Introduction

This list of Questions and Answers (Q&As) complements the Notice to stakeholders on the withdrawal of the United Kingdom and EU rules for national authorised medicines products for human use, which was updated on 1 February 2019.

(NEW) This list of Q&As addresses a 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.

This list of Q&As has been drafted by the CMDh taking into account the European Commission's and EMA's Questions and Answers on the same issues within the framework of the centralised procedure. This version is an update of the initial list of Q&As as subsequently amended and it replaces all previous versions of Q&As. The new text introduced in this version of Q&As is indicated by the word "NEW". The Q&As may be further updated and complemented in the future.

1. What if I am a marketing authorisation holder established in the UK?

According to Directive 2001/83/EC the marketing authorisation holder must be established in the Union. Through the EEA Agreement this is extended to include also Norway, Iceland and Liechtenstein.

For national authorised medicinal products the marketing authorisation holder will therefore normally need to transfer its marketing authorisation to a holder established in the Union (EEA). This means that the addressee of the marketing authorisation decision changes to the new addressee. The transfer of the marketing authorisation must be fully completed and implemented by the marketing authorisation holder before 30 March 2019.

1a. What if I am an applicant established in the UK?

Any marketing authorisation applicant must be established in the Union (EEA). Therefore, for marketing authorisation applications (MAAs) that are expected to receive a national MA in an EU/EEA Member State after 29 March 2019, applicants established in the UK will need to change to a non-UK applicant established in the Union (EEA) before 30 March 2019. It is strongly recommended that
applicants established in the UK consider such change, where possible, in advance of the submission of the MAA.

**1b. What if my Reference Member State (RMS) for a Mutual Recognition (MRP) or Decentralised Procedure (DCP) is the UK?**

According to Article 28(1) of Directive 2001/83/EC the applicant shall request one Member State to act as "reference Member State" (RMS). Reference Member State must be a member state of the Union. Through the EEA Agreement this is extended to include also Norway, Iceland and Liechtenstein.

The Commission submitted on 15 March 2018 a draft withdrawal agreement to the United Kingdom for the purpose of the negotiations. Subsequently, on 19 March 2018, the negotiators of both the EU and the United Kingdom presented the progress made so far in the negotiations in the form of a coloured-coded text. According to this text (notably Articles 121 and seq.), the withdrawal agreement would extend, during a transition period, the EU pharmaceutical acquis to the United Kingdom. In terms of governance, however, as of 30 March 2019 the United Kingdom is no longer going to take part in the decision-making of EU institutions and bodies (Article 6 of the draft withdrawal agreement), nor will it act as Reference Member State (Article 123(6) of the draft withdrawal agreement).

Consequently, after 29 March 2019, UK will not be able to act as a Reference Member State.

For new marketing authorisation applications, if the procedure is not completed before 30 March 2019 (i.e. agreement of the concerned Member States in accordance with Article 28(4) or Article 29(3) or decision of the Commission in accordance with Article 34(1) of Directive 2001/83/EC) the procedure is stopped and the applicant needs to submit a new application to a new Reference Member State. Applicants are advised to take this into account already at the time of submission of the application.

For existing marketing authorisations, marketing authorisation holders are strongly advised to change the Reference Member State before 30 March 2019 in accordance with the CMDh procedural advice on changing the Reference Member State. Marketing authorisation holders should take into account that in accordance with the CMDh procedural advice a change of RMS cannot take place during a pending procedure. Before accepting a change of RMS, the MAH should in cooperation with the RMS close all the pending procedures in the current RMS, should not start new ones and confirm to the new RMS that no procedure is being examined in the current RMS.

After 29 March 2019 the marketing authorisation holder will not be able to make any regulatory submission until a new Reference Member State other than the UK is appointed.

**1c. What will be the effect of UK’s withdrawal on authorisations granted in accordance with Article 126(a) of Directive 2001/83/EC on the basis of Marketing Authorisations issued by the UK? (NEW)**

According to Article 126(a) of Directive 2001/83/EC, in the absence of a marketing authorisation or of a pending application for a nationally authorised medicinal product authorised in another Member State, a Member State may for justified public health reasons authorise the placing on the market of the said medicinal product. Traditionally, some of these authorisations have been granted on the basis of national marketing authorisations granted by the UK.

Authorisations granted by EU27 (EEA) national competent authorities on the basis of Article 126a before the withdrawal date will remain valid. However, new authorisations on the basis of Article 126a

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referring to the national marketing authorisations granted by the UK cannot be granted after the withdrawal date as the UK will become a third country.

In any event, if the products placed on the market on the basis of Article 126a are sourced from the UK after the withdrawal date they will be considered as products imported from a third country and will need to comply with all the requirements of the EU law for imported products.

2. **What if I am an orphan designation holder established in the UK?**

   Not applicable to national authorised medicinal products.

3. **What if I am a UK company with a MUMS (Minor Use Minor Species/limited market) status for my product? (for veterinary medicines)**

   Not applicable to national authorised medicinal products for human use.

4. **What if my Qualified Person for Pharmacovigilance (QPPV) resides and carries out his/her tasks in the UK?**

   According to Article 8 of Directive 2001/83/EC, the qualified person responsible for pharmacovigilance must reside and carry out his/her tasks in the Member State of the Union (EEA). The QPPV will therefore need to change his/her place of residence and carry out his/her tasks in the Union (EEA) or a new QPPV residing and carrying out his/her tasks in the Union (EEA) will need to be appointed. Changes in the QPPV, including contact details (telephone, and fax numbers, postal address and email address) may, for medicinal products for human use, be updated through the Article 57 database only (without the need for a variation) (see Variation Guideline C.I.8).

   In case the marketing authorisation for a national authorised medicinal product has to be transferred to a new legal entity, a new summary of the pharmacovigilance system has to be submitted via variation procedure C.I.8.a as type IAIN variation (see CMDh/v Q/A on variations).

5. **What if my Pharmacovigilance System Master File is located in the UK (PSMF)?**

   According to Commission Implementing Regulation (EU) No 520/2012, the PSMF must be located within the Union (EEA). The supervisory authority for pharmacovigilance is the competent authority of the Member State in which the pharmacovigilance system master file is located. The marketing authorisation holder will therefore need to change the location of the PSMF to a Member State within the Union (EEA). Changes to the location of the PSMF (street, city, postcode, country) may be updated through the Article 57 database only (without the need for a variation) (see Variation Guideline C.I.8).

   In case the marketing authorisation for a national authorised medicinal product has to be transferred to a new legal entity, a new summary of the pharmacovigilance system has to be submitted via variation procedure C.I.8.a as type IAIN variation (see CMDh/v Q/A on variations).

6. **What if my manufacturing site of the active substance is located in the UK?**

   As of the date of the withdrawal of the UK from the Union, active substances manufactured in the UK will be considered imported active substances.
Directive 2001/83/EC state that manufacturing authorisation holders are obliged to use, as starting materials, only active substances that have been manufactured in accordance with the detailed guidelines on GMP for starting materials.

In addition, pursuant to Article 46b(2) of Directive 2001/83/EC, active substances for medicinal products for human use shall only be imported in the Union (EEA) if, inter alia, the active substances are accompanied by a written confirmation from the competent authority of the exporting third country which, as regards the plant manufacturing the exported active substance, confirms that the standards of good manufacturing practice and control of the plant are equivalent to those in the Union (EEA).

7. **What if my manufacturing site of the finished product is located in the UK?**

As of the date of the withdrawal of the UK from the Union, medicinal products manufactured in the UK will be considered imported medicinal products.

The competent authorities of the Union (EEA) shall ensure that the import of medicinal products into their territory is subject to an authorisation in accordance with Article 40(3) of Directive 2001/83/EC. The authorisation is granted when a number of conditions, as defined in Articles 41 and 42 of Directive 2001/83/EC, are fulfilled (e.g. availability of a qualified person within the Union (EEA), GMP inspection).

For national authorised medicinal products the marketing authorisation holder will therefore need to specify an authorised importer established in the Union (EEA) and submit the corresponding variation (see Variation Guideline B.II.b.2).

In addition, in accordance with Article 51(1)(b) of Directive 2001/83 the marketing authorisation holder will need to specify a site of **batch control** in the Union (EEA) where each production batch can undergo upon importation a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of medicinal products in accordance with the requirements of the marketing authorisation.

For national authorised medicinal products the marketing authorisation holder will need to change the location of its current UK based site of batch control to a location established in the Union (EEA) and submit the corresponding variation (see Variation Guideline B.II.b.2).

8. **What if my batch release site is located in the UK?**

In accordance with Article 51(1) of Directive 2001/83/EC, the qualified person of the manufacturing and importation authorisation holder is responsible to certify that each batch of medicinal product intended to be placed on the EEA market was manufactured in accordance with EU GMP requirements and the marketing authorisation. The batch release site has to be located in the Union (EEA).

For national authorised medicinal products the marketing authorisation holder will therefore need to transfer its current UK based site of **batch release** to a location established in the Union (EEA) and submit the corresponding variation (see Variation Guideline B.II.b.2).
9. I am a UK based SME, would I still have access to financial and administrative assistance in accordance with Commission Regulation (EC) No 2049/2005 (the 'SME Regulation')?

The 'SME Regulation' was transposed by some Member States of the Union (EEA) either complete or partially into national legislation and is therefore on a national basis applicable for these Member States.

Further information is available on the website of national Agencies.

10. How does UK’s withdrawal from the Union affect my generic or hybrid marketing authorisation or application based on a reference product authorised in the UK?

A generic or hybrid application in accordance with Article 10 of Directive 2001/83/EC refers to information that is contained in the dossier of a reference medicinal product (RefMP) that is or has been authorised in the Union (EEA).

Generic/hybrid marketing authorisations granted before 30 March 2019 referring to a RefMP authorised by the UK (UK RefMP) remain valid. Applications need to be submitted well in advance in order for the national competent authority to be able to grant the national marketing authorisation before 30 March 2019. Applicants should take into account that in case of a DCP or MRP the national decisions of the Member States are adopted within 30 days after the "end of procedure" (i.e. agreement of the concerned Member States in accordance with Article 28(4) or Article 29(3) or decision of the Commission in accordance with Article 34(1) of Directive 2001/83/EC), subject to the applicant providing high quality national translations of the product information within seven days of the "end of procedure".

Generic/hybrid applications for which marketing authorisations will be granted after 29 March 2019 should refer to a RefMP that is or has been authorised in a EU-27 Member State or a contracting state of the EEA. Applicants are advised to take this into account already at the time of submission of the application.

11. Can medicinal products used in bioequivalence studies be sourced in the UK?

According to Article 10(1) of Directive 2001/83/EC the applicant can submit an abridged application if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised in the EU or EEA for not less than eight years. According to Article 10(2)(b) of Directive 2001/83/EC generic medicinal product means a medicinal product which has the same qualitative and quantitative composition in active substance and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

(NEW) Pivotal studies (bioequivalence, and/or associated in vitro dissolution tests or therapeutic equivalence studies, as appropriate) that have been conducted with a medicinal product sourced in the

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2 See also the electronic application form for marketing authorisation applications, section 1.4.2.2 or 1.4.3.2
3 This will also facilitate management of generic/hybrid product's life cycle in the post-authorisation phase, considering for example the need to implement changes to the product information of the EEA RefMP also for the generic/hybrid products.
4 The (exceptional) situation where a RefMP is or has been authorised in the UK only is addressed in the EU’s "Position paper on Goods placed on the Market under Union law before the withdrawal date" (footnote 7): https://ec.europa.eu/commission/publications/position-paper-goods-placed-market-under-union-law-withdrawal-date_en.
5 See also the electronic application form for marketing authorisation applications, section 1.4.2.3 or 1.4.3.3
UK can be used in generic/hybrid marketing authorisation applications only if the marketing authorisation for that application will be granted before 30 March 2019⁶.

12. How does UK’s withdrawal from the Union affect my biosimilar marketing authorisation or biosimilar marketing authorisation application?

The considerations described under questions 10 and 11 regarding the choice of RefMP are also applicable to biosimilars.

The Guideline on similar biological medicinal products should however be consulted for the available scientific guidance when considering using a non-EEA authorised comparator (i.e. a non-EEA authorised version of the reference medicinal product) in the development of a biosimilar. Batches of the RefMP released by the UK after 29 March 2019 will not be considered as a Union (EEA) authorised comparator.

13. How does UK’s withdrawal from the Union affect the Global Marketing Authorisation (GMA) concept?

The concept of global marketing authorisation within the meaning of Article 6(1) of Directive 2001/83/EC covers the initial marketing authorisation and all subsequent developments of the original medicinal product, irrespective of their authorisation procedures, namely variation or grant of a separate MA⁷. The GMA is accompanied only by a single regulatory data protection period⁸ which applies both to data relating to the original medicinal product⁹ and to data presented for any subsequent developments. That regulatory data protection period begins with the grant of the initial marketing authorisation in the Union (EEA).

Marketing authorisations granted before 30 March 2019 by the UK can still be considered as the initial marketing authorisation.

14. How does UK’s withdrawal from the Union affect well-established use applications?

According to Article 10a of Directive 2001/83/EC it is possible to replace results of the pre-clinical and clinical trials by detailed references to published scientific literature if it can be demonstrated that the active substances of a medicinal product in the claimed therapeutic indication have been in well-established use within the Union (EEA) for at least ten years, with recognised efficacy and an acceptable level of safety. In this regard, the provisions of Annex I of Directive 2001/83/EC shall apply.

Data sourced from the UK, while the UK was a Member State of the Union, can be taken into account to demonstrate that the active substances of a medicinal product in the claimed therapeutic indication

⁶ In exceptional cases where pivotal studies are intended for use in new applications which will be submitted before 30 March 2019 and if these studies have been already completed the national competent authorities will accept submission of such studies in order to avoid unnecessary repetition of studies in humans or animals. Furthermore, in order to avoid unnecessary repetition of studies in humans or animals, applications to extend an existing national marketing authorisation of an EU27 Member State to more EU27 Member States via the mutual recognition procedure (including so-called "repeat use procedure") may be submitted also after 29 March 2019 provided that the applicant is able to demonstrate that the medicinal product used for the studies has been authorised and the batches used for the studies have been released while the UK was a Member State of the Union. (NEW:) In cases where studies have been conducted with a reference product sourced in the UK before 30 March 2019 and when this product is the same as an EU27 or EEA reference product, authorised either via the centralised procedure or mutual recognition or decentralised procedure based on the same dossier, the national competent authorities will accept submission of such studies also after 29 March 2019, in order to avoid unnecessary repetition of studies in humans or animals.

⁷ C-629/15P, para. 72.

⁸ C-629/15P, para. 65.

⁹ See also the electronic application form for marketing authorisation applications, section 1.4.2.1 or 1.4.3.1
and (for veterinary products) target species have been in well-established use within the Union (EEA) for at least ten years, with recognised efficacy and an acceptable level of safety.

15. **How does UK’s withdrawal from the Union affect traditional herbal medicinal products (traditional-use registration)?**

The traditional-use registration procedure allows the registration of herbal medicinal products without requiring particulars and documents on tests and trials on safety and efficacy, provided that there is sufficient evidence of the medicinal use of the product throughout a period of at least 30 years, including at least 15 years in the Union (EEA).

Data sourced from the UK, while the UK was a Member State of the Union, can be taken into account to demonstrate that the product has been in medicinal use throughout a period of at least 15 years within the Union (EEA).

16. **How does UK’s withdrawal from the Union affect the prevalence for orphan drug designation?**

Not applicable to national authorised medicinal products.

17. **How does UK’s withdrawal from the Union affect the local representative located in the UK, if nominated for Member States other than the UK?**

The local representative mentioned in the product information should be located in the Union (EEA). Therefore, any local representative located in the UK and nominated for Member States other than the UK will have to be changed to a local representative located in the Union (EEA).

The corresponding amendments to labelling and package leaflet must be fully completed and implemented by the marketing authorisation holder before 30 March 2019, and is dealt with at a national level.

17a. **How does UK’s withdrawal from the Union affect the name of the product in UK mentioned in the package leaflet?**

After 29 March 2019, the mentioning of the name of the product in UK in the package leaflet (Article 59(1)(g) of Directive 2001/83/EC) will become obsolete.

The deletion of the name of the product in the UK in the package leaflet will need to be incorporated as part of a future regulatory procedure (e.g. variation, renewal and the earliest opportunity after 29 March 2019 should be used) affecting the package leaflet, but no separate notification according to Article 61(3) of Directive 2001/83/EC is expected.

18. **How does UK’s withdrawal from the Union affect the sunset clause?**

According to Article 24(4) to (6) of Directive 2001/83/EC any authorisation which within three years of its granting is not followed by the actual placing on the market of the authorised product in the authorising Member State market will cease to be valid. When an authorised product previously placed on the market in the authorising Member State is no longer actually present on the market for a period of three consecutive years, the authorisation for that product will cease to be valid.
As such there will be no effect of UK’s withdrawal from the Union on national marketing authorisations approved in EU/EEA-Member States.

**19. What if my product is subject to Official Control Authority Batch Release (OCABR) and is currently tested by a UK Official Medicines Control Laboratory (OMCL)?**

According to Article 114 of Directive 2001/83/EC, Member States may require the marketing authorisation holder of a human immunological medicinal product or a medicinal product derived from human blood or plasma to submit samples from each batch of the bulk and/or the medicinal product for examination by an Official Medicines Control Laboratory (OMCL) or a laboratory that a Member State has designated for that purpose before the release on the market. This is referred to as Official Control Authority Batch Release (OCABR).

According to the EU Administrative Procedure for Official Control Authority Batch Release, prior to marketing in the Union (EEA), batches of medicinal products subject to independent testing should obtain an Official Control Authority Batch Release Certificate common to all Member States. This shall demonstrate that the batch of medicinal product has been examined and tested by an OMCL within the Union (EEA) in accordance with this procedure and with Official Control Authority Batch Release guidelines pertaining to the medicinal product and that it is in compliance with the approved specifications laid down in the relevant monographs of the European Pharmacopoeia (Ph. Eur.) and in the relevant marketing authorisation.

For products placed on the market as of the withdrawal date, OCABR cannot be carried out by an OMCL located in the UK. OCABR will need to be carried out by an OMCL located within the Union (EEA) or by a country officially recognised by the Union for mutual recognition of batch release (e.g. Switzerland H+V vaccine, H blood or Israel H vaccine). The marketing authorisation holder will therefore need to identify a OMCL located in the Union (EEA) for official batch release or an officially recognised partner (as stated above) for official batch release. A list of the OMCLs that may be in a position to provide EU OCABR certificates for different products is available to manufacturers from EDQM on request at batchrelease@edqm.eu.

**19a. Can I, as of the withdrawal date, import a medicinal product into the Union (EEA) on the basis of a certificate issued before the withdrawal date by the UK OMCL? (NEW)**

No. As of the withdrawal date, the mutual recognition of Official Control Authority Batch Release (OCABR) stops.

However, the Official Medicines Control Laboratory (OMCL) of an EU27 or EEA Member State may take account of the certificate issued by the UK OCML when issuing a certificate.

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11 For goods placed on the EU market before the withdrawal date, the EU is trying to agree solutions with the United Kingdom in the withdrawal agreement. The essential principles of the EU’s position on goods placed on the market under Union law before the withdrawal date are available here: https://ec.europa.eu/commission/publications/position-paper-goods-placed-market-under-union-law-withdrawal-date_en. The concept of placing on the market refers to each individual product, not to a type of product, irrespectively of whether it was manufactured as an individual unit or in series.
19b. Does the change of the marketing authorisation holder due to the UK’s withdrawal impact on the validity of the Official Control Authority Batch Release issued by a Official Medicines Control Laboratory (OMCL) of an EU27 or EEA Member State? (NEW)

No. The Official Control Authority Batch Release (OCABR) of the OMCL of an EU27 or EEA Member State remains valid even if the marketing authorisation holder changes.

20. What if my product is subject to Official Batch Protocol Review (OBPR) and evaluation is done by a UK Competent Authority? (for veterinary medicines)

Not applicable to national authorised medicinal products for human use.

21. How does UK’s withdrawal from the Union affect the status of inspection outcomes by the UK competent authority?


22. How does UK’s withdrawal from the Union affect CE certification of medical devices by UK notified bodies?

This issue is addressed in the Commission Notice on the withdrawal of the United Kingdom and EU rules in the field of industrial products that also covers medical devices.

23. How does UK’s withdrawal from the Union impact the CHMP scientific opinion for ancillary medicinal substances in medical devices requested by UK notified bodies?

Not applicable to national authorised medicinal products for human use.

24. What should I do if I place my product on the market in a multi-country pack, which includes the UK?

Multi-country packs are medicinal products that are labelled to allow their placing on the market in several Member States with the same packaging. This possibility is subject to the requirements set out in in Title V of Directive 2001/83/EC and requires that the summary of product characteristics is the same in all the markets concerned.

(NEW) Article 57 and Article 62 of Directive 2001/83/EC and Article 63 of Directive 2001/82/EC allow Member States to require inclusion of certain additional labelling information (the so-called “blue box” concept) provided that all the strict conditions for application of Article 57 or Article 62 of Directive 2001/83/EC and Article 63 of Directive 2001/82/EC are fulfilled.
In applying these provisions, multi-country packs with the UK market are only possible if
- the product information is exactly the same in the United Kingdom as in the EU27 (EEA); and
- the Member State has allowed additional information according to the “blue box” concept. This
additional information must be limited to certain administrative information.

In any event the product labelling and package leaflet must be fully in line with the summary of
product characteristics as authorised in the Union (EEA).

25. What if Qualified Person’s for Pharmacovigilance (QPPV) back-up
arrangements are in the UK?

According to Article 2 of Commission Implementing Regulation (EU) No 520/2012 back-up
arrangements shall apply in the absence of the QPPV. As the tasks of QPPV need to be carried in a
Member State of the Union (EEA), the back-up arrangements for cases of absence of the QPPV, which
replace such tasks, also need to be performed in the Union (EEA).

Where a MAH relies on the services of a deputy QPPV as part of its back-up arrangements in the
absence of the QPPV, those arrangements should ensure that the deputy QPPV performs his/her tasks in
the Union (EEA).

26. Who will take over supervision of the manufacturing sites of medicinal
products in third countries (including UK after the Withdrawal date)
previously supervised by UK authorities and when will the next GMP
inspection be conducted? (NEW)

According to Articles 18 and 43 of Regulation (EC) No 726/2004, in case of medicinal products
imported from third countries the supervisory authorities shall be the competent authorities of the
Member State or Member States that granted the authorisation provided for in Article 40(3) of
Directive 2001/83/EC or Article 44(3) of Directive 2001/82/EC respectively to the importer of the
concerned medicinal product.

As of the withdrawal date, UK authorities will no longer undertake the role of a supervisory authority.

The new Union supervisory authority responsible for supervision of manufacturing sites located in UK
and third country sites previously inspected by UK will decide, using a risk-based approach, when an
inspection of the site(s) concerned will be required, in order to confirm or re-confirm GMP compliance.

27. Can I continue to use after 29 March 2019 a manufacturing site for
which the EU GMP certificate has been issued by UK authorities? (NEW)

All medicinal products for human use manufactured or imported into the Union (EEA), including
medicinal products intended for export, are to be manufactured in accordance with the principles and
guidelines of good manufacturing practice.\(^\text{12}\) A certificate of good manufacturing practice (“GMP
certificate”) is issued to a manufacturer if the outcome of the inspection shows that the manufacturer
complies with the principles and guidelines of good manufacturing practice as provided for by the
Union legislation.\(^\text{13}\)

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\(^\text{13}\) Directive 2001/83/EC, Article 111(5).
While the Union legislation does not require a EU GMP certificate issued by a Member State for issuing a marketing authorisation\textsuperscript{14} or importation of a medicinal product,\textsuperscript{15} in practice GMP certificates issued by the Union competent authorities are used to confirm EU GMP compliance in regulatory submissions (e.g. marketing authorisation applications) and for imports from third countries. This means that GMP compliance of manufacturing sites in third countries may also be confirmed through other means, based on a risk-based approach (e.g. based on information on GMP compliance from third country regulatory authorities). GMP certificates issued by the UK competent authority before 30 March 2019 should therefore be considered as such information on GMP compliance from the third country regulatory authority.

28. Shall the information about the unique identifier uploaded to the UK repository between 9 February 2019 and 29 March 2019 be transferred to another repository in the Union? (for medicines for human use)(NEW)

Article 33(1) of Commission Delegated Regulation (EU) 2016/161 requires marketing authorisation holders to ensure that unique identifiers and related information are uploaded to the Union repository system before a product is released for sale or distribution. Any information uploaded to the Union hub or a national repository should be transferred and stored in all national or supranational repositories serving the territory of Member State(s) where the product is intended to be placed on market. Therefore, the information on products released on the market before the withdrawal date will be already present in the national repositories where the product is intended to be placed on the market and there is no need to transfer information from the UK repository.

29. Can activities related to safety features take place in the UK? (for medicines for human use)(NEW)

The manufacturer placing the safety features, as referred to in Articles 14 and 15 of the Commission Delegated Regulation (EU) No 2016/161, is the manufacturer actually affixing the unique identifier and anti-tampering device on the packaging. There is no requirement that such a manufacturer has to be located in the Union (EEA). However, if a manufacturer is not in the Union (EEA), then the obligation to ensure that Articles 14 and 15 of the Delegated Regulation (EU) No 2016/161 are complied with lies with the importer.

The Qualified Person at the batch release site in the Union (EEA) will have to ensure that the safety features have been affixed to the packaging (Article 51(1) of Directive 2001/83/EC). This task may be delegated to appropriately trained personnel or third parties, as set out in Annex 16 to the EU GMP guidelines (section 1.7). For general GMP requirements on outsourced activities, refer to Chapter 7 of the EU GMP guidelines.

The responsibility for ensuring that the information is uploaded in the repositories system lies with the MAH (or the person responsible for placing on the market medicinal products which are parallel distributed/parallel imported). The Delegated Regulation does not prohibit MAHs from subcontracting or delegating data-upload tasks to on-boarding partners (OBPs) acting on their behalf. However, the infrastructures, hardware and software used for data upload must be physically located in the EEA (see question 7.19 in Questions and Answers on Safety Features for Medicinal Products for Human Use).

\textsuperscript{14} Article 8(3)(ha) of Directive 2001/83/EC.
\textsuperscript{15} Article 51(1)(b) of Directive 2001/83/EC, Article 55(1)(b) of Directive 2001/82/EC.
30. **Can parallel trade of medicinal products sourced in the UK and supplied to the EU27 or EEA continue as of the withdrawal date? (NEW)**

Parallel trade of medicinal products in the internal market is possible in particular because of (i) the rules in the internal market for the exhaustion of trade mark rights; and (ii) the fact that the summary of product characteristics and the labelling of medicinal products are – apart from issues of language used – identical.

As of the withdrawal date, the rules for exhaustion of trade mark rights in the Union (EEA) no longer apply in respect of products placed on the UK market. Moreover, the terms of the marketing authorisation will over time differ.16

Hence, parallel trade of medicines sourced in the UK is in practice no longer possible as of the withdrawal date.

However, from the point of view of Union pharmaceutical law, medicines that have been sourced in the UK, and brought into the territory of the EU27 (EEA) before the withdrawal date can continue to circulate on the EU27 (EEA) market if they are authorised.

31. **Does, as of the withdrawal date, Article 76(4) of Directive 2001/83/EC continue to apply to parallel trade of medicinal products sourced in the UK? (NEW)**

Not applicable to national authorised medicinal products.

32. **Will parallel distribution notices under Article 76(4) of Directive 2001/83/EC with UK as the Member State of destination remain valid as of the withdrawal date? (NEW)**

Not applicable to national authorised medicinal products.

33. **Will parallel distribution notices under Article 76(4) of Directive 2001/83/EC for a parallel distributor located in UK remain valid as of the withdrawal date? (NEW)**

Not applicable to national authorised medicinal products.

34. **Will parallel distribution notices under Article 76(4) of Directive 2001/83/EC with a re-packaging site located in UK remain valid as of the withdrawal date? (NEW)**

Not applicable to national authorised medicinal products.

35. **What will change regarding reporting requirements into EudraVigilance of Individual Case Safety Reports (ICSRs) from the UK? (for medicines for human use) (NEW)**

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16 To this may add national rules on parallel trade of medicinal products with third countries.
According to Article 107 of Directive 2001/83/EC suspected serious adverse reactions have to be reported no matter if they occurred in the Union (EEA) or in third countries.

Suspected non-serious adverse reactions occurring in third countries do not have to be reported in the Union (EEA). Thus, as of the withdrawal date
- non-serious adverse reactions that have occurred in the UK before the withdrawal date have to be reported;
- it is no longer mandatory to submit to EudraVigilance reports of suspected non-serious adverse reactions that have occurred in the UK as of the withdrawal date.

For individual cases originating from UK and submitted to EudraVigilance before the withdrawal date, when a follow-up information is received by the marketing authorisation holder as of the withdrawal date, it should be continued to be submitted to EudraVigilance when third country reporting criteria apply.

As of the withdrawal date, UK authorities will no longer have access to EudraVigilance. Marketing authorisation holders are therefore reminded that they will need to submit into EudraVigilance information that they might receive from UK authorities regarding cases occurring in the UK, in line with the reporting requirements for non-EU/EEA cases.

36. What will be the impact of UK’s withdrawal on referral procedures? (NEW)

Referrals of MR/DC applications procedures ongoing on the withdrawal date will continue, irrespective of the Member State that triggered the referral with the exception of MR/DCP referral procedures on applications with UK as the RMS (see question 1b). Where potential serious risk to public health have been identified these will be evaluated within the procedure.

37. How do I handle, as of the withdrawal date, data from UK in the Periodic Safety Update Reports? (NEW)

Periodic safety update reports (PSURs) should present cumulative and interval summaries of global safety data obtained from various sources worldwide. Relevant safety data obtained from UK sources as of the withdrawal date should therefore continue to be included in PSURs as per usual requirements for third country data.

For the calculation of exposure from marketing experience by region, patients exposed in the UK until the withdrawal date should be included in the EU/EEA estimate. Thereafter, UK patient exposure should be considered as part of the non-EU/EEA regions.