EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

EUCOPE

Members Meeting

Brussels, 26 February 2019

Agenda (1/4)

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

II. **Brexit – the State of Play**
Peter Bogaert, Covington

III. **The FMD: Status Quo of Serialisation.**
A manufacturer's perspective
Jörg Plessl, Norgine

Agenda (2/4)

IV. **Recent sanctions against pharma shortages in France**
Olivier Lantrès, Fieldfisher

V. **Incremental Innovation – Recent Work of the European Commission's STAMP Group**
Diego Ardigò, Chiesi

VI. **Rare Diseases Research Challenges**
Laurent Louette, EUCOPE
Diego Ardigò, Chiesi

Agenda (3/4)

VII. Tool for Reducing Uncertainties in the Evidence Generation for Specialized Treatments for Rare Diseases
Laura Batchelor, FIPRA

VIII. Germany: GSAV – Changes on AMNOG, OMPs, ATMPs and Biosimilars
Alexander Natz, EUCOPE

VIII. Biosimilars – Clouds on the horizon?
Laurent Louette, EUCOPE

Agenda (4/4)

X. **Medical Devices**
   - **New requirements for drug-device combination products under the new Medical Devices Regulation**

   Maren von Fritschen, EUCOPE

XI. **European Elections – EUCOPE Engagement Strategy**

   Delphine Roulland, EUCOPE

XII. **AOB / End of meeting**

   Chairs

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

Chairs

Upcoming Events

- 10 - 12 April: World Orphan Drug Congress, USA
- 2 May: Regulatory / PV / Medical Device Meeting, Brussels
- 15 May: OMP Meeting, Brussels
- 4 June: Market Access / Pricing & Reimbursement Meeting, Brussels
- 24 June: Workshop: Innovative contracting in Germany (from the payer perspective)
- 25 June: EUCOPE Members and General Meeting, Brussels

II.

Brexit – State of Play

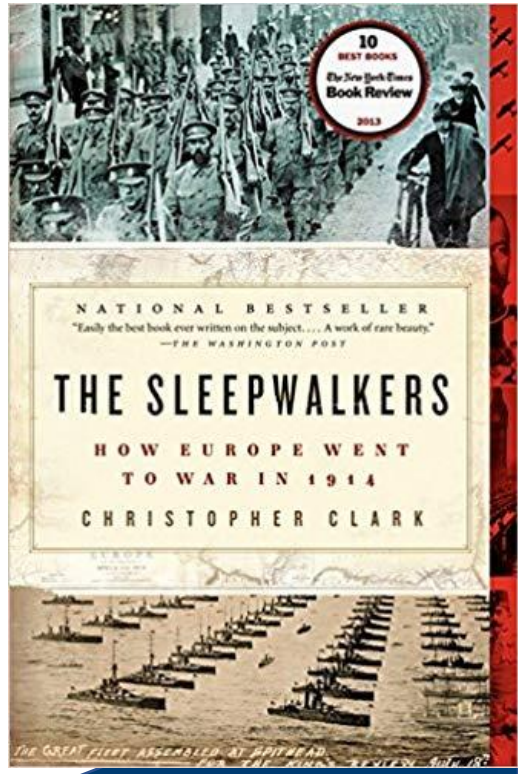
Personal Observations

Peter Bogaert, Covington

pbogaert@cov.com

Brexit State of Play

- Possibilities
  - Withdrawal Agreement without or with short postponement of Brexit (end of June max)
    - With some wording around the backstop
  - Hard Brexit
    - With practical arrangements – if UK pays
  - Longer postponement
  - Withdrawal of Brexit notice



What to Do?

- Regulatory obligations
  - Should be under control
    - Are they?

COMMISSION IMPLEMENTING DECISION

of 12.9.2018

on the transfer of the marketing authorisation granted by Decision C(2018)4458(final) for "Tegsedi - inotersen", an orphan medicinal product for human use

The marketing authorisation granted by Decision C(2018)4458(final) of 6 July 2018 to IONIS USA Limited for the medicinal product "Tegsedi - inotersen", entered in the Community register of medicinal products under No EU/1/18/1296, is transferred to Akcea Therapeutics UK Ltd..

This Decision is addressed to:
1. Akcea Therapeutics UK Ltd., Office 32, 19-21 Crawford Street, London, W1H 1PJ, United Kingdom
and
2. IONIS USA Limited, Tower 42, Level 30, International Finance Centre, 25 Old Broad Street, EC2N 1HQ London, United Kingdom.

Done at Brussels, 12.9.2018

COMMISSION IMPLEMENTING DECISION

of 25.7.2018

concerning the transfer of the designation of "Bardoxolone methyl" as an orphan medicinal product under Regulation (EC) No 141/2000 of the European Parliament and of the Council

The designation of the medicinal product "Bardoxolone methyl" as an orphan medicinal product, entered in the Community Register of Orphan Medicinal Products under number EU/3/18/2019 and held by Dr Stefan Blesse, is transferred to Reata UK Limited.

This Decision is addressed to:
1. Reata UK Limited, 11th Floor, Whitefriars, Lewins Mead, Bristol BS1 2NT, United Kingdom
and
2. Dr Stefan Blesse, Thierschstraße 3, 80538 München, Deutschland.

Done at Brussels, 25.7.2018

What to Do?

- Regulatory obligations
  - Expect pragmatism
    - From regulators
    - But *e.g.*

BfArM's recommendations regarding clinical trials with medicinal products where sponsor or legal representative are established in the United Kingdom (Current note/update from 2019.02.18)

Date2019.02.18

If a so-called hard Brexit occurs, the BfArM will accordingly order the suspension of the approval of such clinical trials,

- *whose sponsors or their representatives are then still resident in the United Kingdom, and*
- *who have not yet notified a change in the sponsor, its representative or their place of business, or*
- *have not yet notified the termination of the clinical trial.*

    - Not from competitors

What to Do?

- Check logistics
  - Your suppliers
    - Actives, intermediates, excipients, etc.
    - Vials, blister packs, leaflets, labels, boxes, etc.
    - Manufacturing tools and products
  - Regulatory obligations suppliers
    - Biocides, REACH, animal origin products
  - Suppliers of suppliers
  - Non-Brexit skeletons in the closet

  - Customs controls

Logistics

- Motor vehicles (2017)
  - EU27 to UK: 2.3 million vehicles
  - UK to EU27: 804,332 vehicles
  - = 8,505 vehicles moved every calendar day
  - More than 2,700 /day in Zeebrugge
  - About 100,000 parts moved per day
- Medicines
  - Almost 2,700,000 packs moving every calendar day

> **Brexit and the potential impact on patients access to medicines and medical devices**

27.03.18

Longer Term

- Preserve role of English
  - Legal challenges possible
  - No Member State with English as first national language

5. (1) The National language of Malta is the Maltese language.

(2) The Maltese and the English languages and such other language as may be prescribed by Parliament (by a law passed by not less than two-thirds of all the members of the House of Representatives) shall be the official languages of Malta and the Administration may for all official purposes use any of such languages:

ARTICLE 8

1 The Irish language as the national language is the first official language.

2 The English language is recognised as a second official language.

III.
The FMD: Status Quo of Serialisation.
A manufacturer’s perspective

Jörg Plessl, Norgine

presentation:**Victorio Hünerberg Coli,** Norgine

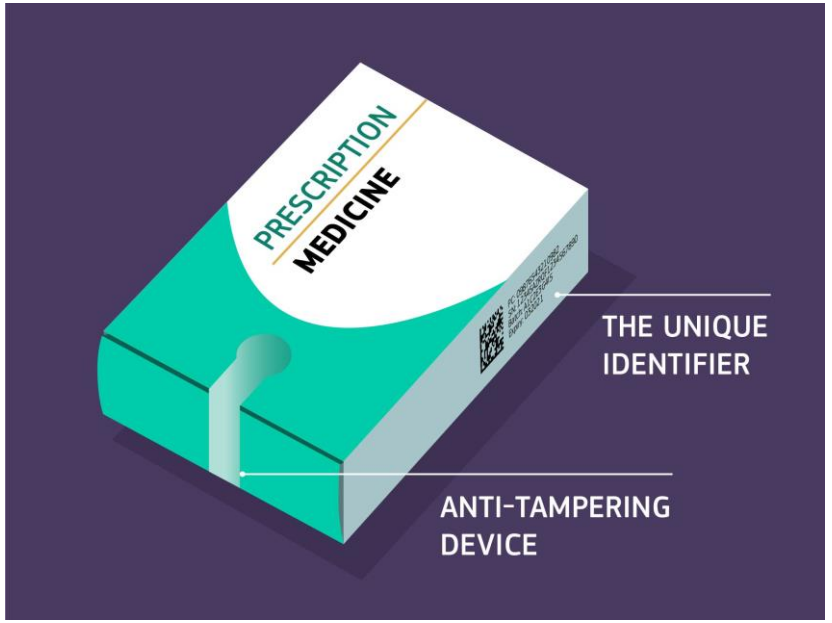
The FMD: Status Quo of Serialisation.

A manufacturer’s perspective

- Why Serialisation?
- Current status
- Challenges

Background & main concepts

- Falsified Medicines Directive (FMD)
- Delegated Regulation 2016/161
- 9th February 2019
- Scope: POM and Annex II of DR
- Safety Features:



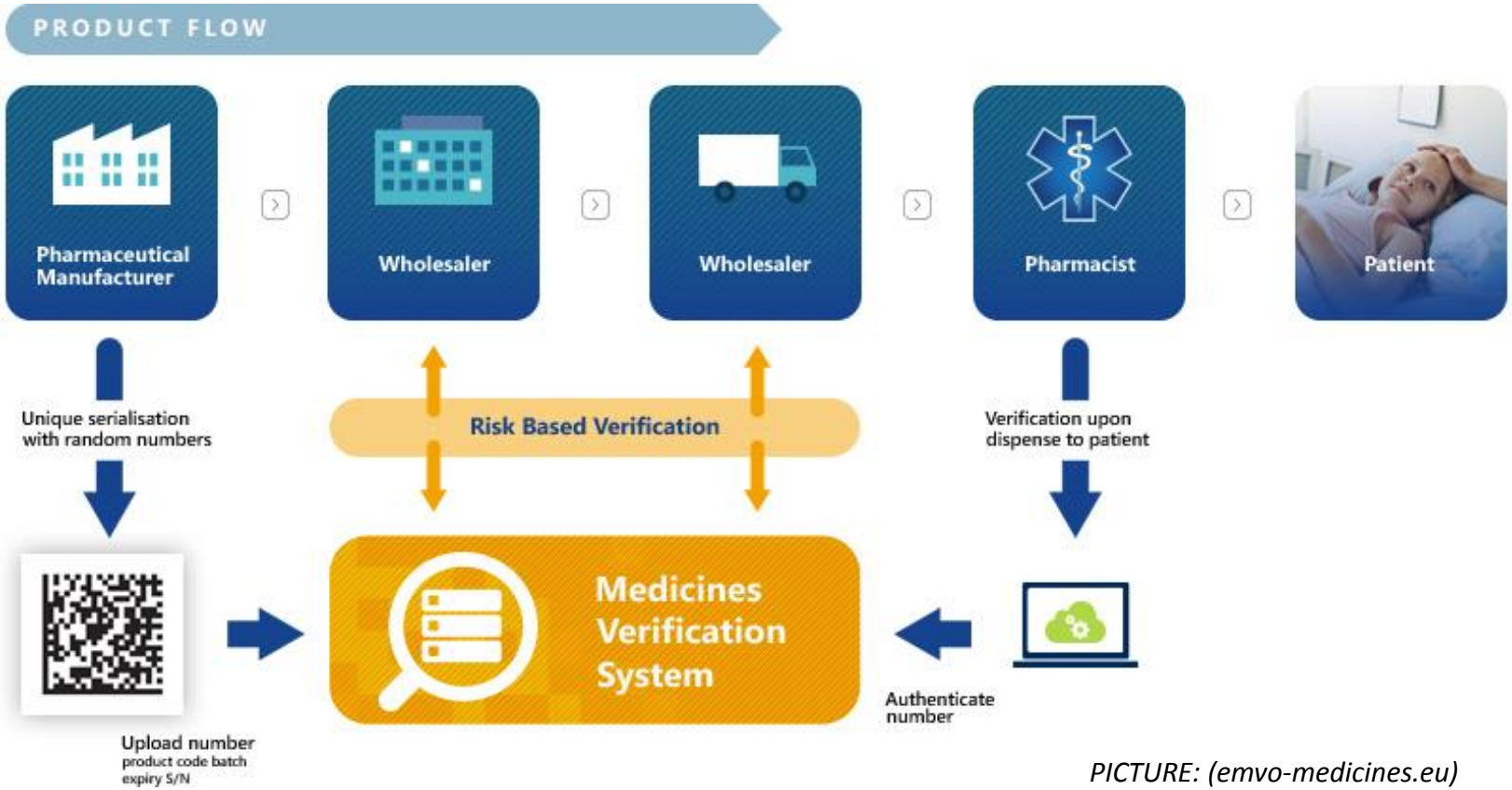
PICTURE: (amvs-medicines.at)

PC	5978564376587
SN	763947AZQE5647238972
Lot	A1C2G3R4K7
EXP	140526

PICTURE: (nmvo.pl)

Background & main concepts

Point of dispense verification:



PICTURE: (emvo-medicines.eu)

Companies adaptation activities

- Regulatory: Update of labelling information in registration dossiers
  - Changes in secondary packaging to be supported by registered information.
- Artwork
  - Text & design changes to include the Safety Features
- Manufacturing & Supply / IT:
  - Production lines & software validation
  - Production planning and prioritization. Stock building

Companies adaptation activities

- EMVO & NMVO contracts signed and technical onboarding completed

- Transfer from Project Phase to BAU:
  - Governance
  - Clear distribution of tasks and responsibilities (int. and CMO's). RACI creation.
  - Costs allocation
- Financial and economic impact
  - CAPEX
  - OPEX

Current challenges

- Hospital decommissioning
  - Hospitals request to the Commission
  - Pre-requisite in tender negotiations?
- Delegated Regulation, Article 23
  - Pack decommission before shipping to certain customers (e.g. prisons, armed forces, nursing homes, dental practitioners….)
  - Readiness and coordination with Storing & Distribution Services (3PLs)
  - Variability between MS
- SOP & Quality Agreements updating
  - New SOP's (e.g. product information upload to EMVO)
  - Product release specifications
  - QA with 3PL
- Technical aspects
  - E.g.: Slowdown in lines due to the inclusion of serialization / ATD application steps and further controls. Resources allocation.

Current challenges

- IT issues
  - Errors in transmissions to EMVO / NMVO
  - Incorrect rejections at point of dispense: E.g. prepared for increase in number of returns and related management. Resources allocation
- BREXIT impact
  - UK will undergo serialization during transitional period
  - No-deal scenario: Options around a national falsified medicines system in the interest of Public Safety
  - Added complexity to manufacturing operations:
    - Split EU joint packs currently shared with UK
    - Update labelling & artwork

EU Commission & Stakeholders

- Working forums
  - Expert Group meetings
  - Meetings with European Associations
- Consistent communication
  - From European Commission
    - Press release and Q&A
  - From EMVO
    - Press release & press conference
    - Guides: “An Introduction to the EMVS” / “The EMVS explained”
  - Stakeholders and Commission
- “Use and learn” phase
  - We are in a learning curve. More stable with system use
  - Effective communication for alert management
  - Maintain trust in the system’s added value and avoid disruption of supply to patients

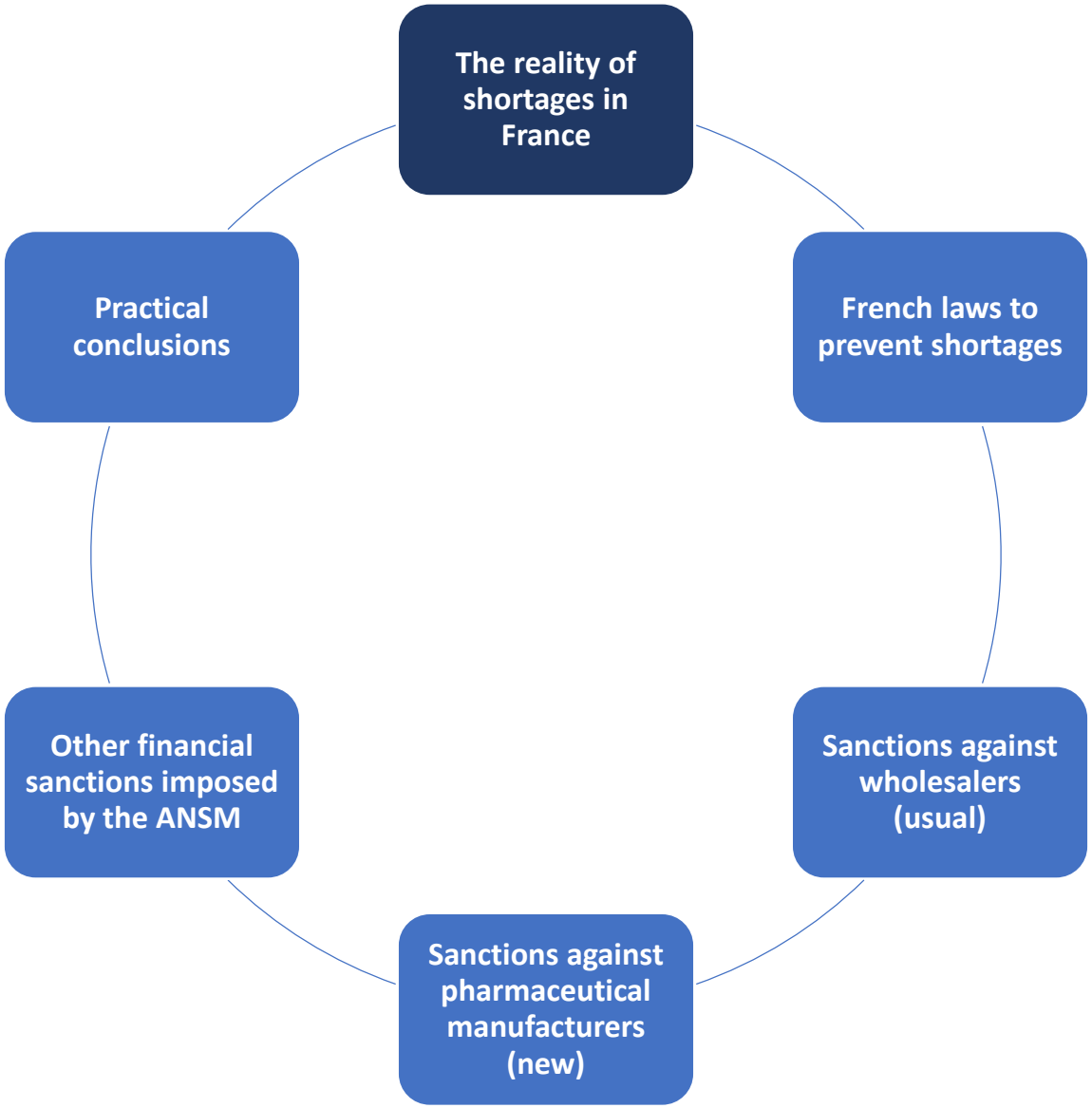
Thanks a lot for your attention!

Any questions?

IV.
Recent sanctions against pharma shortages in France

Olivier Lantrès, Partner, Life Sciences, Fieldfisher (Paris)

Agenda



O. Lantrès, Fieldfisher, Feb. 2019

The reality of shortages in France

Figures

- The situation is becoming more acute
- More and more shortages: X10 in 10 years (more than 500 a year now)
- More identified: amoxicillin, hepatitis B vaccines, Parkinson's

Causes

- Shortages of raw materials (API)
- Manufacturing plants located more and more outside France
- National allocations decided by the pharma companies
- Increasingly complex to produce in the manufacturing chain: medicines for headache ≠ biological medicines

Public and political concerns (see Report from the French Senate, Sept. 2018)

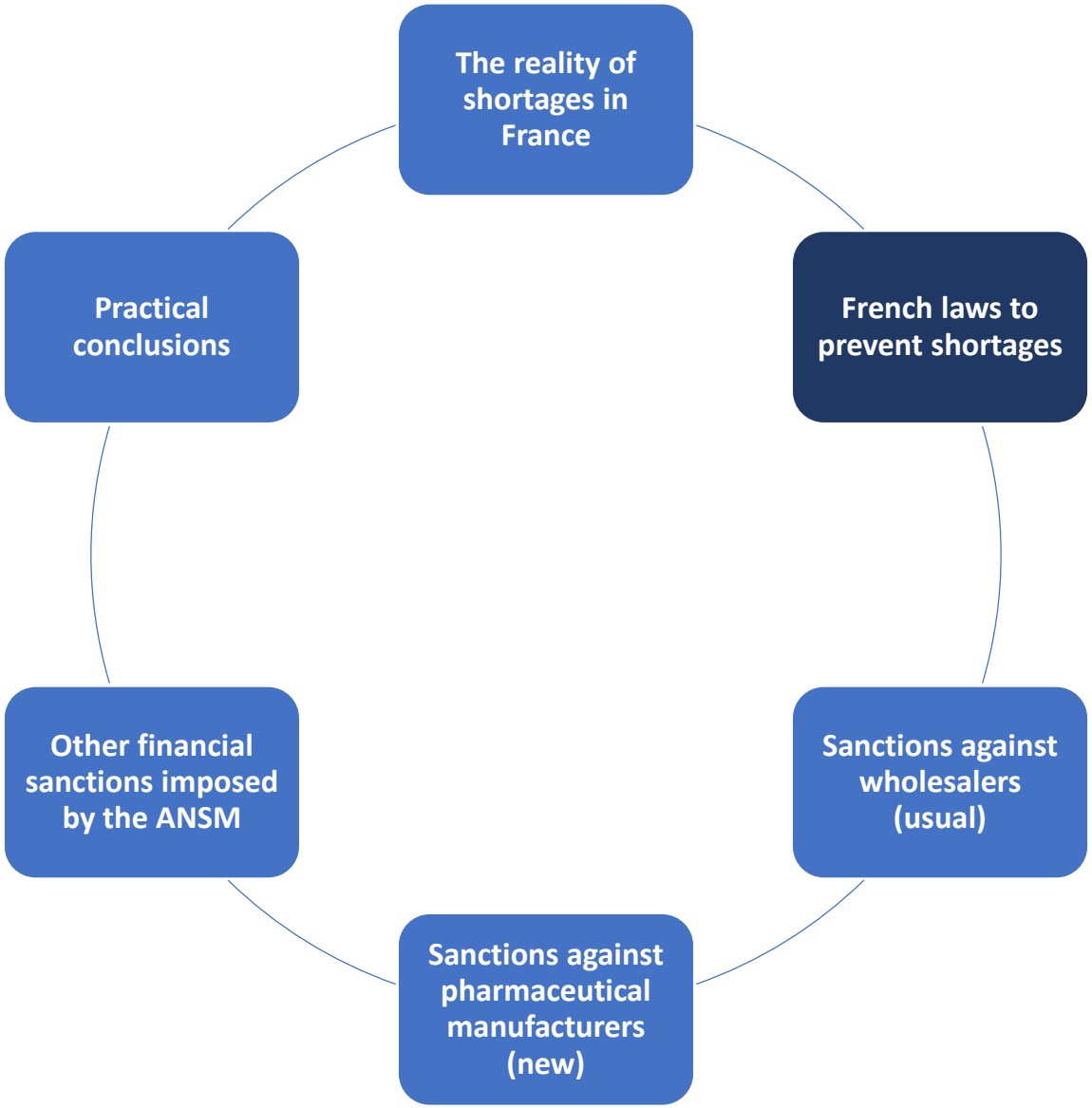
- *"The failure of an operator to fulfill its obligation to provide alternative solutions [and] measures provided for by a [Shortage Management Plan] […] may give rise to financial penalties imposed by the ANSM"*
- *"Any failure by laboratories to supply the market in an appropriate and continuous manner, in particular by not allowing wholesalers-participants to fulfil their public service obligations, shall be financially sanctioned".*

Financial aspects

- There are impacts in terms of turnover for the pharma affiliates in France. E.g. breach of public procurement contract

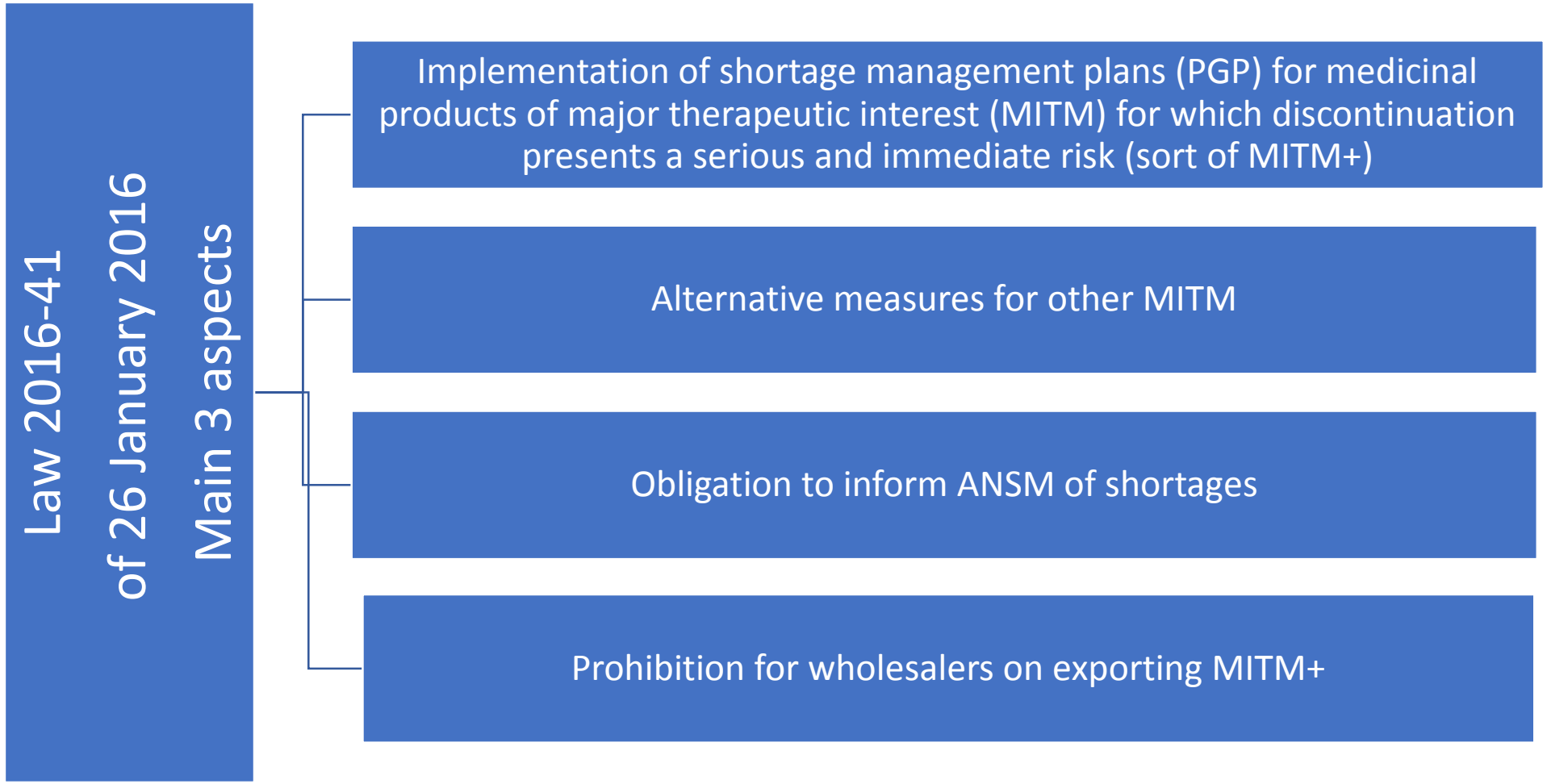
O. Lantrès, Fieldfisher, Feb. 2019

Agenda



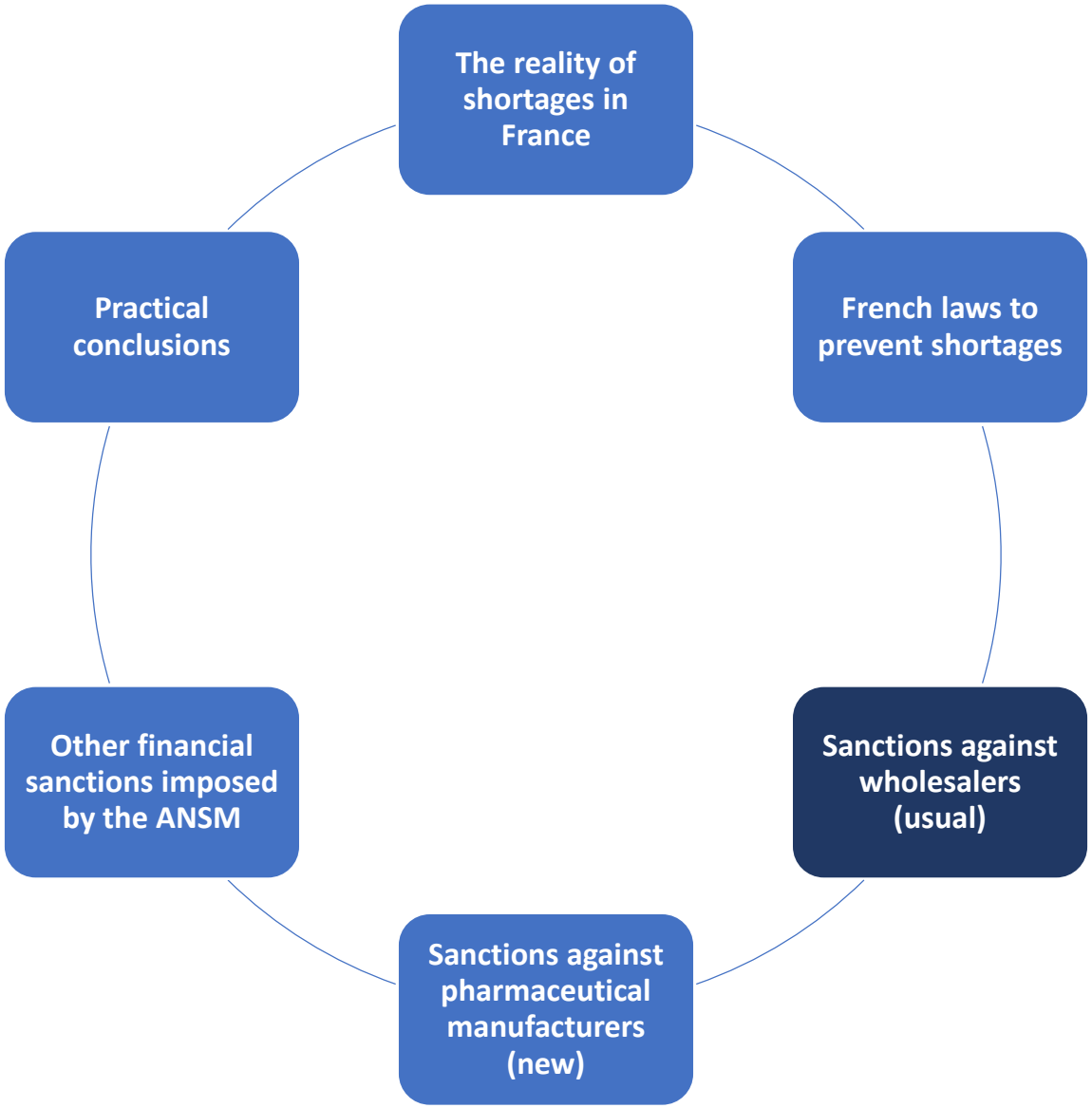
O. Lantrès, Fieldfisher, Feb. 2019

French laws to prevent shortages



O. Lantrès, Fieldfisher, Feb. 2019

Agenda



O. Lantrès, Fieldfisher, Feb. 2019

Sanctions against wholesalers (usual)

ansm
Agence nationale de sécurité du médicament et des produits de santé

Pharmaceutical wholesaler

Obligation to public services

- 90 % of references
- 2 weeks of stock
- Delivery in 24 hours

Sanctions already imposed, mainly against SME wholesalers

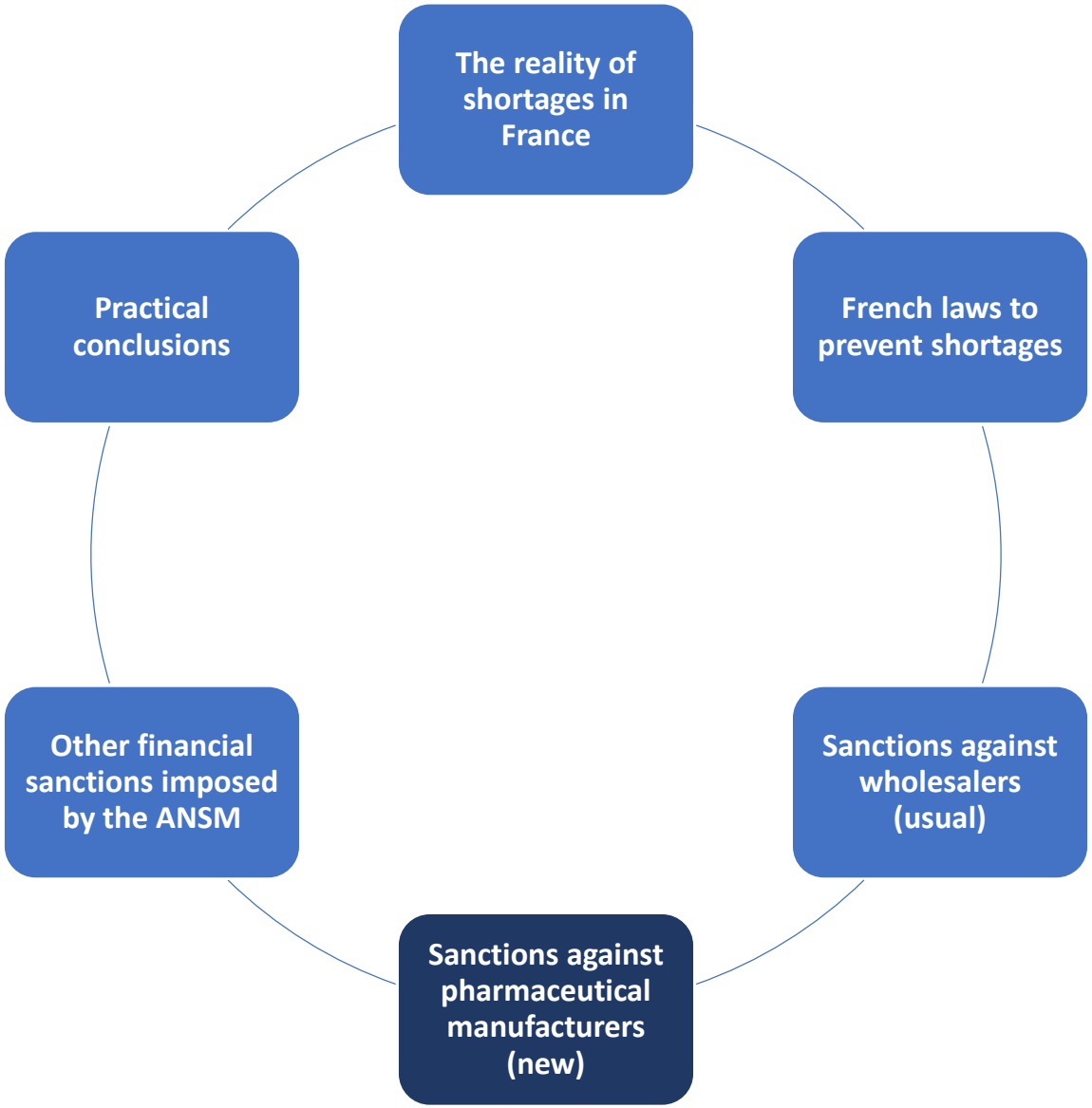
- Injunction
- Financial sanctions (in practice between EUR 50k and 250k, based on the company's turnover)
- Withdrawal of registration licence

Examples of concrete breaches already sanctioned:

- When less than 90 % of references (e.g.: 30 %)
- When mainly export and not delivery to retail pharmacists

O. Lantrès, Fieldfisher, Feb. 2019

Agenda



O. Lantrès, Fieldfisher, Feb. 2019

Sanctions against pharma manufacturers (new)

Decision dated 28 December 2018

Fine: 350,000 EUR. Calculation based on the turnover specific to the product

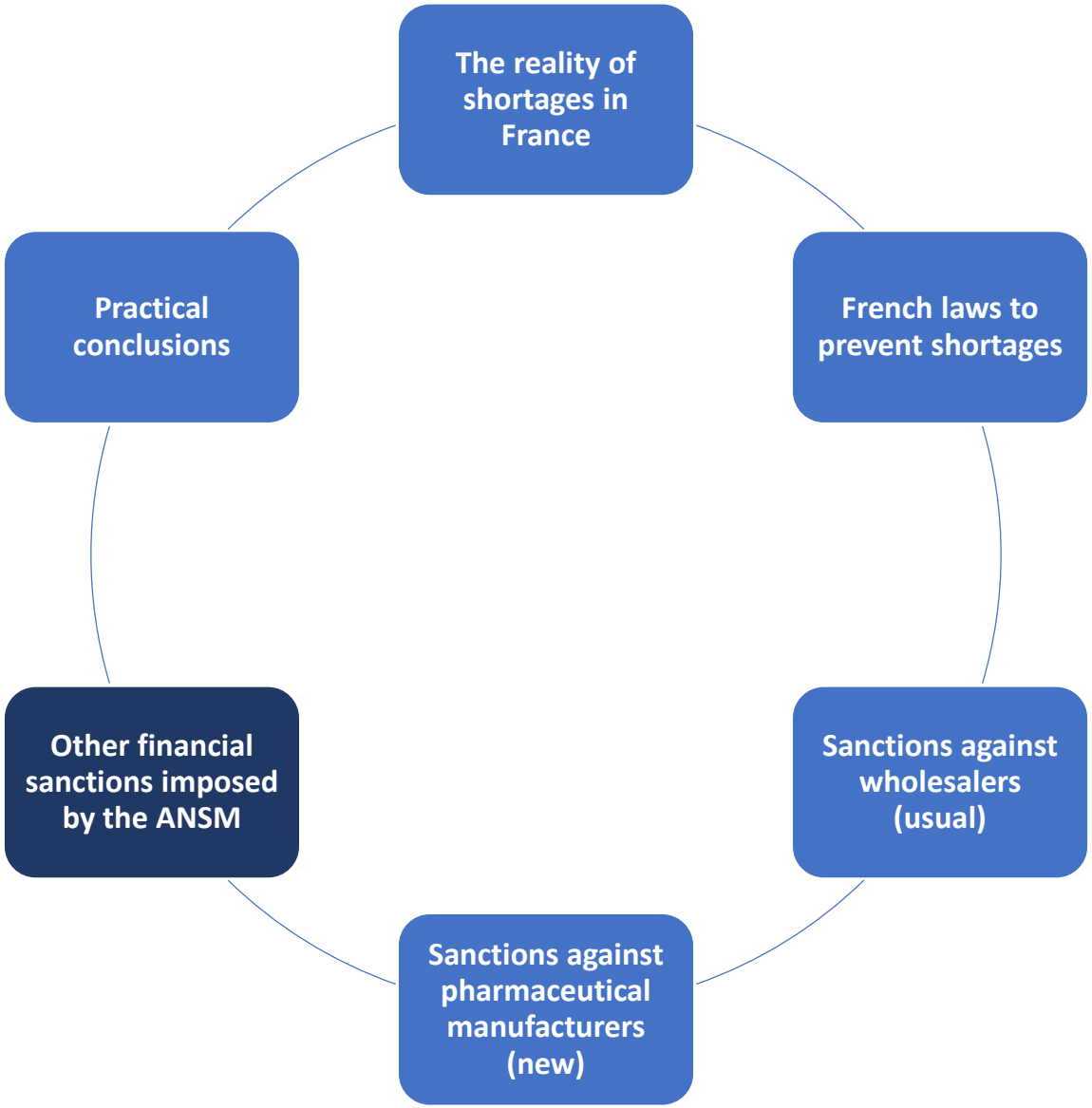
Product: Sinemet (Parkinson's disease)

Reasons:

- the pharmaceutical company did not prepare any PGP even though its product was an MITM for which a shortage presented a serious and immediate risk to patients
- In addition, it did not provide an alternative solution to deal with this situation

O. Lantrès, Fieldfisher, Feb. 2019

Agenda



O. Lantrès, Fieldfisher, Feb. 2019

Other financial sanctions imposed by the ANSM

ansm
Agence nationale de sécurité du médicament et des produits de santé

Pharmaceutical manufacturer

Mainly advertising to customers through websites without authorisation
Between EUR 50 and 300 k

Medical device company

Illegal advertising (need an authorisation for certain MD). In practice between EUR 60 and 90 k
No renewal of CE mark. In practice between EUR 1 and 10 k

Biotech company

So far, there have not been any financial sanctions against biotech companies (to our knowledge)

There have been more than 10 decisions in 2 years
The calculation of the fine is based on the product turnover

O. Lantrès, Fieldfisher, Feb. 2019

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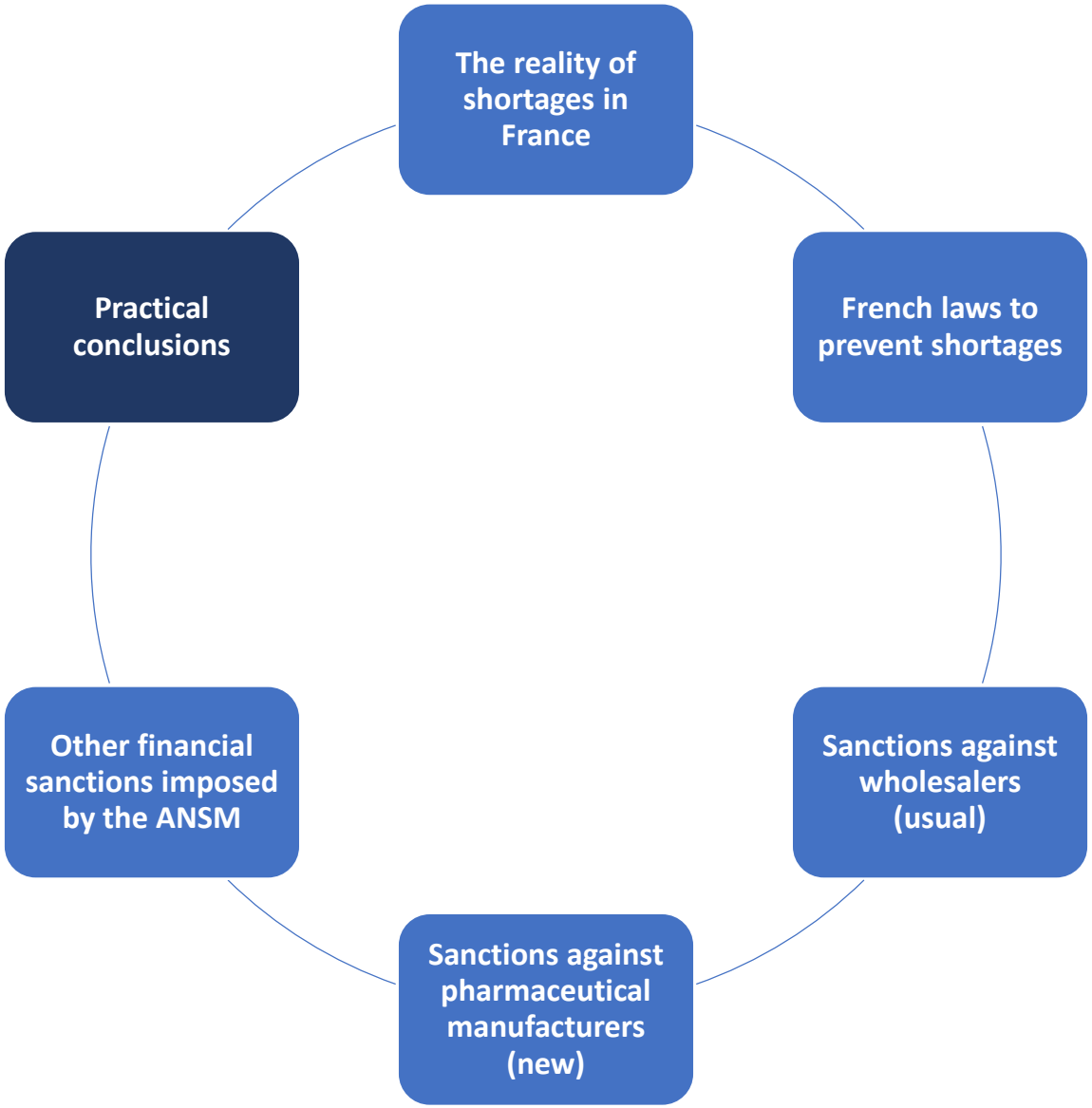

O. Lantrès, Fieldfisher, Feb. 2019

Practical conclusions

In the event of a legal action by the ANSM:

- Check against the French law whether or not your French affiliate complies with this specific regulation concerning shortages
- Challenge the principle of any sanction before the ANSM
- Negotiate the amount of the sanction if any, with the ANSM
- If unsuccessful, lodge an appeal before the administrative court

O. Lantrès, Fieldfisher, Feb. 2019

Olivier Lantrès

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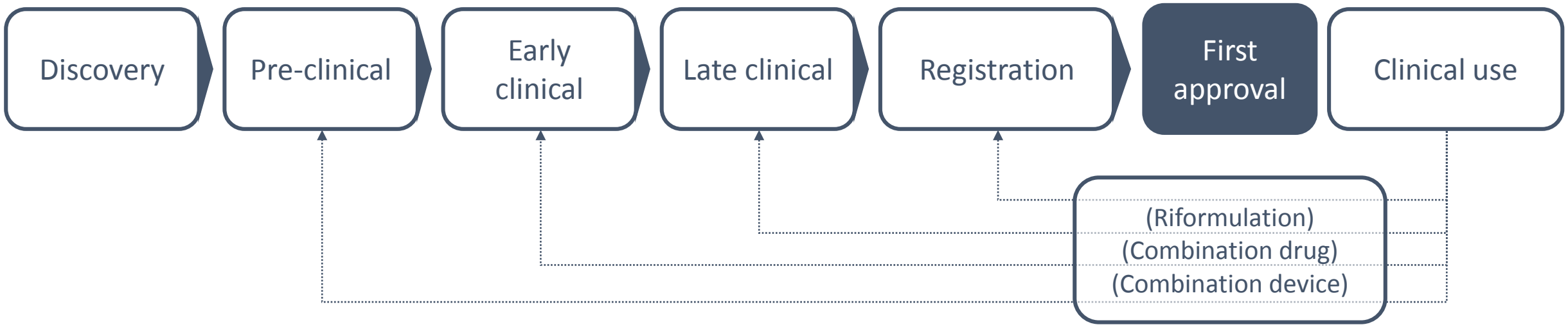
V.

STAMP – Proposal for a repurposing pathway within the current regulatory framework

Diego Ardigo, Chiesi

The concept of repurposing

New use for an existing drug in an indication outside of the scope of the initial indication



What is drug repurposing	The process of identifying a new use for an existing drug/active substance in an indication outside the scope of the original indication
Repurposing includes	finding new therapeutic uses for already known drugs (**repositioning**)
	developing different formulations for the same drug (**reformulation**)
	creating new combinations of drugs previously used as separate products (novel drug combination)

1 – DRUG REPURPOSING

1.1 – Introduction to the STAMP initiative

The issues surrounding the challenges of repurposing of established medicines has been discussed in meetings of the Safe and Timely Access to Medicines for Patients (STAMP) Expert Group – A working group including representatives from:

- Member States (Belgium, Netherlands, Norway, Spain, Sweden, United Kingdom)
- The European Medicines Agency (EMA)
- Stakeholders from industry, patient, healthcare and payer representative organisations (EUCOPE, EFPIA, EURORDIS, EPF, SIOPE, AIM and MfE)

The working group WG is supported by the European Commission:
DG: Health and Food Safety Unit B5 – Medicines: Policy, authorisation and monitoring

1 – DRUG REPURPOSING

1.2 – Scope

- **The aim of the WG:**

In order to address some of the barriers and hurdles identified by STAMP, the aim is to put in place a proposal for a visible supportive framework to non-profit stakeholders (called Champions), who have evidence and scientific rationale with the aim of bringing a new indication on-label.

- The WG proposed a targeted scope, **taking into account the following considerations:**
  - The repurposing framework is the process of facilitating data generation in accordance with regulatory standards of a new therapeutic use for an authorised active substance – outside the scope of the original authorised indication(s) - with the purpose of seeking its authorisation.
  - The elements always discussed in the working group cover only one possible scenario of repurposing of medicinal products, namely the one where medicines are already out of basic intellectual property (IP)/regulatory protection.

1 – DRUG REPURPOSING

1.3 – Working Groups and Objectives

STAMP WG considered objectives for a proposal for a repurposing framework:		The work is led by:
Objective 1	Proposal for a 'repurposing pathway' within the current regulatory framework.	SE, EMA and the UK
Objective 2	'learnings and outstanding issues' to explore how the proposal for a framework would work in practice.	The Anticancer Fund
Objective 3	Possible supporting materials and communication.	Had been briefly discussed by the WG in a teleconference

- During the previous STAMP meetings, the WG made sure to review the essential outstanding issues that needed to be addressed prior to piloting the proposed repurposing framework.
- The leader groups of objective 1 and 2 always prepared an updated document in each meeting to be discussed with the working group as a whole.
- The documents presented to STAMP were an outcome of the working group's activities combined together:
  - **The paper on Objective 1:** contains the working group members comments on the outstanding issues,
  - **The paper on Objective 2:** aiming at providing "real life" examples of products/ indications that could have been put through the pathway and at considering how a pilot for testing the repurposing pathway might be introduced.
  - **The paper on Objective 3:** working on the means to make needed information more visible and accessible in order to promote and support the collection of robust evidence.

1 – DRUG REPURPOSING

1.4 – STAMP repurposing white paper final draft

- **A Champion can be:**
  - person or entity
  - academic unit
  - learned society
  - research fund or payer

  with a particular interest in repurposing an authorised medicinal product for a new indication and who has data evidence/scientific rationale to do so.

- Champions based both within and outside the EU are eligible.

- **A Champion is typically characterised by the following:**
  - Is not a pharmaceutical company or is not financed or managed by private profit organisations in the pharmaceutical sector ("PPO")
  - Is able to coordinate and / or foster the research programme up until the point of full industry engagement
  - Is initially responsible for liaising and leading the interactions with regulatory authorities and industry / other stakeholders such as patient groups
  - Is transparent regarding interactions with relevant pharmaceutical company(s)
  - Files the initial request for scientific/regulatory advice on the basis of the available data

1 – DRUG REPURPOSING

1.4 – STAMP repurposing white paper final draft

- Core components of the targeted repurposing projects:

The proposed **new indication** for an authorised active substance should be in a condition distinct to the currently authorised indication(s)

The targeted indication should be in an area where **important public health benefits** / Union interests are likely to be achieved

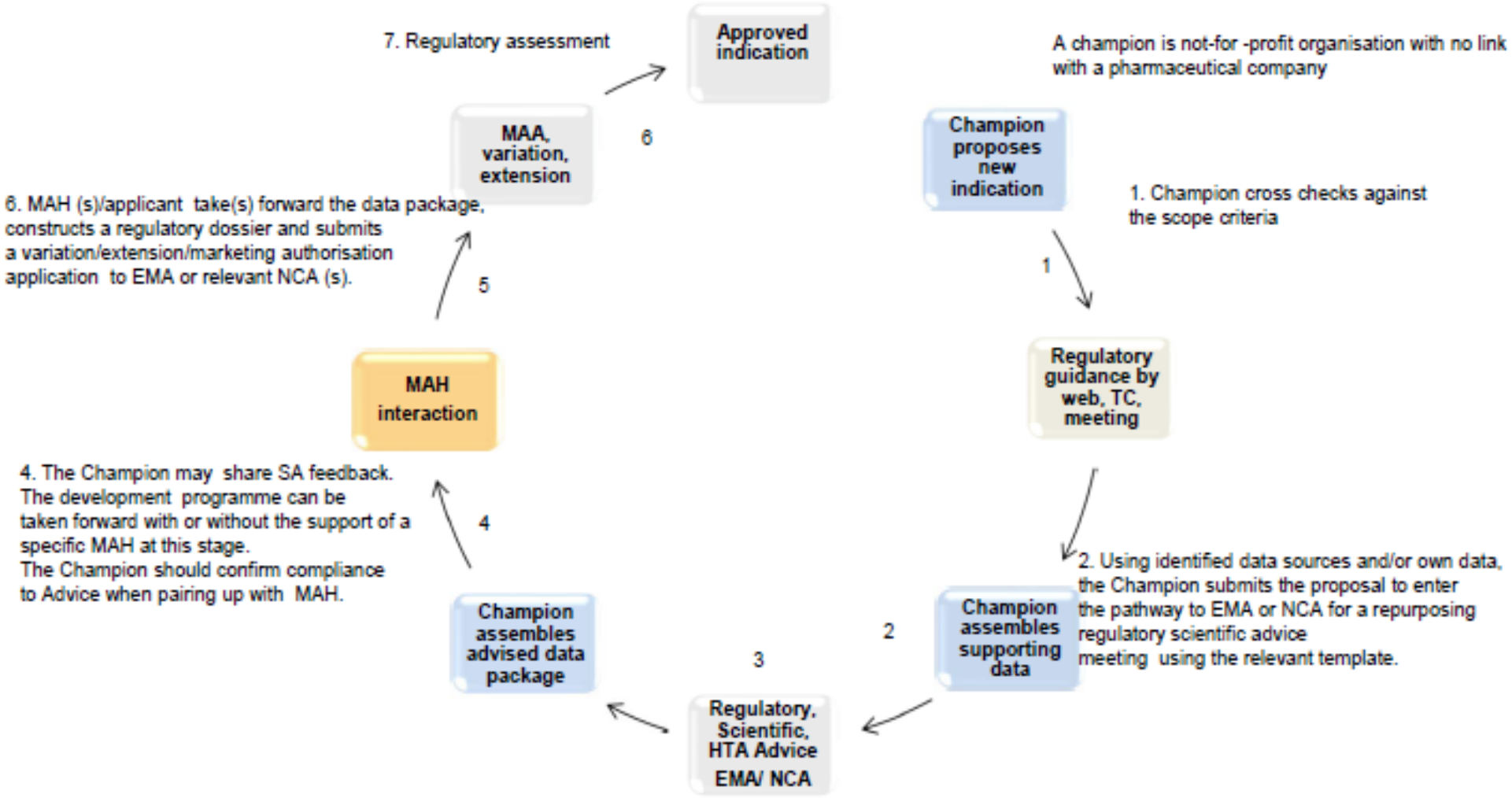
There should be a valid **marketing authorisation** granted in a Member State or in the European Union for the medicinal product containing the concerned **active substance**

Relevant authorised medicinal products containing the concerned active substance should be **out of** basic patent/ supplementary **protection** certificate (SPC) protection, and data and market exclusivity periods

A **Champion takes the initiative** and is willing and able to take forward the roles and responsibilities required of the framework and whose goal is to facilitate the bringing of the new indication to a label.

There should be some **supportive clinical evidence**. It could include documentation from clinical trials, off label use, registry data, or reported case studies.

Repurposing of MP's out of patent & data protection for non-profit organisations



1 – DRUG REPURPOSING

1.5 – Pilot of the STAMP repurposing Framework

In order to test the framework, the WG agreed that a pilot should be conducted to test the proposals, learn from the practical applications of candidates in the framework and build on the concepts identified.

- **Objective:** The overall aim of the pilot is to assess whether the proposed framework is able to facilitate a marketing authorisation application for a new indication for an off-patent medicinal product.

- **Deliverables:**

Short term

Identification of list of specific candidates for repurposing (active substance, target indication) and the respective potential champion(s)

Application(s) for SA, compliant with applicable requirements and understanding of scientific advice scope and outcome letter

Project progress further to SA i.e. continuation of programme development and compliance with scientific advice outcome

Long term

Uptake of a repurposing candidate by one or more business companies or consider lessons learned in case of no uptake of the project by any business company

An application for a variation by a MAH or a new marketing authorisation with the repurposed indication

In case of no uptake by industry and appropriate evidence generated by champion in compliance with SA explore, where possible, what might be the next steps

1 – DRUG REPURPOSING

1.6 – Pilot of the STAMP repurposing Framework - CASES

Potential candidates for repurposing pilot identified by Anticancer Fund

Late stage
(phase 3 & off-label)

- **Clarithromycin** in multiple myeloma
- **Zoledronic acid** in primary breast cancer
- **Letrozole** in epithelial ovarian cancer
- **Docetaxel** in hormone sensitive metastatic prostate cancer

Early stage
(phase 1 and 2)

- **Propranolol** in angiosarcoma
- Combination of 9 repurposed drugs with low-dose chemotherapy **(aprepitant, minocycline, auranofin, captopril, disulfiram, itraconazole, celecoxib, sertralin, ritonavir)**
- **Zoledronic acid** and **sirolimus** in patients with solid tumours with bone metastasis and advanced pretreated osteosarcoma
- Perioperative use of a **propranolol** and **etodolac** in pancreatic cancer
- **Letrozole** in epithelial ovarian cancer
- **Acetylsalicylic acid** and **atorvastatin** in castrate-resistant prostate cancer

1 – DRUG REPURPOSING

1.7 – Next Steps

- **Points discussed at the TC on 22 Feb with the STAMP working group**

- GCP compliance
  - Request by EFPIA to be done by Champion before engaging MAH
- Proposal for creation of an “advisory board” to monitor the pilot project
  - Is EUCOPE interested?

- Funding of the pilot project (regulatory administrative process) remains to be established
  - Fee waiver for scientific advice?
  - Industry support?
  - “Real-life pilot” (as it will be in reality, without specific support)
- Engagement of companies (in pilot and future)
  - Institutional company’s e-mail address for reporting repurposing opportunities
  - Article 57 implications
- List of potential candidates for pilot

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EUCOPE meeting

Any Questions?

VI.
Rare Diseases Research Challenges

Laurent Louette, EUCOPE

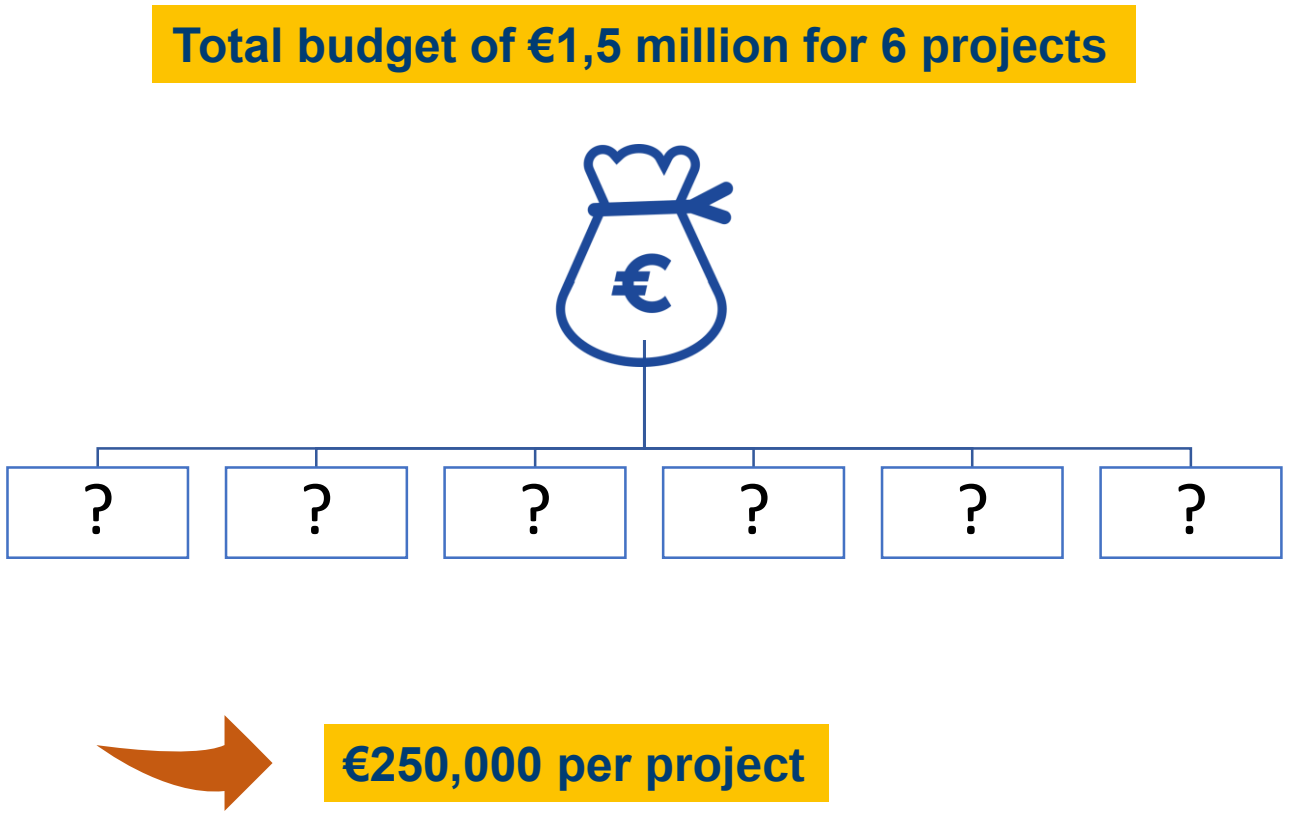
Funding to speficic research challenges

- Part of the European Joint Programme on Rare Diseases (EJPRD) – WP 8
- Solving specific challenges for research in rare diseases
- Industry to identify challenges

Objective: bridging the gap between technologies and industry needs

In practice

- Sponsorship can reach 30% of the project and/or be in an in-kind;
- Challenges should be proofs of concept for specific applications.



Roadblocks

- Scope and timeline: 30 months for a specific challenge
- Amount of grant: what can you do with €250,000?
- 30% of sponsorship is per project, not per sponsor
- End-product should be commercially viable;
- Question of IP?
- Evaluation committee?

VII.

Tool for Reducing Uncertainties in the Evidence Generation for Specialized Treatments for Rare Diseases

Laura Batchelor, FIPRA

TRUST4RD

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

TRUST4RD Objective

To develop a technical but pragmatic tool and methodology that allows the **uncertainties** in evidence for a specialised treatment for a rare disease to be **made explicit**, to **be prioritized** and to **be addressed** in an adequate and timely way.

To provide guidance on the potential of **real-world evidence** to help address such uncertainties.

Multi-stakeholder participation to develop guidance

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Paper Commissioned by

INAMI-RIZIV


Prof. Lieven Annemans
University of Ghent


Dr Karen Facey
University of Edinburgh


Jo De Cock
CEO – INAMI


John Bowis
FIPRA (Chair)


Simone Boselli
EURORDIS


Amr Makady
ZIN

NICE National Institute for Health and Care Excellence

European Reference Networks

Zorginstituut Nederland

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EORTC
The future of cancer therapy

FEDERAL MINISTRY OF LABOUR, SOCIAL AFFAIRS, HEALTH AND CONSUMER PROTECTION
sozial MINISTERIUM

HAS
HAUTE AUTORITÉ DE SANTÉ

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EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

efpia

EuropaBio

EURORDIS
RARE DISEASES EUROPE

BIOMARIN

Celgene

Takeda

Shire

SANOFI GENZYME

ACTELION
A JANSSEN PHARMACEUTICAL COMPANY OF Johnson&Johnson

OBSERVER

European Commission

Proposal for a systematic approach: TRUST4RD

- Taxonomy of evidence gaps
- Setting priorities (important vs unimportant gaps)
- Gaps meet data pre-launch (large potential of RWE pre-launch)
- Post-launch evidence is jointly prepared pre-launch
- Mandatory Dialogue – Dialogue – Dialogue involving patients and clinicians – according to principled compromise

Necessary condition

Supranational data collection (cf. ERN); data governance

TRUST4RD

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

Dissemination

HTAi
June 2019

Finnish EU Presidency
July-December 2019

Orphan Drug Congress
November 2019

Dissemination/ uptake via stakeholders….

2019 - Real World Evidence for Highly Innovative Medicines

Aim: to reach consensus on how to optimize evidence generation to demonstrate the value of highly innovative technologies.

Identification of areas for improvement in existing processes for providing advice, and to discuss the role of RWE to address the uncertainties in order to build trust in conditional payer models and value based agreements.

Finnish EU Presidency focus on 'economy of pharmaceuticals'

'how uncertainties can be reduced in assessing the value of a medicine'

High-level Meeting, 26 and 27 September (Helsinki)

Delivery of policy relevant outcomes (e.g. principles) for consideration by EU Finnish Presidency

Thank You

Laura.Batchelor@fipra.com

IX.

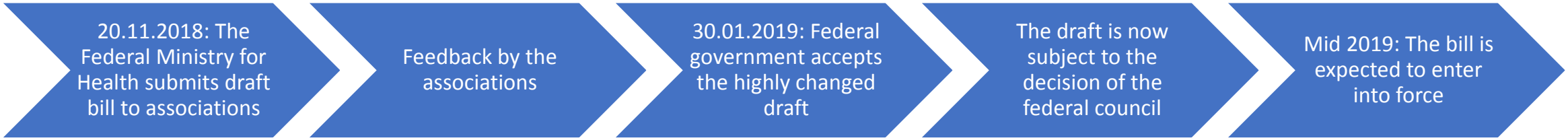
Germany: GSAV – Changes on AMNOG, OMPs, ATMPs and Biosimilars

Alexander Natz, EUCOPE

Outlook

- Status quo
- Content Summary
- Orphan Drugs

Status quo



- GSAV → Law for more safety in the supply of medicines
- The law is a consequence of recent medicine scandals (e.g. Lunapharm, Valsatan)
- Goal: Enhanced control and safety

Content summary

Topic	News
Cannabis	Simplification for approval reservations für cannabis therapy
Recalls	No additional costs for the patients if the medicine was recalled due to minor quality
Discount contracts	Diversity of producers and adequate supply should be taken account of
Products for new therapies	New regulation competencies with the G-BA in order to set out expectations for the quality of medication for new therapies
Imports	Tiered minimum price intervals
Biosimilars	The exchange with biosimilars will enter into force three years after the GSAV
Haemophilia	Subject to pharmacy obligation, price moratorium for haemophilia products
„AMNOG“	New regulations concerning revenue threshold for orphan drugs

Orphan drugs

- Additional benefit threshold: 50 million €
  - Now including in- and outpatient care
  - → Pharmaceutical companies have to present full dossiers earlier

- G-BA can order extra data collections
  - During treatment
  - Additional to EMA controls

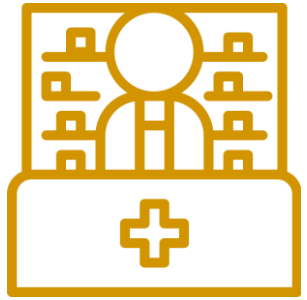
- Considerable sanctions

VIII.
Biosimilars – Clouds on the horizon?

Laurent Louette, EUCOPE

Background & Rationale

- GSAV draft bill
- Future EU trend?
- We need to develop arguments



GSAV Bill

- As far as the **substitution of a reference medicine by a biosimilar at pharmacy level** is concerned, such substitution is permissible only after the **G-BA has issued guidelines on the interchangeability of the product(s) in question**.
- In addition, the bill provides that such **substitution only takes place after a lead time of three years (i.e. according to the current planning as of mid-2022)**. During this three-year period, the switch from the original product to a biosimilar shall only be made by the physician under consideration of the above mentioned guidelines. However, the law also requires the G-BA **to immediately initiate the work on the guidelines on the interchangeability**.
- In addition, the bill stipulates that **targets concerning the uptake of biosimilars have to be defined at regional level**.

GSAV Bill

EUCOPE Reaction (translated from DE)

- Concerning because it places **medicinal products containing the same active substance on an equal footing as far as possible with biosimilars** with a view to substitution by the pharmacist.
- It is undisputed that categorical equivalence is not appropriate since living cells are used for the manufacture of biotechnological medicinal products. This makes it impossible to obtain an exact copy of the original drug […].
- Thus, the substitution of an original preparation by a biosimilar creates the risk of an immunogenic reaction in the patient. The substitution of biopharmaceutical preparations therefore always requires a medical-scientific assessment in the individual case, which must be reserved for the attending physician.

Danger ahead

Changing the practices in place

- Worst-case scenario: Member States follow Germany's example.

- Risks:
  - Unstable market;
  - Restriction of competition;
  - Patient safety;
  - Price as only criteria.

What EUCOPE should do

Developing arguments

- Substitution requires a scientific assessment and should be initiated by the treating physician only;
- Protect the current framework:
  - Incentives for innovators are working;
  - Measures to facilitate uptake are working;
- Specific products, specific rules.

Proposal

- Discuss with members;
- Drafting group;
- Timeline and objective.

XI.

Medical Devices - New requirements for drug-device combination products under the Medical Devices Regulation

Maren von Fritschen, EUCOPE

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Combination products – no legal definition

In the EU, a combination product* is meant as

- a **medicinal product** that has as an *integral part* a **medical device**
- or a **medical device** that has a **medicinal product** as an *integral part*.

Incl. biologics and advanced therapy medicinal products (ATMPs), with a device or diagnostic for medical purposes, without forming necessarily an integrated unit = cATMPs

* Not to be mixed with fixed dose combination nor with combination pack

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Different regulatory frameworks in the EU - either MD or MP

Medical Devices

European Commission

DG GROW
(Internal Market, Industry, Entrepeneurship & SMEs)

NBs
Notified Bodies

Harmonised Standards EN: CEN, CENELEC

CAMD
Competent Authorities for Medical Devices

MDCG
Medical Device Coordination Group

Medicinal Products

DG Sante
(Health & Food Safety)

NCA
National Competent Authorities

HMA
Heads of Medicines Agencies

CMDh
Coordination Group for MRP/DCP

EMA
European Medicines Agency

Committees CHMP etc

"No need for another working group as DG Grow is only 10 people"

Medicinal product or medical device

depends on the mode of action of the PRODUCT in the indication

Primary intended purpose achieved by one of the following means:

pharmacological
metabolic
immonological
(+ ATMPs)

↓

Medicinal product

↓

Drug/Device Combination

Primary intended purpose achieved by other means:

e.g. physical
simple chemical
mechanical
digital

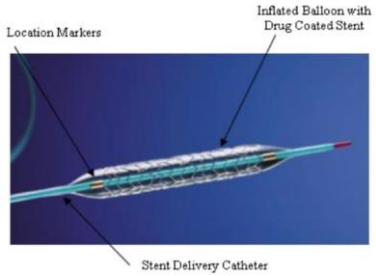
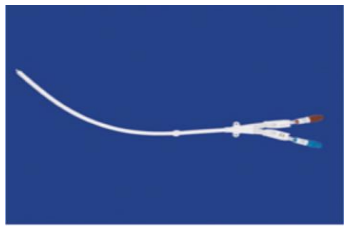
↓

Medical device

↓

Device/Drug Combination

Overall approach - combined products – no legal definition

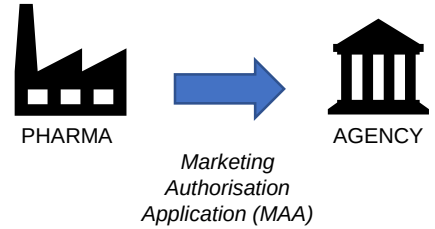
Category	a **medical device** that has a medicinal product as integral part	a **medicinal product** that has as an integral part a medical device
Regulatory pathway	Regulation 2017/745 or /746 amending Dir 2001/83	Directive 2001/83 EC (Community Code, *defined timelines*)
Example	 Drug-coated stent	 Heparin-coated catheter
	 Single use injection pen	

The **two legislative acts** should ensure appropriate **interaction** in terms of consultations during pre-market assessment, and of exchange of information in the context of vigilance activities…

New approach as of 26 May 2020 acc to MDR

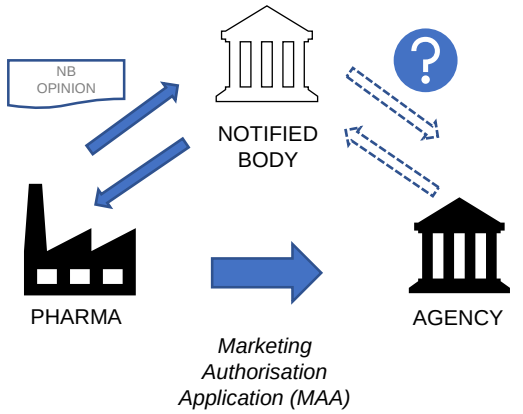
“old” Medical Device Directive (MDD) 93/42/EEC, Art. 1.3

- The relevant essential requirements of Annex I to this Directive shall apply as far as safety and performance-related device features are concerned.



“New” Medical Device Regulation (MDR) 2017/745; Art. 117

- If the dossier does not include the results of the conformity assessment… and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required… **the authority shall require an opinion on the conformity of the device part** with the relevant general safety and performance requirements set out in Annex I issued by a Notified Body…



Challenges ahead

- Not clear how this legal requirement will be implemented and much **uncertainty** across industry (delegated acts?)
- "Cross-border" **business process** between official bodies not well established, yet
- Issue recognized at senior level of regulators (EC, EMA, HMA and NCA, CAMD, NB) > *EC: updated implementation rolling plan published 19.2.2019*
- EMA is taking the lead and working through the Regulatory Network to align across Member States
  - Q&A expected in Jan. 2019: procedural and process issues, impact on legacy products, life cycle considerations & changes that warrant NB opinion
  - BWP/QWP Quality Guideline – by Q2 2019: CMC Module 3 content; variations, EMA in dialogue with NBs

Scope of Notified Body Opinion, **sequential vs parallel reviews**, CMC Module 3 content, LCM and variations, clinical evidence, labelling and instructions for use, QMS vs GMP, pre-submission e.g. scientific advice

Impact on existing MAs for products with a device constituent part particularly for products undergoing significant device change

Notified Body availability (and capacity to take on a new category of pharmaceuticals)

Major challenge ahead – Notified Bodies

Serious loss in NB already now 30% since 2012; current No 58 incl. Turkey (5 NB), UK (4)

Supervision by the competent national authority

Annually

Re-assessment incl. audit at site at least 1/y

Short term

Unannounced audit based on suspicion

After 3 years

Re-assessment
3 years after notification

Every 4 years

Re-assessment every 4 years thereafter

Qualification for the authorisation of personnel

NBOG's Best Practice Guide

applicable for ☐ MDR ☒ IVDR

NBOG F 2017-8

This document has been endorsed by the Medical Device Coordination Group (MDCG) established by Article 103 of Regulation (EU) 2017/745. The MDCG is composed of representatives of all Member States and it is chaired by a representative of the European Commission.

The document is not a European Commission document and it cannot be regarded as reflecting the official position of the European Commission. Any views expressed in this document are not legally binding and only the Court of Justice of the European Union can give binding interpretations of Union law.

Review of qualification for the authorisation of personnel

- Type / level of qualification
- Working experience
- Rationale for roles, functions / limitations (codes)
- Documented training and professional development

Accreditation process complex…

- „Joint Assessment“ > designation process 18 months...
- Acc. to NBOG Codes different **areas of competence**
- **42 applications** received (33 MDR, 9 IVDR) 60% of the NBs designated for the MDD and IVDD have applied so far
  - Serious loss in NB already now 30% since 2012
  - Current No 58 incl. Turkey (5 NB), UK (4), Australia, Switzerland
- Site inspections
- Brexit: > 30% of CE marks have gone via UK NB

BSI first EU notified body to achieve designation to the Medical Device Regulation

E-news: 23 January 2019

BSI was informed on 21 January 2019 by the Medicines and Healthcare products Regulatory Agency (MHRA) that its UK notified body is the first in Europe to be designated to the new MDR (EU 2017/745).

- BSI first NB designation acc to MDR
- 12 months process
- Next 10 designations expected during 2019, amongst BSI Netherlands
- Following processes expected to be faster e.g. 4-5 months

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Next steps and collaboration across stakeholders

- Clearly defined process and **transparent expectations** needed to allow business to plan for:
  - Continued **validity of existing MAs**
  - Avoidance of delays to approval of **new MAAs**
- Welcome clarity on the **accountability**
  - EMA taking the lead and working for alignment
  - Identify gaps between the EMA Q&A/quality guideline and other responsibilities outside EMA's remit
- Industry survey on **planned submissions** of drug-device combinations in 2020
- Are other areas helpful to make constructive proposals e.g. labelling, GMP aspects?

Need for a **collaborative approach to implementation** of Art. 117 across industry, regulators (drug and device) and Notified Bodies

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EUCOPE advocacy on drug-device combination products

- EMA R&D meeting
- CMDh meeting – all NCA
- MDCG stakeholder meetings and working groups
- Notified Bodies (NB) – Notified Body Organisations Group (NBOG)
- Inter-association alignment
- Direct contact with authority representatives, e.g. Armin Ritzhaupt, EMA, Liz Baker, MHRA

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Draft considerations for the Q&A document

When does Article 117 apply for my Marketing Authorisation Application (MAA) containing a medicinal product with an integral medical device?	Apply to MAAs submitted as of 26 May 2020
When must an applicant provide the CE mark certificate / declaration of conformity / notified body opinion for the MAA?	Strongly recommend to submit CE mark certificate / declaration of conformity / notified body opinion already as part of the initial MAA
How will Article 117 impact currently authorised medicinal products with an integral medical device?	Not apply requirements of Article 117 retrospectively to medicinal products with an integral medical device already authorised or to MAAs submitted prior to 26 May 2020
Will I need to provide a (new or updated) CE mark certificate / declaration of conformity / notified body opinion if there are changes to the device post-authorisation?	Submit CE mark certificate / declaration of conformity / notified body opinion if device component will be replaced / new device added / substantial changes

Source: EMA, Armin Ritzhaupt

XI.
European Elections – EUCOPE Engagement Strategy

Delphine Roulland, EUCOPE

Agenda

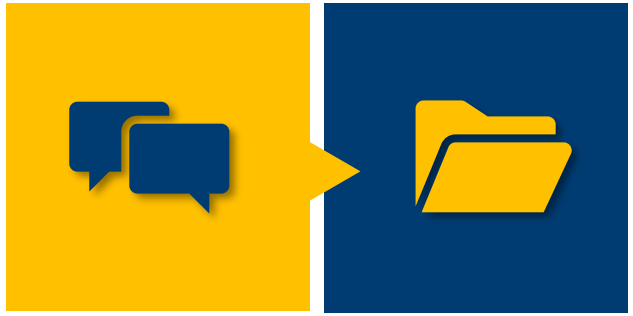
- A. Context
- B. 2019 Engagement rationale
- C. Strategic approach
- D. 2019 Engagement Plan
- E. Proposed resourcing

Context

May 2019: New European Parliament is elected

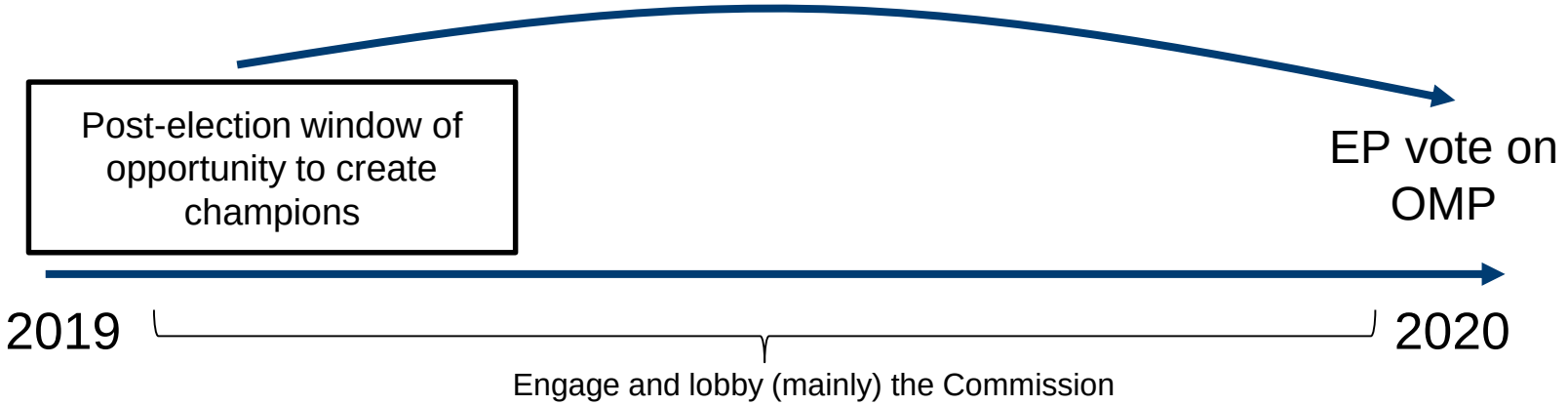
- Expected 60% of newly elected ‘faces’ (MEPs)
- Remaining questions of uncertainty: Post-Brexit seats? The role of anti-establishment parliamentarians? Evolution of ALDE? EPP fragmentation? Splitzenkandidaten system?

?



The Champion gap: High chances that the OMP regulation will be voted in EP in 2020

- We don’t want to be ‘swapping business cards in a crisis’, so the engagement must start early and be meaningful
- It is mission critical to have handful of MEPs to fight the positive OMP case



Timeline of European Elections

Time	Event
Nov 2018	**EPP Congress** elects **EPP Spitzenkandidaten**
Nov 2018	**ALDE Congress** adopts **manifesto**
Dec 2018	**PES Congress** elects **PES Spitzenkandidaten** and **adopts eight resolutions**
Feb 2019	**PES Election Congress** adopts **manifesto** on the basis of eight resolutions
March - May 2019	MEPs campaign in Member States
Feb 2019	**ALDE Electoral Congress** and **Campaign kick-off**
May 2019	**European elections: 23-26 May**
June 2019	**Commission President elected**
Q3 2019	The Commission President publishes their **priorities**
Aug - Sep 2019	**New MEPs will be allocated to committees**
Q3 2019	Appointment of **27 Commissioners** around July **Confirmation hearings in the EP** around September
Aug/Nov 2019	Commission President sends "**mission letters**" to new Commissioners outlining their mandate

Rationale for EUCOPE's engagement

EUCOPE persona	Awareness-raising	Coalition-building
› Differentiate from other stakeholders › Build trust › Demonstrate expertise	Key political dossiers: › OMP Regulation (possible reopening) › Gene & cell therapies (how to address evidential uncertainties? How to pay for one-off, possibly curative treatments)	› Build upon existing relationships › Nurture new relations › Build alliance of MEP Champions

Proposed focus of EUCOPE's engagement

Targeted EUCOPE activities

Focus of EUCOPE's engagement

	Pre-election	Campaigning phase	Post election I: embedding phase	Post election II: performing phase
				
EUCOPE activities	**Jan 2018 – Dec 2018** • Participation in EPP & ALDE congresses to create political capital • Build political network	**Jan 2019 – May 2019** • Prepare runway for post May • Informal engagement with MEP assistants	**May 2019 – Jan 2020** • Introduction of EUCOPE (window of opportunity to differentiate / build champions • **Objective: create or maintain at least 3-5 champions for EPP and ALDE**	**Jan 2020- onwards** • 'Normal' legislative engagement
	• *Influence manifestoes*	• *EUCOPE-led External activities*		

Principles for engagement

Speak with a unique voice

Meaningful and different engagement
Build trust

Be reliable, stay coherent

Engage with allies and build new partnerships

Theme for EUCOPE engagement in 2019-onwards

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The 4th Industrial Revolution in Health

The role of small & mid-sized companies in leading the new EU of innovators

- Genome editing
- Personalised medicine
- Real-world evidence
- Artificial intelligence
- Automation
- Data processing

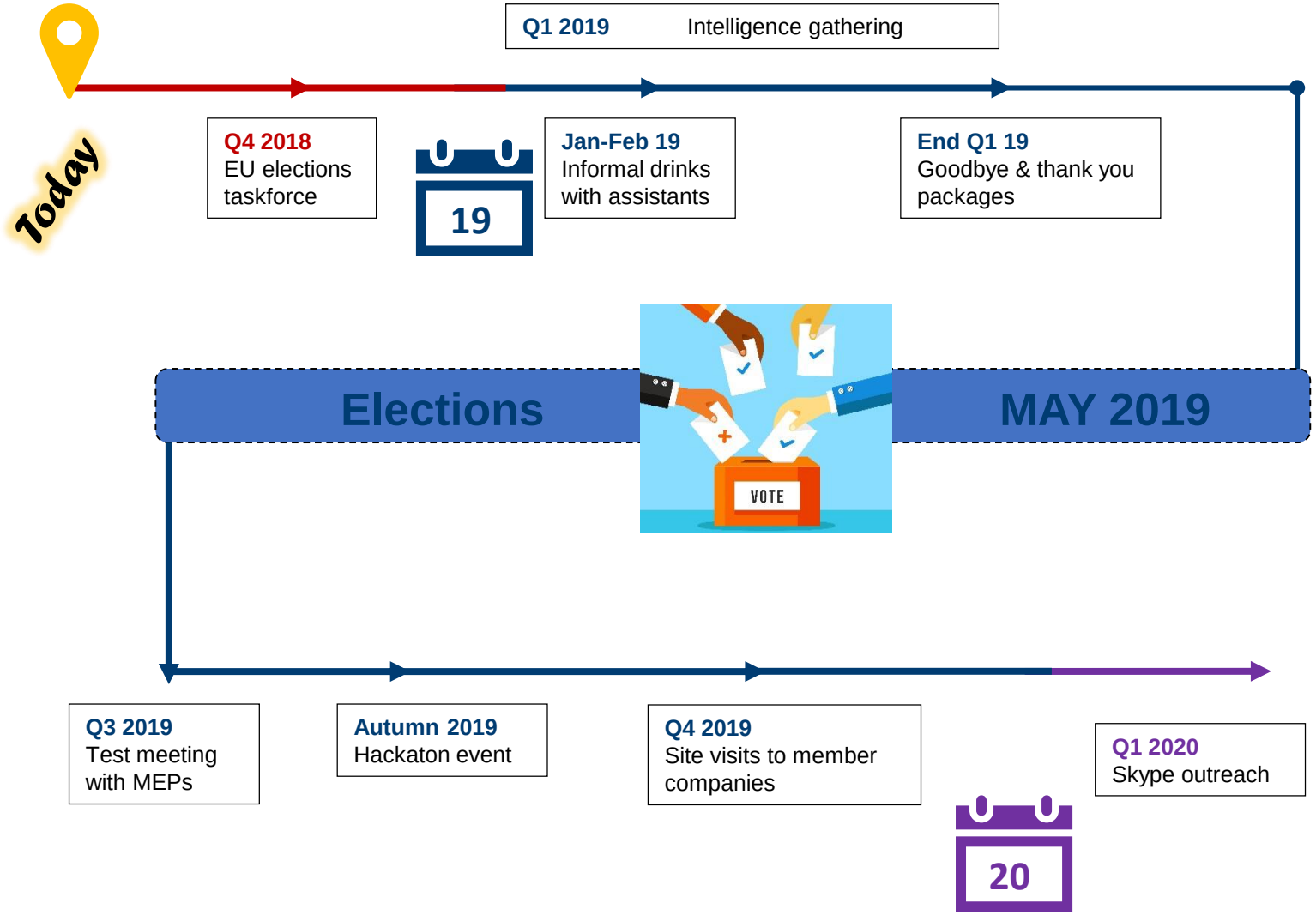
Engagement plan: overview

1. EU elections taskforce
2. Intelligence gathering / mapping of key MEPs
3. Informal drinks / meetup for MEP assistants
4. Goodbye and thank you packages

ELECTIONS 2019

5. Test meetings with MEPs
6. Brussels ‘open space’ / hackathon-type event
7. Site visits to member companies
8. SME-focused Skype outreach

Timeline


Today
Q1 2019 Intelligence gathering
Q4 2018
EU elections taskforce
19
Jan-Feb 19
Informal drinks with assistants
End Q1 19
Goodbye & thank you packages
Elections
VOTE
MAY 2019
Q3 2019
Test meeting with MEPs
Autumn 2019
Hackaton event
Q4 2019
Site visits to member companies
20
Q1 2020
Skype outreach

XII.

AOB / End of meeting

Thank you for your time