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Up-scaling the global univocal identification of medicines

Pharmaceutical products – based on relation from manufactured- to administrable dose form – NoMA's solution to meet needs in clinical practice

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Agenda

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► Presentation of NoMA and the SAFEST project

► Pharmaceutical products and pharmaceutical dose forms

▷ Definitions

▷ Challenges

▷ Clinical use

► NoMAs solution to meet needs in clinical practice

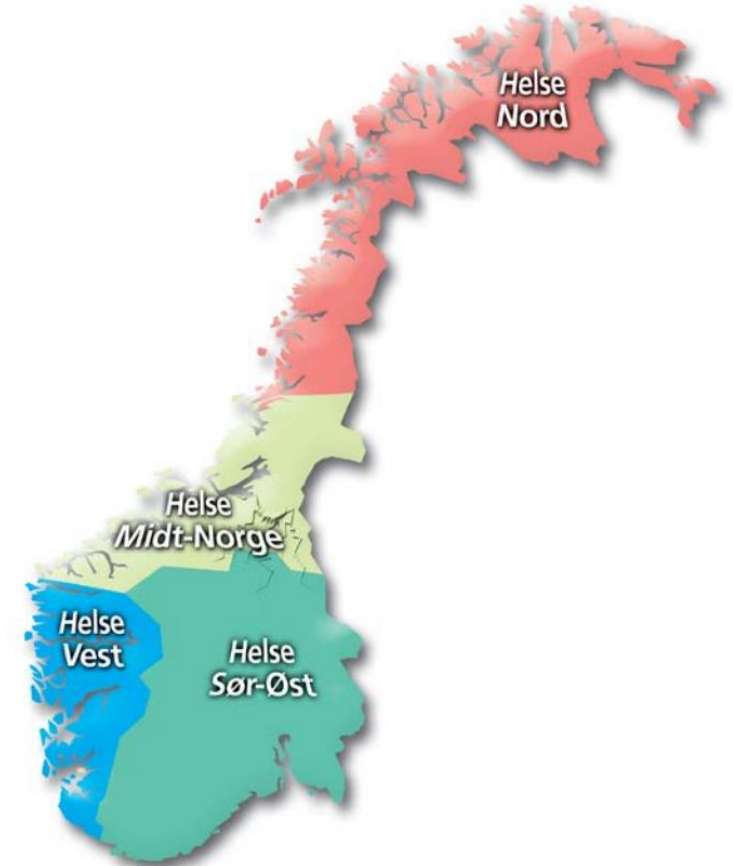► Other aspects for PhPID-generation to meet clinical practice

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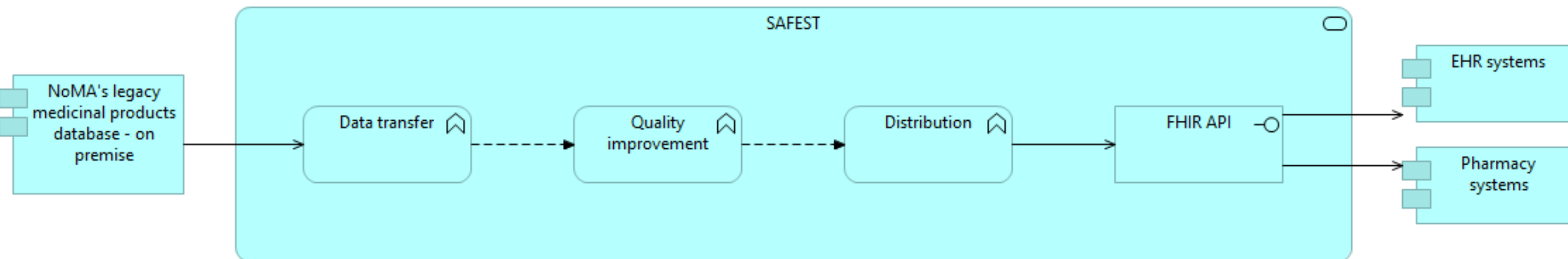
About NoMA (Norwegian Medicines Agency)

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► ≈ 360 employees

► Agency under the Ministry of Health and Care Services

► Our goal is to ensure:

  ▷ That medical products are safe and effective.

  ▷ That the population has access to medicines regardless of ability to pay.

  ▷ The correct medicinal and economical use of medicines.

  ▷ The use of cost-effective medicines.

  ▷ That medical devices placed on the market and put into service in Norway meet the regulatory requirements.

► Responsible for delivery of the Medicinal Product Dictionary

► Facilitate new digital information services based on international standards to meet clinical needs

► Contribute to standardising information about medicinal products nationally and in Europe through European cooperation
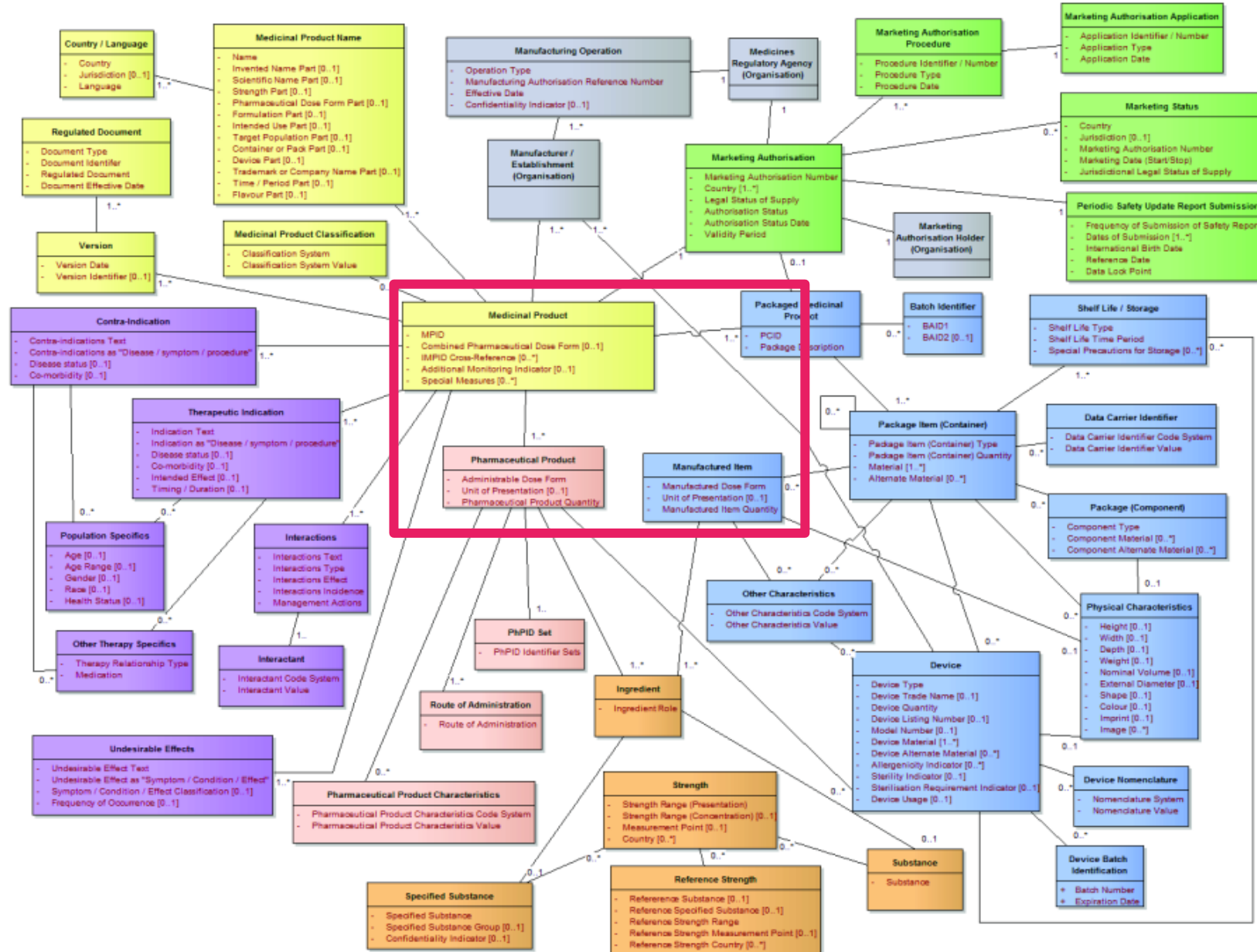
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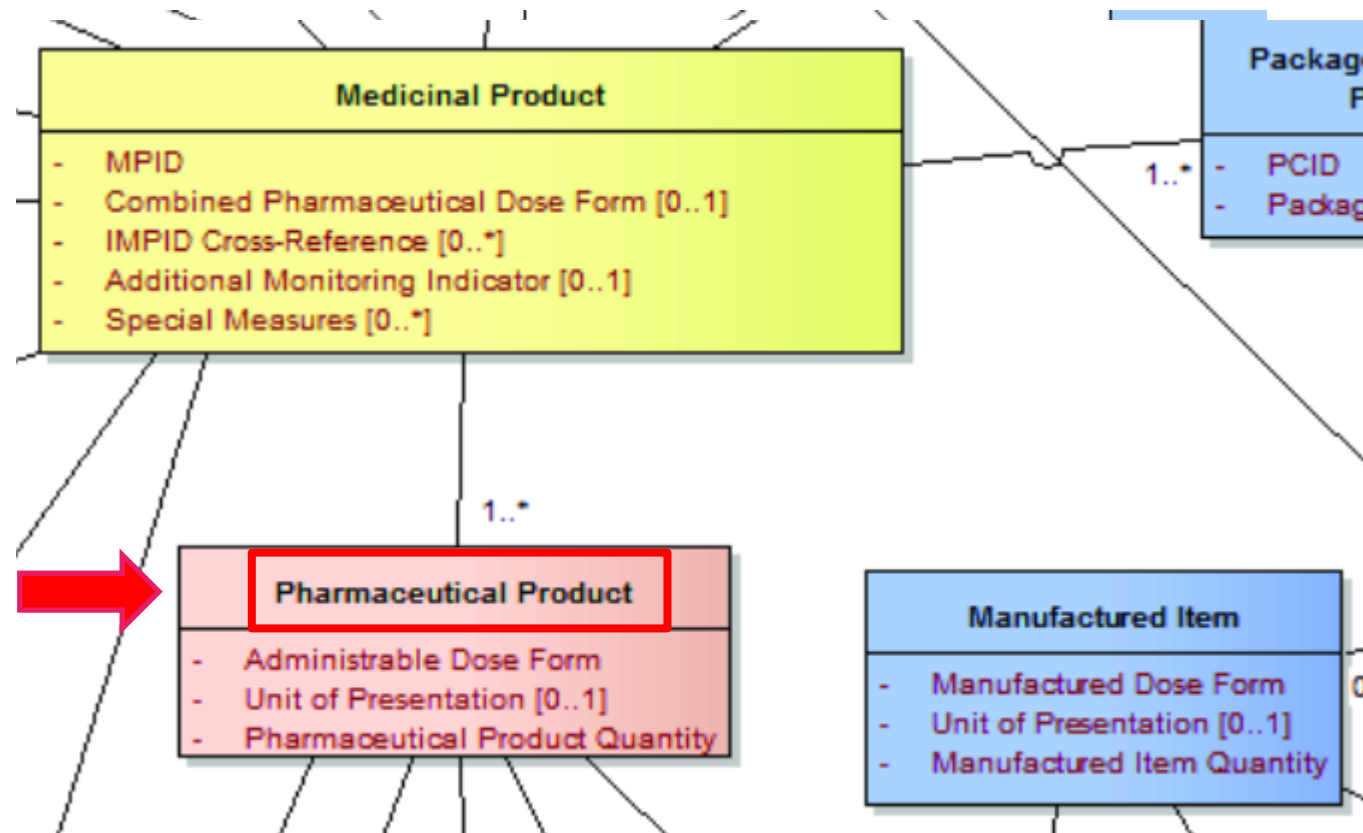
SAFEST project: actors and set-up

- ► 4 health regions – specialized care
  - ▷ The project is financed by the health regions
- ► Background drivers:
  - ▷ Hospitals using different EHRs and other clinical systems.
  - ▷ Reduce manual intervention on the medicinal products data to support clinical use
- ► Goals:
  - ▷ Improved data quality through implementation of IDMP: definition of strength, pharmaceutical dose form, packages, route of administration
  - ▷ Prescription based on active substance (INN)
  - ▷ Data on nutritional products – parenteral medicinal products and enteral nutrition drinks
  - ▷ Product codes on unit level to support Closed-loop medication management
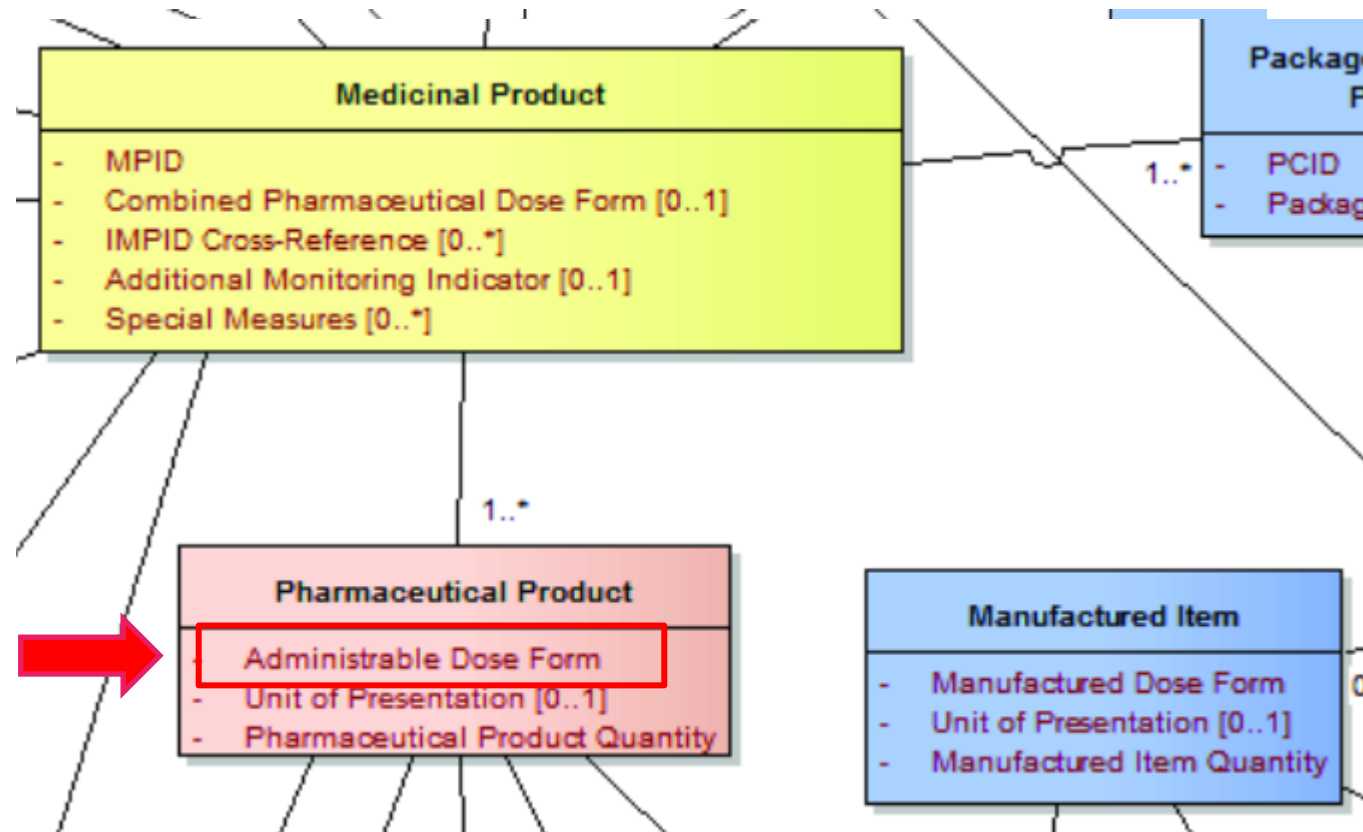- ► Close collaboration with hospitals-/clinician representatives

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SAFEST technical solution

SAFEST-project: status

► First delivery (Q4 2022):

  ▷ Medicinal products, Package and product codes on every package level in FHIR format

  ▷ GUI for management of terms for pharmaceutical dose form, combined term and more

► Next delivery under testing: GUI for management of terms for substance (delivery Q3 2023)

► Analysis and design: Nutrition, Administrable products, Manufactured Item and Ingredient with strength (delivery Q1 2024)

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Medicinal Product

- MPID
- Combined Pharmaceutical Dose Form [0..1]
- IMPID Cross-Reference [0..*]
- Additional Monitoring Indicator [0..1]
- Special Measures [0..*]

Package P

1..* - PCID
- Package

1..*

Pharmaceutical Product

- Administrable Dose Form
- Unit of Presentation [0..1]
- Pharmaceutical Product Quantity

Manufactured Item

- Manufactured Dose Form
- Unit of Presentation [0..1]
- Manufactured Item Quantity

Pharmaceutical product in FHIR: AdministrableProductDefinition

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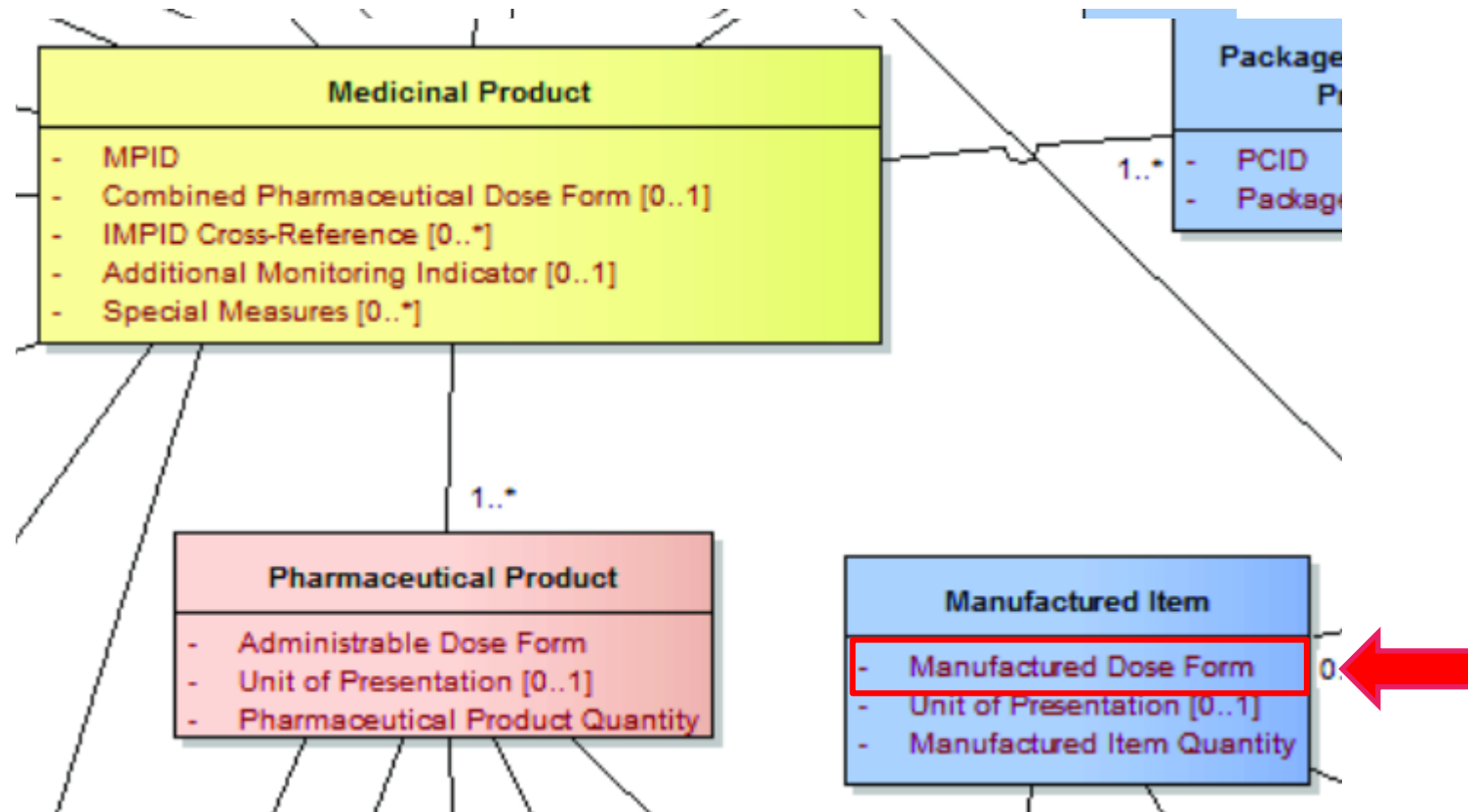
What are the challenges?

► Problem 1: Authorised pharmaceutical dose form is deficient

► Problem 2: Manufactured dose form is too ambiguous to be used as administrable dose form for prescription

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Problem 1: Authorised dose form is deficient

Cefotaxim Navamedic

Authorised pharmaceutical dose form:
Powder for solution for injection

Pharmaceutical product Administrable dose form:
Injection, solution

Cefotaxim MIP

Authorised pharmaceutical dose form:
Powder for solution for injection/infusion

Pharmaceutical product Administrable dose form:
Injection, solution

Pharmaceutical product Administrable dose form:
Infusion, solution

SmPC section 4.2 (Navamedic):

Intravenous administration (injection or infusion):
For intermittent I.V. injections, the solution must be injected over a period of 3 to 5 minutes. During post-marketing surveillance, potentially life-threatening arrhythmia has been reported in a very few patients who received rapid intravenous administration of cefotaxime through a central venous catheter.

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Problem 1: Authorised dose form is deficient

► Authorised pharmaceutical dose form is used to create pharmaceutical products

► Preferred dose form for prescribing to patients

▷ If the authorised pharmaceutical dose form is deficient, then we do not have the correct pharmaceutical products

▷ This is a risk to patient safety

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Different measures taken by NoMA

► Working group for standardised medicinal products information

   ▷ Team of collegues from different
units within regulatory affairs and better use of medicines

   ▷ Prioritise and adress cases where product information is outdated

   ▷ Contact MAH with advise and guidance on how to change and update information
according to standards

► SAFEST:

   ▷ Technical solution which makes room for changes in the relation from manufactured
to administrable dose form
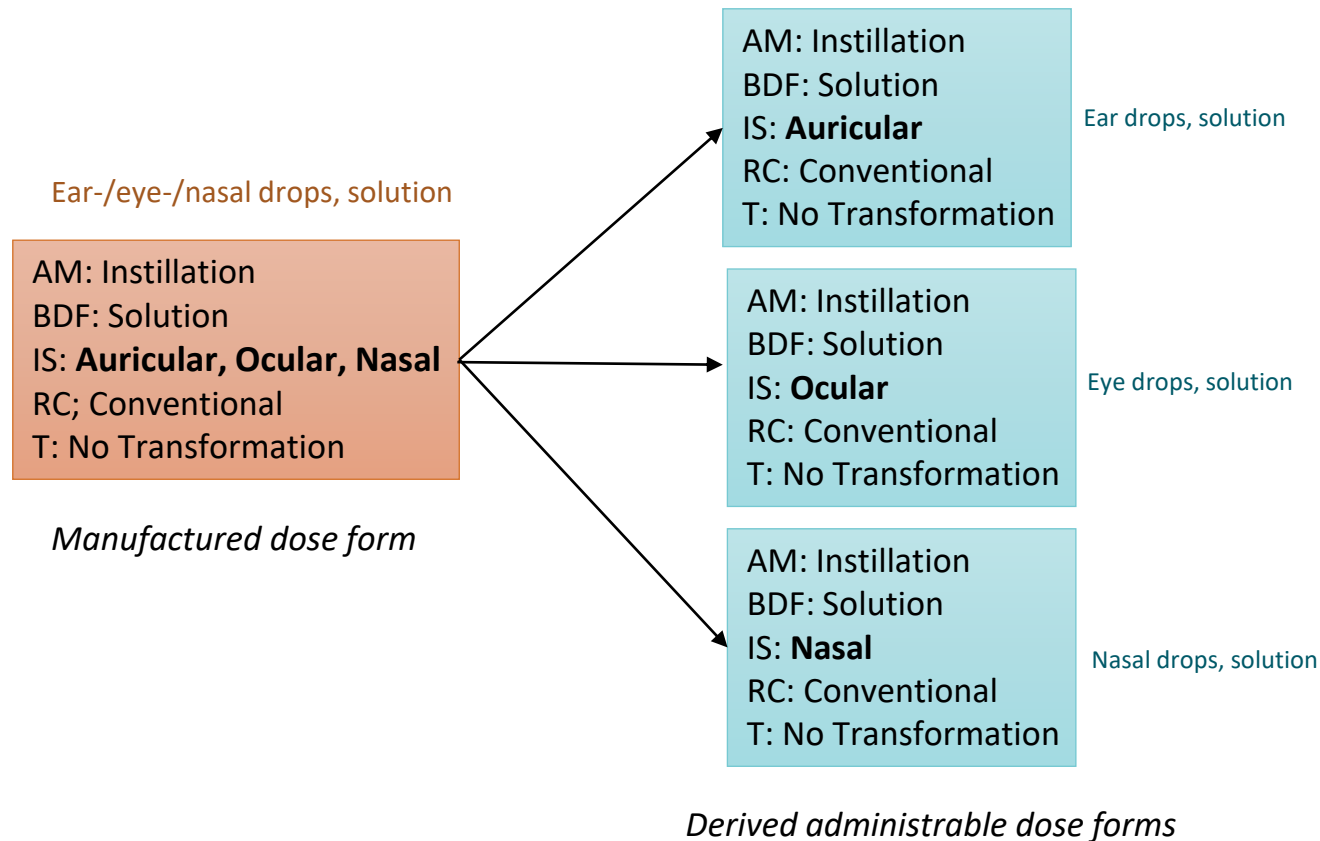
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► IDMP is the chosen standard for expressing data on medicinal products

► PhPID is IDMPs mechanism for the grouping of pharmaceutical products

► PhPID – related use cases assigned to Uppsala Monitoring Centre (UMC):

  ▷ Pharmacovigilance

  ▷ Drug shortages

  ▷ Cross-border Prescription

  ▷ Inpatient care   Clinical use cases

  ▷ Prescription and dispensing within a country

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Ability to identify Medicinal Products is key

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► In general, a PhPID must group all available pharmaceutical products with equal clinical effects across any context (countries, health institutions, systems etc.).

► As a consequence, the clinical use cases require the PhPID, its generating algorithm and its underlying data to have a number of characteristics.

► The following use case in this presentation focuses on one of these characteristics (unambiguous intended site in administrable dose forms)

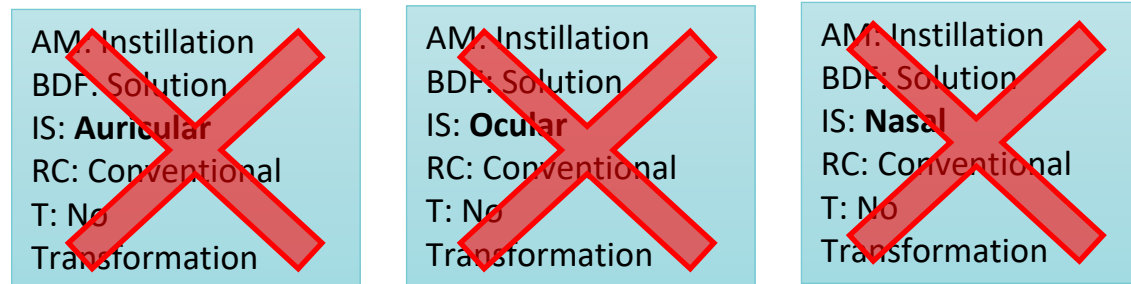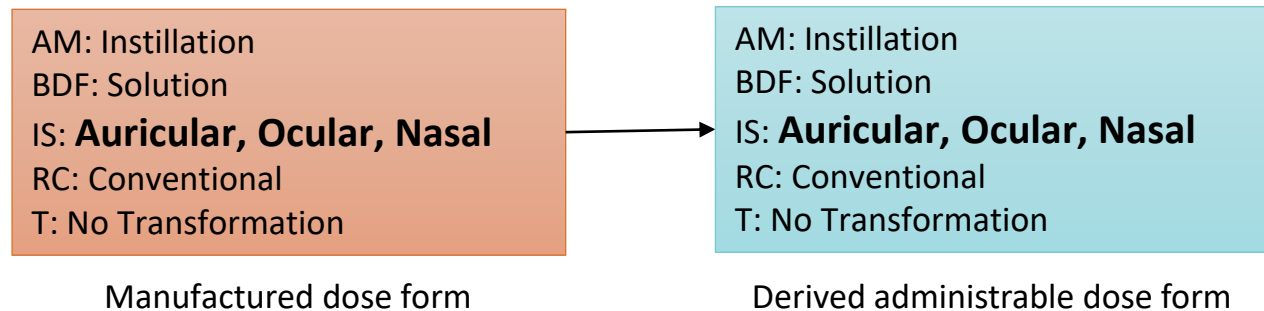► Other characteristics are outlined on the last slide and may be the focus in other workshops and/or presentations

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Ear-/eye-/nasal drops, solution

AM: Instillation
BDF: Solution
IS: Auricular, Ocular, Nasal
RC; Conventional
T: No Transformation

Manufactured dose form

AM: Instillation
BDF: Solution
IS: Auricular
RC: Conventional
T: No Transformation

Ear drops, solution

AM: Instillation
BDF: Solution
IS: Ocular
RC: Conventional
T: No Transformation

Eye drops, solution

AM: Instillation
BDF: Solution
IS: Nasal
RC: Conventional
T: No Transformation

Nasal drops, solution

Derived administrable dose forms

► The clinician must at least provide a concrete Intended site

► The administrable dose forms must define an unambiguous clinical effect and application.

► PhPID generation for clinical use must be based on these unambiguous administrable dose forms

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► E-prescription based on the dose form «Ear-/eye-/nasal drops, solution» would not yield a complete selection of packaged products with equal clinical effect

► Pharmaceutical products with only auricular/only ocular/only nasal use would be excluded

AM: Instillation
BDF: Solution
IS: **Auricular, Ocular, Nasal**
RC: Conventional
T: No Transformation

→

AM: Instillation
BDF: Solution
IS: **Auricular, Ocular, Nasal**
RC: Conventional
T: No Transformation

Manufactured dose form

Derived administrable dose form

AM: Instillation
BDF: Solution
IS: **Auricular**
RC: Conventional
T: No Transformation

AM: Instillation
BDF: Solution
IS: **Ocular**
RC: Conventional
T: No Transformation

AM: Instillation
BDF: Solution
IS: **Nasal**
RC: Conventional
T: No Transformation

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► Just before leaving for her summer holiday, Gitte notices that both her eyes are swollen and red.

► Afraid she might have to cancel her vacation, she consults with her doctor just before leaving for Copenhagen airport.

► The doctor diagnoses a bacterial infection and prescribes eye drops. Since Gitte already is on her way to the airport, an e-prescription is sent to her holiday destination, Austria.

► Gitte is happy not having to cancel her vacation. Sunglasses will have to do before getting the prescribed medication.

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► Upon arrival in Vienna, Gitte quickly rushes to the next pharmacy to collect her medication.

► The pharmacist retrieves the e-prescription, but does not find any matching product.

► Gitte desperately tries to find a pharmacy having her medication in stock, but to no avail.

► After a few days of wearing sunglasses, Gitte arranges an appointment with a local doctor, and she can finally get her eye drops medication "White Eye" at a local pharmacy.

But why didn't "White Eye" show up with her first prescription,
even though the substance, dose form and strength are
seemingly equal?

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►When creating her e-prescription, the doctor in Copenhagen selected

▷ The appropriate **substance** (Ciprofloxacin),

▷ "Ear-/eye-/nasal drops, solution" as **administrable dose form** and

▷ 0.5 mg/ml as (concentration) **strength**.

►This combination is represented by the PhPID "77777" which - together with the dosage - is part of the e-prescription sent to Austria (or a common European e-prescription database).

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► In Austria, there is no pharmaceutical product related to the PhPID on the danish presciption, since the manufacturer of the product marketed in Denmark ("Wide Eye") did not seek market approval in Austria.

► However, a generic version ("White Eye") is available with

▷ The same **substance** (Ciprofloxacin),

▷ "Eye drops, solution" as **administrable dose form** and

▷ The same (concentration) **strength (**0.5mg/ml).

► Since the dose form is different from the one represented by the PhPID "77777", the relevant Austrian product could not be found and dispensed in the pharmacy, and Gitte could not receive her medication.

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Equal clinical effect, different PhPIDs

Denmark: "Wide Eye"

Substance: Ciprofloxacin
ID 100.000.263

Adm. Dose Form: Ear-/eye-/nasal drops, solution
ID 100000074001

Strength: 0,5mg/ml
ID xxxxxxxxxx

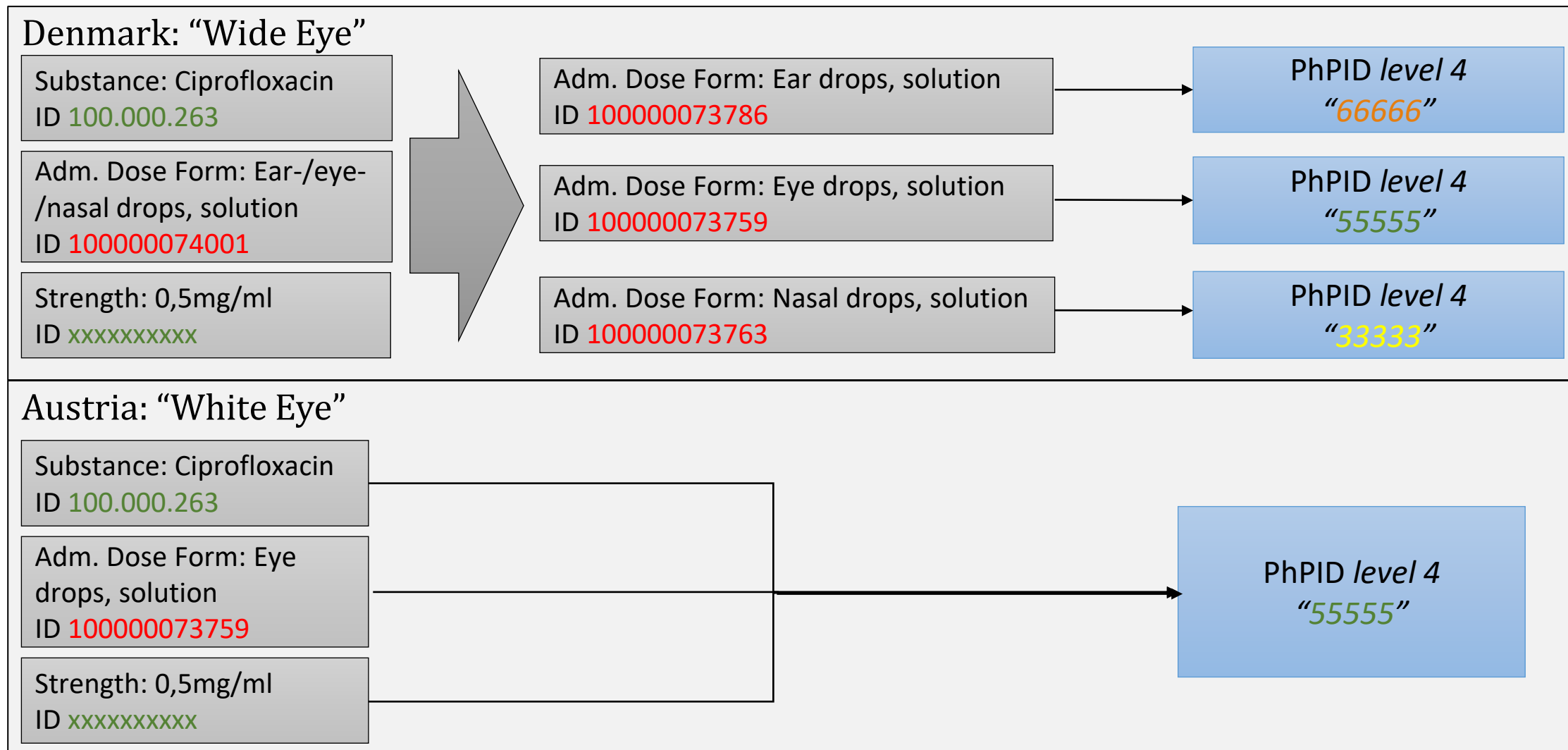→ PhPID *level 4* "*77777*"

Austria: "White Eye"

Substance: Ciprofloxacin
ID 100.000.263

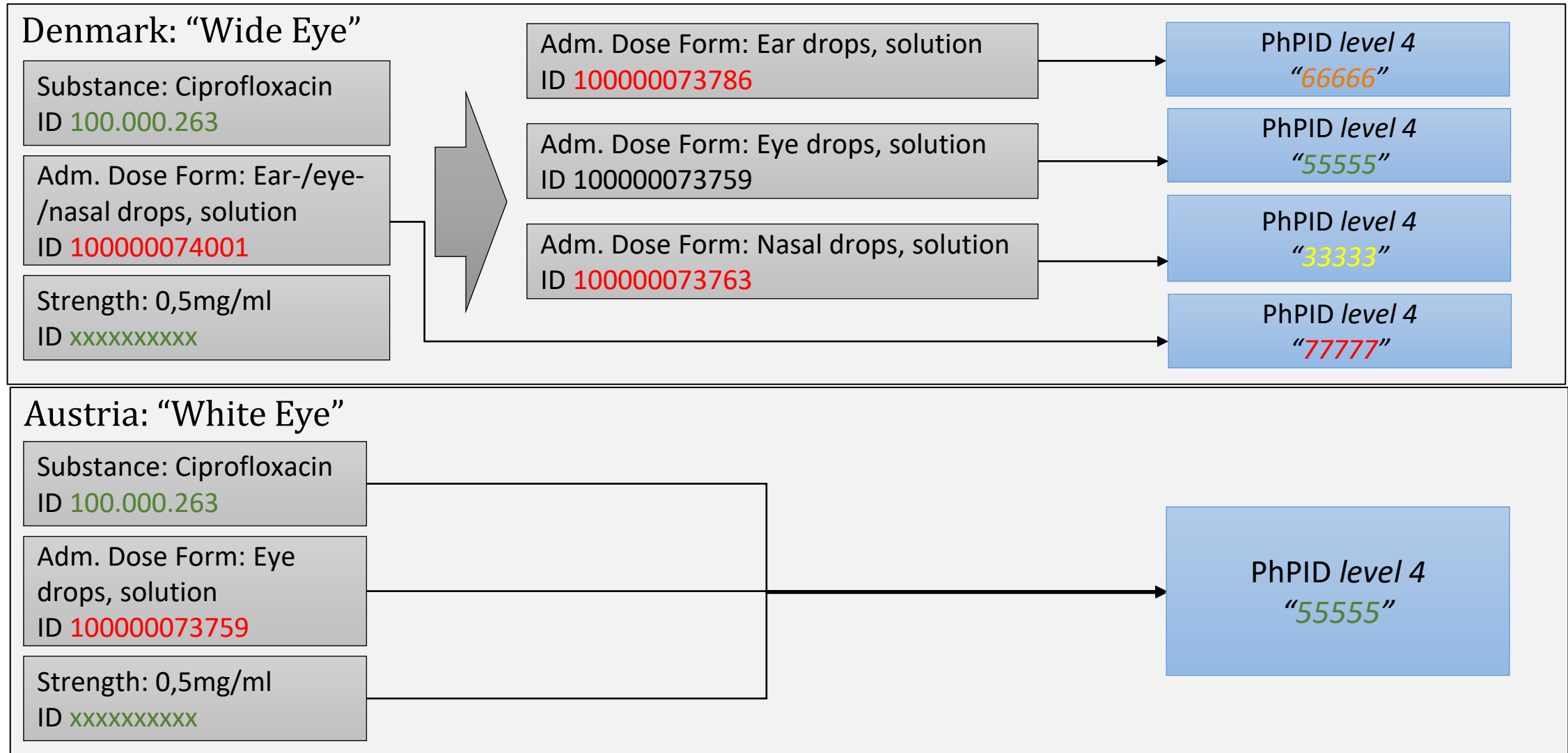Adm. Dose Form: Eye drops, solution
ID 100000073759

Strength: 0,5mg/ml
ID xxxxxxxxxx

→ PhPID *level 4* "*55555*"

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Denmark: "Wide Eye"

Substance: Ciprofloxacin ID 100.000.263	Adm. Dose Form: Ear drops, solution ID 100000073786	PhPID *level 4* "66666"
Adm. Dose Form: Ear-/eye-/nasal drops, solution ID 100000074001	Adm. Dose Form: Eye drops, solution ID 100000073759	PhPID *level 4* "55555"
Strength: 0,5mg/ml ID xxxxxxxxx	Adm. Dose Form: Nasal drops, solution ID 100000073763	PhPID *level 4* "33333"

Austria: "White Eye"

Substance: Ciprofloxacin ID 100.000.263	
Adm. Dose Form: Eye drops, solution ID 100000073759	PhPID *level 4* "55555"
Strength: 0,5mg/ml ID xxxxxxxxx	

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Solution 2: Hybrid

Splitting of manufactured dose form

► Transition from manufactured- to administrable dose form is not stated in the EU implementation guide

► To meet the needs in clinical practice, NoMA has decided to generate multiple pharmaceutical (administrable) products when the manufactured dose form includes multiple characteristics (intended site or administration method).

  ▷ Example 1: products with manufactured dose form ear/eye/nasal drops, will generate 3 different pharmaceutical products, one for each use/intended site

  ▷ Other examples: products with manufactured dose form solution for injection/infusion, will generate 2 different pharmaceutical products, one for each administration method

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Other aspects for the clinical use cases

► The example shown is also applicable to multiple values in other Dose Form attributes (Administration Method, Transformation and, to a lesser extend, Release Characteristics).

► Strength: Two pharmaceutical products with equal clinical effect must be grouped by the same PhPID, independent of their strength and / or Basis of Strength Substance (BoSS).

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NOMA and WHO-UMC are testing the PhPID generation

The Norwegian Medicines Agency is very much aware of its role of interoperabilty enabler and has initiated in 2019 the SAFEST project which aims at the distribution of interoperable medicinal master data for clinical use.

On March 29 and 30, the SAFEST project arranged a face2face workshop with WHO Uppsala Monitoring Center (UMC) in Oslo about **the PhPID generation.** NOMA collaboration with with UMC started in June 2022 and 5 virtual meetings had already taken place.

The UMC has an pivotal role in the generation of a global unique Pharmaceutical Product Identifier (PhPID) for medicinal products (Watch this short interview to undestand why) . The PhPID must be generated based on substance, dose form and strength.

Acknowledgements

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Thank you!