WP-1 / community of expertise

January 2022

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

Vaccine challenges - cleansing, confidentiality and vaccine naming

Annet Rozema
Olof Lagerlund
Jean-Gonzague Fontaine

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SOME RULES FOR THE VIRTUAL MEETINGS

UNICOM

- ✓**Everybody is on mute**
- ✓**You post your question in the Q&A facility**
- ✓**When you speak, please keep concise**
- ✓**You may show your approval !**

After (and during) the introduction presentations, any UNICOM related question / comment may be shared with Q&A

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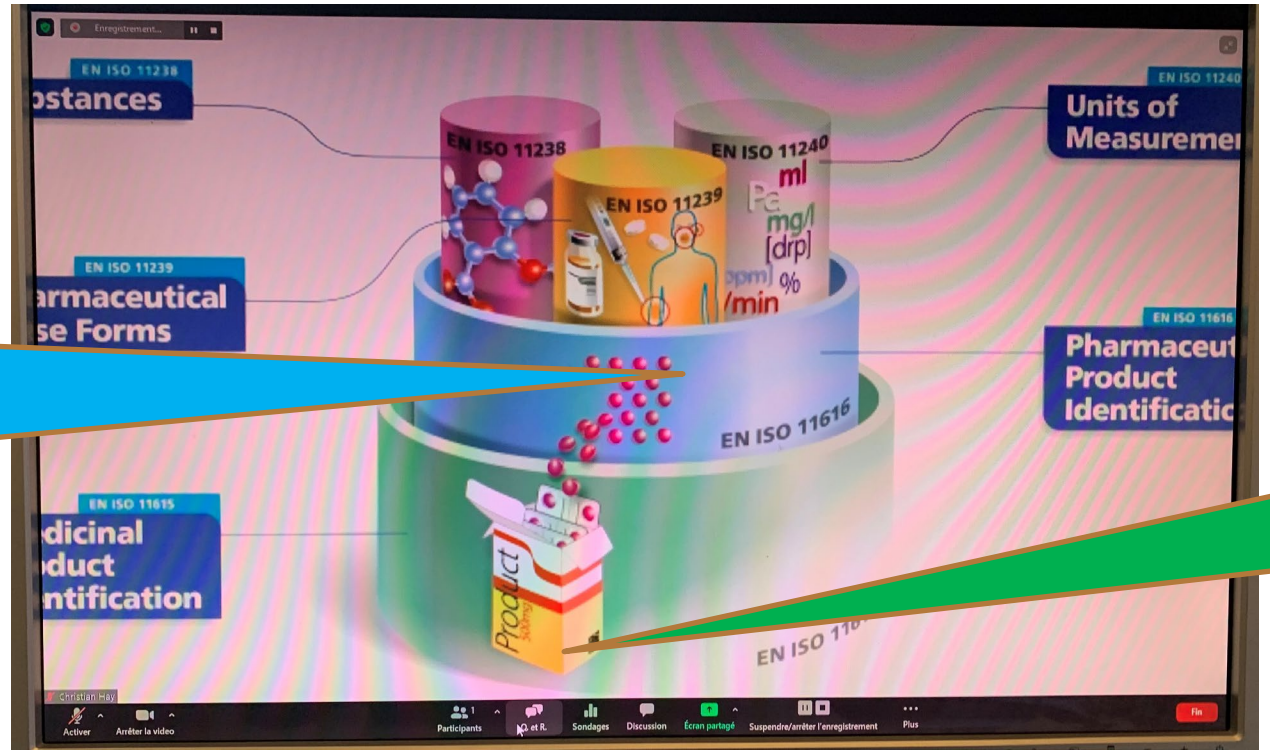
Asking a question or making a comment: please use the Q&A facility

1. Move the mouse on the screen to have the options bar appearing



2. You then select «Q&A» and write your question

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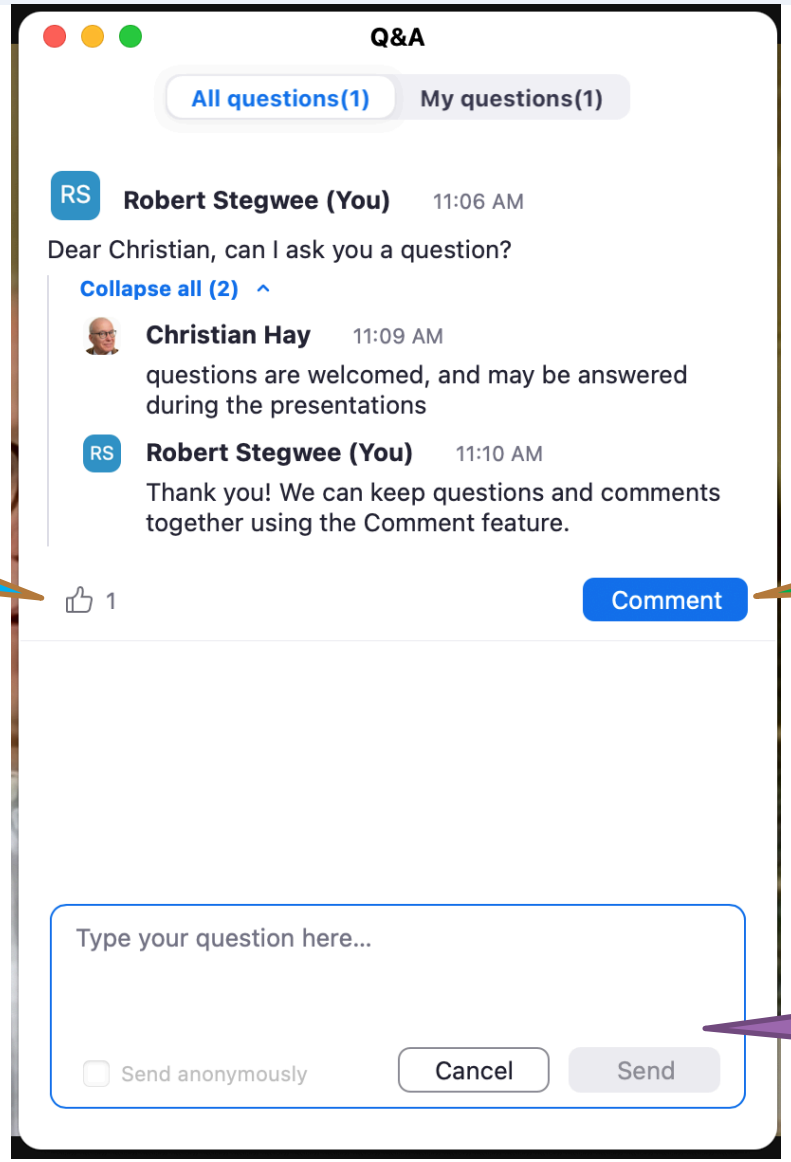
Showing support and providing a comment on a question or answer

You can support a question by clicking the «thumbs up» which moves it up on the list for the presenters



You can comment on a question or answer to engage in a conversation

Typing and sending a new question does not retain the context of your comment

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Security

- Security is our priority
- This session is password protected

Recording of this session is made available on UNICOM's youtube channel.

At the end of the virtual session, a questionnaire will be sent to the participants, to help us understand participant's reactions and needs

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Introductions to our esteemed colleagues and today's speakers

Annet Rozema

Olof Lagerlund

Jean-Gonzague Fontaine

...and our panellist

Raffaella Balocco

Malin Fladvad

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Vaccines – A global perspective

Olof Lagerlund,
WP1, SVG and UMC

2022-01-14

Uppsala Monitoring Centre

Outline

- Global Vaccine Pharmacovigilance
- Global PhPID's
- Global vaccine initiative
- Final remarks

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WHO Program for international drug monitoring (PIDM) and Uppsala Monitoring Centre

- The WHO PIDM was created in 1968 to ensure that evidence about harm to patients was collected from as many sources as possible
- The WHO PIDM had more than 170 full members and associate members in 2021, the program covers about 99% of the world's population.
- UMC has been responsible for the technical and operational aspects of the WHO PIDM since 1978.

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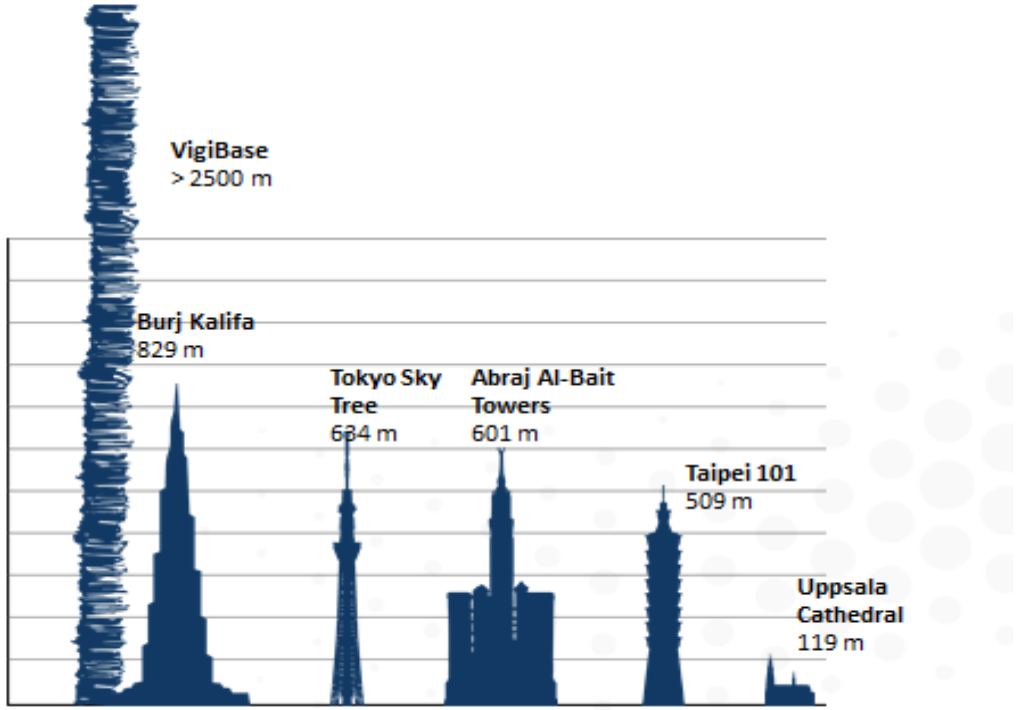
VigiBase- the global data base of ICSR's



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COVID-19 Vaccine ICSR's in VigiBase

COVID-19 vaccine	Number of ICSRs	%
All vaccines	2 720 548	100
AstraZeneca	676 966	25
Comirnaty, Pfizer BioNTech	1 315 056	48
Convidecia	649	0
CoronaVac, Vero Cell, Sinovac	44 583	2
Covaxin, Bharat Biotech	1 566	0
Janssen	114 889	4
Moderna	504 906	19
mRNA, Unspecified	341	0
Sputnik V	4 422	0
Vero Cell, Sinopharm, Beijing	43 730	2
Vero Cell, Unspecified	2 458	0
Other	167	0
Unspecified	10 815	0

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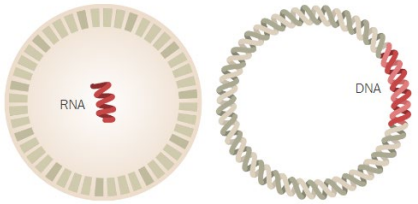
COVID-19 product and substance nomenclature

Genetic Vaccines

Vaccines that deliver one or more of the coronavirus's own genes into our cells to provoke an immune response.



Comirnaty
COVID-19 mRNA Vaccine BNT162b2
Pfizer BioNTech COVID-19 vaccine
Vacuna COVID-19 Pfizer BioNTech

Tozinameran (INN)
PF 07302048
BNT162b2

Spikevax
Moderna COVID-19 vaccine
COVID-19 Vaccine Moderna
Vacuna COVID-19 Pfizer BioNTech

Elasomeran (INN)
CX-024414
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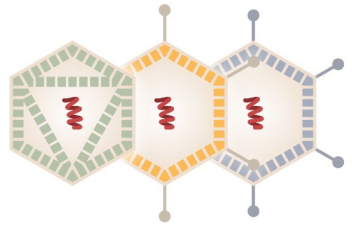


Vaxzevria
Covishield
AstraZeneca COVID-19 vaccine
Vacina COVID-19 (recombinante)
COVID-19 vacuna AstraZeneca

ChAdOx1 nCoV-19
AZD 1222

Sputink
Sputink light
Gam-COVID-Vac
Vacina COVID-19 (recombinante)

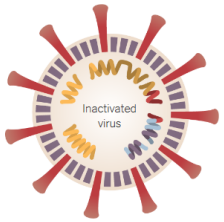
COVID-19 vaccine NRVV Ad26 (Gam-Covid-Vac)
COVID-19 vaccine NRVV Ad5 (Gam-Covid-Vac)
AZD 1222

Convidecia
Ke wei sha
PakVac
Recombinant COVID-19 Vaccine (Adenovirus Type 5 Vector)

COVID-19 vaccine NRVV Ad5 (Ad5-nCoV)
Ad5-nCoV

Inactivated or Attenuated Coronavirus Vaccines

Vaccines created from weakened coronaviruses or coronaviruses that have been killed with chemicals.



CoronaVac
Covid-19 vaccine (vero cell), inactivated
Vaksin COVID-19 bio farma

COVID-19 vaccine inact (Vero)
CZ02

CanSIno COVID Vaccine

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HB02

Sinopharm COVID vaccine, Bejing

Covilo
Covid-19 vaccine (vero cell), inactivated
Zhong kang ke wei

COVID-19 vaccine inact (Vero)
WIV04

Sinopharm COVID vaccine, Wuhan

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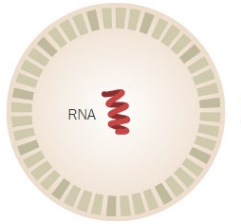
Regional differences - Dose Form

Covid-19 vaccine	
Authority of approval	**AMD dose form**
EMA	dispersion for injection
UK	solution for injection
US	suspension for injection

Pfizer BioNTech COVID-19 vaccine
Tozinameran



mRNA vaccine

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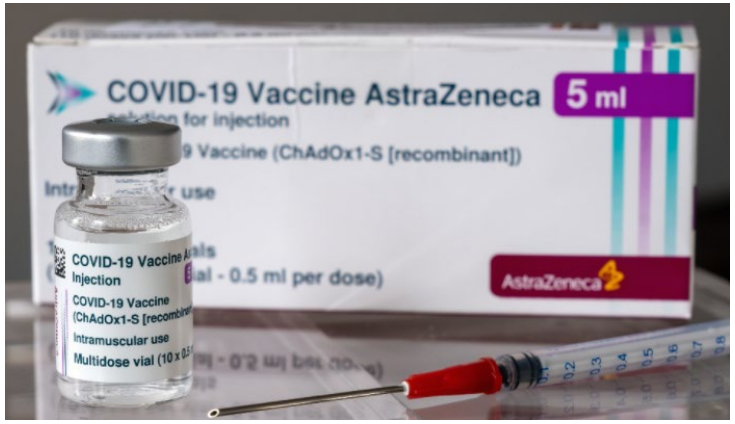
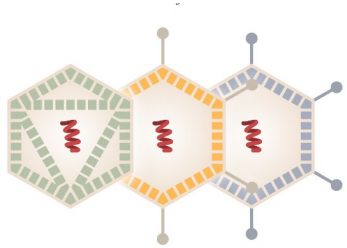
Regional differences - Strength expression

Variation in use of units for strength expression for similar products

Covid-19 vaccine AstraZeneca	
Authority of approval	**Strength per dose (0.5 ml)**
EMA	2.5×10^8 infectious units
UK	5×10^{10} viral particles
Australia	5×10^{10} viral particles



Covid-19 vaccine AstraZeneca
ChAdOx1 nCoV-19



Viral vector vaccine

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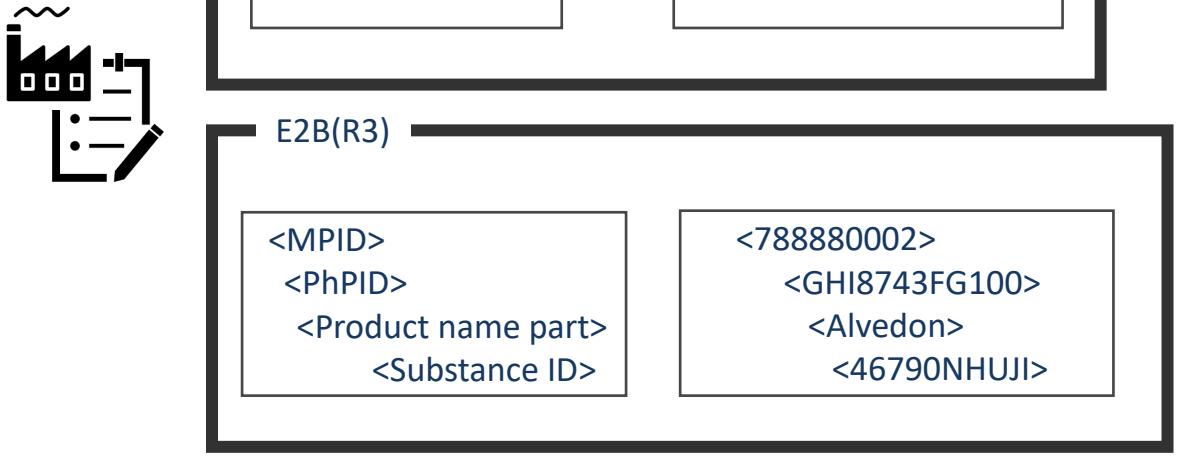
IDMP in post marketing safety ICH E2B(R3)

Each ICH region to implement their own guidelines for ISO IDMP implementation in ICH E2B (R3)

For EU, the five ISO IDMP standards apply to both authorised and developmental medical products that are regulated in the EU and should be used in ICSR submissions to EudraVigilance when available



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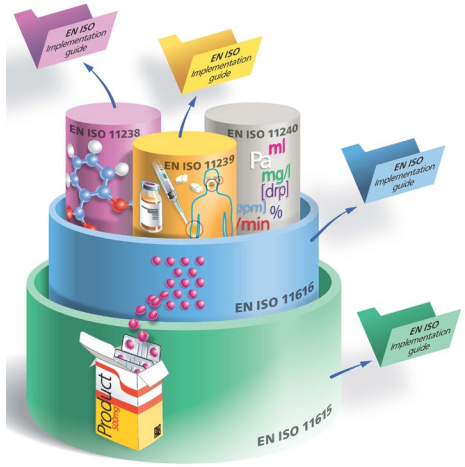
Harmonisation of data using the ISO IDMP suite of standards

PhPID	Substance ID	Strength	Dose form
ISO 11616	ISO 11238	ISO 11240	ISO 11239

PhPID Set

- PhPID Level_L1 → Substance(s) Term
- PhPID Level_L2 → Substance Term(s) +Strength+ reference strength
- PhPID Level_L3 → Substance Term(s) + *Administrable Dose Form*
- PhPID Level_L4 → Substance(s) Term+ Strength + reference strength + *Administrable Dose Form*



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Global PhPID's

- Single database containing global validated PhPID
- Limit unnecessary data redundancies
- Transparent business rules based on the IDMP algorithm for PhPID
- A Global Substance ID is the key for all PhPIDs
- A global Level 3 and 4 PhPID is not possible without a global consensus on Dose Form IDs

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Global vaccine initative

- A collaboration between UMC, US-FDA, NCATS and EU-SRS
- To investigate the feasibility of a having “global” substance management with regards to
  - Technical aspects, global system
  - Scientific aspects

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Global vaccine initative – technical

- Test performed with exchanging (non-confidential) vaccines data between NCATS public GSRS and UMC-SRS
- User requirements were discussed, such as, search function
- Vaccines are complex and feedback for improvements for data exchange were given to the GSRS development team
- Industry has expressed an interest in joining the discussions, especially with regards to data exchange
- Global Substance IDs (and PhPID) generated based on the vaccines in UMC-SRS

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Global vaccine initative - Scientific

Agreement on hierarchy (see next slide)

Discussions on naming

Initial comparison of vaccines in SRS (GSRS vs EUSRS)

- COVID vaccine: Tozinameran
- Meningococcal vaccine: Neisseria
- Comparison side-by-side between regions

Conclusion:

- Some differences in how vaccines were built, but no showstoppers (willingness to align)

Next steps?

- Discuss the differences in building vaccines and the possibility to align globally, and/or if regional differences are acceptable
- Discuss minimal fields for the vaccine substances to be assigned a global Substance ID
- Aim for achieving global agreement on naming of vaccines

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UMC-SRS Vaccine hierarchy

- Organism
- Vaccine (substance)
- Vaccine adjuvant (SSG1)
- Constituents

Basic vaccine hierarchy for the vaccines in UMC-SRS to be shown in the substance hierarchy.

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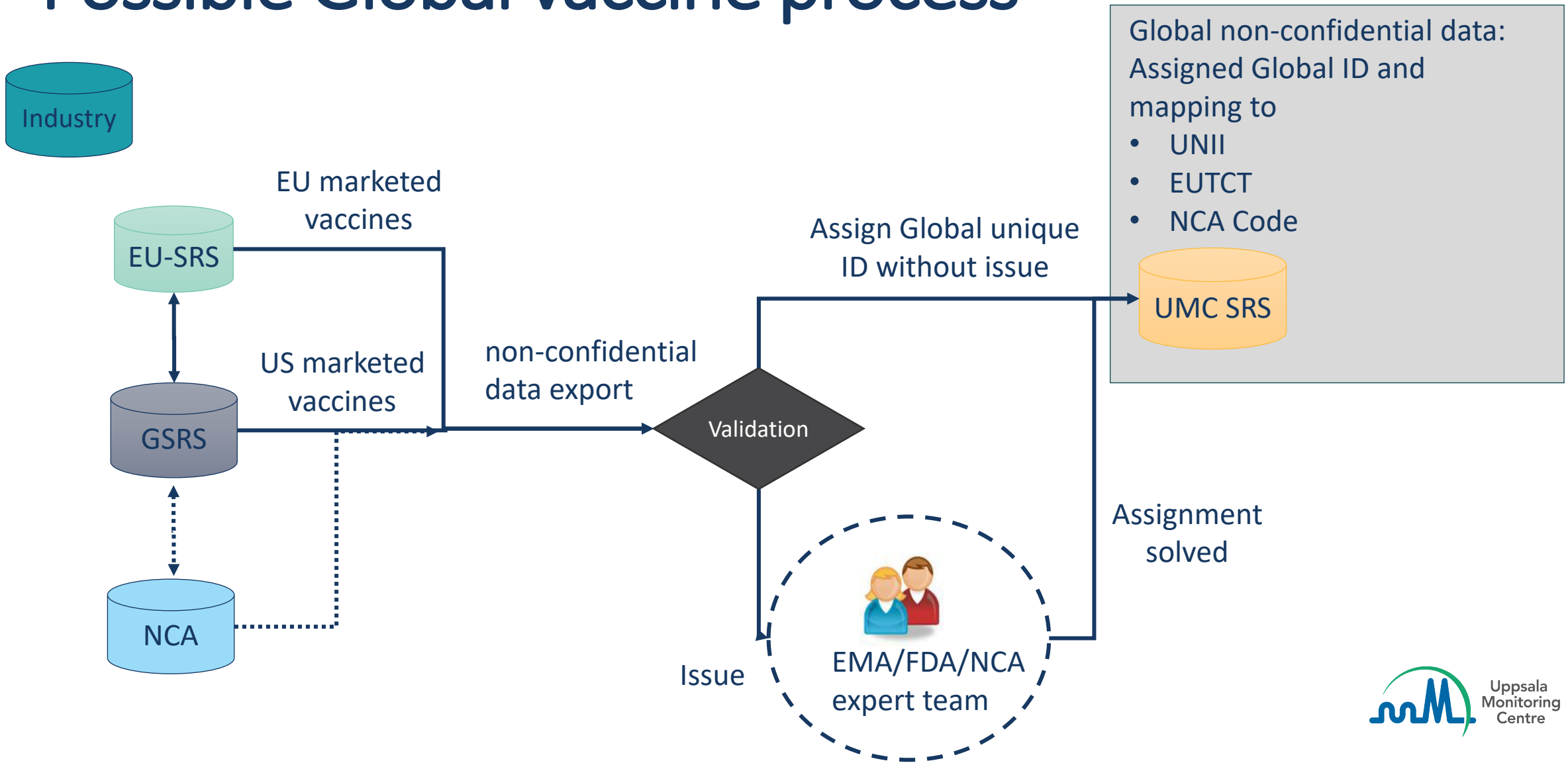
Possible Global vaccine process



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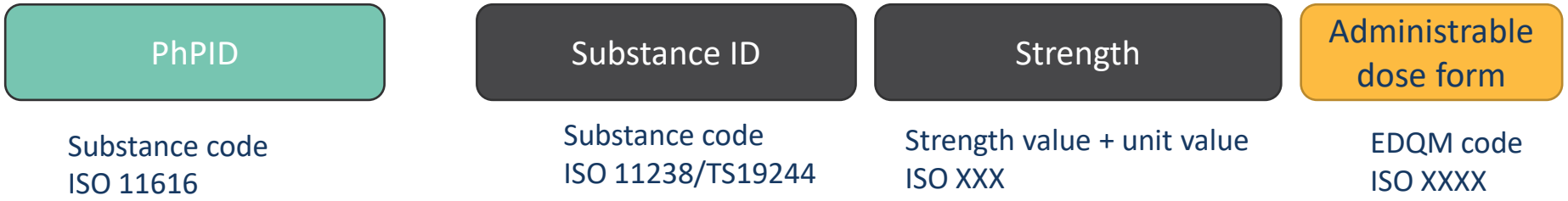
Global Harmonisation of data using the ISO IDMP suite of standards



By using the ISO IDMP suite of standards PhPID's could be assigned for some COVID-19 Vaccines

Product	Substance	PhPID
Covid-19 vaccine Astra Zeneca/ Vaxzevria	COVID-19 vaccine NRVV Ad (ChAdOx1 nCoV-19)	0x26F99364EBCD42F53E5E17D89DC3A2FD
Covid-19 vaccine Moderna	COVID-19 vaccine mRNA (mRNA 1273)	0x2AAED87EBAD551B23869BD1B6C13DE0E
Pfizer COVID-19 Vaccine/ Comirnaty	Tozinameran	0xCF85D49CF8730FEBF44268D12CB115F2
Covid-19 vaccine Janssen	COVID-19 vaccine NRVV Ad26 (JNJ 78436735)	0xD21DC8D29D16257E14D6C57B0FE70157

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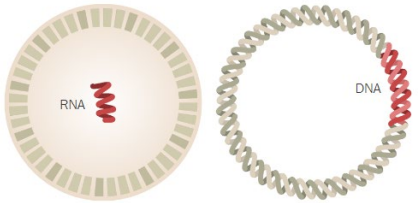

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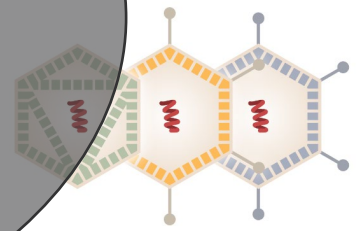

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Global Substance ID
PhPID

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COVID-19 vaccine inact (Vero)
WIV04

Sinopharm COVID vaccine, Wuhan

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Final remarks

- There is a need to work on the global scale and it is feasible
- Global Substance ID’s and PhPID’s can be assigned to vaccines and could improve pharmacovigilance
- The need for umbrella/grouper terms for vaccines

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Questions in the Q & A facility, please

Uppsala Monitoring Centre

Advancing medicine safety ***together***

Uppsala Monitoring Centre (UMC)
Box 1051, SE-751 40 Uppsala, Sweden
Email: info@who-umc.org, www.who-umc.org

Uppsala Monitoring Centre

Vaccines - Substances

WP2: EU-SRS & SMS

On behalf of the experts in the EU-SRS team,
Annet Rozema (project leader EU-SRS)

CoE - 14/Jan/2022

EU-SRS
THE EUROPEAN SUBSTANCE REGISTRATION SYSTEM

TOPICS

- EU-SRS implementation project
- Cleansing (SMS) & building vaccines substances (EU-SRS)
- Vaccines naming and structure
- Collaboration

TODAY'S TOPIC

- Vaccine challenges:
  - cleansing
  - confidentiality
  - vaccine naming

- This is all very relevant to the substance experts working on vaccines in the EU-SRS implementation project

EU-SRS IMPLEMENTATION PROJECT

EU-SRS
THE EUROPEAN SUBSTANCE REGISTRATION SYSTEM

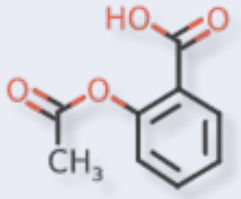
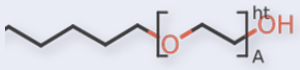
EU-SRS IMPLEMENTATION PROJECT

- GSRS software is implemented in EU:
  - In line with ISO IDMP
  - Open source software
  - Describe substances in a scientifically sound manner
  - Substance class-specific data capturing

EU-SRS
THE EUROPEAN SUBSTANCE REGISTRATION SYSTEM

- Key components of the project:
  - Cleansing SMS substance data (SVG provides feedback to EMA)
  - Building substances in EU-SRS, as well as enriching substances
  - Software installation & validation
  - Establish Substance Validation Group
  - Guidance documentation & procedures available (master data management)

IDENTIFYING ELEMENTS PER SUBSTANCE TYPE

Substance type	Chemical	Polymer	Protein	Nucleic acid	Structurally diverse
Defined by	Chemical structure	Structural repeat unit(s)	Amino acid sequence(s)	Nucleobase sequence	Taxonomic information + part
Example			>A35X00TA2K RCPGCGQGVQAGCPGGCVEE EDGGSPAEGCAEAEGCLRRE GQECGVYTPNCAPGLQCHPP ...	>303159CVH9 TAAACGTTATAACGTT ATGACGTCAT	Organism Family: CANNABACEAE Organism Genus: CANNABIS Organism Species: SATIVA Author: L. Infraspecific Type: SUBSPECIES Infraspecific Name: SUBSP. SATIVA

Vaccine antigens – among the most complex substances to define:

Description starts from pathogen, defined as structurally diverse

- Specific antigens can be described as e.g., proteins or polymers
- Inactivation of toxins and adsorbing to aluminum are described in SSG1

This slide is courtesy of Tyler Peryea, FDA (GSRS team)

DESCRIPTION OF VACCINES IS IMPORTANT…

- Regulatory assessors benefit from insight in
  - Scientific description of vaccines
  - Relationships
  - References, identifiers
  - Naming
  - Hierarchy
  - Access to information of similar or related vaccines

- Rapporteurs across Europe will have access to the “single point of truth”
- Vaccines described through structured data explains more than many words

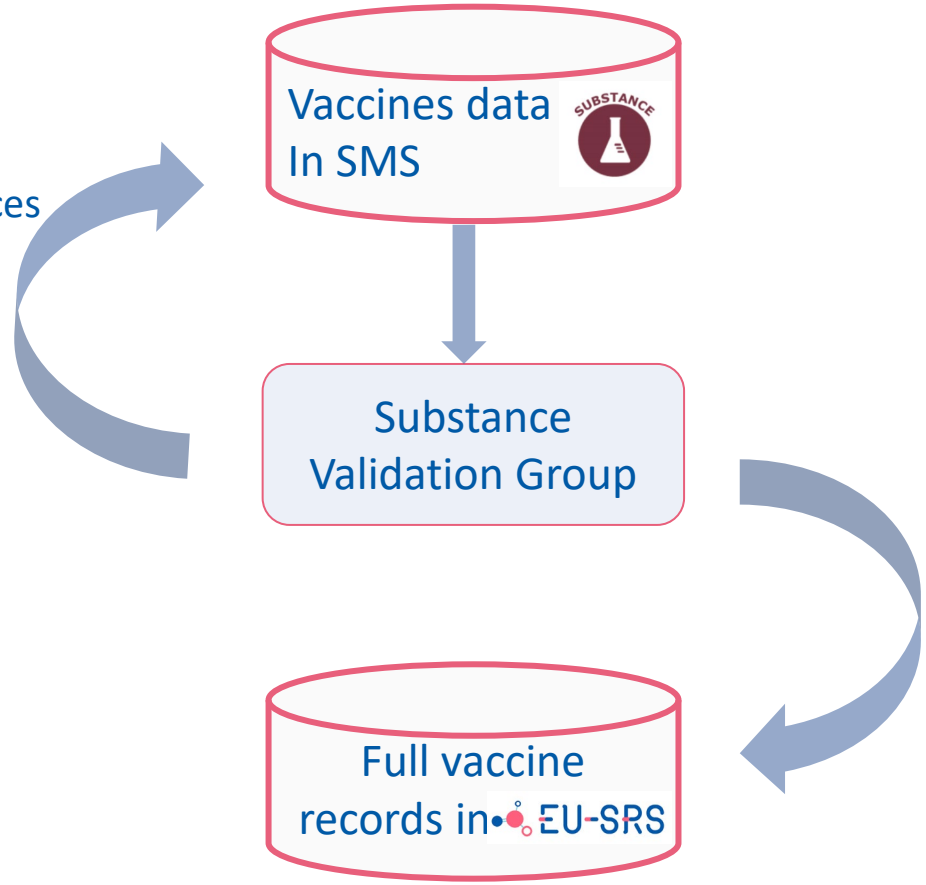
CLEANSING (SMS) & BUILDING VACCINE SUBSTANCES (EU-SRS)

EU-SRS
THE EUROPEAN SUBSTANCE REGISTRATION SYSTEM

CLEANSING + BUILDING VACCINES RECORDS

Identify duplicate vaccine substances
Identify invalid vaccine substances
Confirm vaccine substance names

- Preferred terms
- Aliases



- Build vaccine record in EU-SRS with all necessary information (IDMP)

CLEANSING & BUILDING VACCINES

- ~550 unique vaccine substances received from SMS
- 66 microorganisms
  - 42% Virusses
  - 58% Bacteria
- Each microorganism contains 1 or more vaccine records + 1 or more names (PT/Aliases)
- SVG processes records per microorganism:
  1. Establish the naming rules
  2. Review SMS records
  3. Provide to SMS team
  4. Build example record in EU-SRS
  5. Document how to build the vaccines in EU-SRS
  6. Build records in EU-SRS

VACCINES SUBSTANCES - FACTS & FIGURES (SMS)

Microorganism (main categories)	Unique substances	Total number of names
Influenza virus	172	191
Streptococcus agalactiae	38	57
Neisseria meningitidis	36	69
Bordetella pertussis	34	40
Poliovirus	23	35
Rotavirus	19	22
Haemophilus influenzae	18	54
Hepatitis B virus	18	25
Hepatitis A virus	14	19

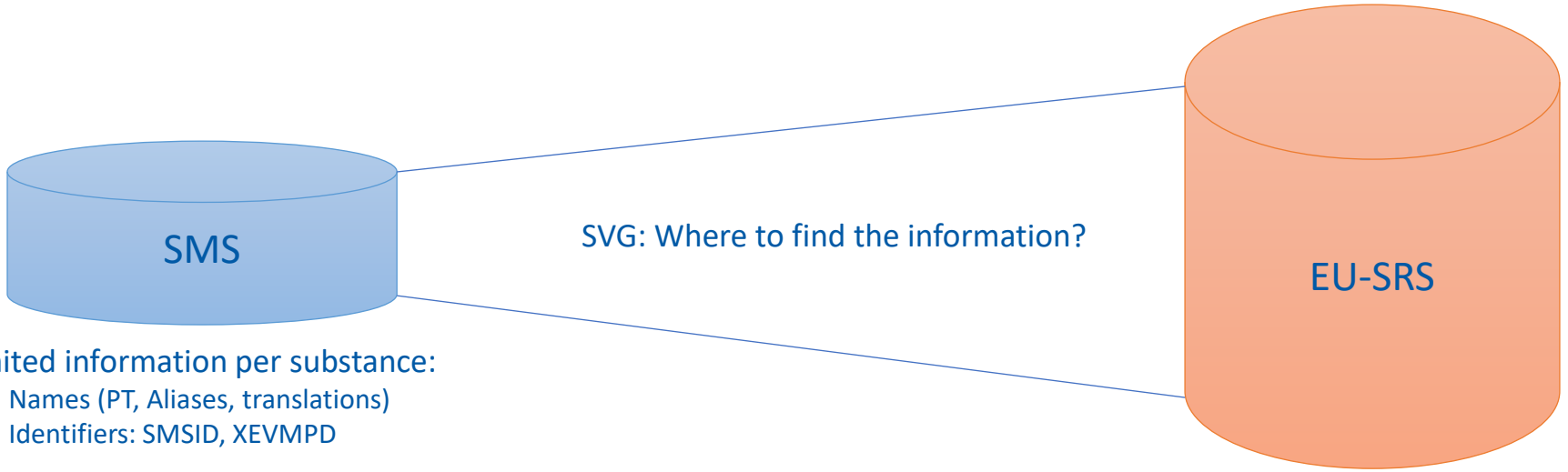
Selection of microorganisms with the largest number of unique substances

~75% of SMS records processed
Examples created in EU-SRS

Note: Significantly more changes to SMS data requested compared to already completed cleansing of chemicals

EU-SRS

CHALLENGES WITH *CLEANSING*



Limited information per substance:

- Names (PT, Aliases, translations)
- Identifiers: SMSID, XEVMPD
- …

- Building records in EU-SRS is maybe not so easy, but certainly doable
- Most time spent is on finding the missing information for existing substances

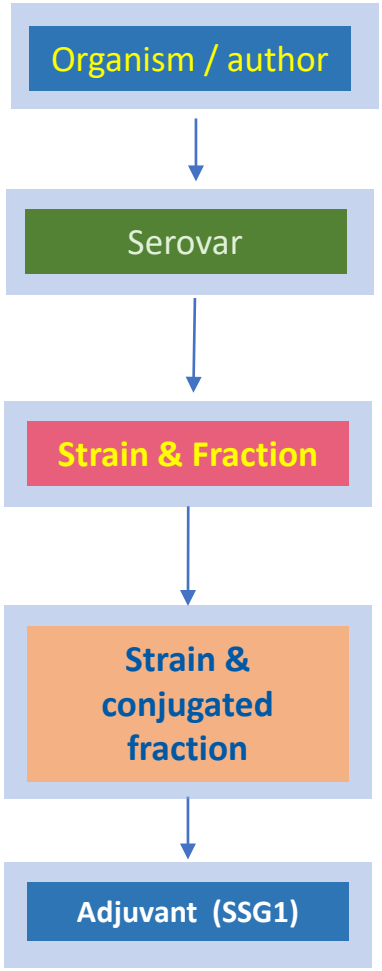
Extensive information per substance:

- Names (PT, Aliases, translations)
- Identifiers: SMSID, EVMPD, UNII, ….
- Hierarchy
- Source materials
- Fractions
- Modifications
- Relationships
- Structural repeat units
- …

VACCINES NAMING & STRUCTURE

EU-SRS
THE EUROPEAN SUBSTANCE REGISTRATION SYSTEM

NAMING SYNTAX OF HUMAN VACCINES BACTERIUM



Example bacterium

Neisseria meningitidis, (Albrecht and Ghon, 1901) Murray, 1929, Whole

Syntax: <Organism>,<Author>,< Year>, <Status> (Whole = Live)

Neisseria meningitidis, Serogroup A, Whole

Syntax: <Organism>,<Serogroup/ Serovar>, <Status>

Neisseria meningitidis, serogroup A, Strain C1, Polysaccharide
(Structurally diverse definition e.g. taxonomic description)
[Addition fields for polysaccharide description
by Alternative Polymer definition by intrisic relationship of both records]

Syntax: <Organism>,<Serogroup>,<Strain>,<Fraction>

Neisseria meningiditis, serogroup A, Strain C1, Oligosaccharide
C. diphtheriae CRM197 conjugated antigen
(Structurally diverse definition e.g. strain & fraction description)
[Additional fields for the conlugated **protein description** by **Alternative Protein definition by intrinsic relationship of both records**

Neisseria meningiditis, serogroup A, Strain C1, Oligosaccharide
C. diphtheriae CRM197 conjugated antigen, Adsorbed on Aluminum hydroxide

Syntax: <Organism>,<Serogroup>,<Strain>.<Fraction>, <Adjuvant>

NEISSERIA RECORDS IN EU-SRS

STRUCTURALLY DIVERSE

Names: Neisseria meningitidis, Whole-HD-TEST
Neisseria meningitidis (Albrecht and Ghon, 1901)…

Codes: ITIS: *ITIS- 964013*
NCBI TAXONOMY: *NCBI-487*

Relationships: 7

Part: WHOLE

Created: a year ago

Last modified: a month ago

Status: pending

Version: 11

Substance Hierarchy

◢ Neisseria meningitidis (Albrecht and Ghon, 1901) Murray, 1929, Whole-HD-TEST	PENDING RECORD
▷ Neisseria meningitidis, Serogroup B, Whole-HD-TEST	PENDING RECORD
Neisseria meningitidis, Serogroup C, Whole-HD-TEST	PENDING RECORD
Neisseria meningitidis, Serogroup Y, Whole-HD-TEST	PENDING RECORD
◢ Neisseria meningitidis, Serogroup A, Whole-HD-TEST	PENDING RECORD
Neisseria meningiditis, Serogroup A, Strain C1, Polysaccharide-HD-TEST	PENDING RECORD
◢ Neisseria meningitidis, Serogroup A, Strain C1, Oligosaccharide C.diphtheriae …	PENDING RECORD
Neisseria meningitidis, Serogroup A, Strain C1, Oligosaccharide C.diphtheria…	PENDING RECORD

{G1SS}

POLYSACCHARIDE RECORD 1) STRUCTURALLY DIVERSE DEFINITION 2) POLYMER DEFINITION

Display of the Monomers

Neisseria meningiditis, Serogroup A, Strain C1, Polysaccharide-HD-TEST

pending record

- Overview
- Alternative Definitions 1
- Names 1
- Identifiers 4
- Relationships 2
- Modifications 1
- Notes 4

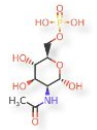
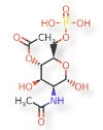
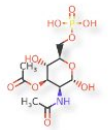
Overview

Substance Class	Structurally Diverse
Source Materials Class	ORGANISM
Source Materials Type	BACTERIUM
Source Materials State	INACTIVATED
Source Materials Parent	Neisseria meningitidis, Serogroup A, Whole-HD-TEST
Development Stage	MATURE
Part	CELL WALL
Fraction Material Type	Polysaccharide

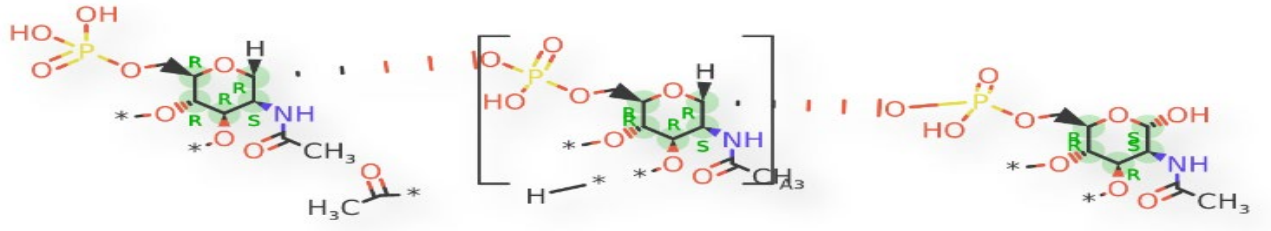
ALTERNATIVE DEFINITION for [Neisseria meningiditis, Serogroup A, Strain C1, Polysaccharide-HD-TEST]

alternative record

- Overview
- Primary Definition
- Display Structure
- Monomers 3
- Structural Units 5
- Relationships 1

Material	Material Name	Amount	Type
	2-Acetamide-deoxy-D-Mannose-6-Phosphate		STARTING_MATERIAL
	4-O-acetyl-2-acetamide-2-deoxy-alpha-D-Mannose-6-phosphate		STARTING_MATERIAL
	3-O-Acetyl-2-Acetamide-2-deoxy-alpha-D-Mannose-6-Phosphate		STARTING_MATERIAL

Display of the structure of the Repeat Unit & end groups



CONJUGATED ANTIGEN RECORD

1) STRUCTURALLY DIVERSE DEFINITION

2) PROTEIN DEFINITION OF THE CONJUGATED CRM197 ANTIGEN

Neisseria meningitidis, Serogroup A, Strain C1, Oligosaccharide C.diphtheriae CRM197 Conjugated Antigen-HD-TEST

pending record

- Overview
- Alternative Definitions 1
- Names 1
- Identifiers 4
- Specified Substances 1
- Relationships 2
- Audit Info
- References 7

Overview

Substance Class	Structurally Diverse
Source Materials Class	ORGANISM
Source Materials Type	BACTERIUM
Source Materials State	INACTIVATED
Source Materials Parent	Neisseria meningitidis, Serogroup A, Whole-HD-TEST
Part	CELL WALL
Fraction Material Type	Conjugated Oligosaccharide
Fraction Name	Oligosaccharide Diphtheria CRM197 Conjugated Antigen

ALTERNATIVE DEFINITION for [Neisseria meningitidis, Serogroup A, Strain C1, Oligosaccharide C.diphtheriae CRM197 Conjugated Antigen-HD-TEST]

alternative record

- Overview
- Primary Definition
- Subunits 1
- Disulfide Links 2

Overview

Substance Class	Protein
Protein Type	PROTEIN
Protein Sub Type	CARRIERPROTEIN
Sequence Origin	Tox197 gene of corynephage beta DNA
Sequence Type	COMPLETE
Record UNII	alternative record
Record Status	alternative
Record Version	2

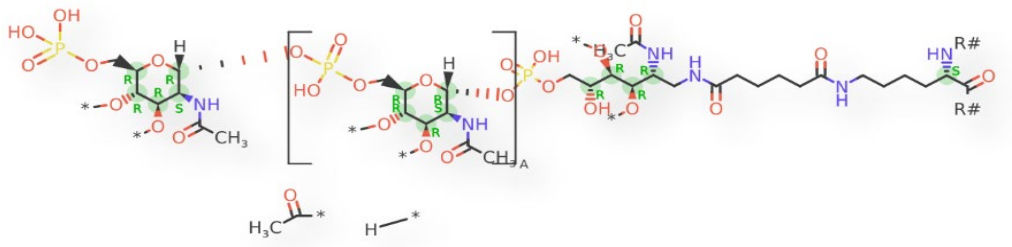
Show Definitional References

Snapshot of partial CRM197 Subunit

Subunit 1

10	20	30	40	50
GADDVVDSSK	SFVMENFSSY	HGTKPGYVDS	IQKGIQKPKS	GTQGNYDDDW
60	70	80	90	100
KEFYSTDNKY	DAAGYSVDNE	NPLSGKAGGV	VKVTYPGLTK	VLALKVDNAE
110	120	130	140	150
TIKKELGLSL	TEPLMEQVGT	EEFIKRFGDG	ASRVVLSLPF	AEGSSSVEYI
160	170	180	190	200
NNWEQAKALS	VELEINFETR	GKRGQDAMYE	YMAQACAGNR	VRRSVGSSLS
210	220	230	240	250

Display of Modified Conjugated Oligosaccharide conlugated to Carrier protein



CHALLENGES WITH *CONFIDENTIALITY OF NAMES*

- In order to define the correct names, more information than the SMS names was needed → time consuming
- The explained naming conventions contrain confidential information
  - Strain name
  - In SMS, the preferred term is always public; therefore the preferred term may be in the SMS database, but not as preferred term
  - EU-SRS will be only accessible to EU regulators, so the confidentiality of names is less of an issue
  - SMS and EU-SRS will need to communicate / stay in synch
  - The team is currently investigating the best solution

COLLABORATION

EU-SRS
THE EUROPEAN SUBSTANCE REGISTRATION SYSTEM

EU-SRS / WP2 IS A *COLLABORATIVE* PROJECT

- SVG members come from a variety of NCA's: Assessors or substance experts (21 members)
- Both human and veterinary experts are involved
- There is a close collaboration with EMA & FDA as well as with WHO-UMC
- **Industry involvement** through Substance Work Group approach

2021: Global Vaccines Initiative

EU-SRS

INVOLVING INDUSTRY IN BUILDING VACCINES

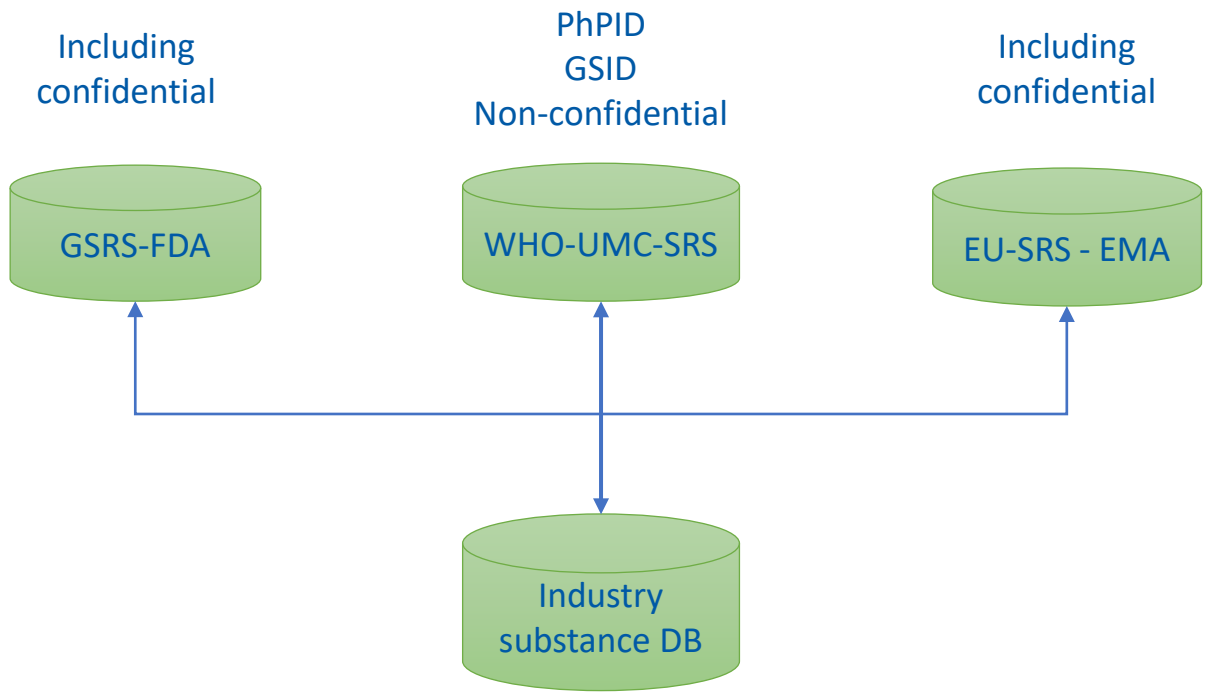
Process details:

- SVG provides guidance on how to build vaccine in the SRS software
- Relevant vaccine is exported in JSON format and shared with industry (Eudralink)
- Industry adds the necessary information based on internal knowledge and exports the updated JSON file to SVG (Eudralink)
- SVG to import the updated substance and validate (peer review) of vaccine in EU-SRS

INDUSTRY INVOLVEMENT IN BUILDING VACCINE RECORDS

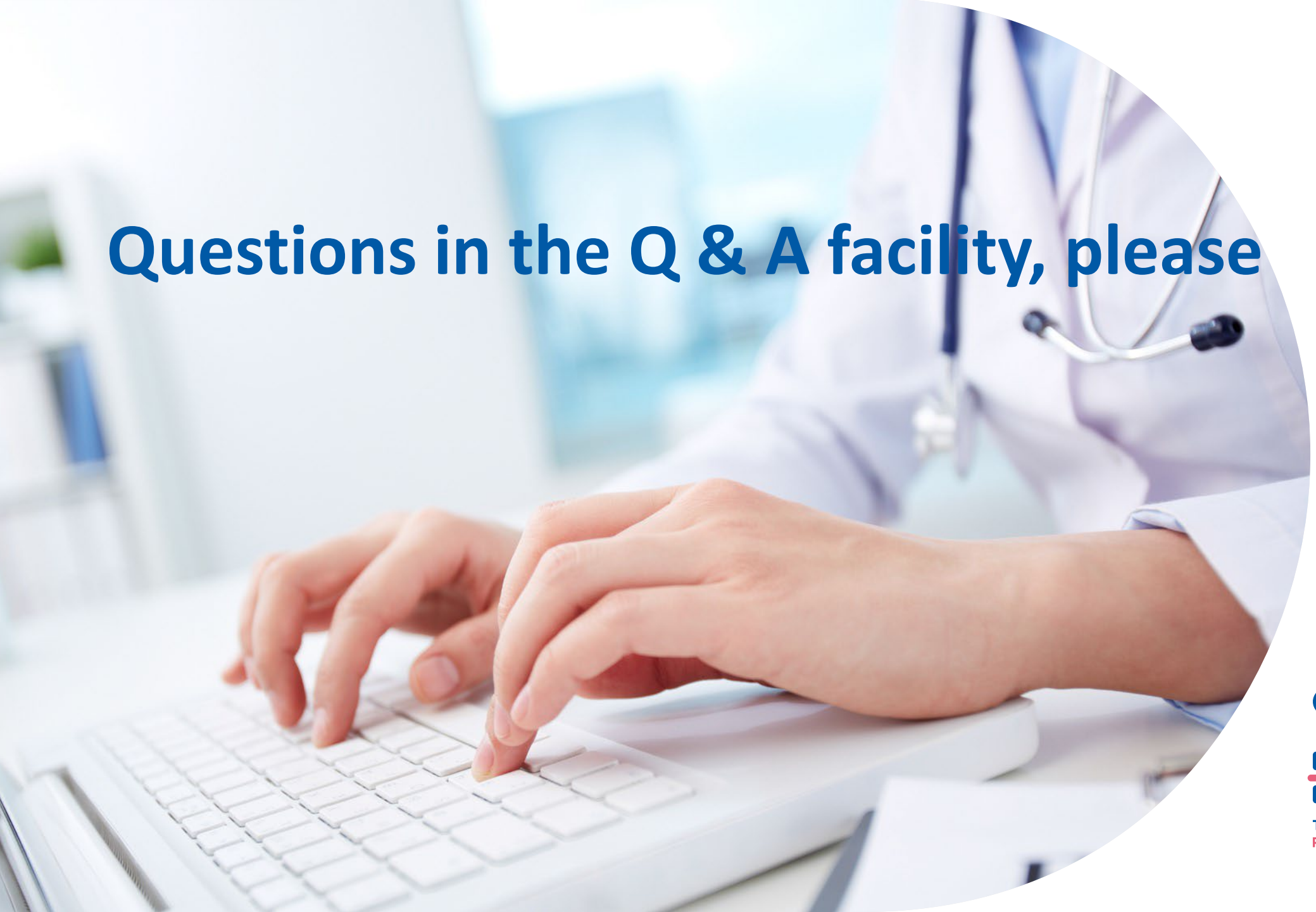
- EU-SRS Steering Committee endorsed industry involvement in building vaccines in SRS (legacy/existing vaccines)
- Whether this would be a future model of exchanging data cannot be confirmed at this stage
- 3 pharmaceutical companies have indicated interest to join this activity
- This activity also fits with the discussions in the global vaccines initiative, and it is expected to provide input into GSRS software requirements for data exchange
- Start: meet early February to confirm next steps

THE FUTURE OF SUBSTANCE MANAGEMENT?



- Substance identifiers (UNII, EUTCT, GSID)
- Global approach, standards
- Same “signature fields” in each SRS
- Data exchange, staging area
- JSON file shared, validated, confirmed
- Share resources (agreed process)
- Scope differences between the instances
  - Early devt substances yes/no
  - Veterinary substances yes/no
  - Food, homeopathics

Questions in the Q & A facility, please



EU-SRS
THE EUROPEAN SUBSTANCE REGISTRATION SYSTEM

14 January 2022

Vaccine challenges – cleansing, confidentiality and vaccine naming
Industry perspective

Presenter: Jean-Gonzague Fontaine
jean-gonzague.x.fontaine@gsk.com

Product and Substance Master Data Lead (IDMP), GSK R&D, Vaccines BU
ISO TC 215 WG 6 « Pharmacy and Medicines Business » expert

This project has received funding from the European Union's
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Agenda

- IDMP, a paradigm shift for pharmaceutical industry
- Product and substance identification implementation, challenges and benefits
- Industry contribution to the GSID and PhPID

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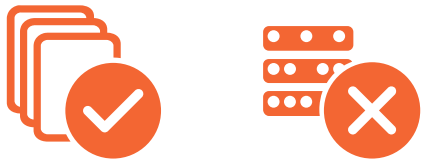
IDMP, a paradigm shift for pharmaceutical industry

IDMP standards implementation is a paradigm shift for Pharmaceutical Industry

Pharma development and regulatory historically deal with documents (with a notable exception of clinical – CDISC)

Regulatory process leverages documents such as IMPD or CTD, PSF, etc., which contain limited structured data in the form of tables.

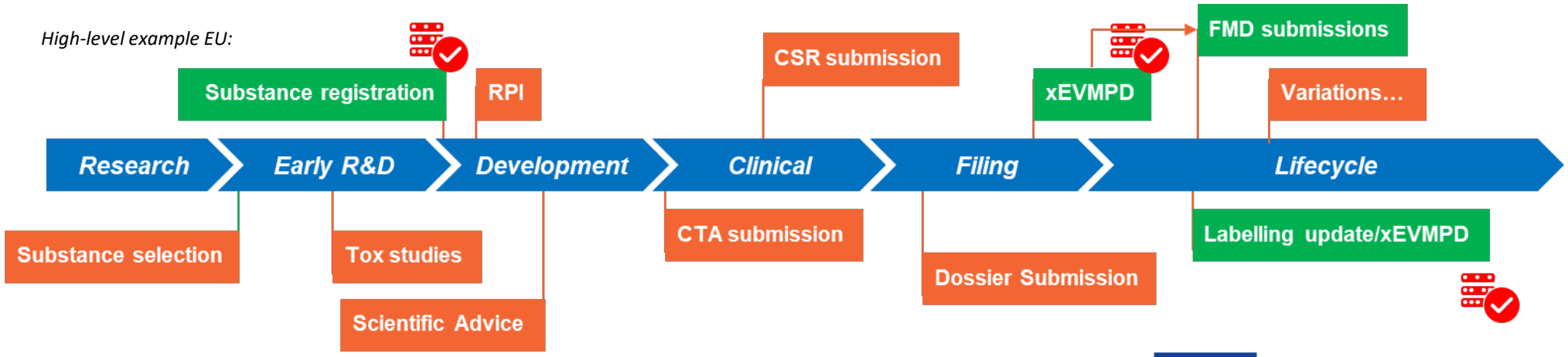


Current situation

Current situation: limited structured information managed post new drug or labelling approval.

- EMA xEVMPD: structured after labelling information has been approved within 15 days from the date of authorization*
- EMA SMS: early registration, with very basic information (name)
- FDA SPL: submission of the label information within 14 days of application approval
- FDA GSRS: registration based on scientific information, for substance identification in the SPL submission

High-level example EU:



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*or 30 days for variation or before CTA form submission for DMP

IDMP standards implementation is a paradigm shift for Pharmaceutical Industry

Recent developments in Europe are driving the industry towards in-process data exchanges:

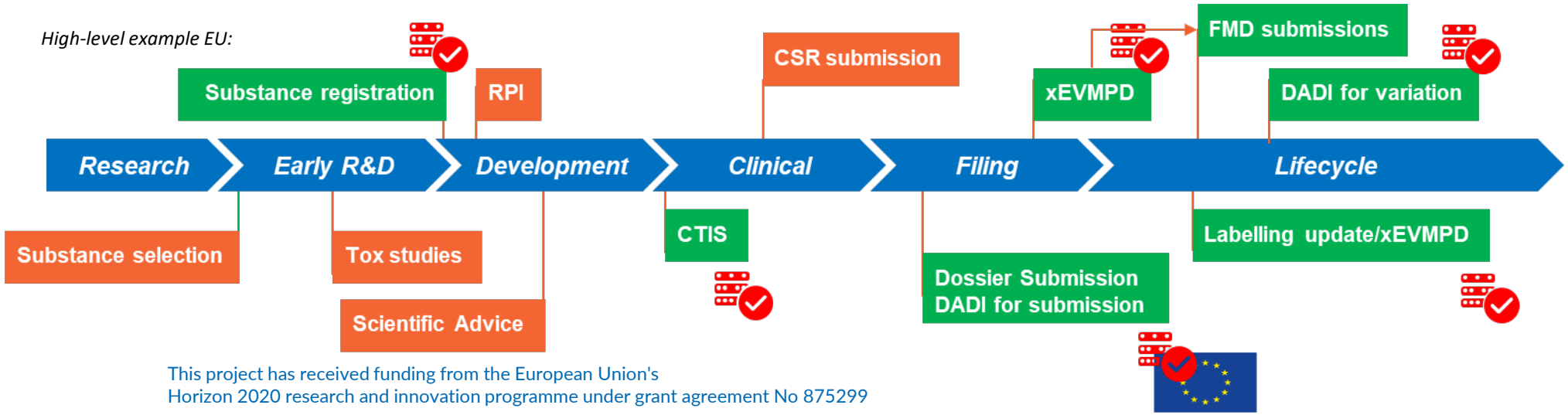
DADI and PMS represent a change in the approach to data submission, where data is submitted **in process, aligned/negotiated with authorities**, as opposed to post-authorization reporting.

Long term

The consequences of this are the need to manage:

- The data lifecycle: both submitted ***AND*** approved data for the same datapoint.
- Scientifically proven information versus regulatory truth for the same datapoint.
- Parallel, desynchronized submissions between regulatory authorities.

Implies the capability to manage as data, in system what is managed today in documents.



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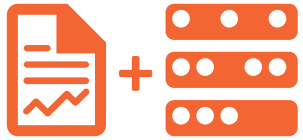
Precise product and substance identification is needed within the regulatory process framework

What are the consequences for regulatory activities (EU focus)?
Additional IDs for the management and identification of the various product dimensions.



Global IDs

Regulatory procedure identification	EMA procedure n°	EMA procedure n°	-
PMS reference	-	PMS ID	***
Authorisation	MA Number	MA number	-
Medicinal Product	PRD code*	MPID (+ PRD code)	***
Package	-	PCID	-
Pharmaceutical Product	-	PhPID	**Global PhPID****
Substance	EUTCT, SUB code	EUTCT (+ SUB code)	**GSID****

*after labelling approval **managed by WHO ***proposal of a technical report for a global and persistent Product identification globally (ISO TC215 WG6)

- In process data exchange:
  - Product and substance identification critical – data quality
  - Improved transparency
  - Improved lifecycle management and PV on products

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Product and substance identification implementation, challenges and benefits

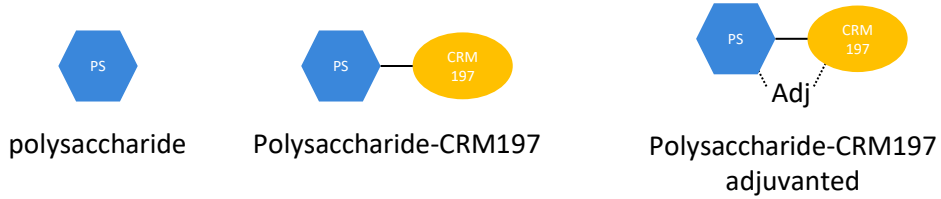
Clear product and substance identification provide transversal and global benefit

Managing data in regulatory procedures presents added challenges…

- Additional datapoints, capabilities, controls, etc.

…but also provides benefits:

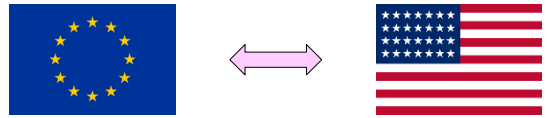
- Straight forward identification of substances (and so products):
  - Do we mean the polysaccharide (active moiety), the conjugated polysaccharide, or the adjuvanted conjugated polysaccharide (active ingredient)?



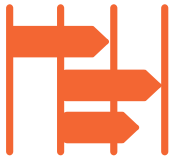
polysaccharide | Polysaccharide-CRM197 | Polysaccharide-CRM197 adjuvanted

  - Do we mean naturally isolated polysaccharide or mechanicaly sized polysaccharide?

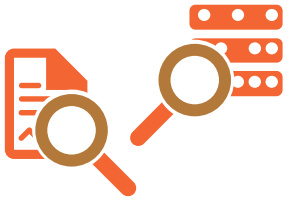
- Straightforward alignment of product across jurisdictions and reusability of information
  Same GSID, same PhPID



- Regulatory processes' efficiency (Pharma and Regulator)



- Transparency: information is easily accessible and structured in a more analysable format



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Substance standard implementation challenges

Implementing the IDMP substance standard presents challenges for industry:

- Additional datapoints: defined and understood by business end-users, business rules and lifecycle – risk!
- Additional capabilities: learning curve/changes for both people and systems
- Additional controls: data quality checks are a must!
- Change in mindset – context is based on a mix of system and document based info → burden for scientific functions which support highly precise antigen information
- Legacy systems, legacy standards
  IDMP substance is another representation of antigens in the company
- Transversal information – first antigen description in early R&D, transferred to development, which will elucidate the complete antigen description as well as its development
- IDMP substance standard focuses on the scientific description of the antigen (incidental, stable information) where development/commercial manufacturing focus on Material Master articles and batches/lots (transactional information)
- IDMP substance standard still regulatory driven: however, the scientific knowledge is in the development functions

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Benefit of PhPID and GSID for Pharmacovigilance

- Vaccine Pharmacovigilence will leverage on PhPID (and GSID) for product identification in individual case safety reports and safety databases.
  - PhPID → Transversal (jurisdiction specific) product tagging
  - GSID → deduced from the Pharmaceutical Product, enabling cross product analysis (sharing the same substance)
- Pharmaceutical Product: leverage dose form characteristics for the administrable dose form description. Improved granularity.
- GSID: Precise substance identification enables answers to transversal research questions.
  For example: a regulatory authority may require the adjuvant safety profile regardless of the antigen.

Challenges in Vaccines safety reporting:

- Reports are often too vague to identify exactly which vaccine was administered:
  - Missing Tradename (e.g. Hepatitis B vaccine)
  - No target population (10 or 20 µg? Child or Adult?)
- PhP (therefore PhPID) does not cover excipients:
  - Impacts identification of side effects from excipients
- Biological substances are not identical: GSK's hep B antigen is not the same one as the Sanofi hep B antigen → GSID (or PhPID) is critical

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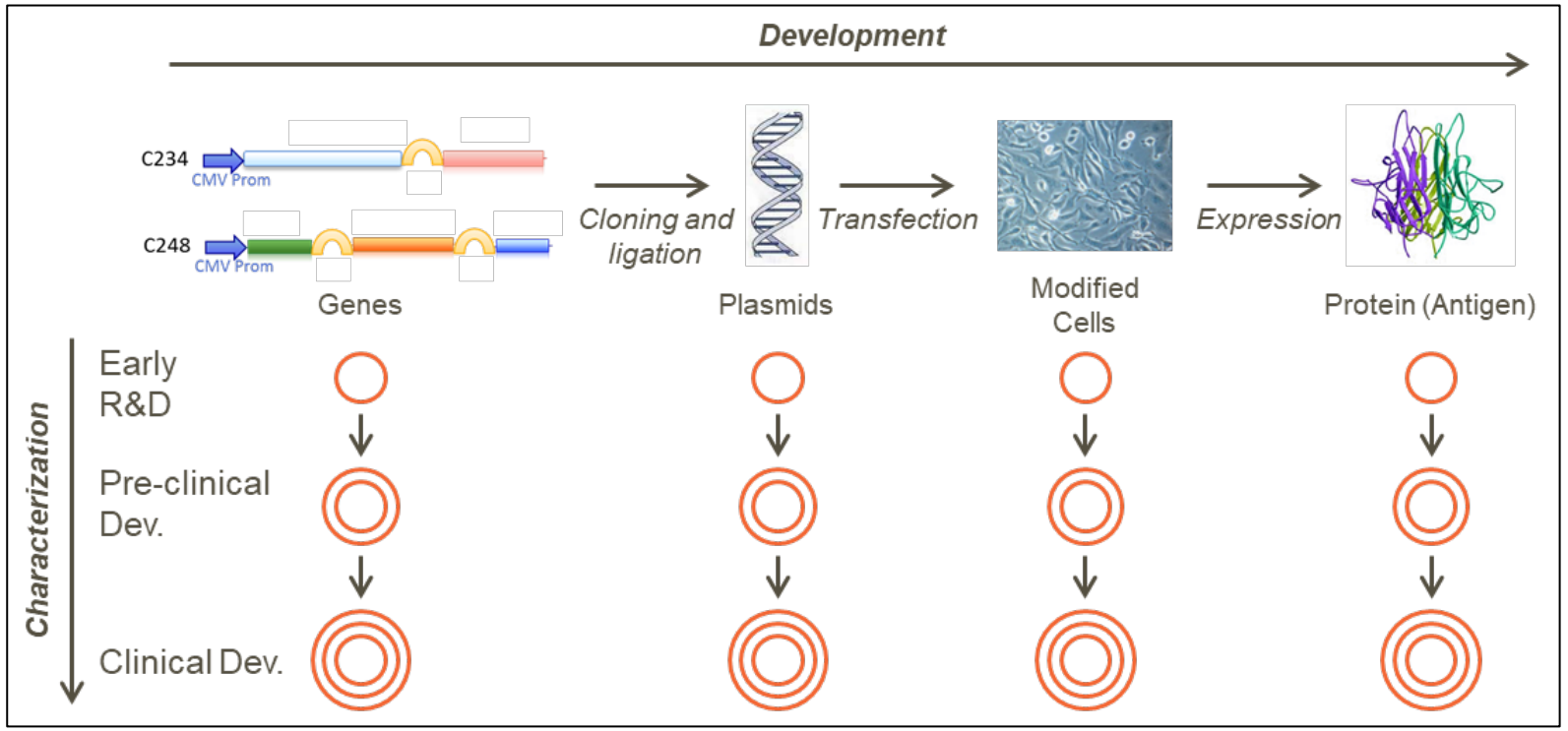
Industry contribution to the GSID and PhPID

UNICOM

- Industry is the **originator, owner and expert on substance information and substance-defining data**
- **Industry involvement in substance creation** and sharing between regulatory authorities
- For vaccines complex substances, antigen is not always characterised at the beginning of development. **Basic substances description** (Minimum substance fields) **is required** in early phases.
- **Lifecycle management of a substance:** creation and enrichment, parent-child relationship, etc.



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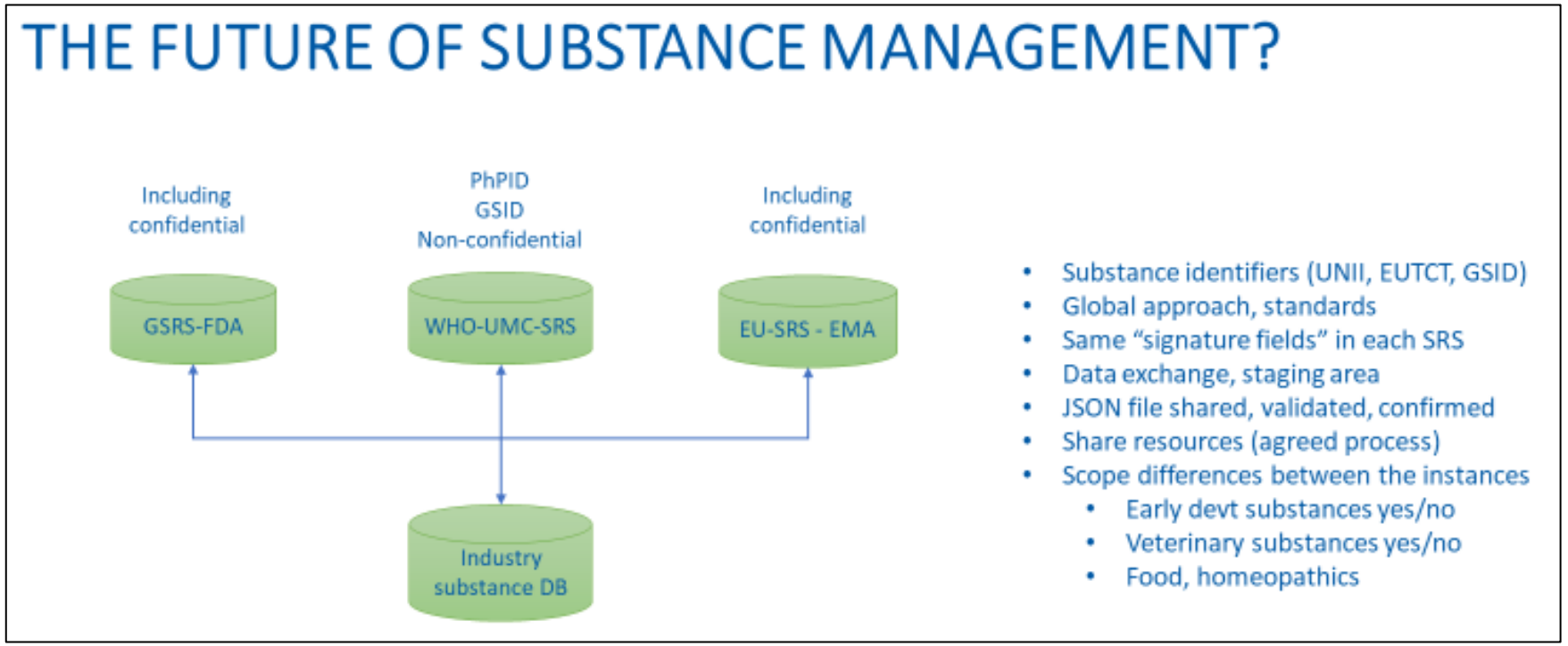
- Confidential information must not be shared between regulatory authorities, nor with the WHO UMC
- **Industry may act as a broker** between regulatory authorities, exchanging the same information, holding a public signature.

A PoC is currently been initiated focusing on data exchange and alignment between EU-SRS team and participating companies (voluntary basis)



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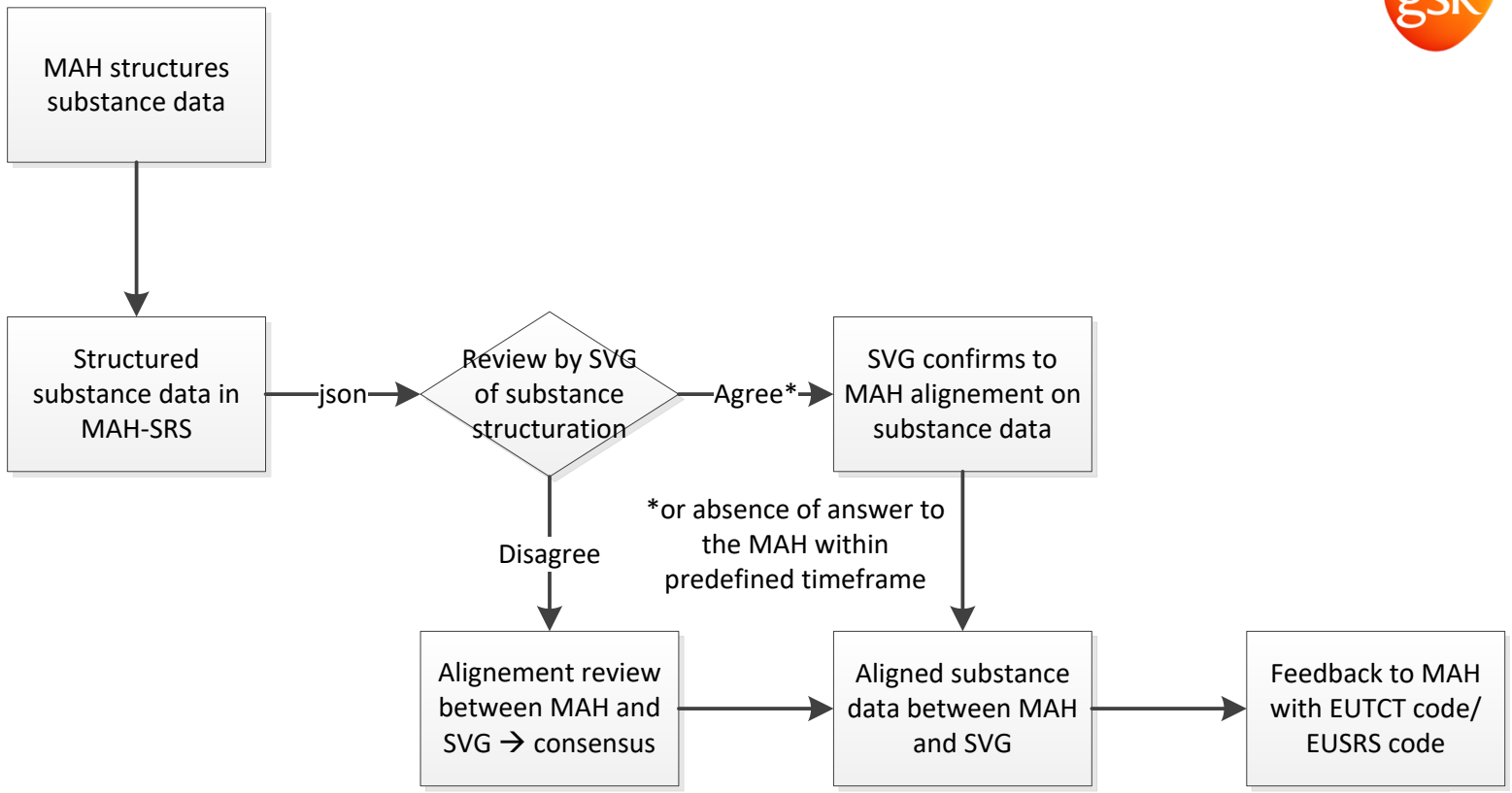
Data exchange and alignment PoC between EU-SRS team and pharma companies

- **System:** leverage GSRS system, MAH instance of SRS and EU-SRS
  - Same system on both Regulatory and MAH sides.

- **Process:**
  - Define roles and responsibilities
  - Define the cleansing process →
  - Define & align on business rules
  - Define hash process



- **Data:**
  - **Substance data ownership: MAH**.
    Regulatory authority (SVG) can not modify a substance data set.
    Enrichment with additional non-definitional data (e.g; references, links, additional codes, etc.)
  - Data is confidential by default, except for the substance ID, substance version and substance hashmap (linked to the version)
    Public data, substance ID, version and hashmap are shared with UMC

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Final remarks

- IDMP Implementation of IDMP represents a paradigm shift for industry, with in-process data exchange in addition to documents.
- There is a need for Pharmacovigilance to define GSID and PhPID for vaccines on a global scale.
- The definition of GSID and PhPID must include the data owner – the pharmaceutical industry, as they are the expert on their own data.
- Both regulators and industry will benefit from having an univocal definition of substances and products.

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Questions in the Q & A facility, please

For feedback, please go to : https://forms.gle/SvePmpHJNwDJHFpL8

Thanks for your time

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Thanks for your time

Questions, comments

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