Policy implications for post-Brexit biotech

To the Editor:

At the one-year anniversary of the Brexit referendum, policymakers remain face to face with the daunting reality of navigating treacherous political, economic, and regulatory waters following Prime Minister Theresa May's authorizing letter invoking Article 50 of the Lisbon Treaty. May's March 29 letter signifies the formal trigger to Brexit, setting the stage for a contentious two-year negotiation that will redefine the UK's national identity and its future relationship with the European Union (EU; Brussels). Effectively, the United Kingdom will need to choose from three pre-determined pathways: the Norwegian model, the Swiss model, or the World Trade Organization model (**Fig. 1**). Irrespective of the pathway taken, Brexit will have uncharted consequences for highly regulated industries, particularly the UK's biotech sector, the largest in Europe. Key concerns relate to access to life sciences funding and capital, research collaboration, professional recruitment and, importantly, continued regulatory cooperation and harmonization with the EU[1,2].

Reviewing the three pathways, even the 'soft' Brexit option (the Norwegian model) fails to achieve status quo pre-Brexit. Under this arrangement, Britain would renounce EU membership before rejoining the European Economic Area (EEA) as a European Free Trade Association (EFTA) affiliate. The arrangement would require consent to contentious EU policies (including 'freedom of movement' rules), while necessitating payment of considerable fees in exchange for EU marketplace access. This option seems increasingly unlikely, given that triggering Article 50 signifies a 'harder' stance toward Brexit (i.e., exiting the single market). Rejoining as an EFTA affiliate additionally obligates UK-based EU regulatory bodies (like the London-based European Medicines Agency; EMA) to relocate to EU-member states and strips the UK of any influence over EU regulation. In anticipation, several countries are actively courting the EMA to be its future home[1,2].

Moving toward 'harder' Brexit options, whereas the Norwegian model blankets all industries, the Swiss model diverges, as it forgoes EEA membership, but carves out specifically negotiated sectors using over a hundred bilateral agreements. The Swiss arrangement allows partial access to the single market and a degree of political autonomy in exchange for EU financial contributions. Like the Norwegian model, this pathway requires Switzerland to abide by key EU policies without representation or the ability to influence and vote in the EU's parliamentary process. Generally, lack of EU membership also restricts access to vital EU-designated R&D investment capital (e.g., the European Investment Fund) and bars non-EU nations from participating in EMA clinical trials. As an example, in response to a 2014 Swiss referendum imposing immigration quotas, the EU froze access to and threatened expulsion from Horizon 2020 funding, only recently reinstating restricted access following a Swiss compromise to 'soften' the referendum's implementation[3].

Lastly, the UK could opt for a 'hard' Brexit and embrace the uncertainty of 'freedom' under the World Trade Organization (WTO; Geneva) model. The immediate downside would be an abrupt dissolution of all existing EU trade and regulatory relationships, coupled with the need to navigate the complexity and short duration of what is likely to become a 'two-phased' negotiation (i.e., Britain first settling the cost of Brexit before negotiating its future relationship with the EU). As a result, commerce with the EU could face severe disruption, leading to market uncertainties and greater transactional expense. UK biotech firms would lose the benefits of free inter-member trade while facing new common external tariffs, anti-dumping duties, and other non-tariff barriers[4]. With 90% of UK exports subject to these duties, the added costs may encourage UK-based firms to relocate into neighboring EU member states[4,5]. The net result may cumulate in fueling a 'Biote[ch]xit' of biotech companies out of the UK.

What is particularly worrying is that the three Brexit pathways fail to provide satisfactory solutions to ensure future growth and sustainability of biotech—one of the UK's most vibrant industrial sectors. Though the softer Norwegian and Swiss models allow the UK to retain limited EU market access through the benefits of EEA and EFTA membership, the political and economic costs, combined with the loss of EU membership benefits, are likely too high. Alternatively, a hard Brexit (mentioned as the "default" in PM May's March letter) envisions a total reconceptualization of UK–EU trading relationships, but currently fails to prioritize the biotech sector and its unique mutual benefits.

The UK's biotech sector has thrived under a synergetic relationship with the EMA, with the Medicines and Healthcare Products Regulatory Agency (MHRA; London) approving nearly one-third of all new drugs on behalf of EMA[6]. In post-Brexit negotiations, emphasis should thus be placed on ensuring special treatment for the biotech sector, including exploring instituting a temporary moratorium or transitional agreement (e.g., phased implementation beyond the two-year negotiation period) and exempting the life sciences industry from EU withdrawal (similar to industry-specific exclusions when Norway joined the EEA). Fees to underwrite continued MHRA–EMA cooperation could also be negotiated as part of EU exit fees until new stabilizing cooperative mechanisms are put into place[7].

A future relationship could include elements of the Swissmedic model, where Switzerland maintains its own regulatory body, with the EMA accepting Switzerland's efficacy, quality, and safety standards, thus authorizing the export of medicines into the EU without additional regulatory approvals. At a minimum, mutual recognition of quality and efficacy thresholds would permit reciprocal recognition of safety standards, thus maintaining regulatory continuity and ensuring timely access to lifesaving innovations.

It is also estimated that Brexit will cost the UK £8.5 ($10.9) billion in lost EU funding over four years[8]. Thus, to prevent a Biotexit,

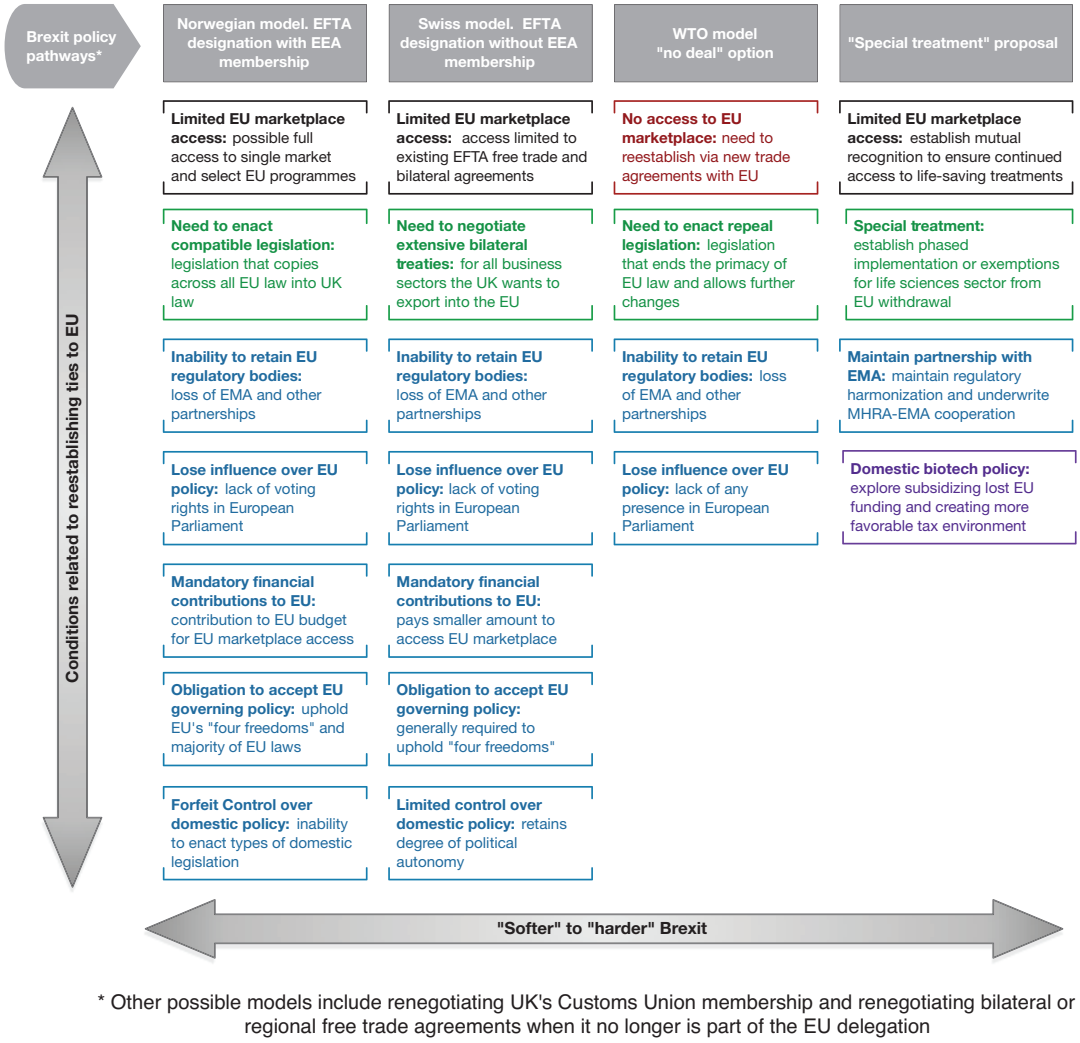

Figure 1 UK 'Brexit' pathways. Visual depiction of different Brexit pathways and the 'special treatment' proposal, and their impact on the UK relationship with the EU.

the UK must pursue domestic legislation to subsidize lost funding and/or investment to counterbalance market uncertainties poised to emerge in the post-Brexit negotiation lull. In this respect, Prime Minister May's government has pledged £4.7 ($6.1) billion in life sciences R&D funding between now and 2020 to safeguard against these impacts[9]. In August 2016, the UK took the first official action to preserve funding for UK-based biomedical companies by guaranteeing it would underwrite lost EU contributions from the Horizon 2020 (ref. 10).

These commitments are important, but fail to mitigate long-term impacts of Brexit for the biotech sector. Additional policy mechanisms to 'mind the gap'—including creating a more favorable tax environment (e.g., reducing biotech-specific corporate tax rates, expansion of R&D tax credits, and encouraging special economic zones)—need to be explored in parallel to EU renegotiation. For example, British institutions receiving EU investment capital are currently unable to exempt R&D expenses from corporate taxes[9]. Although these programs have to be weighed against their public cost, they could provide a stop-gap measure to prevent the exit of firms, especially in biotech enclaves in Scotland and Northern Ireland, which voted to remain in the EU.

The results of the June UK general election may very well orient Britain toward a softer Brexit than before, but much uncertainty remains. Regardless, a no-deal result for the biotech sector should not be an option, as preserving decades-long UK–EU regulatory cooperation post-Brexit must be a priority.

AUTHOR CONTRIBUTIONS

J.A. and T.K.M. jointly conceived the study, wrote the manuscript, and edited the final manuscript.

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