spain, Sweden, Switzerland, UK, Ukraine



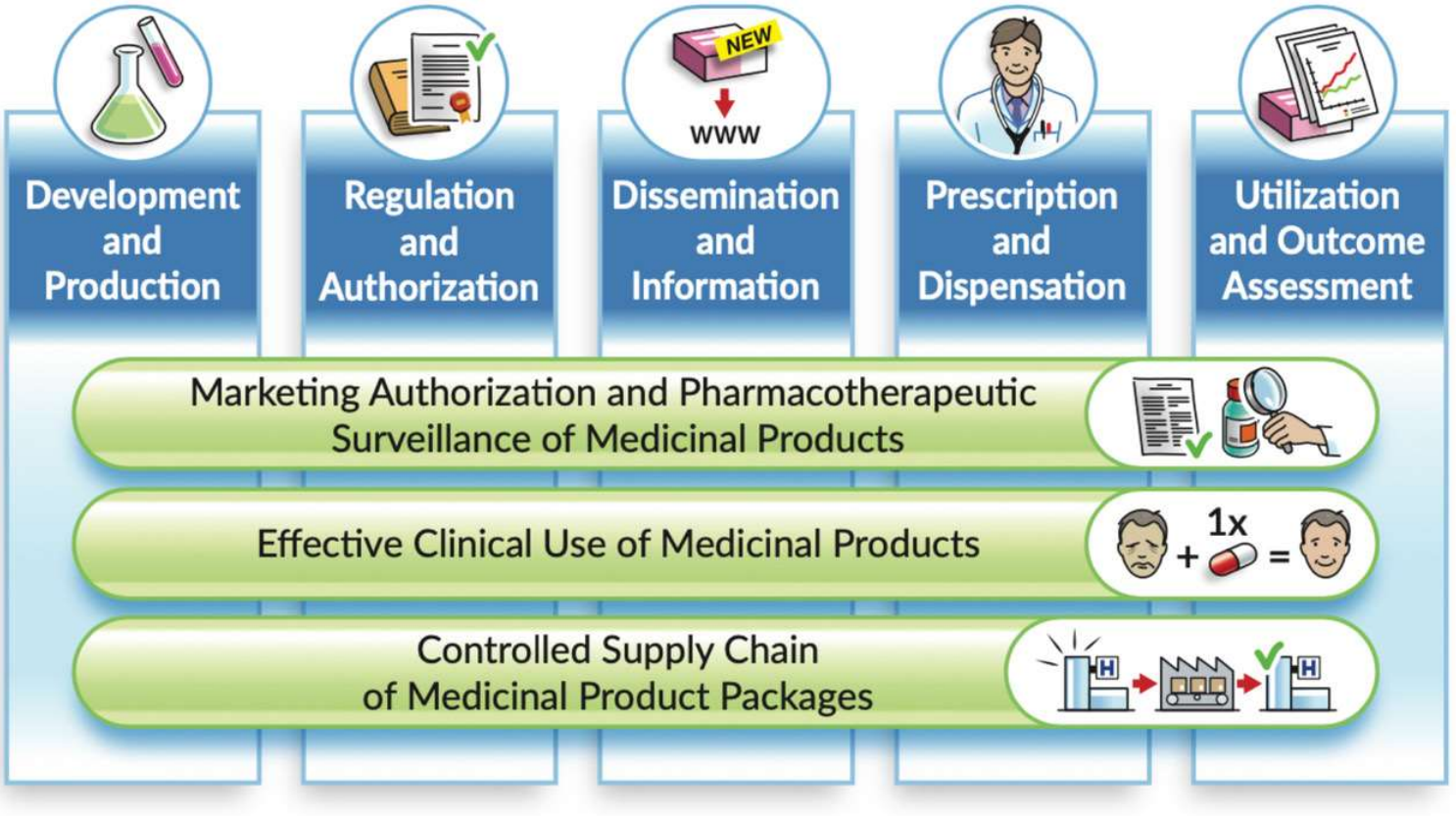
Goals, Activities, IDMP Implementation Challenges

Vision: Improving patient safety and Facilitating better healthcare for all

Mission: Enabling the univocal identification of medicinal products by supporting and accelerating the further development, implementation, and diffusion of ISO IDMP standards (IDentification of Medicinal and pharmaceutical Products) across European health systems, to facilitate the free flow of semantically coded interoperable medicinal product information

Duration: Dec. 2019 – May 2024, Budget: € 21 m; European Commission funding is € 19M, www.unicom-project.eu

UNICOM Supports IDMP Use cases across the medicinal product lifecycle



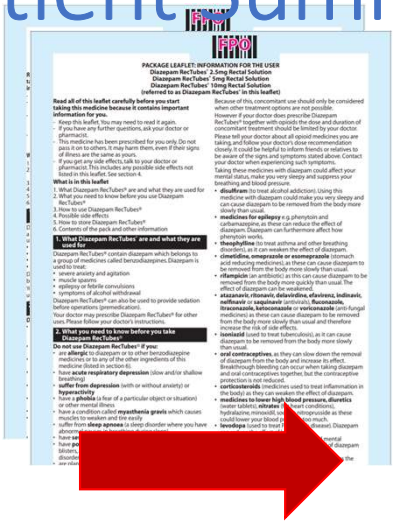
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 875299

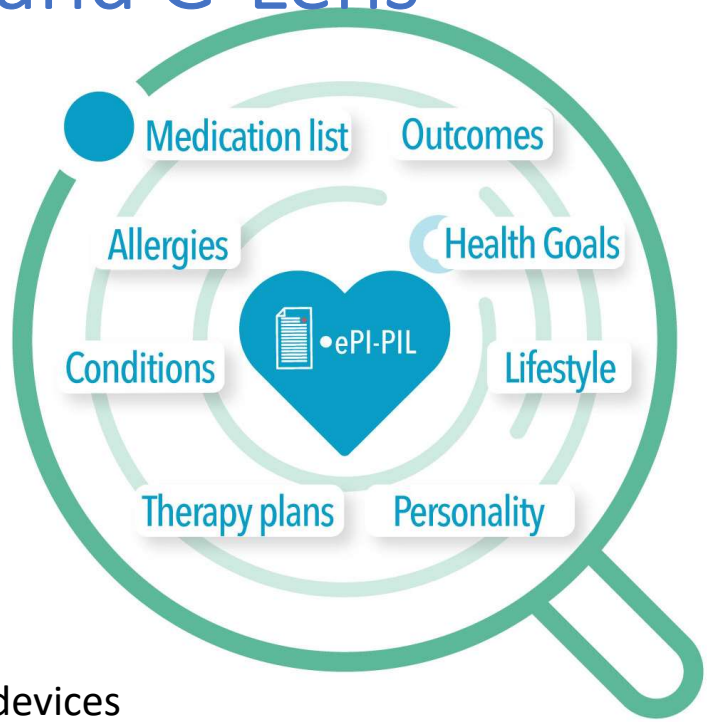
Gravitate Health

Gravitate – Health

Empowering and Equipping Europeans with Health Information for Active, Personal Health Management and Adherence to Treatment

International Patient Summary and G-Lens





- Think of the Patient summary as a window to a person's health or dashboard to get:
  - Medications, allergies, vaccinations, problems and procedures,
  - labs, diagnostic imaging, recent or planned encounters, implantable devices
  - advance directives
- For Gravitate Health it offers the lens to focus on the contents of the medication leaflet

Vision: 80% of the labels digital by 2025
while moving towards a global HL7 FHIR eLabeling/ePI Standard

Global IDMP Working Group

Gravitate-Health has helped connect key initiatives and foster collaborations globally, building on developments in the EU to drive quickly towards a global HL7 FHIR ePI standard

EU ePI Common standard and global use via Vulcan Core ePI

	EU ePI - FHIR Resource Names[1]
1	List
2	Bundle
3	Composition
4	Binary
5	Organization
6	RegulatedAuthorization
7	MedicinalProductDefinition
8	PackagedProductDefinition
9	AdministrableProductDefinition
10	ManufacturedItemDefinition
11	Ingredient
12	ClinicalUseDefinition
13	Substance

[1] Rows 1 to 4 make up the core of EMA's ePI. The ePI cross references out to SPOR, which can provide data of rows 5 to 13. Product data are from PMS, one of the 4 SPOR services.

	Vulcan ePI - FHIR Resource Names[2]
1	List
2	Bundle
3	Composition
4	Binary
5	Organization
6	RegulatedAuthorization
7	MedicinalProductDefinition
8	PackagedProductDefinition
9	AdministrableProductDefinition
10	ManufacturedItemDefinition
11	Ingredient
12	ClinicalUseDefinition
13	Substance

[2] Vulcan ePI is managed as a single self-contained document.

STATEMENT OF COLLABORATION TO SUPPORT THE EU EPI COMMON STANDARD

We are excited to share a joint Gravitate Health - European Medicines Agency (EMA) statement about our collaboration and alignment regarding the EU ePI Common Standard, announced on August, 15th 2022.

Gravitate Health is an IMI funded Public-Private Partnership seeking to empower patients and their support network with better access to trustworthy, up-to-date information that better meets their individual needs. We will develop the Gravitate Lens (G-lens®), which will focus and present relevant information content, and central is use of approved electronic product information (ePI).

Interoperability standards based on HL7 FHIR resources will be an important enabler for progress on the G-lens®, to provide interoperable and standardized means of exchanging trusted product information between digital tools. Within Europe, Gravitate Health will be using and testing the recently adopted FHIR-based EU ePI Common Standard in multiple user scenarios.

- The VULCAN Profile is completely aligned with EU ePI Common Standard, both use FHIR Lists, Bundles, Composition to represent PI documents
- The EU ePI Common Standard includes a link to SPOR (master data system for EU medicines)
- To enable global use for regions without SPOR, VULCAN Profile has option to include data directly

Cross-project collaboration: Global HL7 FHIR ePI/eLabeling

- **Innovative Medicines Initiative (IMI) - Gravitate-Health**
  - 40 partners in Europe and USA; 60 months 11/20 – 10/25; €18.5m
  - Delivering the Gravitate Lens (G-Lens) which focuses on ePI content and offers patients access to trustworthy, up-to-date information that better meets their individual needs
- **HL7 Vulcan - FHIR Accelerator Program**
  - Designed to facilitate the creation and adoption of FHIR Implementation Guides (& related standards) that support global health data interoperability
- **HL7 Biomedical Research and Regulation (BR&R)**
  - Creates standards that facilitate biomedical research and any subsequent regulatory evaluation of the safety, efficacy and quality of medical products.
- **Univocal Identification of Medicinal Products (UNICOM)**
  - UNICOM aims to advance implementation of ISO IDMP (ID of Medicinal Products) standards in EU Member States drug databases to support safe cross-border ePrescription/eDispensation and effective pharmacovigilance.
  - 19 countries are represented, including 26 national Drug and eHealth Agencies. budget € 21 MEuros.
- **H2O IMI Project: Health Oucomes Prepository**
- **European Medicines Agency:**
- https://www.gravitatehealth.eu/statement-of-collaboration-to-support-the-eu-epi-common-standard/

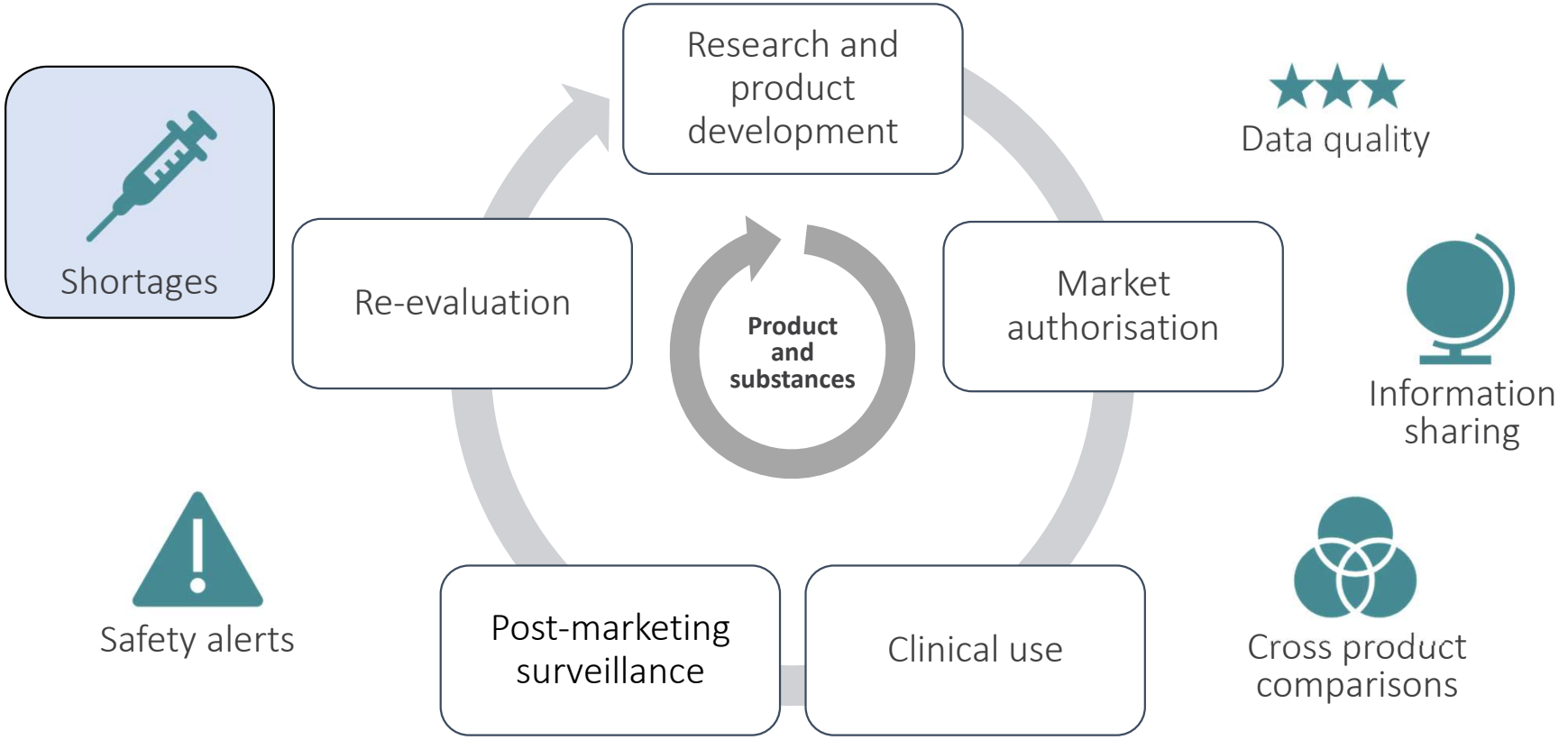
Gravitate-Health Activities 2024 – indicative timeline and deliverables

‘Nordic ePI’ +1 (emc) model, from January 2024

- **Activity:**
  - Harmonizing – strategy for conversion of PIL to ePI; XML – FHIR ePI IG
    - Nordic article numbers
    - PhPID, MPID → multi-lingual, cross border and larger markets
    - Metadata – “tagging” for focusing, support for part of production and regulatory process
  - Procedures – processes for managing updatesm, changes
- **Scope**:
  - ePI in FHIR IG – 5 languages; Norwegian, Swedish, Danish, Finnish, English, with ePI for selection of medicines for IBD, DIA, COPS+, including updates of changes
- **Deliver by end of Q2, 2024:**
  a) Repository of interoperable - ePI in Nordic languages + 1 - will be “G-lens” ready
  b) Methodology – common approach – to ePI conversion, updates / maintenance
  c) Contribute to report - input and experiences to the Gravitate-Health sustainability planning

Objective of GIDWG End-to-End HL7 FHIR Testing

Benefits of IDMP in the medicinal product life cycle

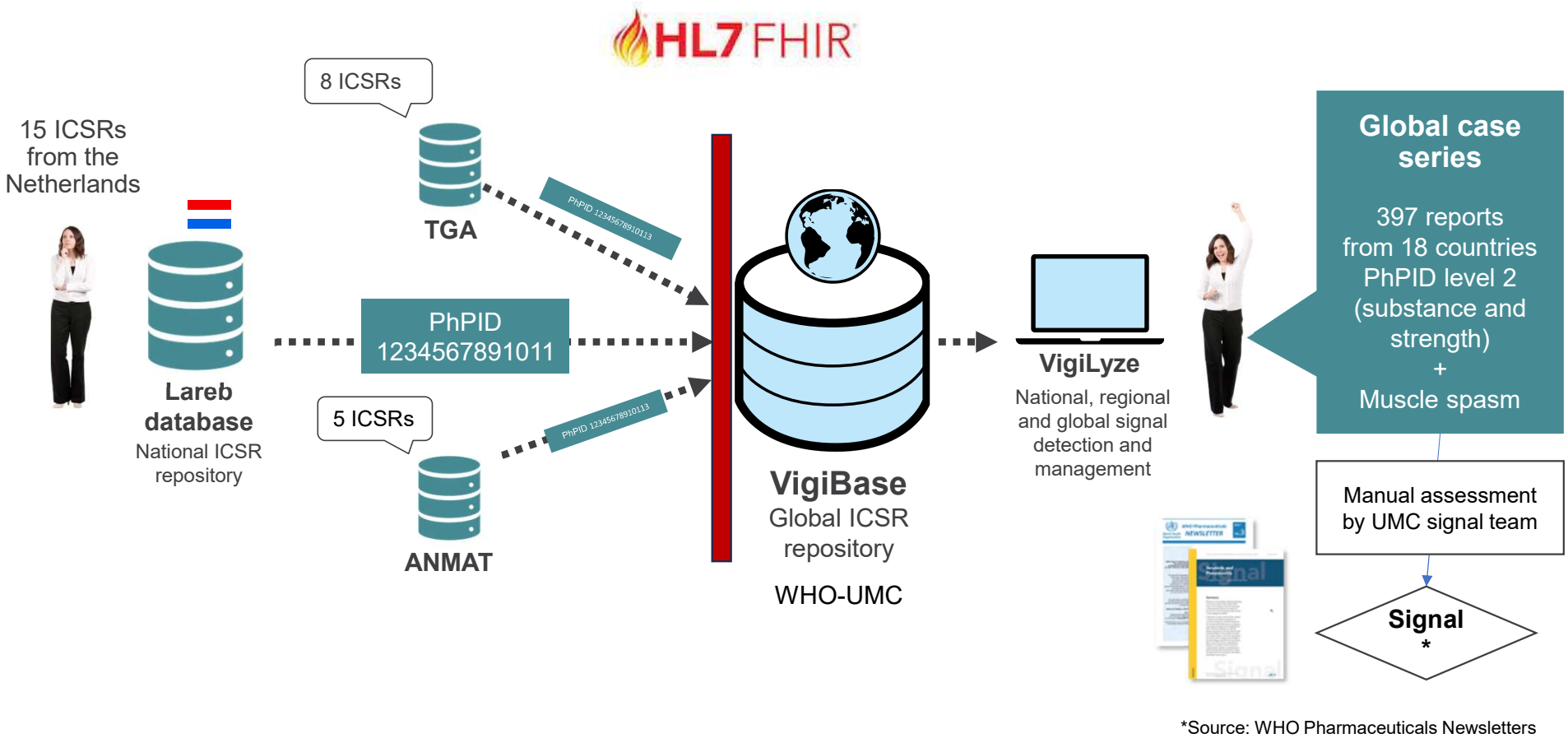


GIDWG End-to-End Testing Plans 2024

- Pharmacovigilance
- Shortages
- Cross-Border Healthcare

1. GIDWG End-to-End Testing in PhV for HL7 FHIR Connectathon:

Example for 2024



*Source: WHO Pharmaceuticals Newsletters

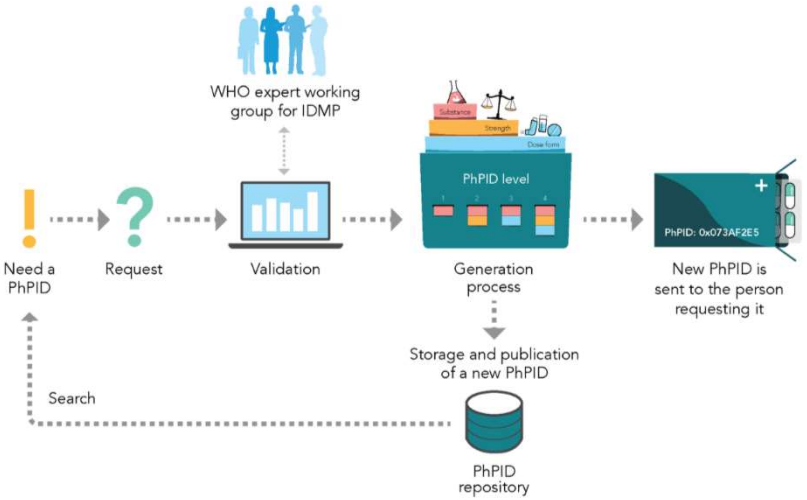
2. GIDWG End-to-End Testing in Shortages for HL7 FHIR Connectathon:
Example for 2024

Global IDMP Working Group

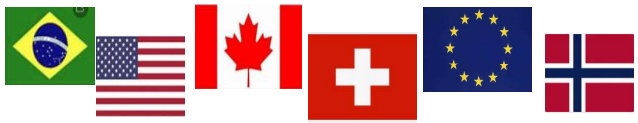
Testing to demonstrate the use cases for GSID/PhPID operating model

SCOPE:

- Validate and generate PhPIDs for products based on the GIDWG/EWG business rules
- EDQM + non-EDQM countries
- Similar products from different countries
- Larger batches & smaller **data sets** for regulators
- Validated Data Sets based on **150 substances** including Chemicals, Biosimilars, Polymers, Nucleic Acids, Structure Divers, 'Mixtures'



Proposed candidate countries:



3. GIDWG End-to-End Testing in Shortages for HL7 FHIR Connectathon :

Example: If we had a global PhPID from Japan to US…

Objective for 2024 HL7 FHIR Connectathons:

- engaging with Pharmacy and EHR system vendors to integrate the lookup of PhPIDs
- test the FHIR API spec also with the UNICOM substitution component for MyHealth@EU

If Global PhPID level 4 is luckily available in the Japanese prescription, a Japanese citizen, can now holds out the prescription confidently, a bridge between languages and cultures. Therapy compliance is successfully ensured preserving patient's health.

Pushing the ISO/IDMP envelop one HL7 FHIR Connectathon at a time…

- GIDWG 2024 End-to-End testing workplan:
  - Athens, Greece 16-18 January 2024
  - Dallas, TX, USA, May 18-24, 2024
  - Atlanta, GA, USA, September 21-27, 2024
- IDMP business use cases in:
  - Pharmacovigilence
  - Shortages
  - Cross Border Use Cases
- For more information:
  - https://who-umc.org/idmp/gidwg-working-group/

HL7 Europe Working Group Meeting

HL7 FHIR CONNECTATHON

HOSTED BY HL7 Hellas

Amsterdam

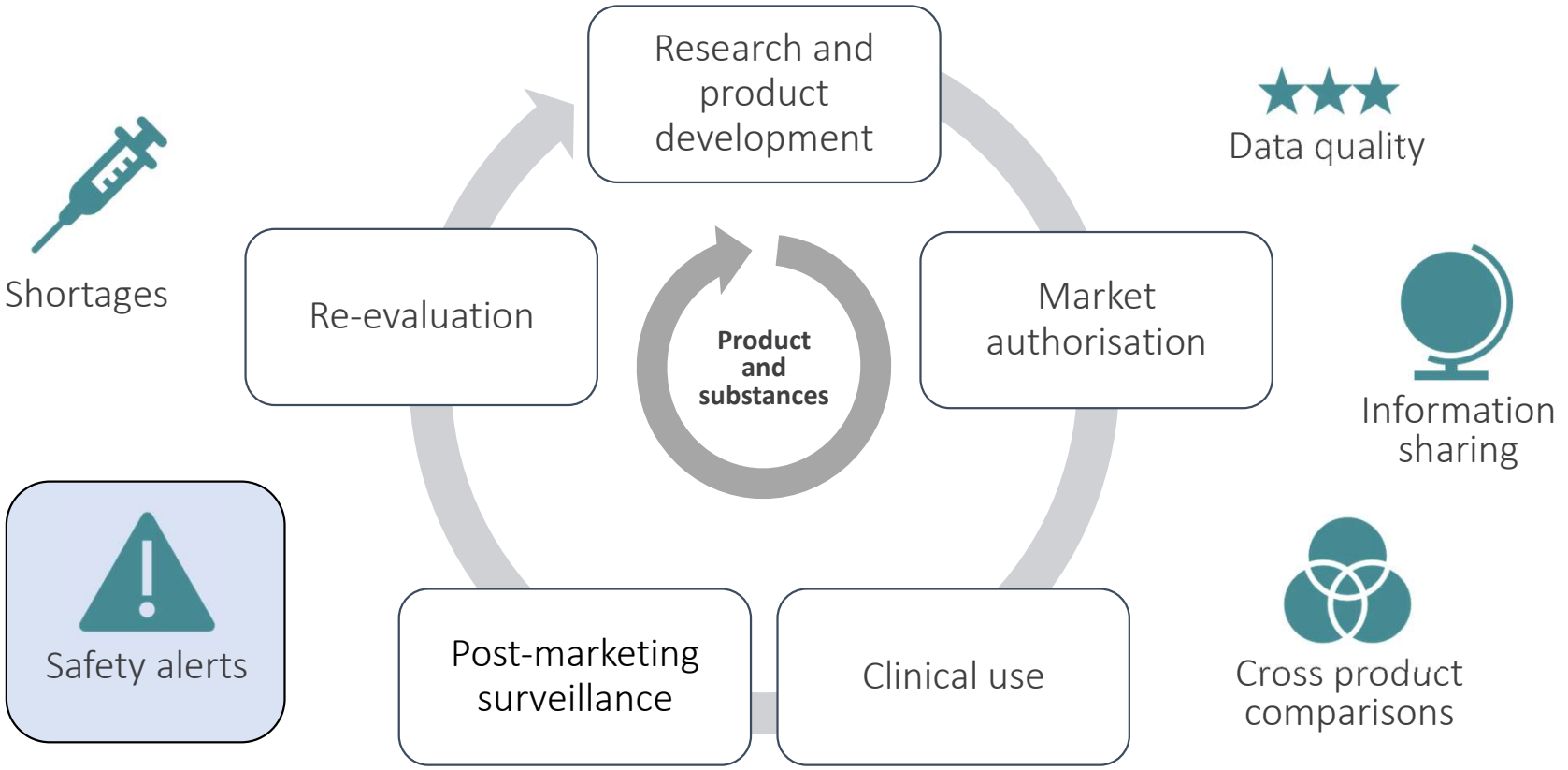
Global IDMP Working Group

Thank you

GIDWG End-to-End Use Cases
Pharmacovigilance

Malin Fladvad(UMC)

Benefits of IDMP in the medicinal product life cycle



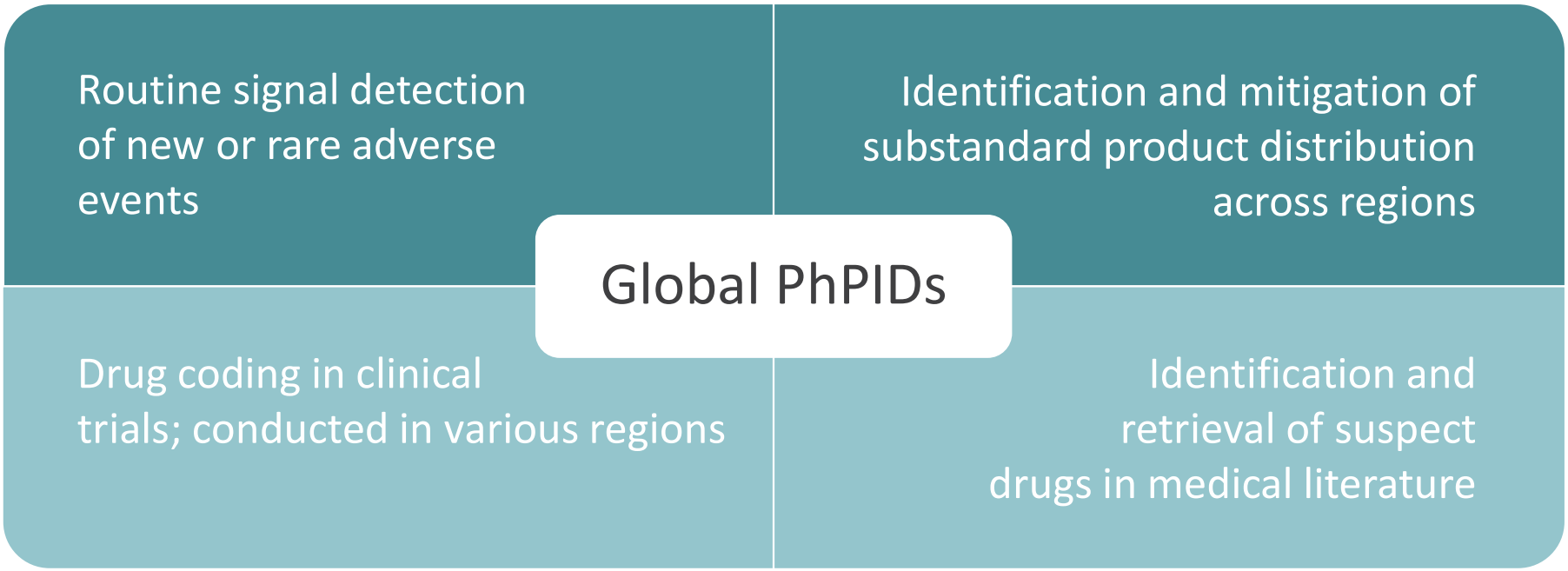
Global IDMP Working Group

Showcase how global Pharmaceutical Product Identifiers (PhPIDs) support faster and more accurate identification of global safety issues

Enabling interoperability at global level

Global IDMP Working Group

Overview of use cases in pharmacovigilance where global PhPIDs would add value



Global IDMP Working Group

Routine signal detection of rare adverse events

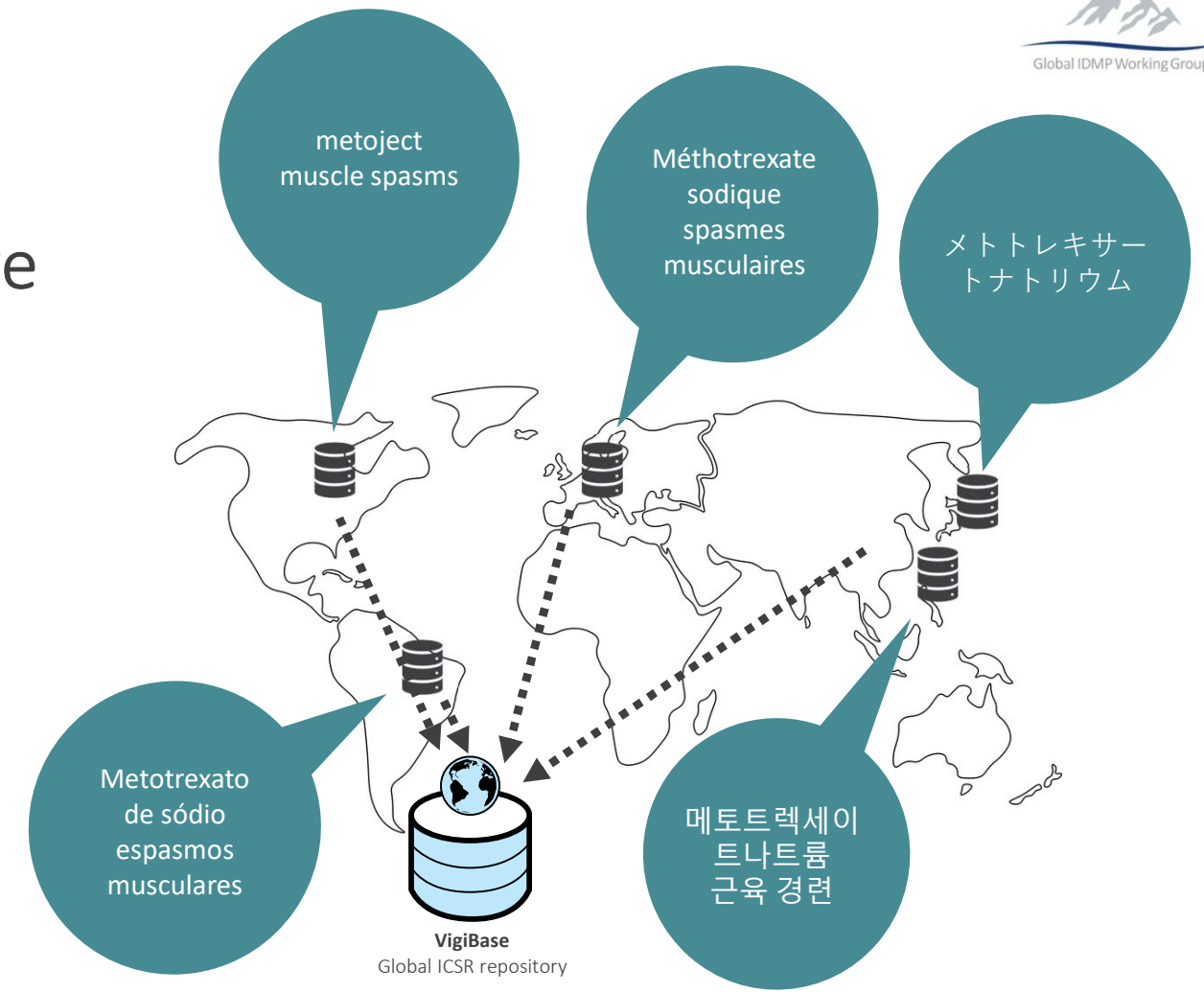
Muscle spasms associated with methotrexate

Methotrexate was delivered via a single-dose pre-filled pen – 15 mg once a week for the treatment of rheumatoid arthritis.

“The intensity of this ADR was described as very intense. Disabling and painful arm or leg pain, with varying frequency, 1 to 3 times a day.”

Spontaneous reports contain local language

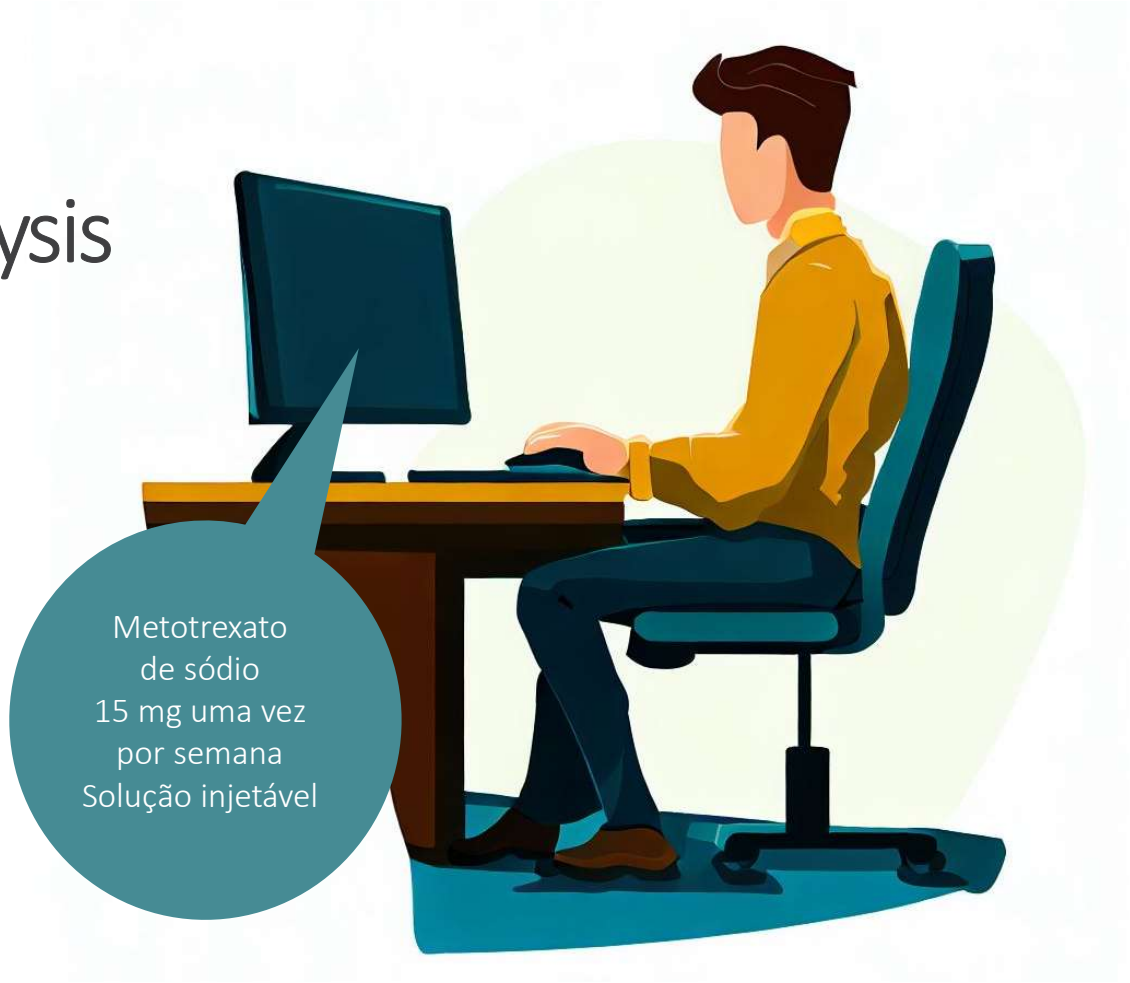
Similar reports are received at various national centres globally, including the Netherlands, US, Canada, Brazil, and Republic of Korea. The information is received in digital format and contains local language in free text data elements.



*https://who-umc.org/vigibase/

Different terminology used for regional analysis

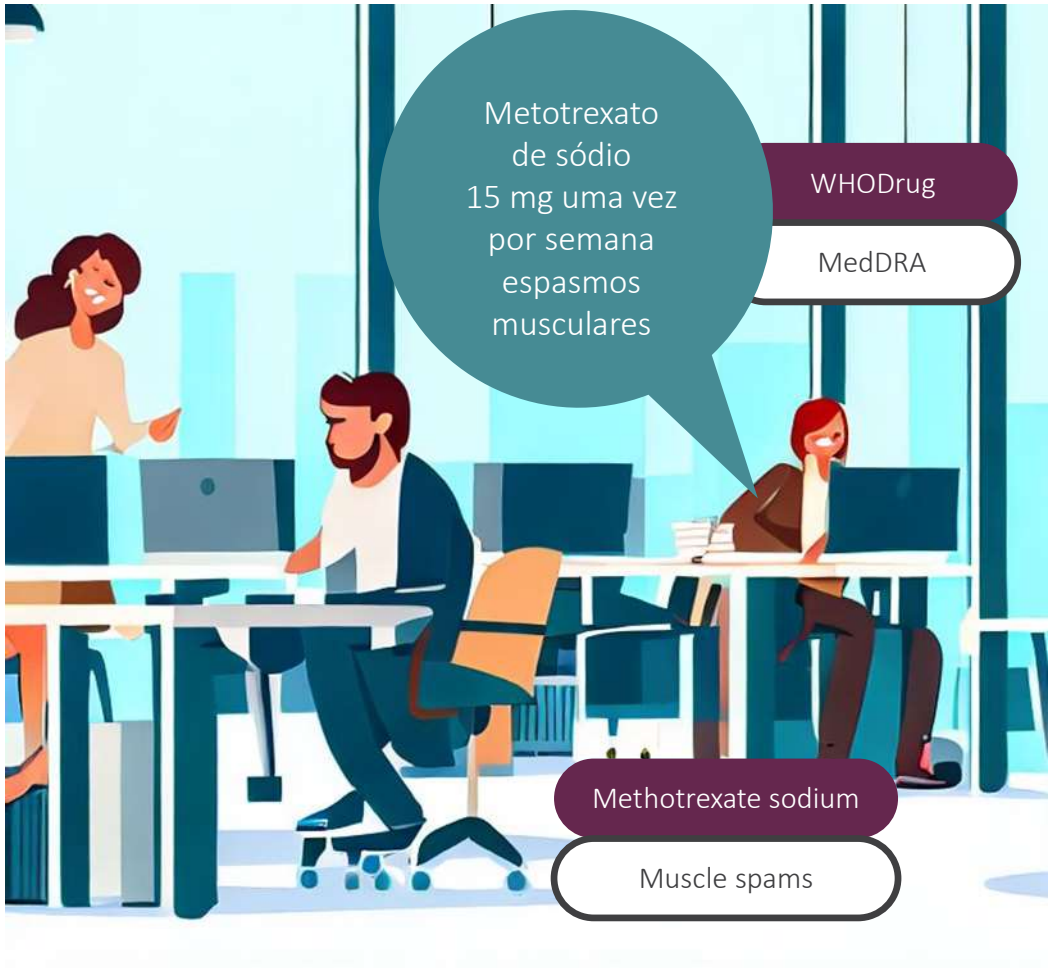
ICSRs undergo standard regional coding to facilitate analysis at each respective Pharmacovigilance centre, highlighting variations in coding standards across countries (Netherlands, Brazil, Republic of Korea, Canada and US).



Additional recoding to global standards at UMC

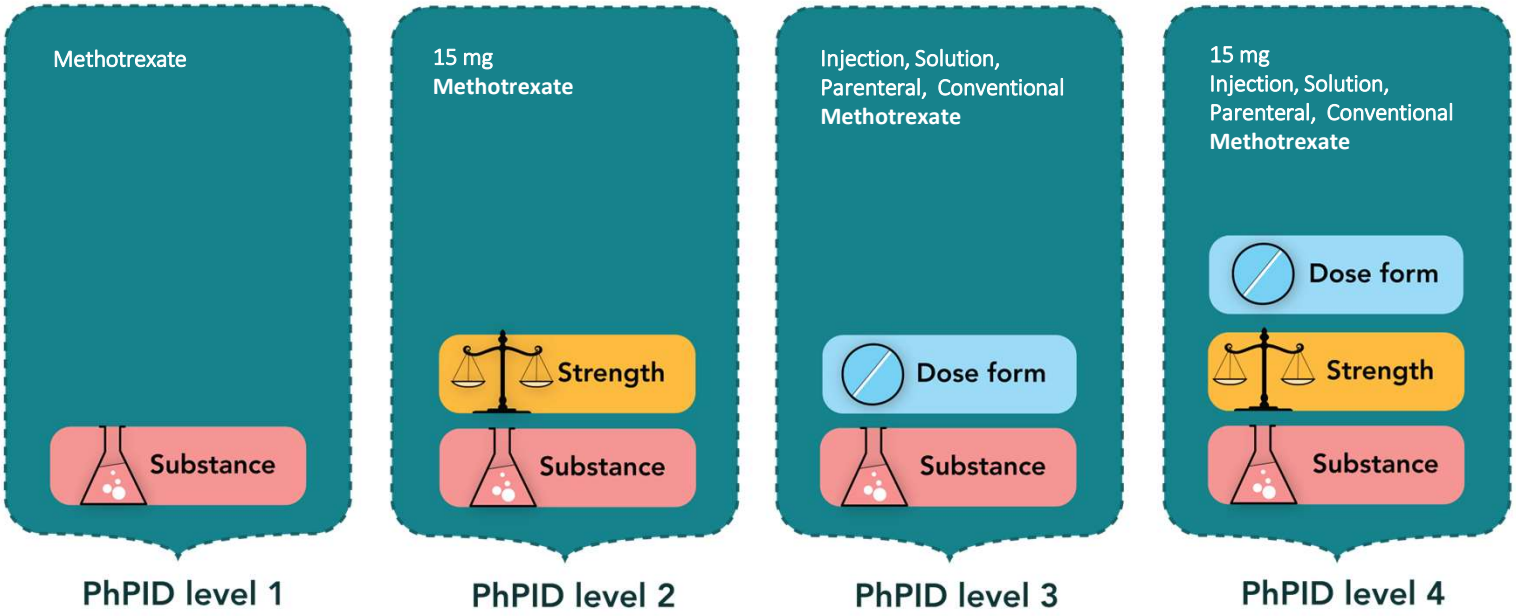
UMC receives these ICSRs continually in VigiBase, WHO's global database of potential side effects of medicinal products.

Manually recoding to a global standard with WHODrug potentially delays analysis.

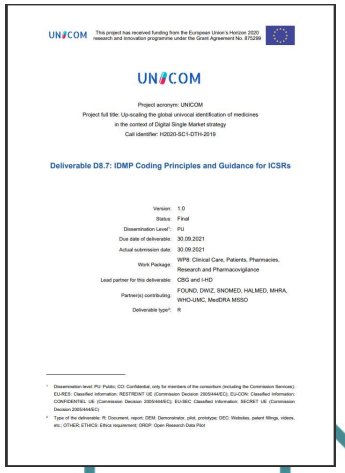


Global IDMP Working Group

What if we had global PhPIDs?



If products were assigned to global PhPID standards, each product name would automatically be linked to active ingredient, strength, dose form.



UNICOM

Project acronym: UNICOM

Project full title: Up-scaling the global univocal identification of medicines in the context of Digital Single Market strategy

Call identifier: H2020-SC1-DTH-2019

Deliverable D8.7: IDMP Coding Principles and Guidance for ICSRs

Version: 1.0
Status: Final
Dissemination Level*: PU
Due date of deliverable: 30.09.2021
Actual submission date: 30.09.2021
Work Package: WP8: Clinical Care, Patients, Pharmacies, Research and Pharmacovigilance
Lead partner for this deliverable: CBG and I-HD
Partner(s) contributing: FOUND, DIWZ, SNOMED, HALMED, MHRA, WHO-UMC, MedDRA MSSO
Deliverable type**: R

* Dissemination level: PU: Public, CO: Confidential, only for members of the consortium (including the Commission Services); EU-RES: Classified information: RESTREINT UE (Commission Decision 2005/444/EC); EU-CON: Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC); EU-SEC: Classified Information: SECRET UE (Commission Decision 2005/444/EC)

** Type of the deliverable: R: Document, report; DEM: Demonstrator, pilot, prototype; DEC: Websites, patent filings, videos, etc.; OTHER; ETHICS: Ethics requirement; ORDP: Open Research Data Pilot

Global IDMP Working Group

ICSRs with heterogeneous information are coded to PhPIDs

Metotrexato de sódio 15 mg uma vez por semana Solução injetável

PhPID Level 4

Méthotrexate sodique; AUTO-INJECTEUR PRÉREMPLI À DOSE UNIQUE, 10 mg/week

PhPID Level 4

Metotrexato de sódio

PhPID Level 1

메토트렉세이트 나트륨 ; 주 1회 15mg 주사 ; 주사액

PhPID Level 4

Methotrexate sodium, injections, 15 once a week

PhPID Level 4

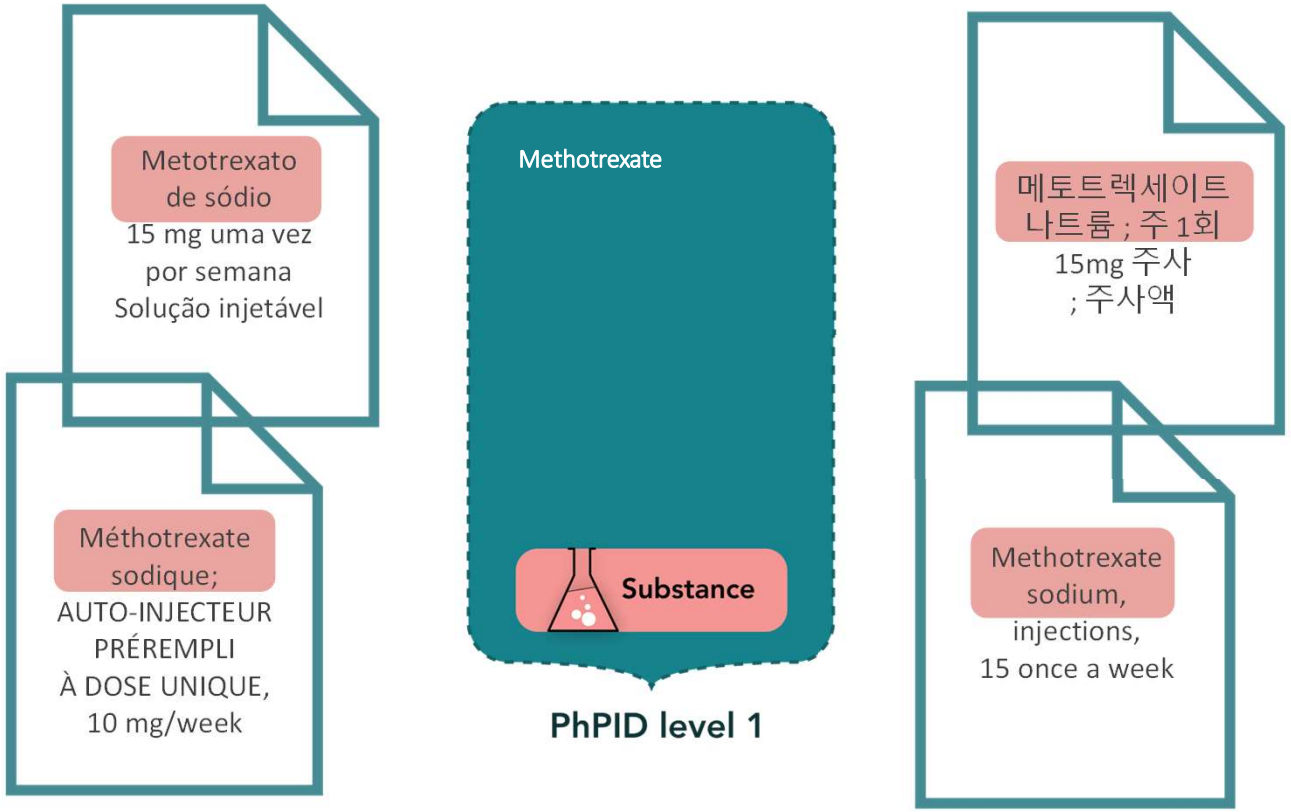
methotrexate 15 once a week

PhPID Level 2

*Deliverable D8.7: IDMP Coding Principles and Guidance for ICSRs: https://unicom-project.eu/wp-content/uploads/2022/01/UNICOM_D8.7_IDMP-coding-principles-and-guidance-for-ICSRs.pdf

Signalling with Global PhPID level 1

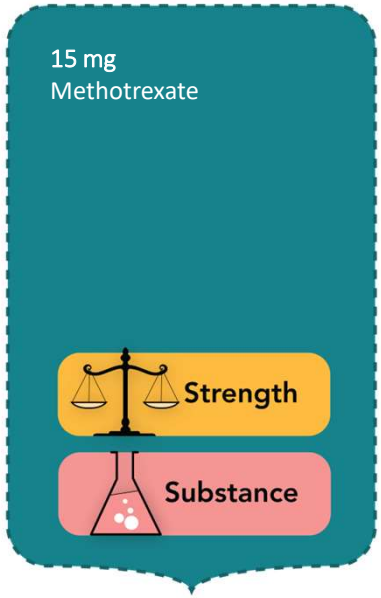
Initiating national centres' coding processes using global PhPIDs will speed up analysis and data sharing between regulators.

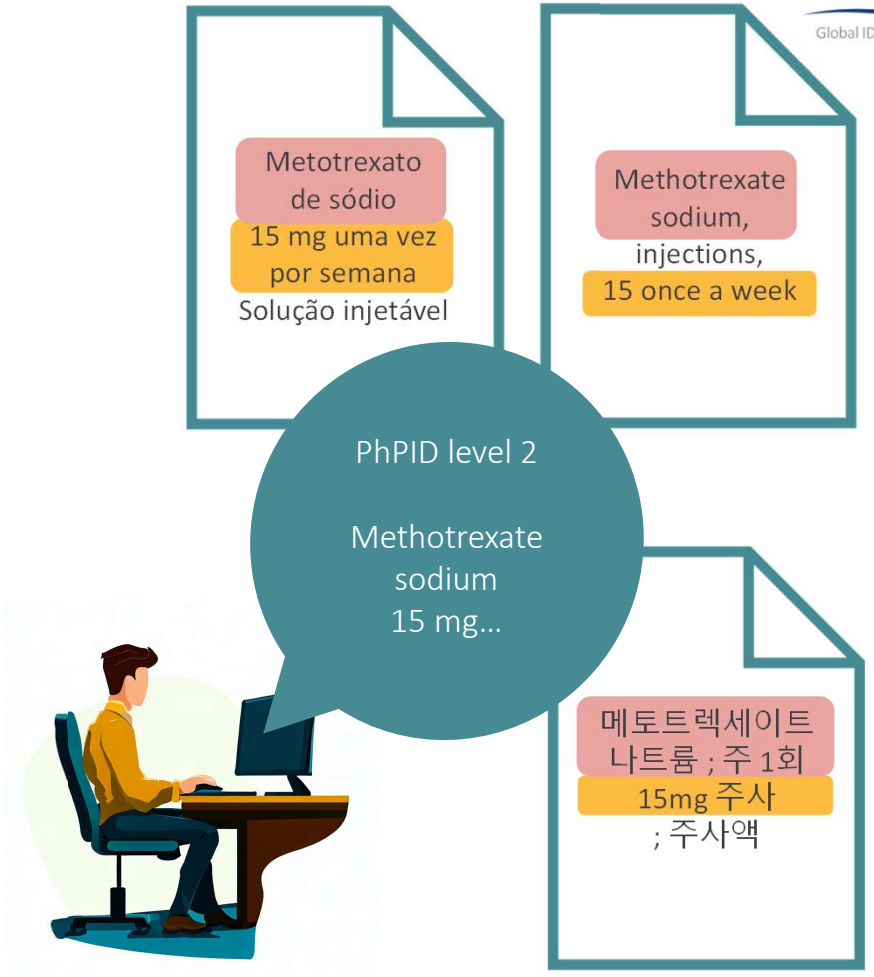


Signalling with additional Global PhPID levels

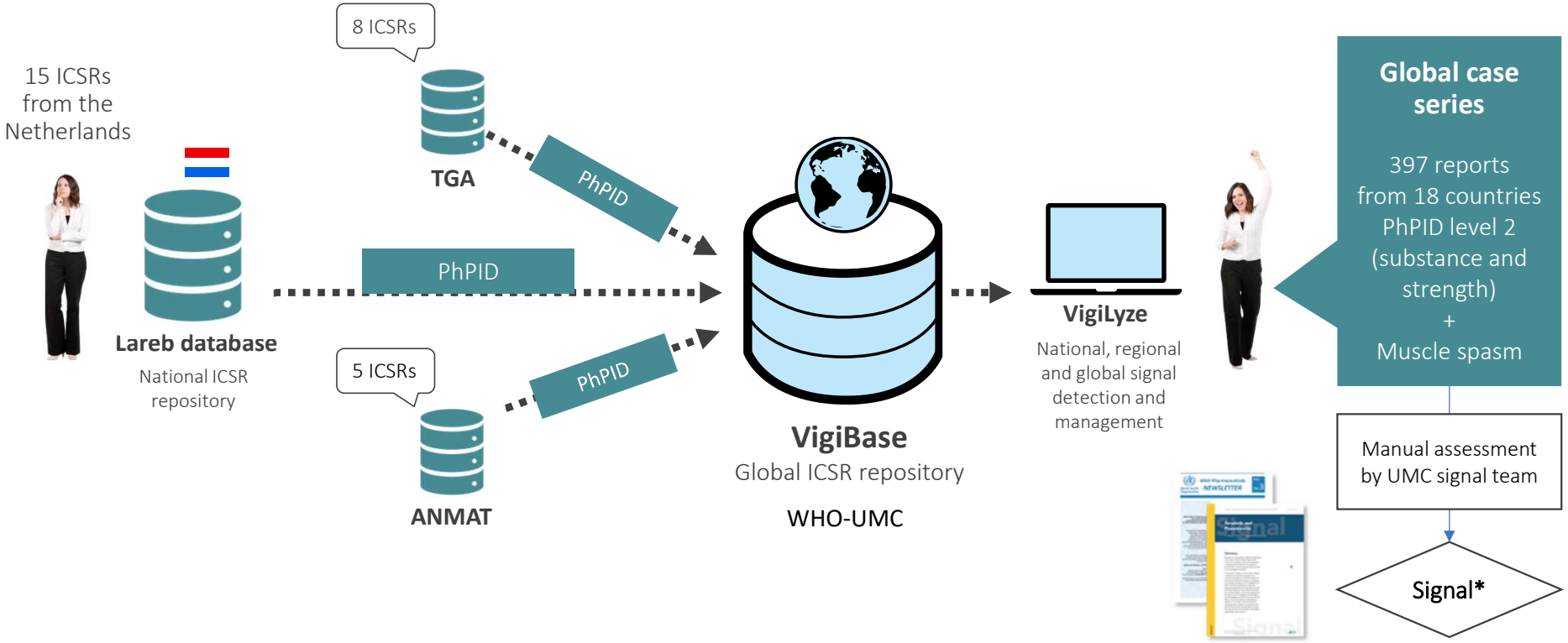
Data coded to the appropriate PhPID level when reports come in facilitates more nuanced analysis, particularly regarding strength or dose form.

This enables not only faster and more granular analysis, but also limits the number of patients harmed.





If we had global PhPIDs



*Source: WHO Pharmaceuticals Newsletters

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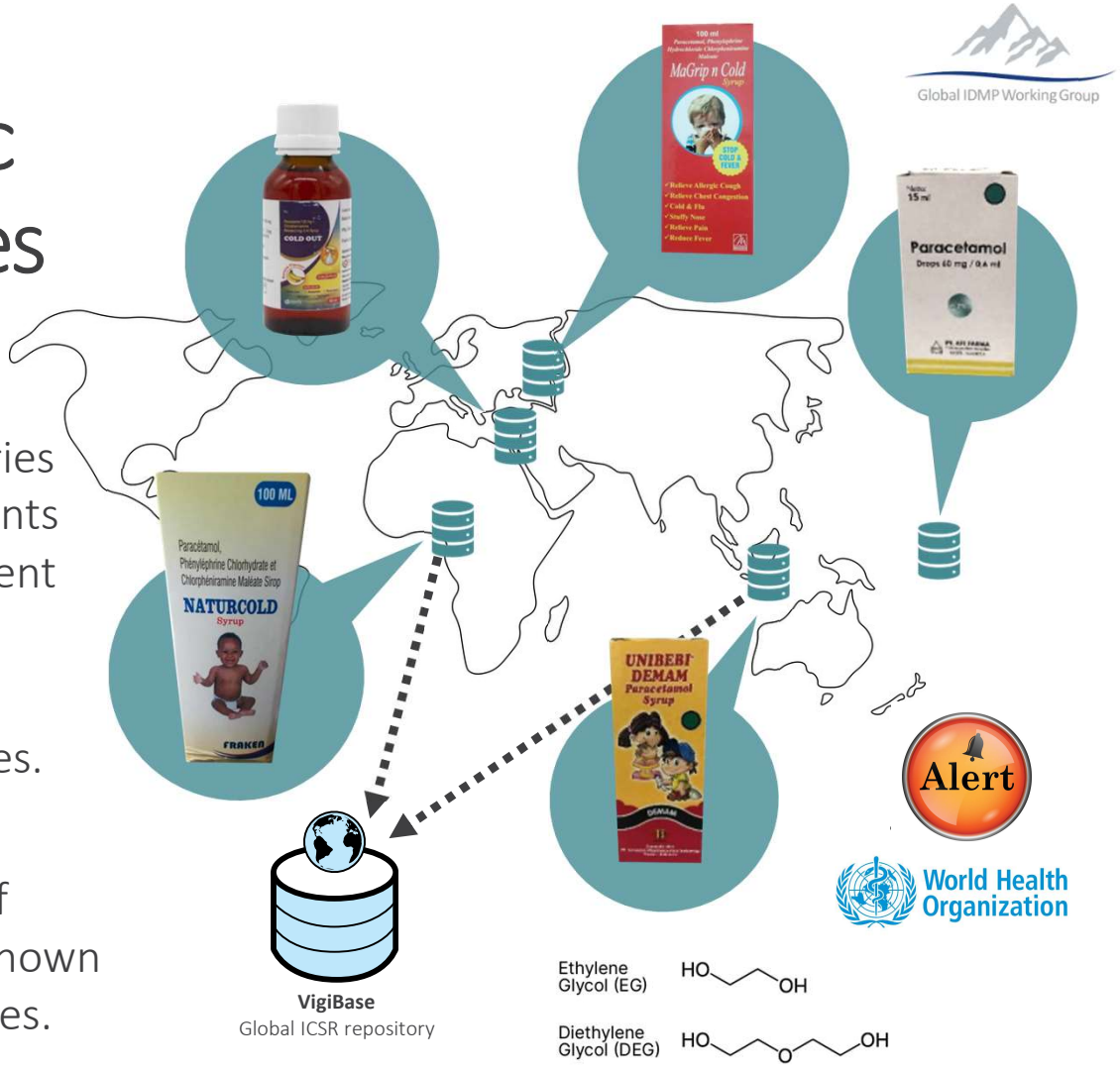
Identification and mitigation of substandard product distribution across regions

Substandard paediatric liquid dosage medicines cause fatalities

- As of January 2023, at least seven countries have reported unexpected serious incidents (adverse events) in children after treatment with over-the-counter cough and cold medications.
- More than 300 fatalities in three countries.
- Mostly children under the age of five.
- The investigation identified toxic levels of **diethylene glycol and ethylene glycol**, known to result in acute renal failure and fatalities.



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What other regions could be affected?

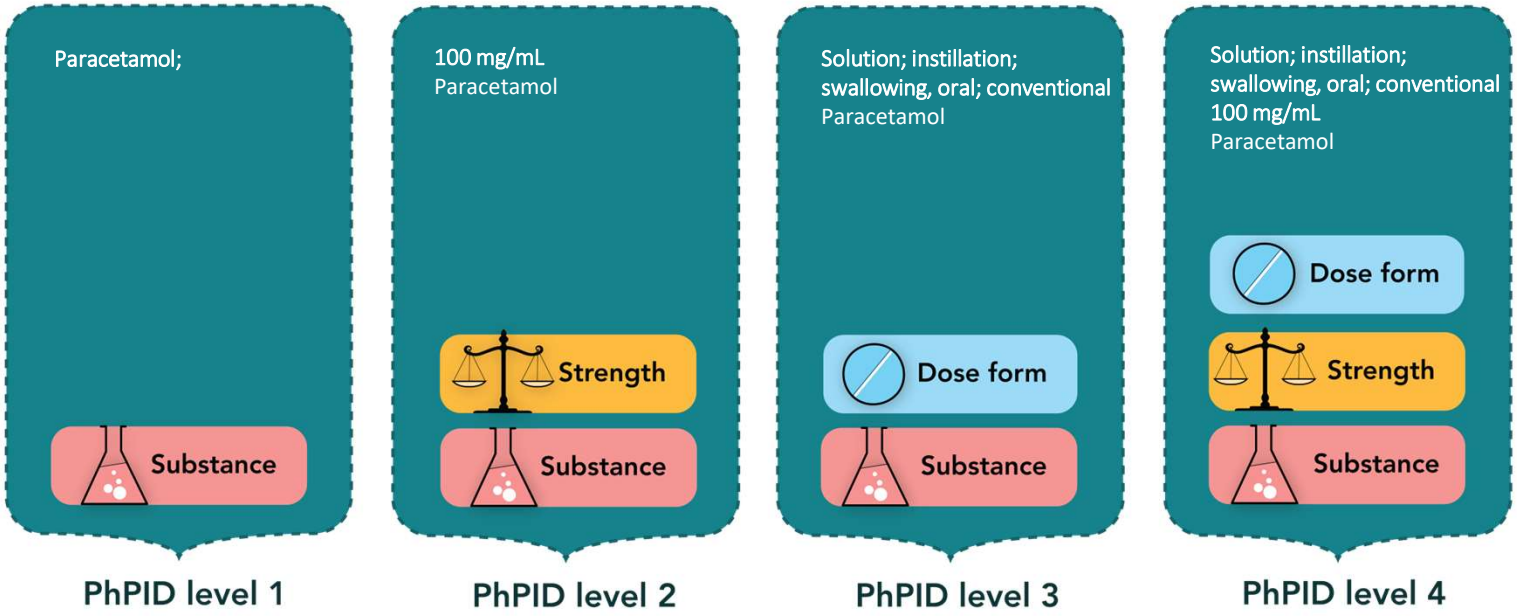
While WHO Medical Product Alerts refer to specific batches of substandard (contaminated) products Identified in a specific country, these products may have marketing authorisations in other countries or regions, or may have been distributed through informal markets to other countries.

VigiBase
Global ICSR repository

Global IDMP Working Group

What if we had global PhPIDs?

If these products were assigned to global PhPID standards, each product name would automatically be linked to active ingredient, strength, dose form.



MC0

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Signalling with Global PhPID level 1

Alert on unexpected child fatalities after treatment with paracetamol in single and multi-ingredient products

Current alert (without Global PhPID level 1) would likely be weakened by different reported product names, necessitating further investigation to determine the active ingredient(s).

MC0 Acetaminophen

Marilina Castellano, 2023-09-28T13:48:24.304

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Paracetamol-containing medicinal products globally

19635 rows

Export | CDG | Add Columns

Product Name B3	Drug Code	Active Ingredients	ATC	Country of Sales	MAH	Pharmaceutical Form	Strength
LITTLE FEVERS	000200 01 954	Paracetamol	**N02BE,** Anilides *official*	Puerto Rico • United States of America	Medtech • Medtech labs • Prestige brands • Vetco	LIQUIDS • LIQUIDS, DROPS	80 mg • 80 mg/ml
INFANTS LITTLE REMEDIES FOR FEVERS	000200 01 A0R	Paracetamol	**N02BE,** Anilides *official*	Canada	Prestige brands	LIQUIDS	80 mg/ml
ACETAMINOPHEN NAEWOE	000200 01 A3J	Paracetamol	**N02BE,** Anilides *official*	Korea (the Republic of)	Nae woi	TABLETS	80 mg
BUBDEL	000200 01 BK3	Paracetamol	**N02BE,** Anilides *official*	Taiwan (Province of China)	Winston	TABLETS	80 mg
CAUSALON [PARACETAMOL]	000200 01 212	Paracetamol	**N02BE,** Anilides *official*	Argentina	Phoenix	LIQUIDS • LIQUIDS, DROPS • SUPPOSITORIES, ADULT • TABLETS • TABLETS, CHEWABLE	80 mg
CHILDREN'S CHEWABLE ACETAMINOPHEN	000200 01 982	Paracetamol	**N02BE,** Anilides *official*	Canada	Vita health products inc	TABLETS, CHEWABLE	80 mg
CHILDRENS MAPAP	000200 01 AXR	Paracetamol	**N02BE,** Anilides *official*	Puerto Rico • United States of America	Major Pharmaceuticals	TABLETS, CHEWABLE	80 mg
CORIVER INFANTIL	000200 01 BBI	Paracetamol	**N02BE,** Anilides *official*	Mexico	Maver	TABLETS	80 mg

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Signalling with Global PhPID level 3

Global PhPID level 3 would enable identification of all medicinal products that share the same substance (paracetamol) and dose form (drops or syrup).

*products circled in blue: Solution; instillation; swallowing, oral; conventional
products circled in red: Suspension; swallowing, oral; conventional

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Global PhPID take-home message

- Quicker and reliable signalling of rare adverse events
- Data analysis can be performed at different levels of granularity globally
- Real-time identification of unexpected serious adverse events/incidents in PV databases thanks to global standards
- **Effective alert communication to stakeholders**
- Immediate generation of accurate safety data for further investigation by regulators for evaluation and regulatory action

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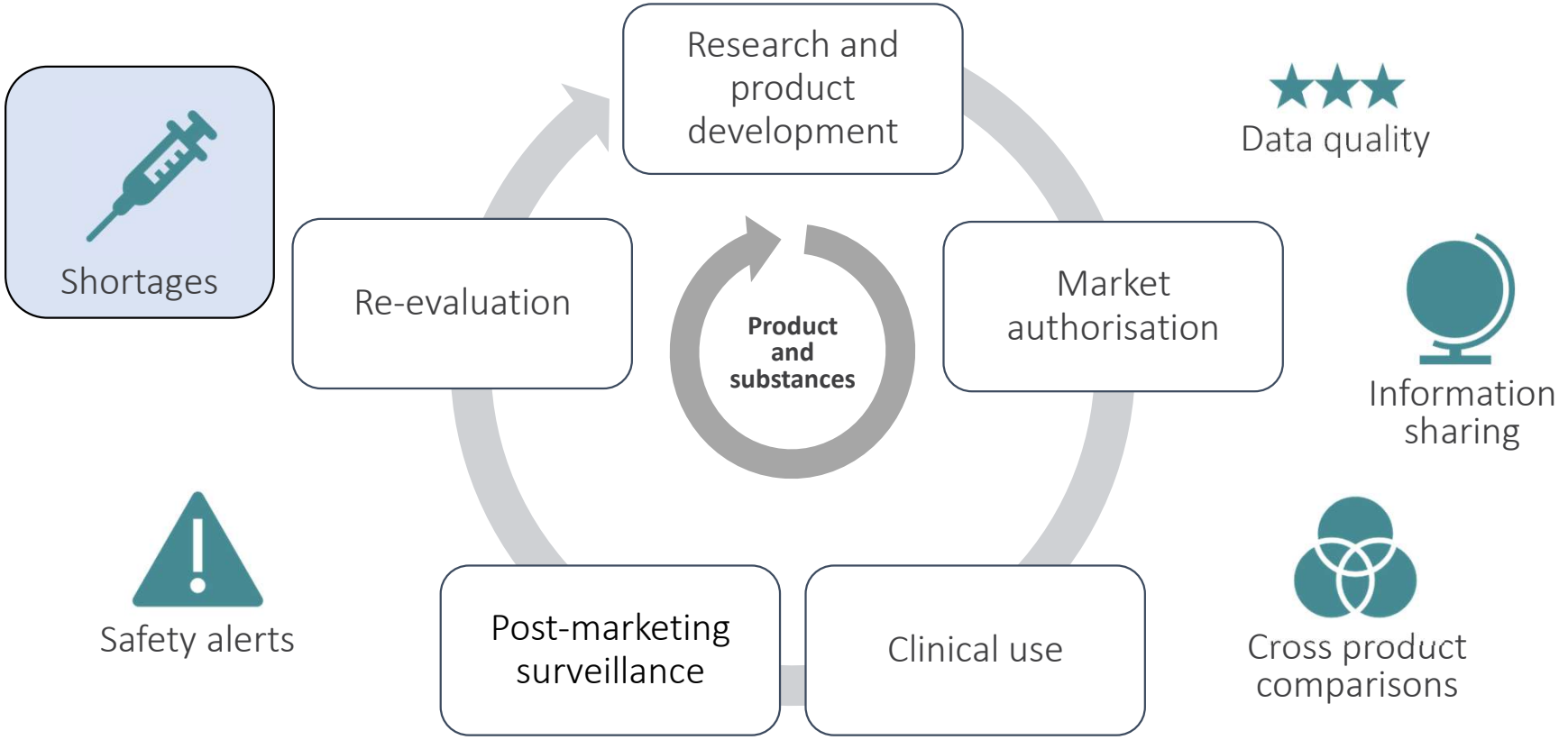
GIDWG End-to-End Use Cases
Drug Shortages

Ron Fitzmartin (FDA)

Benefits of IDMP in the medicinal product life cycle



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Cisplatin Shortage in the U.S.

Global PhPIDs may increase the speed and process for the identification of foreign substitutes

Cisplatin

- To treat a wide range of cancers, including breast, ovarian, throat, lung, testicular, prostate and colorectal cancers.

- For many cancer patients it is the standard of care.

Healthcare demand outstrips MAH's cisplatin supply

A quality-related manufacturing halt at one of the primary foreign production facilities for cisplatin with a US FDA approval causes a ripple effect[1,2].

Other approved marketing authorisation holders (MAHs) are unable to meet the demand for this product.

Regulatory agencies informed of cisplatin shortage

MAHs notify regulatory agencies of the shortage.

Regulators cannot require MAHs to increase production of a drug to meet demand.

Cisplatin shortage investigated

- Once notified regulatory response is swift
  - Initial outreach to approved/pending US application holders.
  - Outreach to other international jurisdictions.
- 3 potential non-US approved products identified.

Challenges:

- ✓Quantity available
- ✓Different strength
- ✓Lack of prospective US distributors
- ✓Time for proposal submission

Shortage communicated to stakeholders

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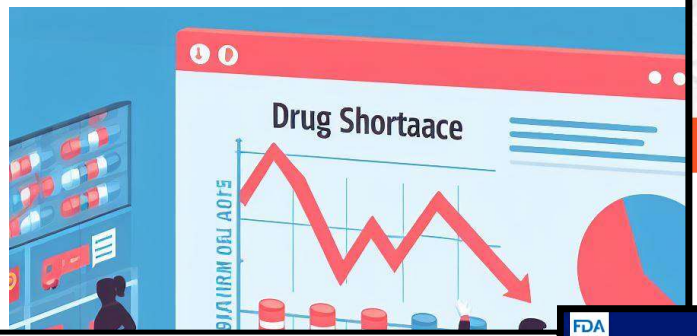
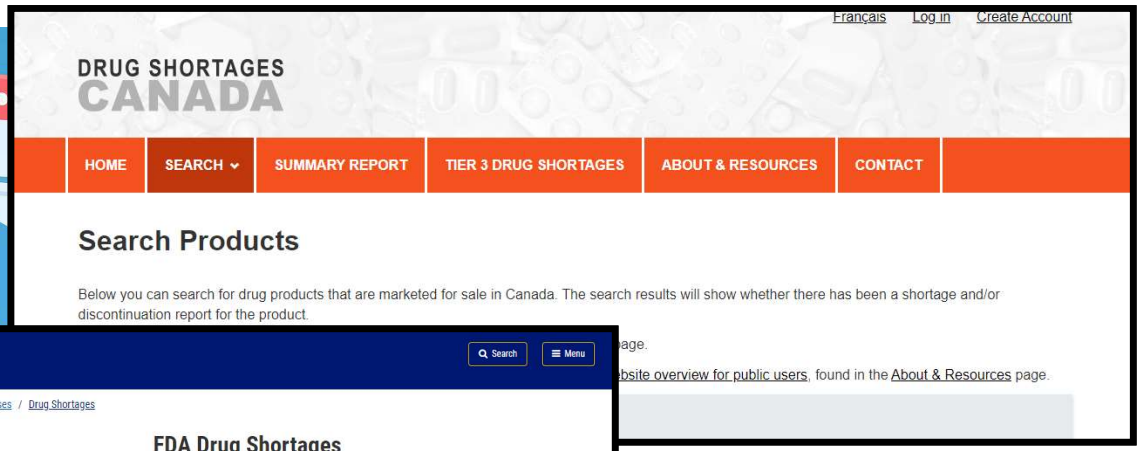
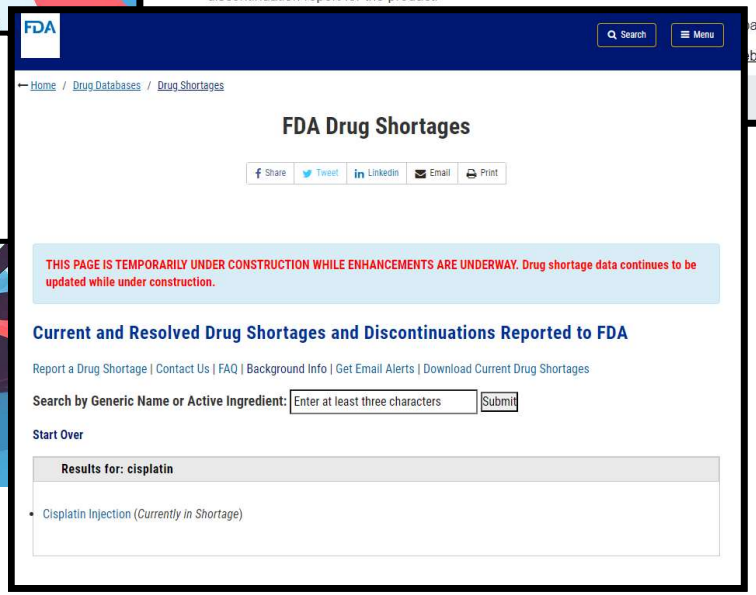


Cisplatin U.S. Drug shortage:
Date first posted:
February 2023



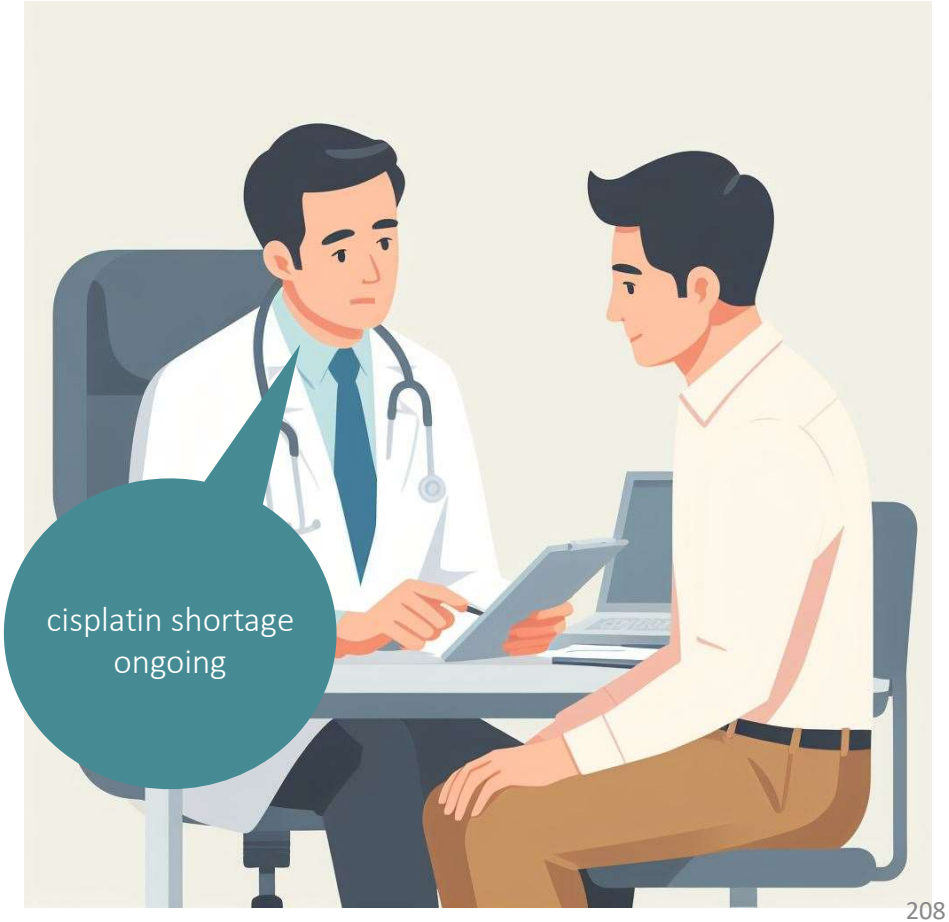


Cancer patient unable to start therapy

March 2023

Stage 3 cancer patient informed by his doctor that he will not be able to commence treatment with cisplatin due to an ongoing shortage.

70% of healthcare centres acknowledged a shortage of cisplatin[3].



Impact of cisplatin shortage

The cisplatin shortage potentially affects **100,000- 500,000 patients** annually[2].

Consequences may include treatment delays, dose adjustments, and transitions to alternative therapies. Such alterations increase the risk of medication errors and adverse events[4].

Challenges and time delay in finding an alternative

- Regulatory action is prompt.
- However, identification of non-US substitutes is challenging and **time** consuming.

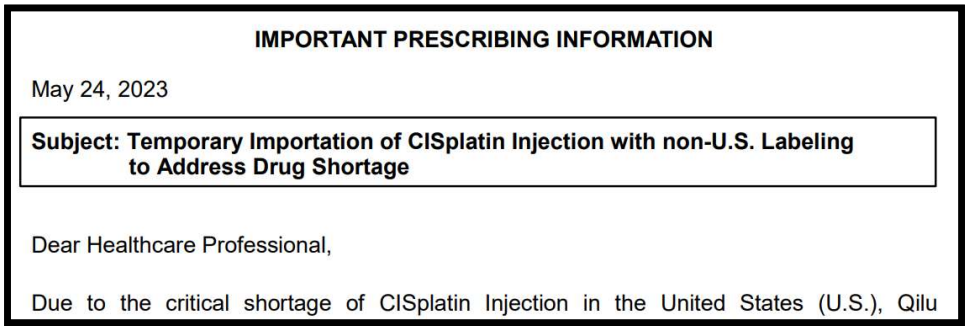
Unavailable global resource

A comprehensive evaluation of available cisplatin products proves challenging due to the lack of a global resource containing information about equivalent medicinal products harmonised with global identifiers.

Drug alternatives and non-US labelling/packaging

The announcement of the temporary importation of non-US labelled Cisplatin Injection, occurring four months later in May 2023, offers a potential solution[5].

The medicinal product, Cisplatin Injection (50mg/50ml), is manufactured by Qilu Pharmaceutical Co Ltd in China[6].



IMPORTANT PRESCRIBING INFORMATION

May 24, 2023

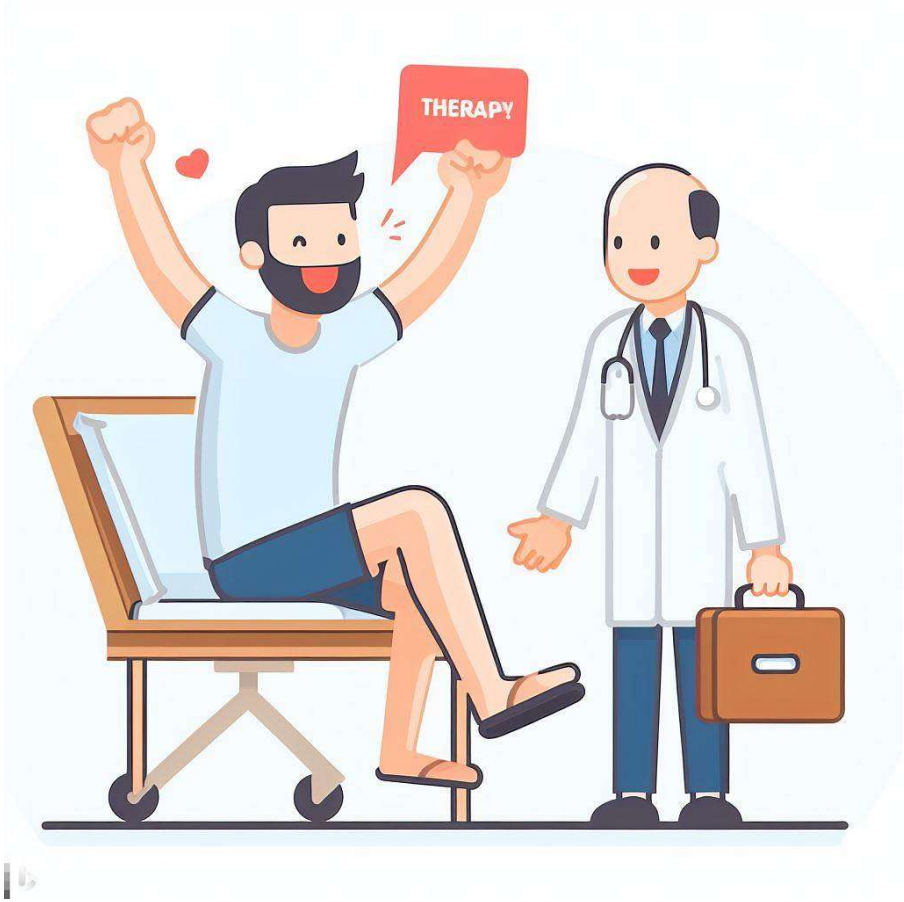
Subject: Temporary Importation of CISplatin Injection with non-U.S. Labeling to Address Drug Shortage

Dear Healthcare Professional,

Due to the critical shortage of CISplatin Injection in the United States (U.S.), Qilu

Healthcare professionals notified in May timeframe

A Dear Healthcare letter is sent out to relevant stakeholders, explaining labelling and packaging distinctions[5].



Start of patient therapy

Following these developments, patients, doctors, pharmacists, and healthcare centres are now equipped to access the necessary medication.

The cancer patient can finally begin therapy.

So, what if we had global PhPID?

Connected to a global resource of medicinal products, global PhPID level 4 can help to identify like medicinal products.

The value of global PhPID in drug shortages

USA Shortage

Cisplatin
1 mg/ml
Concentrate for
Solution for
infusion

China

顺铂注射液
50ml:50mg
Cisplatin
Injection

Global PhPID level 4

D934E701B1FF6B452828E1C6703B257E

Substance	Strength	Basic Dose Form	Administration method	Intended site	Release characteristics
Cisplatin	1mg/ml	Solution	Injection	Parenteral	Conventional

Potential added value of global PhPID Identifiers

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- Initial identification stages – Faster & more accurate
- Drug shortages staff need to know who is **currently marketing** a medicinal product.
  - gPhPID must be connected to MPID
- Global PhPID can be useful in identifying non-US product sources to assist with drug shortages.

Potential added value of global PhPID (cont.)

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Potential to Save days to weeks finding a substitute

- Quick identification of equivalent medicinal products allows drug shortages staff to invest their time more efficiently and effectively.

Better use of resources at healthcare facilities

- Staff hours allocated to managing drug shortages at healthcare facilities can be reduced or used elsewhere.

Prevent harm to patients

- By eliminating the need for alternative regimens, the risk of medication errors and patient harm stemming from less familiar or less effective treatments can be mitigated.

Important Considerations

- Global PhPIDs must be connected to medicinal product information and related marketing status.

GIDWG Use Case End to End

- Test value of global PhPID in drug shortages
  - Cross-region data sets will be based on substances of special interest for drug shortages staff (e.g., amoxicillin powder for solution, methotrexate sodium injection, solution, carboplatin injection, solution, nitro spray)
  - Identify similar medicinal products based on PhPID level 4 nationally and across regions.
  - Locate country of sales and MAHs information for identified similar medicinal products

References

1. Cisplatin U.S. Drug shortage. Date first posted: 02/10/2023 https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Cisplatin%20Injection&st=c
2. Julie R. Gralow, Chief Medical Officer & Executive Vice President, Association for Clinical Oncology testimony to congress. https://cancerletter.com/the-cancer-letter/20230526_2/ https://d1dth6e84htgma.cloudfront.net/Julie_Gralow_Witness_Testimony_06_13_23_7d56adc776.pdf?updated_at=2023-06-12T15:59:08.173Z
3. Survey by the National Comprehensive Cancer Network: https://www.nccn.org/docs/default-source/oncology-policy-program/NCCN-Drug-Shortage-Survey.pdf
4. National survey on the effect of oncology drug shortages on cancer care, McBride et all, 2013 https://academic.oup.com/ajhp/article-abstract/70/7/609/5112445?redirectedFrom=fulltext&login=false
5. Temporary Importation of CISplatin Injection with non-U.S. Labeling to Address Drug Shortage: https://www.fda.gov/media/168657/download
6. Qilu Pharmaceutical cisplatin product: https://www.qilu-pharma.com/products_details/975813724717539328.html

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Thank you

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GIDWG End-to-End Use Cases:

Showcase the value of global PhPID in cross-border healthcare

Robert Stegwee (CEN/TC 251)

Therapy Compliance and Health Concerns

Please meet our Japanese friend Tanaka.

Tanaka is under a treatment regimen with レバチオ, a medication prescribed for his pulmonary arterial hypertension (PAH) condition.

His Japanese physician emphasizes the importance of **therapy compliance**.

Travel from Japan to USA

Tanaka embarks on an international journey from Japan to the United States, poised for his anticipated vacation.

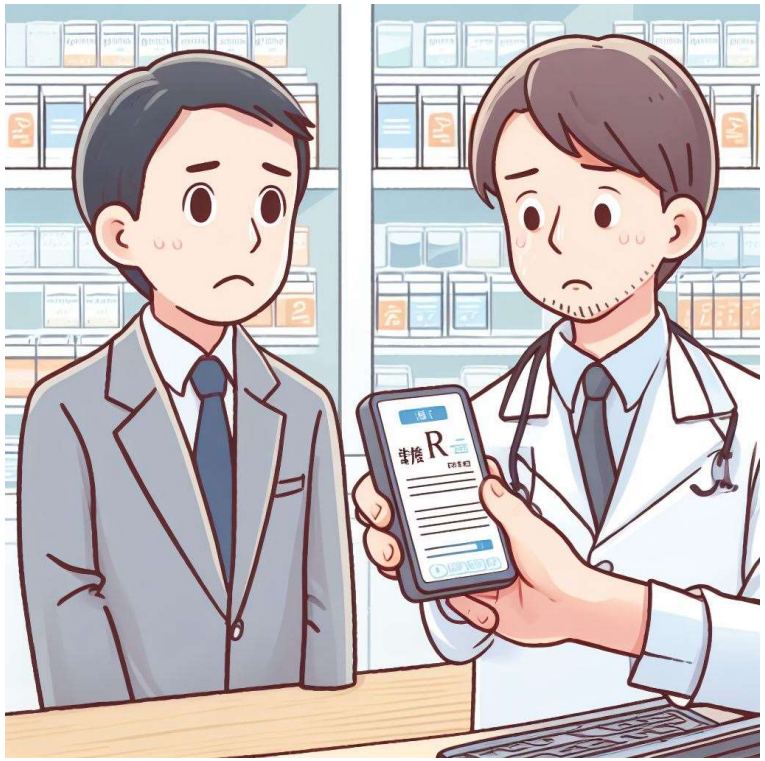
Forgotten Medication

Tanaka inadvertently forgets to carry an adequate medication supply for his three-week vacation in the United States.

Japanese ePrescription

Luckily, Tanaka can leverage a healthcare mobile app to access an electronic prescription for his medication, which he can presents to a U.S. pharmacist.

Challenge: Dispensing a foreign prescription in the US



There are only few pharmacies in the US that can dispense a foreign prescription.

The pharmacist in US cannot type the Japanese brand name in his own software system.

This provokes genuine concern over potential prescription misinterpretation and erroneous medication dispensation.

If we had a global PhPID

Global PhPID level 4 is luckily available in the Japanese prescription.

Tanaka now holds out the prescription confidently, a bridge between languages and cultures.

Therapy compliance is successfully ensured preserving patient's health.

The value of PhPID in cross border healthcare

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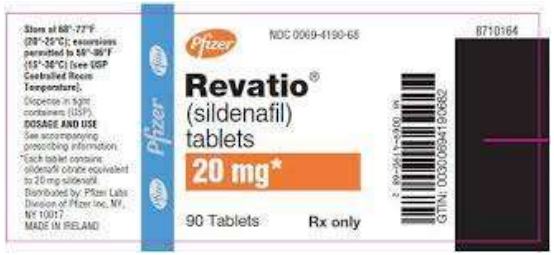
sildenafil
20mg
tablets

sildenafil
20mg
tablets



Global Phpid lvl 4

D934E701B1FF6B452828E1C6703B257E

Global PhPID level 4 is luckily available in the Japanese prescription.

This allows the American pharmacist to search in his own system for medicinal products US FDA approved in the US market that share the same PhPID level 4. Language is no longer a barrier.

Global PhPID connecting the dots

Global PhPID level 4, connected to a federated resource of medicinal products can help to identify medicinal products that are *equivalent to each other*

The PhPID becomes the medicinal product's "common denominator" from country-to-country

End to end testing

Implementing this scenario

- The scenario has been tested as part of the HL7 FHIR Connectathon (Sept 2023)

- Our Japanese friend takes:
  - テグレトール, Tegretol 200mg, SJ214
  - Global PhPID is: FB9808F4FED210183F412F9998622287

- Get the US equivalents for テグレトール, Tegretol 200mg, SJ214
  - https://umc-ext-dev-phponfhirdemo-preview-rg01-webapp.azurewebsites.net/MedicinalProductDefinition?_has:AdminstrableProductDefinition:form-of:identifier=http://www.who-umc.org/phpid|FB9808F4FED210183F412F9998622287&name-country=USA
- Results (with NDC codes):
  - 51672-4005 Carbamazepine
  - 60505-0183 Carbamazepine

Implemented in HL7 FHIR

```
"resourceType": "Bundle",
"type": "searchset",

"entry": [
      "resourceType": "MedicinalProductDefinition",
       "identifier": [
                {
                 "system": "http://hl7.org/fhir/sid/ndc",
                 "value": "51672-4005"
                }
       "name": [
                  "productName": "CARBAMAZEPINE",
       "usage": [
              "country": {
                           "code": "USA"
```

Breaking down the API call

- https://umc-ext-dev-phponfhirdemo-preview-rg01-webapp.azurewebsites.net
- /MedicinalProductDefinition?
- _has:AdminstrableProductDefinition
- :form-of:identifier=
- http://www.who-umc.org/phpid|
- FB9808F4FED210183F412F9998622287
- &name-country=USA

What we have demonstrated

- We now have a FHIR service
- that will support the medication lookup
- based on the global PhPID of a medication
- as prescribed in a country of origin
- for equivalent medication in a particular target country
- resulting in a (list of) MPID(s)
- to be presented to the pharmacist.

Next steps

Guided by questions

In a perfect world, this would be easy

- Do we need to change the scenario?
  - “There are only few pharmacies in the US that can dispense a foreign prescription.”
  - Is a prescription the proper way forward?
  - Prescribing and dispensing are heavily regulated within each jurisdiction, with quite a few differences and incompatibilities between them
  - Bi-lateral legal agreements may be needed to enable cross-border eP/eD
- The UNICOM Demonstrator has a slightly different scenario
- The UNICOM Patient Facing Apps take yet another perspective

How do we truly test end-to-end?

- Do we engage the provider of *“a healthcare mobile app to access an electronic prescription for his medication”*
- Do we engage a provider of *“his own system for medicinal products”* that the pharmacist uses to search and dispense the medication
- Do we need to engage other system providers, like MPD providers?

Do we need visibility of the PhPID?

- Our HL7 FHIR Connectathon scenario was a bit more elaborate:
  - Submit to the PhPID maintenance organization(s) (e.g. Uppsala WHO UMC)
    - country of origin MPID, or
    - Substance, Administrable Dose form, Strength or
    - **PhPID** (covered as part of the country of origin MPID in the first sub-bullet)
    - plus the **target country** (supported by the maintenance organization) (covered in the first sub-bullet)
  - Receive a list of Medical Products (MP) for the target jurisdiction

- We also had discussions on whether to include the PhPID in:
  - The electronic Product Information (ePI/SPL)
  - The medication summary data block of the International Patient Summary

More extensive patient safety

- Would a scenario including cross-border hospitalization make sense?
  - The country of origin medication is key in safely treating a patient in a cross-border situation
  - That is why the Medication Summary is mandatory in the International Patient Summary
  - How do we make sure that the clinicians can introduce the medication list into their Electronic Health Record Systems to guide their processes?

Next HL7 FHIR Connectathon

- 16-18 January 2024
  - HL7 Europe FHIR Connectathon – Athens
  - Virtual HL7 FHIR Connectation
  - Vulcan, Gravitate Health, and UNICOM will continue their work there

- GIDWG proposes to extend the scenario one step, engaging with Pharmacy and EHR system vendors to integrate the lookup
- Will test the FHIR API spec also with the UNICOM substitution component for MyHealth@EU

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Thank you

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Q&A

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Closing Remarks
Public Meeting Adjourned

Panagiotis Telonis (EMA)/
Isabel Chicharo (EMA)

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