

11 October 2017

Health Committee
House of Commons
London
SW1A 0AA

RE: ACRO Comment Submission
Brexit – medicines, medical devices and substances of human origin inquiry--
Inquiry into regulatory arrangements needed to guarantee safe and effective supply of medicines, medical devices and products post-Brexit

Dear Committee members:

The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 130,000 employees engaged in research activities around the world (including 57,000 in Europe), ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 7,000 clinical trials involving 1.3 million research participants in over 100 countries. On average, each of our member companies works with more than 700 research sponsors annually.

Clinical research today is a global and pan-European enterprise. Clinical drug development research knows no borders. Pharmaceutical companies and CROs have a growing number of geographical options for the placement of clinical studies and seek out receptive business environments characterized by regulatory certainty, harmonization, consistency, and predictability. Measured by both CRO employment and clinical study placement statistics, the UK plays a vital role in clinical research compared to other European countries. The results of ACRO's 2013 survey of its members showed that, at that time, ACRO member companies employed 9,418 staff in the UK, compared to 5,337 in Germany, 2,483 in France, 1,967 in Spain, and 1,584 in Italy. In 2013, ACRO member companies placed more clinical trials in the UK and Germany (1,320 and 1,321 respectively) than in France (1,086), Spain (1,046), or Italy (926). ACRO is pleased to provide the following response to the Committee's inquiry.

1. What are the key considerations that arise for companies, healthcare services and regulatory bodies in the UK as a result of the UK's withdrawal from the EU? Focussing on patients and the public, what needs to be done to ensure that any adverse impact is minimised or eliminated, and that opportunities to enhance services are maximised?

Life sciences, including pharmaceuticals and medical devices, are a key part of the UK economy and currently generate £64 billion of turnover, and employ more than 233,000 scientists and staff¹. Unless appropriate agreements are negotiated between the UK and the EU, there is a danger that the regulation of these products will be disrupted, resulting in consequent and immediate disruption of their availability to patients, and of patient participation in ongoing clinical research. In the pharmaceutical sector, the UK accounts for only 3% of the global market by value and 1.7% of the global “market share” for clinical research. A possible long-term consequence, therefore, is that global companies might exclude or delay consideration of the UK when assessing the commercial potential of new products and the placement of clinical research, given the proportionately higher regulatory hurdles to enter a small market compared with those providing access to the 27 countries of the EU. This would lead to delayed access to both innovative and generic treatments for patients in the UK, reduced opportunities for participation in clinical research, and, in turn, a reduction in the UK science base and manufacturing sector.

The UK life sciences industry has identified key considerations that will secure patient access to products and protect public health, therefore minimising the adverse impact of the UK's withdrawal from the EU and maximising opportunities to enhance services^{2,3,4}. These can be summarized as follows:

- Secure the ability to trade freely and move medical and pharmaceutical supplies across borders - this should be ‘frictionless’ and include access to free trade agreements already in place between third countries and the EU.
- Secure access to the best talent - this will require an immigration system that allows global pharmaceutical companies, CROs and research institutes to attract and transfer talented and skilled students, scientists and other professionals from around the world.
- Secure IP protection - the loss or reduction of Intellectual Property protections would disincentivise the development and launch of products in the UK. Protections are key to incentivising the lengthy, risky and expensive process of pharmaceutical, biotechnology and medical device innovation. Europe benefits from a high standard of IP incentives for pharmaceuticals in the form of Supplementary Protection Certificates (SPCs) (essentially compensating for the amount of patent term that is lost during the lengthy development process of a product), regulatory data protection, orphan designation (for rare diseases) and rewards for investigations into paediatric uses and formulations. EU pharmaceutical incentives are currently being reviewed and it is important that the UK actively participates in this review, prior to leaving the EU, and that IP incentives are not weakened.

- Secure predictable access to funding and collaboration for scientific research. This should achieve agreements on existing and future funding and collaboration opportunities such as Horizon 2020 (and its successor), including the Innovative Medicines Initiative; UK life science entrepreneurs should also be able to access the European Investment Bank and European Investment Fund.
- Secure co-operation with the EU on the regulation of medicines, medical devices, the transfer of clinical research and pharmacovigilance data between countries, and the monitoring of medicines to ensure that falsified medicines do not enter the supply chain - this should achieve alignment between the UK and EU regulatory frameworks to deliver proportionate, robust and effective regulation in the UK.

As a means of maximising the opportunities for patients, public health, and the life sciences research and manufacturing sectors following the UK's withdrawal from the EU, ACRO fully supports the conclusions and recommendations of the Life Sciences Industrial Strategy, developed under the chairmanship of Professor John Bell⁵.

2. Following the UK's withdrawal from the EU, what alternative arrangements for the regulation of medicines, medical devices, medical products and substances of human origin could be introduced? What are the respective opportunities, risks and trade-offs involved?

The way in which the UK Life Sciences industry researches, develops, manufactures and brings medical technologies to patients is currently regulated by the EU and benefits from consistency and scale. There is considerable risk to patients associated with the UK divorcing itself from the sophisticated system of EU regulation. This robust regulatory system is critical to deliver safe, effective products and has been built with considerable UK influence and expertise.

If UK regulations were to diverge from those of the EU, duplication of processes, increased costs and a divergence in standards will make the UK a less attractive place to perform clinical research and develop, manufacture and launch new products. Even a UK system designed to improve upon current EU regulations, if separate from the EU, will lead to increased costs and considerable delay or result in no regulatory submission to perform clinical research in the UK. Additionally, the UK will become a second priority market for the launch of new products. This will result in products being made available to UK patients later than to those in the EU. For global companies, the UK market is not sufficiently large to justify significant additional costs, at just 3% of global pharmaceutical sales⁶.

For medical devices, withdrawal from the EU without a new cooperation agreement would mean Notified Bodies in the UK would not be entitled to conduct conformity assessments for the EU. Manufacturers would therefore not be allowed to fix the CE mark to their products. UK manufacturers would have to appoint a Notified Body outside the UK to approve their products for the EU, and appoint an authorised representative in the EU to place their products on the EU market. This would be a costly process with little benefit to the manufacturer.

The life science industry's preferred position, supported by ACRO, is for the UK to maintain continuity with EU regulatory systems, including full participation in EU regulatory processes and alignment of regulations. The industry recommends an overarching regulatory cooperation agreement with the EU in the context of a broader UK/EU special relationship. This should be a long-term, permanent agreement given the complexity, cost and requirement to provide consistent and stable regulation.

The UK could adopt a stand-alone regulatory model. However this would not be preferable and has significant disadvantages associated with it. The resulting additional regulatory burden will add costs for both industry and the UK government. The UK would be deprioritised as an early launch market, delaying patient access to innovative products and offsetting expected benefits. To mitigate this, the UK would need to effectively recognise authorisations granted in other territories for the majority of products, aiming to use the same product dossier, and ensure a quick and simple process for industry. However, other than with the EU (where, as a participant in EU regulatory systems the UK adopts common EU standards), given the disparate regulatory regimes and standards (as well as differing medical practices) in place around the world, the development of recognition agreements of this nature would be only a long-term solution, as considerable time and extensive resources would be required to ensure equivalence such that the safety of patients in the UK is not compromised. The access of UK patients to clinical research opportunities and newly developed products would therefore still be delayed until such agreements have been concluded.

How much time is needed to facilitate a smooth transition to new arrangements? Is it possible, or desirable, to move directly to new arrangements post-29 March 2019, or are transitional arrangements needed?

ACRO believes that transitional arrangements will be needed in order to avoid disruption of the supply of products to UK patients and suspension of clinical trials in the UK while appropriate new arrangements are put in place. The length of time needed will depend on the detail of relevant agreements.

How will withdrawal from the European Union affect the UK's ability to influence international standards in life sciences?

The UK has long been a global leader in life sciences research. A key factor in this is the excellence of research performed in UK universities. However, collaborations are increasingly essential to reach the necessary scale for breakthrough discoveries. The UK currently plays a leading role in EU-wide collaborations; for example, in the Horizon 2020 programme, and in leading the highest number of Innovative Medicines Initiative projects (which speed up the development of better and safer medicines for patients, boosting innovation in Europe). Non-EU countries may now target their collaborations outside the UK if they believe European scale is critical to success.

Uncertainty over the position of EU workers to remain in the UK and the UK's future immigration policy is already making it difficult to attract and retain talent³. The UK is often the European headquarters location of choice for global pharmaceutical/medical device companies and CROs. This has helped foster a deep talent base in areas including research, development, regulatory, manufacturing and commercial skills. These skills exist within a range of organisations in the UK Life Sciences sector, including regulators, industry, CROs, research institutes and support services. However, as the UK's position as an attractive gateway to Europe is challenged, there is a risk that these operations will move to Europe, eroding the UK life sciences ecosystem and the international influence exerted as a result of UK expertise. The loss of influence for the UK within EU regulatory systems will have long-term impacts on the UK, with talented regulatory experts being less attracted to live and work the UK, and EU regulations becoming less favourable to UK interests in the future. The planned relocation of the European Medicines Agency from London represents a further loss of influence and attraction for top regulatory talent and, in turn, may draw highly influential company staff away from the UK to locations near to the Agency. Representation on international bodies that set standards for the development and marketing of pharmaceuticals and medical devices is currently undertaken at EU level (e.g., International Conference on Harmonisation, International Medical Device Regulators Forum) and the UK takes a leading role in these organizations on behalf of the EU. This will stop on withdrawal, and it will be important that, wherever possible, the UK joins the relevant organisations in its own right in order to maintain its influence, which (as a representative of a relatively small country rather than a large trading bloc) will increasingly depend upon maintaining scientific excellence in the UK.

What arrangements are needed to ensure the safe, effective and timely supply of medical radioisotopes over the short, medium and long-term?

This is a highly specialised topic on which ACRO has no comment.

What are the implications for medical research and development, including for the timely patient access to new medicines, technologies and other relevant medical innovations developed within or outside the U.K? How can any adverse consequences be avoided or mitigated and any potential opportunities be enhanced?

The clinical research industry is worth £115billion per year globally and is growing; the current market share of the UK is 1.7%⁷. The UK's withdrawal from the EU creates several challenges for clinical research and timely patient access to new treatments, which were summarised in the responses to questions 1 and 2 above. More detailed responses on key points are as follows:

- New EU regulations for both medicines and medical devices are currently being implemented and are designed to encourage and streamline the approval of pan-EU trials with a single application designed to deliver speed and efficiency, with a simplified process where the product poses less risk. Should the UK be unable to participate in these new processes, the UK could become a less appealing location for clinical trials in Europe, impacting the UK innovation base and the opportunities for UK doctors and academics to conduct trials in the UK and for patients to participate in them. In addition, clinical trial placement is linked to the uptake of innovation within a health system. Participation in this common regulatory framework is pivotal for maintaining investment in research and development, which benefits the NHS and UK patients.
- Around 40% of investigational medicinal products (IMPs) used in clinical trials in the EU are manufactured in the UK (information from the Association of the British Pharmaceutical Industry). It is therefore critical that the supply of these products should continue unhindered, as any additional requirements and/or costs to export IMPs to the EU would likely result in the transfer of manufacturing capacity to EU countries. EU regulations require certification and release of each batch of IMP by a Qualified Person located in the EU. Currently, many of these Qualified Persons are located in the UK and, unless a suitable agreement can be put in place, there is a danger that the role may be transferred to other EU countries. Equally, the UK, post-withdrawal, should accept release and certification by Qualified Persons in the EU and avoid duplication of this activity on importation of IMPs into the UK. Additionally, there is a risk that clinical trials in the UK might need to be suspended while these new arrangements are put in place, to the detriment of companies, researchers, and participating patients.
- EU legislation requires that adverse reactions to medicinal products are reported to a central EU pharmacovigilance database that covers both marketed products and IMPs in clinical trials. A similar EU database is to be developed for medical devices. No longer having UK involvement in these databases and integrated EU vigilance processes will impact the quality and coverage of the systems used to detect side effects and manage safety issues, and may compromise the safety of UK patients. As in the case of batch release outlined above, a Qualified Person located in the EU is required to take responsibility for a company's pharmacovigilance system and there is again a danger that the role may be transferred to the EU, and a risk that clinical trials in the UK might need to be suspended while new arrangements are put in place, to the detriment of companies, researchers, and participating patients.
- A new EU regulation on the protection of personal data will come into effect on 25 May 2018. Pan-European research is supported, in part, by data sharing across the EU. Therefore, in order to ensure the flow of clinical research and pharmacovigilance data between the UK and EU is not impeded post-withdrawal, it is essential that the UK adopts equivalent standards to the EU and reaches a formal equivalency agreement with the EU.

As noted earlier, the life science industry's preferred position, supported by ACRO, is for the UK to maintain continuity with EU regulatory systems, including full participation in EU regulatory processes and alignment of regulations.

ACRO thanks the Committee for the opportunity to provide comment on this inquiry. Please do not hesitate to contact ACRO if we can answer any questions at all or provide additional detail.

Respectfully submitted,



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References

1. HM government, 2016. Strength and Opportunity 2016: The landscape of the medical technology and biopharmaceutical sectors in the UK. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/607193/strength-and-opportunity-2016-bioscience-technology-accessible.pdf
2. Maintaining and growing the UK's world leading Life Sciences sector in the context of leaving the EU - UK EU Life Sciences Transition Programme Report, for the UK EU Life Sciences Steering Committee, 6th September 2016. Available at: <http://www.abpi.org.uk/our-work/library/industry/Documents/UK-EU-Steering-Group-Report.pdf>
3. Association of the British Pharmaceutical Industry - Securing the Opportunity for UK Life Sciences by 2022, 27th April 2017. Available at: http://www.abpi.org.uk/our-work/library/industry/Documents/ABPI_GE2017_Manifesto.pdf
4. Institute of Mechanical Engineers. Medical devices and CE marking – the impact of Brexit, 3rd May 2017. Available at: <https://www.imeche.org/policy-and-press/reports/detail/impact-of-brexit-medical-devices-and-ce-marking>
5. Life Sciences Industrial Strategy – A report to the Government from the life sciences sector, 30th August 2017. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/640696/life-sciences-industrial-strategy.pdf
6. IMS Health. IMS World Review Executive, 2016.
7. International Accrediting Organization for Clinical Research. Actions Needed to Support Significant Growth Opportunity for the UK Clinical Research Sector Pre-Brexit and Beyond, June 2017.