



February 2019
CMDh/373/2018, Rev.3¹

Practical guidance for procedures related to Brexit for medicinal products for human use approved via MRP/DCP

This practical guidance complements:

- [Notice](#) to stakeholders – withdrawal of the United Kingdom and EU rules for medicinal products for human use, and
- The list of [Questions and Answers \(Q&As\)](#) related to the United Kingdom's withdrawal from the European Union with regard to nationally authorised medicinal products for human use.

These documents have been drafted jointly by the European Commission and CMDh and are available on the CMDh website.

The below Practical Guidance addresses the situation where the United Kingdom becomes a third country on 30 March 2019 ("the withdrawal date") without a withdrawal agreement and hence without a transition period provided for in the draft Withdrawal Agreement.

MAHs and applicants of nationally authorised products for human use need to ensure that the necessary changes are made by the withdrawal date, unless indicated otherwise in the guidance below.

This document aims to provide procedural and practical guidance regarding submission of changes.

¹ Revision 3 introduces additional questions and expanded responses to some previously published questions (new text is marked as "NEW"). The introductory text is also updated, in line with the revised Notice and Questions and Answers document.

1. For the switch of the RMS is it sufficient to have the DCP/MRP/RUP finalised or is it necessary to have already received a MA? If so, is it sufficient to have the MA in the proposed new RMS available or is a MA needed in all CMS?

It is sufficient to have the DCP/MRP/RUP finalised with EoP.

2. How can I submit my RMS switch request?

The CMDh has provided a template for a request to switch the RMS (<http://www.hma.eu/90.html>). The template should be sent to the proposed new RMS. Email addresses are available from the contact points list, "Requests for RMS switch" (<http://www.hma.eu/69.html>).

3. When can I apply for a switch of the RMS and when can the switch be implemented?

The switch can be applied for at any point in time after the EoP in a new MAA. However, for the implementation of the switch all other pending regulatory procedures, e.g. variations, renewals, etc., have to be closed. MAHs should preferably discuss the availability and timing beforehand with the proposed new RMS.

4. What can I do if not all strengths have been approved in the proposed single new RMS?

The new RMS can only take over procedures for which a MA is approved in this country. If single strengths are missing in the proposed new RMS there is the possibility to add these MAs by applying for a RUP in the current RMS. Otherwise, the missing strengths have to be switched to a different RMS. It should be assured that the smallest possible number of new RMS is chosen. Furthermore, a worksharing variation could be envisaged to keep the harmonisation.

5. If there are several MAHs in one MRP/DCP which of them can apply for the switch of the RMS?

According to the definition all MAHs within the same procedure are regarded as the same MAH. Generally, it is the task of the MAH in the current RMS to initiate the process.

6. Can I group Brexit-related variations?

Brexit-related variations can be grouped, where the grouping does not delay implementation of changes which need to be in place by the time of UK's withdrawal from the EU. All Brexit-relevant changes may be grouped (<http://www.hma.eu/96.html>).

7. How to classify Brexit-related changes impacting the manufacturing activities for my medicinal product?

Each batch of finished product must be certified by a Qualified Person within the EEA before being released for placing on the market in the EEA or for export. Certification can only be performed by a Qualified Person of the manufacturer and/or importer who is identified in the marketing authorisation and is located in the EEA (see [FudraLex, Volume 4](#), EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use [Annex 16: Certification by a Qualified Person and Batch Release](#)).

Also the site for batch control (where each batch undergoes full qualitative analysis, a quantitative analysis of at least all the active substances and other tests necessary to ensure the quality of the products in accordance with the requirements of the marketing authorisation) needs to be located in the

EEA or a country covered by a mutual recognition agreement. For products manufactured outside the EEA, also an authorised importation site in the EEA is required.

Products that only have batch release and quality control testing sites for finished product in the UK will have to change the batch release and testing sites. For products that have other batch release and testing sites the MAH may choose to delete the site(s) or may choose to replace them. For finished products manufactured in the UK an importation site (in EEA) will need to be introduced.

(NEW) Differently from importation of finished products (including bulk finished products), it is not required to register importation of intermediate finished products undergoing further processing as a separate activity in the MA dossier. However, the respective site still needs to hold a Manufacturing and Importation Authorisation covering this activity.

In many cases, a single site can perform manufacturing, testing, importation and/or batch release activities. In case the MAH decides to move part or all of these activities, the following scenarios, although not exhaustive, may apply:

Manufacturing process	Non-biological/non-immunological	Biological or immunological product
Addition or replacement of site		
The UK site is only a batch release site and/or importation site for the finished product	Type IA _{IN} (B.II.b.2.c.1)	Type IA _{IN} (B.II.b.2.c.1)
The UK site is a batch release and quality control site of the finished product	Type IA _{IN} (B.II.b.2.c.2)	Type IB (B.II.b.2.c.2) if the test methods performed at the site are not biological/immunological/immunochemical methods. Otherwise, it is Type II (B.II.b.2.c.3)
The UK site is only a quality control site of the finished product	Type IA (B.II.b.2.a)	Type IB (B.II.b.2.a) if the test methods performed at the site are not biological/immunological/immunochemical methods. Otherwise, it is Type II (B.II.b.2.b)
At the same UK batch release site, primary and/or secondary packaging also takes place ²	Type IA _{IN} (B.II.b.1a and b)	Type IA _{IN} (B.II.b.1a) – secondary packaging Type II (B.II.b.1c) – primary packaging
The UK batch release site performs manufacturing activities beyond batch release ²	Grouping: A single type II scope B.II.b.1 - Addition of a new finished product manufacturing site: changes to the manufacturing process, batch size and in-process controls to adapt to the new manufacturing site settings. And a type IA _{IN} (B.II.b.2) to add/ replace the batch	Grouping: A single type II scope B.II.b.1 - Addition of a new finished product manufacturing site: changes to the manufacturing process, batch size and in-process controls to adapt to the new manufacturing site settings. And a type IA _{IN} (B.II.b.2) to add/ replace the batch release site

² Only batch control and batch release testing need to take place in a site in EU/EEA, however, other activities can also be transferred between the same involved sites as part of the Brexit related applications, if desired.

Deletion of a manufacturing site		
Manufacturing process	Non-biological/non-immunological product	Biological or immunological product
Deletion of site(s) for batch release, packaging, batch control ³	Type IA (A.7)	Type IA (A.7)

Concerning the rules for grouping of Brexit-related applications please see above Question 6 “Can I group Brexit-related variations?”

8. What variation(s) shall I submit in case of a change of Notified body (previously from UK) for a medical device included in the pack?

For medicinal products that are co-packaged with medical devices (but do not form a single integral product at the time of placing on the market) it is required to include in their dossier evidence demonstrating that the device is CE marked.

The [Notice from the European Commission to Stakeholders on Withdrawal of the United Kingdom and EU Rules in the Field of Industrial Products](#) states the following:

Where economic operators hold certificates issued by a UK Notified Body prior to the withdrawal date and plan to continue placing the product concerned on the EU-27 market as from the withdrawal date, they are advised to consider either applying for a new certificate issued by an EU-27 Notified Body or arranging for a transfer – on the basis of a contractual arrangement between the manufacturer, the UK Notified Body, and the EU27 Notified Body - of the file and the corresponding certificate from the UK Notified Body to an EU-27 Notified Body, which would then take over the responsibility for that certificate.

Therefore, for medicinal products that are co-packaged (but do not form a single integral product) with a medical device for which the conformity assessment to support the CE marking was performed by a UK Notified Body, it will be necessary to either update the MA dossier with evidence supporting the CE marking by a new Notified Body, or remove the medical device from the pack, or replace the device with an alternative medical device with a valid CE mark.

A medical device forming a single integral product with the medicinal product does not require a CE mark, therefore no submission of a new CE marking documentation is required.

The following scenarios, although not exhaustive, may apply to medicinal product packs containing medical devices for which the conformity assessment to support CE marking was performed by a UK Notified Body:

Medical device forming a single integral product with the medicinal product	Medical device is co-packaged with the medicinal product
Same medical device is maintained, but the Notified Body supporting the CE marking is changed	
Variation not required (CE marking not mandatory), but if documentation in the dossier is updated: Type IA _{IN} (B.IV.1.a)	Type IA _{IN} (B.IV.1.a)

³ In case more than one manufacturer in one MA has to be deleted, a single variation of type IA under classification category A.7 to delete all manufacturing sites may be submitted.

Medical device forming a single integral product with the medicinal product	Medical device is co-packaged with the medicinal product
Replacement of the medical device with an alternative CE marked medical device	
Replacement not required (CE marking not mandatory), but if replacement is made: Type II (B.IV.1.c)	For device without significant impact on the delivery of the active substance: Type IA _{IN} (B.IV.1.a) For device with significant impact on the delivery of the active substance: Type II (B.IV.1.a)
Removal of the medical device from the pack	
Not applicable	Type IA _{IN} (B.IV.1.b)

9. Can I submit several changes relating to manufacturing of the active substance or finished product under a single Type II variation?

Introduction of a new manufacturing site for the active substance or for the finished product and their respective consequential changes can be submitted as a Type II variation separately for the active substance and for the finished product, thereby replacing a large grouping of Quality IB (and IA) variations for the consequential changes. Such an approach can be followed for changes of UK manufacturing sites which are related to the Brexit.

The principles for a single Type II variation have already been established and can be found in the respective approved grouping examples (<http://www.hma.eu/96.html>):

- The following complex, related changes could be considered for submission under a single Type II scope B.II.b.1 - Addition of a new finished product manufacturing site: changes to the manufacturing process, batch size and in-process controls to adapt to the new manufacturing site settings.
- The introduction of a new manufacturing site for an active substance supported by an ASMF should be submitted under a single Type II scope B.I.a.1.b. The introduction of a new manufacturer of the active substance not supported by an ASMF that requires significant updates to 3.2.S should be submitted under a single Type II scope B.I.a.1.g).
- In case the introduction of the new active substance manufacturer has an impact on the finished product manufacturer (e.g. changes to the active substance specifications or related analytical methods) separate variations have to be submitted under the corresponding B.I.b. categories and may be grouped together, if related to the introduction of the new active substance manufacturer.

In case there is also a change of the UK batch release site, its replacement requires a Type IA variation (B.II.b.2). If the site also performs Quality control activities please refer to Question 2 above. The variation(s) can be submitted as a grouping with the respective Type II variation.

10. When should I submit Brexit related type IA ("do and tell") variations that have to be implemented before 30 March 2019?

Certain changes that have to be fully implemented before 30 March 2019 can be submitted as type IA variations. Considering the regulatory nature of type IA variations (“do and tell”), and in order to avoid the need to implement such changes even earlier, it is acceptable that corresponding notification of type IA variation(s) is submitted no later than within 2 months after 29 March 2019 provided that the MAH is established in the Union (EEA) by that time.

Type-IA variations requiring immediate notification (‘IA_{IN}’) must in any case be notified (submitted) immediately following implementation of the change.

The MAHs are reminded that actual implementation of such changes must in any case take place before 30 March 2019, irrespective of the variation type.

11. How do I submit changes to Qualified Person for Pharmacovigilance (QPPV) and/or changes in the Pharmacovigilance Master File (PSMF) location? (for medicines for human use)

According to EU pharmaceutical legislation the QPPV must reside and carry out his/her tasks in an EEA Member State; and the PSMF also must be located within EEA.

For medicinal products for Human use, changes to the summary of the pharmacovigilance system i.e. changes in QPPV (including contact details) and/or changes in the Pharmacovigilance Master File (PSMF) location are to be notified to the authorities through the Article 57 database only without the need for a variation. MAHs are therefore not required to notify NCAs of changes to the QPPV or PSMF location by submitting a variation except in cases where there is a transfer of the MA to a new MAH. In those cases the new summary of the pharmacovigilance system still has to be submitted by a type IA IN variation under C.I.8.a. A variation to submit the summary of the pharmacovigilance system will not be necessary in cases where the MA is transferred within companies belonging to the same parent company and the same PSMF will continue to be used. (see Q/A 2.8 on variations - <http://www.hma.eu/20.html>). Upon a change in the QPPV or location of the PSMF, the Article 57 database should be updated by the MAH immediately to allow continuous supervision by the Competent Authorities.

12. What do I need to take into account when I change the PSMF location from UK to a Member State within the Union (EEA)?

In accordance with Article 7(1) of Commission Implementing Regulation (EU) No 520/2012 the pharmacovigilance system master file shall be located either at the site in the Union where the main pharmacovigilance activities of the marketing authorisation holder are performed or at the site in the Union where the qualified person responsible for pharmacovigilance operates. This requirement should be taken into account if the Pharmacovigilance System Master File (PSMF) is located in the UK and the marketing authorisation holder needs to change the PSMF location to a Member State within the Union (EEA).

13. Do I need to change the UK-based addressee of a PIP or waiver decision?

The EU Pharmaceutical legislation does not require the addressee of a PIP or waiver to be established in the EU/EEA. It is therefore not necessary to request a change of an addressee of a PIP or waiver that is located in the UK.

14. What Brexit-related changes to the Product Information can I include as part of other procedures affecting the Product Information?

A change of MAH or of batch release manufacturer require dedicated procedures (MA transfer or variation, respectively), during which any related update within the Product Information should be made, i.e. such amendments cannot be postponed till other, unrelated procedures.

An update of the package leaflet to delete the name of the product in the UK can be included as part of a future regulatory procedure (e.g. variation, renewal) affecting the package leaflet. The earliest opportunity after 29 March 2019 should be used.

Changes to the local representative mentioned in the product information are dealt with at a national level.

15. How should I notify the change of Official Medicines Control Laboratory (OMCL) currently in the UK?

For products subject to Official Control Authority Batch Release (OCABR) this activity needs to be conducted by a designated OMCL located in the Union (EEA) or a country covered by a mutual recognition agreement that includes recognition of OCABR. Products that currently have OCABR conducted only by UK OMCL will have to change their OMCL. For products that have other designated OMCL(s) the MAH may choose to remove the UK OMCL.

When designating a new OMCL and/or removing a previously designated OMCL located in the UK, the Marketing Authorisation Holders should notify such change to the RMS or relevant NCA in writing through submission of a letter in a new eCTD sequence.

16. How shall I reflect UK national scientific advice in submissions made after 29 March 2019?

National scientific advice from UK competent authorities will be regarded, as of the withdrawal date, as a scientific advice from a third country. Information on any third country scientific advice can be included in the application dossier, as appropriate.

17. How can I change the UK based applicant to a non-UK based applicant for an ongoing marketing authorisation application?

For marketing authorisation procedures that are expected to be closed after 29 March 2019, the applicant must be established in the Union (EEA). Where the application was initially planned for a UK based company and it has not been possible to change the applicant to a non-UK entity prior to the submission of the MAA, such change will need to be made during the procedure.

Making such change to an ongoing MA application is possible at certain procedural milestones in case the change of applicant will not create a 'duplicate application' to another pending application or authorised product.

In order to request a change of the applicant, the following documents need to be submitted as part of the Day 106 or Day 160 responses in the decentralised procedures or Day 40 responses for mutual recognition procedures so that by 29 March 2019 the change is implemented:

- A letter requesting the change of applicant and signed by both the previous and the new applicant.
- A confirmation (as part of the cover letter) that complete and up-to-date file concerning the

medicinal product or a copy of this file has been made available to or has been transferred to the new applicant.

- Updated application form and affected annexes (includes proof of establishment of the new applicant within the Union (EEA) issued in accordance with national provisions and which should be no older than 6 months and the power of attorney for a person communicating on behalf of the new applicant).
- Updated summary of the pharmacovigilance system.
- Any other documents of the marketing authorisation dossier affected by the change of applicant, as relevant (e.g. an updated Letter of Access for an application that includes an Active Substance Master File).

The applicants are encouraged to request the changes as early as possible as the acceptability of the proposed changes will need to be assessed.

18. Should I update my ongoing MA application with regards to other entities or activities currently located in the UK?

For marketing authorisation procedures (MAAs) that are expected to be closed after 29 March 2019, the future MAH, QPPV, batch release sites, batch control sites, intended OMCL (if applicable) and nominated local representatives for Member States other than UK must be located in the Union (EEA). Where it has not been possible to amend the application in this regard prior to the submission of the MAA, such change will need to be made during the decentralised procedure.

In order to request the above listed changes, a cover letter highlighting the proposed changes and updated affected dossier documents (e.g. updated product information and mock-ups, if applicable) will need to be submitted as part of the Day 106 or Day 160 responses in the decentralised procedures. The change of future MAH should be accompanied with an updated Summary of the Pharmacovigilance System.

The applicants are encouraged to request the changes as early as possible, in particular with regards to manufacturing sites, as the acceptability of the proposed changes will need to be assessed.

For MRP, necessary updates should be made via the appropriate variation procedure in advance of submitting the application to the CMS. During an ongoing MRP any necessary update of the application should be made with the Day 40 responses and is limited to issues not covered by the variation regulation like the future MAH.

19. How will the UK's withdrawal affect ongoing applications that include manufacturing sites with GMP certificates issued by UK authorities? (NEW)

According to Annex I of Directive 2001/83/EC the manufacturing process shall comply with the requirements of Article 4 of Commission Directive 2003/94 laying down the principles and guidelines of Good Manufacturing Practice (GMP) for medicinal products for human use, published by the Commission in "The rules governing medicinal products in the European Community", Volume 4. GMP certificates issued by EU/EEA competent authorities are commonly used to confirm EU GMP compliance in regulatory submissions (e.g. marketing authorisation applications).

For Marketing authorisation and post-authorisation applications in national procedures that are under assessment at the time of UK's withdrawal from the Union a risk based approach will be applied by the assessing competent authorities concerning the sites with GMP certificates issued by UK. As part of the

assessment of a marketing authorisation application or variation it will be considered whether there is a need to request a GMP inspection by an EU/EEA Competent Authority before concluding the procedure in question, or whether such inspection shall be conducted at a later stage in line with timing decided by the appointed EU27/EEA supervisory authority.

20. How shall I reflect GMP certificates issued by UK authorities in regulatory submissions made after 29 March 2019? (NEW)

In regulatory applications submitted after 29 March 2019 any GMP certificates issued by UK authorities (regardless of the date of issuance) should be included as supportive information on GMP compliance. Such certificates should be listed in the respective application forms as a GMP certificate from a third country authority.

21. How will the UK's withdrawal affect applications relying on clinical studies for which GCP inspections have been conducted by UK authorities? (NEW)

According to Article 8(3)(ib) of Directive 2001/83/EC the marketing authorisation application shall be accompanied by a statement to the effect that clinical trials carried out outside the European Union meet the ethical requirements of Directive 2001/20/EC.

In accordance with Commission Directive 2005/28/EC it is necessary that inspectors ensure the practical effectiveness of the rules on good clinical practice.

As part of the assessment of applications in national procedures it will be considered in a risk based approach whether there is a need to request a GCP inspection by an EU/EEA Competent Authority before concluding the procedure in question.

22. How will the UK's withdrawal affect GLP status of non-clinical studies conducted in the UK? (NEW)

According to Article 2 of Directive 2004/10/EC, when submitting results, the laboratories referred to in Article 1 of that Directive shall certify that the tests have been carried out in conformity with the principles of Good Laboratory Practice (GLP).

Following [Decision C \(97\)186/Final](#) of the OECD Council on the Mutual Acceptance of Data in the Assessment of Chemicals, data generated in the testing of chemicals in an OECD Member Country (including UK), in accordance with OECD Test Guidelines and the OECD principles of GLP, are accepted in other OECD Member Countries.

23. Who will be responsible for the handling of market complaints, quality defects and recalls of batches that have been released by an UK site and supplied to the EU27/EEA before 30 March 2019? (NEW)

According to Article 6(1a) of Directive 2001/83/EC, the marketing authorisation holder shall be responsible for marketing the medicinal product. The designation of a representative shall not relieve the marketing authorisation holder of his legal responsibility.

The overall responsibility for a medicinal product therefore lies with the marketing authorisation holder. The marketing authorisation holders must ensure that market complaints, quality defects and product recalls are handled in accordance with EU requirements, if necessary taking over follow-up activities that otherwise would have been undertaken by the discontinued batch release site.

24. What will change in submission into EudraCT of clinical studies conducted in UK? (NEW)

The impact on the reporting requirements for protocol and result related information, as well as the establishment requirements are addressed in the [European Commission Notice on the withdrawal of the United Kingdom and EU rules in the field of clinical trials](#).

25. What will change regarding reporting requirements to EudraVigilance (EVCTM) for suspected unexpected serious adverse reactions (SUSARs) related to clinical trials conducted in the UK? (NEW)

In accordance with Article 107 of Directive 2001/83/EC suspected adverse reactions occurring in the context of clinical trials shall be recorded and reported in accordance with Directive 2001/20/EC. SUSARs related to clinical trials occurring in the UK before 30 March 2019 should be reported by sponsors in accordance with chapter 7 "Reporting of Suspected Unexpected Serious Adverse Reactions by the Sponsor" of the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3').

Third country reporting requirements will apply for SUSARs occurring in the UK as of 30 March 2019. In accordance with paragraph 69 of chapter 7 of the Detailed guidance i.e. the sponsor of a clinical trial performed in at least one Member State (i.e. where an EU27/EEA Member State is involved in the study) should report the following SUSARs:

- all SUSARs occurring in that clinical trial, irrespective of whether the SUSAR has occurred at a trial site in a Member State or at a trial site in a third country concerned,
- all SUSARs related to the same active substance (regardless of pharmaceutical form and strength or indication investigated) in a clinical trial performed exclusively in a third country or exclusively in another Member State, if that clinical trial, is
 - sponsored by the same sponsor, or
 - sponsored by another sponsor who is either part of the same mother company or who develops a medicinal product jointly, on the basis of a formal agreement, with that other sponsor⁴.

For sponsors conducting clinical trials with a medicinal product in UK, but not in any other Union (EEA) Member State the reporting obligations to EudraVigilance for SUSARs will cease from 30 March 2019.

26. What will be the impact of UK's withdrawal on procedures for single assessment of periodic safety update reports that include UK nationally approved products and related fees? (NEW)

All data submitted for single assessment of periodic safety update reports (PSUSA), including data submitted before the withdrawal date on UK nationally approved products, will be taken into account during the assessment. However, after the withdrawal date, UK products will formally no longer be part of any ongoing PSUSA procedure. As a consequence, after the withdrawal date assessment reports will no longer be shared with marketing authorisation holders for UK products that were previously concerned by the PSUSA procedure. The outcome of the PSUSA procedure will only concern products authorised in the Union (EEA).

⁴ Provision of the IMP or information to a future potential marketing authorisation holder on safety matters should not be considered a joint development.

The fees for PSUSA procedures are determined based on products authorised in the Union (EEA) (as recorded in 'Article 57 database') at the start date of the procedure. Until the withdrawal date this includes UK nationally approved products.

27. What will be the impact of UK's withdrawal on procedures for assessment of protocols and results of imposed non-interventional post-authorisation safety studies that include UK nationally approved products and related fees? (for medicines for human use) (NEW)

After the withdrawal date, UK products will formally no longer be part of procedures for assessment of protocols and results of imposed non-interventional post-authorisation safety studies (PASS). As a consequence, after the withdrawal date assessment reports will no longer be shared with marketing authorisation holders for UK products that were previously concerned by the PASS procedure.

The PASS procedures fees for each study are determined on first submission of the study protocol and on first study results submission. In case of several marketing authorisation holders involved, the fee is split equally by participating marketing authorisation holders at the time of first submission (of protocol or results, accordingly). Until the withdrawal date this includes participating marketing authorisation holders of UK nationally approved products.

28. What will happen to renewals, variations and worksharing procedures with the UK as RMS/reference authority when they are ongoing after March 29, 2019?

Renewals, variations and worksharing procedures with the UK as RMS/reference authority will automatically stop on March 30, 2019 and have to be submitted with a new RMS/reference authority.

The CMDh agreed for those ongoing renewals with the UK as RMS and not finalised by 29 March 2019, that the validity of the original application will be maintained when the amended application is submitted with new RMS and new procedure number. It should be clearly addressed in the cover letter to the amended renewal submission finalised.

29. What will happen to DCP procedures with the UK as RMS when they are ongoing after March 29, 2019?

Ongoing DCP applications with the UK as RMS will automatically stop on March 30, 2019 and have to be resubmitted completely new with a new RMS. For specific products regarded as essential for individual member states exemption from this rule as exceptional cases has been agreed by the CMDh. The respective member states will in these cases be prepared to take over the ongoing procedure and to perform a switch of the RMS during the ongoing procedure. For these specific procedures the proposed new RMS will contact the applicants proactively.

30. Can I still place my product on the market when the MAH, batch release site, local representative, QPPV or PSMF will still be located in the UK after March 29, 2019?

After March 29, 2019, products with these persons/activities still (only) located in the UK may no longer be placed on the market in the EU/EEA. Member states will take the necessary action on these products that are no longer compliant with the EU legislation. Marketing authorisation holders have to submit variations to replace these activities from the UK site to an EU/EEA site. Only after the activities have been transferred to sites in the EU/EEA the products may be placed on the market in the EU/EEA again. If products concerned are already released before March 29, 2019 but are still on the territory of the UK

they may not be placed on the EU/EEA market after March 29, 2019 unless they are imported in the EU/EEA and released again.

Products with these activities still located in the UK but already released and placed on the market on the territory of the EU/EEA until March 29, 2019, do not have to be re-called from the market.

31. What will happen to my ongoing DCP marketing authorisation applications when the applicant, future MAH, batch release site, batch control site, local representative, QPPV or PSMF will still be located in the UK after March 29, 2019?

The procedures will not stop automatically but can be further processed by the RMS (when not being the UK) until the EoP. For all activities as mentioned above the procedure might go on until Day 210 with further possibilities for the applicant to change these activities to an EU site. The respective changes may be submitted with the Day 106 or Day 160 response documents. For changes submitted outside of these official responses it is up to the RMS to accept these changes or not.

When (the only) batch release and batch control site are still located in the UK on Day 210 the procedures will be closed negatively as they cannot be finalised without a valid batch release/control site. They will also be closed negatively in case other activities, e.g. QPPV etc. are still located in the UK as it is not possible to positively close procedures that are not compliant with the EU legislation.

When such procedures have already been positively finalised on Day 210 before March 29, 2019 but the national phase is still ongoing the necessary variations should be submitted to all member states in line with the classification guideline and also updated translations should be submitted, if applicable, during the national phase. Only after transfer of all these activities to the EU MAs might be issued.

32. Can I request a delay for transfer of batch control testing to the EU/EEA?

As indicated in a [communication from the European Commission](#) based on provisions of Article 20(b) of Directive 2001/83/EC and Article 24(b) of Directive 2001/82/EC competent authorities may for a limited time after UK's withdrawal from the Union allow, in justified cases, batch release to continue to rely on quality control testing performed in the United Kingdom. The conditions for accepting such requests are set out in this European Commission communication.

For nationally authorised medicinal products such requests should be submitted to the Reference Member State (RMS) (also copying CMSs) for MRP/DCP and to National competent authorities for products authorised through national procedure. All requests should be based on the template [„Notification of request for a time-limited exemption to continue batch control testing in the United Kingdom \(UK\) after UK's withdrawal from the Union for a nationally authorised medicinal product“](#) and submitted as early as possible, but no later than on 29 March 2019, via e-mail or Eudralink to the national contact point of the relevant national competent authority (NCA). A list of national contact points is available [on the CMDh website](#). The heading of the email is recommended as "Brexit batch control testing exemption <MRP/DCP number> in case of MRP/DCP product or <national MA number> in case of products authorised via national procedure". In order to facilitate a prompt assessment of the request, a scanned signed version and an editable version of the request must be provided.

NCA/RMS will review the request and will inform at the earliest opportunity the marketing authorisation holder whether the exemption has been agreed. If the exemption is granted, the marketing authorisation holder must provide a copy of such exemption to the EU27/EEA competent authority that granted the manufacturing authorisation for the batch release site and to the qualified person of the batch release site. Based on the exemption and batch control testing results from the site located in the UK, the

qualified person can release batches specified in the exemption for placing on the Union market. By the end of agreed exemption period the new batch control testing site(s) in EU27/EEA have to be introduced and the batch control testing site(s) in the UK removed (changes subject to a type IA variation can be notified to the relevant NCAs within 2 months after the end of an agreed exemption).

Batches of authorised medicinal products that had already been placed on the EU27/EEA market before UK's withdrawal from the Union can remain on market. However, in the absence of an exemption as described above, authorised medicinal products that have only undergone batch control testing in the UK and not in EU27/EEA, cannot be placed on the EU27/EEA market after UK's withdrawal from the Union.

Marketing authorisation holders are reminded that such exemptions are limited to batch control testing and cannot be granted for location of batch release sites, qualified person for pharmacovigilance, pharmacovigilance master file or marketing authorisation holder.

33. Where should I address questions regarding continuation of a multi-country packs involving UK?

The requirements for use of multi-country packs are summarised in Question 24 of the [CMDh Questions and Answers](#) document. For any questions regarding continuation of a multi-country packs involving UK, the marketing authorisation holders are encouraged to consult with national competent authorities of respective EU27/EEA Member State(s), in particular in case of doubts about acceptability of any UK specific information as part of the 'blue box' in that Member State.