Impact of Brexit – an industry perspective

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21st DGRA Annual Congress
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The story continues…

- Industry Readiness for Brexit
- Reflection on Current State of Play
- Future Challenges
- UK Perspective - New Opportunities and Risks
- Concluding Remarks

External Voice – Priority of Actions Required

EU urged to safeguard post-Brexit medical supplies from UK

Health

EU urged to safeguard post-Brexit medical supplies from UK

Pharma chiefs see 'lack of focus' in protecting sector after Britain's departure

© Bloomberg

Sarah Neville in London YESTERDAY

European pharmaceutical leaders have called on EU member states to do more to safeguard the supply of medicines post-Brexit, suggesting they had shown a "lack of focus" by prioritising the protection of industries such as fisheries and finance.

The European Federation of Pharmaceutical Industries and Associations called on European leaders to allow medicines and medical devices quality-tested in the UK to be recognised in Europe, and to prioritise the passage of medicines and pharmaceutical ingredients at borders.

March 19th 2019

European pharmaceutical leaders have called on EU member states to do more to safeguard the supply of medicines post-Brexit, suggesting they had shown a ***"lack of focus"*** by prioritising the protection of industries such as fisheries and finance.

FT FINANCIAL TIMES

"…we have been concerned by a certain lack of focus, outside of our industry, on protecting medicines supply."

…***"positive action"*** by the EU in areas such as fisheries, transport and financial services but more needed to be done to protect public health and ensure drugs continued to reach patients

[industry preparations] ***"in what is one of the biggest supply-chain logistics challenges our industry and our health service partners have ever faced"***

Steps should be taken ***"to prioritise medicines, active pharmaceutical ingredients, raw and clinical trial materials"…***

Bayer`s Readiness for Brexit today

Bayer was and continues to remain ready for Brexit

NB = Notified Body
WDLs = Wholesales Dealers and importation Licence

Regulatory Oversight

- Portfolio review started Q1 2017
- EMA pipeline meeting 2018
- Baseline dossier preparation for CP products
- MHRA Portal training/ registration and inflight MAA meeting
- EU QPPV / UK alignment

Portfolio Review

- CP Rapporteur-ships reassigned
- DCP procedures with UK RMS transferred
- MAH transfers completed (MT)
- New SKUs for IE/MT developed
- Notified Body move to NL: Artwork amended

Import & Export

- Additional UK warehousing secured
- 3 months additional stock imported into UK
- UK WDLs amended to prepare for UK Responsible Person
- New UK stock management systems

Clinical Trials

- Review of UK studies conducted – critical studies closely managed (e.g. radioactive materials)
- deletion of QC testing in UK for IMPs
- UK storage site warehousing with QP oversight registered
- Additional stock ready for dispatch to site or warehouse

EFPIA Brexit Survey – Readiness as of March

Summary

95% Companies putting in place Brexit business continuity plans

Financial spend and investments made by companies on business continuity plans — **Up to €100M** (per company)

Procedures

45% Companies with ongoing submissions and regulatory procedures with regulatory agencies

Mitigations

Companies with products having post March 29th approval timelines for Brexit-related changes — **50%**

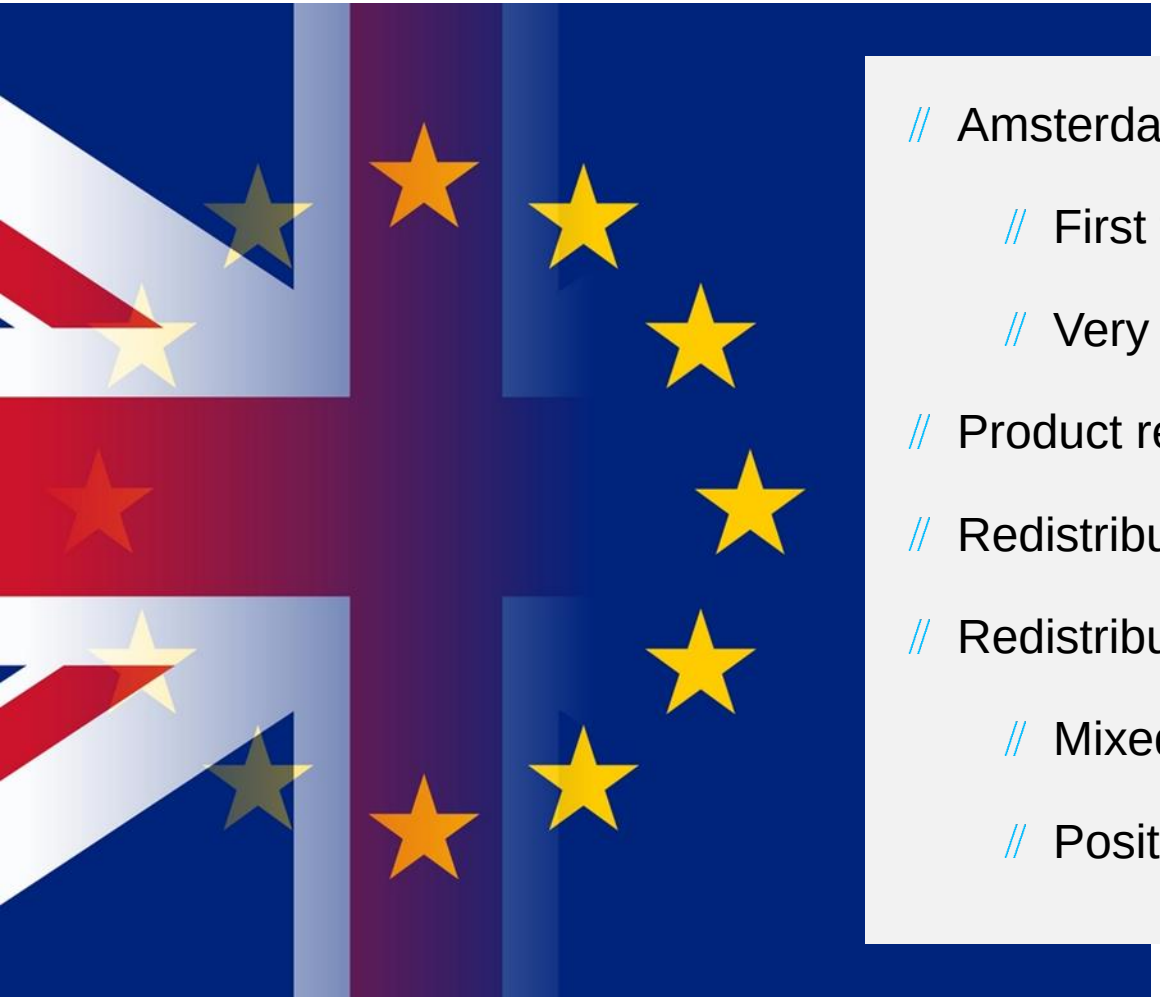
95% Companies with supply and other mitigations in place where post March 29th approval timelines exist

(95% of the above 50% of companies)

%'s shown represent percentage of companies

Survey responses n = 38 (survey as of March 12th 2019)

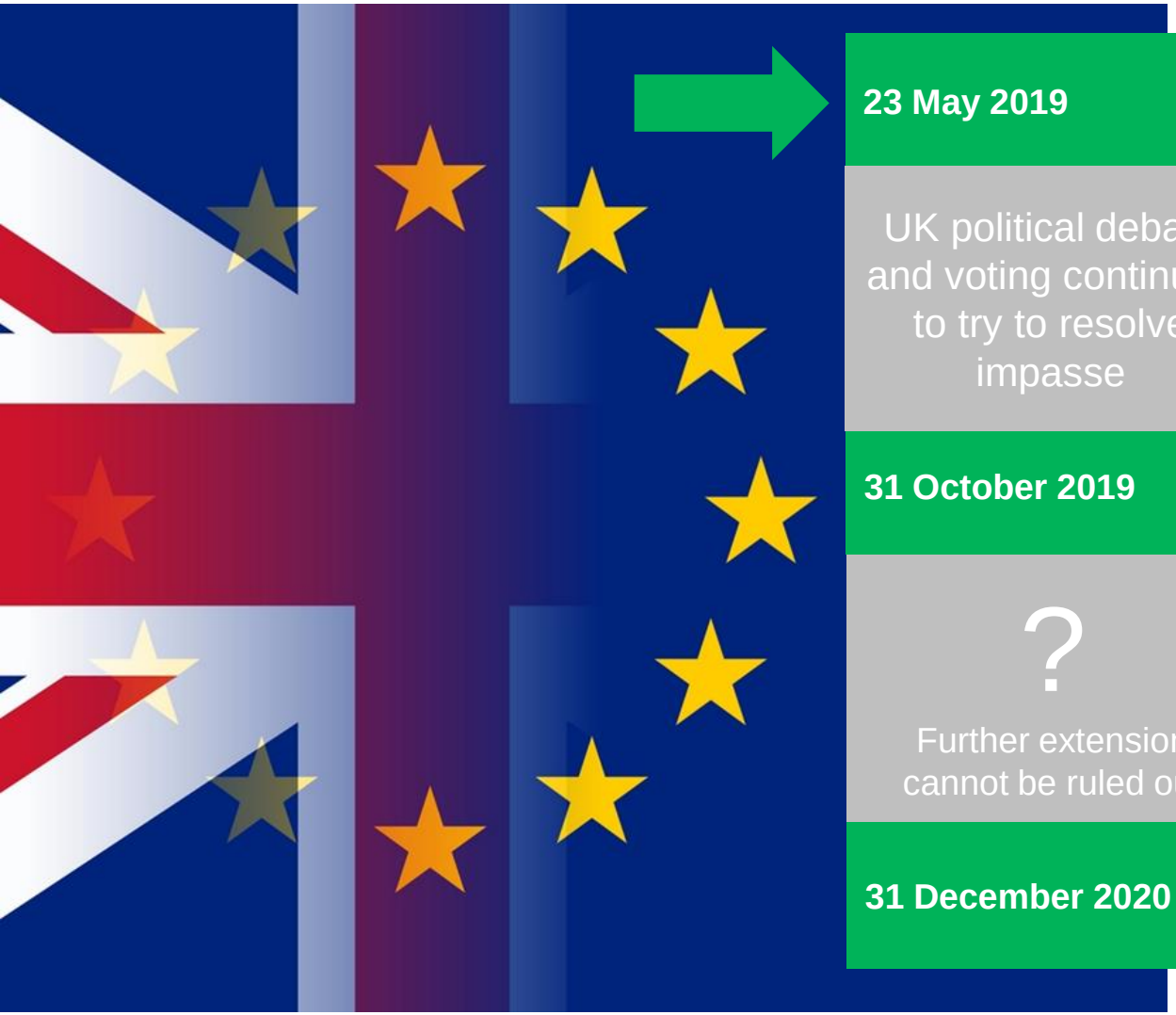
Regulatory Activities – Reflection on Current State of Play



- Amsterdam is welcomed as new home for EMA
  - First feedback on EMA interim building/meeting facilities
  - Very positive to see 75% of staff seems to stay on board
- Product related work in general ongoing without disruption
- Redistribution of CP work to other agencies
- Redistribution of MRP/DCP work from MHRA
  - Mixed industry feedback
  - Positive experience within Bayer

Readiness for Brexit – is uncertainty our future?

Uncertainty will remain – need to mitigate portfolios for a no-deal Brexit



23 May 2019

UK participates in EU EP Elections and avoids no deal Brexit on 1st June 2019

UK political debate and voting continues to try to resolve impasse

31 October 2019

?

Further extension cannot be ruled out

31 December 2020

New EU budget: acceptability of continued uncertainty to EU ?

- Deal
  - Mrs May's deal
  - Amendment?
  - Art 50 further extension
- No deal
  - No deal Brexit
  - Revoke Brexit
- Political Change
  - General election
  - Second Referendum

- UK parliamentary impasse will have to be broken
- If agreement on deal can be reached and ratified, earlier exit into transition period possible
- Currently all possible options remain on the table including
  - UK not exiting
  - UK exiting without a deal
  - UK ratifying existing deal

What future should we plan for?

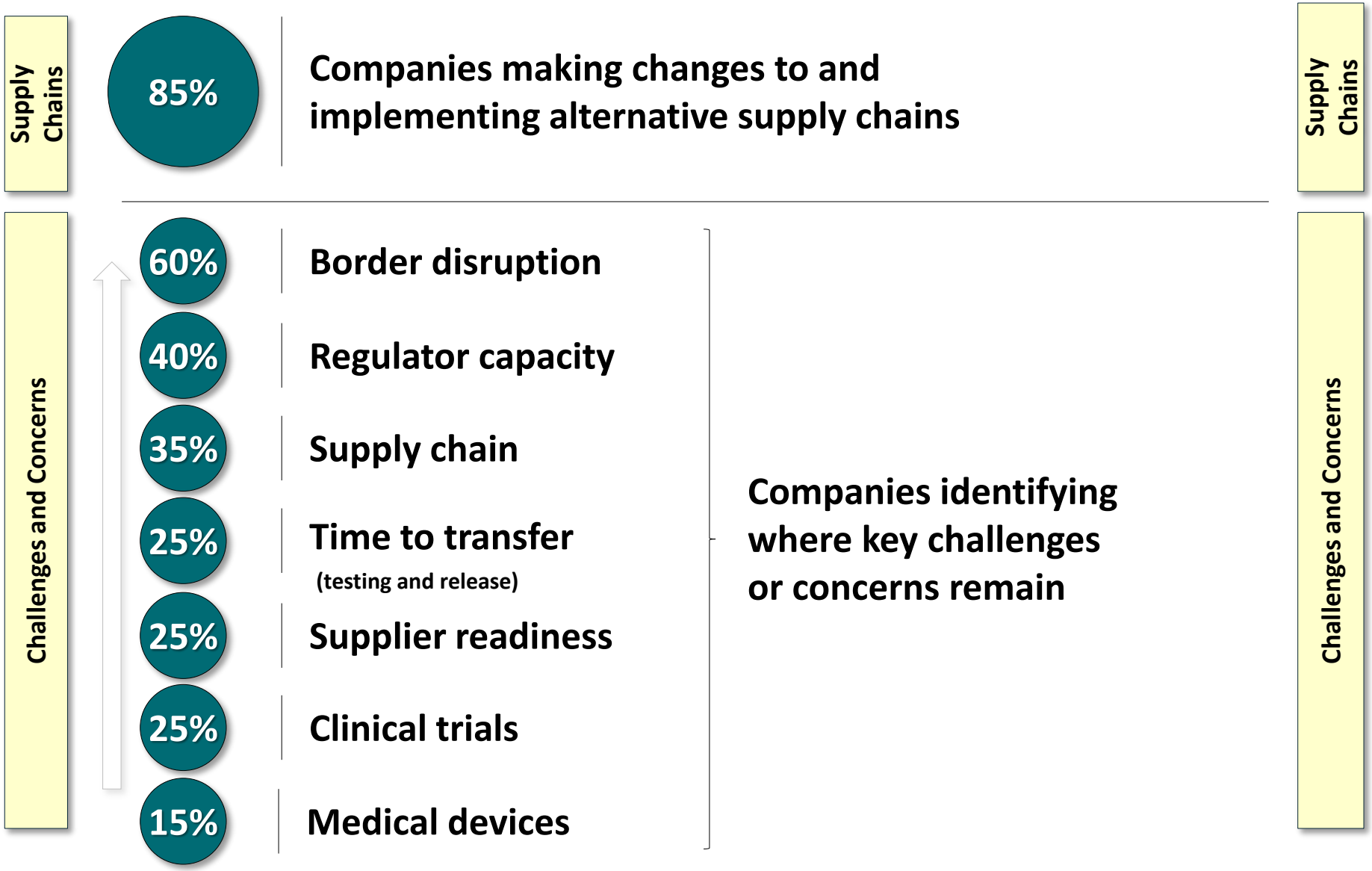
Bayer plans for both a deal and no-deal Brexit

- Preferred option remains a Deal:
  - What will long-term MHRA / EU Network relationship be?
  - Aim for MHRA to be an **active** member of the EU Network
- No deal scenario results in MHRA sovereign regulator:
  - MHRA issued technical guidance on new processes
    - Targeted assessment based on CHMP opinion (67 days)
    - Accelerated assessment and faster national routes (<150 days)
    - Rolling review in development to better manage risk
  - MHRA advice on “in flight” submissions to aid transition
  - Emphasis is on continued alignment with EU, simplified processes and consultation with Industry

Regulatory Activities – Future Challenges for Industry

- Ongoing applications for Innovative products
  - Still unclear if and when UK MHRA would start own assessment
- EMA back to standard operations by January 2020
  - 25% new talents, new hires => takes some time to train and learn
  - Deletion of Procedural Manager role - leaves companies to rely fully on one PTL – high responsibility, need for continuous availability
- EU Regulatory System – some delays in Assessment Reports observed => less time for applicant, no flexibility on industry timelines

EFPIA Brexit Survey – Future Challenges



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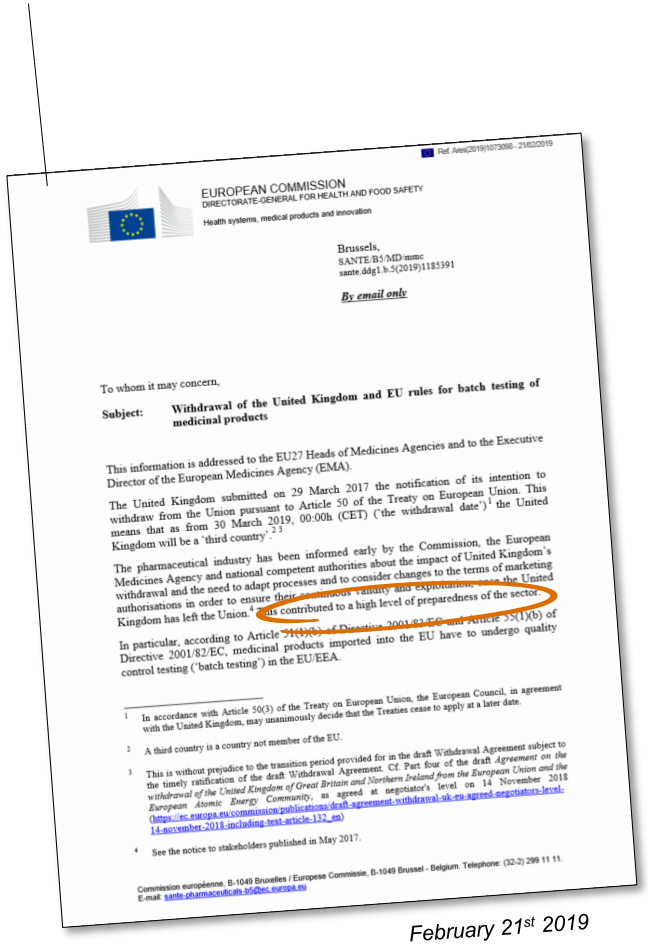
Quality control test: Flexibility acknowledged by EU Commission

Letter from European Commission DG Sante to European Medicines Agency (EMA) and EU-27 Heads of Medicines Agencies (HMA). Temporary exemption from batch testing requirements now available.



EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY
Health systems, medical products and innovation

Brussels,
SANTE/B5/MD/mmc
sante.ddg1.b.5(2019)1185391

By email only

To whom it may concern,

Subject: **Withdrawal of the United Kingdom and EU rules for batch testing of medicinal products**

This information is addressed to the EU27 Heads of Medicines Agencies and to the Executive Director of the European Medicines Agency (EMA).

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 as from 30 March 2019, 00:00h (CET) ('the withdrawal date')[1] the United Kingdom will be a 'third country'.[2,3]

The pharmaceutical industry has been informed early by the Commission, the European Medicines Agency and national competent authorities about the impact of United Kingdom's withdrawal and the need to adapt processes and to consider changes to the terms of marketing authorisations in order to ensure their continuous validity and exploitation, once the United Kingdom has left the Union.[4] This contributed to a high level of preparedness of the sector.

In particular, according to Article 51(1)(c) of Directive 2001/83/EC and Article 55(1)(b) of Directive 2001/82/EC, medicinal products imported into the EU have to undergo quality control testing ('batch testing') in the EU/EEA.

1 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.

2 A third country is a country not member of the EU.

3 This is without prejudice to the transition period provided for in the draft Withdrawal Agreement subject to the timely ratification of the draft Withdrawal Agreement. Cf. Part four of the draft *Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community*, as agreed at negotiator's level on 14 November 2018 (https://ec.europa.eu/commission/publications/draft-agreement-withdrawal-uk-eu-agreed-negotiators-level-14-november-2018-including-text-article-132_en)

4 See the notice to stakeholders published in May 2017.

Commission européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belgium. Telephone: (32-2) 299 11 11.
E-mail: sante-pharmaceuticals-b5@ec.europa.eu

February 21st 2019

…a high level of preparedness of the sector.

↓

However, … there may be objective reasons beyond control of the marketing authorisation holders that may prevent timely transfer … by the withdrawal date.

↓

(conditions apply)

…competent authorities may allow marketing authorisation holders, for a limited period of time, as a justified case, to rely on quality control testing performed in the United Kingdom…

Medical Devices: Patchwork of policies within the internal market

The Commission has not yet developed an EU-wide contingency plan for ensuring the supply of medtech products certified by U.K. notified bodies

Changes to EU NBs and CE labeling updates ongoing

April 2019

A coordinated approach in the area of medicines and medical devices in case of a 'no-deal' scenario.

The medical sector: A priority of the European Commission's preparedness work from the start.

The EU is prepared for a 'no-deal' scenario. EU legislation will allow us to mitigate the impact of such a scenario.

What have we done?

The Commission has called on stakeholders to prepare for a possible 'no-deal' scenario as early as May 2017. Since then, several preparedness notices and guidance documents have been issued on medicines and medical devices. These areas were also carefully assessed in the **Commission Communications of July 2018 and November 2018**.

Economic operators are primarily responsible for taking the necessary measures to ensure their continued compliance with EU legislation. This is also the best way to ensure the continued safety and reliability of medicinal and medical device products in the EU and to avoid supply shortages in the case of 'no-deal'. In addition, the following measures have so far been taken:

Medicines:

- The Commission, the **European Medicines Agency (EMA)** and national authorities have been able to **facilitate the transfer of marketing authorisations for medicines from one UK rapporteur competent authority to another.**
- Notices, Questions and Answers, and Guidance documents on preparedness have been published by the Commission as early as May 2017. They have been regularly updated.
- **The European Medicines Agency has been relocated from London to Amsterdam**.
- The Commission has issued **guidance** to EU27 Member States **on the timely transfer of batch testing sites from the UK to the EU27**.
- **A network has been put in place** bringing together the Commission, national regulators and the European Medicines Agency **to monitor the situation, address any problems of supply and inform patients and doctors** accordingly.

Medical Devices:

- The Commission and Member States have been **closely monitoring the progress of the transfers of certificates from UK notified bodies to EU27 notified bodies** (i.e. private entities designated by Member State competent authorities).
- In justified cases where derogations are granted, **UK certificate holders will be allowed to continue placing their products on the EU27 market** for a limited period of time. The Commission has issued guidance to EU27 Member States.

Managing potential shortages

The risk of shortages of medicines and of critical medical devices in case of a 'no-deal' scenario has been significantly mitigated. No contingency action has been identified as necessary.

Medicine

- National regulators, the European Medicines Agency and the Commission will monitor the situation, address problems and inform patients and doctors appropriately. This structure is built on existing strategies to deal with incidents and shortages.

Medical devices

- The Commission is working closely with EU27 Member States in the context of the Medical Device Coordination Group and the Competent Authority for Medical Devices Network to monitor the progress of certificate transfers and to identify critical medical devices that may be at risk of shortages.
- The Commission will coordinate and ensure transparency with regard to derogations for medical devices certified by a UK notified body. This will ensure a coherent approach and avoid any fragmentation of the internal market.

UK Perspective – New Opportunities and Risks from Brexit

- Opportunities:
  - MHRA/NICE **joint assessment**
  - MHRA role on **global stage**,
  - Co-operation with other NCAs, and groups (ICH, ICMRA IMDRF…):
  - Implementation of **innovative access schemes (AAC)** or authorisation schemes (rolling dialogue)
  - ➢ **increased influence**

- Risks depend on outcome and timing:
  - Remaining in EU Network **without significant Assessment Role**
  - **Long transition** period to becoming sovereign Regulator or
  - Sovereign Regulator national routes slowly implemented, long assessment times or unaligned requirements
  - ➢ **loss of expertise** and decreased influence

NICE = National Institute for Health and Care Excellence
ICMRA= International Coalition of Medicines Regulatory Authorities
AAC = Accelerated Access Collaborative

CH = International Conference on Harmonisation
IMDRF = International Medical Device Regulator Forum
CTR = Clinical Trial Regulattion

Concluding remarks

- Industry has prepared for no-deal scenario or is using the extension of Article 50 to complete the necessary work
- EMA / EU Network slowly recovering from consequences of Article 50:
  - Relocation of EMA and move of work to other HA
  - Resources/expertise loss not yet compensated
  - Loss of MHRA still being felt
- Need to end uncertainty and allow MHRA to move forward as either:
  - A sovereign Regulator with its own international standing or
  - As an active contributing part of the future EU Network

OUTLOOK: NOW IS THE TIME TO SHAPE A WORLD CLASS EU REGULATORY SYSTEM

EFPIAs RSC 4e to 2023 Vision	*To drive for an agile, competitive and world-class regulatory system in Europe and beyond that embraces advances in science, technology and medicines, accelerating access to innovative healthcare solutions and optimised patient outcomes.*

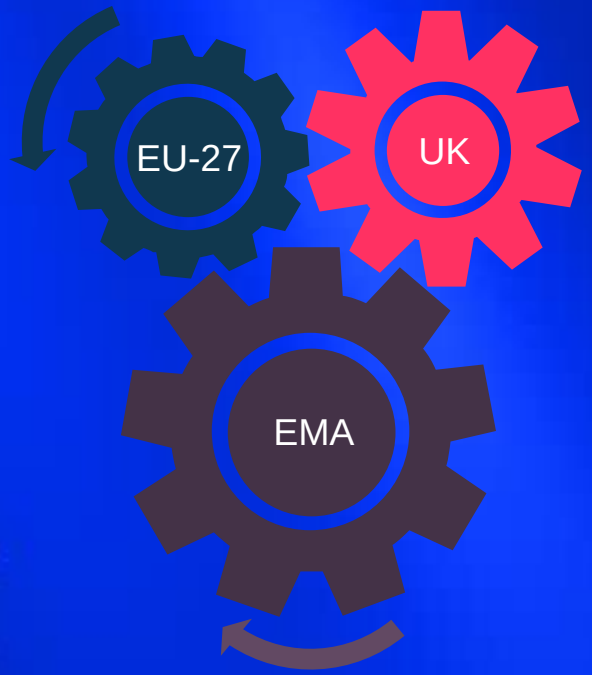
ENSURE
a competitive world-class regulatory system

EVOLVE
the framework for innovation

ELEVATE
multi-stakeholder engagement

EXPAND
global convergence

Time to work together



UK Perspective – Accelerated Access Collaboration

- **Registration:** by Company on HealthTech Connect or UK PharmaScan platforms
- **Time line:** Up to 10 years before availability to NHS
- **Support:** NICE hosts secretariat
- **Products:** medicines, therapeutic, medical technologies, digital, diagnostic
- **Requirements:** evidence of clinical and cost effectiveness, addressing significant unmet need, application to large populations or high budget impact, enabling a novel mode of action or enabling significant changes to the care pathway
- **Support:** dedicated case management offering optimised processes, running processes in parallel and smoother transition between steps in the journey to adoption including:
  - Generation of real world evidence in addition to RCT
  - Potential for flexible and confidential commercial arrangements
  - Pathway transformation funding to drive adoption into the NHS