POST-BREXIT
Marketing and supply of medicines to the European Union

The United Kingdom (UK) is to withdraw from the European Union (EU) later this year and it is critical that UK-based pharmaceutical and other private companies involved in the marketing and supply of medicines begin to prepare.

It is necessary for companies that may be affected to:

- **Establish what regulatory changes will come about**
- **Eliminate potential risk of supply shortages**

What date will the UK withdraw from the EU?

On 10–11 April 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 October 2019.

Is the UK still part of the EU until then?

The UK remains a Member State for the duration of the extension, with all the rights and obligations set out in the treaties and under EU law. On the 31 October 2019, there will be a change of EU-commissioners with no need to appoint one from the UK.

What criteria apply for providing medicinal products to the EU?

Thereafter, for a company from the UK to be able to market or supply a medicine within the EU, the following activities need to be based within the European Economic Area* (EEA):

- The Marketing Authorisation Holder (MAH)/ applicant (MAA).
- The Qualified Person for Pharmacovigilance (QPPV).
- Pharmacovigilance System Master File (PSMF).
- Certain manufacturing sites (q-ty control, batch release, import or manufacturing sites).

Timeline of events leading to the UK's withdrawal from the EU

- **23 June 2016** – Referendum on EU membership (52% voted yes for exit, 48% voted no)
- **29 March 2017** – UK notification of its intention to withdraw from the Union on 29 March 2019
- **November 2018** – Withdrawal agreement between EU and UK ready – (to date, members of the UK parliament voted twice against the motion)
- **22 March 2019** – Extension given at top EU meeting
  - without a deal by 12 April 2019
  - with a deal by 22 May 2019
- **10–11 April 2019 –** EU Council extends withdrawal period until 31 October 2019
- **23 May 2019 –** European Parliament Election in the UK as a prerequisite for extension

* Iceland, Norway and Lichtenstein are included within the EEA.

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Pharmaceutical and other private companies should take note of several regulatory tasks to be fully completed and implemented before 31 October 2019:

Marketing Authorisation Holder/Applicant (MAH/MAA)

- Transfer of marketing authorisation to a holder/ applicant established in the EEA.
- For existing marketing authorisations: MAH's are to change the Reference Member State (RMS) in the Mutual Recognition (MRP) and Decentralised Procedures (DCP) from the UK to another one.
- For on-going applications with the UK as RMS: the applicant needs to submit a new application to a new Reference Member State.
- As of the date of the withdrawal of the UK from the EU, medicinal products manufactured in the UK will be considered imported medicinal products. The MAH needs to specify an authorised importer and a site of batch control established in the EEA and submit the corresponding variation to MA (exemption can be granted for a period of time).
- Transfer of current UK-based site of batch release to a location established in the Union (EEA).
- For designated orphan medicinal products, the UK-based holder needs to transfer its designation to a holder established in the Union (EEA).

Pharmacovigilance

- The QPPV from the UK will need to change place of residence or a new QPPV residing and carrying out his or her tasks in the Union (EEA) will need to be appointed.
- The supervisory authority for pharmacovigilance is the competent authority of the Member State in which the Pharmacovigilance System Master File (PSMF) is located – the MAH needs to change the location of the PSMF to a Member State within the Union (EEA).
- In case the MA for a national authorised medicinal product has to be transferred to a new legal entity, a new summary of the pharmacovigilance system has to be submitted via variation procedure C.I.8.a as type IAIN variation.

Periodic Safety Update Report (PSUR)

- For the calculation of exposure from marketing experience by region, patients exposed in the UK until the withdrawal date should be included in the Union/ EEA estimate. Thereafter, UK patient exposure should be considered as part of the non-EU/EEA regions.

Quality

- The new Union supervisory authority responsible for supervision of manufacturing sites located in the UK and third country sites previously inspected by the UK will decide, using a risk-based approach, when an inspection of the site(s) concerned will be required, in order to confirm or re-confirm Good Manufacturing Practice (GMP) compliance.

Clinical Trials

- Refer to the European Commission Notice on the withdrawal of the United Kingdom and EU rules in the field of clinical trials for further information, available at: https://ec.europa.eu/info/sites/info/files/notice_to_stakeholders_brexit_clinical_trials_final.pdf.

Clinical Trial Supply

Export of IMP from EU to UK:

- If there is a 'no deal', the UK's participation in the EU regulatory network would end. The Medicines and Healthcare products Regulatory Agency (MHRA) would take over this responsibility.
- Investigational Medicinal Products – The UK will recognise QP certification done in an approved country initially including all EU and EEA countries.
- All importers of investigational Medicinal Products (IMP) will require a Manufacturer's Import Authorisation (MIA).
- A UK responsible person, established in the UK, is required to act on behalf of the manufacturers based outside the UK. Evidence supporting the authority to act on behalf of the overseas manufacturer will be required.
- Importers must ensure the devise is appropriately marked (CE) and labelled and registered with the MHRA.

Import of IMP from UK to EU

- The EU's current position is that it will only recognise QP certification undertaken within the EU.
- Imports will require a QP Declaration and a new certification.
- A new certification will require that the API manufacturer, the drug product manufacturer and the packaging site is audit by a EU GMP qualified and experienced auditor.
- A full batch documentation must be made available for the QP who is certifying the batch for import into the EU.
- Further information about clinical trial supply is available at:
  - https://www.gov.uk/government/publications/further-guidance-note-on-the-regulation-of-medicines-medical-devices-and-clinical-trials-if-theres-no-brexit-deal.
  - https://www.gov.uk/guidance/regulating-medical-devices-in-the-event-of-a-no-deal-scenario.

Contact KLIFO Regulatory Affairs Solutions to learn more about BREXIT and the implications for the marketing and supply of medicines in Europe.

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