EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

EUCOPE

Members Meeting

Hybrid, 14 February 2023

Competition Law Compliance Policy

EUCOPE brings together representatives innovative companies to discuss common issues, challenges and trends affecting the pharmaceutical industry. This activity can be perfectly legitimate. However, certain competition law risks may arise in relation to EUCOPE's activities.

EUCOPE's European Union ("EU") compliance policy ("Policy") explains these competition law risks and aims to ensure compliance by all members and EUCOPE staff with the rules applicable in the EU. EUCOPE itself and its members are subject to these rules when engaging in any EUCOPE related activities. Any anticompetitive behavior adopted by a member can result in serious financial, criminal and/or disciplinary penalties, as well as other harm (e.g., reputational harm) for EUCOPE, represented companies and for meeting participants personally.

Competition Law Compliance Policy

There are certain matters which **should not** be discussed with competitors before, during or after any such meetings. These include:

- Territorial restrictions, allocation of customers, restrictions on types of services, or any other kind of market division;
- Prices, price changes, conditions of sale (including payment terms and guarantees), price differentials, discounts;
- Current market conditions and issues, including industry pricing policies or patterns, price levels; capacity (including planned or anticipated changes regarding those matters), except where limited to the discussion of historical or public information;

[cont'd]

Competition Law Compliance Policy

- Individual costs, cost accounting formulas, methods of calculating costs;
- Individual company figures on market shares, sources of supply, capacity;
- Information as to future plans of individual companies concerning technology, capacity, marketing or sales; and
- Matters relating to individual suppliers or customers.

Attention: these rules equally apply to informal discussions before, after, or during each meeting. If any sensitive information is discussed or disseminated, insist that the discussion be terminated immediately and make sure that your objection is recorded in the minutes. If necessary, leave the meeting and immediately inform EUCOPE's General Counsel.

Agenda (1/3)

I. **Welcome / New Members / Next Events**

- EUCOPE´s Initiative on Building a Coalition to Increase Access to Comprehensive Genomic Profiling in Europe

Chairs

II. **The European Commission´s Study on Public Procurement of Medicines**

Laure Geslin, European Commission, DG SANTE

III. **New Commercial (vs Political) Solutions for OMP Access in Europe**

Adam Andrzej Plich, Avanzanite

Agenda (2/3)

IV. **A successful approach for single arm trials in Health Technology Assessments – Cerliponase alfa as an example for the EU-HTA**

Sandra Kiehlmeier, Value & Dossier

V. **The European Commission´s Plans on Compulsory Licensing and SPCs**

Chris Boyle, Sidley

Agenda (3/3)

VI. **Latest Intelligence on the Review of the General Pharmaceutical Legislation, the OMP and Substance of Human Origin Regulations**

Victor Maertens, EUCOPE

VII. **MDR/IVDR Implementation – the European Commission´s Proposal of 6 January**

Axel Korth, EUCOPE

VIII. **AOB**

Chairs

I.
Welcome / New Members / Next Events

- EUCOPE´s Initiative on Building a Coalition to Increase Access to Comprehensive Genomic Profiling in Europe

Chairs

Upcoming Events

https://www.eucope.org/events/

- **16 February:** Genomics Working Group Meeting
- **21 February:** Regulatory Working Group Q1 Meeting
- **01 March:** P&R/Market Access Working Group Meeting
- **22 March:** Cell & Gene Therapy Working Group Q1 Meeting
- **04 April**: OMP Working Group

New Members – February 2023

Nine companies join the EUCOPE network

Admedicum
(Associate)

Ardena
(Institutional)

Avanzanite Bioscience
(Institutional)

Emergent Biosolutions
(Institutional)

Evoke Incisive Health
(Associate)

Insmed
(Institutional)

Lif - SE
(Institutional)

MaaT Pharma
(Institutional)

Omakase Consulting
(Associate)

European Coalition for Access to Comprehensive Genomic Profiling (ECGP)

February 2023

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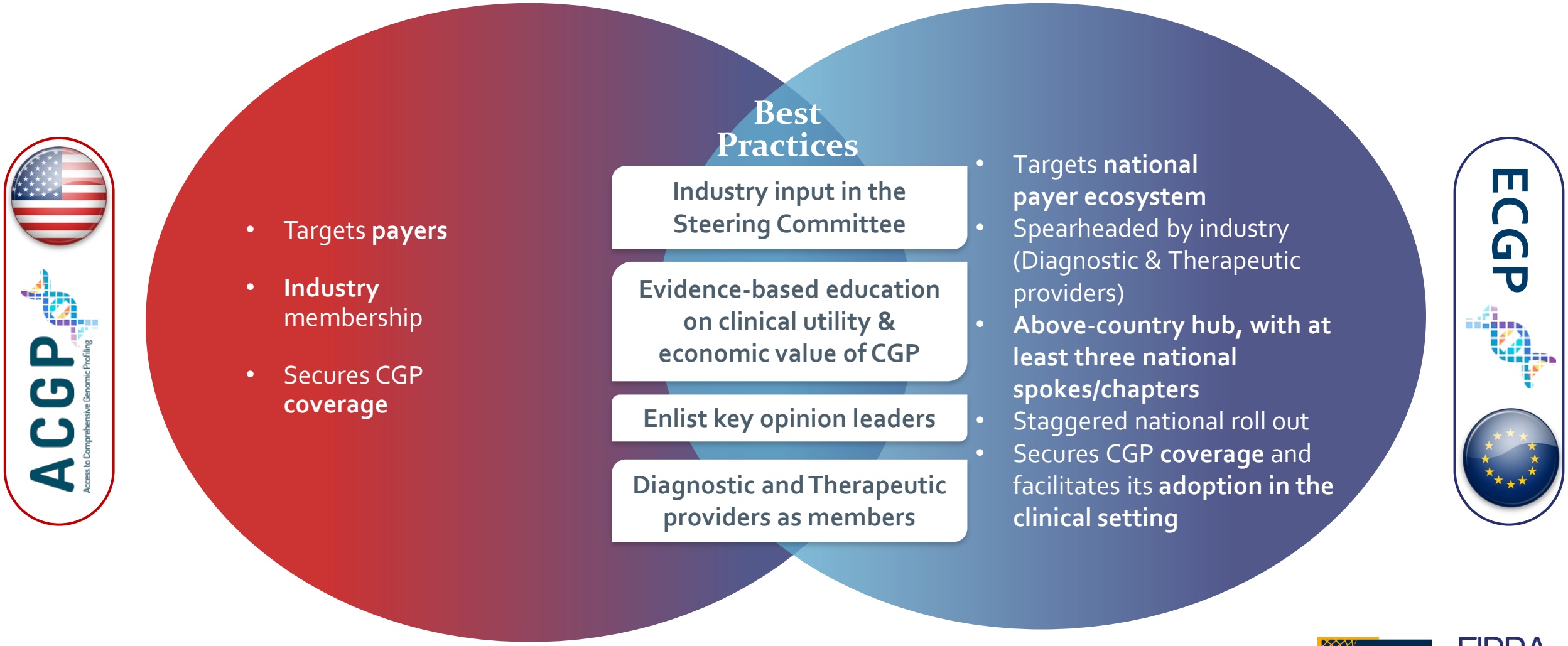
2023 European Coalition for Access to Comprehensive Genome Profiling

A European multi-market initiative promoting the value of CGP for patients and the healthcare system



EUCOPE and members, in collaboration with FIPRA

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FIPRA

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Scope

European CGP Coalition

EUCOPE

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Coalition Scope

Definition of CGP	Comprehensive genomic profiling (CGP) is a method of testing tumors that utilises next-generation sequencing (NGS) to detect the main classes of genomic alterations and signatures in the full exomic gene known to drive cancer growth.
Scope	Technology: Comprehensive Genomic Profiling in Oncology. For multiple biomarkers in already diagnosed cancers: - in numerous tumour types k(Tumour type agnostic (breast, lung…)) - in different tumour stages (Tumour stage agnostic, though may focus on late-stage tumours initially)

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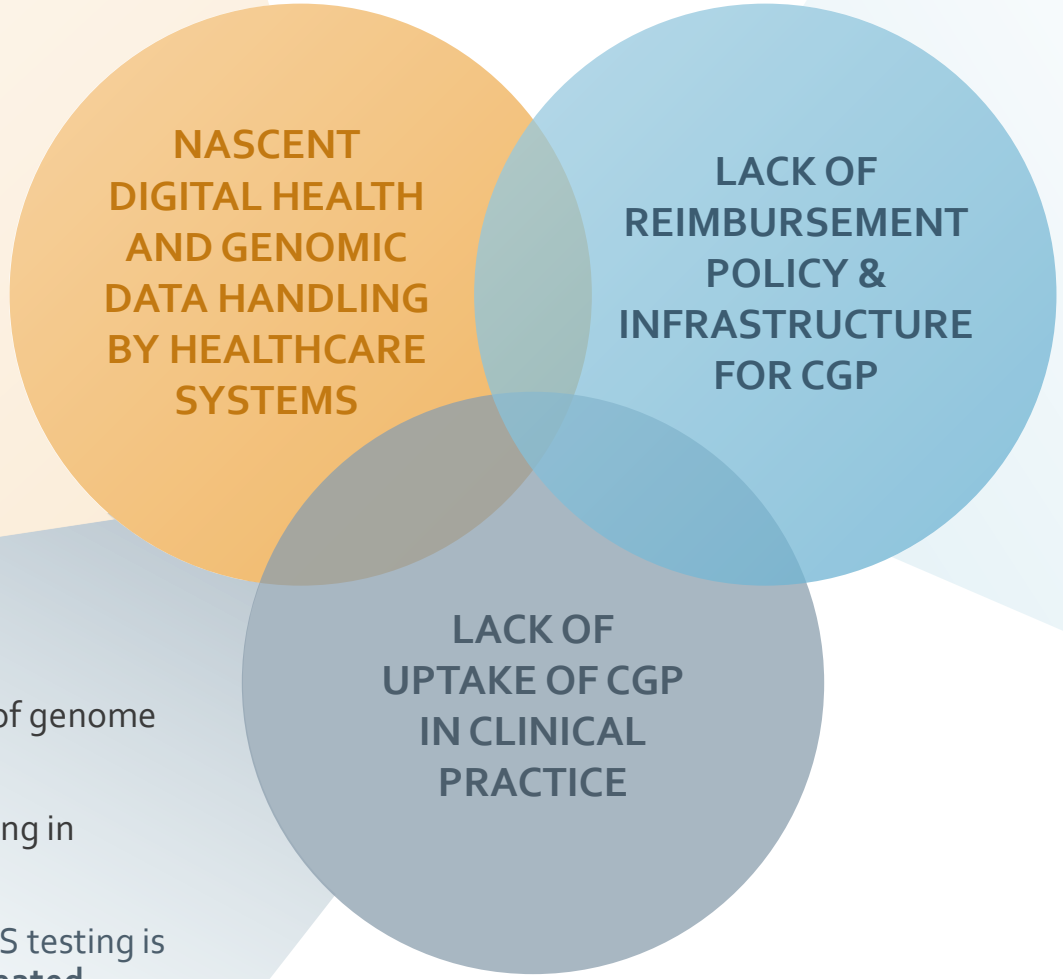
The barriers to CGP in Europe are interlinked and cannot be tackled in isolation

- **Lack of digital infrastructure & uncoordinated genomic data collection process, storage and access** limiting opportunities for care and research
- **Uncertain approach to harmonized data usage** and concerns over GDPR rules
- **Poor awareness and knowledge of data sets** creating an inability to interpret accurately CGP results and, consequently, reduced access



- **Varied recognition of personalised medicine in value assessment guidelines** & delays in updating screening guidelines
- **Evidentiary requirements** for reimbursement decisions, unsuited to advanced diagnostics with little flexibility to reflect available evidence
- **Insufficient funding** of testing services & high costs of genetic testing
- **Insufficient diagnostic testing capacity** & limited use of novel tests in labs

- **Different levels of prioritization** of genome testing at national level
- Lack of inclusion of mutation testing in **clinical guidelines**
- Access to multiple-gene panel NGS testing is limited, **especially for patients treated outside large cancer centres**

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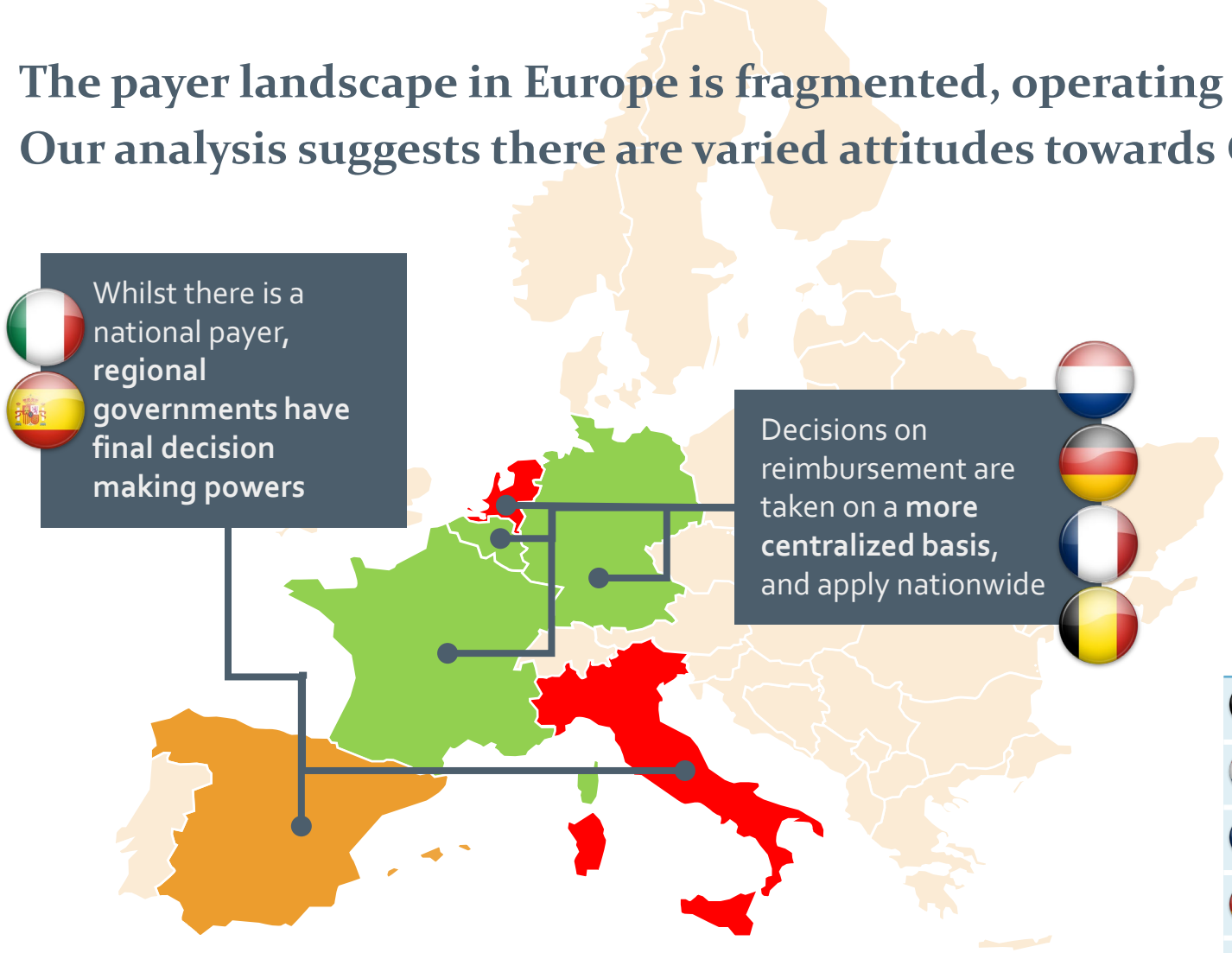
The payer landscape in Europe is fragmented, operating at the national and regional level

Our analysis suggests there are varied attitudes towards CDx/CGP reimbursement



National attitudes towards CDx/CGP in key markets
See Annex for full analysis

Most favourable — *Least favourable*

	Reimbursement / regulatory environment (e.g. Existence of reimbursement schemes for IVD/CDx, timeline for reimbursement) Scored out of 4	**Policy / political environment** (e.g. Existence of national precision medicine plan, focus on digital health) Scored out of 3
Belgium	✓✓✓✗	✓✓
Netherlands	✓✗	✓✗
France	✓✓✓✗	✓✓✓
Germany	✓✓✓✗	✓✓✓
Italy	✓✗	✓✗
Spain	✗✗	✓✓✓

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Note: Subject to validation

Coalition Aim & Objectives

Aim

Unlock value for patients and the healthcare system through access to CGP

Objective(s)

Create multi-stakeholder outputs to support wider CGP coverage and reimbursement in view of the development of personalised medicine

Actions

Raise awareness on the role of CGP

Convening decision-maker and stakeholder roundtables to progress a common understanding around the implementation of CGP, and current patient access challenges

Promoting exchange of best practice to foster the use of CGP in clinical practice

Gather clinical, economic and operational evidence

Assembling evidence and identify data sources (Real World Data) to improve access to CGP in the cancer ecosystem

Evolve funding and P&R frameworks

Gathering evidence and aligning stakeholder perspectives on optimal access pathways (e.g. HTA, payer, clinician, pathologist, patient, industry)

Identify cross-market learnings on the patient diagnostic journey in support of HTA/payer decision making

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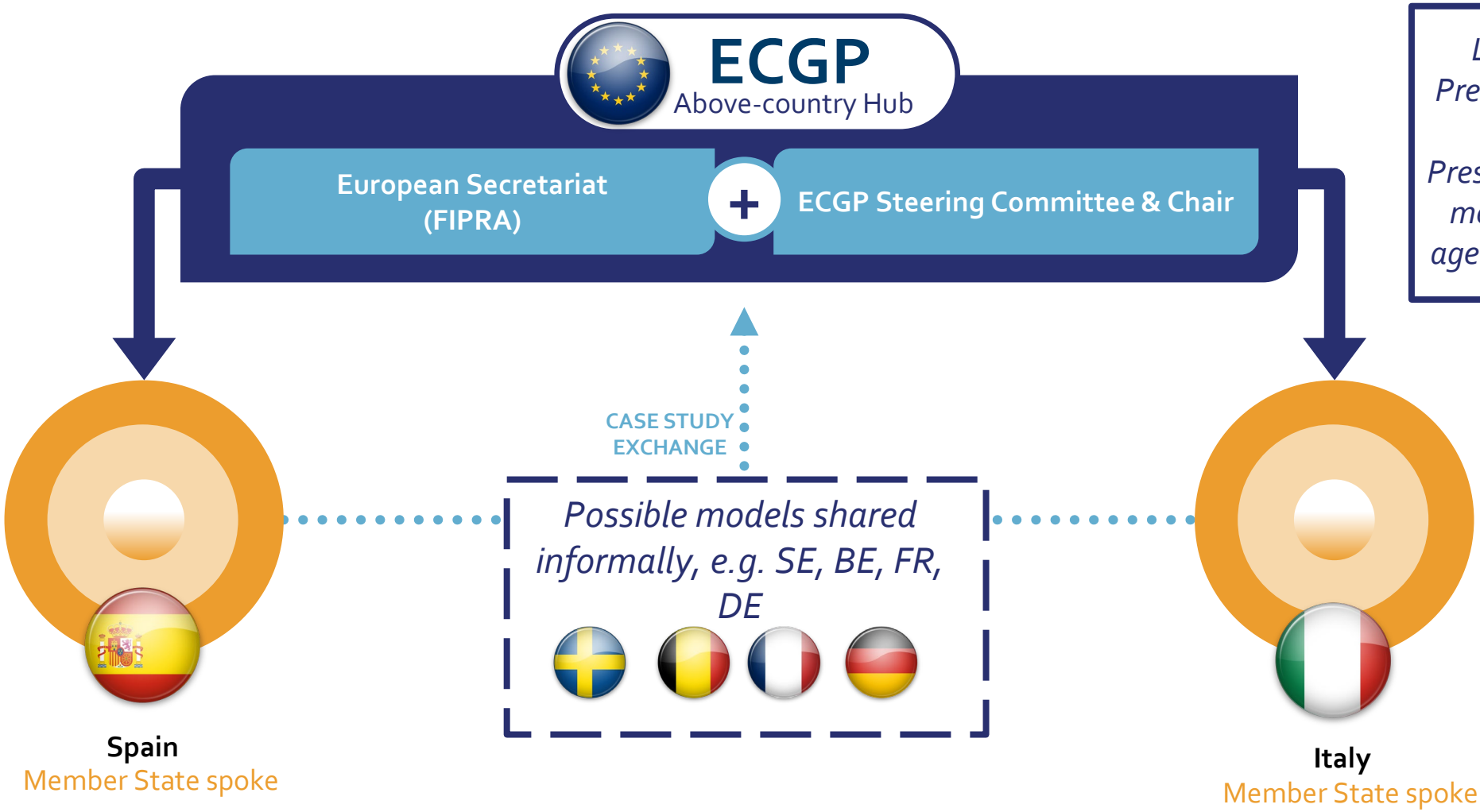
European Coalition structure – Hub & Spoke



Leveraging EU Council Presidencies where relevant (e.g. Swedish 2023 Presidency focus on precision medicines via life sciences agenda (26 June conference)

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Phase I: Project plan for first 6 months

2022		2023			
NOV	DEC	JAN	FEB	MAR	APR

Scope

REVIEW KEY MARKET ANALYTICS

- Informed market analysis and landscape assessment
- Identify 'white space'

COALITION FRAMING

- Agree on scope, aims and objectives of coalition
- Develop coalition model and governance for European Secretariat and national roll-out (select x3 national markets)
- Develop roadmap for strategic engagement, onboarding/ recruitment

Establish

EUROPEAN STEERING GROUP

- Establish ECGP Steering Group:
  - Sponsors, potential chairs and leading players, KOLs (e.g. cancer organisations)
  - Max 20 - 25 stakeholders
  - Ensure robust compliance
  - Agree above-country and local language engagement hooks and strategy

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II.
The European Commission´s Study on Public Procurement of Medicines

Laure Geslin, European Commission, DG SANTE

Study on Best Practices in the Public Procurement of Medicines (PPM)

Study overview and key findings

Laure GESLIN, DG SANTE
14 February 2023
EUCOPE Members Meeting

Acknowledgements

The study on best practices in PPM was conducted by **Gesundheit Österreich Beratungs GmbH** (Austrian National Public Health Institute / GÖ B) and **Tetra Tech Sp. z o.o.**

The study was commissioned in the frame of the SC 2020 7304 under the FWC SANTE/2016/A1/039 – Lot 1 by the European Health and Digital Executive Agency (HaDEA) as contracting authority under the mandate of the European Commission.

Gesundheit Österreich Beratungs GmbH

TETRA TECH International Development

European Commission

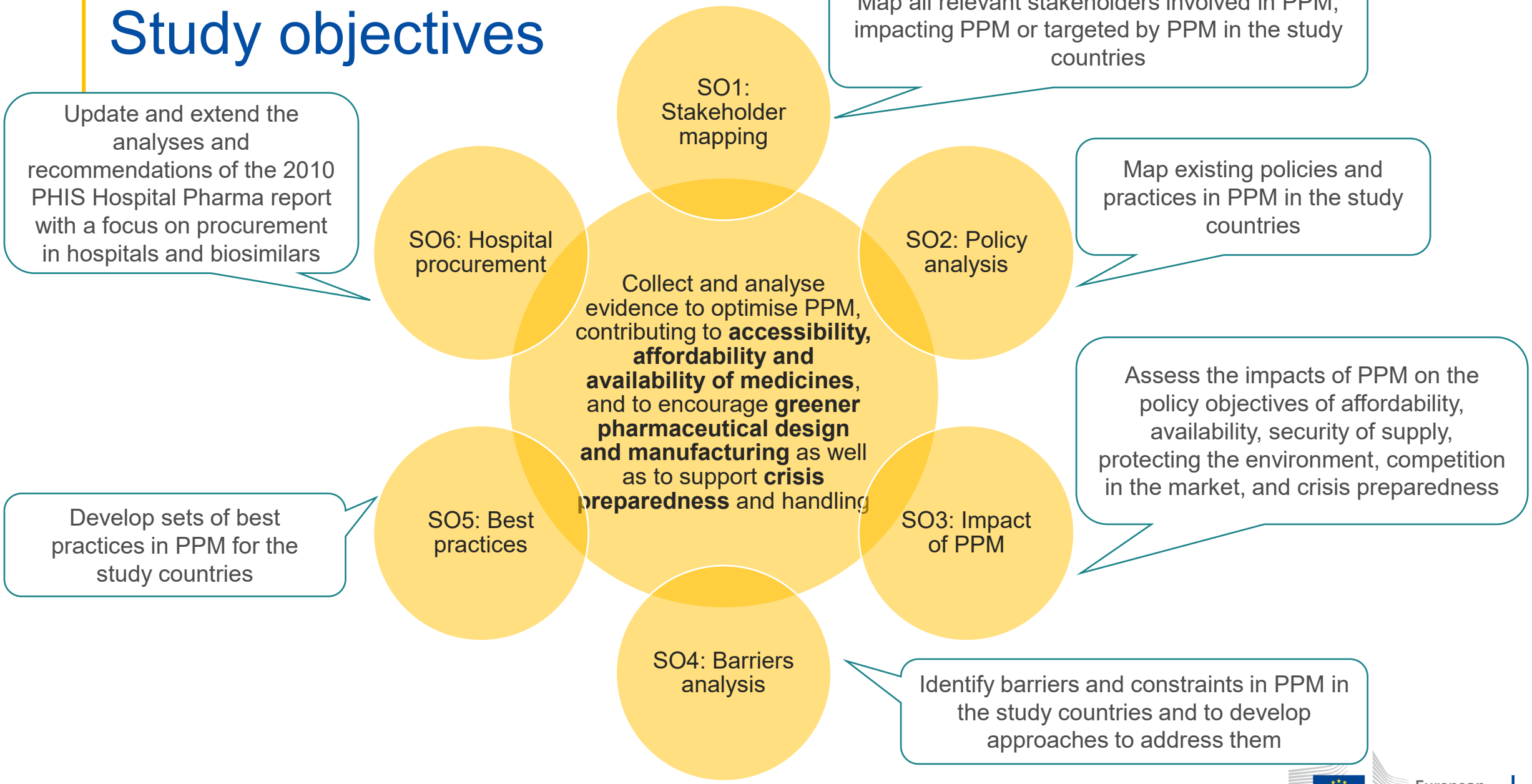
Background and motivation for this study

- Public procurement is a **commonly applied policy option** to achieve and improve sustainable access to affordable medicines, and strategic procurement is **recommended by the WHO** (contingent on awarding contracts using other criteria than price alone)
- Potential benefits include:
    - Reduced unit prices
    - Improved availability of medicines
    - Increased competition
    - Improving accountability and anti-corruption
    - Rational selection of medicines
- Public procurement of medicines (PPM) is highlighted as an action area to improve access to medicines and foster competition in the "**Pharmaceutical Strategy for Europe**"
- In the EU, legal guidance on public procurement exists through Directive 2014/24/EU
- **Use of the different public procurement practices and their potential impacts** have not been systematically assessed across European countries

Methods

European Commission

Study objectives



European Commission

Study scope

All medicines for human use in both sectors:

- outpatient and
- hospital

32 countries:

- EU-27
- EEA/EFTA
- UK

Definition of PPM for the purpose of the study

All aspects surrounding the **process of purchasing medicines** by a contracting authority, such as a body of public law (e.g. governments, local health authorities, and social health insurance institutions) or an institution affiliated to the public sector, **from economic operators chosen by the contracting authority**. The study acknowledges the importance of **supporting policies** in the pharmaceutical value chain (such as managed-entry agreements and policies to encourage uptake of generic and biosimilar medicines) and analyses their contribution towards effective PPM.

Mix of methods

Literature reviews

Review of general and country-specific literature

Stakeholder engagement

Interviews

Stakeholder workshops

Stakeholder survey

Data analysis

Analysis of data on public procurement (TED) and sales (IQVIA)

Triangulation of methods to address research questions

No single method to address each question

Mix of methods (continued)

				Stakeholder consultation			Quantitative data			
Specific objective	**General question**	Literature review	Country fiches and expert review	Workshops	Interviews	Online survey	TED data	IQVIA data	Impact analysis	Presentation of findings in online dashboard
SO1	**Which stakeholders are involved in PPM, and in which role?**									No
SO2	**What are current national PPM policies in the studied countries?**									Yes
SO3	**What are possible impacts of PPM?**									Yes
SO4	**Barriers to optimise PPM?**									Partly
SO5	**Which are best practices to optimising PPM?**									Partly
SO6	**Which are current hospital PPM practices?**									Yes

Major data source
Supplementary data source / use in some cases
Method not used for this question

data collection and analysis
field research method

European Commission

Mapping of PPM practices in European countries

European Commission

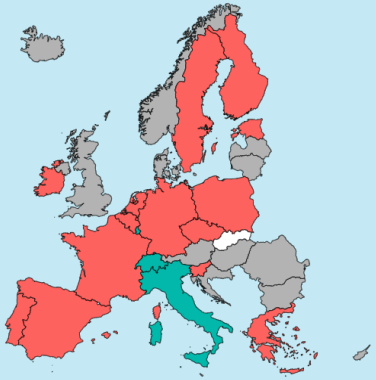
Organisation of PPM

- **Hospital medicines** are commonly procured by individual facilities and less frequently through voluntary group procurement

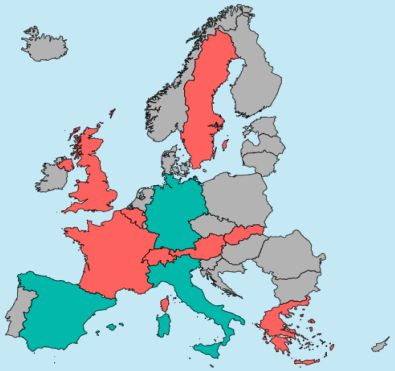
- **Centralised purchasing bodies (CPB)**
  - regional level : focus on hospital medicines
  - national level : scope varies (all medicines, all hospital medicines, vaccines and national health programmes only)

Facility-based procurement

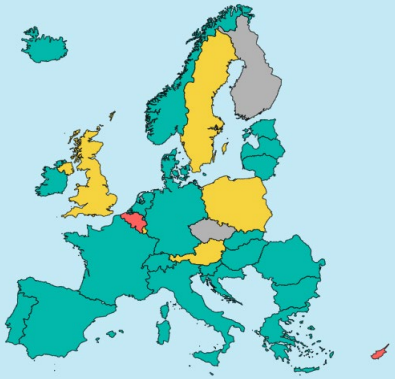
Group (joint) procurement



Centralised procurement (regional level)



Centralised procurement (national level)



Applied in outpatient and inpatient sector

Applied only in inpatient sector

Applied only in outpatient sector

Not applied

No information

Open tenders are the dominant form of procedure for PPM overall and across different types of medicines

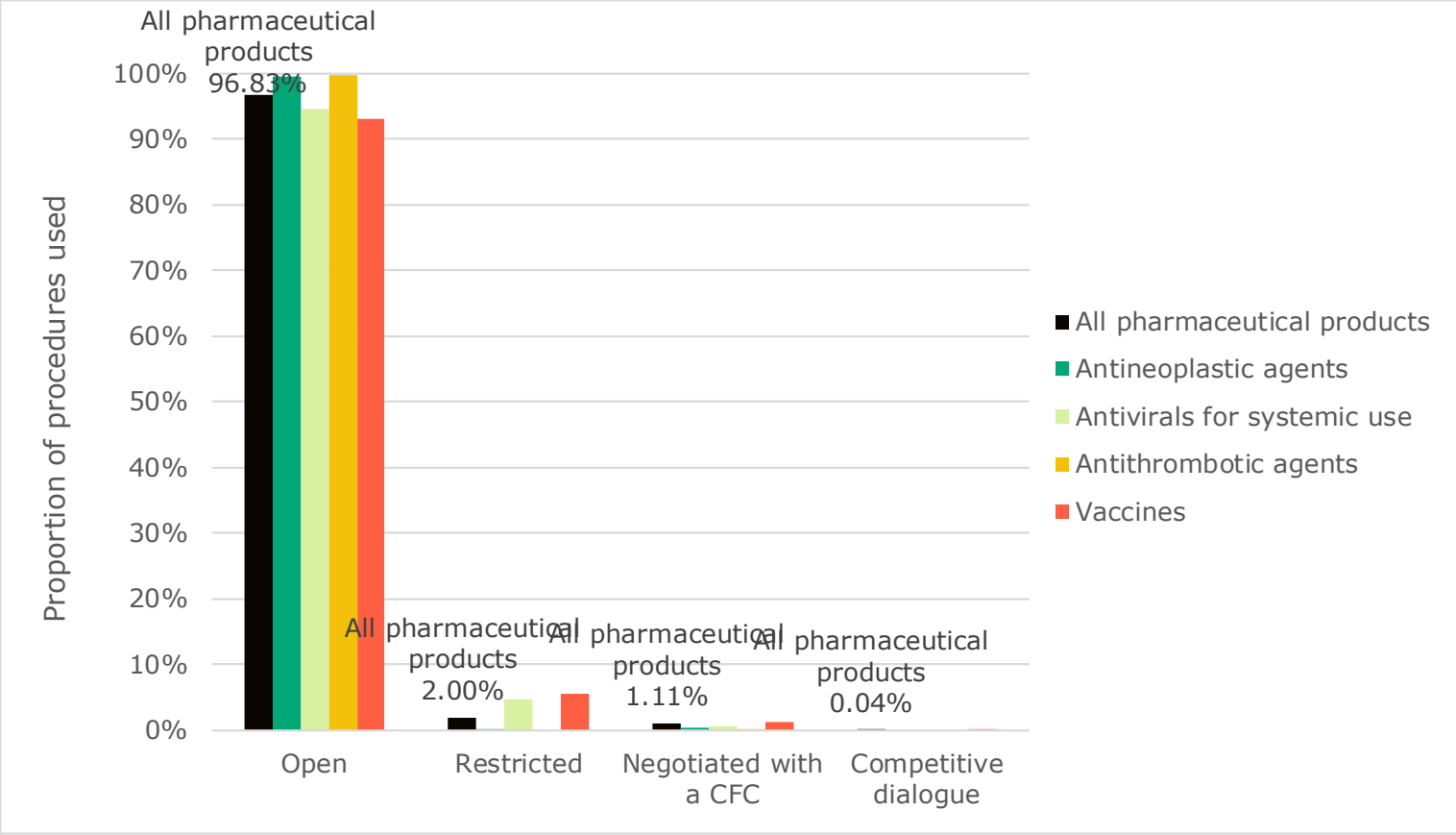


Figure shows the proportion of different types of publicly listed procedures from 2008-2021, aggregated for all study countries, and for all pharmaceutical products and selected groups of products.
CFC: call for competition

- Open tenders are seen as the **simplest procedure form** to implement
- Open procedures are sometimes used to establish framework agreements
- Negotiated procedures and competitive dialogue tend to be used for **products without competition**
- Restricted procedures are more common when a Dynamic Purchasing System is in place

European Commission

Price only remains the key award criterion for procurement of medicines overall and across different product groups

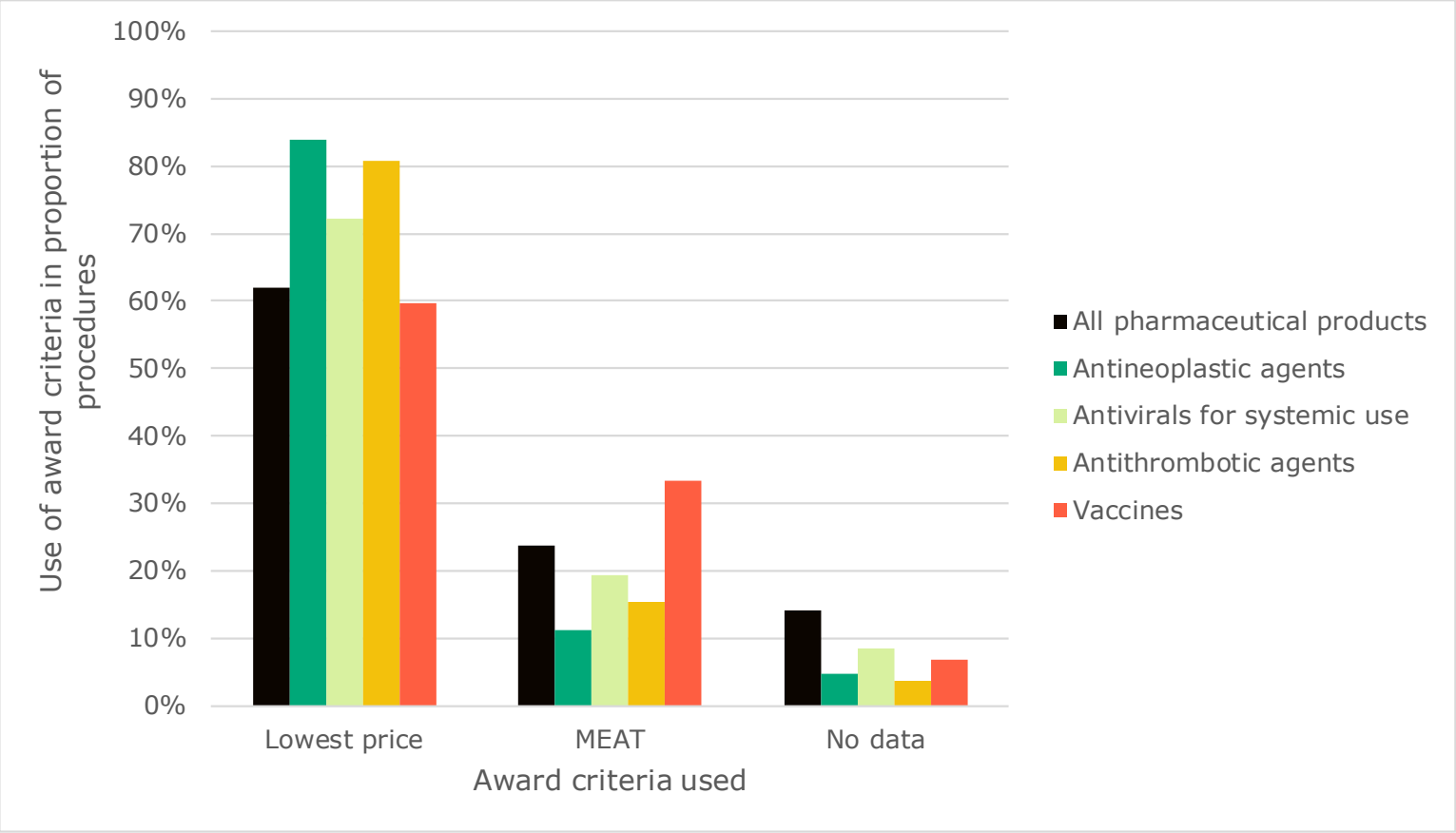


Figure shows the proportion of publicly listed procedures from 2008-2021 across all study countries that were awarded according to lowest price or most economically advantageous tender criteria. Source: TED.
MEAT: Most Economically Advantageous Tender

- MEAT (Most Economically Advantageous Tender) requires an assessment about the willingness to pay for other (non-price) criteria, which may be **challenging to implement**
- Reasons for using **price only**:
  - Ease of implementation
  - Other criteria cannot distinguish a limited number of suppliers (in small markets)
  - Quality criteria are set as minimum criteria or are otherwise not expected to vary between suppliers
  - To avoid appeals when awards are based on other criteria

European Commission

Contracting authorities in the study countries have also used other non-price criteria

Security of supply

- Security of supply is a key issue for procurers and therefore features as award criterion. Procurers may **use other tools** to address this issue, e.g. multi-winner awards.
- Award criteria may include requirements to hold stock (potentially within the country) or other guarantees. Local production is not commonly used as criterion.

Environmental criteria

- While environmental criteria are not yet widely used, **pilot projects** are underway (e.g. packaging, transport, and existence of environmental policy as criteria). The **Nordic countries** are playing a pioneering role and have used environmental criteria in national tenders (Denmark, Norway) and cross-country joint procurement, although other countries are using such criteria as well.

Added therapeutic value

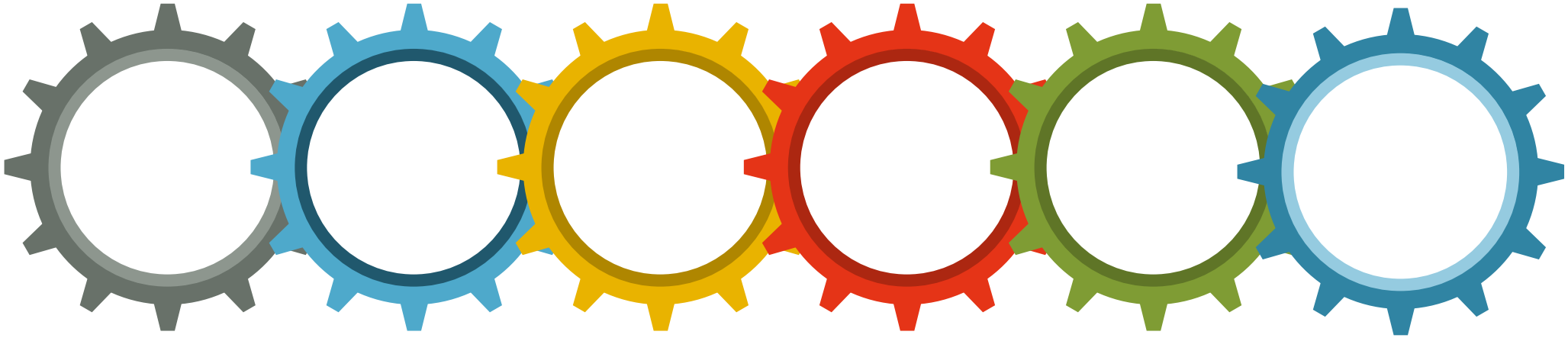
- Not commonly used (mostly in the inpatient setting).
- Added value may be assessed by external bodies, e.g. **HTA bodies** or other institutions collaborating with procurers.

Procurement is supported by other pharmaceutical policy tools

Procurement strategy
To spell out visions for procurement, major reforms, as well as operational principles

Horizon scanning
Being aware of new technologies as well as monitoring patent expiries and emerging competition

Managed-entry agreements
Commonly used for medicines with high price tags or budget impact, but procurers may not be involved in concluding them



Capacity-building
Providing training to procurement staff and issuing guidance and support documents

HTA
Rarely integrated into procurement process, but a valuable resource for negotiations.

Engagement with suppliers & prescribers
Market research in preparation for tenders and needs assessment with prescribers / users of products to be procured

Note that only a selection of major supporting policies are presented.
Further policies can provide important complementary functions to procurement.

Cross-country collaborations in PPM

European Commission

Cross-country joint procurement in Europe

- There is increased **interest in cross-country collaborations** to improve affordable access to medicines in Europe
- Cross-country joint procurement between European countries has been used for vaccines and hospital medicines. Joint PPM at EU level was used during the Covid-19 pandemic (for vaccines and therapeutics).
- Key **reasons for conducting joint procurement** (within-country or cross-country) include the following:
  - Achieving lower prices
  - Improving availability of medicines (ensuring the market is attractive to suppliers)
  - Ensuring access to high-quality products
  - Improving efficiency in procurement
  - Strenghtening capacity of procurers and procurement processes, including improvement in transparency, accountability and anti-corruption

Cross-country initiatives involving joint procurement in Europe

All EU member states participated in joint procurement of Covid-19 vaccines and therapeutics

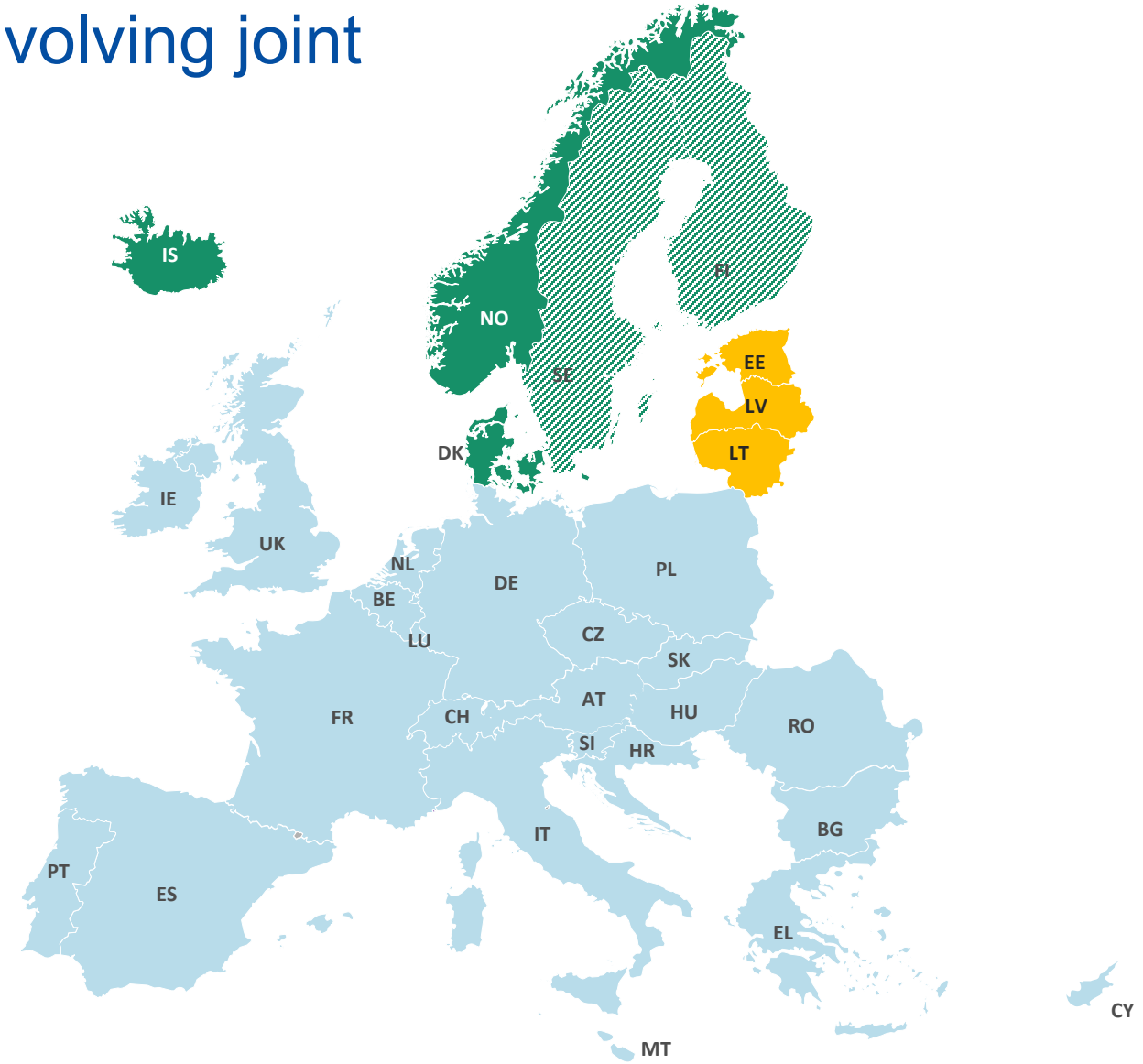
Nordic Pharmaceutical Forum:

Participating in joint Nordic tenders

Members of the initiative but not participating in joint procurement

Baltic Procurement Initiative:

Participating in joint procurement



Note that only initiatives with joint procurement are shown. Other European countries are also involved in further voluntary cross-country initiatives working on other policies and tools (e.g.horizon scanning, HTA, joint negotiations) to improve access to medicines.

European Commission

Two cross-country initiatives have successfully conducted joint procurement

Baltic Procurement Initiative

- Estonia, Latvia, Lithuania
- Joint procurement of medicines (so far, only for vaccines that are in the immunisation schedule of at least two of the three countries)
- Lending of medicines and medical devices among the countries without charging any costs in cases of shortages
- 4 procedures successfully conducted
- Lead partner (one country) for each tender

Nordic Pharmaceutical Forum

- Denmark, Finland, Iceland, Norway, Sweden
- Platform for exchange between the Nordic countries on issues related to access to medicines and identify areas for collaboration
- Joint procurement to increase purchasing power and ensure security of supply
- 2 joint tenders for off-patent hospital medicines successfully conducted (DK, IS, NO only)

Cross-country joint procurement of medicines at EU level was conducted during the Covid-19 pandemic

Joint procurement agreement (JPA)

- Developed following the H1N1 pandemic influenza to improve crisis preparedness and create a framework for procuring medical countermeasures
- Voluntary participation, but with set processes
- Signed by 37 countries, including all EU member states
- During the COVID-19 pandemic, the JPA was used in 12 joint procurement procedures to purchase medical equipment and therapeutics

EU COVID-19 vaccines procurement

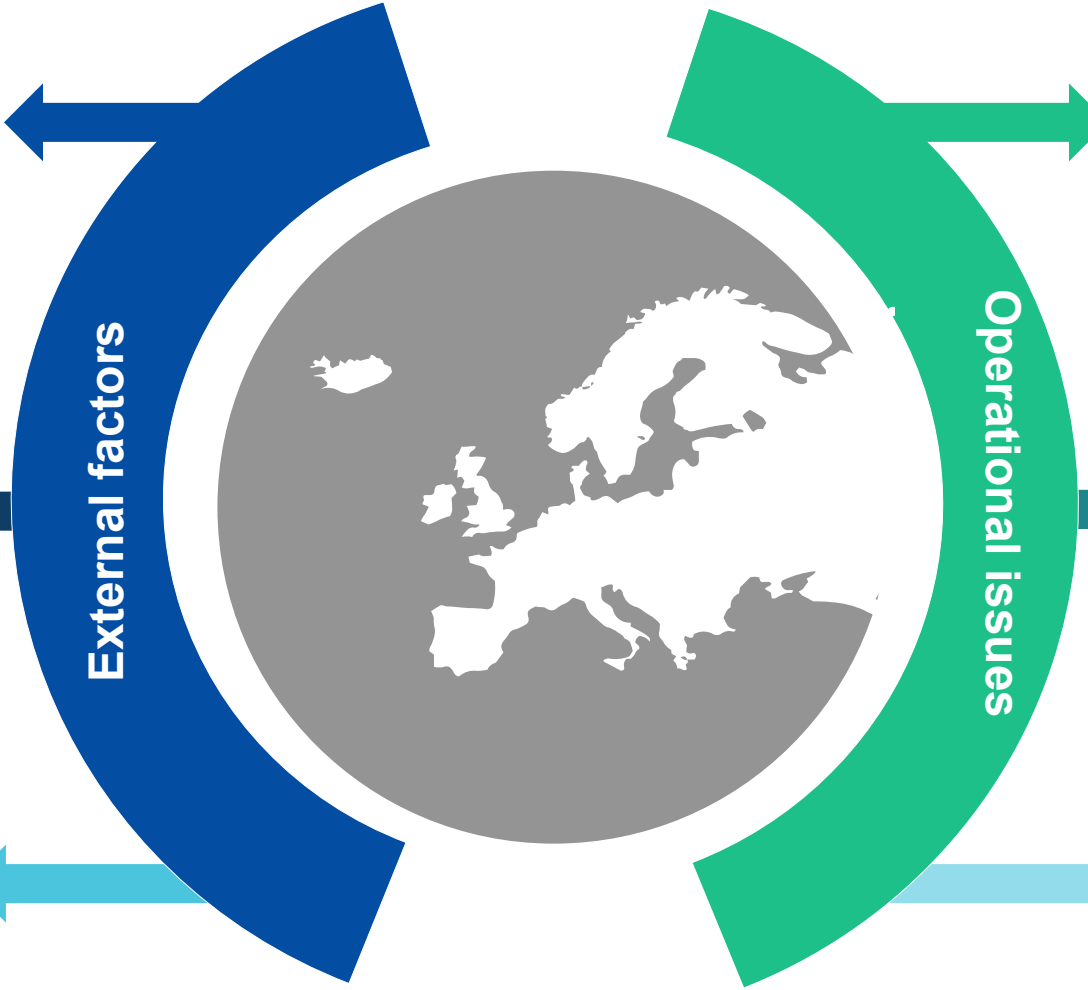
- JPA was not seen as suitable for procurement of COVID-19 vaccines; instead, a centralised approach led by the EC was used
- Vaccines procurement in the early stages of the pandemic included up-front investment through advance purchase agreements

Key learnings from cross-country joint procurement

Need for awareness of **differences in national legislation and procedures** (related to PPM, pricing and reimbursement, supporting tools such as HTA)

Fragmented health systems may limit or prevent country's participation in cross-country procurement

Suppliers may be hesitant to respond to calls for a cross-country tender



Cross-country joint procurement is more **resource-intensive and time-consuming** than national procurements

Need to address language issues due to different countries and legislations (including regarding the packaging of procured medicines)

Need for clarity about **leadership** and lead procurer

European Commission

Impacts of PPM

European Commission

Methods: impact analysis

Aimed to assess possible impacts of PPM practices on **six policy objectives:**

- Affordability
- Availability
- Security of supply
- Crisis preparedness
- Competition in the market
- Environment

Triangulation of data sources:

- **IQVIA** – pharmaceutical sales data (list prices, not real prices; restricted data availability for some study countries)
- **TED** – public procurement data (contract notices and contract award notices)
- Analysis conducted for **tracer groups of medicines** and at the **aggregate level** (countries were grouped by PPM practices)
- Online **stakeholder survey** (58 participants)
- Qualitative data from **stakeholder workshops and interviews**
- Evidence from **published literature**

PPM and affordability of medicines

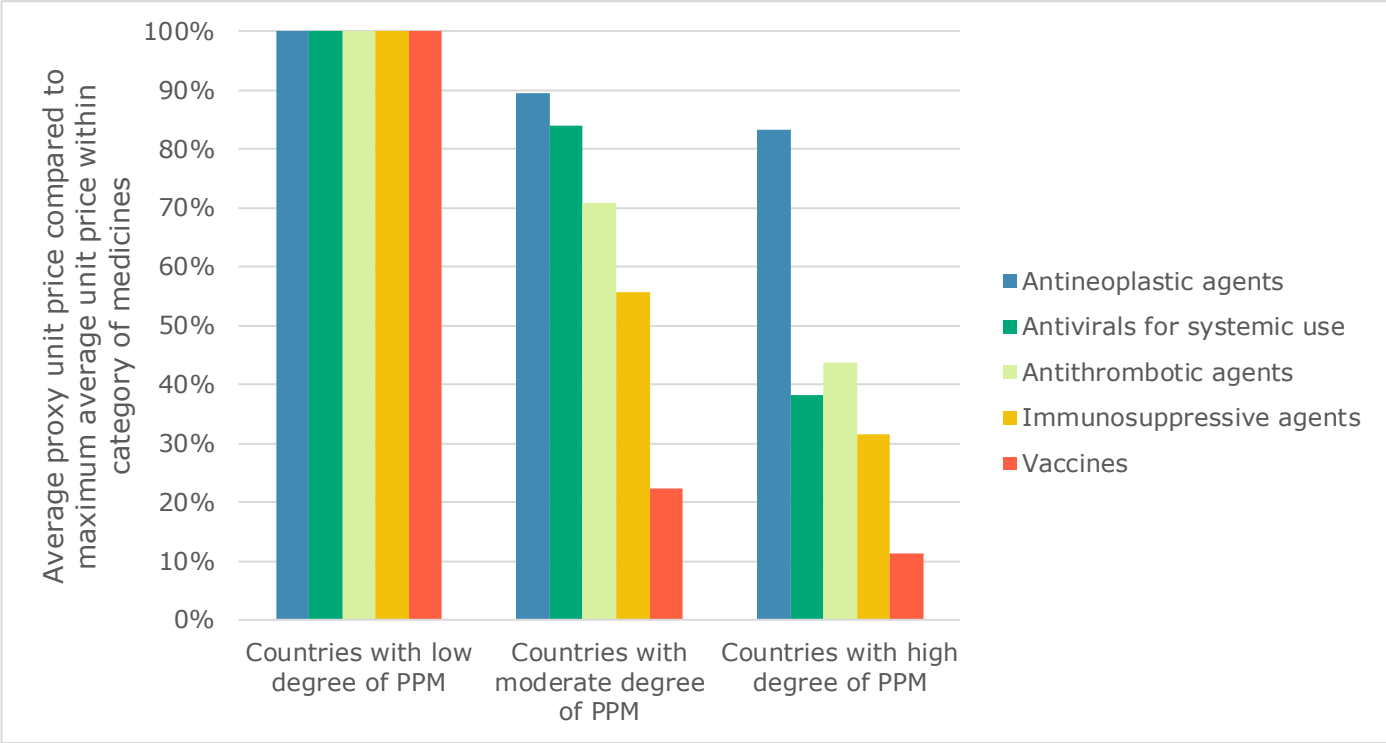


Figure shows aggregated data for 2008-2021 for countries with low, moderate, or high degree of PPM and the average proxy unit price in those countries for five categories of medicines. Pharmaceutical sales data were obtained from IQVIA; degree of PPM was constructed based on literature, publicly available data and expert interviews.

- At the aggregate level, **lower unit prices** were observed in countries with **higher degree of PPM**, i.e. countries that
  - use more centralised forms for procurement
  - use different procedures and techniques
  - apply the MEAT criteria
  - use supporting policies
- In line with evidence from previous studies
- Reported **savings** through centralised procurement ranging from 1% (Croatia) to 40-50% (Cyprus, Denmark, Norway).

European Commission

Stakeholders views on affordability

PPM procedures

- All stakeholders participating in an online survey assessed **more competitive procedures** (open procedure tenders, restricted procedures) to have higher potential for impacting on affordability compared to less competitive ones (competitive dialogue, competitive procedure with negotiation).
- **Suppliers** considered negotiated procedures to have a potential negative impact.

PPM techniques and tools

- Awarding **multiple winners** was considered to impact positively on affordability by all stakeholders, while awarding a single winner may have a negative impact according to suppliers.
- **Framework agreements** and **DPS** were considered to contribute to affordability by all stakeholders. **Electronic auctions** and **electronic dialogue** were assessed positively by procurers and authorities, and negatively by suppliers.

Trade-offs

- Stakeholders mentioned possible trade-offs between affordability and other policy objectives, in particular **security of supply**, promoting **green manufacturing and transport**, and maintaining sustainable levels of **competition** in the market.
- Suppliers in particular raised concerns that practices that drive down prices lead to lower levels of competition, with potential impacts on security of supply.

PPM and availability of medicines

Aggregate level analysis

- Number of individual molecules available was **lower in countries with more advanced PPM practices**.
- **No causal link** between PPM practices and availability of different molecules or individual products was assessed.

Country-level experience

- **Pooled procurement** associated with improved availability of medicines (although mostly in LMICs).
- Icelandic experience: gaining access to some medicines for the first time through **joint Nordic tenders**.

Stakeholder views

- Stakeholders disagree on the contribution of **joint procurement**
- Overall positive views on **awarding multiple winners** and using **additional criteria other than price**

Security of supply

- **Empirical data** are lacking
- PPM practices to address security of supply:
  - Awarding **multiple winners** (anecdotal reports of **shortages** after awarding single winners)
  - **Joint (cross-country) procurement**, in particular for smaller markets
  - Security of supply criteria (but possible trade-offs with price)

Crisis preparedness

- **PPM perceived as important tool** for crisis preparedness, particularly for vaccines
- Role for **joint procurement** forms at national or cross-national level (including joint procurement at EU-level)
- Joint procurement of **Covid-19 vaccines** at EU-level was overall seen as success

PPM and the environment

- **Environmental criteria** starting to be used, but no evidence on impact on the environment
- Possible **trade-offs** between environmental criteria and price and competition
- At the *aggregate level*, **higher price levels** were observed in countries that use environmental criteria compared to countries that do not or only rarely use these criteria.
- **Experience from Nordic countries** suggests that suppliers are able to comply with criteria without impacting on prices or levels of competitors submitting bids.
- Challenges with implementation: what criteria can be assessed?

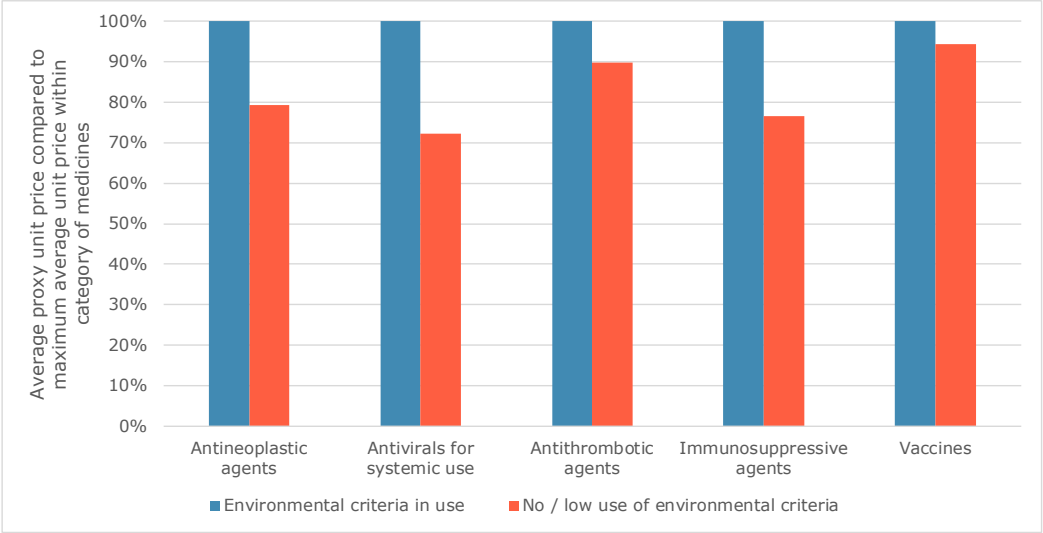
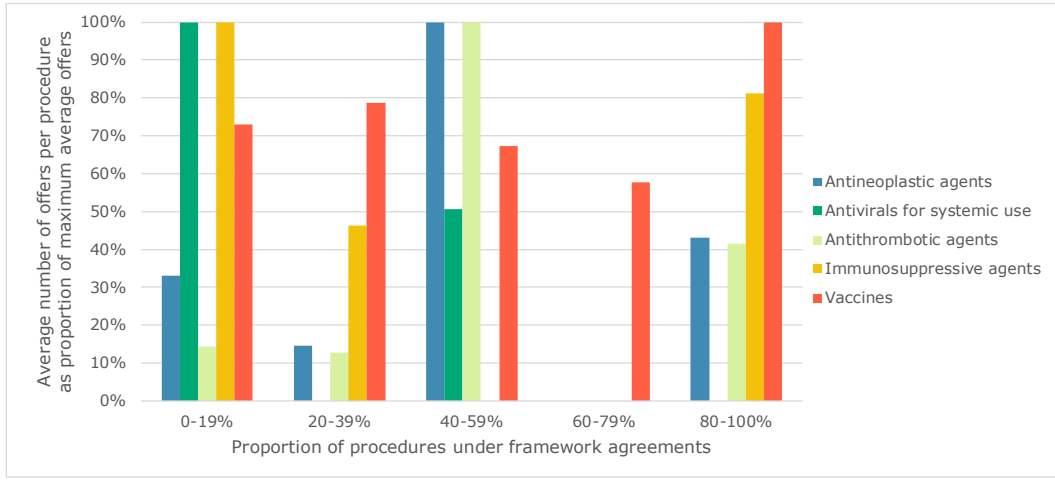


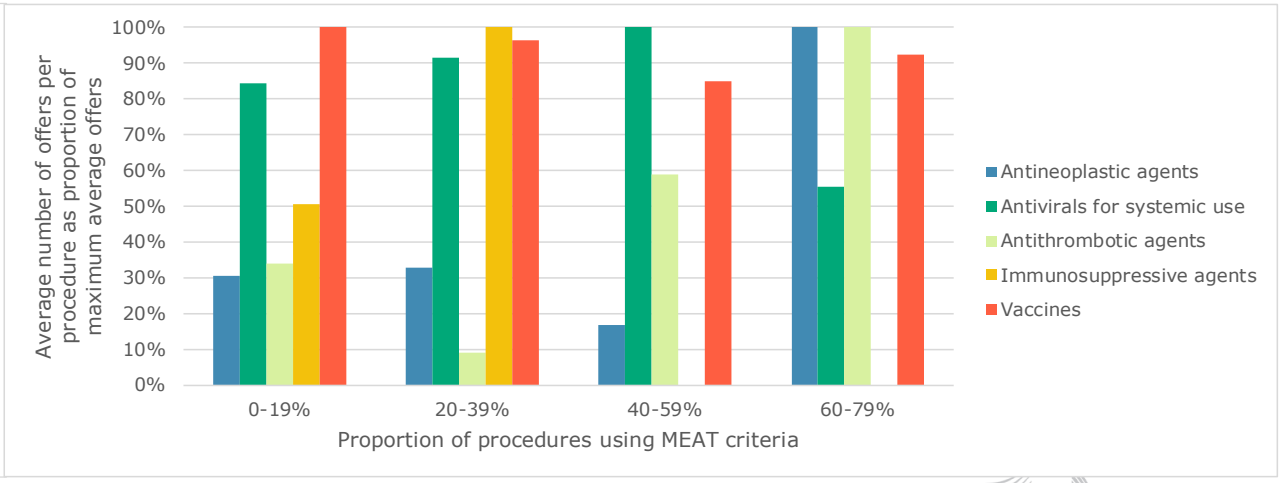
Figure shows aggregated data for 2008-2021 for overall application of environmental criteria in a country and average proxy unit price in that country for five categories of medicines. Information on use of award criteria was obtained from literature and expert interviews and relates to general use of the criteria in the country, rather than individual tenders for specific products. Price data are from IQVIA.

European Commission

PPM and competition

- According to stakeholder assessments, PPM processes contributing to competition in the long run include **multi-winner contracts** and using **MEAT criteria**.
- Countries with **more frequent use of advanced PPM processes** (framework agreements and MEAT criteria) tended to attract **higher numbers of bids** per procedure.
- **Joint procurement** is seen as detrimental to competition in the market by industry representatives as well as some individual procurers. However, joint procurement may also create competition in the first place: some countries only become attractive markets for (multiple) suppliers by pooling purchase volumes.





Figures show aggregated TED data for 2008-2021 for overall proportion of procedures including a framework agreement (left) or using MEAT criteria (right) and the average number of bids received for procedures in five groups of products.

European Commission

Key findings and policy recommendations

Key findings

1/ PPM practices vary across Europe

- Medicines are most commonly procured by individual health care facilities or through centralised procurement at national level; the roles of centralised procurement bodies differ across countries
- Open procedure tenders dominate PPM in Europe (97% of procedures recorded in the TED database); use of award criteria other than price alone is still developing

2/ Well-designed PPM can improve access to medicines

- More mature PPM systems were observed in countries with lower unit prices; these countries also have higher overall pharmaceutical expenditure
- Procurers' experience and published evidence show that lower prices can be achieved through PPM, and more medicines can become available
- Stakeholders highlight the need for strategic use of PPM tools, such as multi-winner awards and joint procurement

3/ A strategic approach is needed to balance different policy objectives

- PPM can impact on different policy objectives, including affordability, availability, and security of supply of medicines, protecting the environment, competition in the market, and crisis preparedness and handling
- Trade-offs exist, in particular between affordability and maintaining a competitive market with secure supply levels, as well as green manufacturing & transportation
- New developments and legislation (e.g. EU HTA Regulation) may impact on future procurements of medicines

Key findings

4/ There is scope for optimising procurement of medicines used in hospitals

- The share of pharmaceutical expenditure that is spent in hospitals in increasing, highlighting the importance of optimising procurement practices in this setting
- Procurement of biosimilars needs to be seen together with factors that could impede biosimilar uptake, including hesitancy among prescribers and patients, and manufacturer behaviour to impede market entry and uptake of competitor products

5/ Best practices and recommendations

- Joint procurement, including within country and cross-country, can help achieve lower prices and making small markets attractive for suppliers, as well as providing other benefits, such as information sharing and capacity building; however, implementation is resource-intensive
- A strategic approach to procurement should be applied that takes into consideration the product life-cycle and uses procurement tools accordingly, including balancing different award criteria
- Multi-winner awards for products with off-patent competition can help address issues with security of supply and maintain a competitive market

Policy recommendations for national policy-makers

1/ Develop and communicate a PPM vision and strategy

2/ Support implementation of the PPM strategy through investments

3/ Monitor and adapt the strategy

4/ Consider intra-country and cross-country collaboration as a key principle

5/ Select PPM practices strategically, applying a product life-cycle approach

6/ Facilitate exchange of experiences among procurers

European Commission

Recommendations at technical-operational level: PPM strategy to consider following PPM features

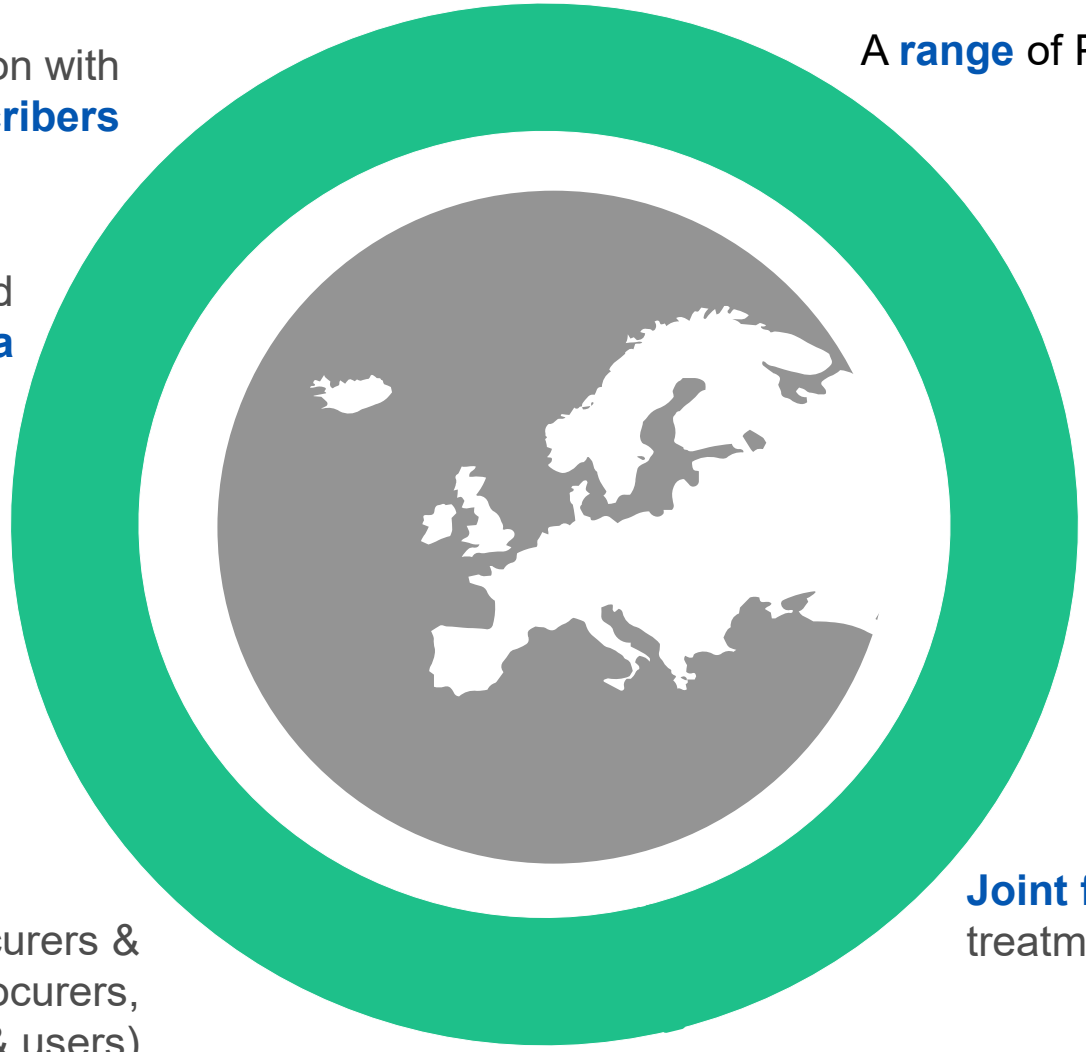
Communication with **prescribers**

Collection and analysis of **data**

Optimised **IT environment**

Transparent, clear **processes**

Regular **dialogue** (procurers & suppliers, between procurers, procurers & users)



A **range** of PPM polices and practices

MEAT criteria

Multiple winner awards

Collaboration, overcoming fragmentation (e.g. centralisation)

Joint formularies and treatment recommendations

European Commission

Keep in touch

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EUTube

EU Spotify

European Commission

Thank you

European Commission

III.

New Commercial (vs Political) Solutions for OMP Access in Europe

Adam Andrzej Plich, Avanzanite

New Commercial (vs Political) Solutions for OMP Access in Europe

EUCOPE Members Meeting

14 February 2023

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BIOSCIENCE

Our inspiration come from the challenges faced by our first partner

FABRIZIO CHINES
Chairman & CEO

Solution

SIFI ANNOUNCES LICENSE AGREEMENT WITH AVANZANITE BIOSCIENCE FOR AKANTIOR®

NEWS PROVIDED BY
SIFI S.p.A. →
Jan 10, 2023, 02:00 ET

SHARE THIS ARTICLE

- *Collaboration offers potential access to hundreds of patients across several European Countries.*
- *SIFI will focus its European market access and commercial activities on existing markets, and the new markets Germany and the United Kingdom.*
- *SIFI expects a potential positive opinion by the Committee for Medicinal Products for Human Use and New Drug Application to the US Food and Drug Administration (FDA) in 2023.*

26

Avanzanite countries

500

patients[1]

[1]In Avanzanite countries [2] https://www.prnewswire.com/news-releases/sifi-announces-license-agreement-with-avanzanite-bioscience-for-akantior-301716731.html .


What are the OMP-access problems and drivers in Europe?
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Launching OMPs in Europe is Often Unsuccessful and Creates Enormous Inequities

Key Challenges

1. **Pricing** & **Market Access**
2. **Complexity** & **Costs** of EU operations & logistics
3. **Talent** Shortage & Lack of **Know-How**
4. Increasing **competition**
5. Applying same **business model** as "big pharma" in the non-OMP space

Consequences

Non-oncology OMPs approved in years 2017–20 in EU[1]		
Country	% available[4]	Days to access
DE	93%	79
IT	70%	522
ES	41%	769
BE	29%	711
SE	26%	526
IE	24%	789
PL	7%	750

80%

European launches of medicines for rare diseases fail to meet their goals[2,3]

Bluebird Exits Europe, Casting Clouds Over Gene Therapy Commercial Effort

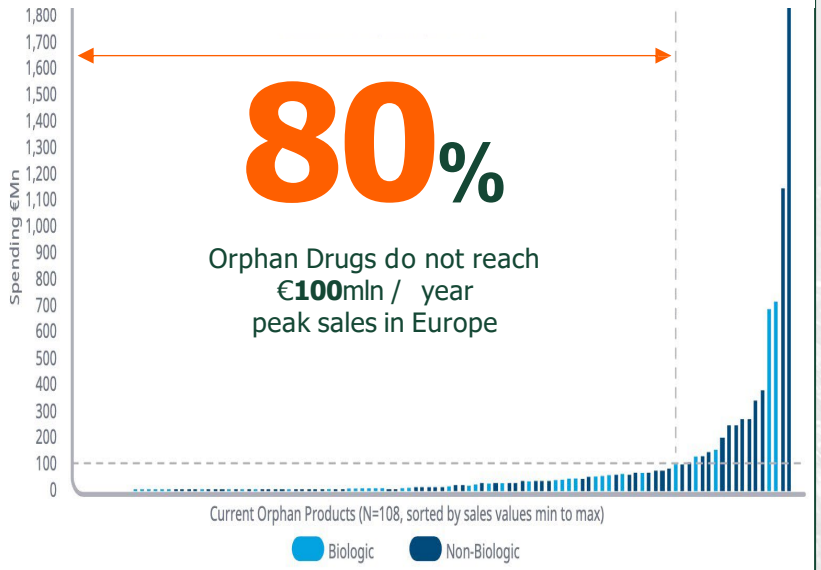
09 Aug 2021 | NEWS

[1]EFPIA. Patient W.A.I.T. Indicator. Apr 2022. https://www.efpia.eu/media/636821/efpia-patients-wait-indicator-final.pdf [2]SKP. In-house research. April 2021. [3]Scrip. 9 Aug 2021. [4]Meaning with national reimbursement or other not-limiting sources of funding as of 1Jan 2022.

Most OMPs in Europe are overlooked and particularly tricky

Market Size Challenge

Average Sales of Newly Approved Orphan Drugs in Europe, 2019[1]



Source: EMA approvals 2019; MIDAS MAT, Q2 2019
Notes: Excludes withdrawn products

Niche Orphans

€ 50 mln

Max peak sales per year

No one cares to make these products available to all European patients as they are perceived to have **low ROI**:

- Ultraorphan
- Repurposed
- No Orphan Drug status
- Neglected diseases

Problem

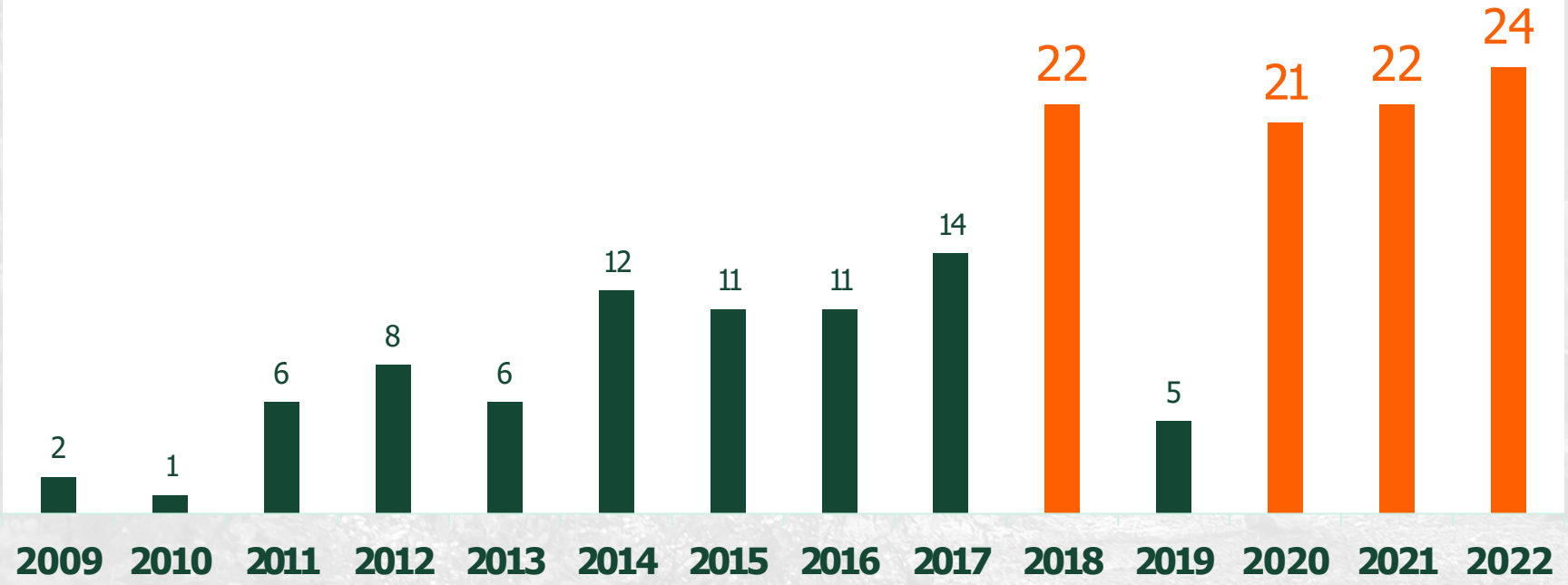
- Unmotivated biotechs to establish **European operations** or to enter **certain markets**
- **Not on radar for in-licensing** for any mid-to-large pharma suitor
- Most view them as unnecessary **distraction** for HQ given priorities on the US launch and research & development (R&D)

[1]IQVIA. The Prospects for Biosimilars of Orphan Drugs in Europe. 21 Jul 2021. https://www.iqvia.com/insights/the-iqvia-institute/reports/the-prospects-for-biosimilars-of-orphan-drugs-in-Europe. **CoGS** =cost of goods sold. **ROI** = Return on Investment

We need to fix this problem now given anticipated Astonishing Growth of the Orphan Approvals and the hope these drugs create for patients

OMP–Approvals in Europe

Positive CHMP decisions[1,2].



Future Potential

800+

New Orphan Drugs in development (Dec '21)[4,5]

[1]PinkSheet EU CHMP tracker (years 2021–22); EMA Report (years 2017–2020); Eurordis (2009–2016). **[2]**For year 2021, includes also 2 medicines for rare diseases that did not maintain Orphan Drug status for formal reasons. Not included in the statistics in other years. **[4]**PhrMA Dec 2021. https://catalyst.phrma.org/new-report-nearly-800-new-medicines-in-development-to-treat-rare-diseases **[5]**Only accounts for those in active clinical trials that are undergoing FDA review in the US.
CHMP = Committee for Medicinal Products for Human Use at the European Medicines Agency.

Everyone in Europe – like Juliette – should benefit from approved orphan medicines regardless of where they live, how rare their disease is or how challenging commercialization is.

It is a shame and unfair otherwise

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Juliette
Acanthamoeba Keratitis eye infection survivor


OMP-access
Political Solutions
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- Launch conditionality, RDP and other OMP Incentives

- EU-HTA Europe

- Joint procurement for OMPs; EU rare disease fund


What if we can build a
Commercial Solution to
OMP-access in Europe?
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Options for Biotechs to make their OMPs accessible regardless of where patients live

Comparison	**Pharmaceutical firms, mid-size**	Regional or country **distributors**	Contract-**services companies**	**Ideal Business Model**
Ultra–OMP / overlooked-OMP focus	✗	✗	✗	✓
Bespoke deals across biotechs's all **non-core markets**	✗	✗	✓	✓
Pan-European technical operations	✓	✗	✗	✓
Covers **end-to-end** commercialisation and distribution **costs**	✓	✓	✗	✓

STORY - 15/12/2022

Multi-drug in-licensers could help tackle critical issues in the European orphan drugs space - Avanzanite CEO

What are the pillars of such a commercial OMP-tailored approach?

Portfolio

30 OMPs
by 2030

All countries

32[1]

OMP

commercial model

[1] European Economic Area, United Kingdom and Switzerland.

OMP Commercial Solution – New Business Model

Model	Our Deal Types	Value Proposition for Biotechs
Locating **overlooked market-ready orphan** drugs and commercializing them **where nobody else will.**	**Tailored partnering**: EU[1] countries that the biotech **does not plan to enter** – could be all or selected **Royalty**-based exclusive in-licensing or distribution deal	No **financial** and **commercial risk** of European or country operations Early earnings generator through **royalty stream without HQ distraction** from key corporate priorities **Efficiency** and little resources in managing 1alliance for **all EU countries.**

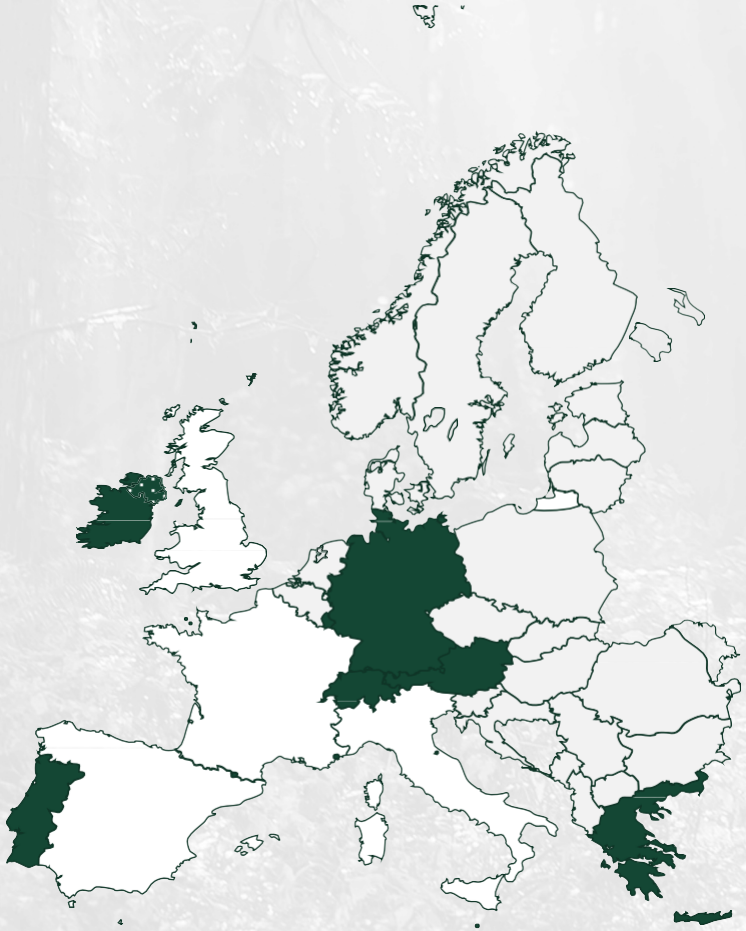
[1] As well as the UK, CH, NO.

Motivation of R&D originators to find better way to accelerate patient access

EXPANSION	TROUBLE	EFFICIENCY
Biotech has no desire to build a **European infrastructure** or risk **distracting** senior manageme nt teams	Biotech does not know how to deal with **formal HTA / P&R issues** leading to a severe underappreciatio n of their asset	Biotech wants to work with only **one distributor** across all **non-core territories**, to maximie value across a diverse range of countries

HTA – Health Tech

Examples of how new model can be tailored



Q&A: How do we ensure that our OMPs – in particular ultra-orphan or otherwise tricky ones – are reaching patients in Europe regardless of where they live?

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IV.

A successful approach for single arm trials in Health Technology Assessments –Cerliponase alfa as an example for the EU-HTA

Sandra Kiehlmeier, Value & Dossier

Value & Dossier
Reimbursement Specialists

A successful approach for single arm trials in Health Technology Assessments

Cerliponase alfa as an example

EUCOPE Members Meeting 14.02.2023

Dr. Sandra Kiehlmeier, Dr. Willi Schnorpfeil

Objectives of the presentation

Value & Dossier
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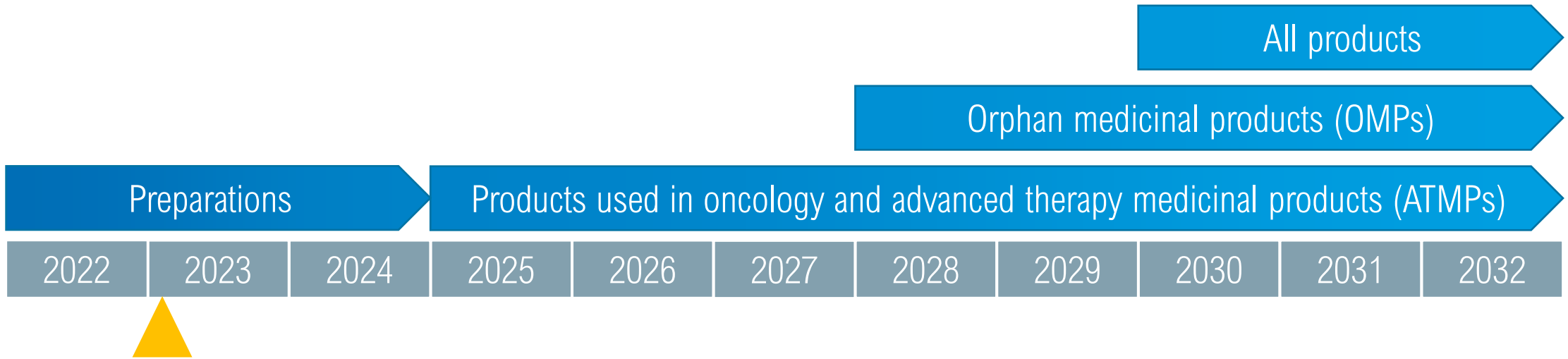
- Challenges of the EU-HTA
- Best practice example
- Quality criteria for natural history comparisons

EU-HTA Timeline – Assessments of single arm trials may be necessary starting in 2025



→ Approximately 30 - 40 % of the OMPs are also used in oncology

→ For some products (e. g. oncologic drugs in 3rd or 4th line, OMPs, ATMPs, paediatric populations), randomized controlled trials (RCTs) may not be possible and the clinical evidence is based on single arm trials

What does this mean for the upcoming EU-HTA and how to handle single arm trials?

Sources: Regulation (EU) 2021/2282, Bundesverband pharmazeutischer Industrie – AMNOG Daten 2021

Challenges of the proposed EU-HTA methodology

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Reimbursement Specialists

→ Comparison with ≥1 other health technology required for Joint Clinical Assessments

→ According to the regulation, specificities of OMPs and ATMPs are to be considered

→ The EU-HTA guidelines have been adjusted

REGULATION (EU) 2021/2282 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 15 December 2021

on health technology assessment and amending Directive 2011/24/EU

Article 2

(6) 'joint clinical assessment' of a health technology means the scientific compilation and the description of a comparative analysis of the available clinical evidence on a health technology in comparison with one or more other health technologies or existing procedures, in accordance with an assessment scope agreed pursuant to this Regulation, and based on the scientific aspects of the clinical domains of HTA of the description of the health problem addressed by the health technology and the current use of other health technologies addressing that health problem, the description and technical characterisation of the health technology, the relative clinical effectiveness, and the relative safety of the health technology;

Article 4

1. The Coordination Group shall ensure that the joint work carried out pursuant to Articles 7 to 23 is of the highest quality, follows international standards of evidence-based medicine, and is delivered in a timely manner. For that purpose, the Coordination Group shall establish procedures that are systematically reviewed. When developing such procedures, the Coordination Group shall consider the specificities of the health technology to which the joint work relates, including orphan medicinal products, vaccines and advanced therapy medicinal products.

Strategies and methodological standards for HTA of single arm trials need to be followed.

ATMP: advanced therapy medicinal products. HTA: health technology assessment. OMP: orphan medicinal product.

Sources: Regulation (EU) 2021/2282

Chances for the EU-HTA – Indirect comparisons

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→ Deliverable D4.6:

Data of a single-arm trial can be used coupled with an external source of data as a control to allow for a comparative statistical analysis. In the context of a JCA, the assessment of such external comparisons is explicated in the EUnetHTA 21 methodological and practical guidelines *Direct and indirect comparisons*. Such a comparison requires an adequate use of a method of causal inference. In such a

→ D4.3.1 and D4.3.2 describe statistical methods for adjustment of populations

- → Matching adjusted indirect comparison (MAIC)
- → Simulated treatment comparison (STC)
- → Propensity score
- → Methods using individual patient data are prefered over aggregated data

Deliverable D4.3.1 and D4.3.2 provide a statistical framework which can be used to generate comparative data with single arm trials. Indirect comparison with natural history cohorts may be a feasible approach.

Sources: EUnetHTA Deliverable D4.3.1, D4.3.2, D4.6

IQWiG analysis of indirect comparisons in AMNOG assessments

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AMNOG assessments of OMPs (2014 – 2018)
n = 67 resolutions on n = 85 questions

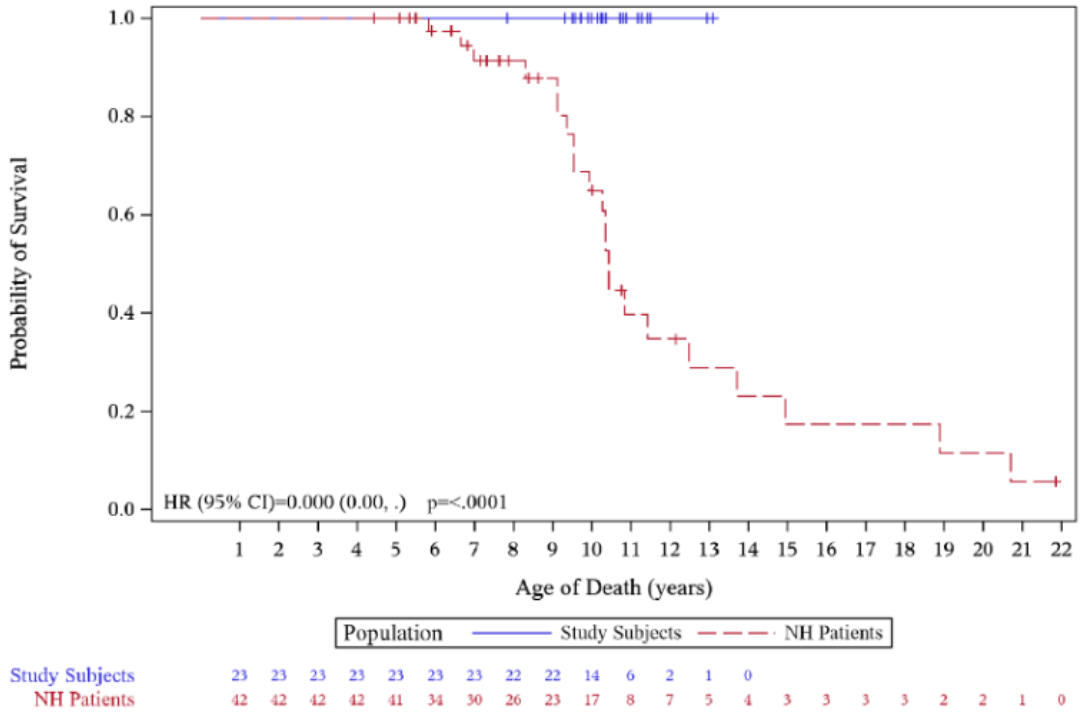
Non-quantifiable added benefit: n = 61 (72 %)	Quantifiable added benefit: n = 24 (28 %)
Based on randomized studies: n = 33 (54 %) Based on non-randomized studies: n = 26 (43 %)	Based on randomized studies: n = 24 (100 %) Based on non-randomized studies: n = 0
Increase of resolutions based on non-randomized studies observed over the past 2 years (2021 – 2022): n = 20/22 with non-quantifiable benefit	Libmeldy and **Cerliponase alfa** were the first OMPs to achieve a **major added benefit** based solely on **non-randomized** studies.

HTA: health technology assessment. OMP: orphan medicinal product.

Sources: IQWiG Rapid Report A19-43

Cerliponase alfa – Overview

- → Enzyme replacement therapy for the treatment of neuronal ceroid-lipofuscinosis type 2 (CLN2)
- → Orphan drug status
- → Market authorization under exceptional circumstances in 2017 based on a single arm phase I/II trial and comparison with a natural history cohort
  - → highly effective treatment
  - → no therapeutic alternatives
  - → ultra orphan disease
  - → randomized controlled trials would be unethical
- → 1st AMNOG assessment in 2017: non-quantifiable benefit
- → 2nd AMNOG assessment in 2022: major added benefit



Success factors

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Major added benefit

Quality criteria for natural history comparisons

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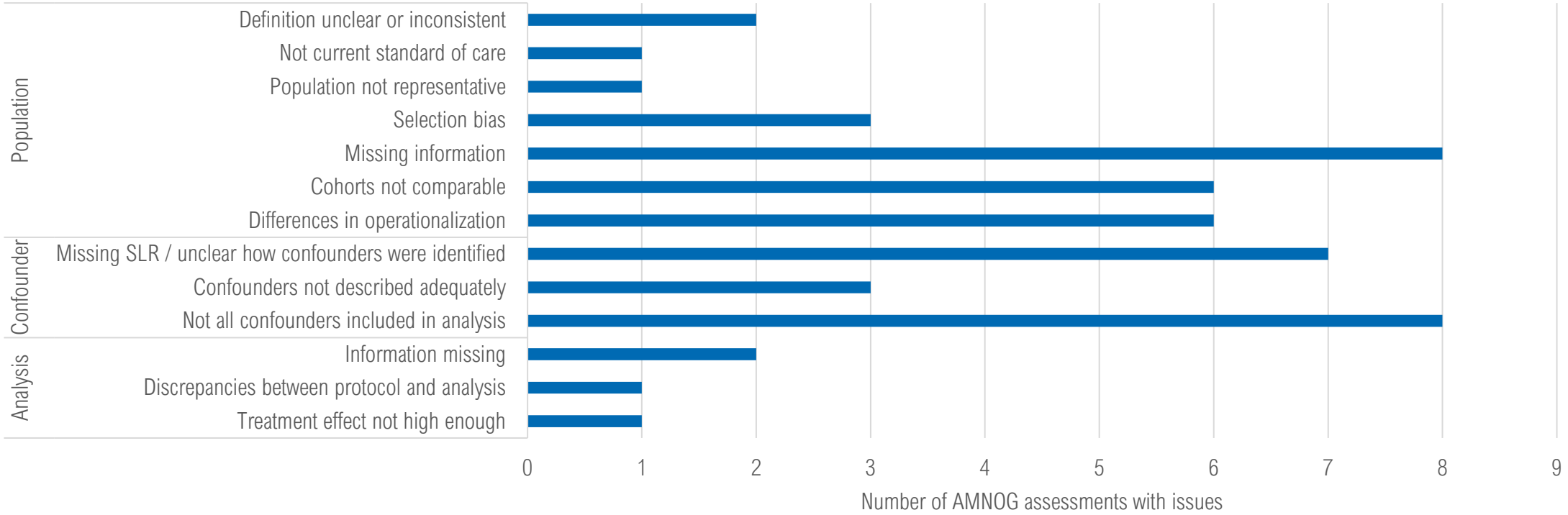
Natural History Cohort	Confounders	Analysis
• Systematic literature research	• Systematic literature research	• Pre-specified in the study protocol and the statistical analysis protocol
• Population must be strictly defined, representative and comparable to the study population	• Explain and justify the rationale of each confounder	• Statistical methods described in deliverables D4.3.1 and D4.3.2
• Availability of all necessary measurements (confounders, endpoints)	⚠ All identified confounders need to be accounted for	⚠ Patient-individual data are necessary for at least one cohort

An indirect comparison of single arm trials with a natural history cohort needs to be planned ahead of time.

Critical points of previous assessments in Germany (2021 – 2022)

In n = 20/22 assessments, indirect comparisons of non-randomized trials were not accepted for various reasons



Choice of the population and confounders are the biggest challenges.

Summary and outlook

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→ An alternative approach for single arm trials is necessary in HTA and useful to strengthen the value story

→ Deliverables D4.3.1 and D4.3.2 describe statistical methods needed for indirect comparisons

→ Natural history cohorts and the methods used for comparison must meet certain requirements to optimize the external validity

Pharmaceutical companies and Member States should align on a common approach.

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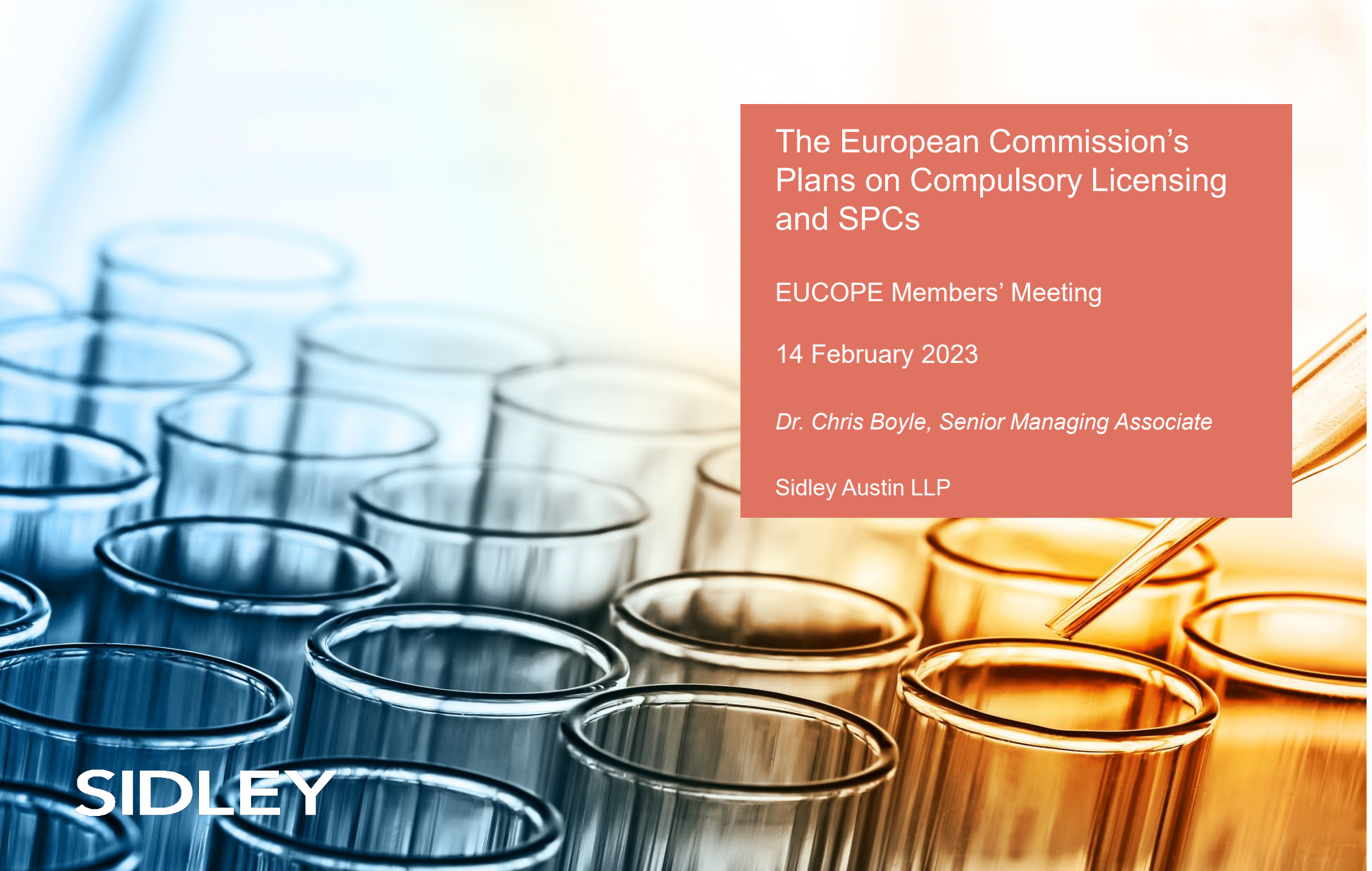
V.
The European Commission´s Plans on Compulsory Licensing and SPCs

Chris Boyle, Sidley



The European Commission's Plans on Compulsory Licensing and SPCs

EUCOPE Members' Meeting

14 February 2023

Dr. Chris Boyle, Senior Managing Associate

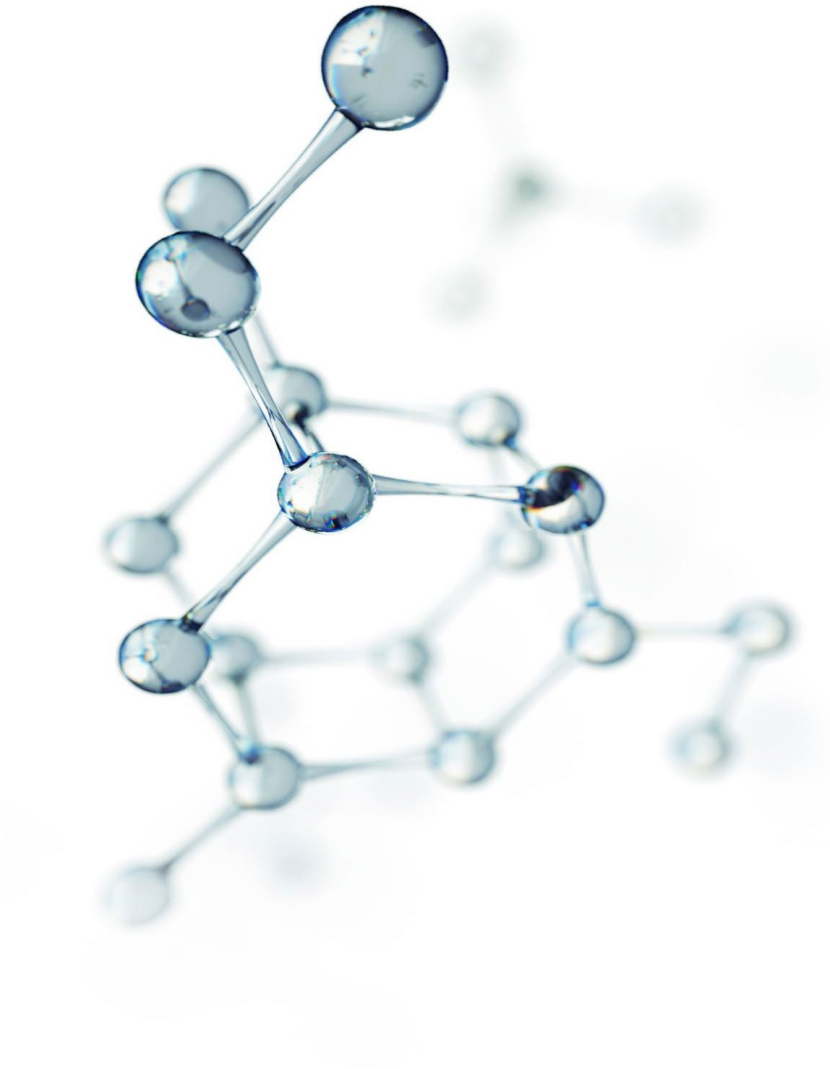
Sidley Austin LLP

SIDLEY

TALENT. TEAMWORK. **RESULTS.**

Agenda

1. Timeline: EC Review of CLs and SPCs
2. Current Framework for CLs
3. EC Report: Compulsory Licensing of IPRs
4. EC Report: CL Policy Options
5. SPCs: Call for Evidence for an IA
6. Max Plank 2: USPC vs. Unified Procedure
7. General Pharmaceutical Legislation: Leak



Timeline: EC Review of CLs and SPCs

- October 2015: EC Single Market Strategy (inc. unitary SPC and man. waiver)
- 2017 – 2018: Various SPC studies (inc. Max Planck 1)
- June 2019: SPC Manufacturing Waiver introduced
- November 2020: IP Action Plan (CL & SPC) and Staff Working Document (SPCs)
- 8 March 2022: Call for evidence on single procedure for granting SPCs
- March – Sept 2022: Call for evidence, Feedback and Public Consultation on CL
- 8 September 2022*: Study on the Options for a Unified SPC (Max Planck 2)
- 24 January 2023: EC Report: Compulsory Licensing of IPR
- 31 January 2023: EC General Pharmaceutical Legislation Proposals Leaked

Current CL Frameworks

Primarily National Law

International Agreements

– TRIPS (effective 1 January 1995, as amended 23 January 2017)

Art 31: *"Where **the law of a Member allows for other use of the subject matter of a patent without the authorization of the right holder,** including use by the government or third parties…"*

Art 31*bis*: A WTO Member may grant a CL to the extent necessary for the **production of pharma products** and its **export** to an eligible importing Member (for cases of public health emergencies)

WTO Decision regarding waivers for the production and supply of COVID-19 **vaccines,** from 17 June 2022, for **five years** (may be extended). In essence, it facilitates the granting of CLs, by "waiving" some of the requirements set out in Art. 31 TRIPS. Negotiations are ongoing to possibly extend the scope of the waiver to COVID-19 "**therapeutics**" and "**diagnostics**" (product scope to be defined).

→ Spill over to negotiations of – legally binding – WHO Pandemic Treaty

EU Treaties/Legislation

– Regulation 2100/04 (Plant variety rights)

– Regulation 816/2006 (CL for export purposes, inc. RDP)

– Art. 102 TFEU & Reg 1/2003 (Competition law)

EC Report: Compulsory Licensing of IPR

Aims: **Identify problems** and assess **policy options** to improve **coherence and effectiveness** of the CL system in the EU

Focus: **Public emergencies** and in particular **health-related crises**. CL remains a '**last-resort**'

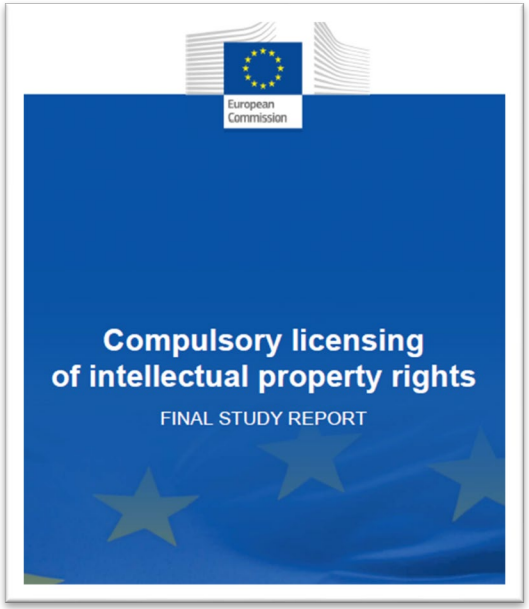
Problem Definitions:

1) Obtaining CLs for manufacturing or import

2) CL for export/import from/to the EU

Examples of cited challenges:

- Diversity/heterogeneity of MS CL legislation
- Cross-border CLs
- RDP
- Lack of exhaustion of IPR



EC Report: Policy Options

*"…**the two most relevant options** to face the crisis described in the baseline scenario are **policy option 4 and policy option 3**"*

0: Maintaining the status quo

1: Member State Coordination

– Building upon the existing national-based CL procedures by formalizing a regulatory network of institutions

2: Member State Coordination & Harmonisation

– Harmonizing national legislation and practices, aligning the definitions and conditions for granting a CL in all EU MS (inc. SPC, RDP etc.), in addition to enhancing MS coordination

3: EU-level compulsory licence

– Designated authority/authorities (existing or new) to declare a "crisis" in the EU CL issued at the EU-level

4: Exhaustion (not included in EC Call for Evidence for an IA)

– EU-wide exhaustion of IPR after product placed on EU market pursuant to CL

– Only one CL procedure issued in one MS is required for the applicant to be authorized to produce and then sell the product in the whole EU market (!)

*"[Option 4]…the **most logical and most effective remedy** to resolve many of the problems described in this study."*

*"…policy option 4 offers the **most threatening solution** for right-holders compared to all the other alternatives, including policy option 3, as the CL outcome would impact the whole EU market through parallel imports".*

SPCs – Call for Evidence for an Impact Assessment

Objectives:

1) Increase legal certainty about procedure for granting SPCs
2) Provide unitary SPC protection in relation to unitary patents
3) Increase transparency
4) Reduce the cost/burden of obtaining and maintaining SPCs

Policy Options:

A) Baseline scenario (no change)

B) Non-legislative instruments (guidelines based on best practice)

C) Legislative changes:

C1) **Unitary SPC** or **Unified Procedure** for **granting national SPC**; or

C2) Targeted amendments to SPC Regulations

Max Planck 2: Unitary SPC vs. Unified Procedure (C1)

Recommends a unified procedure:

- The unified procedure would lead to granting a European certificate which **in some states** has **national effect** and in **other states unitary effect**, according to the law applicable to the designated basic patent.

Recommends the following 'pillars':

- **Central examining body** with a representative from each national agency (similar to CHMP);
- **A system of appeal against refusals before the General Court** supplemented by a Board of Appeal within the agency;
- **Option for a central 'attack'** to be filed with the agency by any person irrespective of a commercial interest; and
- **Applicant may choose** between either a bundle of national applications or a single regional application for a European certificate.

Alternative option: a central body examines regional applications and prepares an opinion on eligibility for an SPC, while the NPOs decide whether to grant or refuse the certificate.

General Pharmaceutical Legislation Leak – SPC and CLs

1. **RDP Waiver – Paving the way for EU CL?**
   - When a CL has been granted
   - To address a "**public health emergency**"
   - Data and market protection would be "**suspended**" for duration of the CL

2. **Shortages Reporting**
   - **Potential trigger for CL?**
   - **Potential trigger for OME derogation?**

3. **Missed opportunity**
   - No 12 extra months of SPC extension for UMN PIP
   - No SPC extension for AMR transferable exclusivity voucher

What's Next?

1st Quarter 2023?

- Proposal on General Pharmaceutical Legislation Package
- Adoption of a Proposal for Single Procedure for the Granting of SPCs
- Adoption of Compulsory Licensing Proposal
- Adoption of a Proposal for Standard-Essential Patents (SEPs)
- And more…

ANY QUESTIONS?

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VI.

Latest Intelligence on the Review of the General Pharmaceutical Legislation, the OMP and Substance of Human Origin Regulations

Victor Maertens, EUCOPE

The revision of the EU pharmaceutical framework

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Current framework

General Pharmaceutical Legislation (GPL)

Medicinal Products Directive (2001/83/EC)

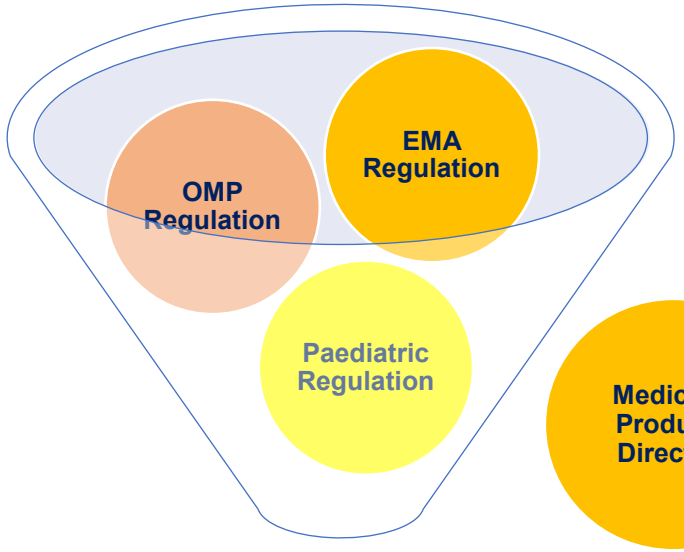
Dual legal path approval

EMA Regulation (no. 726/2004)

OMP Regulation (no. 141/2000)

Paediatric Regulation (no. 1901/2006)

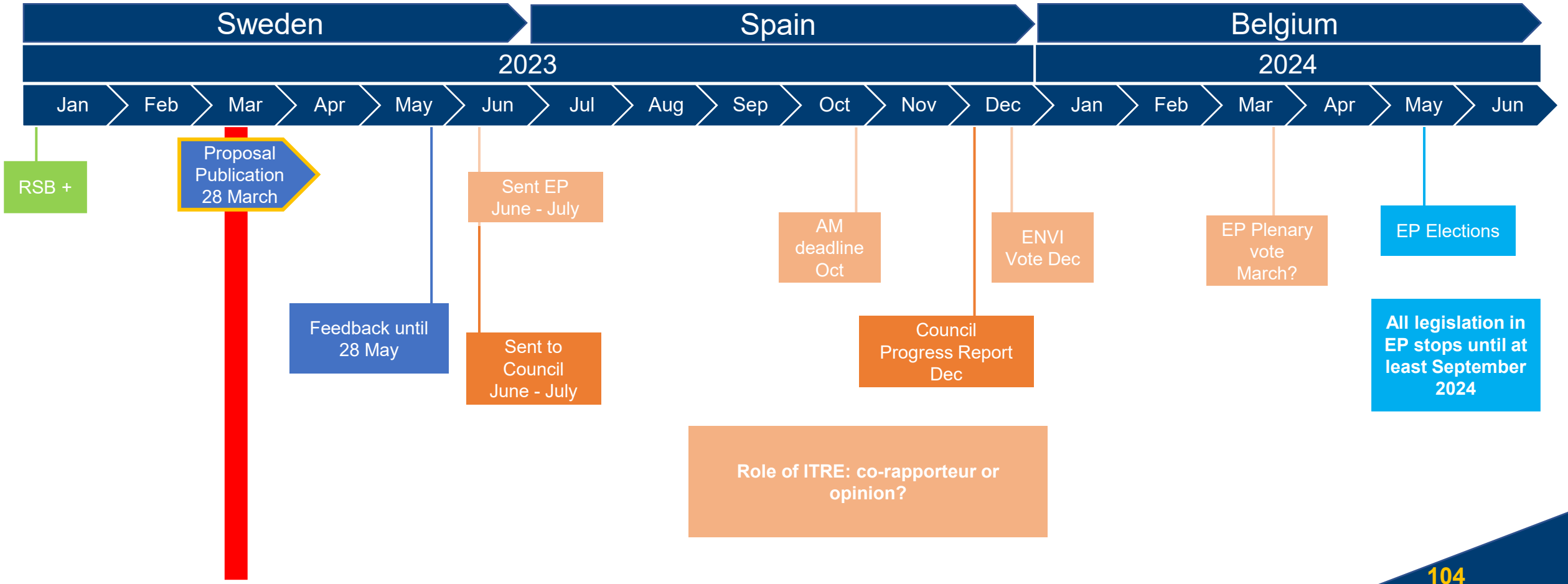
Planned review



Merged into a 'Master Regulation'

Legislative Process Overview

European Parliament will have **less than 11 months** to effectively discuss the proposal



NB: These timings are indicative and rough estimates, not official – it assumes a 'fast' process

EUCOPE Initial Key Priorities

1. (H)UMN
2. Orphan Market Exclusivity
3. Regulatory Data Protection
4. Launch conditionality
5. Regulatory provisions
6. ATMP Policies
7. Shortages and supply chains

1. (H)UMN

Unmet Medical Needs (UMN)

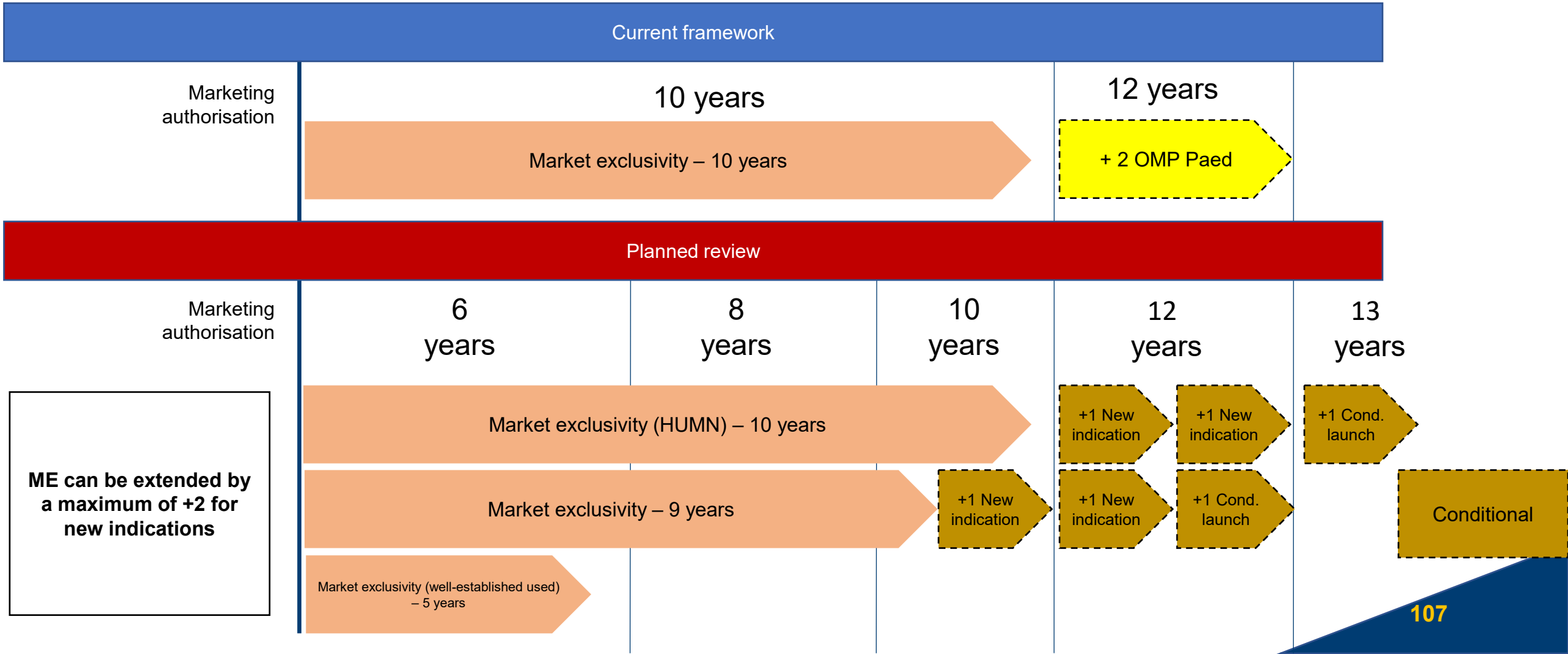
- A medicinal product is designated as UMN if:
  - At least one of its indications relates to a life-threatening or **severely** debilitating conditions ("disease level"); and
  - no medicinal products is authorized in the EU or it does not offer satisfactory method of diagnosis, prevention or treatment of the disease; and the use of a medicinal product results in **meaningful** reduction of **morbidity or mortality** for the relevant patient population ("product level")
- All OMPs are designated as UMN

Highest UMN (HUMN)

- At least one of the product's indications diagnoses, prevents or treats an orphan condition for which:
  - No satisfactory diagnosis, prevention or treatment method exist; or a satisfactory diagnosis, prevention or treatment method exists and it has been demonstrated by the applicant that such a product will bring **exceptional therapeutic advancement**; and
  - The product must **meaningfully reduce** disease morbidity or mortality for the **relevant part of the population**
- The EMA will develop additional scientific guidelines to define HUMN

Crucial aspect: who will decide which products address (H)UMN in real-life (besides the definition)

2. Orphan Market Exclusivity (OME)



2. OME Modulation (Art. 67)

- Introduces a ‘Global Orphan Marketing Authorisation’ (GOMA)
- Orphan Paediatric incentive is removed
- Three types of product are created (Maximum of 12/13 years of protection)

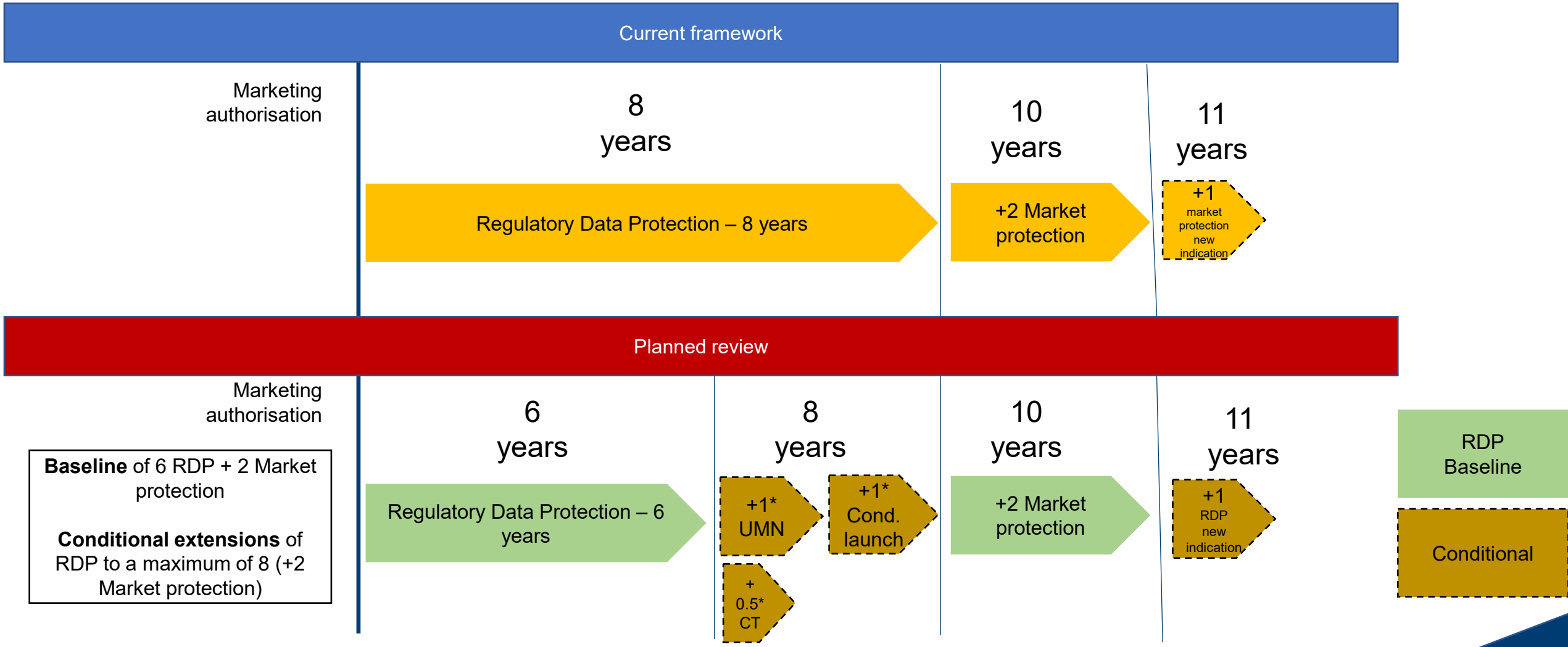
- **Significant benefit definition**: clinically relevant advantage or a major contribution to patient care of an orphan medicinal product ***if such an advantage or contribution benefits a substantial part of the target population***

2. OME Modulation

How do the different elements interact with and impact Orphan Designation?

- Product that is intended for the diagnosis, prevention or treatment of a life-threatening or debilitation condition (Regulation Art. 60):
  - Affects no more than 5 / 10,000 people, and;
  - There exists no satisfactory method of diagnosis, prevention or treatment that has been authorized, or if such method exists, that medical product will be of **significant benefit**. All existing methods should be taken into account that at least party overlap with the medical product referred.
- **Significant benefit** (Regulation Art. 2): clinically relevant advantage or a major contribution to patient care of an orphan medicinal product ***if such an advantage or contribution benefits a substantial part of the target population***
- An orphan designation will be **valid for seven years** – this can be extended and a decision will be made by the Agency (Regulation Art. 61)
- **(H)UMN assessment** (Regulation Art. 65) – in case a treatment exists, the new therapy must provide '**exceptional therapeutic advancement**' and **meaningfully reduce mortality and morbidity** in the **relevant part of the population**

3. Regulatory Data Protection (RDP)

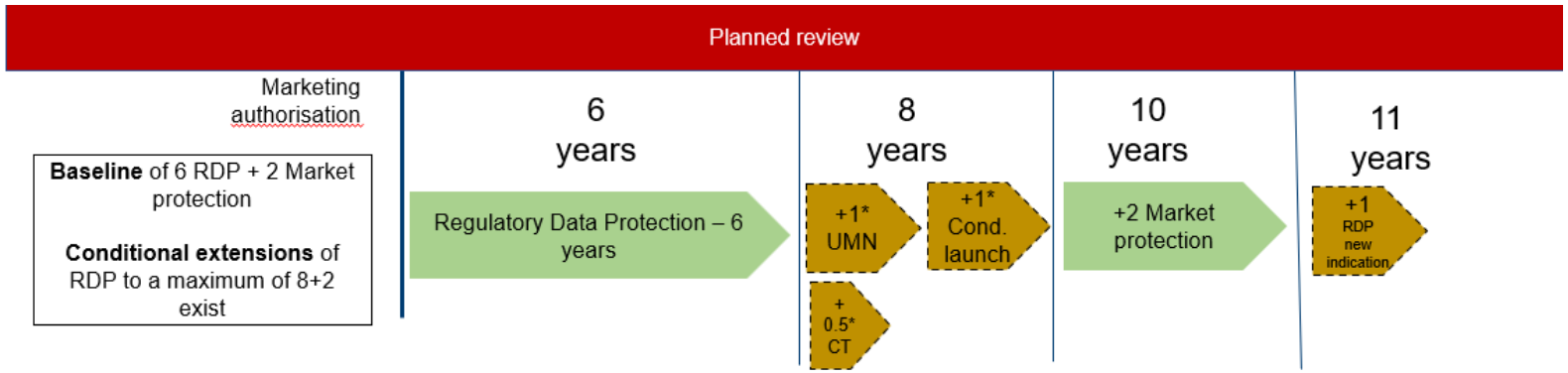


*RDP can be extended, upon conditions to 6.5, 7, 7.5 or 8 years (as a cap)

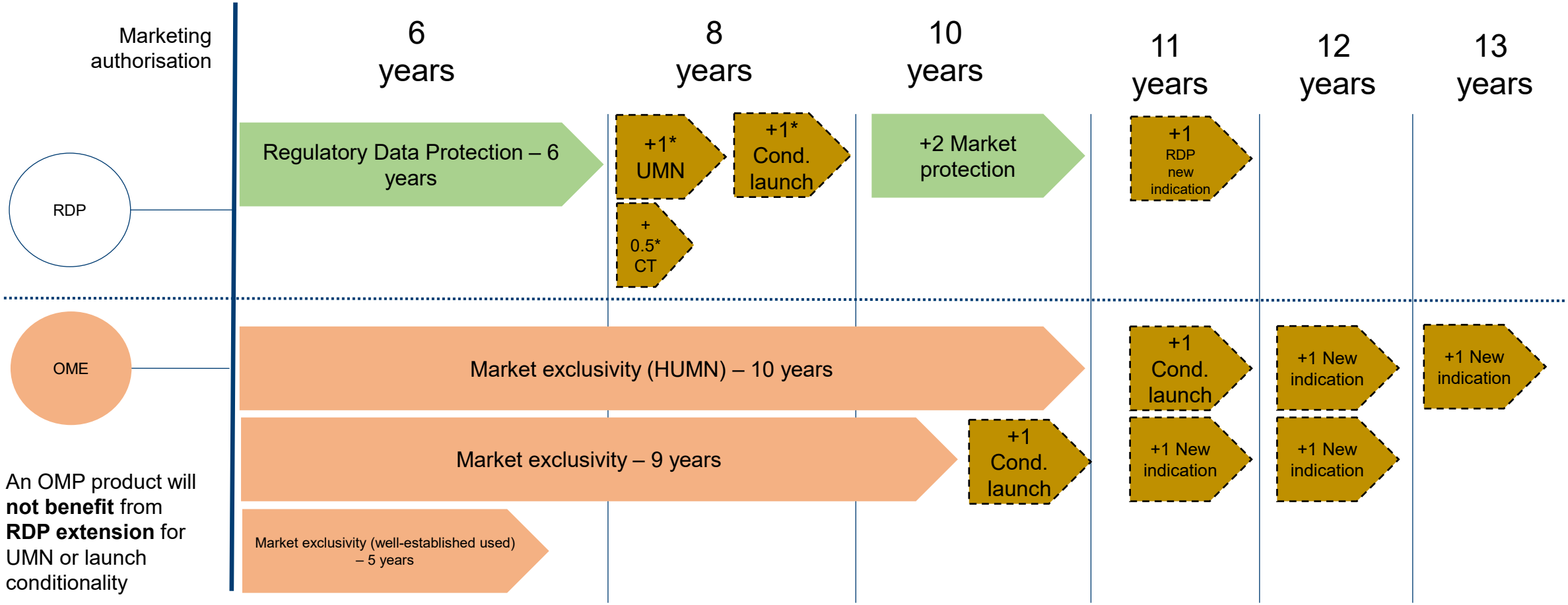
3. RDP Modulation

- Baseline:
  - 6 years RDP + 2 years market protection (MP)
- Conditional extension:
  - Maximum 8 years RDP + current 2 years MP
- Conditional RDP:
  - +1 year for UMN
  - +1 year for launch in all EU Member States
  - +6 months for comparative clinical trials
- +1 year extension for new indication remains in place as now, 8 years limitation does not apply
  - Not clear whether it will provide RDP (per Directive) or MP (per Regulation)

4 years RDP for repurposed medicinal products, but only once for each product, if it provides significant clinical benefit in comparison to existing therapies



RDP and OME: how they interact



*RDP can be extended, upon conditions to 6.5, 7, 7.5 or 8 years (as a cap)

4. Launch Conditionality

- Launch in all EU Member States (unless MS opt-out):
  - +1 year RDP
  - +1 year OME
- "The medicinal product should be released and continuously supplied in a sufficient quantity and in the presentation necessary to cover the needs of the patients in the Member States in which the MA is valid"
  - Within 2 years from MA or
  - In case of SMEs, **within 3 years from MA**
- MAH shall apply for variation of MA between 34-36 months, or 46-48 months for SMEs, after initial MA
- Within 60 days from MAH request, Member State shall issue a confirmation of compliance, a statement of non-compliance or provide a waiver

5. Regulatory Provisions

Context – Regulatory Ecosystem

EUROPEAN COMMISSION

Brussels, XXX
PLAN/2021/10601
[…](2023) XXX draft

SENSITIVE*

Pharmaceutical package

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006

(Text with EEA relevance)

Reasons

- Substantive developments in the past 20 years
- Better collaboration in the overall ecosystem (whole cycle for medicines and medical devices) between administration and stakeholders
- International competitiveness

Objectives

- Simplify regulatory framework, reduce the regulatory burden and provide a flexible regulatory framework
- Improving effectiveness and efficiency, reducing administrative costs borne by companies and administrations
- Streamlining and acceleration of procedures
- Enhanced coordination of the European medicines regulatory network
- Enhanced digitisation (re-use of data, eSubmissions, ePI, etc.)
- Promoting innovation and novel technologies

Context – Regulatory Ecosystem

Additional Tasks to be carried out by EMA

Main areas:

- Enhanced pre-authorisation scientific and regulatory support
- Decision-making on orphan designations and management of Union Register on designations of orphan medicines
- Active substance master file assessment and certification
- Inspection capacities for inspections in third countries and support to Members States
- Environmental Risk Assessment strengthening
- Shortage management and security of supply

Enhanced pre-authorisation scientific and regulatory support

Broadened role and additional competences for EMA

- Scientific and regulatory support by EMA will be strengthened, in particular, for developers of UMN products (Art. 55 ff. Reg NEW)
- Experienced gained with PRIME scheme broadened, i.e. phased review of data (Art. 57 Reg NEW)
- Enhanced legal framework for scientific advice (SA) and accelerated assessment and authorisation of medicines if they offer exceptional therapeutic advancement in areas of UMN (Art. 57 Reg NEW)
- Dedicated support scheme for SMEs and not-for-profit entities
- EMA will be able to provide SA to developers in **parallel** with the SA given by HTA bodies under the HTA Regulation or by expert panels (Art. 56)
- EMA will be able to provide scientific opinions related to the classification of products, advising developers and regulators on whether a particular product is a medicine or not (Art. 58 Reg NEW)
- Orphan criteria and designation through EMA (Art. 60 – 66 Reg NEW), criteria for HUMN in Art. 65 Reg NEW), OME in Art. 67 Reg NEW
- Protocol assistance and R&D support for OMPs, Art. 68 Reg NEW
- EMA – coordinate a mechanism of consultation of public authorities active along the medicines lifecycle, to promote the exchange of information and pooling of knowledge on general issues of scientific and technical nature relevant for the development, evaluation and access to medicines

Temporary emergency marketing authorisation

Situation of public health emergency

- Possibility to grant temporary emergency MAs to address public health emergencies
- Balancing act between immediate availability and requirement to collect additional comprehensive quality pre-clinical and clinical data

Enhancing security of supply of medicines

Addressing shortages of medicines

- Very comprehensive framework for activities to be deployed by Member States (Art. 175 ff DIR NEW) and EMA (Art. 122 ff Reg NEW) to enhance EU's capacity to react efficiently and coordinated to support shortages management and security of supply of medicines, particularly **critical medicines**, to EU citizens at all times
  - MSSG to adopt "Union list of critical medicinal products", provide recommendations on appropriate security of supply measures to MAH, MS, EC or other entities
  - EMA to develop common methodology to identify critical medicinal products and specify procedures and criteria for establishing/reviewing the list as well methods and criteria for reporting
  - EC to implement measures taking MSSG recommendations into account, coordinate between MAH and other relevant entities; consider the need for guidelines
- Broad EMA competences in the monitoring and management of shortages (Art. 122 ff Reg NEW)
- MAH to prepare shortage prevention plan (SPP) and, depending on the circumstances, Shortage Mitigation Plan (SMP)
- Proposal complements and further develops the core tasks already given to the Agency in EMA Extended Mandate Regulation (EU) 2022/123
- Complements HERA's mission to ensure availability of medical countermeasures in preparation of and during crisis
- EMA to be equipped with additional inspection capabilities to inspect sites in third countries (compliance)
- Joint Audit Programme (JAP) established at EMA level to ensure Member States conduct regular GxP audits

Reducing regulatory burden and ensuring flexible regulatory framework for innovation and competitiveness

*Improved **structure** and **governance** of EMA and regulatory network*

Reasons

- Agility of European regulatory system as key component for generics, biosimilar and cutting edge medicines
- Continue to optimise the functioning and efficiency of the regulatory system
- EMA and NCAs confronted with increasing number of procedures, duplication of work, challenges with innovative/complex therapies
- Capacity limitations exacerbated during Covid-19

Measures

- EMA committee structure simplified and reduced from 5 to 2 main Committees
  - CHMP
  - PRAC (as main safety committee)
- CAT, COMP, PDCO and HMPC to be organised in working parties and pool of experts to provide specific input to CHMP, PRAC and CMDh
- CHMP/PRAC – experts from MS and **first-time patient representative**
- **Model of rapporteurs remains unchanged**
- Representation of patients and HCPs with expertise (especially rare/paed diseases) will be increased
- More resources for **early SA** to promising medicines and repurposing, lifecycle approach
- Training opportunities and capabilities enhanced (assessment and monitoring of cutting-edge innovative and complex therapies
- Responsibility of orphan designation (adoption) shifted from EC to EMA

Reducing regulatory burden and ensuring flexible regulatory framework for innovation and competitiveness

Other simplification, streamlining and future proofing measures

Facilitation by measures related to more agile procedures and making use of digitisation

- Electronic submissions
- Electronic Product Information (ePI) – MS to decide if paper or electronically
  - EC empowered to adopt delegated acts to make ePI mandatory from 2035 onwards
  - If qualified majority of MS allowed ePI, package leaflet always to be provided on patient's demand
- Abolishment of the renewal and the sunset clause
- Simplified committee structure eases interactions between companies and Agency
- Emerging developments in science
  - Adapted clinical trials (CT)
  - Use of RWE
  - Secondary use of health data
  - **Regulatory sandboxes** (can be linked to an adapted approval framework, Art. 115 - 117)
- **Evolutionary** and simplified Paediatric Investigation Plans (PIPs) subject to conditions regarding timing and substance (Art. 75 ff.)
- SA for paediatric developments (Art. 86)

Reducing environmental impact of the pharmaceutical product lifecycle

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European Confederation of Pharmaceutical Entrepreneurs AISBL

More comprehensive requirements for Environmental Risk Assessment (ERA)

- **Context**:
  - European Green Deal, COM(2019) 640 final
  - EU Action Plan “Towards a Zero Pollution for Air, Water and Soil”, COM/2021/400 final
  - European Union Strategic Approach to Pharmaceuticals in the Environment, COM (2019), 128 final
- **Complementary to the main environmental legislation**
  - Revision of the Urban Waste Water Treatment Directive(91/271/EEC)
  - Revision of the Industrial Emissions Directive (2010/75/EU)
  - Revision of the list of surface and groundwater pollutants under the Water Framework Directive (2000/60/EC)
  - Environmental Quality Standard Directive (2008/105/EC)
  - Groundwater Directive (2006/118/EC)
  - Drinking Water Directive (2020/2184)
- **Consequence and overall objectives**:
  - Tighter requirements for Environmental Risk Assessment (ERA) **in the marketing authorisation**
  - Evaluation of risk, limitation of potential adverse effects to the environment and public health
  - Scope of ERA extended to cover the entire product lifecycle
  - New protection goals such as risks for antimicrobial resistance (AMR)

Environmental Risk Assessment (ERA)

Market authorisation applications must include an ERA

- **General requirements ERA, Art. 14**
  - Evaluation of the risks to the environment due to the use and disposal (Art. 14 (2), Annex II)
    - For Manufacturing, ERA shall provide information on discharges and emissions of the active substance and other environmentally relevant substances (Annex II of DIR)
  - Proposed risk mitigating measures to reduce discharges and emissions of the medicinal product (Art. 14 (3))
  - ERA shall also include information whether the risk mitigation measures take the main environmental standards **under any applicable legislation** into account
  - Antimicrobial MoA: ERA shall include an evaluation of the AMR selection and specific requirements in Art. 17
  - Ongoing obligation to update the ERA (Art. 14 (6)) and resubmission in accordance with Art. 87 (2) if new information becomes available including updates on the emissions (manufacturing), relevant information from environmental monitoring (Dir 2000/60/EC), from eco-toxicity studies, new or updated risk assessments under other legislation and the collation of sales data
  - In any event 5 years after issuance of the MA (Art. 14 (7))
  - EMA to coordinate with ECHA, EFSA, EEA and draw up scientific guidelines to specify technical details in Annex II to Directive
- **Medicinal Products authorised prior to October 2005 (prior to submitting an ERA)**
  - Specific provisions to be introduced to set up a programme for the ERA of those products potentially harmful, Art. 15
- **Environmental Monograph**: EMA (in collaboration with NCAs) shall setup system of monographs of the environmental properties of active substances that are used in an authorised medicinal product and identified as potentially of concern to the environment
- **Issuing of MA** with AR regarding ERA, Art. 34 (4)
- **Conditional MA** – conduct post-authorisation ERA studies, collection of monitoring data, AMR (Art. 35 (1) lit. (h)
- **Refusal of MA regarding insufficient ERA** – Art. 38 (1) para. (d)
- Rx requirement where active substance contains hazardous property for the environment and Rx as risk mitigation measures (Art. 46 (1) lit. (f) (2), special Rx requirements for antimicrobial products, Art. 46 (2), (4) (d)

6. ATMPs

GMO provisions – Regulation Art. 172: Investigation medical products will be exempt from the relevant GMO Directive articles and instead submit an ERA

CAT – recital 35: The CAT will be dissolved as a permanent body, ATMPs are now considered more common

Hospital Exemption (HE) – Directive Art. 3: Principle remains unchanged. However, stricter data collection requirements are put in place regarding the safety, efficacy, and use of HE. The Commission will have the option to **create a pathway for less complex ATMPs 3 years after the Directive goes into effect**

7. Medicine shortages and supply chains

- MSSG to adopt “Union list of critical medicinal products”, provide recommendations on appropriate security of supply measures to MAH, Member States, Commission or other entities
- **MAH to prepare and keep updated a shortage prevention plan** (SPP) and, depending on the circumstances, Shortage Mitigation Plan (SMP)
- MAH shall notify a Member State on:
  - the intention to cease marketing of a medicinal product (12 months before last supply)
  - the intention to temporarily suspend marketing of a medicinal product (6 months before temporary disruption)
  - the request to withdraw MA (12 months before last supply)
  - temporary disruption in supply (as soon as MAH is aware and no less than 6 months before expected disruption)
- **In case a MAH wants to permanently withdraw a MA, it shall first offer to transfer MA to a third party**

Other provisions

- If **compulsory licensing** is issued by a relevant authority in the EU due to a public health emergency, also RDP and market protection shall be suspended during the period of compulsory licensing

- 6-month **SPC extension** remains in place as reward for the PIP completion

- The Commission will also introduce a notification to report public funding for **transparency of R&D costs**. MAH shall list public funding or financial support to conduct any clinicals trial relevant to MA, and this report shall be accessible to public

EUCOPE “Townhall”

Open to all EUCOPE Members

- **7 March at 14.00**: strategic meeting to discuss main **concerns** from the leak proposal and streamline **priorities**

- April (after the official proposal is released): strategic meeting to define **EUCOPE position** and broader **strategy**

- Additional strategic meetings focused on Pharma Package to follow, upon need

VII.

MDR/IVDR Implementation – the European Commission´s Proposal of 6 January

Axel Korth, EUCOPE

Context of the Proposal

EUROPEAN COMMISSION

Brussels, 6.1.2023
COM(2023) 10 final

2023/0005 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards the transitional provisions for certain medical devices and *in vitro* diagnostic medical devices

(Text with EEA relevance)

Reasons

- Insufficient overall capacity of conformity assessment ('notified') bodies
- Lack of preparedness by manufacturers to meet regulatory requirements of MDR by the end of the transition period (26 May 2024)

Objectives

- Prevent imminent risk of shortages
- Maintain patient access to a wide range of medical devices while ensuring transition to new framework
- More time for manufacturers to certify devices

Context of the Proposal

Legal basis and Consultations

- Art. 114 TFEU
- Art. 168(4) point (c) TFEU
- Subsidiarity and Proportionality
- Urgent calls and broad support from EP, MS and stakeholders through MDCG framework
  - **EUCOPE intervention in MDCG Meeting on 24 August 2022**
  - **Presentation of EUCOPE/France Biotech Survey regarding shortfalls of MDR implementation**
- Parliamentary debate on 24 November 2022
- EPSCO Health Council on 9 December 2022 > broad support for urgent adoption

Supporting measures

- Policy actions coordinated in the MDCG
- **MDCG 2022-14** (26 August 2022) position paper setting out **19 non-legislative actions** where work is in process as well as completed
- 2 delegated acts by EC on 1 December 2022
- **MDCG 2022-18** position paper on 9 December 2022

Content of the Proposal

Transition periods' extension for 'legacy' devices

Staggered regime modifying Art. 120(3) MDR depending on risk class from 26 May 2024 to

- **31 December 2027** – for class IIb implantable and class III devices
- **31 December 2028** – for other class IIa, class IIb and class I devices placed on the market in sterile or having a measuring function

Regulation is directly applicable law in all MS so that notified bodies do not have to change validity dates of certificates, validity dates are extended by operation of law (*legal certainty principle*).

Content of the Proposal

Which devices are benefitting from the extension provisions?

Legacy devices, i.e.

- Covered by a certificate or a declaration of conformity issued **before 26 May 2021** under the Medical Device Directive 93/42/EC (MDD) or Active Implantable Medical Device Directive 90/385/EEC (AIMDD)
- Certificate was **valid** and has **not** been **withdrawn**, or
- Certificate **expired before entry into force of Proposal** but manufacturer and notified body entered into **written agreement** for the conformity assessment of the device (or substitute device) or competent authority of a MS granted derogation (Art. 59(1) or 97(1) MDR) for the device in question

No benefit without conditions

Manufacturers must ensure compliance with MDR

- Compliance – devices continue to comply with MDD/AIMDD
- No **significant** changes in **design** and **intended purpose**
- **No unacceptable risk** to the health and safety of patients / public health
- **QMS** in accordance with Art. 10 (9) MDR by no later than **26 May 2024**
- Formal application for conformity assessment by no later than **26 May 2024** and **written agreement** between NB and manufacturer by no later than **26 September 2024**

Content of the Proposal

Special provision for custom-made implantable devices

Class III custom-made implantable devices also benefit from an extension from 26 May 2024 until

- **26 May 2026** if
  - By not later than **26 May 2024**, a formal application for conformity assessment has been launched by manufacturer, and
  - By not later than **26 September 2024**, the manufacturer and the notified body entered into a **written agreement** for the conformity assessment of the device (or substitute device) or competent authority of a MS granted derogation (Art. 59(1) or 97(1) MDR) for the device in question.

”Sell-Off” requirement removed

No unnecessary disposal of safe devices

- Safe medical devices and *in vitro* devices placed on the market can remain on the market without restrictions provided that devices were in compliance with previous legal requirements under the applicable EU directives (MDD/AIMDD)
- “Sell-Off” dates in new Art. 120 (4) MDR and Art. 110 (4) IVDR removed

Accelerated Procedure

Prevention of a public health crisis and continued access

- Co-decision procedure by European Parliament and Council with an exception to the standard 8-week period that shall elapse between a draft legislative act being made available to national parliaments and the date when it is placed on the provisional agenda for the Council for its adoption
- No formal time limit for the EP and Council's first reading but timely adoption is very likely given the broad political support by all involved stakeholders and the goal to ensure continued access to imminent and safe devices

MDCG Meeting 6 February 2023

Industry raised various practical questions

- Implementation of automatic extension of the transition periods
  - Visibility and certainty in the certifcate towards authorities, bodies and commercial partners in the supply chain and third countries (e.g. export compliance)
- Scope of MD
- Clarification on NB expectations and requirements
  - Written agreement?
  - Application for assessment?
- Transfer of surveillance from MDD to MDR
- Non-legislative measures (MDCG position paper 2022-14) partly fragmented across Members States
  - Structured dialogue with Notified Bodies

Thank you for your attention!