EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

EUCOPE

Members Meeting

Brussels, 26 February 2020

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 / Working Groups

Chairs

II. Reopening of the OMP Regulation

- Risks and opportunities
  Peter Bogaert, Covington
- Core messages from EUCOPE's study on the OMP Regulation

III. The OECD report on performance-based managed entry agreements

Eliana Barrenho, OECD

Agenda (2/3)

IV. Germany: Recent developments concerning reimbursement, data generation and quality management - **Hans-Jürgen Seitz**, IGES

- Focus on ATMPs
- Outlook on further envisaged reforms

V. The outcome of the activity of European Commission Expert Group on Safe and Timely Access to Medicines for Patients – STAMP

Helen Lee, European Commission

VI. Real World Evidence Initiatives – engagement strategy in 2020

Laura Batchelor, FIPRA

- TRUST4RD
- RWE4Decisions

Agenda (3/3)

VII. The German presidency of the EU Council and the upcoming legislative dossiers

Max von Olenhusen, Acumen

VIII. Update on recent EMA activities

- Regulatory Science – examples of future innovative therapies and diagnostics based on new technologies
- New approach for Drug-Device combination products

IX. AOB / End of Meeting

Chairs

I.
Welcome / New Members / Next Events / Working Groups

Chairs

Upcoming Events

https://www.eucope.org/calendar-of-events/

- **4 March 2020:** ISG Meeting, Brussels
- **5 March 2020:** OMP Working Group Meeting, Brussels
- **10 March 2020:** Pricing & Reimbursement / Market Access Working Group, Brussels
- **19 May 2020:** Regulatory & Medical Devices Working Group Meeting, Brussels
- **17 June 2020**: Members General Meeting, Brussels

II.
Reopening of the OMP Regulation

Risks and opportunities

Peter Bogaert, Covington

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Reopening of the OMP Regulation
Risks & Opportunities

February 2020

Peter Bogaert
pbogaert@cov.om

Reopening of the OMP Regulation

- Very difficult to predict
- Commission proposal may get changed dramatically during process
- Many policy choices possible
  - Abolishing
  - Major review (products covered, incentives, etc.)
  - More technical changes

- Always also look for opportunities

Basic Structure of OMP Regulation

- Orphan designation
  - Initial
  - Maintenance (at MA, variation,...)
- Market exclusivity
  - Initial
  - Revision
  - Grounds for breaking

Policy Drivers

- OMP Regulation a success, but ...

- Many orphan diseases still have no approved treatment
- Access to approved orphan medicines:
  - Price
  - Geographical

Examples of Risks

- Exclude certain therapeutic categories?
- Exclude subsequent designations for same product (*e.g.* maximum five)
- Stricter prevalence criteria
- Stricter standard for significant benefit
- Tighten the review procedure for designations

Examples of Risks

- Reduced market exclusivity
- Stricter review of market exclusivity
- “Stick” provisions
- Other

Opportunities

- Rebalance review of designation (at time of MA and variations)
  - Reconcile with conditional MA
- Modulated market exclusivity periods
- Strengthen market exclusivity
- Orphan designation fixed for *e.g.* 10 years after MA, even when market exclusivity falls away
- Allow mixing orphan and non-orphan indications
- Flexible electronic labelling
- Create framework for stakeholder collaboration to stimulate EU R&D
  - European Reference Networks; academia; industry; regulators

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Many thanks

?

pbogaert@cov.com
Covington & Burling, Brussels

Core messages from EUCOPE's study on the OMP Regulation

Chairs

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

OMP KEY MESSAGES AND NEXT STEPS

Vittoria Carraro

CONTEXT: 2020-2021 developments

Expected next steps

March/ April 2020

Publication of the Technopolis report on the OMP Regulation

+

Staff Working Document on the Evaluation of the OMP & Paediatric Regulations

Q1 2020

Industrial strategy with roadmap to pharmaceutical strategy – March 10th

Q2-Q3 2020

Expected EC proposal for a revision of the EU Regulation n° 141/2000

Impact assessment (4 weeks, summer)?

Q4 2020 - Q1 2021

Pharmaceutical Strategy and OMP legislative proposal

RATIONALE TO PROPOSED STRATEGY

Only defending the status quo wont work

WHY?

- There is political will to redefine the current pharmaceutical innovation framework, we need to be realistic in the face of a changing political environment
- Need to put the strategy in the broader context and come up with/leverage existing proposals to tackle the underlying issues

Strategy at a glance

Objective: Halt or limit the possible negative impact of the incentives review on OMP and possible ripple effects on other pharma incentives to innovation

Approach: Combine reactive arguments (to counteract main risks of regulation reopening) with proactive arguments, inter alia, on OMP developers value to European economy

OHE Study: Key takeaways + other messages

Report is final

The results will inform our strategic approach along with complementary messages

1. There are significant financial challenges in developing orphan drugs
2. There has been an increase in development of OMP therapies, produced by small to medium sized companies
3. Net Present Value Model shows that policy changes have negative impacts on OMP development
4. The value of OMPs stretches beyond healthcare budgets alone, also OMP expenditure is sustainable
5. Competition is increasing, but the market has not yet fully matured

Framing the OHE Report

Message 1

Data shows that small to medium companies are **bringing innovation** to Europe but also face **higher volatility rates** than other parts of industry

- EUCOPE wants to bring in the voice of these smaller companies

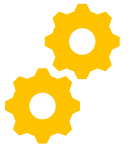
Message 2

There is **more competition** coming from more OMPs, but there is **still a high unmet medical need**

Message 3

Legislation is working – what is needed is improved **access at national level**

- Today there are over 160 OMPs available due to current system
- We can expect **more OMPs (and a steady growth rate)** in the scenario of status quo
- High prices under current framework make the news, but these examples are not representative of all of industry



Additional messages Example: OMP expenditure

Headroom for innovation (Celgene study)

Another recent study shows that Growth in OMP expenditure in Europe is not impacting the stability of total pharmaceutical expenditure

- The OMP market is growing; however, the growth rate has been stable since 2006
- In 2017, the **OMP share of total pharmaceutical expenditure** was **5.6%** of adjusted total expenditure, **versus 4.5% in the forecast**
- Although the orphan market is having a **greater impact** on budget than **forecasted**, the growth of the **non-orphan market** has **slowed**
- **Taking into account this factor and the saving due to the entry of biosimilars in the market to date**, the **OMP share** of total pharmaceutical expenditure is **more aligned with the predicted budget impact in the forecast**

INFORMING KEY ACTIVITIES

OHE Report is final and needs to be framed in the policy context to inform our strategic approach to legislation reopening

Along with the evidence from the report, providing a base for reactive messages, we should bring in our strategy different viewpoints and leverage existing narratives. This is of particular importance to build our proactive messages.

Looking at the **external environment, key risks and their likelihood, 4 key activity areas have been identified**:

1. **Broaden the scope of the debate**
2. **Strengthen partnership with relevant stakeholders within and beyond the rare community**
3. **Engage with 'swing' Member States**
4. **Build simple and comprehensive messages**

Leverage broad industry messages (complement EUCOPE's position)

- Healthcare systems sustainability (% Pharma and rare)
- Pharmaceutical industry role in the EU Innovation ecosystem

DISSEMINATION & STAKEHOLDER ENGAGEMENT

FEBRUARY
OHE Study publication
ISG strategy & key messages

MARCH Preparations of a EUCOPE reaction to Technopolis report + SWD and EUCOPE Position

OMP WG : 5.03

Use leave behind for stakeholder engagement

OMP WG: 11.05 TBC

Continue engagement in legislative phase

Q1

EUCOPE activity around **Rare Disease Day** 28.02

DIA Brussels – 19.03 EUCOPE sessions on OMP and G&CT

Technopolis + SWD Early April

Q2

EUCOPE Breakfast Brief: 23.04 OHE+ Additional Key Messages

WODC Washington – 29.04

Q3

ERCD Stockholm 15 -16.05

EUCOPE 4TH industrial revolution event – May: include relevant messages

Q4

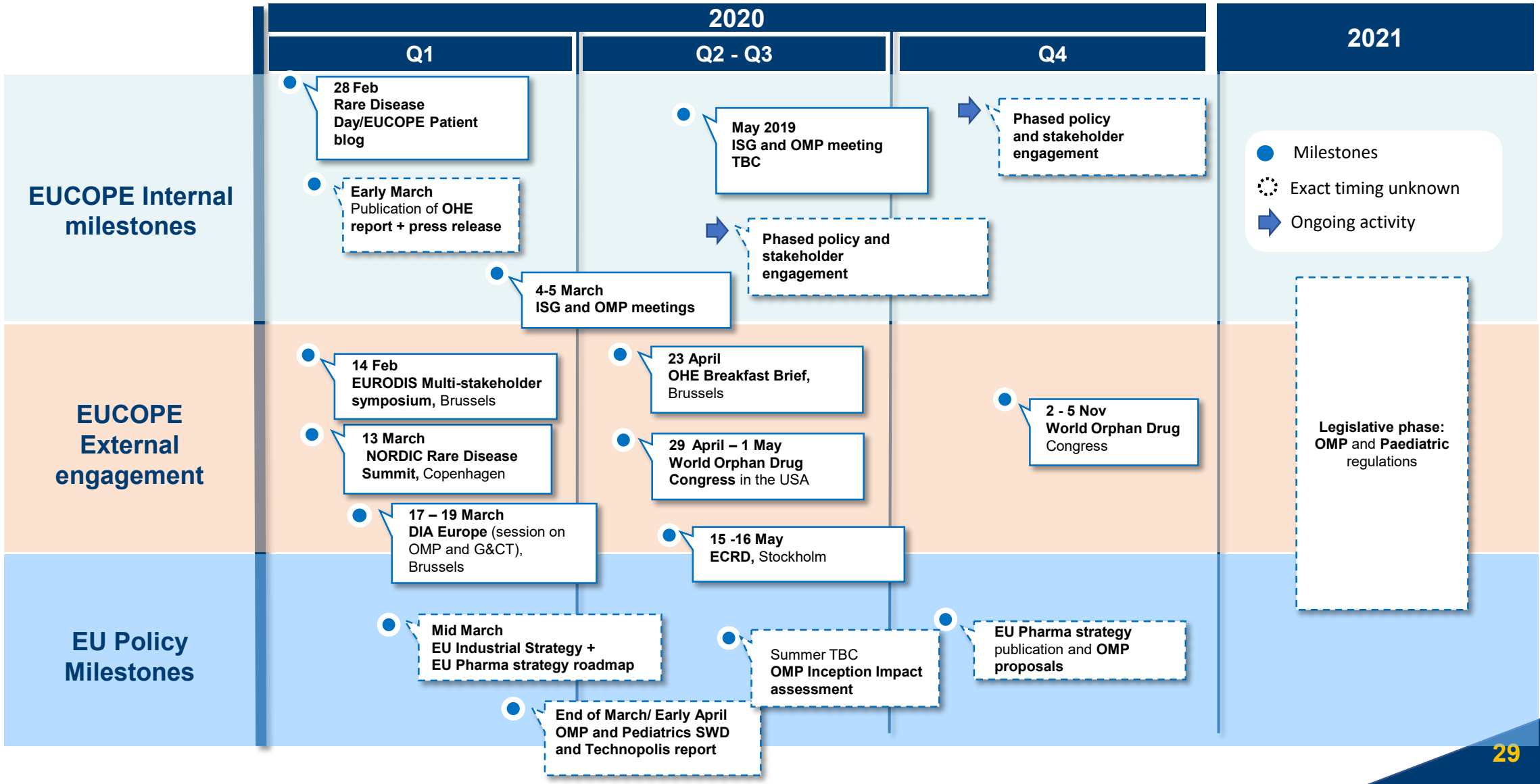
EUCOPE engagement with attachés + key MS health ministries

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

INTERNAL TIMELINES

EXTERNAL ENGAGEMENT

Timelines 2020-2021



What's next?

- ISG and OMP WG to
  - discuss risks and opportunities and refine key messages based on report and complementary sources
  - Define plan for stakeholder engagement – 4 and 5 March

- EUCOPE's external engagement to start positioning policy messages (incl. report launch) – March/April

III.

The OECD report on performance-based managed entry agreements

Eliana Barrenho, OECD

PERFORMANCE-BASED MANAGED ENTRY AGREEMENTS

How they work and possible improvements

EUCOPE meeting, 26 February, Brussels

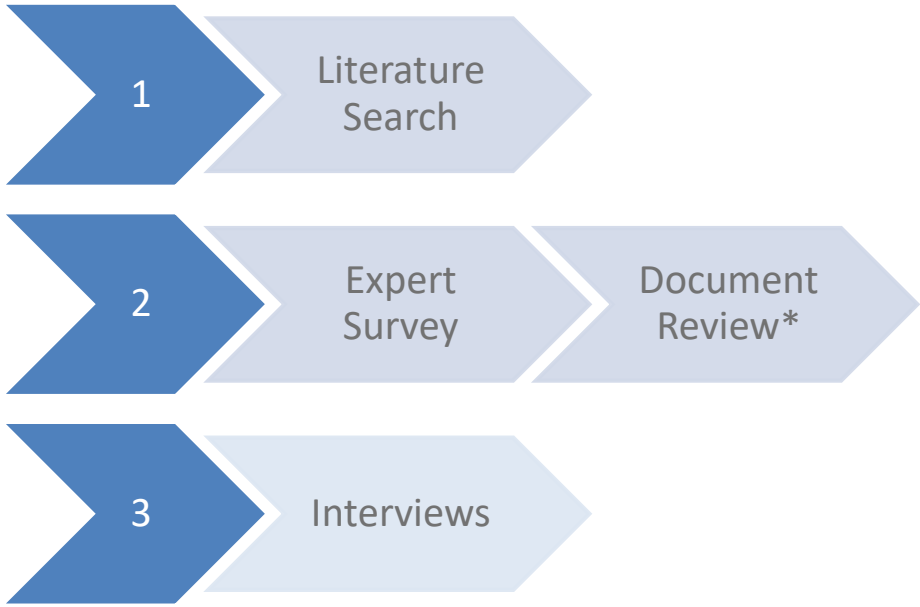
Eliana Barrenho, Health Economist/Policy Analyst
OECD Directorate for Employment, Labour and Social Affairs

BETTER POLICIES FOR BETTER LIVES

Objectives and methods of OECD work

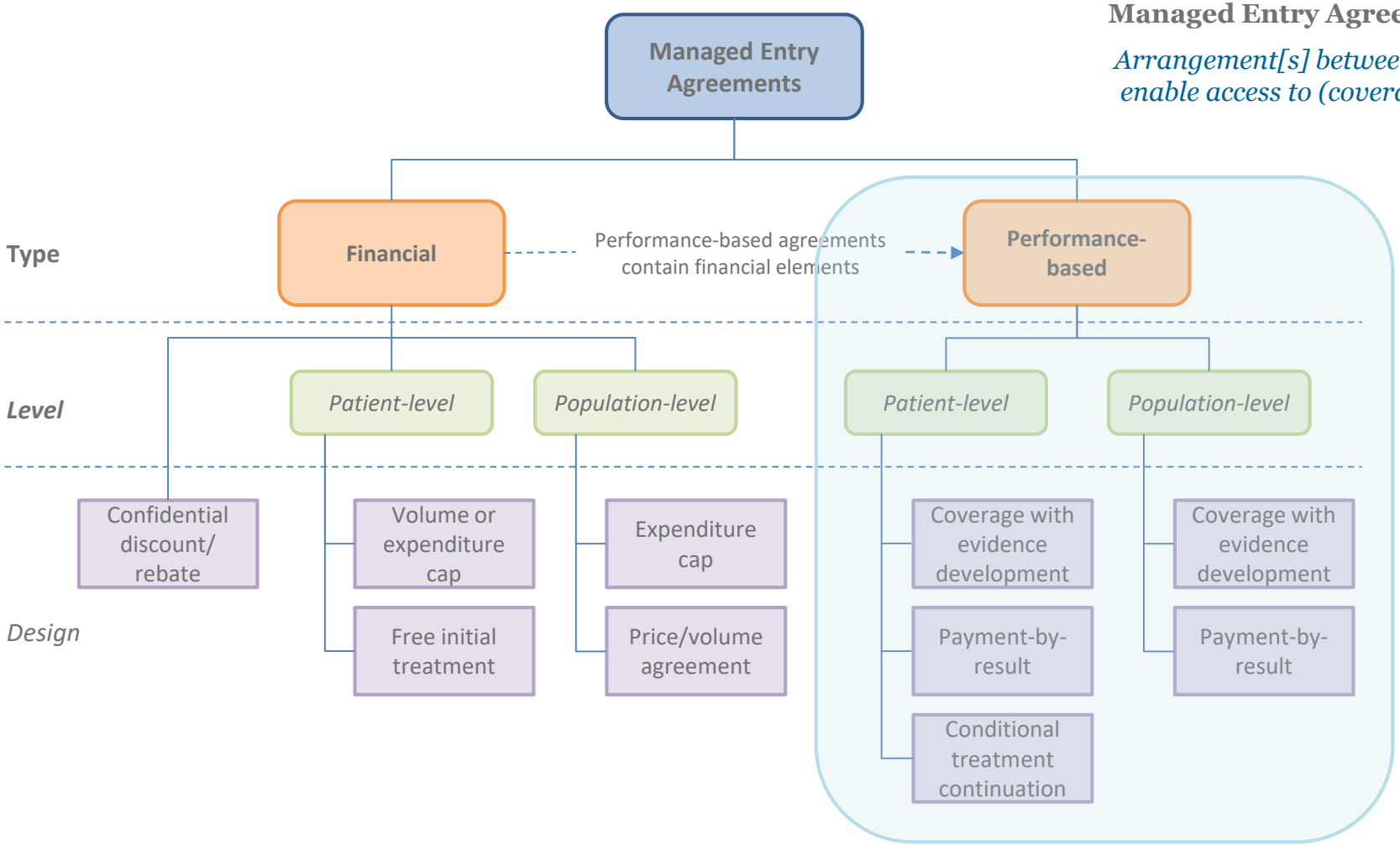
Objectives

1. Critically assess *effectiveness* of performance-based MEAs in achieving their stated goals
2. Identify *good practices* with performance-based MEAs and opportunities for improvements in use and design
3. Outline options for *collating and sharing information* on performance-based MEAs, in particular evidence on the performance of medicines



*Subject to data availability

Focus of OECD work on managed entry agreements:
Performance-based MEAs



Managed Entry Agreements are defined as

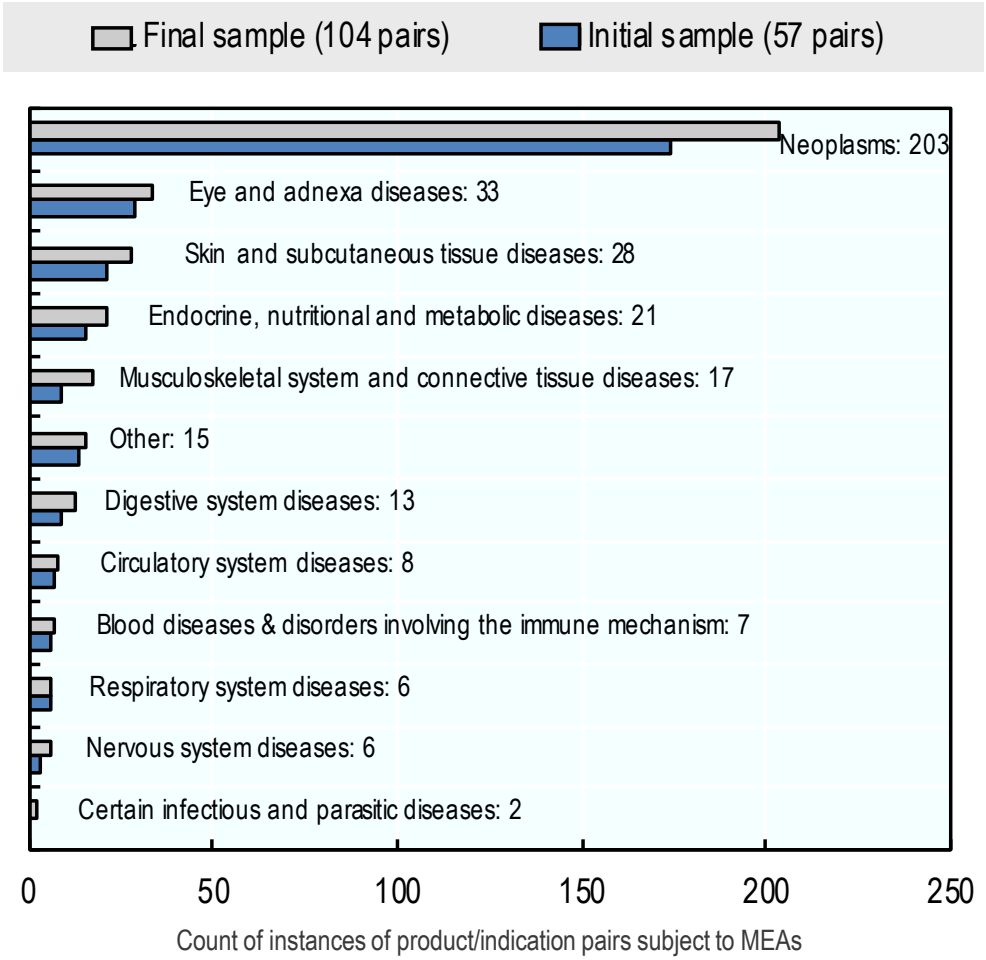
Arrangement[s] between a manufacturer and payer/provider that enable access to (coverage/reimbursement of) a health technology subject to specified conditions.

These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize their effective use, or limit their budget impact.

(Klemp, Frønsdal and Facey, 2011)

Responses to OECD survey / interviews

Country	Responded to survey	Responded to survey question on existence of MEAs for product/ indication sample	Participated in interview
Australia	Yes	Yes	Yes
Belgium	Yes	Yes	Yes
Czech Republic	Yes	No[1]	Yes
Estonia	Yes	Yes	Yes
France	Yes	Yes	Yes
Hungary[2]	Yes	Yes	Yes
Italy[3]	No	No	Yes
Japan[4]	Yes	No	No
Korea	Yes	Yes	Yes
Lithuania	Yes	Yes	Yes
Netherlands	Yes	Yes	Yes
Norway	Yes	Yes	No[5]
Portugal	Yes	Yes	No[6]
Spain	Yes	Yes	No[6]
Sweden	Yes	Yes	Yes
England[7]	Yes	Yes	Yes
United States[8]	Yes	No	No
Country count	**16**	**13**	**12**



Sources: OECD survey and AIFA (2018) for Italy

Existence of Managed Entry Agreements

General

- Overall, MEAs used in about 2/3 of OECD countries and EU member states
- Financial agreements are common
- Most countries also use performance-based MEAs but less frequently

Number of MEAs in sample based on OECD survey (14 countries)

Country	Number of product / indication pairs in sample			
	Data available for	Subject to MEAs (active[1] / total)	Subject to performance-based MEAs (active[1] / total)	Subject to performance-based MEAs by type (total)
Australia	72	n.d.[2] / ≥43	Confidential	Confidential
Belgium	58	25 / 28	Confidential	Confidential
Estonia	64	n.d.[2] / 11	n.d.[2] / 8	Patient-level PbR: 8
France	59	n.d.[2] / 48	≤3[2] / 4	Patient-level PbR: 3 Population-level CED: 1
Hungary	70	16 / 16	7 / 7	n.d.
Italy[3]	n.d.	25[4] / 37	16[4] / 22	n.d.
Korea	58	≤8 / 10	0 / 1	Patient-level CED: 1
Lithuania	57	n.d.[2] / 22	n.d.[2] / 1	Patient-level CTC: 1
Netherlands	19	10 / 13	n.d.	n.d.
Norway	67	1 / 2	0 / 0[5]	n.a.
Portugal	66	43 / 43	3 / 3	Patient-level PbR: 3
Spain	3	3 / 3	3 / 3	Patient-level PbR: 3
Sweden[6]	58	22 / 26	0 / 0	n.a.
United Kingdom (England only)[7]	n.d.	n.d[7]. / 57	n.d.[8] / ≥27	Population-level CED: ≥22 Others: n.d.

Sources: OECD survey and AIFA (2018) for Italy

Performance-based MEAs often have financial objectives

Objectives of performance-based MEAs

based on OECD expert interviews (12 countries)

Country	Reduce uncertainty around comparative effectiveness	Reduce uncertainty around cost-effectiveness	Manage budget impact
Australia[1]	Yes	Yes	Yes
Belgium	Yes	Yes	Yes
Czech Republic		Yes	Yes
Estonia		Yes	Yes
France	Yes	Yes	Yes
Hungary		Yes	Yes
Italy	Yes	Yes	Yes
Korea[2]			Yes
Lithuania		Yes	Yes
Netherlands[3]	Yes	Yes	
Sweden	Yes	Yes	Yes
United Kingdom (England only)[4]	Yes	Yes	Yes
Total (count)	7	**11**	**11**

Source: OECD expert interviews

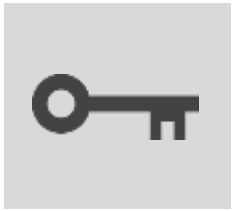
Experience with performance-based MEAs is mixed

- Published evidence suggests performance-based MEAs not very successful at reducing uncertainty around product performance
  - Australia: unclear if CED reduced uncertainty around product performance; can be costly to implement (Tuffaha and Scuffham 2018; Kim et al. 2018)
  - Belgium: performance-based MEAs allowed for coverage at lower prices at "cost" of reduced transparency; do not reduce uncertainty around product performance (Gerkens 2017)
  - Netherlands: CED ("*conditional financing*") did not reduce uncertainty around product performance and did not achieve its objectives (Makady et al. 2018 and 2019; Pouwels 2019)
  - Sweden: studies conducted under CED schemes of poor quality and unable to answer research questions (Ekbom et al. 2007; Merlo 2007)
- Limited evidence available
  - Few countries have formally evaluated their experience
  - Confidentiality of the content of MEAs and their results continues to be a barrier to independent evaluation

Experts also report varying experiences

- Performance-based MEAs considered successful in accelerating coverage decisions in the face of uncertainty
  - Payment-by-Result considered an effective means of managing budget impact
  - Coverage with evidence development also allows for faster coverage decisions despite uncertainty around comparative effectiveness or cost-effectiveness, but experts question its ability to reduce such uncertainty
- Main concerns include
  - Limited ability to reduce uncertainty around product performance
    - Poor data quality or methodological issues in studies – difficulties with interpreting study results
  - Difficulties with making appropriate coverage decisions, in particular withdrawing coverage
  - High level of confidentiality
  - High burden of executing performance-based MEAs
  - ➢ *Financial objectives of Payment-by-Result could also be achieved by lowering prices*

Good practices emerge from existing experience



Using performance-based MEAs strategically

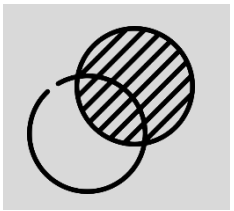
- Formulating a clear policy and strategy on when and when not to use performance-based MEAs
- Embedding the decision process with HTA to ensure uncertainties are identified
- Using a value-of-information framework

Designing performance-based MEAs to address uncertainties at hand

- Choosing the most appropriate MEA design
- Defining clear research questions to address uncertainties
- Ensuring that informative data are available, sound study designs and appropriate follow-up times

Adopting a governance framework

- Ensuring transparency of process and accountability of stakeholders
- Providing mechanisms to act on new evidence – e.g. exit from MEAs and withdrawing coverage
- Avoiding conflicts of interest and creating the right incentives for firms



Ensuring transparency of information on product performance

- At a minimum, publishing information on product performance
- Keeping only commercially sensitive information (e.g. prices) confidential

New **Cancer Drugs Fund** (England)

- Clear entry criteria
- Embedded in NICE appraisal process
- Temporary coverage conditional on evidence generation
- Data collection arrangements public
- Defined exit mechanism

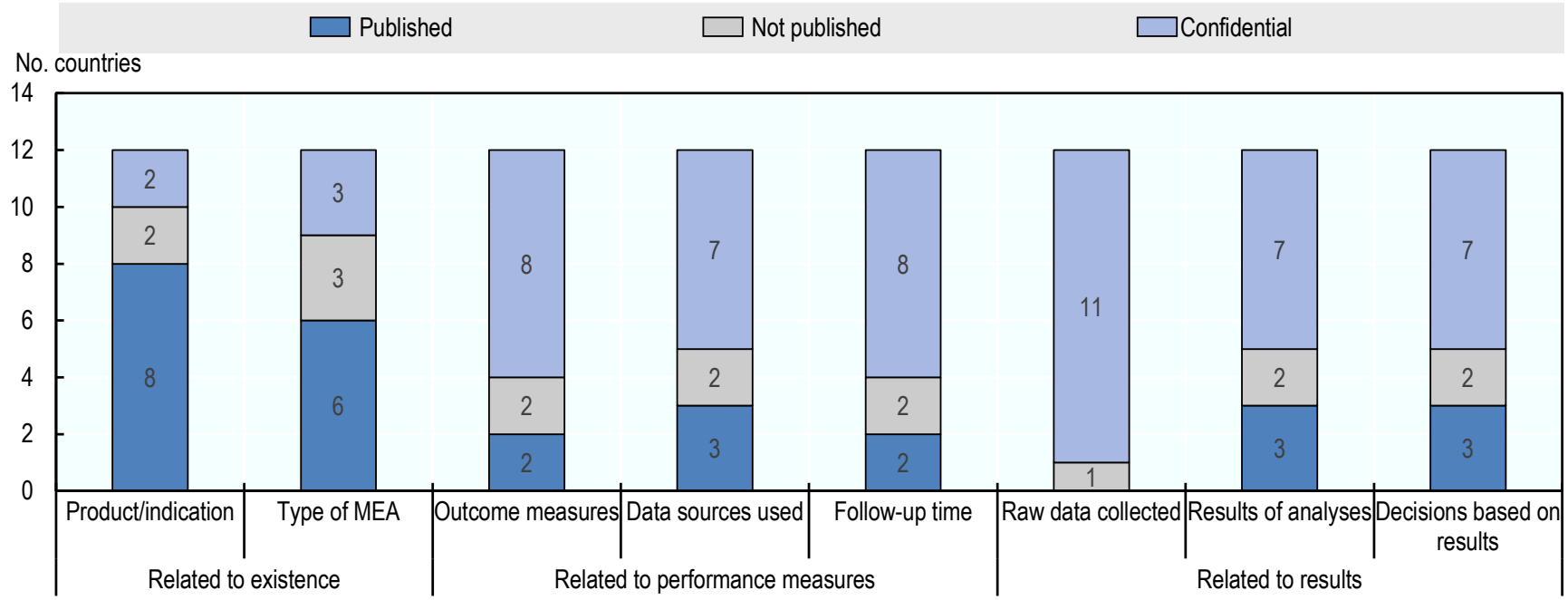
However: too early to evaluate success

- *Operational since 2016*
- *Two products so far*

International sharing of information is uncommon…

Number of countries in which information is published, not published and confidential

Based on OECD survey and expert interviews (12 countries)

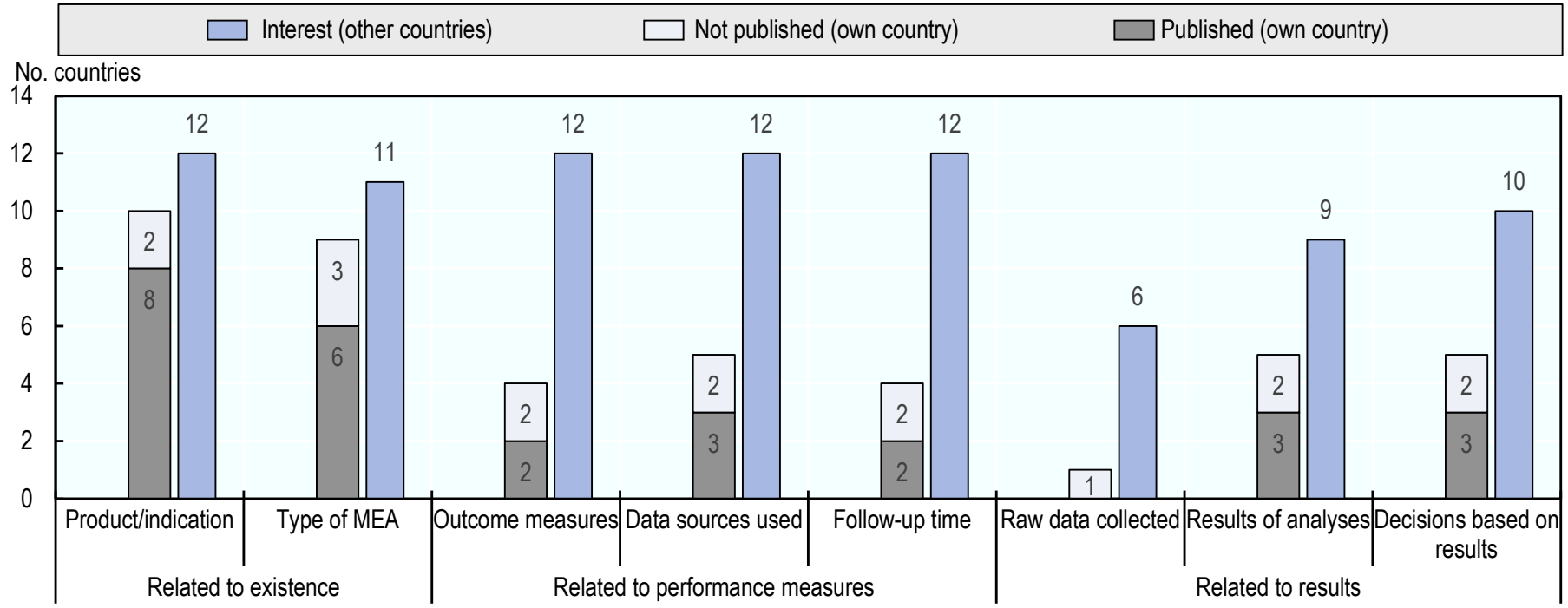


Sources: OECD survey and expert interviews

…despite interest expressed by experts in many countries

Number of countries in which information is not confidential and interest in such information from other countries

Based on OECD survey and expert interviews (12 countries)



Sources: OECD survey and expert interviews

Various options available for information sharing

- Publishing information individually (e.g. on websites)
  - Existing MEAs and MEAs in negotiation by product/indication
  - Data sources and health outcome measures used to determine product performance
  - Study results and coverage decisions made
- Creating a shared repository (e.g. similar to Euripid)
- Integrating information on product performance into existing information sharing frameworks (e.g. with patient registry data, pharmacovigilance and other data on product performance)

➢ *All options would require that new MEAs do not contain confidentiality clauses that apply to the above information*

Staying in touch with the OECD

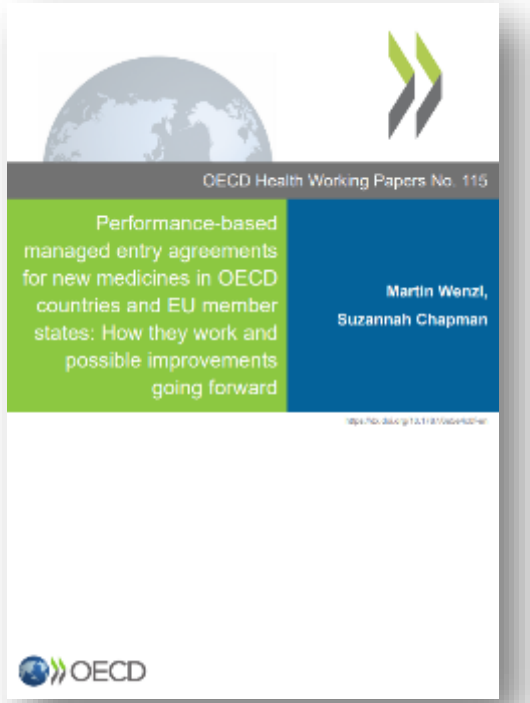
Your Name eliana.barrenho@oecd.org

Follow us on Twitter @OECD_social

Visit our website http://www.oecd.org/health

Final report on MEAs available as OECD Health Working Paper

https://www.oecd.org/els/health-systems/pharma-managed-entry-agreements.htm



IV.
Germany: Recent developments concerning reimbursement, data generation and quality management

Hans-Jürgen Seitz, IGES

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Germany: Recent developments concerning reimbursement, data generation and quality management

(Dr. H.J. Seitz, IGES)

Members Meeting

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Topics

1. Background
2. New legislation and Impact
   - Act for more safety in supply of pharmaceuticals (GSAV)
     - Mandatory Data Collection
     - Pricing
     - IQWIG Rapid report
   - Statutory Sickness Funds - Fair Competition Law (GKV-FKG)

Rising Expenditures of Sickness Funds

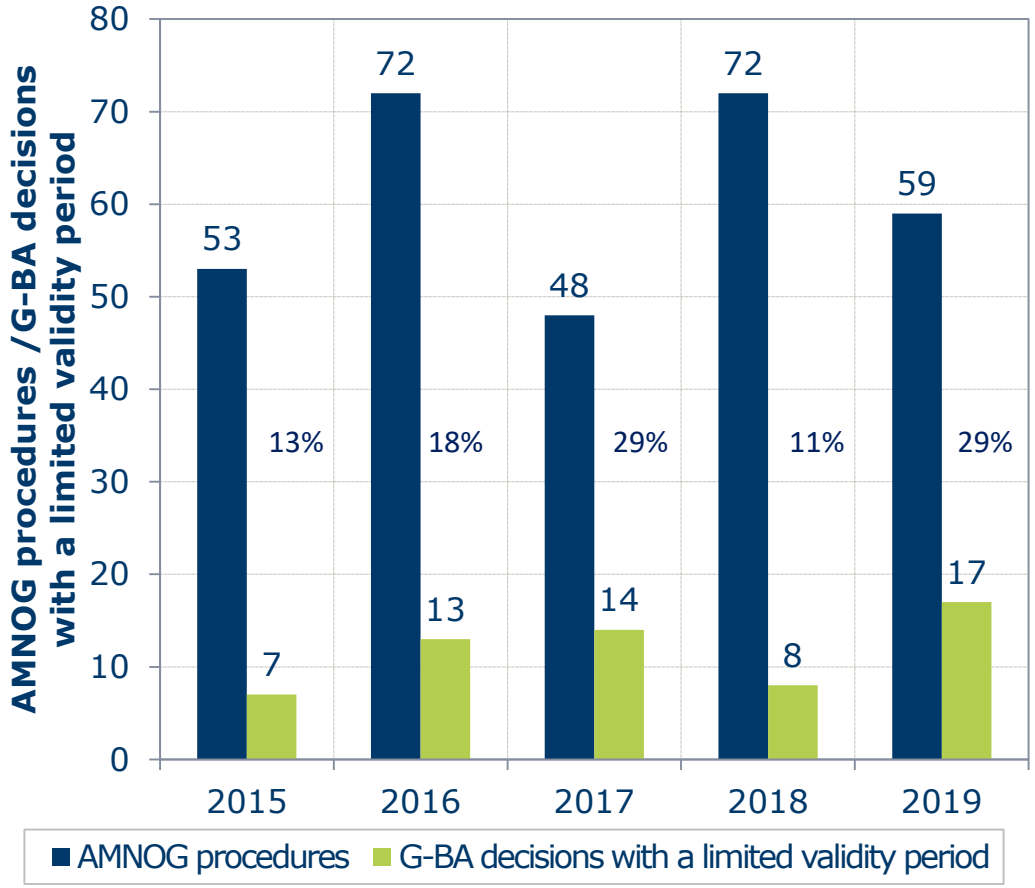
Some Facts to keep in mind

- 2019: Drug expenditures Statutory Sickness Funds increased by 4.7% (41.7 bio € or 1,9 bio €) (IQVIA)
  - 42% of increase is due to oncologicals
- Oncologicals:
  - 1.1% of prescriptions, 17.5 % of expenditures (Prof. Hecken)
- Orphan Drugs:
  - 0.05% of prescriptions, 9.1% of expenditures (Prof. Hecken)
- After several years of surpluses, expenditures of statutory sickness funds exceed contributions by members (deficit 2019: approx. 1.6 bio €; surplus 2018: approx 2 bio €)

G-BA Decisions with limited validity period are increasing

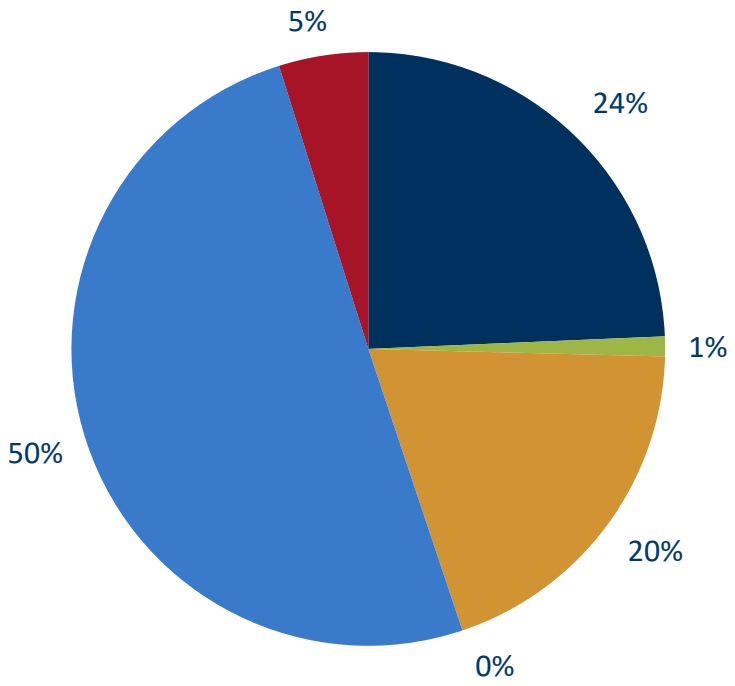
In recent years, the number of G-BA decisions with a limited validity period in AMNOG has increased.

- The reason for this is often the limited level of evidence at AMNOG Dossier submission
- 34% of all new substances evaluated under AMNOG are Orphan Drugs (Jan.-August 2019)

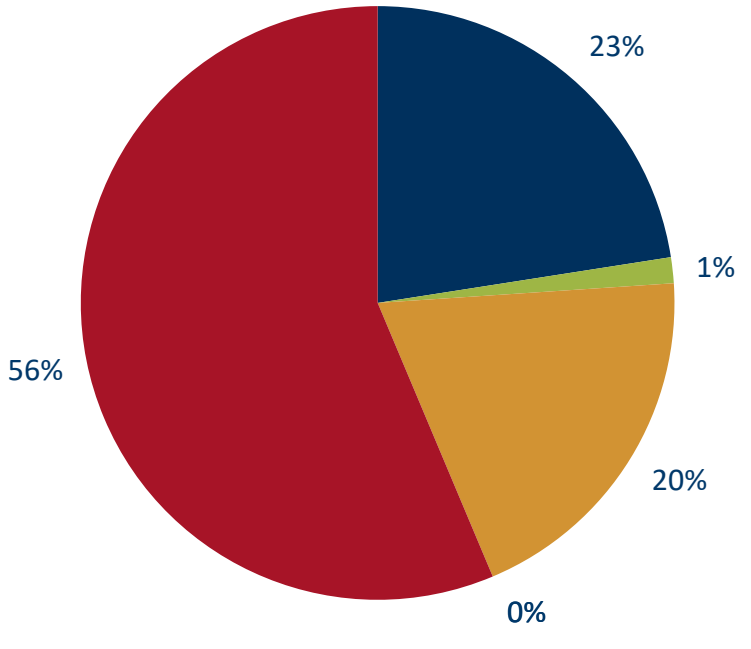


AMNOG: Almost 80% of non-quantifiable additional benefit concentrates on OD*

AMNOG products without orphan (n=185)

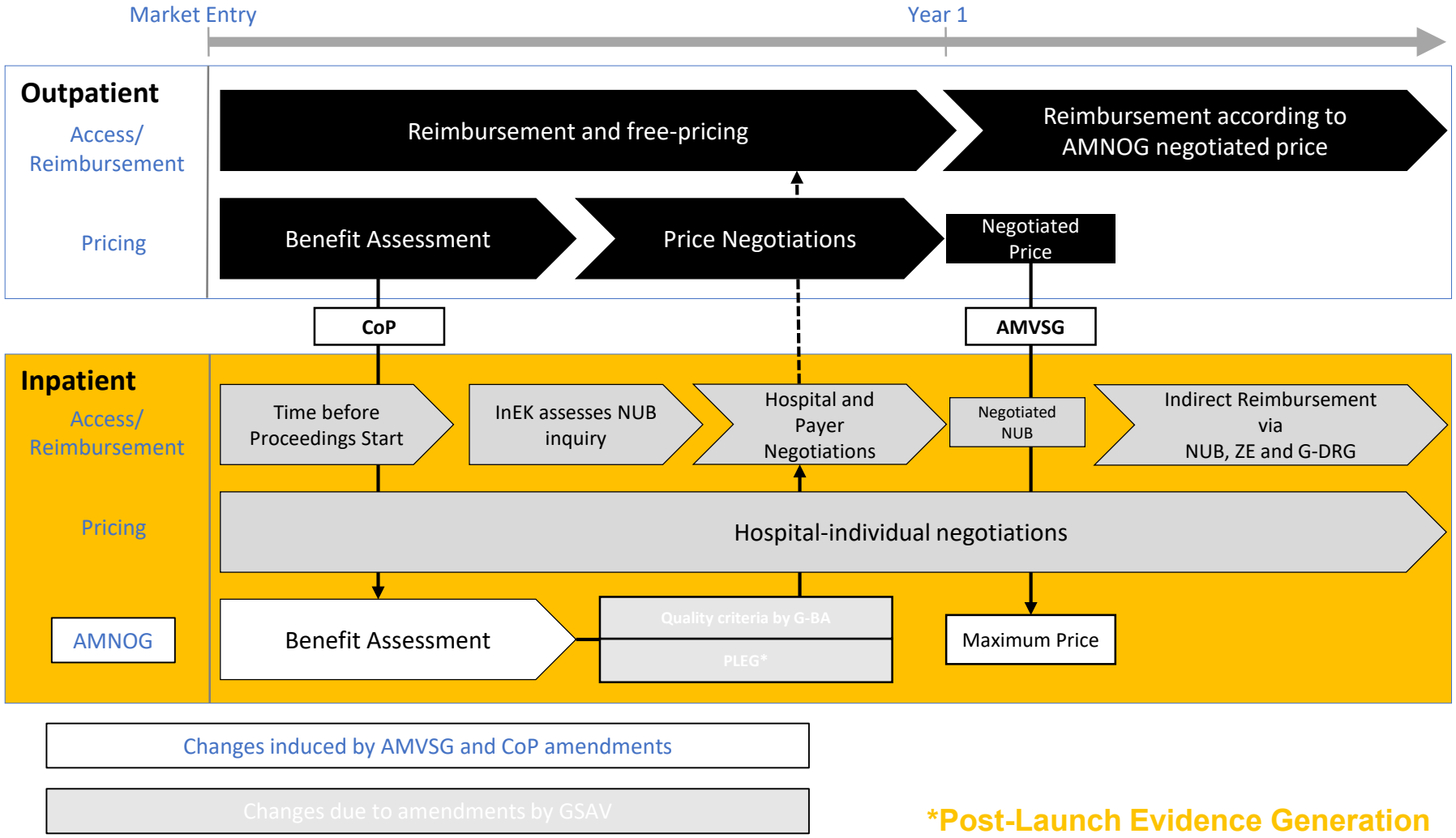


Orphan products in AMNOG (n=71)



Source: IGES-ARA, as of November 2019; a total of 49 ZN "not quantifiable", 40 of which are orphan drugs

AMNOG is gradually expanding in the hospital sector



*Post-Launch Evidence Generation

GSAV (August 2019): Quality Assurance criteria for ATMPs

Quality assurance criteria passed with G-BA decision (AM-UA) for ATMPs

- minimum requirements for structure, process and outcome quality,
- These may also be defined with regard to indications or groups of drugs.
- Relevant aspects are focused by the quality assurance guidelines:
  - the necessary qualifications of the service providers,
  - structural requirements and
  - Requirements for other quality assurance measures
  - May define according to § 136a Abs. 5 SGB V quality criteria for the application of ATMP according to § 4 Abs. 9 AMG within the framework of its resolution.
- The Federal Institute for Drugs and Medical Devices and the Paul Ehrlich Institute must be involved before a measure according to § 136a sentence 1 SGB V is enacted.

GSAV (August 2019): Mandatory Data Collection

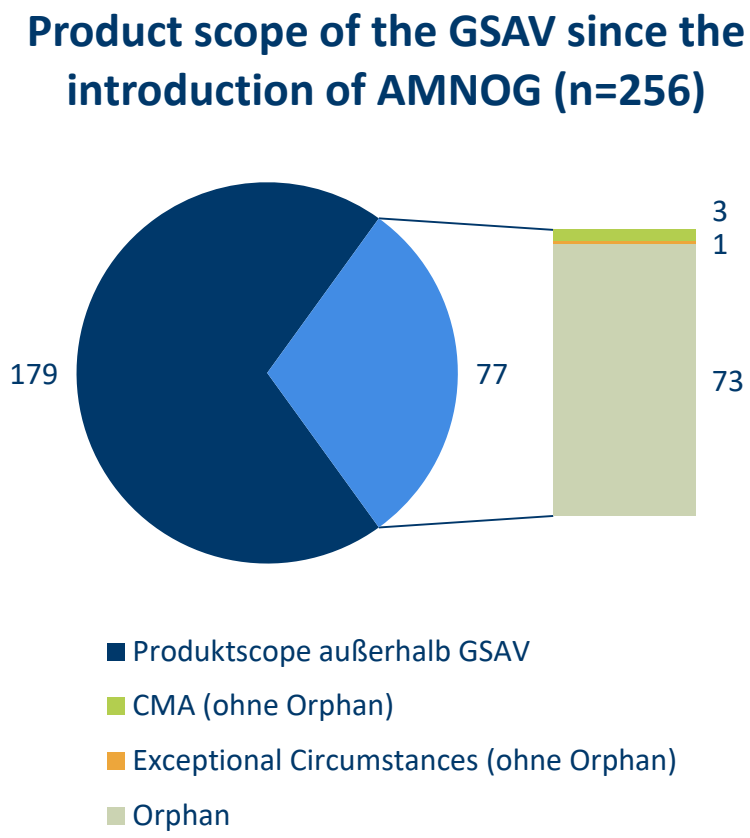
The Federal Joint Committee (G-BA) can demand data collection and evaluations to accompany the application for the purpose of benefit assessment.

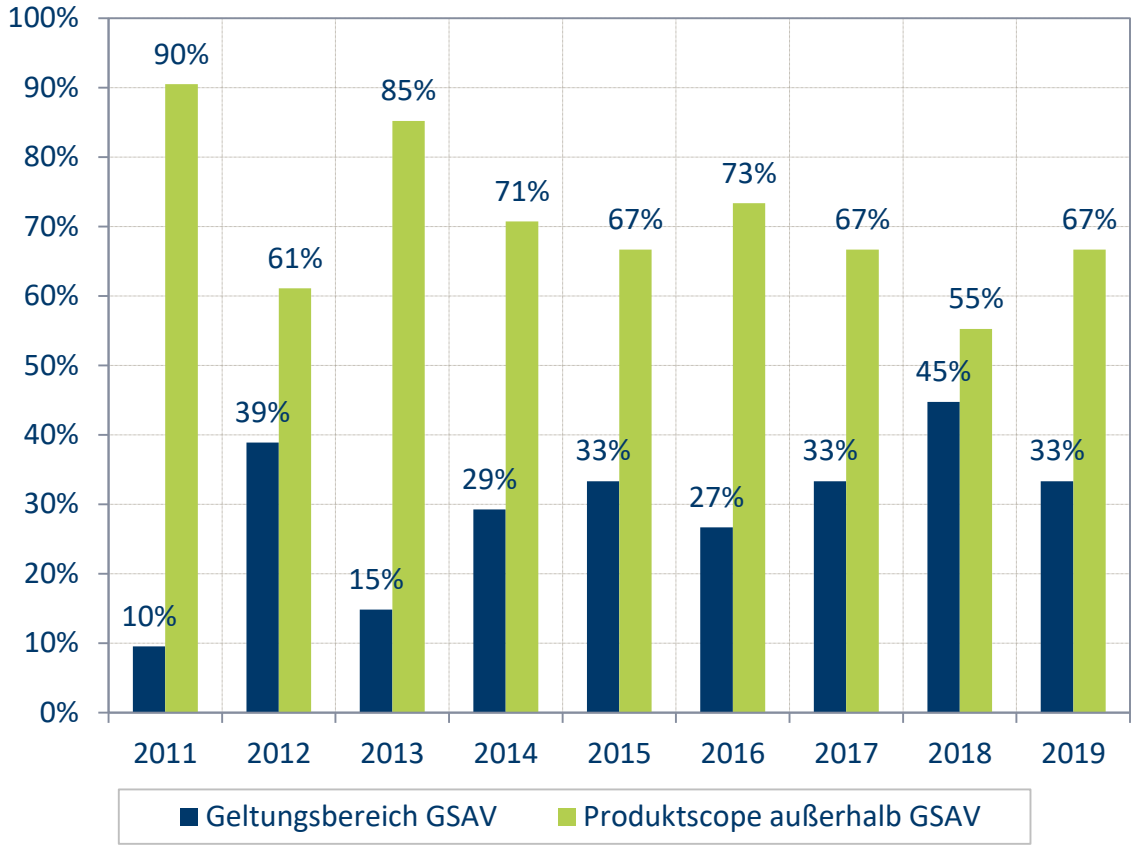
- orphan drugs
- medicinal products with a conditional marketing authorization
- marketing authorization under exceptional circumstances

The G-BA

- Determines duration, type and scope of data collection and evaluation as well as the format to be used
- commissioned IQWiG to submit a concept for the generation and evaluation of application-related data
  - Criteria for the quality and the methodological requirements
  - Requirements for the reporting, preparation, structure and statistical evaluation

Product scope of the GSAV: Mainly - but not only - Orphan Drugs





2019: Products with present G-BA decision until 15.11.2019

IQWIG Rapid Report: January 2020

AMNOG Evaluations of ODs (2014-2018)

- 67 Evaluations
- 85 Questions
  - 28% quantifiable additional benefit
  - 72% non-quantifiable additional benefit
- No or insufficient data on control groups in all cases of non-quantifiable additional benefit
- 67% of all OD-Dossiers with RCTs !
- OD-Market Authorizations: Prevalences (vfa presentation 18.2.2020)
  - 40%: less than 1/10.000 = below 8000 (Germany)
  - 49%: 1-3/10.000 = 80000-24000 (Germany)
  - 11%: more than 3/10.000 = more than 24.000 in Germany

IQWIG Rapid Report: January 2020

Concept for generating supply-related data (proposed method)

Commissioned by G-BA in May 2019 (GSAV came into force in August 2019)

Concept intended to be used in exceptional cases at the fNB to generate missing evidence - for example ODs - ; but: ODs are anything but the exception in AMNOG

- Original legal argument: Observational studies, case control studies or registry studies ...should be possible
- High quality register data yes (studies based on high quality registers
- Data from ePAs and billing data no (at least "current and not usable for the foreseeable future")
- For the time being only registers remain, see details in the report; must be comparative
- And now: G-BA position and implementation ?

GSAV: Key issues

Key issues for ATMPs:

- G-BA limits treatment and reimbursement to appropriate service providers (ATMPs)
- G-BA limits reimbursement to participation in the required application-accompanying data collection (ATMPs)
- The data obtained and the obligation to collect data must be reviewed by the G-BA at regular intervals, but at least every 18 months
- Repeated assessments of additional benefits lead to repeated negotiations of reimbursed prices
- Poor RWE study results or failures to carry them out will lead to discounts on the reimbursement price.

Ongoing legislation: GKV-FKG
What is to be expected

Key topics (selection)

- In Force: March/April 2020 (expected)
- Improvement of morbi RSA
  - More Indications coded
  - Risk pool for expensive procedures/therapies (curative or significant delaying progression)
    - Refund of 80% of costs above 100 K €
- ATMPs are Pharmaceuticals
  - follow AMNOG pathway for additional benefit and Reimbursement
    - Are readily available for use (ambulant/hospital care)
  - Exception: biotechnologically engineered tissue products (TEP)
    - Case by case decision of G-BA continues

And what about reimbursement ?

No explicit adaptations of hospital system yet

But: Political Will is expressed to adopt reimbursement system accordingly

Back up

IQWIG Rapid Report: January 2020

Quality criteria for registers

- Basic suitability of results from register data studies but mandatory comparative evidence e.g. indication registers or historical comparisons
- List of quality criteria; if the criteria are not met, discuss the effects on validity

Study design & protocol

- emulation of a comparative study with randomization for study design of non-randomized studies.
- PICO scheme, (the most accurate possible reproduction of inclusion and exclusion criteria and a detailed definition of interventions and patient-relevant outcomes)
- Presentation of the final study protocol & analysis plan before data review, → credible documentation

Identification and control of confounders

- Pre-specification of all confounders from scientific literature and, if necessary, consultation with clinical experts as well as appropriate control/adjustment within the framework of statistical analyses

IQWIG Rapid Report: January 2020

Statistical analyses

- Specify all adjustment approaches in detail a priori, but recognize that certain methodological decisions can only be made after the data are known. This must be mapped in SAP.
- Extensive sensitivity analyses are recommended
- Propensity-Score-based approaches
  - Trimming of populations as a fallback option; then, however, only the recognition of an additional benefit for the resulting sub-population
- Recommendation of meta-analytical aggregation when evaluating several data sources versus pooled analyses

Effect thresholds for additional benefits

- The effect threshold for relative risk is between 2-5 for a small additional benefit (or harm).
  - For a significant or substantial additional benefit, a relative risk above a threshold of 5 is required.
  - These threshold value ranges apply if the methodological requirements/QA criteria for the register and evaluation methodology are (optimally) fulfilled, otherwise the effect remains dramatic with a relative risk of at least 5-10 in non-randomized studies.
- the impossibility of a complete confounder control (unknown confounders) in the setting without randomization means that maximum statements can be made on the certainty of results of a reference point.

IGES ARA: All information on benefit assessment (§ 35a SGB V) in one tool

All AMNOG procedures since the start of the AMNOG benefit assessment on 1 January 2011

Monthly update

All important results and information prepared

- e.g. products, active substances, orphan status, cause of action, manufacturer, additional benefit, populations, appropriate comparative therapy, costs
- Methodological aspects, endpoints and their consideration in the benefit assessment
- Published documents from PU, G-BA, IQWiG, EMA, FDA, and the Journal of Medical Information
- Health economic aspects (annual therapy costs, negotiation results and reimbursement amounts)
- In preparation: all arbitration proceedings

Web-based application that is intuitive to use

Various search and filter options

Supplementary graphical representations

Analyses and reports

V.

The outcome of the activity of European Commission Expert Group on Safe and Timely Access to Medicines for Patients – STAMP

Helen Lee, European Commission

Repurposing of medicines European Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP)

EUCOPE Members Meeting

26 February 2020

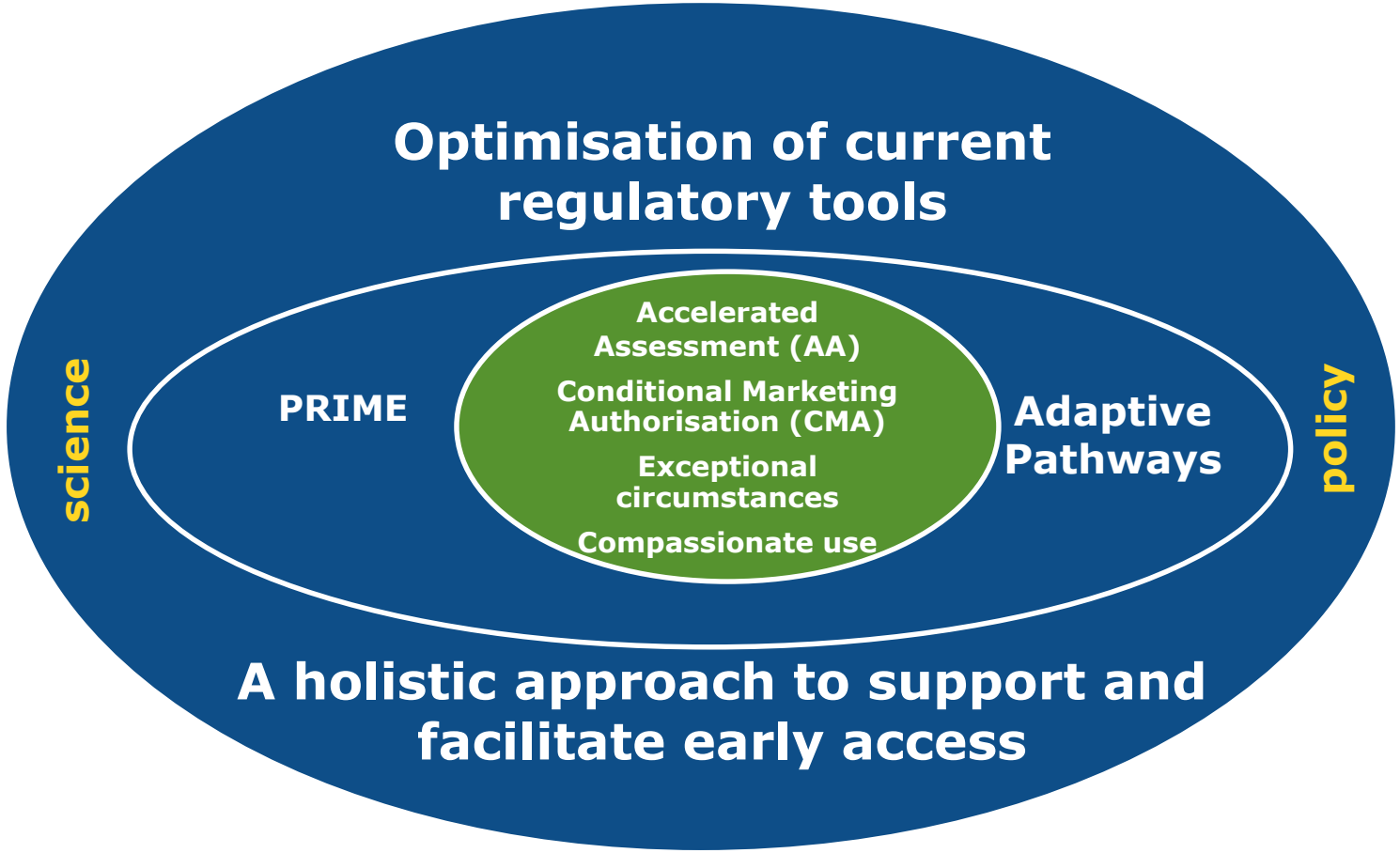
Helen Lee
European Commission
Directorate-General for
Health and Food Safety

Health and Food Safety

STAMP - Safe and Timely Access to Medicines for Patients

- Sub-group of the Pharmaceutical Committee
- Identify ways, to use more effectively the existing EU regulatory tools
- Explore, where possible, ways to increase information-sharing and cooperation among Member States
- Improve implementation of EU Pharmaceutical legislation and speed up access to innovative and affordable medicines
- Synergy HTA/regulators

Access to medicines - STAMP



Repurposing and its opportunities

- a new use for authorised medicines / known active substances

✓ already **tested in humans**

✓ **available infomation** on pharmacology, formulation, dose, toxicity

- **common molecular pathways**
- potential to **reduce cost**, **risk** and development **time**

➢ **early access**

STAMP – Repurposing discussions

- Since March 2016 repurposing of medicines discussed in STAMP
- June 2018 proposal for a framework on repurposing discussed and further developed
- July 2019 framework presented to Pharmaceutical Committee
- Pilot to test and monitor the framework

Repurposing Framework - Aim

- Aim to provide a visible supportive framework to not-for-profit stakeholders who have the data and scientific rationale for a new indication, and who have the aim to see this new use on-label

STAMP discussion scope of repurposing

- STAMP repurposing discussion scope
  - ✓ multisource medicinal products
  - ✓ evidence generated by a third party
  - ✓ MAHs have not updated product information
  - ✓ no incentives

X withdrawn products reintroduced with a new indication

X not for an update of product information

Key principles (1)

- Promotes a process for facilitating data generation in accordance with regulatory standards, described as voluntary steps within the existing regulatory framework

- Elements of the framework cover only one possible scenario, some key milestones are not regulatory activities

- Applicable to both EMA and NCA activities, and driven by 'Champions'

Key principles (2)

- A Champion is not a pharmaceutical company, is able to coordinate, transparent, files initial request for scientific advice, provides information to MAH

- Core components: new indication in areas of public health benefit / Union interests, valid out of protection marketing authorisation exists

Champion engagement with regulators

- Main tools are scientific and regulatory advice
- Scientific advice instrumental to discuss the data package in relation to regulatory requirements – current and future development plans
- Outcome of advice can be made available to marketing authorisation holders

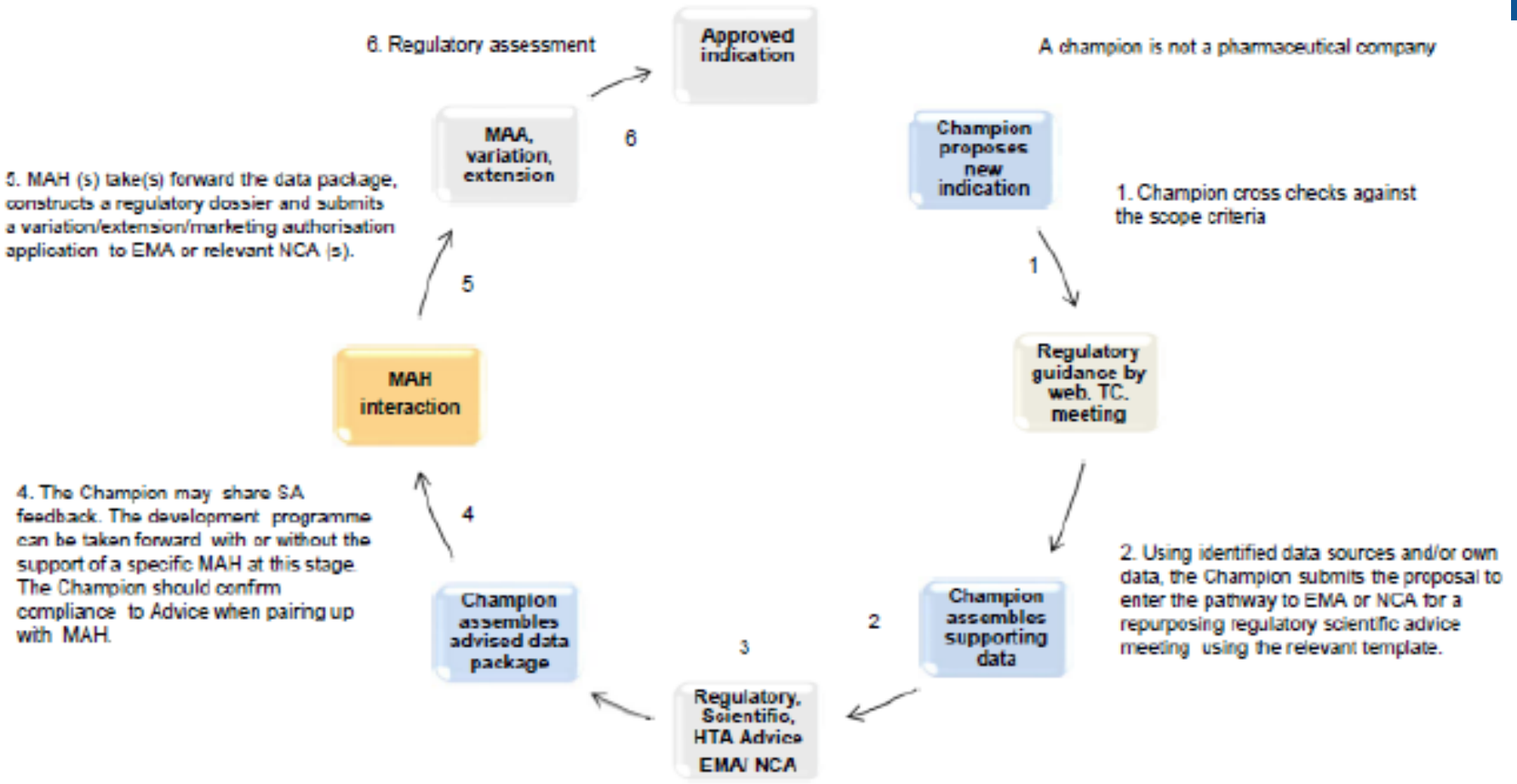
Champion engagement with industry – before scientific advice

- Before the Champion seeks scientific advice in order to seek views or input
- Identification of marketing authorisation holder using the European Medicines Agency's Article 57 database
- Companies will be encouraged to create dedicated email addresses for repurposing queries
- Input may range from none to data sharing or even collaboration

Champion engagement with industry – after scientific advice

- After the Champion has sought scientific advice – key engagement
- Champion to share output from scientific advice with marketing authorisation holders (MAH)
- MAH consider if interested in varying their marketing authorisation
- Champion to be ready to provide relevant information for regulatory submissions

Repurposing of MP's out of patent & data protection



Pilot to test framework

- assess whether the proposed framework is able to facilitate an application for a new indication for an unprotected off-patent medicinal product

- learn from the practical applications of candidates within the framework and build on the concepts identified

Repurposing Observatory Group – voluntary group led by Spain

- Objectives:
  - conclude on the practical aspects of the implementation
  - promote interaction
  - report on the challenges, successes and opportunities
  - make recommendations to facilitate the cooperation between parties
- Contact point for regulatory authorities and other stakeholders
- **not involved** in selecting Champions or medicines for the pilot nor any individual assessment or decision making role for the individual pilot projects

Thank you

More information:

STAMP:

http://ec.europa.eu/health/documents/pharmaceutical-committee/stamp/index_en.htm

Link to framework for repurposing document presented to Pharmaceutical Committee:

https://ec.europa.eu/health/sites/health/files/files/committee/pharm773_repurposing_annex_en.pdf

VI.

Real World Evidence Initiatives – engagement strategy in 2020

Laura Batchelor, FIPRA

RWE4Decisions REAL WORLD EVIDENCE

EUCOPE European Confederation of Pharmaceutical Entrepreneurs AISBL

The use of Real World Evidence (RWE) to support HTA/payer decisions

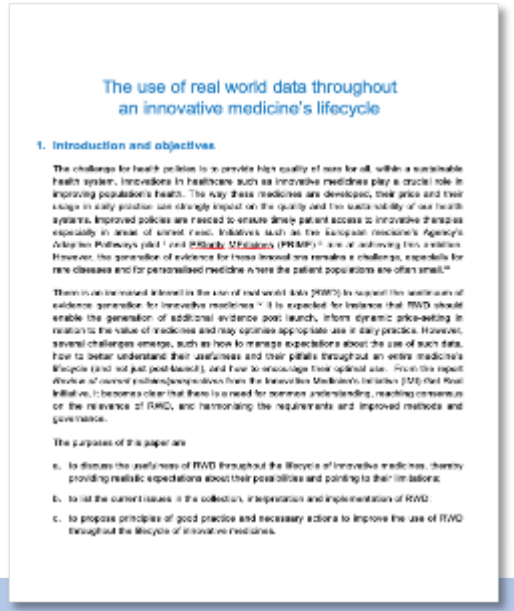
EUCOPE Members Meeting | 26 February

Laura Batchelor, Secretariat (FIPRA)
Ivana Cattaneo, Novartis

INAMI papers

Foundations for consideration of RWE

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL


The use of real world data throughout an innovative medicine's lifecycle

1. Introduction and objectives

2016

The use of real world data throughout an innovative medicine's lifecycle

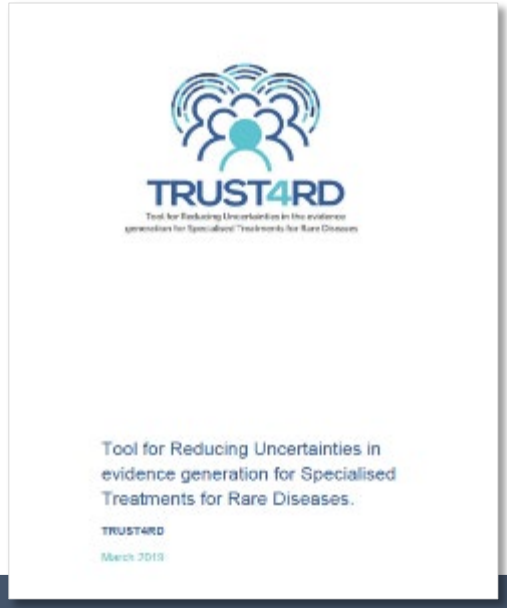

Outcomes based pricing and reimbursement of innovative medicines with budgetary limitations

Discussion document for the multistakeholders meeting on pharmaceuticals (Meeting DG GROW 12th September 2017)

1. Introduction

2017

Outcomes based pricing and reimbursement of innovative medicines with budgetary limitations



2018

TRUST4RD – Tool for Reducing Uncertainties in the evidence generation for Specialised Treatments for Rare Diseases

Multi-stakeholder participation to develop guidance

Paper Commissioned by

INAMI-RIZIV

Secretariat:

FIPRA

Authors

Jo De Cock
INAMI

Dr Karen Facey
University of Edinburgh

Piia Rannanheimo
Finnish Medicines Agency (FIMEA)

TASK FORCE
(drives initiative forward by providing input during regular meetings)

REVIEW GROUP
(consulted throughout the development of the guidance and provided feedback during the consultation period)

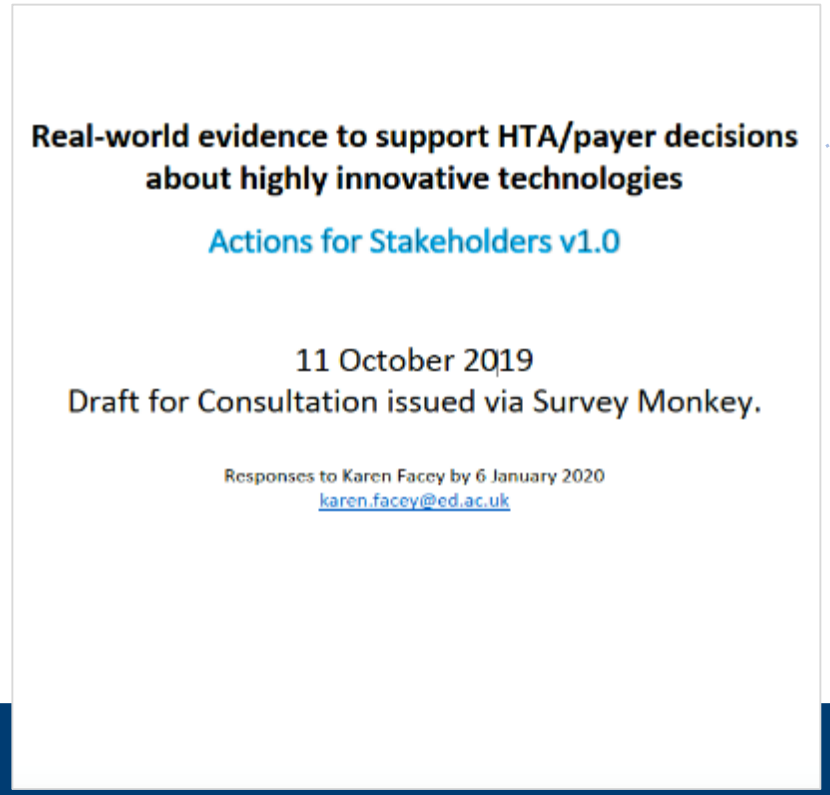
Participation of:

- **HTA authorities** (NICE, NoMA, ZIN, KCE, FIMEA, NCPE…)
- **Payers** (INAMI)
- **Regulator** (EMA)
- **Patient representatives** (EURORDIS, EPF, ECPC)
- **Industry**
- **Researchers/clinicians** (EORTC, ECCO)
- **Policy-makers** (Finnish EU Presidency)

RWE4 Decision Vision

Stakeholders agree **what** RWD can be collected for highly innovative technologies – **when**, **by whom** and **how** – in order to generate RWE that meets the needs of patients and healthcare systems.

Stakeholder actions



Policy-makers and national/European authorities

HTA bodies/payers

Regulators (EMA) and NCAs

Industry

Registry holders

Clinicians, Patients & Patient groups

2019-2020

Real-world evidence to support HTA/payer decisions about highly innovative technologies

Actions for Stakeholders

A multi-stakeholder Learning Network

on the use of RWE for highly innovative technologies

Building on TRUST4RD, RWE4Decisions Stakeholder Guidance and linking to existing policy initiatives, the “Learning Network” will:

- ❑ share case studies of challenges about use of RWE in HTA/payer decisions
- ❑ develop learnings to continuously improve approaches
- ❑ develop guidance on use of RWE
- ❑ monitor progress of implementation and discuss other emerging issues with all stakeholders

2020 Engagement Plan

WORK STREAM 1

Piloting the actions for stakeholders about the use of RWE in HTA/payer decisions

INAMI-RIZIV

EMA
HTA bodies
Payers
Clinicians
Academics

Scientific advice

Industry

WORK STREAM 2

Advocating for an EU framework for RWE within the EU Health Data Space through engagement with:

European Commission

European Parliament

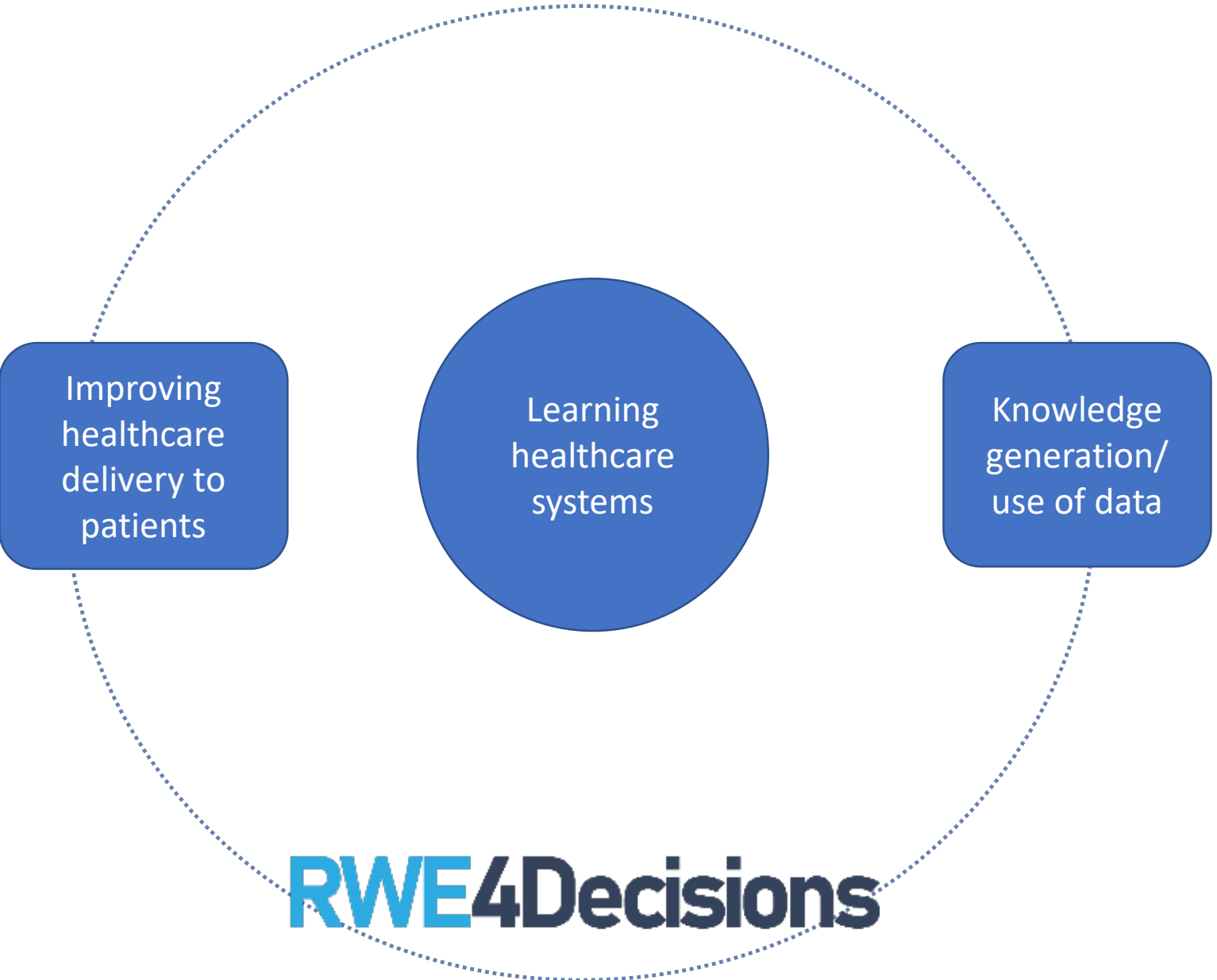
Council of the European Union

DG CNECT
DG SANTE

STOA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

WORK STREAM 2: Advocacy



European Commission
EU Strategy for Data (Health Data Space)
EU Pharmaceutical Strategy, industrial strategy
Beating Cancer Plan
Review of incentives / OMP legislation
European Medicines Agency
EMA/HMA Big Data Taskforce (DARWIN Network)
European Parliament
Engagement with STOA
MEPs engaged on Resolution on Digital Transformation of Health and Care
Other initiatives to build upon
IMI GetReal
IMI PARADIGM
EUnetHTA WP 5b – PLEG and registries
Data Saves Lives (EPF)
Etc…

RWE4Decisions advocacy – 2020

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

14 FEB
Meeting with Prof Ricciardi, EU Cancer Mission

6 MAY
Case studies workshop (INAMI-led)

INAMI

4 JUN
RWE4Decisions Stakeholder meeting on RWE for Learning Healthcare Systems

15 OCT
RWE4Decisions Conference on the use of RWE within the European Health Data Space

STOA

JAN | FEB | MAR | APR | MAY | JUN | JUL | AUG | SEP | OCT | NOV | DEC

CROATIAN EU PRESIDENCY

GERMAN EU PRESIDENCY

17 MAR
DIA EUROPE workshop, Brussels

1-2 APR
Practical applications of RWE in rare diseases, London

The Evidence Base

8 JUN
HTA SIG session

20-24 JUN
HTAi, Beijing

18-19 NOV
ECCO 2020 European Cancer Summit

ECCO

Engagement with EU Commission, EMA, EU Parliament, Cancer mission

Expert meeting

Real World Evidence for Learning Healthcare Systems

4 June (11h00-16h00)

University Foundation, Brussels

Session 1: What is the Way Forward? (11.00-13.00)

EMA: The case for DARWIN (Data Analysis and Real World Interrogation Network)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

RWE4Decisions and the need for a multi-stakeholder approach
Karen Facey

Panel discussion

FDA The Food and Drug Administration

fimea

Zorginstituut Nederland

INAMI

EPF European Patients Forum

European Commission

Industry rep.

LUNCH & NETWORKING (13.00-14.00)

Session 2: Case studies learnings (tbd) (14.00-15.30)

The experience of recently launched CAR-T cell therapies and use of RWE

Roche

NOVARTIS

Panel discussion

EURORDIS RARE DISEASES EUROPE

Gemeinsamer Bundesausschuss

HAS HAUTE AUTORITÉ DE SANTÉ

AIFA Agenzia Italiana del Farmaco

European Commission

Industry rep.

Conclusions & next steps (15.30-16.00)

How to realise a EU learning network?

INAMI

Public meeting

RWE4Decisions

How to foster learnings from the use of RWE for highly innovative technologies within the European Health Data Space?

STOA
Science and Technology Options Assessment

15 October (10h30-16h30)

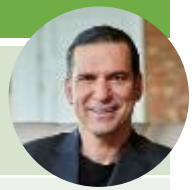
European Parliament, Brussels

Keynote: The use of Real World Evidence and the need for an EU Health Data Space
Stella Kyriakides

Keynote: Why do we need a multi-stakeholder Learning Network on RWE and how can we best collaborate?
Maggie De Block

Panel 1: The need for RWE across the lifecycle of a product

Presentation of TRUST4RD
Lieven Annemans



Panel discussion — Gemeinsamer Bundesausschuss; EURORDIS RARE DISEASES EUROPE; EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH — **Industry**

LUNCH & NETWORKING

Panel 2: Considering the realisation of a multi-stakeholder 'Learning network' and implications for stakeholders

Presentation of RWE4Decisions Stakeholder Guidance
Karen Facey

Panel Discussion — Federal Ministry of Health; EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH; INAMI — **Industry**

Panel 3: Meeting the innovation challenge for sustainable patient access to innovative technologies

Presentation on the EU Mission Board for Cancer
Christine Chomienne

Panel discussion — Spitzenverband; EPF European Patients Forum; European Commission; ECCO — **Industry**

Conclusion & the Way Forward
Mariya Gabriel

Thank you!

For further information, please contact Laura.batchelor@fipra.com

Annexes

Opportunities & Challenges

OPPORTUNITIES

- Increasing availability and quality of RWD in electronic form
- Emergence of tools for advanced analysis of large volumes of data
- Increasing limitations of clinical trials, e.g. due to feasibility, time and costs
- Increasing appreciation of the potential value of RWD for patient health and healthcare systems
- The planned establishment of a **European Health Data Space** by the European Commission (2022)
- Prioritisation of **health data** by the German Presidency

CHALLENGES TO BE ADDRESSED

- Patient privacy
- Data quality and interoperability
- Legal and regulatory barriers
- Build trust in the use of RWE to support earlier access.

Recommendations to industry (DRAFT)

1. **Create a RWE generation plan** early in development, which addresses essential data elements for HTA not covered in the clinical trial program and that might be studied in a real-world setting.
2. **Discuss the RWE generation plan at various stages** throughout the technology life cycle with regulators, payers, HTA bodies, clinicians and patients.
3. **Ensure the study (protocol) and statistical analysis plans for RWE studies** that are answering major HTA questions **are available to HTA bodies** to provide transparency about the methods used to obtain and analyse data.
4. **Support the development of a public portal** that provides details about the design and results of major RWE studies (ala RCT registries), particularly hypothesis evaluating treatment effect (HETE) studies.
5. **Drive non-competitive, multi-company and multi-stakeholder collaborations** about the development of robust RWE for diseases treated by highly innovative technologies .
6. **Enact recommendations from the ISPOR and RWE Transparency Partnership**.
7. **Use reliable data collection methods for RWD**, including ehealth and digital tools and develop best practices as digital approaches evolve.

VII.

The German presidency of the EU Council and the upcoming legislative dossiers

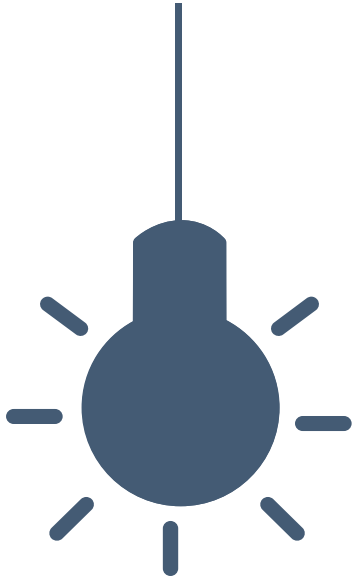
Max von Olenhusen, Acumen

German EU Presidency Priorities

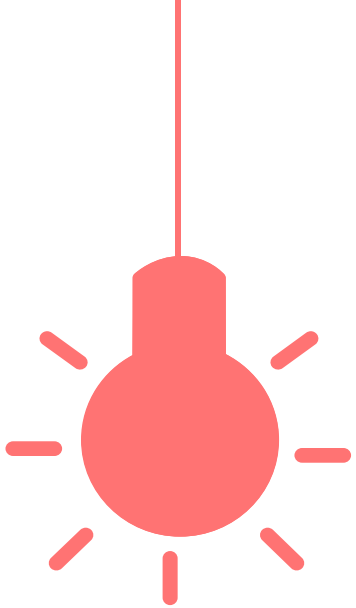
26 February, 2020

About Acumen

Acumen Public Affairs is an **independent consultancy** set up in 2010 to combine the very best of big agency experience with hands-on senior support.



Our philosophy is to provide clients with **value adding strategic counsel and high quality execution** – by the same people. When we commit to an assignment, this means personal supervision and implementation by the acumen senior team from beginning to end. That way, we can ensure that we deliver results and surpass expectations, at competitive prices that only an independent agency can offer.



We believe in the power of taking an **integrated approach to advocacy and communication** to achieve outcomes that have a tangible impact. We have a track record of developing winning strategies that are sustainable, by identifying a confluence of interest among key stakeholders.

Why Acumen?

- Deep level of healthcare expertise
- Committed to innovative clients in healthcare
- Proven track record in healthcare for strategy and execution
  - ✓ Advcocacy & lobbying
  - ✓ Market access
  - ✓ Communications
  - ✓ Patient groups
- In biotech & pharma, animal health, vaccines, health insurance

Our team

- Team of > 25 people working in healthcare policy or communication projects at global (WHO level), EU and country levels.
- Senior people closely involved
- Combined expertise of more than 100 years in public affairs

What others say about us

acumen
public affairs

Current and past clients

acumen public affairs

Table of contents

Structure of EU Presidency Team

EU Presidency Health Team: Brussels

Ambassador Susanne Szech-Koundouros
Deputy Permanent Representative of Germany
to the EU (Coreper I)

Ortwin Schulte
Health Attaché at the Permanent
Representation of Germany

Katharina Wunderlich
Health Attaché at the Permanent
Representation of Germany

Bettina Gallitz
Health at the Permanent
Representation of Germany

Lea Pfefferle
Spokesperson on health at the Permanent
Representation of Germany

EU Presidency Leadership in Health

Jens Spahn
Federal Minister of Health

Thomas Steffen
State Secretary, Federal Ministry of Health

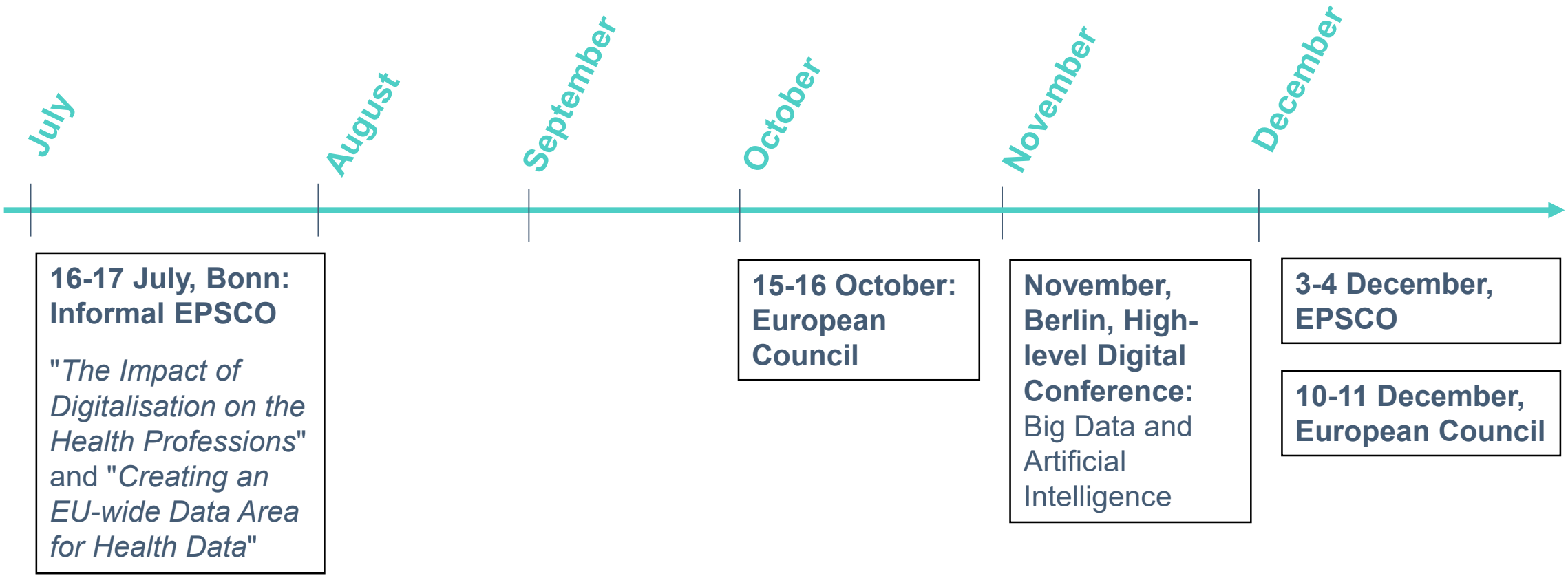
Sabine Weiss
Parliamentary State Secretary to the Federal Ministry of Health

Thomas Müller
Head Of Directorate General Drugs, Medical Devices, Biotechnology, Federal Ministry of Health

Thomas Gebhart
Parliamentary State Secretary to the Federal Ministry of Health

Timeline of main events

Key events during the Presidency



German Presidency Priorities

Expected key priorities of the Presidency I

The German Presidency
(July-December 2020)

Digitization, Big Data and Artificial Intelligence

- Priority issue of the trio programme with Portugal and Slovenia
- Deliverable: an e-Health Strategy

The Role of the EU in Global Health

- Priority issue of the trio programme with Portugal and Slovenia, emerged during the current trio and will be taken up by France in 2022.
- Deliverable: recommendations on the EU's strategic role in global health

Expected key priorities of the Presidency II

The German Presidency
(July-December 2020)

Ensuring a sufficient supply of medicines and tackling shortages

- Deliverable: possible package with measures to ensure supply chains

Health Technology Assessment

- Deliverable: completion of trilogue negotiations

Europe's Beating Cancer Plan

- Deliverable: Action Plan Against Cancer

Other potential deliverables

The German Presidency
(July-December 2020)

Medicines

- Discussions on **EU Pharmaceutical Strategy**
- Discussions on **Orphan Medicinal Products**
- Discussions on **Antimicrobial Resistance (AMR)**
- Communication on the benefits of **vaccination**
- Discussion on evaluation of **EU legislation on blood and tissues and cells**

Other

- (Potential) new regulatory approach to tobacco products
- **Farm to Fork Action Plan**
- Implementation of the phytosanitary regulations

Legislative files

Open legislative files in health: HTA

Proposal on Health Technology Assessment and Amending Directive 2011/24/EU

Commission
DG SANTE, Unit B4 – Medical Products: Quality, Safety, Innovation

Council
Working Party on Public Health
Working Party on Pharmaceuticals and Medical Devices

Parliament

ENVI Committee

Rapporteur
- Tiemo Wölken (S&D, DE)

Shadows:
- Nathalie Colin-Oesterlé (EPP, FR)
- Veronique Trillet-Lenoir (RE, FR)
- Michèle Rivasi (Greens/EFA, FR)
- Joelle Melin (ID, FR)
- Joanna Kopcinska (ECR, PL)
- Katerina Konecna (GUE/NGL, CZ)

December 9, 2019:
Discussion in EPSCO

Expected development during Presidency

Completion of trilogue negotiations

Rapporteur: Tiemo Wölken (S&D, DE)

acumen public affairs

Open legislative files: collective redress

Proposal on representative actions for the protection of the collective interests of consumers

Commission
DG JUST, Unit E3 – Consumer enforcement and redress

Council
Working Party on Consumer Protection and Information (**WPCP**)

Parliament

JURI Committee

Rapporteur
Geoffroy Didier (EPP, FR)

Opinions:
IMCO – Dennis de Jong (GUE/NGL, NL), TRAN - Georg Mayer (ENF, AT)

Rapporteur: Geoffroy Didier (EPP, FR)

acumen
public affairs

Open legislative files: programme for single market competitiveness

Programme for single market, competitiveness of enterprises, including small and medium-sized enterprises, and European statistics 2021–2027

Commission
DG GROW, B1 – Single Market Policy

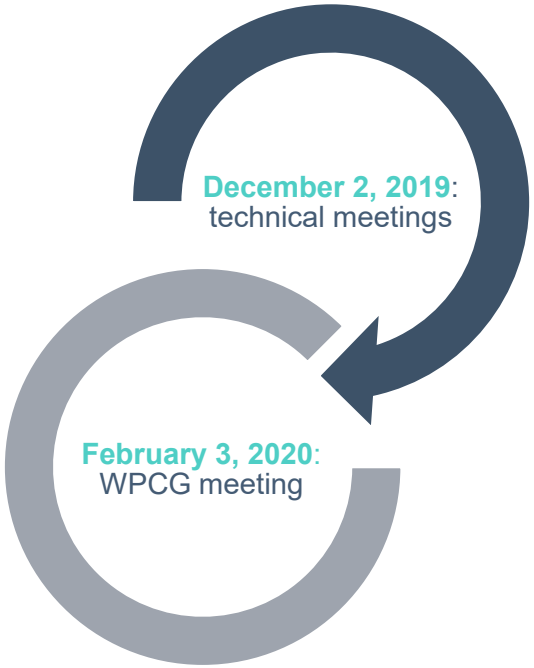
Council
Working Party on Competitiveness and Growth **(Industry)**

Parliament

IMCO Committee

Rapporteur:
Brando Benifei (S&D, IT)

Opinions:
BUDG – Paul Rübig (EPP, AT), ECON – Ralph Packet (ECR, BE), ENVI – Lukas Mandl (EPP, AT), ITRE – Patrizia Toia (S&D, IT), AGRI – Sofia Ribeiro (EPP, PT)



Rapporteur: Brando Banifei (S&D, IT)

acumen
public affairs

Open legislative files: Horizon Europe I

Proposal for a Regulation establishing Horizon Europe – the Framework Programme for Research and Innovation, laying down its rules for participation and dissemination

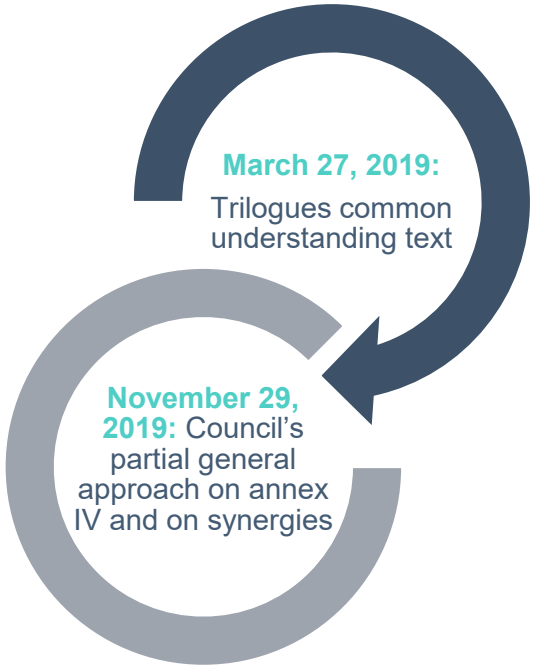
Commission
DG RTD, Dir. A – Policy Development and Coordination

Council
Working Party on Research

Parliament

ITRE Committee

Rapporteur
• Dan Nica (S&D, RO



Rapporteur: Dan Nica (S&D, RO)

acumen
public affairs

Open legislative files: Horizon Europe II

Proposal for a Decision on establishing the specific programme implementing Horizon Europe – the Framework Programme for Research and Innovation

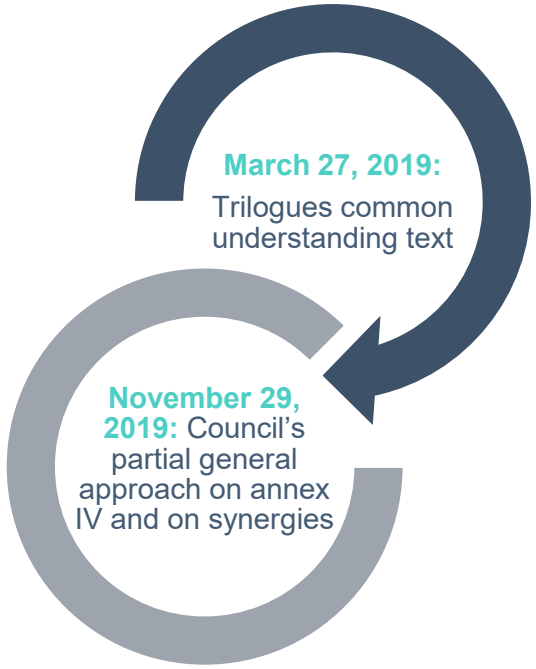
Commission
DG RTD, Dir. A – Policy Development and Coordination

Council
Working Party on Research

Parliament

ITRE Committee

Rapporteur
• Christian Ehler (EPP, DE)



Rapporteur: Christian Ehler (EPP, DE)

acumen
public affairs

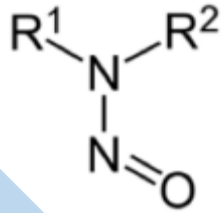
VIII.

Update on recent EMA activities

Chairs

Nitrosamines in Sartans - other chemicals?

N-nitrosodimethylamine (NDMA), N-nitrosodiethylamine (NDEA)



June 2018	Jul 2018	Aug 2018	Mai 2019	June 2019	Sept 2019	Oct 2019	4 Nov 2019
NDMA in Valsartan Zhejiang Huahai	FDA / EU recall of several Valsartans	EDQM review of CEPs	EMA Art 31 Review	Update of five Ph. Eur monographs	detection of NDMA in Ranitidine	All MP to be reviewed	EMA-Stakeholder meeting

All authorised human medicinal products containing chemically synthesized APIs are to be reviewed


EMA reviewing medicines containing valsartan from Zhejiang Huaha following detection of an impurity: some valsartan medicines being recalled across the EU

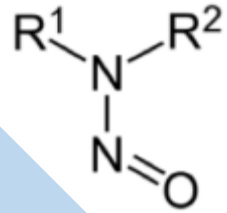

FDA Updates and Press Announcements on Angiotensin II Receptor Blocker (ARB) Recalls (Valsartan, Losartan, and Irbesartan)


Control of nitrosamine impurities in sartans: revision of five Ph. Eur. monographs


EMA advises companies on steps to take to avoid nitrosamines in human medicines

Nitrosamines Latest status

"Presence in medicines is considered unacceptable"



4 Nov 2019 EMA-Stakeholder meeting	5 Nov 2019 Industry letter to EMA	29 Nov 2019 **WHO** Note	17 Dec 2019 EMA – stakeholder TC	20 Dec 2019 EMA/CMDh Q&A Update	13 Dec EDQM new monogr	Jan 2020 Several TCs with EMA	20 Feb 2020 EMA stakeholder meeting	Bi-weekly TCs

All authorised human medicinal products containing chemically synthesized APIs are to be reviewed.
"… consider whether to **broaden the scope**…" e.g. biological products containing excipients at risk

APIC, EUCOPE, EFPIA, AESGP and Medicines for Europe take note of the notice EMA/189634/2019: 'Information on N-nitrosamine for marketing authorisation holders and API manufacturers - Request to assess the risk of N-nitrosamine impurities in human medicinal products containing chemically synthesised APIs' and appreciates the accompanying Q&A EMA/428592/2019.

Ref. EMP/RHT/Information Note_Nitrosamine impurities

WHO Information Note

UPDATE ON NITROSAMINE IMPURITIES

The EDQM's response to nitrosamine contamination

20 Nov. 2019

20 December 2019
EMA/CHMP/428592/2019 Rev. 2

Questions and answers on "Information on nitrosamines for marketing authorisation holders"

Detection of N-nitrosamine impurities: the Ph. Eur. launches a public consultation on the revised general monograph Substances for pharmaceutical use (2034)

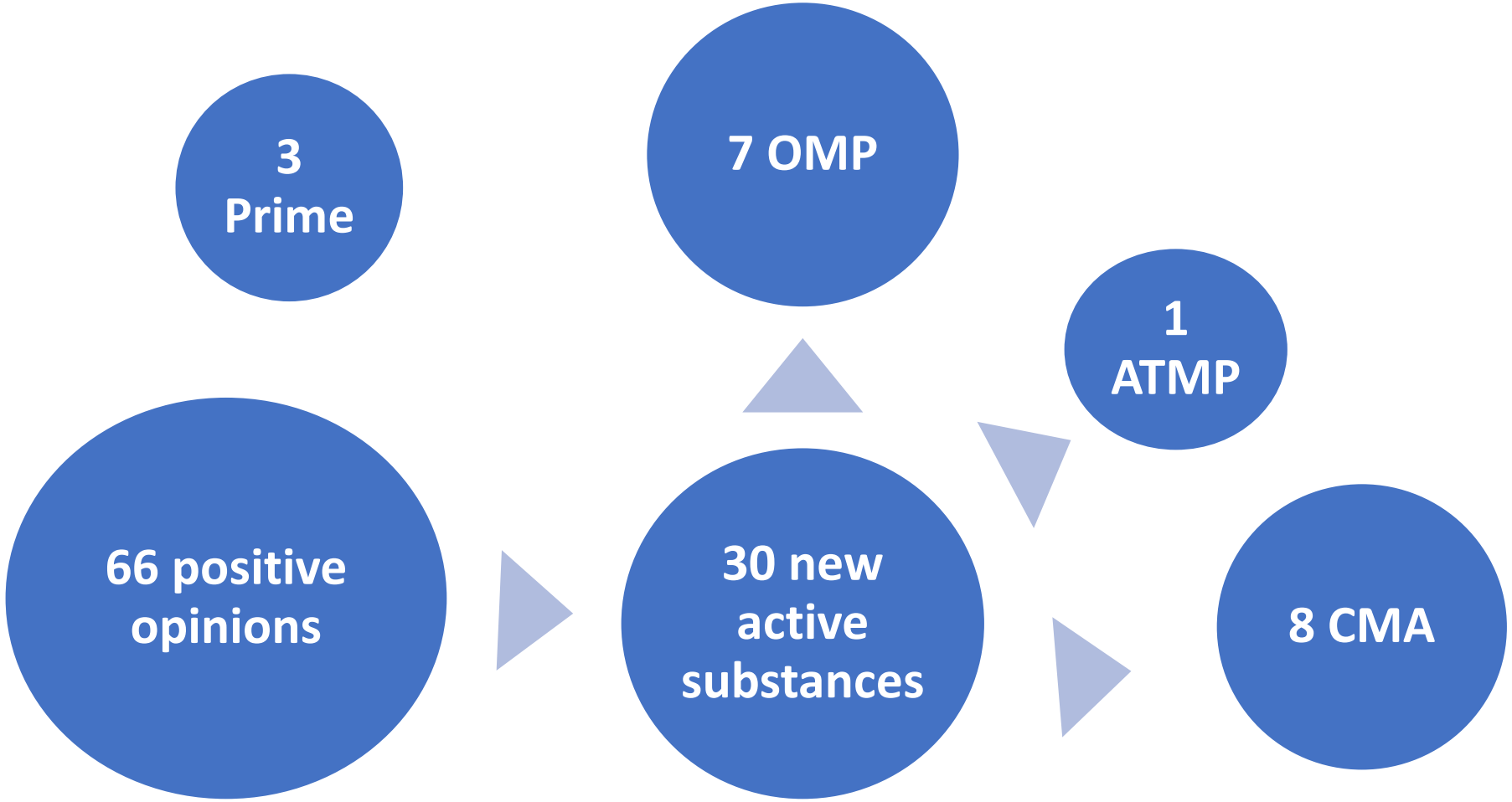
EMA to support development

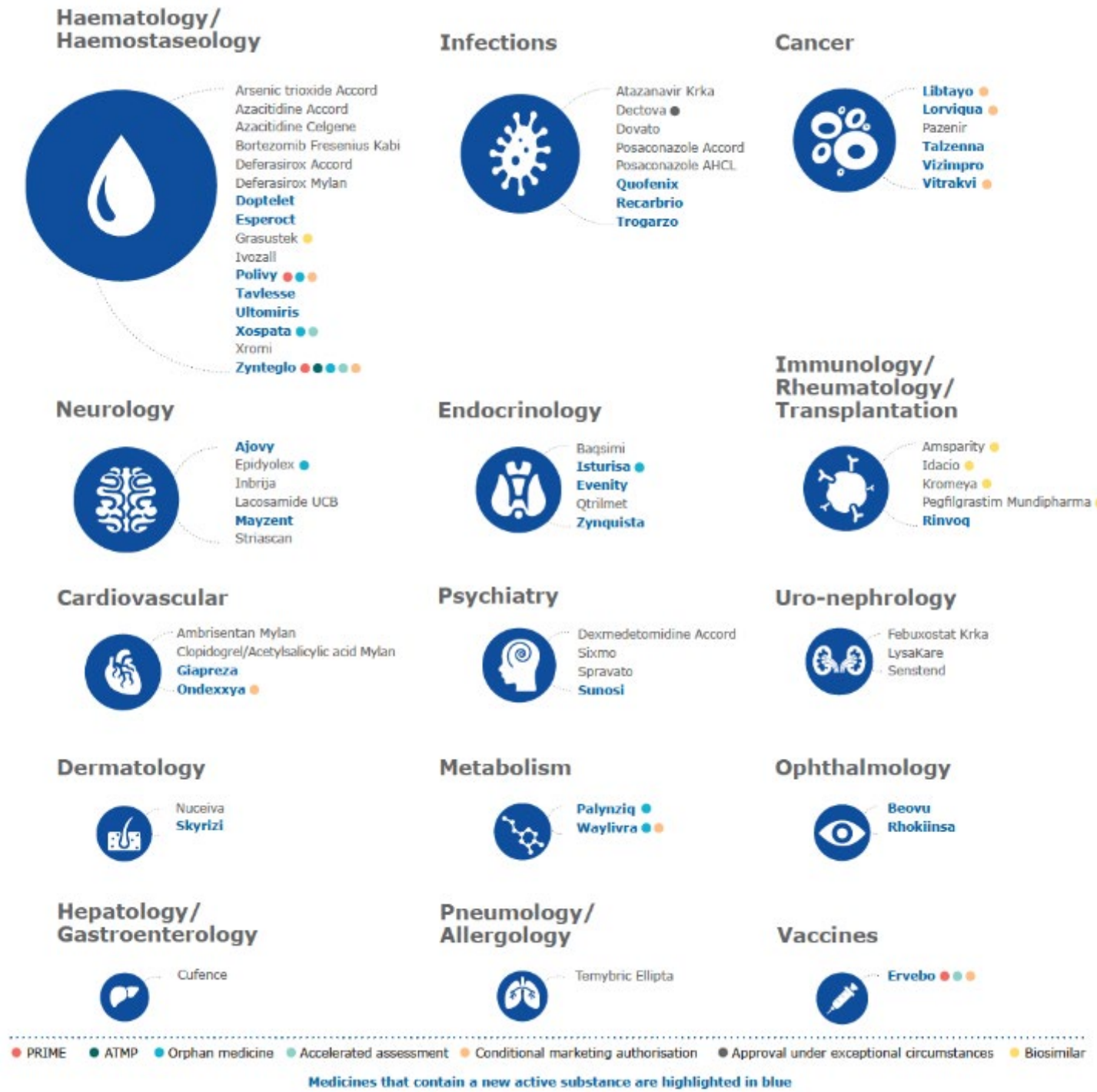
of vaccines and treatments for novel **coronavirus** disease (COVID-19)

EMA encourages developers of potential vaccines or treatments for novel coronavirus infection to **contact EMA as soon as possible** to discuss their strategy for evidence-generation, by emailing 2019-ncov@ema.europa.eu.

EMA: human medicines in 2019

66 positive opinions, 4 negative, 12 withdrawals





PRIME:

Zynteglo, Polivy, Ervebo

ATMP:

Zynteglo

OMP:

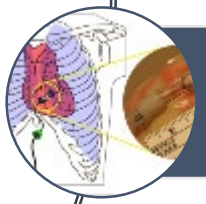
Isturisa, Palynziq, Waylivra, Zynteglo, Xospata, Polivy, Epidyolex

Huge number of DDC products

DDC products - Digital innovations

Digital Medicines: e.g. Digital ingestible sensor measuring medicine physiology: **AbilifyMycite**: sensor embedded in an ingestible oral pharmaceutical form with active substance

Interoperable automated system that adjusts medicine delivery based measurement: **Tandem Diabetes Care Control-IQ**: controller-enabled insulin pump (ACE pump) + integrated glucose monitor (iCGM) + Software



Innovative **drug delivery systems**: **Headlander**: a miniature mobile robot (caterpillar) that delivers minimally invasive therapy to the surface of the beating heart.

Digital supported **Services for better Compliance**: **Onduo** Virtual Diabetes Clinic, where patients can access high-quality, evidence based support, personalized recommendations and special care for better Patient Outcomes

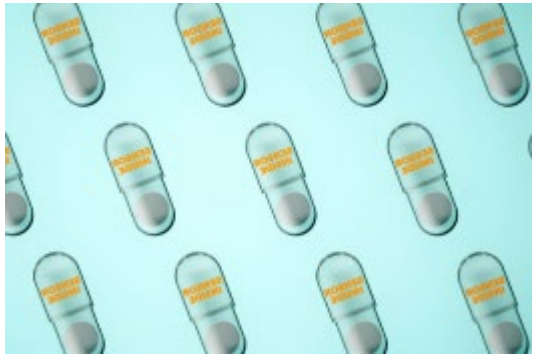
Digital Medicines

Digital ingestible sensor measuring medicine physiology

Abilify Mycite pill with a tiny e-sensor, approved by FDA in Nov 2017

Digitally records ingestion developed by **Proteus Digital Health** provides a unique way **to measure medication adherence and physiologic response of patients**.

Technology to measure and identify adherence in real time and share information with health care providers can play a role in developing better communication and counselling interventions.



Digital Chemotherapy pills in Minnesota Fairview Health Service

After patients swallow a capsule, the sensor activates when it gets wet in the stomach and then pings a signal to a patch that patients wear on their torso. That transmits data on the time of day, the size of the dose, and the type of medication taken to an online portal that the patient can view.

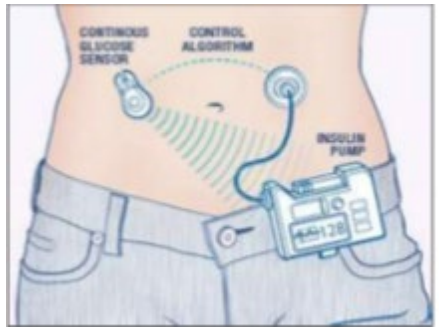
Interoperable automated system

adjusts medicine delivery based measurement

Tandem Diabetes Care Control-IQ Technology, approved by FDA Dec 2019, is an **interoperable automated glycemic controller device** that automatically adjusts insulin delivery by connecting to an

1. integrated continuous **glucose monitor / measurement** (iCGM)
   - Sensor + transmitter + monitor
2. alternate controller-enabled **insulin pump** (ACE pump) and
3. **Software** to control the system

FDA definition: Alternate controller enabled infusion pump



"Do-It-Yourself (DIY)" automated insulin delivery (AID)

„Rapid pace of recent advancements in diabetes technologies suggests that multiple AID systems will be commercially available in the near future."*

*Nature: Open source automated insulin delivery: addressing the challenge , Nick Oliver, Monika Reddy, Claire Marriott, Tomas Walker , Lutz Heinemann, Digital Medicine Dec 2019

Innovative digital drug delivery systems

HeartLander - still in preclinical studies stage

a **miniature mobile robot** (caterpillar) that **delivers minimally invasive therapy to the surface of the beating heart**.

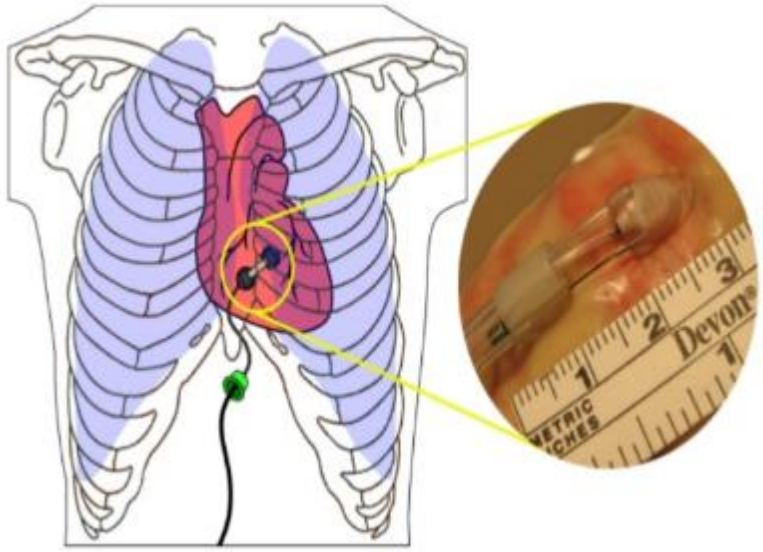
HeartLander provides a single device for stable and localized sensing, mapping, and treatment over the entire surface of the heart.

Under physician control by joystick, the robot:

- enters the chest through an entry below the sternum,
- adheres to the surface of the heart,
- travels to the desired location and
- administers the therapy

Used in cardiac therapies:

- ablation for atrial fibrillation
- lead placement for biventricular pacing
- delivery of myocardial regenerative treatments



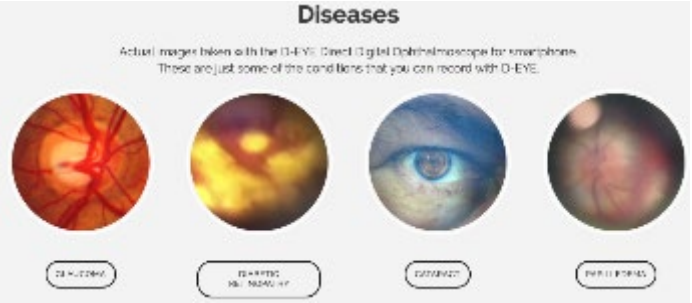
Services for better Compliance

Medical Device

D-Eye Retina – FDA 510k class 2 and CE class 1

turns an iPhone into a **Digital Direct Ophthalmoscope**, capable of recording and transmitting high-definition photos and videos of the fundus oculi for clinical assessment.

The D-EYE system allows **regular screenings of the eye**, providing information about noticeable eye diseases and capturing images for further evaluation of specific medical conditions. The D-EYE system covers the camera aperture and LED light source of the smartphone to turn the phone into a **portable retinal imaging tool**. The examiner uses the D-EYE App on the smartphone display to enter patient information, focus the retinal camera and record, archive, view and transmit images.



EMA Regulatory Science Strategy 2025

to address **upcoming innovations**

"...catalyse and enable regulatory science and innovation to be translated into patient access to medicines in evolving healthcare systems"

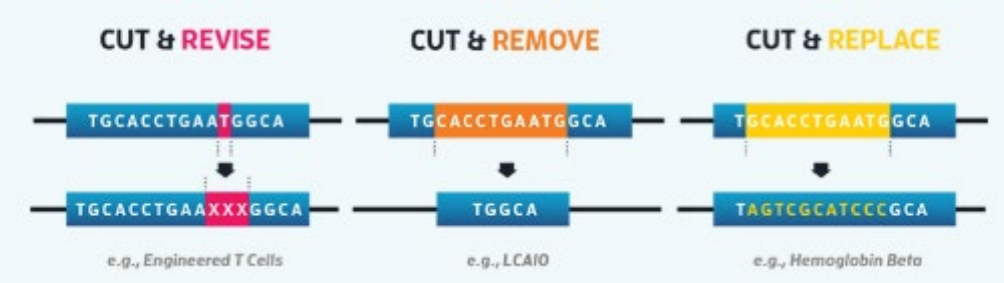
Five key goals of the strategy:

1. catalysing the **integration of science and technology** in medicine development;
2. driving **collaborative evidence generation** - improving the scientific quality of evaluations;
3. advancing patient-centred access to medicines in **partnership with healthcare systems**;
4. addressing emerging **health threats**;
5. enabling and leveraging **research and innovation** in regulatory science.

Other innovations to be addressed

requiring new evaluation approach

- **CRISP-CAS9**: gene editing technology that allows for precise, directed changes to genomic DNA



- **Nanotechnology**
  - Nano delivery systems for targeted drug delivery
  - Nanomesh as an antibiotic drug delivery system using electrospinning in a mesh with gold nanoparticples
  - Nanomesh sensor

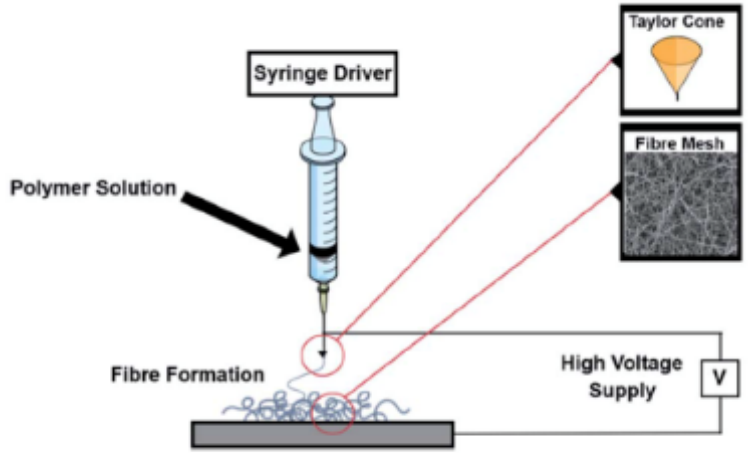


Fig. 1 Schematic of the electrospinning instrument showing the Taylor cone and mesh formation.

Picture source: RSC Adv. 2019, 9, 30064: Nanoparticles in an antibiotic-loaded nanomesh for drug delivery

IX.

AOB / End of Meeting

Chairs

Thank you for your attention!