# Regulatory consequences of "Brexit" for the development of medicinal products



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# The regulatory consequences of 'Brexit' for the development of medicinal products.

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## Introduction

**The United Kingdom (UK)voted in a referendum in June 2016 to leave the European Union (EU) after 45 years of membership. Among the many political , social and scientific consequences are those for the regulation of health care products. No longer will the efficacy, safety and quality of medicines in the UK be subject to a EU regulatory framework. The European Medicines Agency ( EMA) currently located in London , will move elsewhere in Europe. The pharmaceutical industry will reassess its commitment to the UK health scene.**
**(75 words)**

In the UK, the regulation of medicines takes place almost entirely through the incorporation into UK law of a series of European directives, through what is now the Medicines Regulations 2012 In addition to being regulated by EU-wide laws, the European regulatory framework for medicinal products has evolved to facilitate the collation of post-marketing efficacy and pharmacovigilance safety metadata across the EU. The European Medicines Agency (EMA), based in Canary Wharf in London, is ultimately responsible for good pharmacovigilance practice, and for the evaluation of the causation of safety-related events across Europe. It has developed the necessary infrastructure and expertise for the rapid evaluation of post-licensing safety and efficacy data from the 28 countries within the EU, and another three in the European Economic Area (EEA). This enables it to identify and act upon any changes to the risk-benefit profiles of new medicines in a robust and timely manner. The EMA has also acquired the necessary expertise to issue marketing authorisations for more complex new medicinal products, for cancer and orphan indications, for example. Decoupling the UK's regulatory system from that of the EMA would be likely to cause delays and additional costs for manufacturers seeking to market innovative products in the UK, which in turn could result in slower access for patients and increased costs for the NHS.

As an agency of the EU, the EMA will almost certainly have to relocate when the UK leaves the EU, and there is currently a bidding war among several European nations keen to host an agency that brings jobs, expertise and benefits for the domestic healthcare system. Anders Lönnberg, the Swedish government's life sciences coordinator, explained to *The Times* why Sweden is keen to inherit the EMA from the UK: 'We get 900 jobs and a network of highly skilled researchers. It will help a lot with national healthcare'. Loss of the EMA is also likely to affect future pharmaceutical investment in the UK. As a statement released by the Japanese Ministry of Foreign Affairs has explained: 'If the EMA were to transfer to other EU member states, the appeal of London as an environment for the development of pharmaceuticals would be lost, which could possibly lead to a shift in the flow of R&D funds and personnel to continental Europe'.

In addition to losing the EMA, leaving the EU will mean that the UK will no longer automatically comply with amendments to the European Medicines Directive and ancillary European legislation regarding, for example, clinical trials and pharmacovigilance. It is also unclear whether European consumer protection legislation such as the Products Liability Directive and General Products Safety Directive will remain enshrined in UK law. Even if existing medicines regulations are consolidated into UK law when the UK leaves the EU, they would no longer be subject to automatic updates as EU law adapts to the changing landscape of medicines regulation.

It could be argued that changes in the development of innovative medicinal products make this an especially unpropitious time to depart from an effective, pan-European regulatory framework. The taxonomy of disease is changing in order to define pathologies, like cancer, based on molecular mechanisms, rather than target tissues. As new medicines become more precise and personalised, their target markets shrink. Coupled with the public health imperative to accelerate approval regimes for innovative therapies, it is increasingly possible – through mechanisms such as conditional licensing schemes – for innovative medicines to enter the market at earlier stages in their development, in the absence of large-scale clinical trial data. Innovative licensing schemes for new medicines necessitate the initial evaluation of risk-benefit profiles on the basis of much smaller clinical trial data. With smaller clinical trials, the rigorous collection, monitoring and evaluation of post-licensing safety and efficacy data becomes ever more important. Similarly, for medicines for rare diseases, designated for orphan indication status, composite clinical studies carried out throughout Europe are needed in order to maximise statistical power when safety and efficacy data are evaluated at increasingly early stages of a new drug's clinical development.

The safety of medicines within the UK is enhanced by its membership of an EU-wide regulatory framework. Drug development throughout the EU benefits from the infrastructure and scientific resources and expertise in the EMA, and in other member states. Leaving this regulatory framework will certainly not enhance the UK's capacity to evaluate robustly the risk-benefit profiles of new medicines. To the contrary, there is a real danger of a reduced ability to detect safety signals in new medicines, especially in the immediate post-launch period when the first evidence of as yet undetected safety risks might be likely to emerge. Given the profile of many new and increasingly specialised medicines, any reduction in the effectiveness of the UK's pharmacovigilance regime is to be lamented, on public health grounds

THERE ARE ALSO REGULATORY CONSEQUENCES OF BREXIT FOR THE EMA AND THE EU. THE UK REGULATORY AUTHORITY , THE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA) CURRENTLY SHOULDERS A SUBSTANTIAL PROPORTION OF THE WORK OF THE EMA. SOME 30% OF THE APPLICATIONS FOR EUROPEAN MARKETING AUTHORISATIONS ARE ASSESSED BY THE MHRA; UK PLAYED AN IMPORTANT ROLE IN THE FORMULATION OF BOTH THE EUROPEAN CLINICAL TRIALS

REGULATIONS(2014) AND THE EUROPEAN PHARMACOVIGILANCE REGULATIONS (2012). FURTHER, SEVERAL OF THE COMMITTEES OF THE EMA ARE CHAIRED BY UK REPRESENTATIVES. DECOUPLING THE MHRA FROM THE EMA WILL RESULT IN A LOSS OF THE PRAGMATISM, EXPERTISE AND RESOURCE OF THE MHRA. A FUTURE EMA WITHOUT THE MHRA WILL NOT BE AS STRONG. IN CURRENT PARLANCE! THIS HAS THE APPEARANCE OF A 'LOSE-LOSE' SITUATION.

As far as we are aware, there has been little discussion of the public health consequences of this particular implication of Brexit. The dangers would be minimised if the UK continued to be part of the single market, as a result of joining Iceland, Liechtenstein and Norway in the European Economic Area, but the price of membership of the EEA is freedom of movement. Outside of the single market, the UK might try to negotiate an exit from the EU which retains the supremacy of European medicines regulations and directives, and therefore access to the centralised procedure for marketing authorisations and the pharmacovigilance infrastructure. But whether it would be possible to secure the ongoing primacy of European law in one area of business remains open to question. Cross-European pharmaceutical legislation celebrated its 50th anniversary in 2015, and the EMA now serves a population of more than 500 million EU citizens. In the context of increasingly specialised new medicinal products, subject to innovative early-licensing schemes, there is strength in numbers, and, conversely, a serious risk to public health from isolationism.

748 words
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