KCR Memo: What's Next for Brexit

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BREXIT: WHAT TO KNOW

- The UK will be leaving the EU on **30 March 2019** (the withdrawal date set by the timeframe provided in Article 50 of the Treaty on European Union) and will be officially deemed a '**third country**' as of that date.

- **The European Medicines Agency will relocate to Amsterdam** where it will begin operations. The move from London should be completed by 1 March 2019. There should be no impact on EMA procedures for sponsors (e.g. scientific advice, orphan designation, pediatric investigation plans (PIPs), applications for marketing authorization, post-authorization activities) and Sponsors are advised to submit applications and requests to EMA as normal.

- As agreements discussion between EU and UK are collapsing, the **'no deal' scenario is the most probable.** Namely, no arrangements will be made between the UK and EU.

- There will be **no transition or implementation period** which would give businesses and organizations additional time to respond to the changes.

- **As of 30 March 2019, Sponsors will need to navigate two sets of regulatory guidelines for pharma industry – one established by the UK and the other in the EU. The EU rules and regulations on clinical trials, in particular Directive 2001/20/EC, will cease to apply to the UK as of the withdrawal date.**

OVERVIEW OF EUROPEAN GEOGRAPHY AS OF 30-MAR-2019

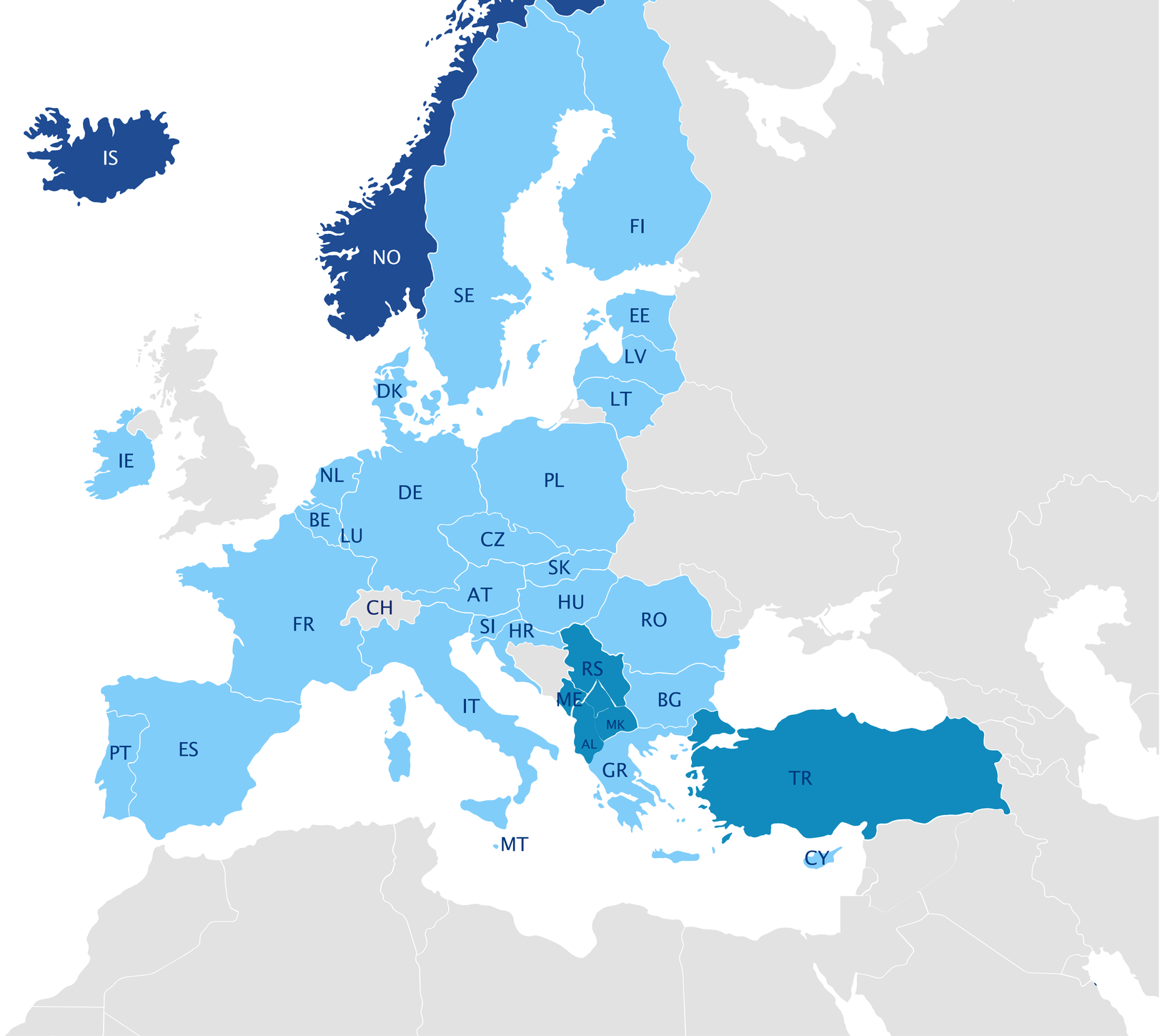
EU Member State

EEA member state

EU / EEA candidate

EU – European Union

EEA - European Economic Area



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EMA BREXIT PREPAREDNESS BUSINESS CONTINUITY PLAN' (BCP)

- BCP is an official and publicly available action plan that helps the EMA respond to the consequences stemming from Brexit. EMA entered **phase 4** of BCP on 1 January 2019.
- According to EMA, 2019 is a '**year in transition**', where 2020 will be a 'year of paving the way for the future'.

Currently, EMA priorities for 2019 are the following:

January – June	July – December
➔ Existing category 1 activities from phase 3 will be maintained with no new activities. EMA will prepare for the implementation of new veterinary legislation. ➔ Brexit-related activities to be maintained, but gradually less FTEs will be involved. ➔ Only critical category 2A and 2B activities to be upheld, as well as the minimum required corporate governance activities from category 3 ➔ There are no changes to category 2B and 3 activities compared to BCP phase 3 ➔ All remaining category 2A and 2B activities to be temporarily suspended ➔ Specific arrangements to be made for the physical relocation from London to Amsterdam (until 15 March 2019 inclusive), whereby focus will be on maintaining category 1 activities	➔ A list of priorities for further consideration will be drawn-up for discussion in June ➔ Before restoring activities, where relevant and feasible, a reflection on longer term sustainability will take place
During this period EMA mainly will have to: • Address important staff loss • Cope with the consequences of the physical relocation to Amsterdam • Cope with an important workload increase as a direct result of the Brexit arrangements As for the highest priority activities (category 1), the focus will be on the authorization, maintenance and supervision of medicinal products, ongoing Brexit implementation activities and preparation for the implementation of the new veterinary legislation	**During this period EMA mostly will:** • Gradually take up previously suspended reduced/activities in line with the priorities identified in the strategy to 2020, at the same time looking for the most efficient way to achieve longer term fit-for-purpose applications/processes/tools • Prepare for the future (2020-2025 strategy) with particular emphasis on Regulatory Science Strategy and Corporate ICT strategy

EU-BASED CLINICAL TRIALS WITH THE UK COMPONENT

Legal basis	Directive 2001/83/EC , Directive 2001/82/EC
QP release	Qualified person of the manufacturing and importation authorization holder is responsible to certify that each batch of medicinal product intended to be placed on the European Economic Area (EEA) market was manufactured in accordance with the Union GMP requirements and the marketing authorization. The batch release site has to be located in the EEA.
UK manufactured substances	• As of the date of withdrawal from the UK from the Union, active substances manufactured in the UK will be considered imported active substances and will require certification from the MHRA that the API manufacturing site active substance complies with EU GMP. • Drug products manufactured in the UK will be subject to a value-added tax (VAT) if they are shipped outside of the UK. • The corresponding amendments to labelling and package leaflet must be fully completed and implemented by the marketing authorization holder before 30 March 2019, either as part of a regulatory procedure affecting the annexes (e.g. variation, renewal), or through a notification under an Article 61(3) of Directive 2001/83/EC or (for veterinary products) through a Type IA_{IN} variation (see Variation Guideline (2013/ C 223/01), classification C.II.6.a).

EU-BASED CLINICAL TRIALS WITH THE UK COMPONENT

(Co)-rapporteur

The UK will no longer be able to engage as a (co)-rapporteur for new marketing authorization applications for which the centralized procedure would finish after 30 March 2019. The rapporteurs or co-rapporteurs in centralized procedures will need to be transferred to new rapporteurs and co-rapporteurs from the EEA.

Insurance

According to European Insurance and Occupational Pensions Authority (EIOPA), insurance agreements concluded by UK insurers with policyholders from the EU before 30 March 2019 are valid after that date. After that date, the insurers from the UK will not be authorized to carry out insurance activities with regard to cross-border insurance contracts by way of freedom of establishment or freedom to provide services within the EU.

In order to ensure service continuity, insurers from the UK affected by Brexit may need to:
transfer insurance contracts offered to EU policyholders by their UK undertakings to an insurance subsidiary established in an EU Member State, establish a third country branch in the EU Member State of the policyholder, or go through the process of changing the domicile of the company to an EU Member State.
e.g. Lloyd's decided to launch its Brussels subsidiary.

Legal presence

The local representative mentioned in the product information should be located in the EEA. Therefore, any local representative located in the UK and nominated for Member States other than the UK will have to be changed to a local representative located in the EEA.

RUNNING A TRIAL IN THE UK

- 2004 Regulations in force, modified using powers under the EU (Withdrawal) Act (EUWA) to make sure they still work in the UK after exit from the EU.
- Alignment with EU Clinical Trial Regulation (CTR) 536/2014 will be subject to usual parliamentary approvals.

Registration	As clinical trials are currently managed nationally, UK clinical trial applications will continue to be authorized by the MHRA and ethics committees as they are now.
IMP testing and certification	(..) stakeholders will not need to QP certify IMP in the UK, if it has already been certified in one of the countries on the approved country list.
Safety Reporting	The UK currently requires to submit all suspected unexpected serious adverse reactions (SUSAR) reports to the MHRA, and will continue to do so in the future via UK-based systems. Annual safety reports for all UK trials must still be submitted to the MHRA.
Insurance	Insurers from the EU will lose their right to conduct business in the UK by way of freedom of establishment and freedom to provide services.

THE IMPACT OF BREXIT FOR THE US-UK TRADE RELATIONSHIPS

Changes in FDA European Office	FDA to follow EMA with move from London to Amsterdam within its Office of International Programs.
FDA-EMA Mutual recognition agreements	'Mutual recognition agreements' concluded between the EU and the US that contain a sectoral annex on the mutual recognition of good manufacturing practice (GMP) inspections and batch certification of human and veterinary medicines ceases to apply to the UK after withdrawal date.
Current and future trade agreements between the UK and the US	The US will negotiate a bilateral free trade agreement with the UK, once the UK leaves the EU on 30 March 2019. As part of the U.S.-UK Trade and Investment Working Group, the US and the UK have already signed agreement on Mutual Recognition Between the U.S.-UK (including Good Manufacturing Practices). These U.S.-UK agreements will ensure that there is no disruption in trade of some specific products and services between the United States and the UK when the UK leaves the EU.

IMPLICATIONS ON CORPORATE LEVEL

Circulation	The free circulation and movements of goods and services between the UK and EU ends. EU nationals who are currently present in the UK may be at risk of losing some of their EU-derived rights, which depend on the new legislation prepared by the UK government.
Customes	The UK & the EU apply the same customs and excise rules to moving goods that are currently applied in cases where goods move between the UK/the EU and a country outside of the UK/the EU. Customs declarations would be needed when goods enter the UK/the EU or when they leave the UK/the EU, along with the safety and security declaration.
Trade conditions	Trade with the EU will be on non-preferential World Trade Organization terms. EU's Most Favored Nation tariffs and non-preferential rules of origin would apply to consignments between the UK and EU.
Data protection	The UK will become a "third country" also for the purposes of personal data transfers from the EEA to the UK. The European Data Protection Board's guidance on personal data transfers between the EEA and the UK requires a data transfer instrument (like standard or ad hoc contractual clauses, binding corporate rules or certification mechanism) to be implemented by the company prior to data flow in case there is no adequacy decision for data transfer issued by EC.

FEW RESERVATIONS

- No Member State has previously decided to leave the EU, so there is no precedent for this situation.
- Last EMA Brexit-related guidelines for pharma were issued on 1 February 2019. As there are still a lot of uncertainties, the information provided in this presentation may not be sufficient to ensure continuous validity and exploitation of the company after this date.
- Stakeholders should check EMA page* for new information as both EMA and the EC are updating their procedural guidelines and information notices for pharma industry on regular basis.
- Next UK MPs vote on the deal scheduled for March 12.

*https://www.ema.europa.eu/en/about-us/uks-withdrawal-eu/brexit-related-guidance-companies