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Insights

Brexit and the European Medicines Agency—What Next for the Agency and UK Drug Regulators?

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The UK formally left the European Union (EU) on January 31, 2020, but disengagement is a process, not an event. Its future relationship with the EU remains highly contested. All foreseeable scenarios pose risks to health in the UK,[1-3] but the implications for both the European Medicines Agency (EMA) and drug review and approval in the UK have attracted little attention.

Given that it was based in London, the EMA, which evaluates and supervises medicinal products, has been particularly affected by Brexit. In March 2019, it relocated to Amsterdam, taking with it around 900 high-skill jobs and an annual budget of more than $300 million. This disruption has decreased staff retention and harmed business continuity, as documented by the agency.

The EMA, which relies heavily on the expertise and resources of more than 40 national regulatory agencies in EU member states, has also had to divert resources to fill the gap left by the departure of the UK Medicines and Healthcare Products Regulatory Agency (MHRA). Prior to the UK's withdrawal from the EU, the MHRA provided substantial scientific input to EMA marketing approvals of new drugs. As of 2016, when the Brexit vote took place, a large share of EU clinical trials were conducted in the UK, and UK experts played a disproportionate role in EMA evaluations.[4]

In the UK, which is home to 2 of the world's largest biopharmaceutical companies, AstraZeneca and GlaxoSmithKline, there are fears about collateral damage to the life sciences sector. The EMA was a magnet for private investment in the UK, with biopharmaceutical companies jockeying for closer ties with and easier access to 1 of the world's most important drug regulators. Faced with uncertainty over future EU-UK relations, some biopharmaceutical companies with UK manufacturing plants, including AstraZeneca, have preemptively set up so-called batch control sites and pharmacovigilance teams in EU member states to make sure they can continue to lawfully supply drugs in the EU.

The UK government has promised a Medicines and Medical Devices Bill in its current legislative proposals, which would change the regulation of medical products and clinical trials in the country. However, details are scant.[5] Some UK ministers have argued for a continued close regulatory alignment between MHRA and the EMA in the post-Brexit era. The closest possible alignment would be modeled on the European Economic Area membership of Norway, Liechtenstein, and Iceland. Regulatory authorities in these countries are legally and practically equal to EU agencies in terms of drug licensing, although they cannot vote on regulatory issues or raise objections. However, this model is based on alignment with EU rules, something that may be unacceptable to the current UK government.

Alternatively, the UK could, in principle, unilaterally recognize EMA authorization, either across the board or in specific areas in which capacity is constrained. For example, Singapore will accept evaluations undertaken by a number of other agencies, including the US Food and Drug Administration and the EMA, subject to a 60-day Verification Route.[6] However, this would rest uneasily with the UK government's pledge to "take back control."

An increasingly likely scenario is that the UK will have to set up its own drug review and approval process. The UK's health minister recently argued that an independent MHRA could cut bureaucracy. There are also opportunities for the MHRA to collaborate with the EMA as a third party, along the lines of collaborations between the EMA and the US Food and Drug Administration. However, questions remain regarding whether the MHRA could fill the gap left by the EMA in the

near term, given than the UK has outsourced technical responsibilities to the agency for decades. These challenges are exacerbated by the fact that the MHRA previously derived a sizable share of its funding from the EU, both from contract work for the EMA and from other EU research funds. Government investment will be needed to compensate for this loss, and it is worth noting that the reduced scale of the organization may lengthen the time it takes to review drug applications.

If the UK sets up a separate approval process, with minimal harmonization with EU procedures, such as the EU Clinical Trial Regulation, some drug companies may decide to first seek approval from the EMA for the EU (representing a market of approximately 500 million patients) before trying to launch a product in the UK (population of approximately 66 million). This could mean delayed access to new therapies for UK patients, especially for children and those with rare diseases.

Losing access to the infrastructure and systems that will be created by the EU Clinical Trial Regulation is a particular problem for the UK. The regulation, not yet in effect, aims to harmonize the application and authorization procedures for clinical trials conducted in EU member states. The government's briefing on the proposed new Medicines and Medical Devices Bill suggests less demanding processes for initiating clinical trials in the country. In the briefing, the government stated its aim to remove "unnecessary bureaucracy for the lowest risk clinical trials, to encourage rapid introduction of new medicines."[5] This is likely to cause concern that the UK might engage in regulatory competition to retain investments and clinical trials by setting unsafe standards.

Close ties between the MHRA and the EMA, including the harmonization of regulatory procedures, would help minimize inevitable disruptions stemming from Brexit.[7] British politicians and commentators[8,9] have argued that this is in the interests of both sides. But the EU is legally and politically constrained from deep collaboration with a country that has chosen to diverge from the bloc's rules. The challenges faced by Switzerland, which has a much closer relationship with the EU than that envisaged for the UK, should serve as a reality check.[10]

What will happen post-Brexit will ultimately depend on the outcome of EU-UK negotiations over future trade relations.[1,3] Currently, the UK seems to be advocating a Canada-style trade deal, although this could take years to settle and would preclude many forms of collaboration. Meanwhile, the EU may favor a Ukraine-style Association Agreement, which would be much easier to implement but would require closer alignment than the UK government wishes. Both sides will have to work to mitigate the inevitable harm to drug regulation. The UK must decide what it wants in its future relationship with the EU, but it must also accept that its choices will be limited and will have consequences.

ARTICLE INFORMATION

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