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SCIENCE MEDICINES HEALTH

Relocation of EMA
Challenges and Consequences

DGRA – 20th annual congress
14 June 2018

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An agency of the European Union

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Relocation of EMA - Challenges and Consequences

EMA preparedness following the UK referendum

- Internal task force (Operation and Relocation Preparedness (ORP) Task Force) established on 24 June 2016
- Focus on three pillars simultaneously:
  - The physical relocation of the Agency (from London to Amsterdam, and from the temporary to the permanent premises)
  - Operational preparedness and workload redistribution
  - Communication to external stakeholders, focusing on pharmaceutical companies

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01 Jan	2019	Temporary building
30 Mar	2019	Staff relocation
15 Nov	2019	Permanent building
31 Dec	2019	Staff relocation

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Progress report on the EMA – NL collaboration for relocation

Workstream 1A
Permanent building

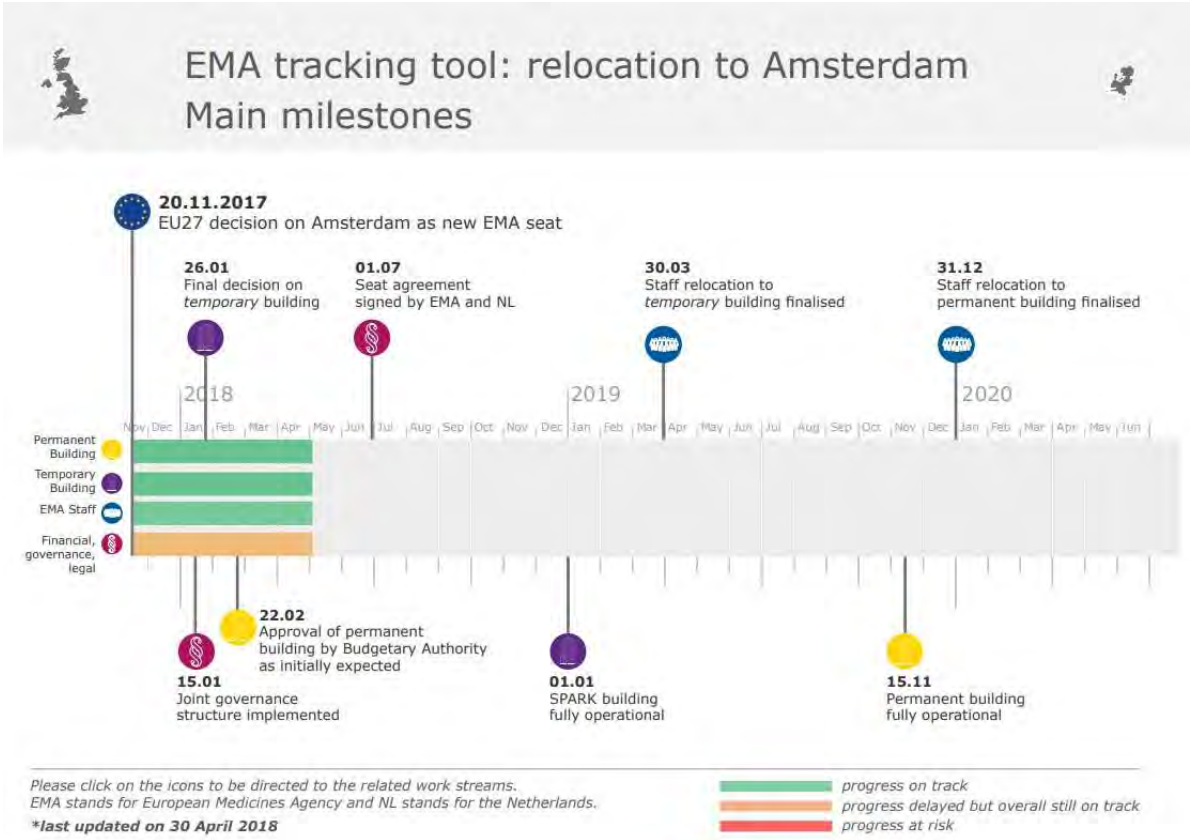
Workstream 1B
Temporary premises

Workstream 2
Staff relocation

Workstream 3
Financial and legal aspects

Workstream 4
External communication

Tracking tool published



Operational preparedness and workload redistribution

Operational preparedness (1/3)

EC and EMA published a **Notice to MAHs** of centrally authorised medicines products for human and veterinary use

Unless a ratified withdrawal agreement establishes another date, **UK** will become a **'third country**' from 30 March 2019, 00:00h (CET).

Companies reminded to **plan in advance in order to avoid any impact on the continuous supply of medicines** for human and veterinary use within the Union (EEA).

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DIRECTORATE-GENERAL HEALTH AND FOOD SAFETY

EUROPEAN MEDICINES AGENCY

Rev 01, published on 29 January 2018

Notice to marketing authorisation holders of centrally authorised medicinal products for human and veterinary use

The United Kingdom submitted on 29 March 2017 the notification of its intention to withdraw from the Union pursuant to Article 50 of the Treaty on European Union. This means that unless a ratified withdrawal agreement[1] establishes another date, all Union primary and secondary law ceases to apply to the United Kingdom from 30 March 2019, 00:00h (CET).[2] The United Kingdom will then become a 'third country'.[3]

Preparing for the withdrawal is therefore not just a matter for EU and national authorities, but also for private parties.

In view of the considerable uncertainties, in particular concerning the content of a possible withdrawal agreement, marketing authorisation holders of centrally authorised medicinal products for human and veterinary use are reminded of legal repercussions, which need to be considered when the United Kingdom becomes a third country.

Subject to any transitional arrangement that may be contained in a possible withdrawal agreement, as of the withdrawal date, the EU rules in the field of medicinal products for human and veterinary use no longer apply to the United Kingdom. This has, in particular, the following consequences in the different areas of EU law on medicinal products:

- EU law requires that marketing authorisation holders are established in the EU (or EEA);
- Some activities must be performed in the EU (or EEA), related for example to pharmacovigilance, batch release etc.

Marketing authorisation holders may be required to adapt processes and to consider changes to the terms of the marketing authorisation in order to ensure its continuous validity and exploitation, once the United Kingdom has left the Union.

Marketing authorisation holders will need to act sufficiently in advance to avoid any impact on the continuous supply of medicines for human and veterinary use within the European Union.

In particular, the Commission and the European Medicines Agency expect marketing authorisation holders to prepare and proactively screen authorisations they hold for the need for any changes. The necessary transfer or variation requests will need to be

[1] Negotiations are ongoing with the United Kingdom with a view to reaching a withdrawal agreement.

[2] Furthermore, in accordance with Article 50(3) of the Treaty on European Union, the European Council, in agreement with the United Kingdom, may unanimously decide that the Treaties cease to apply at a later date.

[3] A third country is a country not member of the EU.

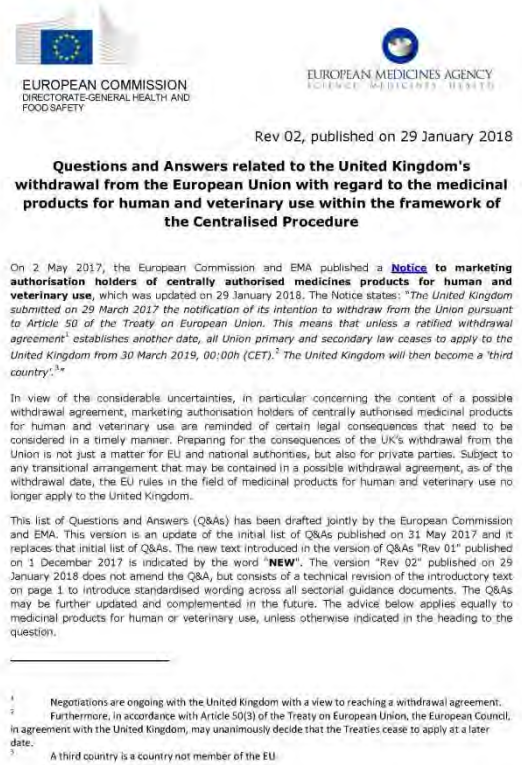
Operational preparedness (2/3)

Questions and Answers Document (Q&As) published jointly by EMA & EC

Provides a **legal interpretation** of principles to be applied in a consistent manner across the pharmaceutical network (human and veterinary) and across sectors

Corresponding guidance for MRP/DCP has been published in parallel by CMDh/CMDv

Several updates since the initial version in May 2017



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Rev 02, published on 29 January 2018

Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the Centralised Procedure

On 2 May 2017, the European Commission and EMA published a **Notice to marketing authorisation holders of centrally authorised medicines products for human and veterinary use**, which was updated on 29 January 2018. The Notice states: "*The United Kingdom submitted on 29 March 2017 the notification of its intention to withdraw from the Union pursuant to Article 50 of the Treaty on European Union. This means that unless a ratified withdrawal agreement[1] establishes another date, all Union primary and secondary law ceases to apply to the United Kingdom from 30 March 2019, 00:00h (CET).[2] The United Kingdom will then become a 'third country'.[3]*"

In view of the considerable uncertainties, in particular concerning the content of a possible withdrawal agreement, marketing authorisation holders of centrally authorised medicinal products for human and veterinary use are reminded of certain legal consequences that need to be considered in a timely manner. Preparing for the consequences of the UK's withdrawal from the Union is not just a matter for EU and national authorities, but also for private parties. Subject to any transitional arrangement that may be contained in a possible withdrawal agreement, as of the withdrawal date, the EU rules in the field of medicinal products for human and veterinary use no longer apply to the United Kingdom.

This list of Questions and Answers (Q&As) has been drafted jointly by the European Commission and EMA. This version is an update of the initial list of Q&As published on 31 May 2017 and it replaces that initial list of Q&As. The new text introduced in the version of Q&As "Rev 01" published on 1 December 2017 is indicated by the word "**NEW**". The version "Rev 02" published on 29 January 2018 does not amend the Q&A, but consists of a technical revision of the introductory text on page 1 to introduce standardised wording across all sectorial guidance documents. The Q&As may be further updated and complemented in the future. The advice below applies equally to medicinal products for human or veterinary use, unless otherwise indicated in the heading to the question.

[1] Negotiations are ongoing with the United Kingdom with a view to reaching a withdrawal agreement.
[2] Furthermore, in accordance with Article 50(3) of the Treaty on European Union, the European Council, in agreement with the United Kingdom, may unanimously decide that the Treaties cease to apply at a later date.
[3] A third country is a country not member of the EU.

Operational preparedness (3/3)

EMA Procedural Guidance provides more practical guidance and complements the EC-EMA Q&A.

Covers submission of applications for changes and related fees in centralised procedure

Covers both human and veterinary medicinal products

Aimed at, where possible, a simplified approach nevertheless respecting legal requirements.

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29 January 2018
EMA/478309/2017 Rev. 1[1]
Human Medicines Evaluation Division
Veterinary Medicines Division

Practical guidance for procedures related to Brexit for medicinal products for human and veterinary use within the framework of the centralised procedure

On 2 May 2017, the European Commission and EMA published a **Notice** to marketing authorisation holders (MAHs) of centrally authorised medicines products for human and veterinary use, stating: *"The United Kingdom submitted on 29 March 2017 the notification of its intention to withdraw from the Union pursuant to Article 50 of the Treaty on European Union. This means that unless the withdrawal agreement establishes another date or the period is extended by the European Council in accordance with Article 50(3) of the Treaty on European Union, all Union primary and secondary law ceases to apply to the United Kingdom from 30 March 2019, 00:00h (CET). The United Kingdom will then become a 'third country'."*

In view of the considerable uncertainties, in particular concerning the content of a possible withdrawal agreement, MAHs of centrally authorised medicinal products for human and veterinary use are reminded of certain legal consequences that need to be considered in a timely manner. Preparing for the consequences of the UK's withdrawal from the Union is a significant matter for European and national administrations, and also equally important for private parties. Subject to any transitional arrangement that may be contained in a possible withdrawal agreement, as of the withdrawal date, the EU rules in the field of medicinal products for human and veterinary use no longer apply to the United Kingdom.

In order to consider the necessary changes, a list of Questions and Answers (Q&As) related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the Centralised Procedure drafted jointly by the European Commission and EMA is available on the EMA website.

The below Practical Guidance has been developed taking into consideration that as of 30 March 2019 the United Kingdom will become a third country. As a result, MAHs and applicants of centrally authorised products for human or veterinary use need to ensure that the necessary changes are made by the 30 March 2019, unless indicated otherwise in the guidance below.

This document complements the EC-EMA Q&A to provide procedural and practical guidance regarding submission of changes and related fees.

[1] Revision 1 does not amend the guidance, but revises only the introductory text on this page, aligning it with the amended introductory text in corresponding EC-EMA Q&A.

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Methodology: Redistribution of the UK Centralised H/V product Portfolio

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- The redistribution follows a multifaceted approach and takes into account the diverse expertise in the European medicines regulatory network and the workload associated with each medicine
- Building on existing knowledge, medicines are allocated to the current co-rapporteur or to the peer reviewer involved in the initial marketing authorisation application
- Allocation is also based on current expertise with a class of medicines (ATC code);
- Clusters of products with the same INN and belonging to the same MAH are allocated to a single rapporteur in order to facilitate review of post-authorisation procedures.

Implementation: Redistribution of the UK portfolio

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EMA Working Group has developed a methodology for the redistribution of the work currently carried out by the UK,

The methodology was endorsed by the EMA Management Board at its December 2017 meeting,

The **first step** of the implementation started in Q1 2018 and was finalised in April 2018,

The new (Co)-Rapporteurships has been communicated to the MAHs by 30 April 2018,

To support knowledge transfer, EMA will provide a knowledge transfer package to the new (Co)-Rapporteurs.

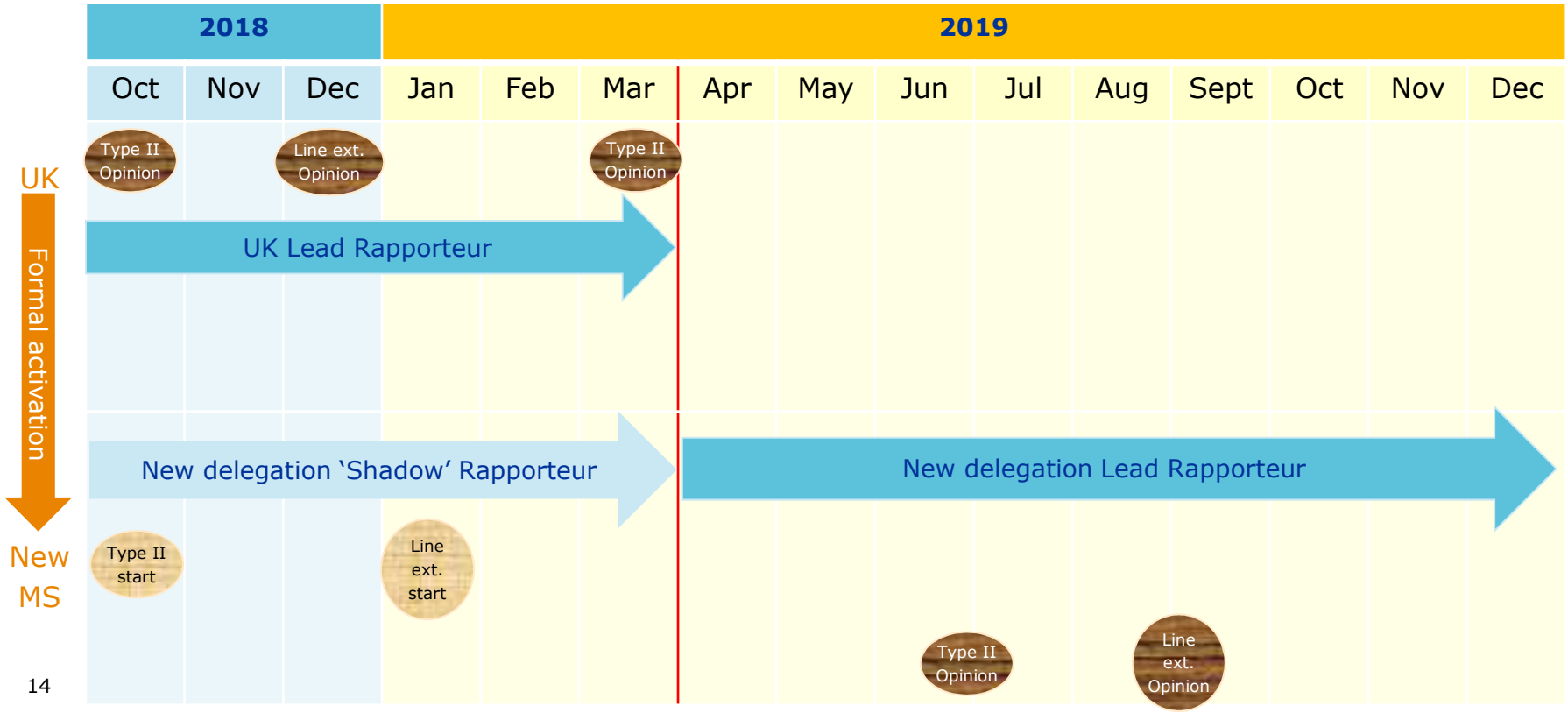
Implementation of the redistribution of the UK centrally authorised products portfolio (1/3)

- The redistribution of the UK product portfolio was finalised on 4 April 2018 and the new (Co)-Rapporteurships were communicated to the MAHs on 30 April 2018
- To support knowledge transfer, a stepwise approach is applied
  - EMA to provide the new (Co)-Rapporteurs with a knowledge transfer package
  - Option for the new (Co)-Rapporteurs to liaise with the MAHs in order to gather further information on the allocated medicinal products, including forecast of post-authorisation procedures
  - If any outstanding issues remain, new (Co)-Rapporteur to liaise with MHRA/VMD

Implementation of the redistribution of the UK centrally authorised products portfolio (2/3)

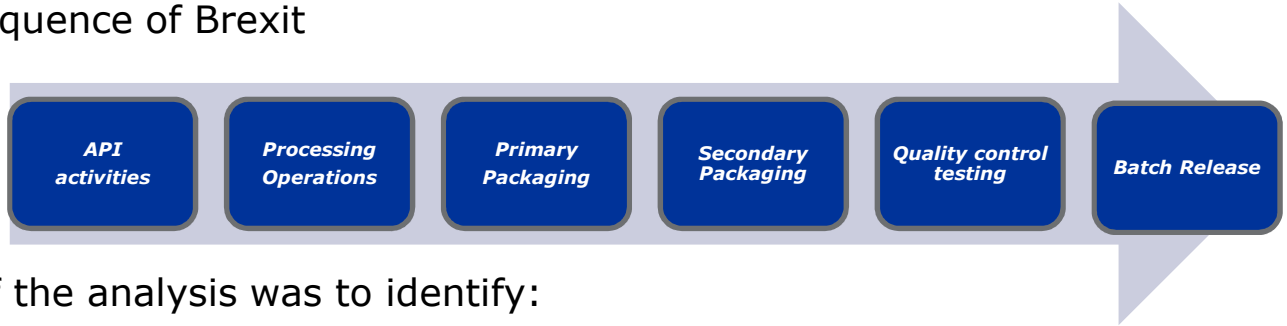
- The new (Co)-Rapporteurs will only take full responsibility for the re-allocated medicinal products as of 30 March 2019 when the UK withdraws from the Union and becomes a third country. However, they may be required to handle, from Q4 2018 onwards, post-authorisation procedures that are likely to be finalised after 29 March 2019

Implementation of the redistribution of the UK centrally authorised products portfolio (3/3)



Update on EMA work on the potential impact of Brexit on the supply of CAPs (1/2)

- EMA has undertaken an analysis of the potential supply issues due to the required changes as a consequence of Brexit



- The aim of the analysis was to identify:
  - The manufacturing operations currently located in the UK for CAPs
  - The type of manufacturing operations affected by Brexit
  - The potential risk of disruption as a number of these operations will need to be relocated to the EEA

Update on EMA work on the potential impact of Brexit on the supply of CAPs (2/2)

- EMA also launched a survey to MAHs on 23 January with a deadline for response by 9 February. The survey has received a response rate of 90%
- The aim of the survey was to complement the EMA analysis by further identifying the CAPs potentially at risk of supply shortages and obtaining information on the timelines for submission of the necessary regulatory changes
- The survey was sent to MAHs of 690 CAPs (657 human and 33 veterinary products) who are located in the UK or who have quality control, batch release and/or import/manufacturing sites or a QPPV or pharmacovigilance system master file (PSMF) in the UK
- The responses to the EMA survey have been received and analysed and a high level summary will be published in due course

Update on EMA work on the potential impact of Brexit on the supply of medicines: Next steps

- EMA will liaise with MAHs that have batch release, quality control and/or importation sites located in the UK only and that have indicated in the survey that they do not plan to submit changes required before 30 March 2019 or have not responded to the survey, as this could potentially lead to supply disruptions
- Following feed-back from the MAHs further reflection is needed how to best address identified (temporary) supply problems (link with the work undertaken in the joint EMA/HMA Task Force)
- EMA will monitor and track the submissions of required changes for the affected CAPs
- Workload analysis will be used to ensure an adequate resource planning within EMA and the Network, where relevant

EMA’s Business Continuity Plan

EMA in a Brexit preparedness business continuity scenario

- Challenge for EMA is to strike the right balance between achieving:
  - A **short to mid-term objective** in terms of ensuring continuity of operation by adequately addressing an unprecedented staff loss
  - A **longer term objective** (as per the EMA mission statement) in terms of continuing to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health
- EMA aims to strive for both objectives, acknowledging that this is fully dependent on the ultimately available human resources

EMA Brexit Preparedness BCP in a nutshell

- To operate the EMA Brexit Preparedness BCP, EMA activities have been grouped in **3 categories** which can broadly be described as follows:

Category	Activities covered
Category 1 (highest priority) activities	Core scientific activities and supporting IT applications, corporate/communication/other IT activities necessary for EMA's operation, legal obligations put on EMA
Category 2 (medium priority) activities	Either strategic activities or other core activities, sub-classified into 2A and 2B
Category 3 (lowest priority) activities	Non-strategic activities such as governance and support activities

EMA Brexit Preparedness BCP in a nutshell

- Activities are **temporarily suspended or scaled back** (in the latter case the reduced output should continue to the same high standards although it may result in a reduction of volume or a delay in the time to achieve the agreed deliverables)
- A **stepwise implementation** has been put in place
  - First targeting category 3 (the lowest priority) activities
  - Followed by category 2 (medium priority) activities
  - When needed, targeting category 1 (the highest priority) activities

Current environment as regards the available EMA human resources

- Situation in terms of staff retention is difficult to predict, staff surveys have been run to estimate numbers that will relocate
- Plan to address **staff loss** by:
  - Speeding-up the **recruitment of new staff**
  - Continuing the discussions with the EU Budgetary Authorities as regards the **requested additional resource**
  - Reviewing **approach towards short-term contract staff** to take due account of the different situation in the Netherlands
- For its **legal obligations** EMA will prioritise its resources to meet such obligations in compliance with the legal deadlines and the expected quality of the output, in a worst-case scenario introducing a further priority to focus only on the activities legally required relating to the authorisation, supervision and maintenance of medicines

Next phases of the BCP: Principles and methodology

- Management Board in June endorsed **next phase of BCP**
- This will result in a **further re-prioritisation** of EMA's activities throughout 2019 to maintain as far as possible the Agency's core activities in relation to the evaluation, maintenance and supervision of medicines.
- Will come into effect on **1 October 2018** to enable staff to be mobilised to cover critical functions where needed. It will be monitored and the need for further reduction of activities will be reviewed on an ongoing basis. More information will be provided in due course.

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Why do we need a new approach to innovation?

Gatekeeper or enabler?

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Regulatory Agencies: a changing role?

- From treatment to potential cure
- From treatment to prevention
- From anatomical to molecular (and beyond?) driven diseases taxonomy
- From RCT to **?**CT (RWE, AI)
- From drug prescription to therapy delivery
- From risk/benefit to clinical added value
- From approval to access

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New role for regulators

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*"Regulators need to take a **new role** at the **crossroads between science and national healthcare systems**: in order to promote public health in the current environment, they can no longer be just a gateway between those two worlds; they need to become a catalyst, an enabler for science to be translated into patient-centred healthcare and fit in the reality of healthcare systems."*

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Regulators as **enablers** between science and healthcare systems

Scanning the horizon

Identifying the main gaps

Connecting various stakeholders together, in order to bridge gaps

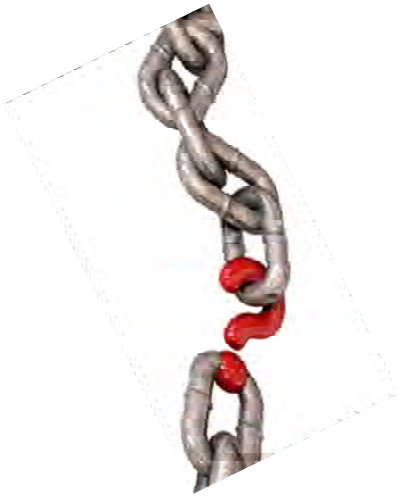
"Evidence by design" – facilitating patient access through data that serves the entire decision-making chain

Starting point: Decision makers (regulators, HTAs and payers)

- answer different questions
- have different requirements in terms of evidence

Aim: Alignment of the design of the evidence generation plan

1. Planned studies (populations / comparators / design of trial / endpoints)
2. Requirements for post-licensing evidence generation (e.g. registries)



Expectation: Optimised evidence generation plan ➔ Improve access for patients

Can Parallel Advice help?

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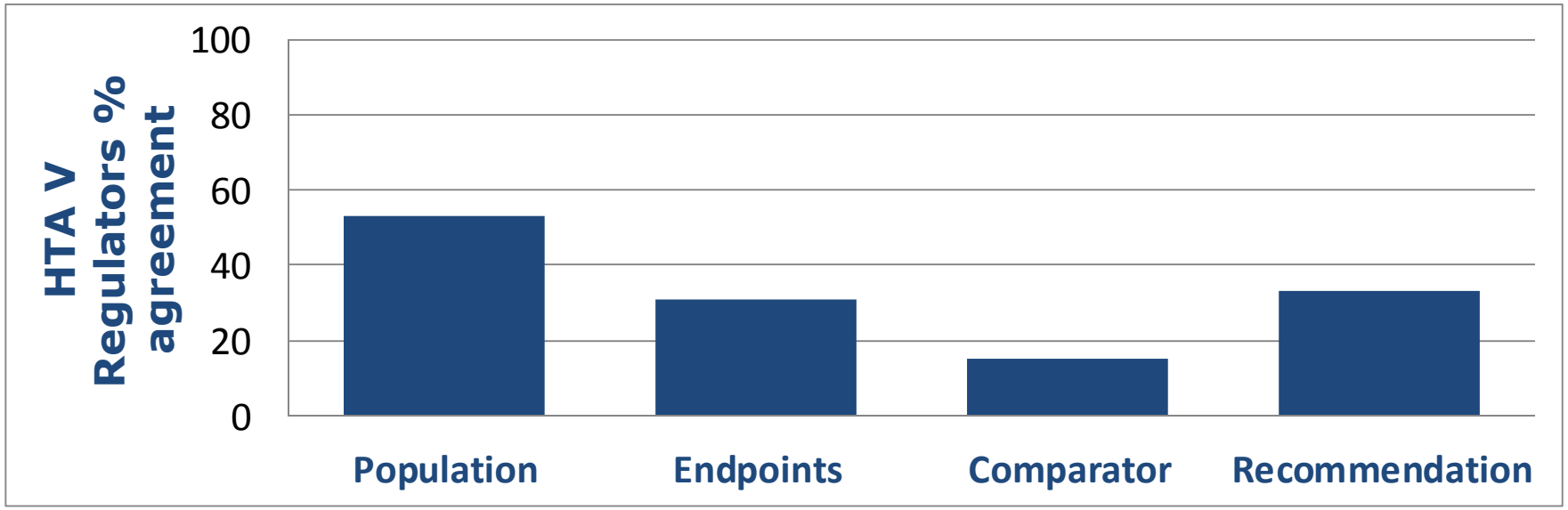

Can Parallel Advice help?

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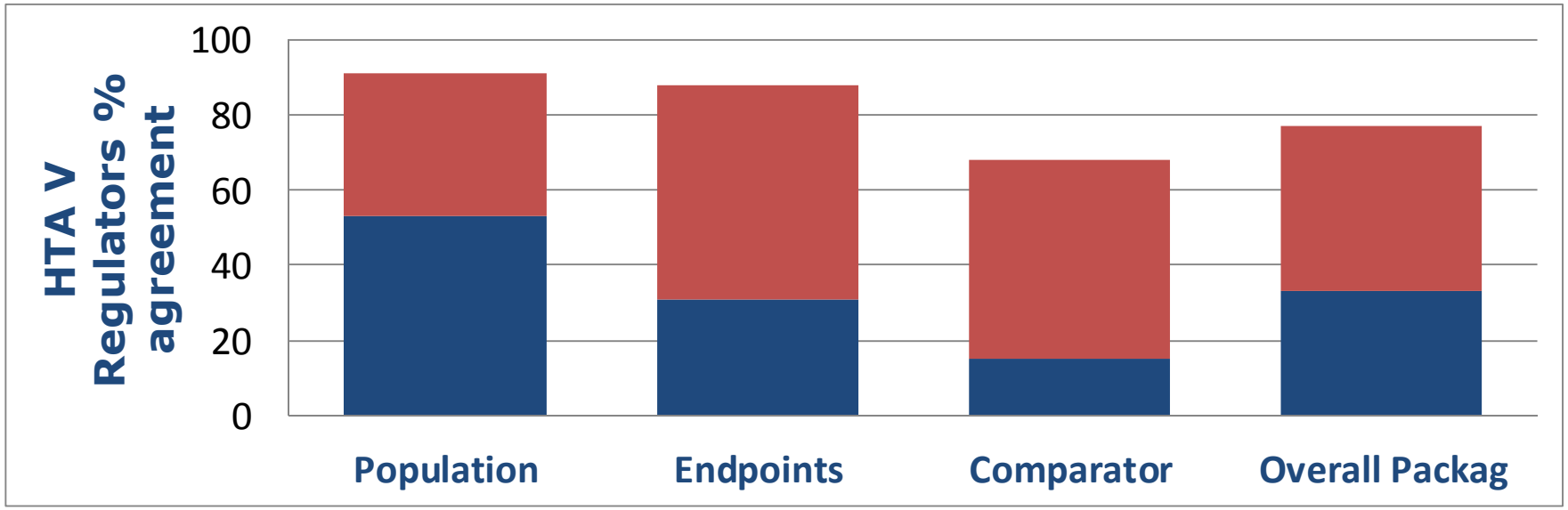
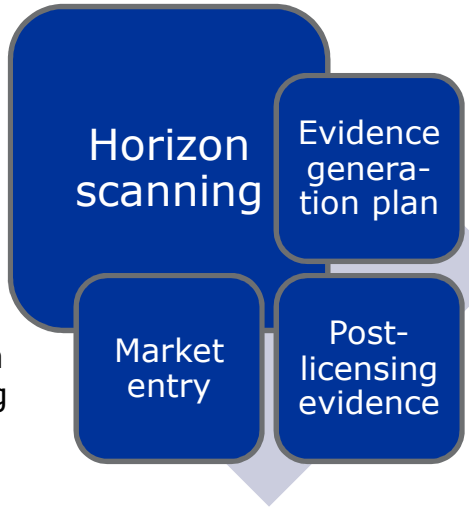


How can players along the technology lifecycle work together to support the introduction of innovative health technologies

- Collaboration on topic identification and prioritisation by various players
- Early flag of innovation that would benefit from closer engagement across decision makers



e.g. parallel consultation (scientific advice) involving various decision-makers to ensure evidence generation meets different needs

e.g. readiness for subsequent decision making in a timely manner, respecting different remits

e.g. preparedness of patient registries to collect relevant information in a robust manner

Collaboration between decision makers on Horizon Scanning activities can enable better preparedness of the healthcare systems for development and introduction of innovation.

Closing remarks

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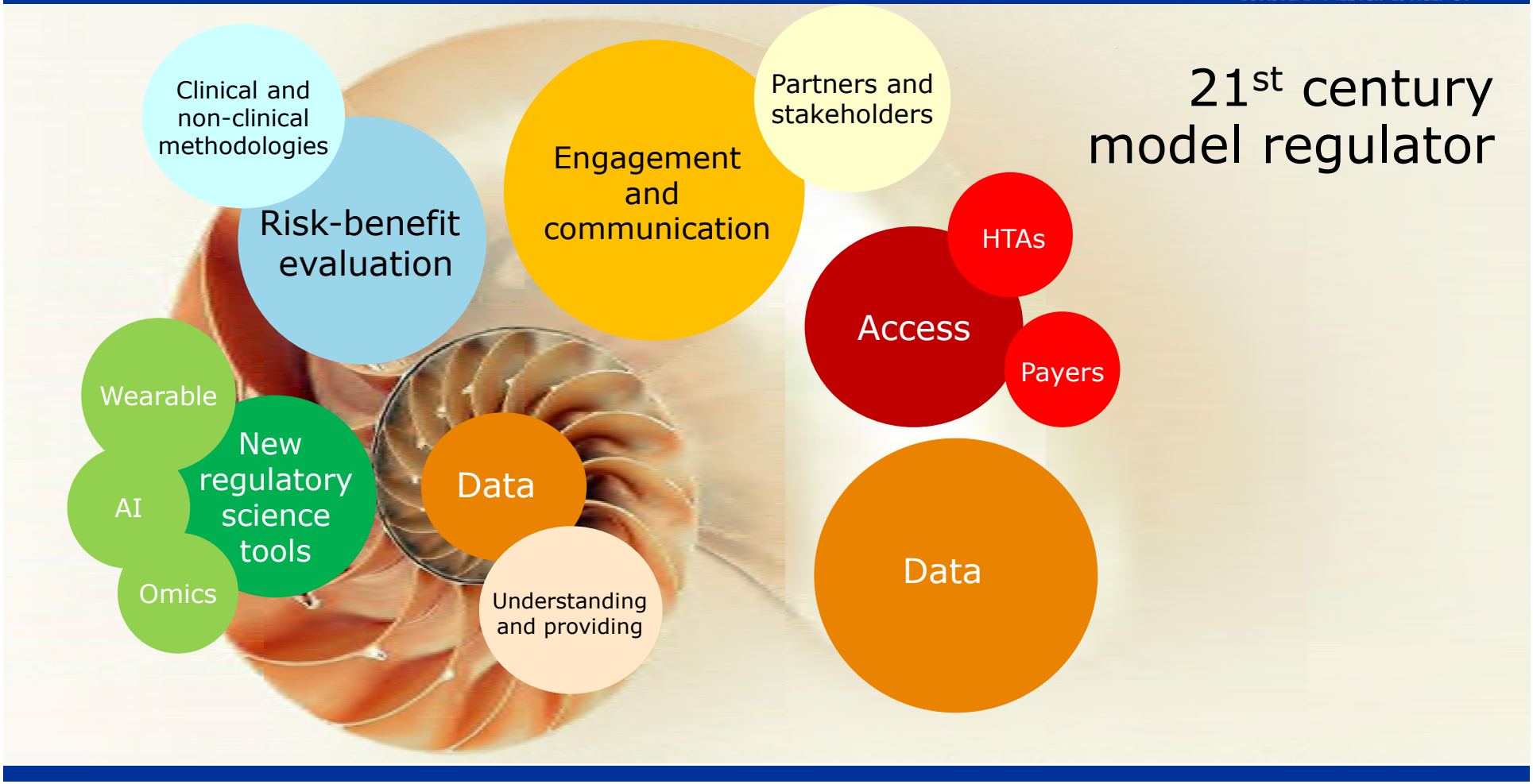

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Thank you for your attention

Further information

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