THE UK’S FUTURE RELATIONSHIP WITH THE EUROPEAN MEDICINES AGENCY
OCTOBER 2019

SUMMARY

Many cancer patients rely on access to innovative cancer medicines to reduce disease symptoms and often allow them to live longer. But before new medicines are made widely available to patients, they must go through a multi-stage process, known as the drug development pathway. This involves clinical trials to test if a drug is safe and effective, and subsequent market authorisation or ‘licensing’ to approve their use in individual countries’ health systems.

In the UK, the way new medicines are developed is governed by legal frameworks arising from the European Union, with the European Medicines Agency (EMA) playing a central role. This approach allows researchers to collaborate effectively on clinical trials – particularly those that need to recruit patients from multiple countries – and allows patients to access newly-approved medicines more quickly through a centralised process of licensing.

A strong future partnership between the UK and the European Medicines Agency (EMA) will be therefore be crucial to ensure the NHS can continue to secure the best possible outcomes for cancer patients after EU Exit. If the UK diverges from the EMA’s common regulatory framework for clinical trials and medicines licensing, this risks delaying patient access to potentially lifesaving treatments. By contrast, a continued collaborative approach will enable researchers across Europe to continue to make advances that benefit patients and ensure UK patients’ access to new safe and effective cancer drugs continues to improve.

The Government should seek the closest possible future UK relationship with the EMA and must prioritise avoiding delays to patient access to new treatment options (including medicines used in clinical trials) after the UK’s exit from the EU. This should include seeking the MHRA’s active participation in the EMA’s processes, building on its reputation and expertise, to the benefit of patients in the UK and across Europe.

To achieve this:

- The UK and the EU must come to an agreement to ensure the UK can fully participate in the regulatory system created by EU Clinical Trials Regulation (CTR), including seeking full and direct access to the EU portal and database for UK trial sponsors.
- The Government should explore and implement legal mechanisms to automatically recognise EMA marketing authorisations as valid in the UK. It should also seek an agreement with the EU which would allow the MHRA to continue to participate fully in the EMA marketing authorisation process, on a similar basis to EEA countries’ regulators.

We recognise that a range of alternate models for regulation of medicines and clinical trials are possible after EU Exit, such as the option for the Medicines and Healthcare Products Regulatory Agency (MHRA) to act as a standalone regulator and/or increase its cooperation with medicines regulatory agencies elsewhere in the world. However, we do not believe that these can protect patient safety and treatment outcomes to the same extent as continued collaboration with the EMA, at least in the short to medium term.
This statement was informed, in part, by a study commissioned by Cancer Research UK (CRUK), which engaged with researchers, regulators, patients and policy makers from the UK and EU. The resulting report, *The future of clinical trials after Brexit*, outlines the short and long-term factors affecting clinical trials in different EU exit scenarios. For further information, see our policy positions on *The future of clinical trials as the UK exits the EU* and *Drug licensing following the UK’s exit from the EU*.

**BACKGROUND**

**THE WORK OF THE EMA**

Cancer is a global phenomenon, and improvements in outcomes for people affected by cancer are achieved most quickly through international collaboration. The EMA works across and beyond the EU to protect and improve public health, with input from national medicines regulators such as the UK’s MHRA. The UK has been a major contributor to, and beneficiary of, the EMA’s activities since its inception.

The EMA manages the database of clinical trials carried out in the EU, which is used by national authorities to enter vital clinical trial data. The EMA also manages the EU Clinical Trials Register which provides a subset of this data, and forms part of the EudraPharm database for medicines. Most importantly, the EMA is developing the infrastructure crucial to the functioning of the new and improved regulation on clinical trials, the EU Clinical Trials Regulation (CTR).

The EMA also approves new medicines for use in Europe, by evaluating applications for market authorisation. This certifies a medicine’s safety, efficacy, and manufacturing quality, allowing the treatment to be routinely used in EU Member States’ healthcare systems (a new medicine’s cost-effectiveness is then evaluated separately at a UK level). The EMA therefore plays a central role in both the development and licensing of new treatment options for cancer patients in the UK.

**THE IMPORTANCE OF COLLABORATION**

The EMA’s marketing authorisation procedures rely on input from national regulators, and the UK’s MHRA is recognised as a world-class organisation key to these efforts. Between 2008 and 2016, the MHRA acted as Scientific Advice Coordinator in over 20% of centralised EMA medicine approval procedures, and Rapporteur or Co-Rapporteur in around 15% of centralised procedures. As has been noted by the Executive Director of the EMA, loss of this expertise could mean that the EMA’s decision-making processes slow down, at least in the short term, to the detriment of patients across Europe.

International collaboration is also crucial when it comes to research. Cooperation between countries is fundamental to improving cancer diagnosis and treatment, especially when conducting clinical trials. The UK is currently conducting nearly 700 oncology trials. 409 (58%) of these trials are also being run in the EU, compared to just 17 (2%) being run internationally outside of the EU. Over 1 in 3 (34%) of CRUK-supported clinical trials involve countries outside of the UK. Most of our cross-border trials work with EU nations (28% of our total trials). The current EU Clinical Trial Directive (CTD) means that it is generally simpler than collaborating with nations outside of the EU.

Cross-border trials are especially important for paediatric and rare cancers (such as in the BEACON trial, illustrated in the figure below), where individual countries do not have large enough patient populations to make the evidence meaningful. More generally, as the patient populations involved in individual cancer trials become increasingly stratified, the number of patients available for individual trials will decrease. This will increasingly require UK researchers to work with other nations to ensure trials recruit enough patients.
CLINICAL TRIALS
THE VALUE OF ASSOCIATION WITH THE EMA

Currently, trials are regulated by the EU Clinical Trials Directive (CTD). While, the CTD was a step forward at the time, different implementation of the CTD in Member States has resulted in a lack of harmonisation and led to delays when setting up cross-border trials. Therefore, CRUK and other UK organisations worked with the EMA, European Commission and other Member States’ organisations to develop the new Clinical Trials Regulation (CTR), due to be introduced in 2020.

This new regulation will be a significant improvement on the current system, harmonising the regulatory environment for clinical trials across the EU, to benefit both patients and researchers. The CTR will allow for more efficient setup of cross-border clinical trials, which are particularly important for rare and paediatric cancers as individual countries do not have large enough patient populations.
Crucial to the functioning of the CTR is new technological infrastructure, including a portal and database which will simplify trial application and approval procedures. This infrastructure is being set up and maintained by the EMA. EU Member States will have automatic access to this portal and database, allowing faster trial setup and quicker enrolment of patients onto research into new treatment options.

**CRUK’S PREFERRED OPTION POST-EU EXIT**

We welcome the commitment from the UK Government to align with the CTR as closely as possible, including seeking access to the portal and database. Without access to the new technological infrastructure supporting the CTR, the UK risks being left out of, and losing the benefits of, the harmonised process which it has worked to create. This could negatively impact patient access to treatment options as they are being tested, and harm the UK’s standing as a location for research.

We therefore see it as vital that the UK and EU now reach an agreement to enable the UK to access this infrastructure so that researchers and patients across Europe can continue to collaborate and participate in clinical trials, and the UK can continue to contribute to this research.

**The UK and the EU must come to an agreement to ensure the UK can fully participate in the regulatory system created by EU Clinical Trials Regulation (CTR), for the benefit of patients in the UK and the EU.**

Building on the commitment to adopt the CTR as far as possible when implemented, the UK Government must now prioritise seeking access to the EU portal and database. The ability for UK-based organisations to act as the Sponsor of clinical trials with EU partners should also be safeguarded, this is key for academic trials.

If the UK is unable to negotiate access the portal and database associated with the CTR, one option would be for the UK to implement a parallel system. In this case, the full advantages available to the rest of the EU through the CTR would not extend to the UK as the benefit of a single approval process would be lost. This could cause inefficiencies meaning longer approval times for cross-border UK-EU trials, as there would still be the need for multiple applications, one for the UK and the other for EU nations. Therefore, the UK risks becoming a less attractive place to conduct trials.

Another option would be for the UK to set up a bespoke trials approvals system that does not aim to mirror the portal and database associated with the CTR. There is a greater risk of the UK becoming a less attractive destination for clinical trials with this scenario. A bespoke UK system could lead to additional burden as multiple submissions would be required for trials with sites both in the UK and other EU countries. The system could also take time and cost money to implement.

**ACCESS TO NEW MEDICINES**

**THE VALUE OF ASSOCIATION WITH THE EMA**

The UK’s membership of the EMA is a major advantage for UK patients, since companies generally prioritise launching new products in the European pharmaceutical market relative to other countries. This is because the EMA covers an area responsible for 25% of global pharmaceutical sales, and companies are able to access this entire market based on one regulatory submission; the UK on its own makes up only 3%. The UK’s inclusion in this integrated market therefore provides faster access to new treatment options for UK patients.
But if the UK is outside of the EMA after it exits the EU, companies will have to submit separate marketing authorisation applications to the EMA in the EU, and to the MHRA in the UK. Companies would likely submit to the larger EU market before the application to the UK – meaning patients in the UK would get delayed access to the newest medicines.

Companies submit drugs for licensing to the European Medicines Agency before they do to many individual countries

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<thead>
<tr>
<th>Country</th>
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<tr>
<td>Switzerland</td>
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CRUK’S PREFERRED OPTION POST-EU EXIT

Post-Brexit arrangements which result in delays in access to the most innovative medicines would be unacceptable to patients and could have significant implications for the research and life sciences industry in the UK. Our preferred option is therefore for the UK Government to continue to recognise EMA marketing authorisation decisions after EU Exit, and to seek an agreement with the EU which would allow the MHRA’s continued participation in EMA decision-making and shaping the regulatory environment.

This would ensure the UK remains a priority launch market for new medicines and minimise any disruption to current routes to market, preserving the swift and comprehensive access to new innovative treatments UK patients currently have. Crucially, this would also help protect the wider UK life science ecosystem, as well as benefitting the EMA by providing continued access to the MHRA’s expertise and resource.

The pharmaceutical industry has also repeatedly signalled that it considers avoiding the short-term uncertainty caused by divergence from the EMA to be extremely important. Its preference is for the UK to remain part of the larger single European regulatory space, rather than seeking to develop an independent UK approach to medicines regulation.

Continued alignment with the EMA’s marketing authorisation processes therefore represents the best way to maintain the industry’s positive engagement with the UK’s market access procedures, and to maximise the benefits of recent reforms made to streamline drug approval processes in the UK, that have together resulted in an increase in the number of new cancer drugs becoming available for patients in recent years.

93% of people affected by cancer we surveyed want the UK and EU to agree close cooperation on the licensing of new medicines.
The Government should explore and implement legal mechanisms to automatically recognise EMA marketing authorisations as valid in the UK. It should also seek an agreement with the EU which would allow the MHRA to continue to participate fully in the EMA marketing authorisation process, on a similar basis to EEA countries’ regulators.

Another option would be for the MHRA to act as a sovereign regulator for a separate UK medicines market after EU Exit, and/or to establish new forms of collaboration with other regulators in countries such as Australia or Canada. However, as noted above, the UK’s smaller share of the global medicines market means that in this scenario, the UK would likely become a second-priority market relative to the EMA area for new medicines launches (as is already the case for countries like Australia and Canada). This would result in new treatments reaching UK patients more slowly.

In addition, while it is crucial to ensure regulation keeps pace with the innovative medicines now emerging from research and development, it is doubtful that any additional flexibility the MHRA may have as a sovereign regulator would outweigh the broader costs which would be caused by divergence from the EMA’s regulatory framework. The pharmaceutical industry’s preference for the UK to remain aligned with the EMA suggests it is similarly concerned about the balance of benefits and costs associated with developing an independent UK regulatory approach.

This could lead to a long-term reduction in the industry’s engagement with the UK as a location for research and early launch market for new medicines, especially given ongoing concern from industry about slow uptake of medicines in the UK relative to other countries. Ultimately, it will be patients who feel the impact of this, through delayed access to new medicines and fewer opportunities to participate in research.

As noted above, the MHRA could also step up its collaboration with regulators in other countries, such as Canada, Australia or the US. However, this approach could cause considerable uncertainty for industry and patients in the short-term. This is because of the level of regulatory realignment which may be required to accommodate differences in the healthcare and regulatory systems of the UK and other countries. It would also be a highly resource-intensive approach to have to implement within a short timeframe.

OTHER EMA ACTIVITY

ORPHAN AND PAEDIATRIC DRUG DEVELOPMENT

In addition to its work licensing new medicines and coordinating clinical trial setup, the EMA also plays a key role supporting research into new treatments for paediatric and rare diseases. It administers a system of incentives to encourage the development of new medicines and operates schemes to accelerate the regulatory approval of new treatments for these cancers. Collaboration with the EU therefore allows the UK to participate in research and swiftly access new drugs for these cancer types which might not otherwise be possible because of the limited numbers of patients affected by these diseases.

The UK should continue to work with EMA to shape future regulation in this space and maintain broadly harmonised systems in interests of future research collaboration and UK participation in that research.

MEDICINES SAFETY AND MONITORING

The EMA coordinates the oversight of pharmaceutical companies’ compliance with their drug safety monitoring obligations and provides publicly-available information on medicines’ safety. The UK benefits from being a part of this system that operates through cooperation between Member States, allowing safety issues to be picked up more quickly. The EMA also has bilateral agreements in place with a number of third countries’ regulators – including Switzerland, the United States, Australia and Canada – which allow for sharing of data on issues such as medicines’ safety or manufacturing quality.
The future partnership between the UK and the EMA must not allow for any fall in standards of patient protection, but promote continued sharing of expertise.

CONCLUSION

The UK’s participation in the EMA’s processes facilitates and accelerates cancer patients’ access to new, potentially lifesaving treatments at all stages of the drug development pathway. Continued collaboration between the MHRA and the EMA after EU Exit will therefore be essential in securing the best possible outcomes for people affected by cancer in the UK.

By contrast, an independent UK approach to medicines regulation would be incompatible with minimising the short-term negative impact of EU Exit for patients. As such, Government must prioritise seeking both the short-term and long-term agreements with the European Union that will deliver the closest possible working relationship between the UK and the EMA after EU Exit.

For further information or to discuss this statement please contact duncan.sim@cancer.org.uk or angeliki.yiangou@cancer.org.uk

REFERENCES

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