Brexit

How to be prepared and how we can help

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DEVELOPMENT • REGULATORY • MARKET ACCESS

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Brexit – Art 50 application

- 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.
- As a consequence all European law ceases to apply to the UK from the "withdrawal date" and the UK will become a standalone country (third country) separated from EU legislation and processes.
- Brexit was originally due to happen on 29 March 2019. The deadline was delayed twice. The new deadline has been set for 31 January 2020.
- On 29 October 2019, the European Council agreed to a further extension of the date for the UK's withdrawal from the EU. The extension will last as long as necessary and, in any event, no longer than 31 January 2020.

Withdrawal agreement

- On 19th March 2018, the Draft text of the **Withdrawal agreement** of the UK and Northern Ireland from the European Union and the European Atomic Energy Community was published. The EU and the UK have agreed, at negotiators' level, on the colour-coded text, indicating areas of agreement, disagreement or where further clarifications are needed. **The withdrawal agreement needs to be ratified by both sides.**

- The "**Transition period**", **until 31st December 2020** (inclusive) is part of the Withdrawal agreement. This Withdrawal agreement **is still not agreed upon** ("nothing is agreed before everything is agreed") and not yet ratified by the concerned parties.

EMA calls for preparedness

- The Commission, EMA, national competent authorities along with the MAH have a **collective responsibility to ensure preparedness of the system** so that we can continue to deliver on the expectations and needs of patients for continuous supply of medicines

- In view of the considerable uncertainties, **industry should not rely on the "transition period"**. Even if there is commitment to reaching an agreement on the UK's orderly withdrawal, this should not dispense from ensuring 'preparedness'. The Withdrawal agreement needs to be ratified by the UK and the EU by the end of January 2020. Therefore preparedness is a matter of today.

EMA & CMDh recommendation

CMDh and EMA are continuously publishing notice to MAH's.

"..Marketing Authorisation Holders (MAH) will need to **act sufficiently** in advance to avoid any impact on the continuous supply of medicines for human use within the European Union.

In particular, the CMDh expects marketing authorisation holders to prepare and proactively **screen authorisations** they hold for the need for any changes..."

Do a risk evaluation and take actions in a proactive manner!

Risk Evaluation

- It can't be foreseen whether the negotiation and transition agreements will cover a more suitable situation than third country status nor whether they will be finished within the given time period.

- A risk evaluation should be prepared based on the worst case scenario i.e. UK will become a third country as of 31 January 2020.

Main topics which will be impacted

- **UK is/will be RMS** – For medicinal products authorized/planned to be submitted via MRP/DCP - need to change the RMS to an agency of a member state of the EU (EEA).
- **Marketing Authorisation Holdership** - MAHs located in the UK will need to transfer their EU MAs to a holder established in the EU (EEA). And for UK license a UK located MAH will be needed.
- **Batch testing and release site(s) in the UK** – The MAH will need to transfer its current UK batch testing and release site(s) to a location established in the EU (EEA) whilst for UK license a site in UK is required.
- **PV - PSMF & QPPV location** must be inside EU/EEA for EU27 whilst for UK PV - PSMF & QPPV location must be in UK
- **Influence on Generic/Hybrid application types** – RefMP and BE studies

UK as Rapporteur/Co-Rapporteur or RMS

UK can't act as Rapporteur/Co-Rapporteur in a Centralised Procedure nor as RMS in MRPs/DCPs anymore.

- CP:
  CHMP will decide which country takes over responsibility of activity

- MRP/DCP:
  The MAH should switch the RMS as part of the lifecycle plan of the development.

UK in planned or running procedures

- National:
  No influence due to Brexit – the procedure is and remains national.

- MRP/DCP – **UK as RMS**:
  Initial Procedure: Evaluate carefully when and if to start a procedure
  Life Cycle – Variation: Close communication with RMS
  Life Cycle – Renewal: Close communication with RMS
  Life Cycle – PSUR: CHMP will take care for
  Line Extensions: Evaluate carefully when and if to start a procedure

- MRP/DCP – **UK as CMS**
  UK will be out of the "boat" and treated as pure national in future

MAH location for EU27 MAs

- MAH/Applicant based in the UK will need a legal establishment in the EU/EEA
- The legal construct of a MAH must be in line with EU/EEA requirements (a UK Ltd company is no longer possible)

⇒ Do you have a site in EU/EEA?

⇒ Transfer of Ownership (national variation)

MAH location for UK MAs

- MAH/Applicant of UK MAs needs a legal establishment in the UK

⇒ Do you have a site in UK?

⇒ Transfer of Ownership

PV – PSMF & QPPV location

- For EU27
  - PSMF location must be inside EU/EEA
  - QPPV location must be inside EU/EEA

- For UK
  - PSMF location assumed to be located in UK
  - QPPV location assumed to be located in UK

⇒ PSMF and/or QPPV within the same organization
Notification via Art 57 database (no variation)

⇒ PSMF and/or QPPV from new System
Variation (grouping/worksharing)

Batch Testing location

- For EU27 must be inside EU/EEA or a so called Mutual Recognition Agreement (MRA) with EU27 is in place for the country of the site
- For UK it is assumed to be located in UK or a so called MRA with EU27 is in place for the country of the site

⇒ Worst Case: Method transfer to a new/additional batch testing site

⇒ Worst Case: Variation (grouping/worksharing)

Batch Release / QP / Import location

- For EU27 must be inside EU/EEA
- For UK it is assumed to be located in UK

⇒ Method transfer to a new/additional batch release site

⇒ Supply Chain re-organization

⇒ Variation (grouping/worksharing)

Generic/Hybrid type of application

- UK Reference product (RefMP) for generic or hybrid MA:
  General: Reference can be made to a RefMP for which a marketing authorisation has been granted in the Union in accordance with Articles 8(3), 10a, 10b or 10c of Directive 2001/83/EC.
  =>
  UK RefMP MA granted before 31 January 2020 remains valid to calculate the data protection time line.
  UK MAs approved afterwards can not be used as RefMP in EU-27.
  (supported by Sträter Rechtsanwälte)

  Brexit Q&A from CHMP & CMDh No 13.

Generic/Hybrid type of application

- Bioequivalence studies (BE studies):
  Notice to applicants Vol 2 already describes: “In case, the RefMP is no more produced and placed on the Union market , demonstration of the bioequivalence with the RefMP through BE-studies should however be performed on batches which have been authorised within the Union.”
  BE-studies that have been conducted with a medicinal product sourced in the UK can be used only if the new MAA using those BE studies will be granted before Brexit. *See Brexit Q&A from CHMP & CMDh No 10-13*

⇒ Meeting EMA-Industry stakeholders March 2018: industries should get in touch with local authorities to ensure that BE studies with reference UK products can suitably support new MAAs after Brexit.

⇒ “BE studies are fast to run, companies should plan to re-do the studies with appropriate EU reference products”.

How Dr. Regenold GmbH & regulanet® can help?

- Marketing Authorisation Holdership (MAH) - MAHs located in the UK will need to transfer their EU MAs to a holder established in the EU (EEA) and *vice-versa*.
  - We can support marketing authorization applications & holdership through our legal entities in the EU (and UK).
  - We can assist you with all the necessary changes, variations & wholesaler or distributor licenses, if you require them.
  - We can help you establishing your own legal entity or use an outsourced option and provide advice concerning any supply chain, tax and legal issues which may arise.
- UK is RMS – For medical products authorised via MRP/DCP the MAH will need to switch the RMS to an agency of a member state of the EU (EEA).
  - We can help you choosing the optimum RMS and assist with all regulatory tasks.
- Other Regulatory issues
  - We have extensive experience with procedural activities. We closely follow up the discussions of CHMP/CMDh and are in close communication with agencies.

How Dr. Regenold GmbH & regulanet® can help?

- PV - PSMF & QPPV location must be inside EU/EEA for EU27
  - ➢ We have PV and QPPV capabilities both in the EU and the UK (for MAs to be held there).
- Batch release (incl. testing) site(s) in the UK – The MAH will need to transfer its current UK batch testing and release site(s) to a location established in the EU (EEA)
  - ➢ We can support clients who require a batch testing and release site(s) within the EU and obtain authorization by the local authorities.

➢ In addition, as EMA and national agencies prepare and issue further guidance, we will continuously monitor them and assess the impact upon your plans.

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