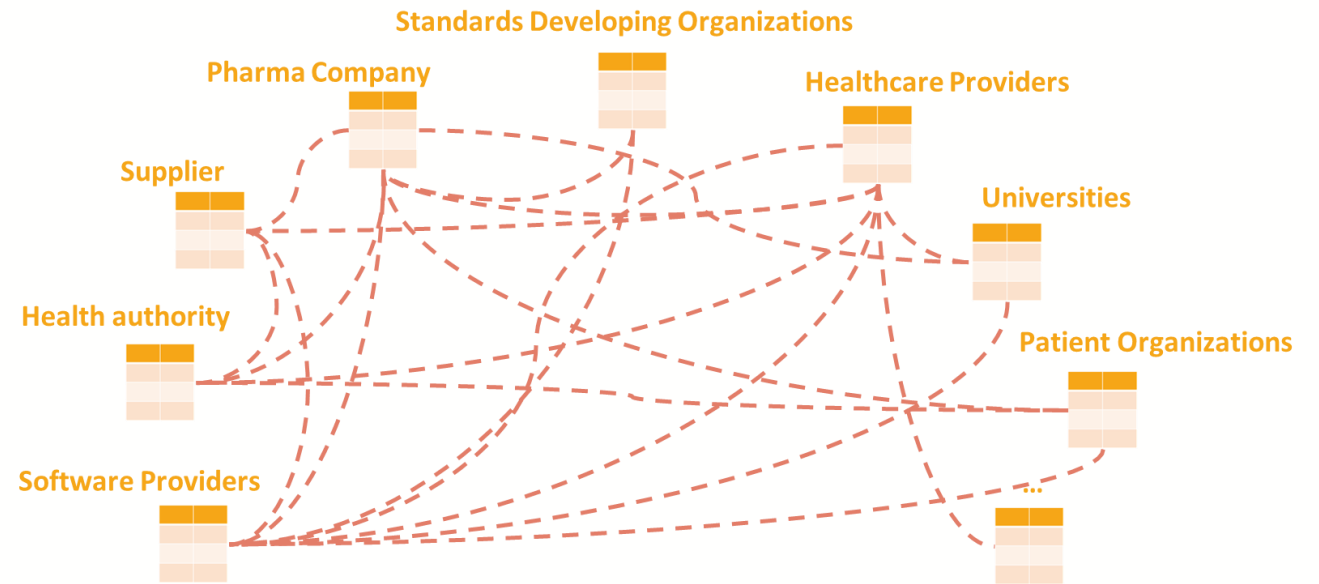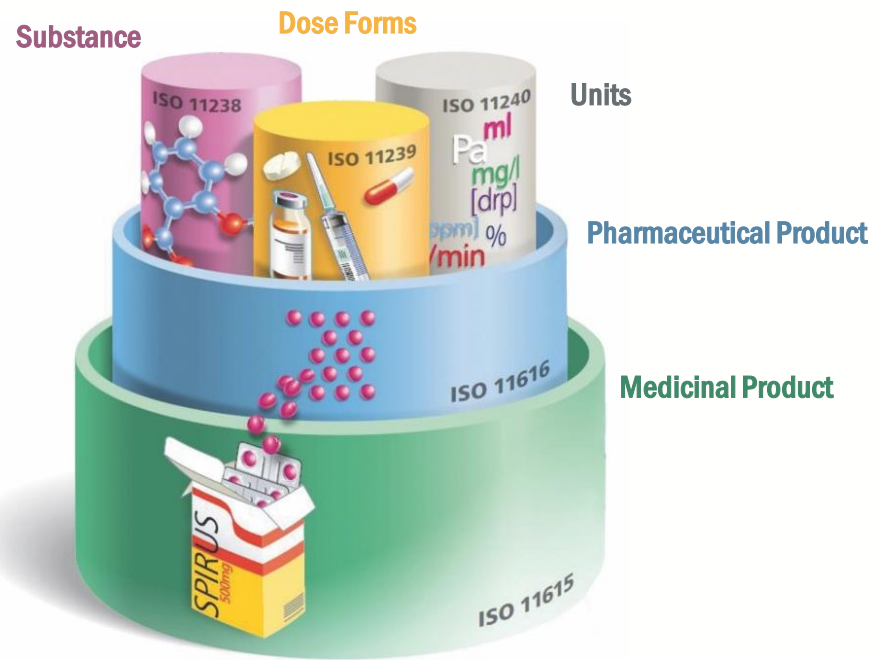# IDMP Ontology

Collaborative Implementation of IDMP in Pharma

15 Juni 2023, Interop-Forum - HL7 Germany

Rafail Kasapis, OSTHUS GmbH

The Problem: Diverging IDMP implementations create more silos and are a risk for envisioned standardization benefits of IDMP for drug safety, innovation and operational efficiency.


Substance · Dose Forms · Units · Pharmaceutical Product · Medicinal Product

ISO 11238 · ISO 11239 · ISO 11240 · ISO 11616 · ISO 11615

ISO IDMP Standards

Standards Developing Organizations · Pharma Company · Healthcare Providers · Supplier · Universities · Health authority · Patient Organizations · Software Providers

Silos and many costly point-to-point integrations

The IDMP Ontology provides a universal implementation of the IDMP product data model as a common language to effectively bridge the gap between people, processes, and systems.
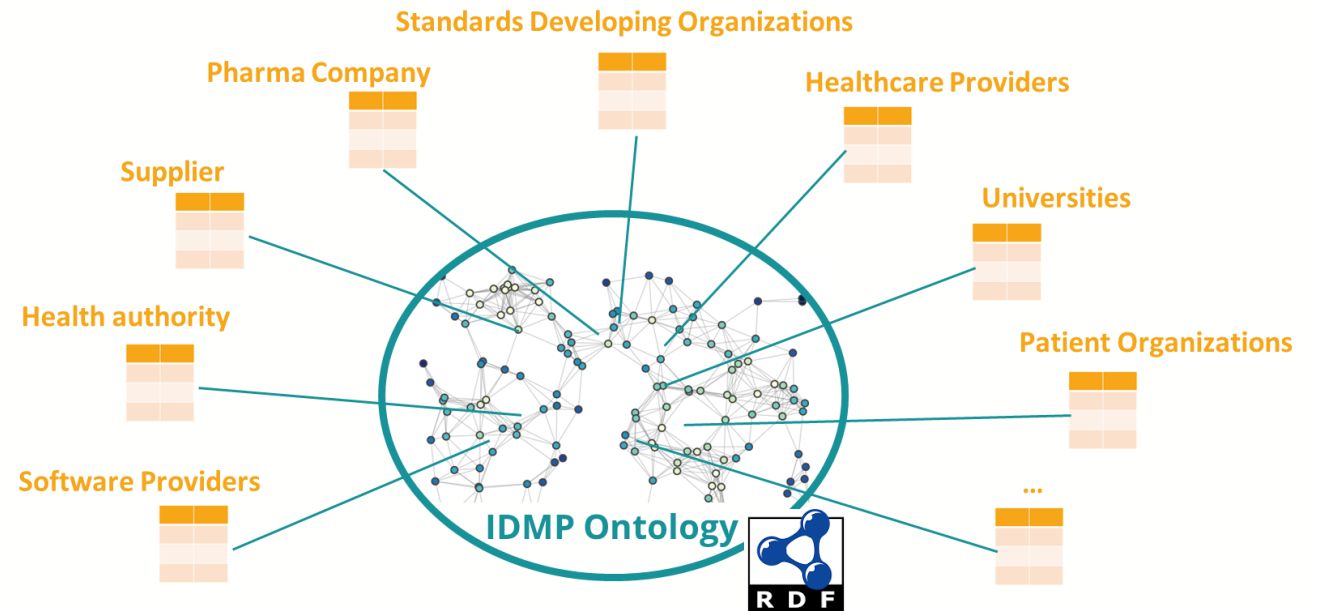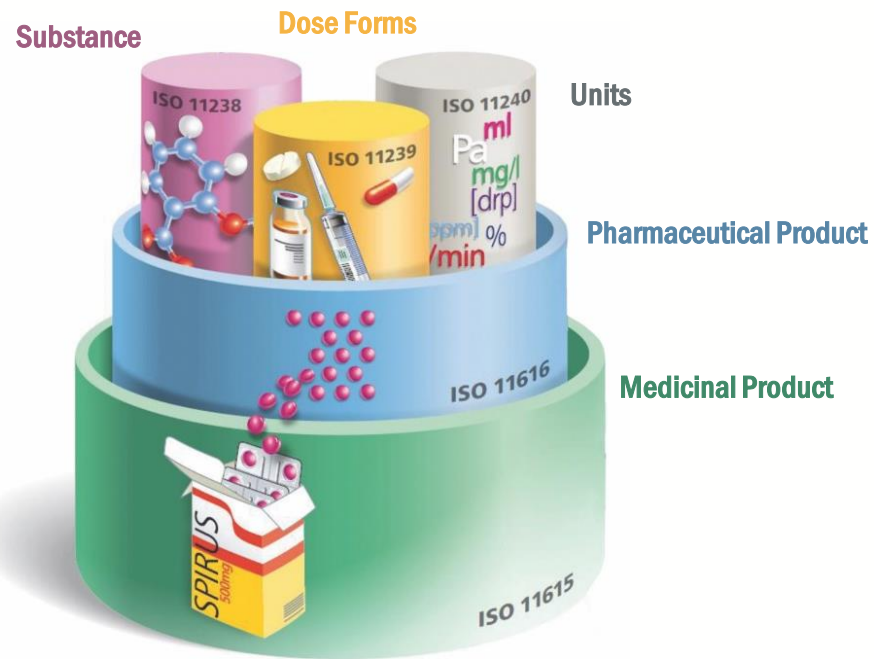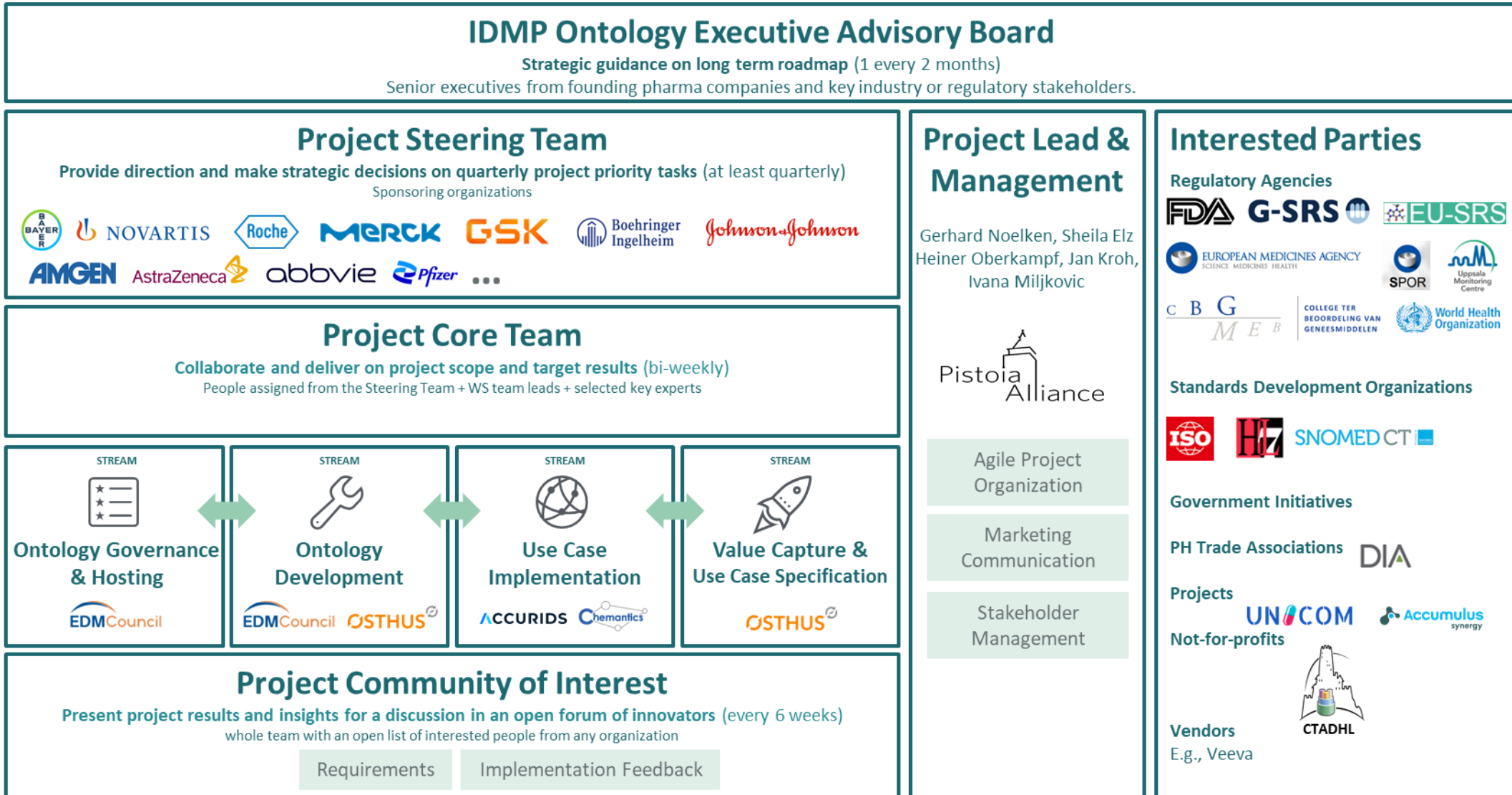

ISO IDMP Standards

Collaborative implementation creates interoperability by design

© Pistoia Alliance

Our agile governance framework ensures effective industry alignment.

IDMP Ontology Executive Advisory Board
Strategic guidance on long term roadmap (1 every 2 months)
Senior executives from founding pharma companies and key industry or regulatory stakeholders.

Project Steering Team
Provide direction and make strategic decisions on quarterly project priority tasks (at least quarterly)
Sponsoring organizations

BAYER · NOVARTIS · Roche · Merck · GSK · Boehringer Ingelheim · Johnson&Johnson
AMGEN · AstraZeneca · abbvie · Pfizer · ...

Project Core Team
Collaborate and deliver on project scope and target results (bi-weekly)
People assigned from the Steering Team + WS team leads + selected key experts

STREAM	STREAM	STREAM	STREAM
Ontology Governance & Hosting	**Ontology Development**	**Use Case Implementation**	**Value Capture & Use Case Specification**
EDMCouncil	EDMCouncil OSTHUS	ACCURIDS Chemantics	OSTHUS

Project Community of Interest
Present project results and insights for a discussion in an open forum of innovators (every 6 weeks)
whole team with an open list of interested people from any organization

Requirements · Implementation Feedback

Project Lead & Management

Gerhard Noelken, Sheila Elz
Heiner Oberkampf, Jan Kroh,
Ivana Miljkovic

Pistoia Alliance

Agile Project Organization

Marketing Communication

Stakeholder Management

Interested Parties

Regulatory Agencies

FDA · G-SRS · EU-SRS
EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH · SPOR · Uppsala Monitoring Centre
CBG MEB · COLLEGE TER BEOORDELING VAN GENEESMIDDELEN · World Health Organization

Standards Development Organizations

ISO · HL7 · SNOMED CT

Government Initiatives

PH Trade Associations DIA

Projects UNICOM · Accumulus synergy

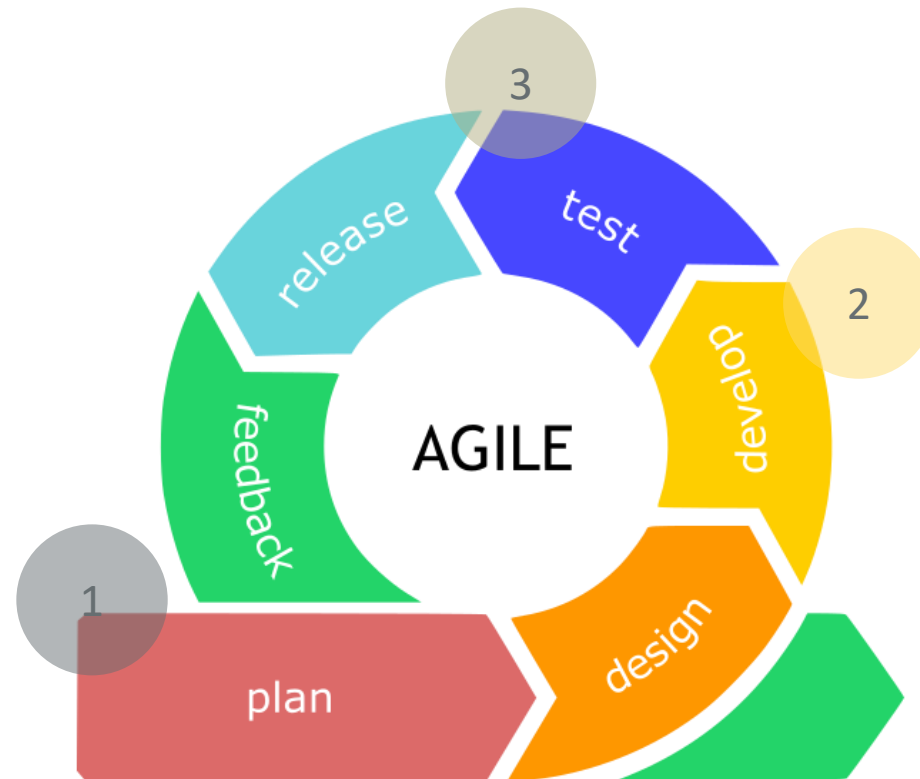**Not-for-profits** CTADHL

Vendors
E.g., Veeva

Agile IDMP Ontology Development

ISO IDMP Standards
Use Cases / CQs
Challenging Examples
Implementation Feedback

Terminology Clarification
Draft Modelling Diagrams

Ontology Engineering
Specifying Examples
SPARQL Queries
Public Data Alignments

Ontology Hygiene Tests
Execution of SPARQL Queries
Mapping Challenging Examples
SME Review

Documentation
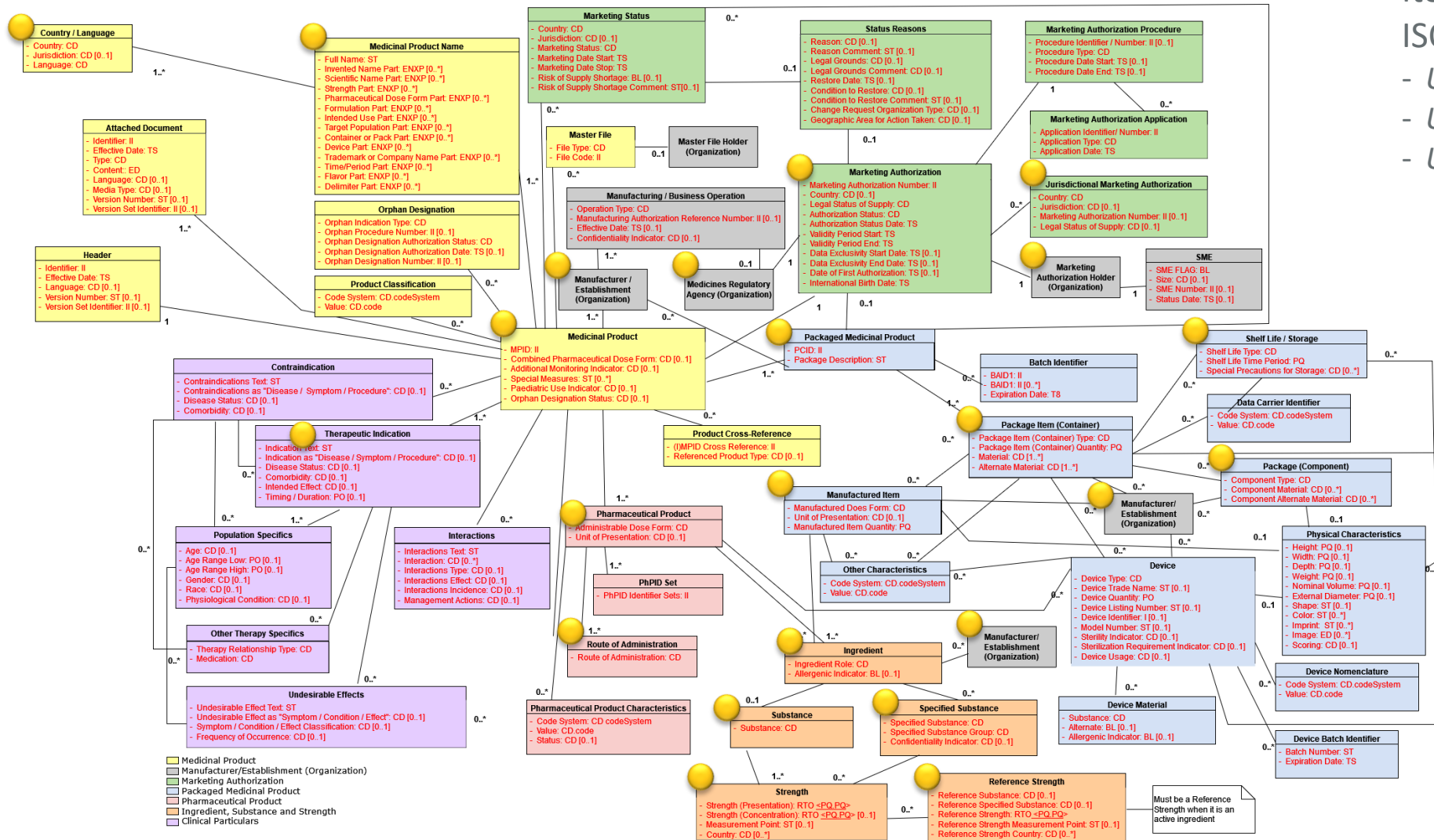Publication

Pharma Implementation
Further SME Review

Incremental Use Case driven development

Iteratively covering the ISO standards
- *UC1: Substance*
- *UC2: Reg-Manuf.*
- *UC3: Therapeutic Indication*

ID   Competency Question

UC1-CQ1	Which substances have the common active moiety <X>?
UC1-CQ2	What is the active moiety of substance <X>?
UC1-CQ3	What are the products that contain substances with common active moiety <X>?
UC1-CQ3.1	What is the basis of strength for substance <S> in product <P>?
UC1-CQ4	Which EV code (future SMS code) does the substance <S> have?
UC1-CQ4.1	In addition to CQ4: What FDA UNII code, ATC Codes, ... Does the substance <S> have?
UC1-CQ5	In which clinical trials were the authorized medicinal products <P> administered?
UC1-CQ6	Which investigational/authorized medicinal products contain the substance <S> or its active moiety <M> or any other substance related to active moiety <M>?
UC1-CQ7	Which manufactured items contain substance <S> as an ingredient of type "active"?
UC1-CQ8	Which investigational medicinal products are related to manufactured item <M>?
UC1-CQ9	What is the molecular structure of substance <S>?
UC1-CQ10	Are two substances <A> and <B> the same? If not, what is their relationship, if any?
UC1-CQ11	What is the non-salt, non-hydrated, non-ester form of substance S? (aka: What is the parent substance of substance <S>?)
UC2-CQ1.1	In which manufactured item is substance <S> used?
UC2-CQ1.1a	In which substances (active, excipient, packaging materials etc.) is substance <S> found?
UC2-CQ1.1b	In which (Global) SKUs is substance <S> used?
UC2-CQ1.1c	In which materials (package item (container) constituent) is substance <S> used?
UC2-CQ1.1d	In which packaging is substance <S> used?
UC2-CQ1.2	In which production/manufacturing steps is substance <S> used?
UC2-CQ2.1	Which Marketing Authorization Number(s) does a sellable article (Material in ERP) have?
UC2-CQ2.2	Which marketing authorization does this supply material <M> relate to?

CQs from MVP Phase (refinements)

Further substance CQs (ongoing)

Phase 2: 2023-Q1 Scope (ongoing)

Ontology Modeling Example: accurate representation of active moiety

GSRS

ARIPIPRAZOLE LAUROXIL

Relationships: Active Moiety

Related Record	Type

W9C3Q6D4HE

ACTIVE MOIETY (FOR EXCLUSIVITY)
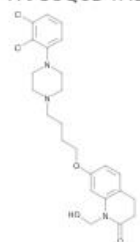
N-HYDROXYMETHYL ARIPIPRAZOLE

82VFR53I78
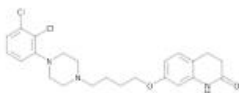
ACTIVE MOIETY

ARIPIPRAZOLE

simple active moiety relation

ISO-11238 Definition (Substance)

moiety = "Entity within a substance that has a complete and continuous molecular structure"

"The **active moiety** of a stoichiometric or non-stoichiometrical substance molecule is considered that part of the molecule that is the base, free acid or ion molecular part of a salt, solvate, chelate, clathrate, molecular complex or ester."

Challenges in accurately modelling (active) moiety

- **The term "active" moiety leads to confusion** -> many parts of a substance can have some pharmacological or physiological impact.
- **Moieties cannot be classified as "active" without context** -> the same molecule can be "active" as part of one substance and "not active" in another.

Finding

Active moiety concept (aka 'parent substance') is different in different organizations or even within one organization. This requires **specifying roles and contexts correctly**, e.g. regulatory, chemical, biological..

Ontology Modeling Example: Interoperability between Regulatory with Manufacturing

GSK: Remove HSA from all **manufacturing steps of Varicella vaccine**

Novartis: Remove a toxic/restricted substance - Identify all manufacturing processes containing a potential source of Nitrosamine or Titanium dioxide

Bayer: A supplier gets replaced – identify which substances are procured from this supplier and in which products these are used, to access impact

Roche/J&J/Merck/…: Enable **back traceability** from late product lifecycle stages back to the earliest molecule stages

IDMP Ontology

IDMP ISO Standards	**Enrichment** of ISO Standards to define **standardized concise** definitions needed to create a **bridge to the Manufacturing domain**

IDMP Perspective

Manufacturing Perspective

- Pharmaceutical Product
- Medicinal Product
- Packaged Medicinal Product
- Package Item (Container)
- Manufactured Item
- Substance
- Ingredient
- Specified Substance

In a box, with label and leaflet specific to market

with label — with container, but no label

with specific dosage — without volume

substance in a media

- Finished Product
- Filled Product
- Manufactured Article
- Manufactured Article (Starting material)

IDMP Knowledge Graph: IDMP Ontology + IDMP Data Graph

Testing the ontology along concrete use cases and data

IDMP Ontology

Formal semantic definition of concepts, relationships and attributes from the ISO IDMP standards.

→ *A few hundred concepts*
→ *Need accurate and agreed patterns*
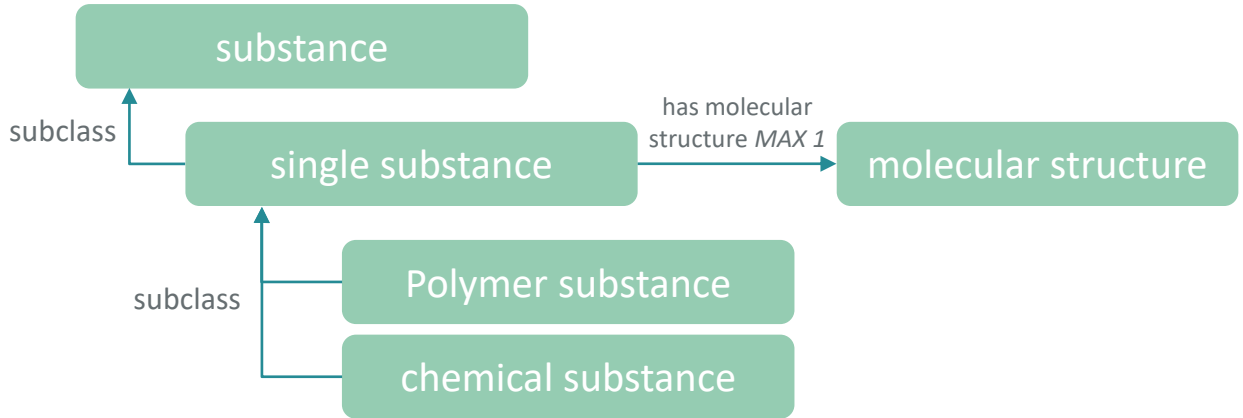
IDMP Data Graph

Any data object that are described by the concepts of the IDMP Ontology

→ *Many millions of objects*
→ *Our test data*
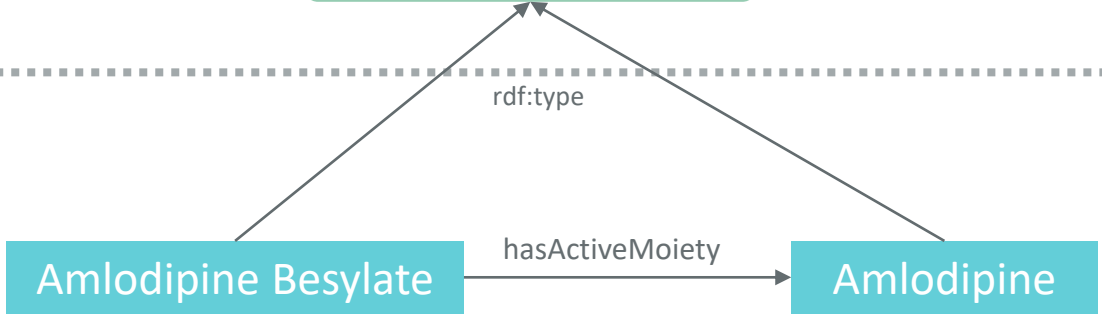
Enable business users to answer questions

What substances have a common active moiety?

Which products contain titanium dioxide?

YOUR USE CASE

Demo: Give me all substances with a common active moiety Amlodipine

Demo: In which clinical trials were Enegerix B administered?

Pilot Implementation Setup for initial Feasibility Assessments

Business question: "Which products contain titanium dioxide and where are these products registered?"

Bayer Product Data Model Backbone

IDMP Ontology
ISO-11238, ISO-11239, ISO-11615, ISO-11616, ISO-11240 + Common Augmentations

Bayer Augmentation of IDMP Ontology Model
Some additional classes, relationships, and attributes to address internal needs

Harmonized Bayer Product Data Knowledge Graph

synchronize

Public IDMP-O aligned data graph*

alignment   alignment   alignment   alignment   alignment

| EMA SPOR | FDA GSRS | RIM | Master Data | Product Supply |
| Excel Exports | JSON Dump | Veeva Exports | RDF Graph | SAP |

Alignment to IDMP Ontology Concepts
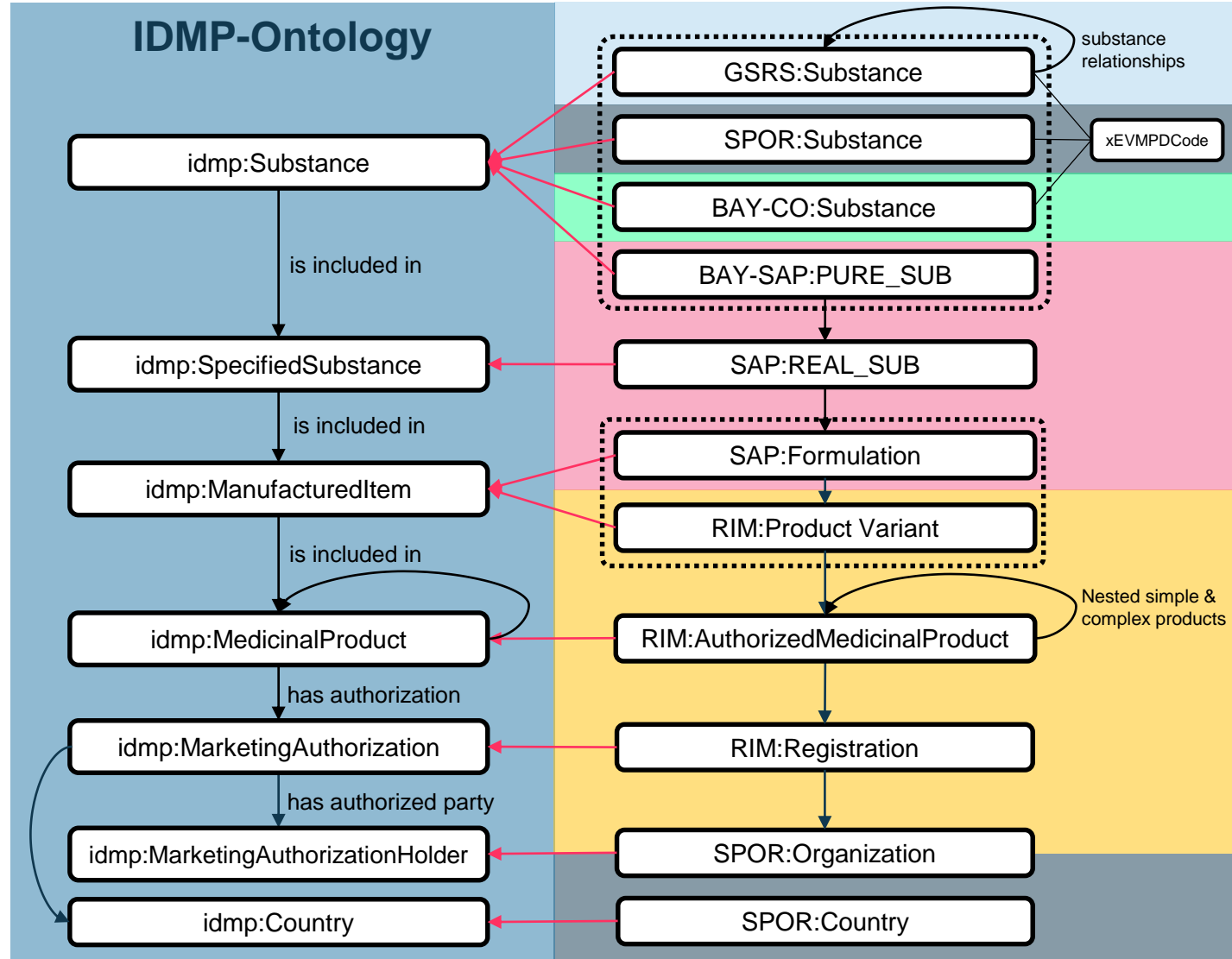
Business Questions:
- "In which manufactured items is titanium dioxide used?" (UC2-CQ1a)
- "In which medicinal products is substance "titanium dioxide (xEVMPD:SUB12611MIG) used, and where are they registered?"
- …

Qlaira (26+2), Film-coated tablet, 3 mg + 3 mg (Marketing Authorization for Austria)

BAY-RIM

type	marketing authorization Registration
Label	Qlaira (26+2), Film-coated tablet, 3 mg + 3 mg (Marketing Authorization for Austria)
URI	https://pid.bayer.com/
applies to	Qlaira (26+2), Film-coated tablet, 3 mg + 3 mg
has authorized party	Bayer Austria Ges.m.b.H. LOC-100002234

The marketing authorization is linked to the product

BAY-RIM

type	marketing authorization holder
Label	Bayer Austria Ges.m.b.H. LOC-100002234
URI	https://pid.bayer.com/k
is played by	Bayer Austria Ges.m.b.H.

The authorization holder is linked to SPOR OMS

SPOR-OMS

type	legal entity
Label	Bayer Austria Ges.m.b.H.
URI	https://spor.ema.europa.eu/omswi/#/organisations/ORG-100000122
address	LOC-100002234
broader	Industry Pharmaceutical company

RMS-OMS-Party-Category

The authorization holder is linked to SPOR RMS

type	OMS Party Category
Label	Pharmaceutical company *(en)*
URI	https://spor.ema.europa.eu/rmswi/#/lists/200000000015/terms/200000000081
definition	Support all the medicines regulatory use cases. These are commercial businesses licensed to research, develop, or participate in the marketing and/or distribution of medicines, most commonly in the context of healthcare. CROs will be regarded as pharmaceutical companies since they can also act as one. *(en)*

IDMP-O Implementation at Boehringer Ingelheim

Five competency questions implemented.
Continuous progress on additional QCs

Which substance corresponds to a given identifier?	Which substances have a common active moiety M?	What is the active moiety of substance S?
What are the products that contain substances with common active moiety M?	Which EV code (future SMS code) does the substance S have?	In which clinical trials were the registered products administered?
Which investigational/authorized medicinal products contain the substance S and active moiety M?	Which manufactured items contain substance S as ingredient of type "active"?	Which investigational medicinal products are related to this manufactured item?

User interface for answering questions up and running

Which substances have a common active moiety?

An answer to this question are substances that have the given active moiety as active ingredient

Data source(s)   MDM Product

Active Moiety   calcium

e.g., calcium

Get answers   Reset

Quick search

Substance

calcium hydrogen phosphate anhydrous

CALCIUM LACTATE

calcium hydrogen phosphate dihydrate

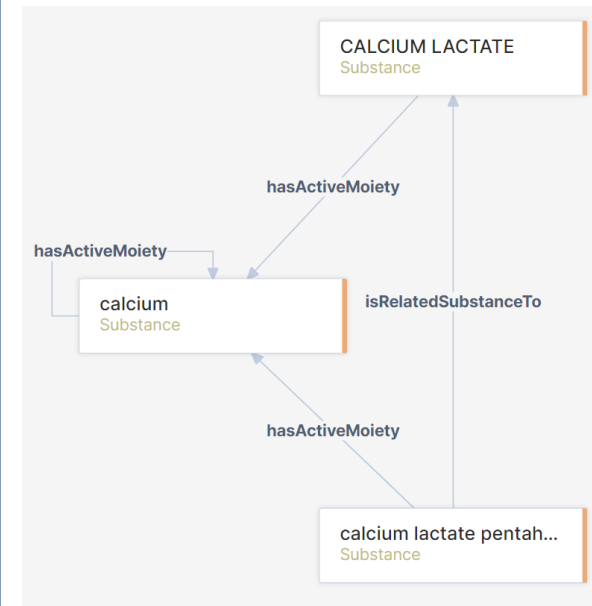calcium pantothenate

calcium carbonate_hp

calcium lactate pentahydrate

calcium fluoride

Knowledge graph for internal data available

CALCIUM LACTATE
Substance

hasActiveMoiety

hasActiveMoiety

calcium
Substance

isRelatedSubstanceTo

hasActiveMoiety

calcium lactate pentah...
Substance

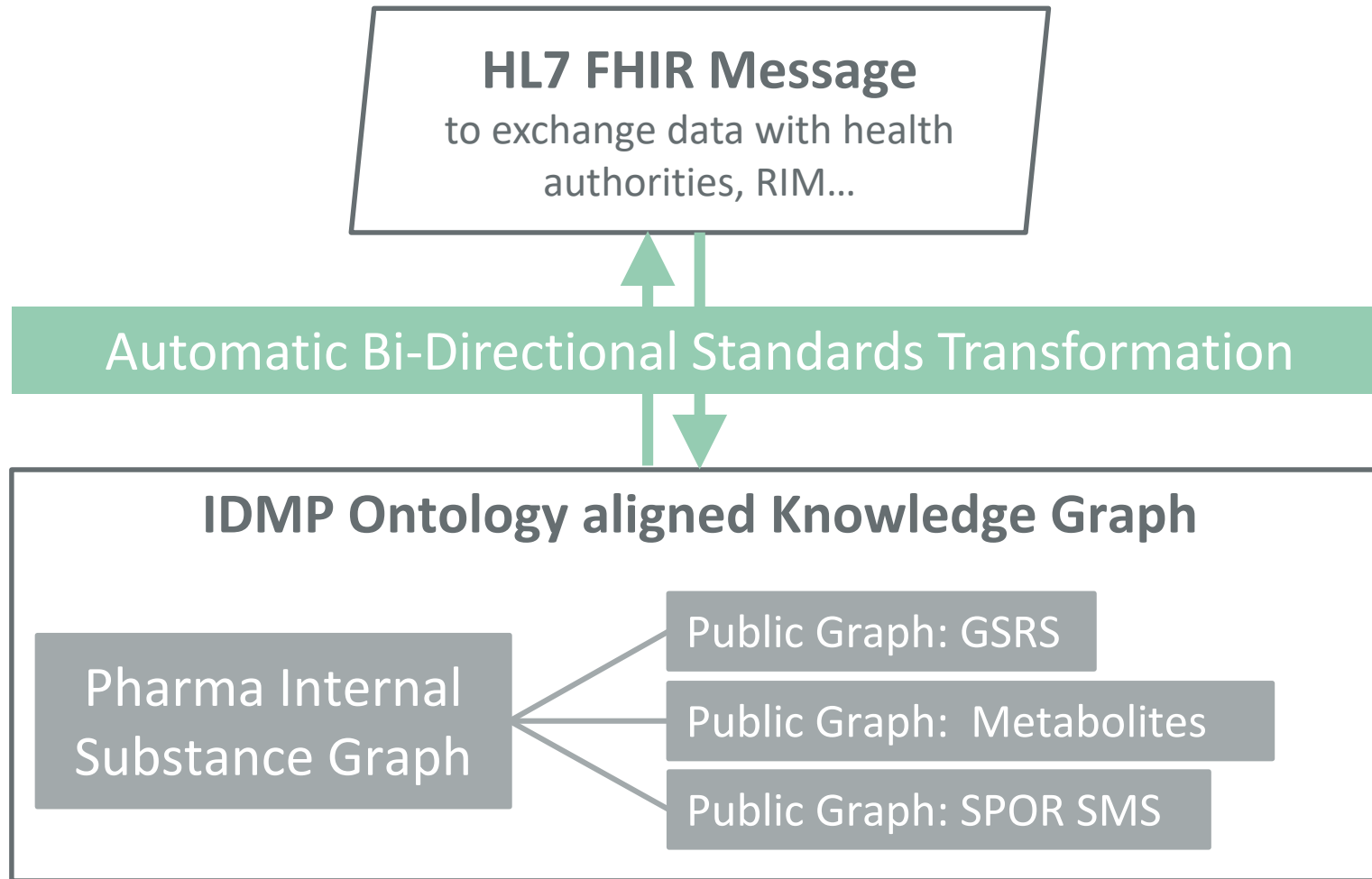# WHO-UMC: Harmonized Dose and Strength Information

IDMP Ontology aligned product information, combined with FDA GSRS substance data, allows to automatically harmonize strength information

National data						Characteristics assignment	Harmonized data for PhPID		
Product name	Active ingredient	Country	Local dose form	MAH	Strength	Characteristics from original dose form	Dose form Characteristics	Substance	Strength
Diclofenac Orifarm	Diclofenac diethylamine	Sweden	Gel	Orifarm	11,6 mg/g	Gel / Application / Cutaneous/Transdermal / Conventional	Gel Application Cutaneous/ Transdermal Conventional	Diclofenac diethylamine	11,6 mg/g
Kinespir	Diclofenac diethylamine	Belgium	Gel	Teva	10 mg/g	Gel / Application / Cutaneous/Transdermal / Conventional			
Neo dolaren	Diclofenac diethylamine	Mexico	Gel	Carnot laboratorios	1 g/100 g	Gel			
Artridene	Diclofenac diethylamine	Colombia	Gel	Siegfried	1 %	Gel			

11,6 mg/g refers to diclofenac diethylamine which is the actual ingredient. 10 mg/g and 1 % refers to diclofenac sodium

Partially missing dose form characteristics

© Pistoia Alliance

Alignment with other Standards: Example HL7 FHIR

HL7 FHIR Message
to exchange data with health authorities, RIM…

Automatic Bi-Directional Standards Transformation

IDMP Ontology aligned Knowledge Graph

Pharma Internal Substance Graph

Public Graph: GSRS

Public Graph: Metabolites

Public Graph: SPOR SMS

FHIR Resources for Interoperability PoC

MedicinalProductDefinition
PackagedProductDefinition
AdministrableProductDefinition
ManufacturedItemDefinition
Ingredient
ClinicalUseDefinition
RegulatedAuthorization
SubstanceDefinition
…

Getting Started with the IDMP Ontology

⬡ **Learn More**
www.pistoiaalliance.org

@ **Contact Us**
ProjectInquiries@PistoiaAlliance.org

Schedule an Exchange
with our Pharma Champions

🚀 **Join the Initiative**
use and help build the IDMP Ontology