Title: Contingency legislation to establish MHRA as a standalone medicines and medical devices regulator in a result of no-deal on EU exit.

IA No: DHSC IA 4074

RPC Reference No: N/A

Lead department or agency: Medicines and Healthcare Products Regulatory Agency (MHRA)

Other departments or agencies: Department of Health and Social Care (DHSC)

Impact Assessment (IA)

Date: 21/09/2018

Stage: Consultation

Source of intervention: EU

Type of measure: Secondary legislation

Contact for enquiries: MHRA EU Exit
euexit@mhra.gov.uk

Summary: Intervention and Options

RPC Opinion: Not Applicable

Cost of Preferred (or more likely) Option				
Total Net Present Value	**Business Net Present Value**	**Net cost to business per year** (EANDCB in 2014 prices)	**One-In, Three-Out**	**Business Impact Target Status**
£m	£m	£m	N/A	Out of scope

What is the problem under consideration? Why is government intervention necessary?

The UK is currently part of the European medicines and medical devices regulatory framework. Contingency legislation is needed in order for the MHRA to be able to take on regulatory processes for human medicines and devices that are currently undertaken by the European Medicines Agency (EMA) and other bodies in the unlikely event of no deal being agreed with the EU before 29 March 2019. Regulatory continuity would be essential in order to ensure the ongoing safety of medicines and medical devices being placed on the UK market and to avoid disruption to supply chains. A trusted standalone sovereign UK regulator would also be essential to minimise uncertainty amongst patients, practitioners and businesses and to provide suppliers with incentives for innovation in medical products where buyers would not be prepared to pay the prices necessary to cover the costs of innovation.

What are the policy objectives and the intended effects?

The objectives of the policy are, in the unlikely event of no deal, to maintain a high level of public health protection by the UK regulator ensuring that existing processes are mirrored or provided by the MHRA where appropriate, in the short term. The intended effects are to ensure continuity in the safety of medicines and devices in the UK whilst retaining the UK regulator's ability to take regulatory action to protect public safety. These objectives are intended to be met with minimum disruption and burden on businesses and with minimum disruption to the supply of medicines and devices in the UK. Examples of this approach are converting European Centrally Authorised Products (CAPs) issued before Exit Day to UK Marketing Authorisations (MAs) and time-limited recognition of the CE mark for medical devices.

What policy options have been considered, including any alternatives to regulation? Please justify preferred option (further details in Evidence Base)

Options are assessed against a 'dual baseline' of Options 0 and 1

Option 0.1: Baseline - the 'status quo' with the UK part of the European medicines and devices regulatory framework. This is the baseline which options are primarily assessed against

Option 0.2: Do nothing

Option 1: Establish MHRA as a standalone UK regulator following a principles-based approach in order to protect public health and to minimise impact and disruption for business

Option 2:UK accepts decisions of cross-European regulatory bodies without any oversight, influence or additional assessment

Option 3: MHRA becomes a standalone regulator requiring full assessment of all products, not taking into account any information already provided to cross-European regulatory bodies.

Option 1 is the preferred option in the unlikely scenario of no deal with the EU.

Will the policy be reviewed? It will not be reviewed. **If applicable, set review date:** /				
Does implementation go beyond minimum EU requirements?				
Are any of these organisations in scope?	**Micro**	**Small**	**Medium**	**Large**
What is the CO_2 equivalent change in greenhouse gas emissions? (Million tonnes CO_2 equivalent)		**Traded:**	**Non-traded:**	

I have read the Impact Assessment and I am satisfied that, given the available evidence, it represents a reasonable view of the likely costs, benefits and impact of the leading options.

Signed by the responsible: ..... Date: .....

Summary: Analysis & Evidence

Policy Option 1

Description:

FULL ECONOMIC ASSESSMENT

Price Base Year	PV Base Year	Time Period Years	Net Benefit (Present Value (PV)) (£m)		
			Low: Optional	High: Optional	Best Estimate:

COSTS (£m)	Total Transition (Constant Price) Years		Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	N/A		Optional	**Optional**
High	N/A		Optional	**Optional**
Best Estimate				

Description and scale of key monetised costs by 'main affected groups'

Compared to the status quo baseline (Option 0), this IA assumes that UK remains part of the European medicines and medical devices regulatory frameworks, and as such there are no costs or benefits as the legislation would never come into effect. In the unlikely event of no deal being agreed with the EU before 29 March 2019, there are costs and benefits which are described in narrative terms. Although the approach aims to minimise business burden, there would be ongoing costs for businesses currently operating in the UK as they would need to adhere to additional UK only regulatory requirements if they currently sell in the EU/EEA. This includes additional fees, legal and administration costs. There would be familiarisation and set up costs as businesses transition into dealing with both systems. There would be costs to the MHRA of establishing and sustaining new regulatory capabilities; these will be largely recouped through fees.

Other key non-monetised costs by 'main affected groups'

As the UK would become a standalone regulator, only medicines approved through the MHRA would be able to reach the UK market and therefore there is a possibility that some medicines that would have been authorised in the UK because of the UK's involvement in the EMA will not be submitted to the MHRA due to business decisions. This could have an impact on access to certain medicines and therefore to public health. The extra costs of complying with a new UK regulator could be passed onto the purchaser through higher prices of medicines.

BENEFITS (£m)	Total Transition (Constant Price) Years		Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low	Optional		Optional	**Optional**
High	Optional		Optional	**Optional**
Best Estimate				

Description and scale of key monetised benefits by 'main affected groups'

Compared to a situation where there is no standalone regulator or other regulatory provision available in the unlikely event of no deal being agreed with the EU before 29 March 2019, the preferred option minimises the risk to businesses and offers regulatory continuity. The ability of the MHRA to operate as a trusted and comprehensive UK regulator will allow consumers to have confidence in medicines and devices on the market and allow businesses to innovate.

Other key non-monetised benefits by 'main affected groups'

The UK regulator would have the ability to protect public health and make its own decisions to ensure patients have confidence in the safety of medicines and devices on the UK market. Retaining a comprehensive UK regulator means that the scientific expertise that the MHRA holds would be retained to an extent, reducing a possible flight of scientific knowledge and skills which could have negative spillover effects for the UK's life sciences industry and the UK's ability to regulate medicines and devices. This contingency legislation also aims to benefit business by helping them prepare for a no-deal scenario.

Key assumptions/sensitivities/risks (%)	Discount rate	3.5%

Although this contingency legislation aims to help business to in their preparations for a no-deal scenario, there is a risk that due to the requirements set out, businesses will not have sufficient time to prepare. In the unlikely event of no deal being agreed with the EU before 29 March 2019, the MHRA will have regulatory processes in place so that businesses will have the relevant information to prepare for this scenario. The MHRA is not able to estimate the proportion of businesses that now apply through the European centralised procedure that will apply for an authorisation through the MHRA.

BUSINESS ASSESSMENT (Option 1)

Direct impact on business (Equivalent Annual) £m:			**Score for Business Impact Target (qualifying provisions only) £m:**
Costs:	**Benefits:**	**Net:**	

Evidence Base (for summary sheets)

Contents

	● Small and micro business assessment (SaMBA)
SECTION 9 SUMMARY, IMPLEMENTATION PLAN AND REVIEW	● Preferred option summary ● Post implementation Review

Introduction: The UK's withdrawal from the EU and preparations for no-deal

1. The UK will leave the EU on 29th March 2019. The UK and EU27 have agreed an Implementation Period, lasting until 31st December 2020 as part of the draft Withdrawal Agreement. While the UK is clear in its commitment to reaching agreement on the Withdrawal Agreement with the EU, it is prudent to be prepared for all possible outcomes, and the consultation that accompanies this Impact Assessment forms part of these preparations.

Medicines

2. The UK is currently a member of the European medicines regulatory framework. This means:

- Being a part of the European Medicines Agency (EMA) and its committees.
- Being a member of the European Heads of Medicines Agencies network.
- Participating in the EMA's 'centralised procedure' (CP) marketing authorisation (MA) process for medicines, which grants a medicine for sale across the EU.
- The UK is also part of the decentralised (DCP) and mutual-recognition (MRP) marketing authorisation procedures, which allows medicines to be brought to market across specific EU27/EEA countries through mutual-recognition of regulatory approval decisions.
- Participating in a pan-European GxP inspections process, which grants mutual-recognition of inspections across the EEA, reducing the number of duplicate inspections on the medicines supply chain, and the number of inspections individual national regulators need to carry out. GxP refers to the series of laws, regulations, and guidance that govern various areas of the research, development, testing, manufacturing, and distribution of medicines. Examples of these include: GLP (Good Laboratory Practice), GCP (Good Clinical Practice), GMP (Good Manufacturing Practice), GDP (Good Distribution Practice) and GPvP (Good Pharmacovigilance Practice).
- Being part of the Official Control Authority Batch Release (OCABR) network, which allows for a mutually-recognised batch testing and release of biological medicines, vaccines, blood and plasma products across the EEA by a single Official Medicines Control Laboratory (OMCL), reducing duplicative scientific testing for sensitive or time-critical products.

- Participating in pan-European pharmacovigilance processes, allowing for signal detection and management across the EEA.
- Taking part in the agreement of orphan designation and paediatric investigation plans to ensure that patients experience the benefits of EU incentives for the development of 'orphan' and paediatric medicines, supporting the increased access to medicines for rare clinical conditions and child-specific formulations, including clinical trials for these.
- Sharing of several EU-owned systems that enable sharing and exchange of data, such as EudraVigilance, EudraCT for clinical trials, CESP and the Common Repository.

Medical Devices

3. The UK is currently a member of the European devices regulatory framework. This means:
    - Being a member of the Medical Devices Coordination Group (MDCG) and its committees
    - Being a member of the Competent Authorities Medical Devices (CAMD) network (former chair and current member of the elected Executive Group) and its sub-committees
    - Recognising the CE mark and having Notified Bodies (NBs) based in the UK which are able to certify the CE mark on medical devices.
    - Participating (currently leading) in Joint Actions with other member states designed to improve coordination and collaboration across the network in relation to the performance of market surveillance responsibilities.
    - Access to databases (e.g. EUDAMED) providing information on products on the market and pooling information about performance and safety.

Regulation in the context of a no-deal scenario and the EU (Withdrawal) Act

4. As this is contingency legislation, the costs and benefits of the preferred option compared to the baseline (Option 0.1) are zero. Where there are impacts compared to Option 0.2 (no deal being agreed with the EU before 29 March 2019), the effects are discussed. Without membership of these European medicines and devices frameworks in the unlikely event of no deal being agreed with the EU before 29 March 2019, the UK would need to make arrangements for its regulator to take on regulatory processes of medicines and medical devices currently performed at EU level where necessary.
5. Although the EU (Withdrawal) Act would bring EU law into UK law in the unlikely event of no deal being agreed with the EU before 29 March 2019, the rationale of this legislation is that the law on

medicines and medical devices regulation would continue to function in an effective way in such a scenario.

Description of options considered (including status-quo)

6. Options are assessed against a 'dual baseline' of Options 0.1 and 0.2. Given that this is contingency legislation, the costs and benefits of the Option 0.1 baseline are expected to be zero. Where there are costs relative to Option 0.2, they are described throughout the rest of the IA.

   Option 0.1: Baseline - the 'status quo' with the UK a member of the European medicines regulatory framework, and pan-European CE marking system for medical devices, and this is the baseline which options are primarily assessed against

   Option 0.2: Do nothing

   Option 1: The MHRA to become a standalone UK medicines and devices regulator following a principles-based approach to protect public health and to minimise impact and disruption for businesses

   Option 2: The UK accepts decisions of cross-European regulatory bodies without any oversight, influence or additional assessment

   Option 3: The MHRA becomes a standalone regulator requiring full assessment of all products, not taking into account any information already provided to cross-European regulatory bodies.

7. The principles determining the preferred option are as follows:

   - Pragmatic and proportionate approach in establishing standalone UK regulatory requirements.
   - The UK regulator's continued ability to take regulatory action to protect public safety.
   - Minimum disruption and burden on business as the UK exits the EU.

8. These principles ensure that:

   - Public health is not adversely affected through disruption to the regulation of medicines while at the same time as minimising additional regulatory requirements for businesses need to comply with.
   - Businesses have the ability to implement changes and familiarise themselves with regulatory changes within a reasonable timeframe, where possible; this necessitates a pragmatic approach to legislation.
   - The UK public continues to have confidence in the safety, quality and efficacy of medicines and medical devices on the UK market through the MHRA continuing to be able to licence medicines and providing relevant safety information about them. This also ensures that businesses are

willing to bring new products to market as only medicines and medical devices that meet UK standards would make it to market and would not have to compete with sub-standard products.

9. On this basis, Option 1 is the preferred option in the unlikely event of no deal being agreed with the EU before 29 March 2019. Option 2 is not feasible because it does not protect the UK regulator's ability to take regulatory action to protect public safety and is discounted from this analysis. Option 3 is not feasible because it does not minimise burdens on businesses as the UK exits the EU and is also discounted from this analysis.

Policy objective and overall rationale for intervention

10. The overall approach in the unlikely event of no deal being agreed with the EU before 29 March 2019 is for the Secretary of State for Health and Social Care and the Minister for Health, Social Services and Public Safety in Northern Ireland, acting through MHRA as a stand-alone medicines and devices regulator, to take any decisions and carry out functions that are currently taken or carried out at EU-level. These would include deciding on applications for marketing authorisations (MAs) which are currently obliged to use the centralised procedure, paediatric matters and orphan status.

11. The MHRA would continue to carry out the wide range of work it currently does on a national basis including medicines licensing, pharmacovigilance, inspections, standards and enforcement. the MHRA would also take an expanded role in registration, assessment, and post-market surveillance of medical devices.

12. More specific details around how these principles are applied to specific policy decisions are outlined in the costs and benefits sections for each policy issue.

Section 1: Medicines

Batch testing and Qualified Person certification of human medicines

Summary of policy proposal in preferred option

13. As described in the Technical Notice for Batch testing medicines if there's no Brexit deal, in order to continue to protect safety and minimise disruption and protect the medicines supply chain, the UK would recognise batch testing carried out in countries named on a list set out by the MHRA for a limited time. In this scenario, on Exit day, this list would include EU and EEA countries and those third countries with whom the EU has already made arrangements under article 51(2) of the Directive on the day the UK leaves the EU.

Benefits and rationale of approach

14. This approach would preserve the status quo and protect the supply chain of medicines in the short term through accepting batch testing, certification and release from trusted countries, including the EU and EEA on Exit day.

Costs: Direct Costs

15. As this option preserves the status quo in terms of UK recognition of EU/EEA batch testing, there is no additional cost to industry.

Data and marketing exclusivity for Marketing Authorisations

Summary of policy proposal in preferred option

16. It is not proposed that there will be any change as a result of EU exit to the data and marketing exclusivity periods enjoyed by the holders of UK national MAs or converted EU MAs.

17. After the UK's withdrawal, the start of data and/or market exclusivity will be the date of authorisation in the EU or UK, whichever is earlier.

Benefits of preferred approach

18. This approach does not represent a change to the status quo. It has been adopted to encourage companies to submit applications for innovative products to the UK as soon as possible (see the wider impacts section a full description of the issue of possible delays) and therefore is beneficial in protecting public health in the UK.

Costs: Direct costs

19. There will be no additional cost to industry unless individual businesses decide to delay their UK market authorisation applications. In this case, they will lose any additional revenue in the UK as a result of a shortened UK exclusivity period and earlier possible generic entry.

Change M1: Legal presence

Summary of policy proposal in preferred option

20. At present, the UK as part of the EU medicines regulatory network, requires a marketing authorisation holder to be located in the EU/EEA. In the unlikely event of no deal being agreed with the EU before 29 March 2019, a Marketing Authorisation Holder (MAH) would have to be established in the UK by the end of 2020. Until a UK MAH is established, the UK would require a contact in the UK. This person (MAH or interim contact person) would be responsible for taking urgent action in the event of a safety concern. The MAH would retain ultimate legal responsibility during this period.

21. As is the case today, the UK require a Qualified Person for Pharmacovigilance (QPPV) to be responsible for delivery of a pharmacovigilance system that covers UK authorised products. In the unlikely event of no deal being agreed with the EU before 29 March 2019, given that the EU QPPV would not have legal responsibility towards UK authorised products, a QPPV would need to be established in the UK by Exit day. Those without a current UK presence would have until the end of 2020 at the latest to establish a UK presence but would nevertheless be required to make arrangements for providing the MHRA with access to the relevant safety data related to UK Marketing Authorisations (MAs) at any time, and comply with UK inspection requirements, during that interim period. Companies may choose to have the EU QPPV take on responsibility for UK MAs until the UK QPPV could be established. A variation should be submitted to the MHRA to change the QPPV.

Benefits of this option (rationale for approach)

22. Legal presence is important in protecting public health by giving the ability to prosecute in enforcement cases. In the event of an adverse incident, MHRA needs to be able to contact companies at any time. The ability to prosecute a MAH in appropriate circumstances is important to deter unsafe practice.

23. The requirement for a QPPV that resides in the UK allows the MHRA to gain access to the pharmacovigilance system data and documentation applied to UK MAs, in order to maintain MHRA's supervisory role over MAH compliance with pharmacovigilance.

Costs: Direct Costs

24. From Exit day, there would be a cost to industry in establishing a contact person, MAH and QPPV presence in the UK for those who do not already have a UK presence, compared to the status quo, including a direct cost to change the MAH to a UK MAH. This would include the costs of establishing any premises, familiarisation and administration for the interim contact person or MAH, and QPPV to comply with the new legal requirements, and labour costs for these representatives.

Change M2: New marketing authorisation (MA) assessment routes

Summary of approach in preferred option

25. As the UK would no longer be part of the European medicines regulatory framework in the unlikely event of no deal , the MHRA would offer the following new assessment procedures for applications for products containing new active substances alongside our existing 210-day national licensing route (which would continue to operate as now):, which would represent additional costs to those firms who currently apply to the EMA for authorisation in all member countries.

26. A targeted assessment of new applications for products containing new active substances or biosimilars which have been submitted to the EMA and received a Committee for Medicinal Products for Human Use (CHMP) positive opinion, based on submission of all relevant information and the CHMP assessment reports. New fees for marketing authorisations under a new national targeted assessment route would be: £62,421 for a new active substance; and £17,330 for a biosimilar.

27. A full accelerated assessment, for new active substances, with a reduced timeline of no more than 150 days. The fee for this would be the same as the current national assessment route major fee of £92,753.
28. The MHRA would also offer a 'rolling review', for new active substances, which would allow companies to make an application in stages.

29. The existing (210-day) national assessment route would also remain available for MA applications. This route would continue to be available for all MAs, including all new active substances and those that would have gone through the centralised procedure. The existing MHRA national fees for such applications would apply (see gov.uk: https://www.gov.uk/government/publications/mhra-fees/current-mhra-fees).

Benefits of option (rationale for approach)

30. This approach is proposed to ensure that the principle of the UK's ability to protect public safety is upheld while still minimising burdens and processes on business.

31. For targeted assessment, the MHRA would not be seeking to repeat questions or work - it would be focusing its contribution on ensuring the quality, safety and efficacy of the product in the context of clinical use in the UK. The UK decision would only differ from EU in the situations where there is a significant public health concern about the risk/benefit of the product.

32. The proposed targeted assessment fees are based on the incoming mutual recognition (IMR) fee for a marketing authorisation for major application for a new active substance (£62,421) and for a complex abridged application (£17,330) for a biosimilar. The MHRA considers that basing the proposed fees for targeted assessment on existing fees for IMR is merited as targeted assessment requires a similar amount of work by the assessment team as IMR assessment, and therefore the costs to MHRA are similar. Two fees are required to reflect the different amount of assessment work required for applications involving a new active substance and a biosimilar.

33. The accelerated assessment route would be made available for those products containing a new active substance in order to support the quickest route to the UK market.

34. The 'rolling review' would allow for companies to better manage development risk.

Costs: Direct Costs

35. This would represent an additional direct cost to industry for each application for a new active substance or biosimilar compared to the status quo of applying through the European centralised procedure at the EMA and receiving approval across all EU countries. The level of cost would depend on the UK route selected.

36. For those marketing authorisation holders who previously used the decentralised (DCP) or mutual recognition (MRP) procedures, these routes would no longer exist to obtain a UK MA, and they would now have to apply for a UK MA separately. MHRA fee income changes and costs to business would depend on which proportion of firms selected the UK as a Reference Member State (whereby the MHRA lead the assessment) and how many selected the UK as a Concerned Member State (CMS) (whereby the MHRA decide whether to accept the decision of the RMS), and also on the level of the CMS and RMS fees in other countries.

37. There would also be the administrative cost of the additional application and maintenance of the marketing authorisation, and also the cost of the additional periodic fees associated with keeping the marketing authorisation.

Change M3: Converting centrally authorised products (CAPs) to UK MAs (grandfathering)

Summary of policy proposal in preferred standalone option

38. Currently the UK is part of the European Medicines Agency, where products can be authorised centrally through a single application. To protect medicines supply, existing CAPs at the EMA would be converted automatically into UK MAs and issued with a UK marketing authorisation (MA) number on Exit day. Marketing Authorisation Holders (MAHs) would be given the opportunity to opt out of conversion prior to Exit day. No fee would be charged for the grandfathering process.

39. MAHs would have one year from Exit Day to provide MHRA with baseline data for CAPs that are converted to UK MAs. Baseline data should be submitted before any variations can be accepted by the MHRA. Under exceptional circumstances, the MHRA would allow variations to be submitted prior to baseline data.

40. Any product that is granted a UK licence as of 1st April 2019 would be charged a periodic fee almost immediately under existing periodic fee rules (see gov.uk:

https://www.gov.uk/government/publications/mhra-fees/current-mhra-fees)

Benefits of this option (rationale for approach)

41. The rationale of this option is to provide continuity of licences and the medicines supply chain. The proposed approach aims to have the minimum possible additional burden on industry.

Costs: Direct Costs

Industry

42. In terms of transition costs, we anticipate that there would be additional administrative costs to industry who currently sell in the UK and EU27 of providing MHRA with the baseline data in terms of staff time. There are also costs to these businesses of maintaining their UK MA, including the Periodic Fee, legal costs, and administrative costs. This is the same as the recurring costs for new marketing authorisations as outlined in the fees section.

MHRA (HM Government)

43. There would be one-off costs to the MHRA for staffing and IT in order to convert CAPs and variations from EMA to UK MAs. As MHRA is a trading fund, it must operate on a cost recovery basis. In order to incentivise conversion, cost recovery would not be front loaded through a conversion fee. Rather, costs would be recovered by periodic fees on those converted, to reduce burden on industry.

Change M4: Packaging

A) Amending packaging and leaflets for a product on the market

Summary of policy proposal in preferred option

44. Packaging of medicines in the UK currently reflects the UK's status as part of the European medicines regulatory network and would therefore need to be amended to reflect regulatory changes implemented in a no-deal scenario. We would give industry until end of 2021 (i.e. an additional year after the time required to change MAH) to amend packaging and leaflets for a product already on the market. The amendments should be necessary to include UK administrative information such as UK MAH name and address, UK PL number and details of the batch release site. However, any regulatory intervention that impacts on public health, and would require a change to the public facing information as a result, should be accompanied by amended packaging components reflecting those changes along with the necessary administrative updates as above.

45. The UK would continue to approve shared packs that include administrative information from other jurisdictions, so long as the entirety of the information complies with UK requirements.

Benefits of preferred option (rationale for approach)

46. This approach balances the need to protect public health through the provision of UK-required administrative information with a proportionate and pragmatic response which should allow business sufficient time to provide this information.

Costs: Direct Costs

Industry

47. There would be the administrative and manufacturing cost to industry of amending packaging to include their UK information, however this is likely to be minimised as the UK would accept shared packs which share information from other jurisdiction(s), so long as the entirety of the information complies with UK requirements. This means that although there would be the cost of changing the packaging itself initially, in terms of administration, it should be possible to use the same pack in more than one territory if that is acceptable to the other jurisdiction(s). There would also be cost of variation fees to change the packaging.

B) Falsified Medicines Directive (FMD)

Summary of policy proposal in preferred option

48. The UK is expected to implement the Falsified Medicines Directive 'safety features' element in February 2019. In the unlikely event of no deal being agreed with the EU before 29 March 2019, we expect the UK would not have access to the EU central data hub, and therefore stakeholders would be unable to upload, verify and decommission the unique identifier on packs of medicines in the UK. Therefore, the legal obligation related to this would be removed for actors in the UK supply chain. Packs containing the FMD safety features would still be accepted in the UK, provided that they are in line with other UK packaging requirements. In the interests of public safety, we will evaluate the options around a future national falsified medicines framework, which would inform the detail of any short or longer-term modifications.

Benefits of preferred option (rationale for approach)

49. By accepting packs containing FMD safety features in the UK, provided that they are in line with other UK packaging requirements, this approach minimises burden on business and protects the medicines supply chain.

Costs: Direct costs

50. This approach has no additional costs on industry, provided that manufacturers are in line with other UK packaging requirements.

Change M5: Paediatric investigation plans (PIPs) and studies

Summary of policy proposal in preferred option

51. MA applications for new medicinal products and applications for new indications, including paediatric indications, routes of administration and new pharmaceutical forms for products with supplementary

patent protection would need to demonstrate compliance or partial compliance with a UK Paediatric Investigation Plan (PIP) or have a waiver.

52. Paediatric Use Marketing Authorisations (PUMAs) maybe granted through any appropriate national licensing route and are eligible for 8+2 years data exclusivity/market protection.

53. Class waivers, product-specific waivers and deferrals would be possible as per existing EU system.

54. Reward of a 6-month extension for a UK Supplementary Protection Certificate (SPC) (which extends the patent period) based on a UK MA that complies with a PIP and paediatric information in the Summary of Product Characteristics (SmPC)/Patient Information Leaflet (PIL) would be granted in the UK on the same basis as it is currently granted.

55. There would be 2 years additional market exclusivity for orphans complying with a PIP, as at present.

56. Newly completed paediatric studies would need to be submitted for assessment by UK MA holders.

57. Where an application has already been made to the EMA and a positive Paediatric Committee (PDCO) opinion has been given, the EU PIP may be adopted as the UK PIP on provision of the same information already submitted to the EMA including the EMA Paediatric Committee (PDCO) summary reports and PDCO opinion.

58. An exception to this would be in cases relating to UK public health where a focussed assessment would be conducted. This would be particularly considered for products covering rare paediatric conditions, including medicines with paediatric only development, or medicinal products to be developed in therapeutic areas that have been identified in the UK as unmet needs. The focussed assessment would include consultation with expert advisory groups and/or Commission on Human Medicines to ensure the proposed drug development plan agreed in the PIP for the product covers the needs and context of clinical use in the UK.

Benefits of preferred option (rationale for approach)

59. In the unlikely event of no deal being agreed with the EU before 29 March 2019, where the UK chooses to take a ‘standalone’ approach to medicines regulation, the MHRA would seek to provide incentives for marketing authorisation holders (MAHs) of paediatric medicines to bring these medicines to the UK.

60. If an incentive structure is not in place to incentivise MAHs to carry out this work following EU Exit, public health in the UK could face one of two possible scenarios:

    1. New paediatric medicines may come to the UK later than to EMA members, or;

    2. New paediatric medicines may not come to the UK at all.

61. An additional consequence is the potential loss of participation of UK paediatric patients in ground-breaking research aiming to support the development of therapeutic options in areas of unmet clinical needs.

62. The introduction of a UK PIP would assist in ensuring the UK public health system has access to new medicines for paediatric use, by having processes and procedures in place so that the MHRA can continue to carry out licensing assessment work for this category of medicine and that MAHs and developers of paediatric medicines have incentives to bring these medicines to the UK. UK has played a significant role in increasing research in medicines for children in Europe; since 2006, the percentage of paediatric clinical trials has risen, and the UK government has supported the development of research infrastructure through the NIHR, an investment that could be lost if the pharmaceutical industry chooses to conduct studies in jurisdictions only where they have regulatory obligations.

63. Adopting the EU PIP as the UK PIP, given a positive PDCO opinion and provision of the relevant documents, supports the UK's global collaboration in drug development within the limited paediatric population and thus avoids unnecessary duplication of paediatric clinical trials.

64. The rationale for focussed assessment is to provide the option to ensure that the proposed drug development and paediatric clinical trial(s) meets unmet paediatric needs in the UK, for example in rare conditions or medicines requiring paediatric only development. It would also provide the option to take action if there is a strong objection to the proposed paediatric investigation plan on public health grounds – further strengthening the UK's capabilities to promote ethical and scientifically robust paediatric drug development.

Costs: Direct Costs

65. As with current paediatric work that the UK undertakes on behalf of the EMA, this would be covered by the periodic fee, therefore there is no additional cost to industry beyond the administration costs associated with the additional submission of the PIP to the UK.

Change M6: Orphan designation

Orphan products

66. An orphan drug is one developed for the treatment of a rare condition. In the unlikely event of no deal being agreed with the EU before 29 March 2019 , where the UK chooses to take a 'standalone' approach to medicines regulation, in order to incentivise medicines in a similar way as the EMA does at present, the MHRA would seek to provide incentives for marketing authorisation holders (MAHs) of orphan drugs (following the EMA definition and amending where necessary) to bring these medicines to the UK.

Summary of policy proposal in preferred option:

67. The EU orphan criteria would be amended so that they have UK-specific criteria (in relation to the prevalence of the rare disease in the UK and the satisfactory methods of treatment in the UK and significant benefit).

68. The MHRA proposes to explore retention of the most important orphan incentive – namely 10 years market exclusivity from competition from similar products in the approved orphan indication. This incentive would be conferred at the time of MA approval and the evaluation of compliance with orphan criteria would be conducted in parallel with the review of quality, safety and efficacy at the time of the MA application.

69. However, the MHRA does not propose to duplicate the EU pre-approval orphan designation, given that this will be available at EU level and that a separate UK only designation is unlikely to further incentivise industry to warrant the investment required to resource a separate system. As it is proposed to have UK specific criteria, it would not be possible to simply copy the EU designation for these high value drugs.

Benefits of this option (rationale for approach)

70. In the unlikely event of no deal being agreed with the EU before 29 March 2019, where the UK chooses to take a 'standalone' approach to medicines regulation, the MHRA would seek to provide incentives for MAHs of orphan drugs to bring these medicines to the UK.

71. If an incentive structure is not in place to incentivise MAHs to carry out this work following EU Exit, public health in the UK could face one of two possible scenarios:

    - New orphan drugs may come to the UK later than to EMA members, or;
    - New orphan drugs may not come to the UK at all.

72. The exclusivity award has been highlighted by stakeholders as being very important to MAHs who develop orphan drugs, and this should be preserved.

Costs: Direct Costs

73. As this option preserves the status quo, there is no additional cost to industry, except for the fee waiver as described in the fees section, change F1.

Change M7: Abridged applications

Summary of policy proposal in preferred option:

74. In the unlikely event of no deal being agreed with the EU before 29 March 2019, the MHRA would not have access to the data provided in support of EU approved products. Therefore, new generic applications would need to be based on reference products that have been authorised in the UK, including CAPs that have been converted in UK MAs.

75. Existing MAs for generic products which are based on a reference product authorised in the EU would remain valid.

76. It is proposed that the various abridged procedures to getting an MA (generic applications/hybrid abridged/biosimilars/well-established use and new combinations of existing products/consent) would remain in place, but with modifications to reflect the UK's exit from the EU. The legal basis for these

applications is currently described in Articles 10 – 10c of the Directive, which in turn cross-refer to Article 6. There would be amendments to the HMRs to transpose these requirements.

77. It is proposed that amendments would be made to the effect that it would not be possible to rely on a European reference product post-Exit, the reference product would have to have been authorised in the UK (this would include products which have a UK MA because they are converted EU MAs). However, for applications relying on well-established use (Article 10a), the use could continue in the UK or the EU / EEA post-Exit.

78. Comparators used in bioequivalence studies for the purpose of approval of generic medicines should be authorised for the UK market, if not then the batch(es) selected for use in bioequivalence study(ies) should be shown to be representative of the product(s) authorised in the UK.

Benefits of option (rationale for approach)

79. This option allows for a pragmatic approach to abridged applications, preserving the status quo as far as possible, given that MHRA would not have access to the data provided in support of EU approved products.

Costs: Direct Costs

80. We expect the impact of this requirement to be minimal because the overwhelming majority of new active substances are approved through the EU centralised procedure and the already approved products would be grandfathered by the UK. Additionally, our experience is that there are very few applications made in the UK relying on an EU reference product.

Change M8: Increased requirements for needing a manufacturer's licence for import or a wholesale dealer's licence

Summary of policy proposal in preferred option

81. An existing manufacturer's licence for import (MIA) or wholesale dealer's licence would remain valid. However, it is proposed that human medicines with a UK MA, which are imported into the UK from the EU/EEA, should require a MIA post-Exit.

82. The UK MIA used for importation into the UK would allow the naming of Qualified Persons (QPs) in countries that are on the relevant MHRA designated country list.

83. It is proposed that a transitional provision would be put in place for those who need a different type of licence as a result of the changes.

Benefits of preferred option (rationale for approach)

84. This approach is vital in helping to protect the medicines supply chain the unlikely scenario of no deal with the EU. Upon the UK exiting the EU, EU/EEA countries would become third countries. As a result, a manufacturer's licence for import (MIA) would be required to import human medicines into

the UK from the EU/EEA. Currently, medicines manufactured in, or imported into, the EU/EEA under the control of a EU-based MIA are supplied to the UK via a UK wholesale dealer, who would hold a wholesale dealer's licence, or through direct sale from a EU wholesale dealer or manufacturer to an 'end user', e.g. a NHS trust.

Costs: Direct Costs

85. There would be an additional fee and administration costs associated with the MIA requirement for those companies that do not currently have a MIA for importing medicines with a UK MA into the UK.

Change M9: Recognition of prescriptions

Summary of policy proposal in preferred option

86. EU and EEA countries currently mutually recognise prescriptions issued by qualified professionals in any other EU/EEA country.

87. Human Medicines Regulations 2012 define who is eligible to issue prescriptions that can be dispensed in the UK.

88. The regulations would be amended so that the UK recognises prescriptions from those countries on a designated country list from day one. This list would initially include EU and EEA countries.

Benefits of preferred option (rationale for approach)

89. At present the EU cross border healthcare directive means that prescriptions issued in any member (or EEA) state can be dispensed across the EU. This would cease to apply to the UK after the end of the implementation period or from March 2019 in the case of no-deal. By recognising EU and EEA states in the legislation, the status quo is preserved, and the UK continues to take a pragmatic approach to safety while enabling business continuity.

Costs: Direct Costs

90. As this option preserves the status quo in the UK, there is no additional cost to industry.

Section 2: Clinical Trials

Change CT1: Legal presence – clinical trials

- **Summary of policy proposals in preferred option**

91. Currently, a sponsor or legal representative for clinical trials in the UK can be located in the EU/EEA. In the unlikely event of no deal being agreed with the EU before 29 March 2019, the UK would require the sponsor or Legal Representative to be in the UK or a country on a designated country list from Exit Day. This list would initially include EU and EEA countries. Where the sponsor or legal representative are not based in the UK, we propose introducing a duty on the sponsor to ensure that the chief investigator (CI) in the UK is contactable, and UK-based to provide real assistance and facilitate action if needed.

Benefits of preferred option (rationale for approach)

92. The proposal would ensure that as now, someone will be contactable who has the ability to halt a clinical trial if required, in order to protect patient safety.

93. The use of a designated country list helps to maintain the status quo for trial sponsors and legal representatives and does not put an additional burden on organisations wishing to hold a trial in the UK above what is required today.

Costs: Direct Costs

94. There would be a small administrative transition and recurring cost of having a contactable person in the UK for organisations who do not already have one, which would include staffing and other administrative costs.

Change CT2: Transparency

- **Summary of policy proposals in preferred option**

95. To ensure continued transparency of clinical trials, in keeping with the current situation, a change would be made for there to be a requirement for sponsors to publish information on UK trials, in line with what is currently published about them in the EU clinical trials register.

Benefits of preferred option (rationale for approach)

96. For transparency, the publication of clinical trial information is proposed in order to ensure that information published in the UK on trials is as transparent as they are at present in the EU.

Costs: Direct Costs

97. There would be a small administrative burden for organisations (in submitting information) and for MHRA in publishing the information about clinical trials.

Change CT3: Use of designated country lists, including for legal presence and importation of investigational medicinal products

- **Summary of policy proposals in preferred option**

98. The MHRA would develop lists of countries where activities relating to clinical trials can be performed. There would be three such designated country lists:

    1. A designated country list where a sponsor or legal representative could be established.

    2. A designated country list from which:

        - The UK would accept the summary of product characteristics (SmPC) (in English) as an alternative to the investigators' brochure in an ethics application, where the IMP has a MA in that country.

        - advanced therapy medicinal products (ATMPs) that have an MA in the designated country would not be subject to usual special provisions for ATMPs when used in trials in the UK.

    3. Countries from which a UK MIA (IMP) holder could import IMPs that have already been certified by a QP, for which further certification would not be required in the UK (for IMPs both manufactured in or imported to that designated country).

99. On exit day, all EU/EEA states would be on all three lists. ICH countries would be included in the second list.

Benefits of preferred option (rationale for approach)

100. The designated country list would minimise burden on business by allowing certain activities relating to clinical trials to be performed in countries where the UK deems this safe to do so due to regulatory equivalence, thus maintaining the status quo where possible. This proposal would also protect public health by excluding countries where it is not deemed safe to carry out these activities.

Costs: Direct Costs

101. As these activities would be permitted to be carried out in EU/EEA states as at present, there would be no additional cost to industry.

Section 3: Medical Devices

Unilateral recognition of CE-marked medical devices and in-vitro diagnostic (IVD) medical devices

Summary of policy proposal in preferred option

102. The UK currently is part of the European CE-marking system for medical devices. In the unlikely event of no deal being agreed with the EU before 29 March 2019, the UK would unilaterally recognise the CE-mark for medical devices and in-vitro diagnostic (IVD) medical devices for a time limited period. In parallel, the MHRA would strengthen its market surveillance and assurance role to ensure the UK has sufficient ability to protect patient safety. The MHRA would retain the right to take enforcement action in respect of devices on the UK market, but only for justified safety grounds or non-compliance, as per status quo.

Benefits of preferred option (rationale for approach)

103. This option would ensure the continued supply of medical devices in the UK by allowing devices which are permitted in the EU/EEA to be marketed in the UK as at present.

104. However, recognising the principles of our overall approach in ensuring the UK is an effective standalone regulator, the market surveillance and assurance role of the MHRA will be strengthened to offset the broader benefits lost from being part of the EU devices regulatory network.

Costs: Direct costs

MHRA (HM Government)

105. There will be an additional cost to the MHRA in terms of labour and capital (IT) costs for strengthening its market surveillance and assurance role from building and running an expanded registrations system.

Change D1: Registration of medical devices

Summary of policy proposal in preferred option

106. The UK is currently part of the European medical devices regulatory framework. Registration requirements would be expanded to cover all medical devices and IVDs that are placed on the UK market in order to continue to ensure safety of devices on the UK market.

107. The responsibility for registering the medical device or IVD would fall to the economic operator (e.g. an importer, distributor or manufacturer) that first 'places the device' on the UK market. This economic operator (or UK 'sponsor') would need to be established in the UK and provide a registered address. There would be a grace period to allow time for compliance, which would – at least initially – require a small administrative fee broadly in line with the current registration charge for class I devices.

Benefits of preferred option (rationale for approach)

108. Implementing the above changes would enable MHRA's ability to carry out effective market surveillance on medical devices through enhancing its knowledge of the number and type of devices on the UK market, segregated by risk class.

a. This approach would allow for a straightforward regulatory route for manufacturers of medical devices, supporting them to place products on the market.

b. The grace period allows the UK to balance consumer safety with the need for businesses to be able to prepare for these changes.

109. However, these benefits are limited compared to achieving a common rulebook for goods, as set out in the Government's White Paper on the Future Relationship with the EU.

Costs: Direct Costs

110. This option would impose a direct cost on industry – exact costs could depend on the scope and scale of the registration process. There would also be costs associated with non-UK medical devices manufacturers having to nominate a UK 'sponsor' to place their products on the UK market.

111. We assume that acting as a 'sponsor' for an overseas devices manufacturer would be cost-neutral to the sponsor. This assumes that any regulatory costs incurred by the UK 'sponsor' would be passed on to the overseas manufacturer through any commercial agreement between the two parties, allowing the 'sponsor' to reclaim the direct costs of regulatory burden.

Section 4: Fees

Change F1: Fee waivers for orphan products

Summary of policy proposal in preferred option

112. The EMA currently offers waivers for orphan pharmaceutical products. The MHRA as a standalone regulator in the unlikely event of no deal being agreed with the EU before 29 March 2019 propose to offer fee waivers for orphan products for initial marketing authorisation (MA) applications, and variations in the first year after the initial marketing MA is granted. This would include:

- 100% fee waiver for small-medium enterprises (SMEs) (for initial MA applications, and for variations in the first year after the initial MA is granted);
- 10% fee waiver for all other manufacturers (for initial MA applications only).

Benefits of preferred option (rationale for approach)

113. Incentives are important to ensure that MAHs continue to carry out this work and bring orphan products to the UK market. The fee waivers help to incentivise bringing orphan products to the UK.

Costs: Direct Costs

HM Government

114. The preferred option would introduce additional costs to HM Government if the waiver was offered.

Change F2: New/amended MHRA fees for six processes/services previously provided centrally by EC/EMA

- **Summary of policy proposal in preferred option**

115. In the unlikely event of no deal being agreed with the EU before 29 March 2019, six other processes/services currently undertaken by the EU / EMA would need to be carried out in the UK in order to protect medicines supply and provide regulatory continuity. The MHRA is therefore proposing new MHRA fees for those existing EU/EMA processes for introduction on Exit day. The proposed MHRA fee levels are based on analogous existing products/services in the MHRA's existing statutory fees tariff and are competitive when set against the associated fees for the comparable existing EU/EMA processes/services. These are additional costs for businesses who currently sell in the UK and the EU27.

116. MHRA would charge fees for this work, which includes:

117. A fee of £8,309 for certification of a new Plasma Master File (PMF); a fee of £277 for a certified annual update of a PMF involving epidemiology updates only; and a new fee of £734 for a certified annual update of a PMF where there are significant changes to safety-related information.

118. A fee of £8,309 for certification of a new Vaccine Antigen Master File (VAMF).

119. Fees of £8,309 to undertake assessment of a Pharmacovigilance Post-Authorisation Safety Study (PASS) protocol, and £8,309 to undertake assessment of a PASS results.

120. A fee of £51,286 to undertake a Pharmacovigilance Major Safety Review.

121. A fee of £890 to undertake a single assessment of Pharmacovigilance Periodic Safety Update Reports (PSURs).

122. Amend Renewals fees so that all new medicinal products (new active substances), whether authorised nationally, or through a centralised procedure that will become a national licensed medicine from EU Exit day one, are subject to a renewal fee of £9,682 five years after the licence was first granted

123. Additionally, the MHRA would explore the possibility of offering fee waivers for MA applications for medicines considered to be orphan products to encourage such products on to the UK market (see Orphans section above).

Benefits of this option (rationale for approach)

124. By charging fees to industry, the MHRA is able to continue protecting UK public health by bringing regulation of medicines currently assessed by the EMA in-house. The implications of this option are that:

a) The MHRA is able to take on work in the above areas, as the Agency would be able to recover its costs – in compliance with Trading Fund rules against cross-subsidy.

b) The MHRA recovers its costs when undertaking work in the above areas, avoiding the need for the Department of Health and Social Care (DHSC) or HM Treasury (HMT) to subsidise MHRA activities – in violation of Trading Fund rules – which would have implications for other public spending priorities.

125. Charging these fees would allow consumers of medicines in the UK to continue to have confidence of the safety and efficacy of medicines on the UK market and incentivise manufacturers to place them on the UK market.

Costs: Direct Costs

126. These fees represent an additional cost to industry per product for the services listed in order to stay eligible for sale on the UK market in addition to the remaining EU27 countries. This analysis does not take into account that EMA fees could change following the UK's departure from the EU.

Section 5: NIBSC

Change N1: Independent UK batch testing of biological medicines and associated fees

Summary of policy proposal in preferred option

127. The UK is currently part of the EU Official Control Authority Batch Release (OCABR) network. In the unlikely event of no deal being agreed with the EU before 29 March 2019, where the UK is not part of this network, a new power in the Human Medicines Regulation HMRs would enable the licensing authority to require UK certification of batches (immunological medicinal products or a medicinal product derived from human blood or plasma) requiring batch testing by the National Institute for Biological Standards and Control (NIBSC), and a prohibition on sale or supply until such testing takes place. However, the UK may decide on a risk-based approach to waive the associated laboratory testing for some products/batches and replace it with a paper-based assessment of data.

128. EU Official Control Authority Batch Release (OCABR) certificates issued prior to 29 March 2019 would be accepted by the UK, whether they have been issued by the UK or another EU OCABR laboratory.

129. There would be a new statutory fee to enable NIBSC as the UK Official Medicines Control Laboratory (OMCL) to charge for OCABR certification and testing in the UK, broadly the same as the current fees charged by NIBSC in its role as an EU OCABR laboratory. Proposed fees are shown below, based on the existing fees tariff.

Price Bands	Proposed Certification Fee (£)	Proposed Laboratory Testing Fee (£)	Proposed Combined certificate/lab testing fee	Current NIBSC batch testing fee
Plasma pools	£90	£90 for 3 tests plus £25 for each additional test	£180 for 3 tests plus £25 for each additional test	£180 for 3 tests; £215 for 5 tests; £230 for 6 tests
Band A	£305	£1,355	£1,660	£1,660
Band B		£1,605	£1,910	£1,910
Band C		£2,035	£2,340	£2,340
Band D	£677	£3,013	£3,690	£3,690
Band E		£5,733	£6,410	£6,410
Band F		£9,673	£10,350	£10,350

Authorised copies	n/a	n/a	£50	£50

Benefits of this option (rationale for approach)

130. Introducing a fee tariff for NIBSC that enables the UK competent authority to continue its critical role in protecting public health. This would allow NIBSC to certify or re-test products to ensure their safety and efficacy for use in the UK.

Costs: Direct Costs

Industry

131. The preferred option would bring about increased costs to industry, as batch-release activities carried out in the EU27 would now require either certification or re-testing and certification for use on the UK market. At a minimum, this would mean paying a certification fee. At most, it would require the costs of full re-testing and certification.

Section 6: Rationale and evidence that justify the level of analysis used in the IA (proportionality approach)

Context in terms of EU Exit

132. This impact assessment relies on costs and benefits identified through policy development, research and initial meetings with industry.

133. Work is ongoing to analyse the costs, benefits, risks and wider impacts of no-deal plans. Information gathered during the consultation would assist MHRA and DHSC in understanding the costs, benefits and wider impacts of the UK becoming a standalone regulator.

Section 7: Risks and assumptions

Risk that industry is not sufficiently prepared for the additional requirements of a no-deal EU Exit under a standalone UK regulator in the proposed preferred option

134. Overall, this contingency legislation is aimed to be of benefit to businesses and help them to prepare for the possibility of no deal being agreed with the EU before 29 March 2019. The approach taken in the preferred no-deal option is to minimise burden on business while protecting public health. However, there is a risk that some businesses would not be prepared in time for these changes in legislation, in particular those changes which are resource intensive – particularly if the legislation is activated with little notice. This could cause disruption to the medicines supply chain. There are also risks associated with medical device manufacturers not getting re-certified by an EU27 Notified Body in time and the impact on the supply of medical devices in the UK.

135. There is some evidence that businesses are taking steps to prepare for EU exit in a July 2018 report - the EMA[1] contacted over 180 marketing authorisation holders (MAHs) of 694 human and veterinary centrally authorised medicinal products that are based in or have control procedures undertaken in the UK and found that overall, MAHs of centrally authorised medicines are taking steps to make the necessary changes to their marketing authorisations to prepare for the withdrawal of the UK from the EU.

136. However, one of the principles of MHRA's approach to this contingency legislation is to take a pragmatic and proportionate approach to regulation and ensure where possible that businesses have adequate time to implement changes. The MHRA and DHSC would take into account consultation responses on the proposed regulations and the timeframes needed for industry to implement them. As outlined in the preferred policy option, transitional arrangements for the majority of changes have been provided to mitigate these impacts.

137. The government has published technical notices relating to certain elements of EU exit and medicines and devices regulation in order to assist business in preparing for the possibility of no deal being agreed with the EU before 29 March 2019 and to minimise this risk. These are available here.

138. MHRA and DHSC will continue to review business preparedness for a no deal being agreed with the EU before 29 March 2019 and act accordingly.

Other risks and assumptions

Medicines

139. There is some uncertainty around the desirability for businesses in applying to a UK regulator and how this would affect public health and access to medicines.

[1] http://www.ema.europa.eu/docs/en_GB/document_library/Report/2018/07/WC500251842.pdf

140. Specifically, there is uncertainty on what proportion of businesses that would continue to pay the periodic fee for grandfathered CAPs. Also, as discussed in the public health impacts section which follows in the next section of this document, there is uncertainty around when companies would submit applications for new and innovative medicines to the UK as a standalone regulator and to what extent this would impact on public health. MHRA will continue to review the evidence in this area.

Section 8: Wider impacts

Indirect costs

141. In the unlikely event of no deal being agreed with the EU before 29 March 2019, duplicating regulatory processes between the EU could have a number of effects on pharmaceutical businesses and other organisations. For manufacturing authorisation holders (MAHs) of generics, biosimilars, and established new medicines authorised through the centralised procedure, there would be duplication of MA maintenance for CAPs and other additional processes to comply with as outlined in this Impact Assessment. It is likely manufacturers would seek to recoup these additional regulatory costs through price increases, which would affect NHS budgeting and spending choices.

142. For prospective manufacturing authorisation holders of these medicines, duplicated licensing procedures may act as a disincentive to apply for marketing authorisation in the UK, delaying patient access to new treatments and biosimilars. In this instance there is the possibility of NHS cost savings due to the high price of innovative medicines, however the wider economic costs of any public health impacts from inferior treatment options could cancel out any financial savings made.

143. It is also important to note that this IA only examines the impacts on business in terms of UK fees and does not examine any possible changes in EMA fees if the UK was to leave the EMA, and how this could impact businesses.

Public health impacts

144. In the unlikely event of a no deal being agreed with the EU before 29 March 2019, some third-party analysis has suggested that there could be delays in new innovative medicines coming to the UK market, once the UK has legislated to become a standalone regulator.

145. The evidence base for this area of concern is summarised below.

146. Centre for Innovation in Regulatory Science (CIRS) data analysed by the Office for Health Economics[2] for authorisations in the years 2013-2015 shows a 2-3 month median submission lag between applying to the EMA versus selected third country authorities, namely Health Canada, SwissMedic, and Australia's Therapeutic Goods Agency (TGA).

147. Using the same dataset, between 5% and 15% of submissions were submitted one year after the EMA.

148. Using the same dataset, 45% of submissions to EMA were not submitted to all three of the above comparators – SwissMedic did not receive 22%, TGA did not receive 29%, Health Canada did not receive 38%.

[2] https://www.ohe.org/sites/default/files/Technical%20Annex%20-%20final.pdf p.24

149. Separate CIRS analysis[3] showed that the size of the submitting company could also be a key factor – companies with a 2016 R&D budget under $3bn were shown to have larger submission gaps between the EMA and the US Food and Drug Administration (FDA), and third countries.

150. As the circumstances of EU Exit are without precedent, the CIRS figures have used proxy data from comparable national regulators outside the EMA network. However, this does not consider ways in which the UK may be a more attractive market than these proxies, or ways in which the UK can make itself a more attractive market, or the regulatory alignment of these proxy countries.

151. The pragmatic and proportionate approach to targeted assessment as outlined in this document is designed to mitigate the risk outlined above.

Small and micro business assessment (SaMBA)

152. The EMA Small and Medium Enterprises (SME) waiver for orphan medicines would be mirrored in legislation (excluding pre-approval designation stage). MHRA notes the importance of financial assistance for small and medium businesses and the UK would continue to provide incentives that it currently provides domestically, including the current 'Payment Easements for Small Companies' scheme. In order to provide a pragmatic response to a no-deal exit from the EU, other EMA SME waiver incentives would not be brought into UK law immediately on exit, rather they would be reviewed as part of the overall fees policy cycle (See post-implementation review section at the end of this document.)

3 Bujar M, McAuslane N, Liberti L. 2018. *R&D Briefing 67: New drug approvals in six major authorities 2008 – 2017: Focus on the availability of medicines and company size*. Centre for Innovation in Regulatory Science. London, UK. p.14

Section 9 Summary and preferred option, with description of implementation plan and review

Preferred option

153. The preferred option, in the context of this impact assessment, is for the MHRA to become a standalone medicines and devices regulator in the unlikely event of no deal being agreed with the EU before 29 March 2019 in UK-EU negotiations and implements the changes as outlined in this impact assessment and in more detail in the main consultation document.

154. The MHRA and DHSC will use the results from the consultation, including stakeholder views and quantitative analysis provided, to help inform detail of regulatory processes for no deal and to ensure that this achieves its objectives of protecting public health through a standalone UK regulator while minimising burdens on business where possible.

Post implementation Review

155. Better Regulation guidance[4] on inclusion of statutory review clauses for secondary legislation is as follows:

- *'The inclusion of review clauses in all EU withdrawal secondary legislation would create a large volume of concurrent reviews and potential challenges for regulatory stability and legal certainty. Furthermore, government takes the view that reviews of such correcting regulations would be impractical, and any potential benefit would be outweighed by the potential adverse effects in terms of cost and use of resource'*.

156. Based on the above guidance, a ministerial statement rather than a full Post-Implementation Review will be provided if this legislation is enacted.

157. However, the MHRA regularly reviews its fee levels internally, and this will be the case with fees introduced as a result of EU Exit. The MHRA, with support from DHSC, will also be producing a review of the incentives introduced as part of the EU Paediatric Regulation in late 2018 which will inform any future policy decisions in that area.

(ends)

[4] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/674755/small-business-act-s31-statutory-review-requirements.pdf p.7