

Brexit Guidance for Stakeholders

Human and Veterinary Medicines

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only. The content provided is subject to change and may be updated as required by the HPRA without notice.



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1 BACKGROUND

The HPRA's strategic objective in regard to Brexit is to protect public and animal health by supporting the continued supply of health products. The HPRA has been planning for Brexit for the past ~~two~~three years to ensure that the organisation is sufficiently prepared to manage the regulatory challenges presented by the UK's departure from the EU. Our focus, and the work of the internal task force and the management team, has from the outset planned for all possible scenarios. ~~However, since January 2019, the HPRA has moved from operational planning to focussing our efforts on 'no deal' contingency planning.~~

The UK left the European Union on 31 January 2020 on the basis of the Withdrawal Agreement which was agreed by the European Council on 17 October 2019. The agreement includes a transition period until 31 December 2020. The period for the UK government to seek an extension to the transition period has now expired.

Negotiations are ongoing between the EU and the UK on a new future relationship agreement which, if agreed, is due to come into effect from 1 January 2021. There is a possibility that no agreement on a future relationship is reached, effectively resulting in a 'no deal Brexit' on 1st January 2021. The HPRA is continuing operational planning and focussing our efforts on 'no deal' contingency planning.

The HPRA approach has been consistent with the work of the Commission and the EU human medicines, veterinary medicines and medical device networks calling on all stakeholders to ensure that they are prepared for every eventuality, including the worst-case scenario of a 'no-deal' Brexit. The guidance in this document is based on a potential 'no-deal' scenario. However, should the evolving political situation allow for the preparation of a more central case scenario, the document will be updated as appropriate.

2 IMPACT OF BREXIT ON EU/EEA REGULATORY NETWORK

The HPRA's priority, working with all relevant stakeholders, is to ensure continuity in the supply of health products and continued access for patients. It is essential that companies ensure continued communication with the HPRA for guidance and support as they prepare for Brexit.

The HPRA is working to continue supporting all stakeholders already present on the Irish market or stakeholders who need to relocate to an EU/EEA country as a result of Brexit. We are open to working together to address any areas of risk or difficulty and to support the implementation of the required regulatory changes within the existing framework.

The HPRA works with the UK's Medicines and Healthcare products Regulatory Agency (MHRA) and Veterinary Medicines Directorate (VMD) on many regulatory issues both bilaterally and at EU level. The HPRA wants to assure stakeholders that it is our intention to continue working closely with the UK to ensure continued product supply to the Irish market. Ireland is actively

assuming a greater role in EU regulatory activities and has increased further our already significant contribution to the EU regulatory networks.

In light of the ~~pending~~ withdrawal of the UK from the EU, information which may be useful to stakeholders is provided below.

3 KEY INFORMATION FOR HPRA STAKEHOLDERS

The guidance provided in this document on the key issues facing the HPRA and our stakeholders is based on the premise that ~~there will be a 'no deal' Brexit and~~ result of future relationship negotiations the UK will become a third country ~~by~~ at the withdrawal date end of the Transition Period. It incorporates the latest information provided in the updated European Commission's notice to stakeholders, the 2019 European Commission's Q&A and batch testing rules as well as questions compiled from the HPRA's Brexit Stakeholder event on 1 February 2019. It is also based on our current understanding of the potential legal impact of exit. However, it is important to note that guidance is evolving and ~~must be agreed in respect of so-called 'grey' areas. Therefore, the advice currently provided~~ may require updating as the negotiation process continues. ~~In the event that a transition period is agreed, this guidance will be updated to reflect the terms of the transition.~~

4 MEDICINES AVAILABILITY

The HPRA views the management of medicines availability as a key priority in the protection of public and animal health. This is reflected in our Strategic Plan for 2016-2020, which includes access to health products as a key strategic goal. The HPRA is therefore actively working with companies to ensure that the impact of Brexit on medicine availability is assessed and proactively addressed by all relevant stakeholders and that, where necessary, timely actions are taken to ensure continuity of supply.

The HPRA is offering support to companies in managing any problems that might impact on the supply of medicines when responsibilities relating to marketing authorisations have to be transferred from the UK to other EU member states as a result of Brexit. Actions under this initiative include:

- We are reviewing critical products with potential regulatory issues and collaborating with MAHs to ensure that there is a pathway in place to achieve compliance prior to the withdrawal date.
- We are assisting companies in developing multilingual packs and in implementing the revised requirements for joint/dual IE/UK labels with the UK to maintain products on the Irish market.
- We are working with stakeholders on addressing company specific issues arising as a result of Brexit.
- Changes to the HPRA MAH transfer procedures to alleviate pressures on the supply chain following transfer of authorisations (see section 6.4 of this guidance document). Willingness to act as RMS for all products where Ireland (IE) is currently CMS and a change of RMS is required. No fees will apply to the process for changing RMS to IE. In addition, where possible we are working with companies both to simplify the transfer of RMS and to minimise the administrative burden.

5 **MULTILINGUAL PACKAGING AND JOINT LABELLING**

The HPRA views the management of medicines availability as a key priority in the protection of public health and therefore is actively working with companies to ensure that the impact of Brexit on medicine availability is minimised.

The use of multilingual packaging can be key to companies retaining medicines on the Irish market. The HPRA is therefore committed to working with companies to develop multilingual labelling while remaining compliant with regulatory requirements to safeguard continued patient access. The HPRA 'Guide to labels and leaflets of Human Medicines' available on the HPRA website gives specific guidance on the development of multilingual labelling. To encourage the use of multilingual labelling the HPRA is proactively working with other European regulators to help optimise opportunities for multilingual labelling. To this end, the HPRA has worked with the Co-ordination group for Mutual recognition and Decentralised procedures – human (CMDh) to draw up the CMDh Best Practice Guide on Multilingual Packaging rev 2 (June 2020). This guidance contains useful principles for companies to follow when developing multilingual packaging and is complementary to the existing guidance in the HPRA Guide to Labels and Leaflets of Human Medicines.

On the veterinary side, the HPRA has worked with the Co-ordination group for Mutual recognition and Decentralised procedures – veterinary (CMDv) to recently revise the Best Practice Guide for processing of SPC, Labelling and Package Leaflet in support of MRPs and DCPs (May 2020) with a focus on assisting applicants to develop multilingual packaging.

The HPRA recognises that the maintenance of joint labelling with ~~other markets~~ the UK can be key to companies retaining medicines on the Irish market. We are committed to facilitate such joint labelling while remaining compliant with regulatory requirements and thereby safeguarding continued patient access.

As outlined in the Commission's ~~Q&A update of 1 February 2019, Notice to Stakeholders: Withdrawal of the United Kingdom and EU Rules for Medicinal products for Human Use and Veterinary Medicinal products (March 2020)~~ the possibility of multi-country packs is subject to the requirements set out in Directive 2001/83/EC in Title V or Directive 2001/82/EC in Title V. Multi-country packs with the UK ~~(as a third country)market~~ are possible if the ~~summary of product characteristics information~~ is exactly the same in ~~all the markets concerned~~ UK as in the EU, and if the Member State has allowed additional administrative information labelled in the 'blue box'. 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). Applicants should also consider the notice to stakeholders where guidance on safety features is provided.

~~The~~ Thus the HPRA will accept the name and address of the IE and the UK MAHs, the IE and UK marketing licence authorisation numbers and the name and address of the IE and UK sites of batch release on the joint packaging subject to: (1) the MAH for each country being clearly distinguishable and (2) there being sufficient space to ensure legibility of the product information.

For veterinary medicines, the HPRA and the VMD have enjoyed a close working relationship and have successfully operated a bilateral joint labelling procedure for in excess of 10 years. It is the intention of the HPRA to maintain a close working relationship with the VMD and that this procedure will continue after the ~~UK leaves end of the EU transition period.~~

~~Consideration should also be given to the use of multilingual labelling and the HPRA will work with the MAH and other European regulators to help facilitate this for both human and veterinary medicines.~~

Information on labelling issues for both human and veterinary medicines are available at the links below:

[Human medicines](#)

[Veterinary medicines](#)

6 POST BREXIT LICENSING SCENARIOS FOR MARKETING AUTHORISATION HOLDERS

~~The implications of Brexit with regard to the UK's role in the licensing of medicines will be determined by the terms of the ongoing exit negotiations. However, inAs from the end of the transition period, the Protocol on Ireland/Northern Ireland ('IE/Ni Protocol') applies. The IE/Ni Protocol provides that the EU pharmaceutical acquis applies to and in the United Kingdom in respect of Northern Ireland and thus a medicinal product placed on the market in Northern Ireland has to comply with the EU acquis for medicinal products. Marketing authorisation applicants who wish to obtain a marketing authorisation for the United Kingdom in respect of Northern Ireland have to include Northern Ireland in the scope of their marketing authorisation application in the decentralised procedure (DCP) or the mutual recognition procedure (MRP). A further outline of the applicable rules in Northern Ireland after the end of the transition period is outlined in the EC Notice to Stakeholders. The IE/UK Protocol also outlines further restrictions on UK involvement in respect of Northern Ireland in decision making in the EU. HPRA will provide further guidance on the practical application of these rules as our understanding of the future relationship between the EU and UK in respect of existing medicinal products develops.~~

~~As outlined above, due to Brexit the UK's role in the licensing of medicines has changed. In Due to Brexit the UK's role in the licensing of medicines has changed. In~~ accordance with Directives 2001/82/EC and 2001/83/EC, the marketing authorisation holder (MAH) must be located within the EU/EEA. ~~(apart from the specific situation of medicines authorised by UK in respect of Northern Ireland, where an MAH in NI could be established as outlined in the notice to stakeholders).~~ In addition, for marketing authorisations issued through the mutual recognition procedure (MRP) or decentralised procedure (DCP), the Reference Member State (RMS) must be based in the EU/EEA.

~~The HPRA is recommending that~~At this time MAHs ~~plan for a situation where the UK becomes a third country which involves selecting~~who have not already done so are requested to select a RMS based in the EU/EEA and ~~ensuring~~ensure that the MAH is also based in the EU/EEA, ~~as UK may no longer act as RMS for upcoming regulatory activities.~~

Practical guidance

The Heads of Medicines Agencies, via the Coordination Groups for Mutual Recognition and Decentralised procedures for both human and veterinary medicines, have updated information regarding Practical Guidance for procedures related to Brexit for products approved via MRP/DCP.

~~Human Medicines Practical Guidance (February 2019)~~

~~Veterinary Medicines Practical Guidance (March 2019)~~

- ~~- CMDh Practical guidance for procedures related to Brexit for medicinal products for human use approved via MRP/DCP (April 2020)~~
- ~~- CMDv Practical guidance for procedures related to Brexit for veterinary medicinal products approved via MR/DC procedures (June 2020)~~

The EMA have also developed;

~~Practical Guidance (March 2019) for procedures related to Brexit for both human and veterinary products within the centralised procedure. Practical guidance for procedures related to Brexit for medicinal products for human and veterinary use within the framework of the centralised procedure (March 2020)~~

Questions and answers documents

~~The Q&As from the CMDh/v and the EMA were updated in February 2019. These may continue to be updated periodically with further questions and answers pending negotiation outcomes. The lists of CMDs Q&As have been drafted taking into account the European Commission's and EMA's Question and Answers on the same issues within the framework of the centralised procedure.~~

~~CMDh Q&A and notice to MAHs (Update February 2019)~~

~~CMDv Q&A and notice to MAHs (Updated February 2019).~~

- ~~• EMA and European Commission updated Q&A and notice to Stakeholders related to centrally authorised products (Updated February 2019).~~

6.1 Why select Ireland as your RMS?

The HPRA has a proven track record of conducting high quality and timely assessments, and will be happy to receive requests to act as RMS for all product types including all products for which the UK is currently the RMS and IE is a CMS. There will be no fees charged for switching the RMS from the UK to IE. The HPRA commits to an efficient and simple process for handling these requests (for example allowing the inclusion of multiple products in one request where applicable) and for taking on the role of RMS.

6.2 What is the timeline for changing RMS?

The procedure itself is a straightforward administrative procedure which can be completed within a matter of days. In order to ensure the successful change of RMS to IE, MAHs are requested to contact the HPRA as soon as possible to plan work volumes and to ensure continued supply of product on the EU market prior to the UK's exit from the EU. ~~The critical issue will be the timing of when the change in RMS should occur, as it is required to occur when there are no open regulatory activities for a product. It is therefore advisable that all planned regulatory activity with products requiring a change in RMS takes into account the expected duration of the procedures to ensure the RMS change is completed prior to the withdrawal date~~

6.3 Procedures for MAHs to change RMS

For both human and veterinary medicines, when making a change to the RMS, the following guidance, as agreed by CMDh and CMDv, applies:

- Where the UK is RMS and there is only one concerned member state (CMS), then that CMS will automatically become the new RMS. In instances where IE is that CMS, the HPRA will become the RMS.
- Where there are two or more CMSs, it is the responsibility of the MAH to secure a new RMS based in the EU/EEA.
- The choice of a new RMS will be a decision for the MAH, subject to agreement with the relevant national competent authority. MAHs are advised to communicate with their preferred new RMS and the UK to submit the official notification of change in a timely manner in order to facilitate completion of the change of RMS before the UK exits the EU. IE is very willing to become the RMS for any product where the UK is RMS and IE is CMS.

For human medicinal products, all queries in relation to IE acting as RMS should be sent to the following e-mail address: article50changes@HPRA.ie-brexit@hpra.ie

For veterinary medicinal products, all queries in relation to IE acting as RMS should be sent to the following e-mail address: vetinfo@hpra.ie.

6.4 Procedures for MAHs to transfer MAH to EU/EEA based MAH

A marketing authorisation may be transferred from the existing authorisation holder to another holder using a **transfer procedure**. The transfer procedure must be used where the **legal entity** of an authorisation/licence holder **is changed** as marketing authorisations are transferred to a new company number. It is possible to transfer the MAH while there are ongoing/open variations. If the transfer is processed/issued, the new MA holder details will transfer onto the open/ongoing variations.

NOTE: Important changes to the HPRA transfer procedure:

HPRA transfer procedures have recently been changed to allow MAHs up to six months to implement packaging changes following issue of the transferred authorisation, for Brexit related transfers. In addition, the HPRA no longer requires stock to be recalled from wholesaler level six months following the issue of the transferred authorisation / licence / registration.

6.4.1 Bulk MAH Transfers

Bulk transfers are accepted by the HPRA and reduced fees apply. Please contact submissions@hpra.ie prior to submission to discuss dates and timelines.

If transfers need to be processed on a particular date, please **include** this in the **application form and** highlight it in the cover letter accompanying the applications. Note that transfer applications are generally listed for approval within the HPRA on a Friday. Please bear this in mind when proposing your preferred transfer date.

For bulk transfer applications, only one application form is required. Please include an annex listing of the product authorisation numbers, full product names and strengths with all applications.

6.4.2 Issuing of PA numbers

To facilitate the preparation of your application, the HPRA Receipts and Validation section can provide you with the new PA numbers in advance of your application. Requests for PA numbers should be sent to submissions@hpra.ie. Typically, each request takes ten working days to process. When requesting new PA numbers please specify the existing product name and PA number as well as the current and new MAH.

6.4.3 Art work requirement with transfer application (Human Medicines Only)

An updated package leaflet is required to be submitted with a transfer application so that this can be displayed on the HPRA website. The package leaflet should reflect the new MAH details. A Word version of the package leaflet is acceptable.

If the only changes proposed relate to MAH details and a new PA number, an Article 61(3) application is not required. However, if there are additional changes to the labels and package leaflet, an Article 61(3) application must be submitted. This can be submitted in parallel to the transfer.

Further information on transfers can be found on our website:

[Human Medicines](#)

[Veterinary Medicines](#)

6.5 Meeting licensing requirements for products under development

~~A series of questions and answers have~~[Guidance has](#) been developed at a European level (~~listed above under 6 – Questions and Answers documents~~)([Notice to Stakeholders](#)) to manage specific scenarios for products, including those under development. Examples of ~~these include queries relating to specific guidance includes~~ reference products for generic/hybrid or biosimilar applications, the well-established use legal basis and traditional use registrations for herbal products. For products under development for which data has already been generated, it is recommended that all data is screened to ensure that the data will comply with EU requirements following the UK's exit from the EU.

6.6 Authorised generic medicinal products which refer to an UK reference product

Marketing authorisations for generics/hybrids granted in accordance with Directives 2001/82/EC and 2001/83/EC prior to withdrawal date will continue to be valid authorisations notwithstanding that a reference medicinal product (RefMP) may no longer be an EU authorised product.

Further guidance regarding bioequivalence studies and generic/hybrid marketing authorisations is available in the [EMA Q&A EU notice to stakeholders \(March 2020\)](#) and the [EMA practical guidance \(March 2020\)](#) for centralised products and in both the [CMDh/CMDv Q&As](#)[CMDh/CMDv practical guidance](#) for MRP/DCP procedures.

6.7 Medical devices containing an ancillary medicinal substance

Manufacturers of medical devices containing an ancillary medicinal substance wishing to transfer an existing competent authority consultation to the HPRA are advised to contact the HPRA to discuss the transfer.

Transfers of medical devices containing a medicinal ancillary substance with a valid CE certificate are considered administrative only. Transfers typically take less than 30 days from validation of the submission to be completed. No fees will apply to this transfer process.

All queries in relation to IE acting as a consulting authority should be sent to the following e-mail address: article50changes@HPRAbrexit@hpra.ie

6.8 Parallel Product Authorisations

Parallel product authorisations (PPAs) can only be granted for medicines imported from an EU Member State or a country within the EEA. Therefore, PPAs issued for products imported from the UK will cease to be valid ~~post at the withdrawal date~~[end of the Transition Period](#).

If the UK is listed as one of a number of source countries on a PPA, this will need to be removed by way of a type IA variation (category 5).

A PPA holder must be located within the EEA. Therefore, where the holder of a PPA is located within the UK, the authorisation will need to be transferred to a holder located within the EEA. This transfer can be conducted using the transfer procedure as outlined in section 6.4 above.

The repackaging activity and subsequent certification of the repackaging activity by the Qualified Person must take place within the EEA. Variations to change the repackaging and/or certification of the repackaging activity site (if different to the repackaging site) from the UK to the EEA should be completed prior to the ~~withdrawal date~~ end of the transition period. Amendments to the details of the repackaging and or certification of the repackaging activity site can be submitted using the PPA variation category No 9a.

All repackaging of parallel imported products must take place within the EEA as by the end of the ~~withdrawal date~~ transition period. The European system is predicated on the products being sourced in one Member State and remaining within the EEA throughout repackaging, certification of the repackaging activity and placing on the market.

7 CLINICAL TRIALS FOR HUMAN MEDICINES

The European clinical trial regulation EU No. 536/2014 ~~is which was~~ due to come into force in 2020 has been postponed to 2021 due to the Covid-19 pandemic. Key features of this Regulation will include:

- Identical rules for conducting clinical trials throughout the EU.
- Increase in the efficiency of the approval process for clinical trials.
- Single submission and approval of multinational clinical trial applications through an EU 'Clinical Trial portal and database'.
- A harmonised procedure for assessment by member states, divided in two parts:
- Strictly defined deadlines for assessment.
- Involvement of the ethics committees in the assessment procedure.

It is recognised that the UK is involved in many European clinical trials and it is hoped that the UK will fully adopt the new regulation, which aims to increase the number of clinical trials conducted in Europe.

[The EU Commission issued a Notice to Stakeholders \(May 2020\) regarding the UK withdrawal and EU rules in clinical trials in September 2018. Replacing the previous notice to stakeholders \(September 2018\) and the guidance on well-established clinical trial applications in Q14 of the EC Q&A](#)

7.1 UK based sponsor or legal representative listed on clinical trial application

Under the current clinical trial directive, Article 19 of Directive 2001/20/EC requires that the sponsor or a legal representative of the sponsor is established in the EU/EEA. This does not exclude the possibility that this establishment is a branch or subsidiary of a legal person having its principal seat outside the EU. This establishment could be the sponsor or act as legal representative of the sponsor established outside the EU.

Sponsors are requested to consider the impact of Brexit on this legal requirement. A change to the application form can be made prior to approval of a clinical trial. For approved clinical trials, a change to the sponsor or legal representative requires the submission of a substantial amendment. The HPRA strongly advises that amendments are submitted for review and approval in advance of the ~~withdrawal date~~ end of the Transition Period, in order to avoid a possible suspension of a clinical trial where both sponsor and legal representative are based in a third country.

In the new clinical trial regulation (article 74, paragraph 1), where the sponsor of a clinical trial is not established in the EU, that sponsor is required to ensure that a natural or legal person is established in the EU as its legal representative. Member States may choose not to implement paragraph 1 for clinical trials to be conducted solely on their territory, or on their territory and the territory of a third country, provided that they ensure that the sponsor establishes at least a contact person on their territory in respect of that clinical trial, who shall be the addressee for all communications with the sponsor provided for in this regulation.

With regard to clinical trials to be conducted in more than one Member State, all those Member States may choose not to apply paragraph 1 provided that they ensure that the sponsor establishes at least a contact person in the EU in respect of that clinical trial who shall be the addressee for all communications with the sponsor provided for in this regulation. While the full impact of Brexit is still unclear, the HPRA remains committed to supporting sponsors during this period of change.

7.2 UK site of batch release listed on clinical trial applications

In accordance with article ~~34~~13(1) of Directive 2001/20/EC the site of EEA importation of investigational medicinal products (IMP) must hold a manufacturing authorisation which permits this activity. This authorisation is required if any aspect of the manufacture or packaging of the product is conducted outside the EEA.

Article 13(2) of Directive 2001/20/EC requires the holder of this authorisation to have, permanently and continuously at their disposal, the services of at least one qualified person ~~located within the EEA.~~

As per article 11(2) of Directive 2003/94/EC mandatory testing of IMPs, manufactured in third countries, upon importation into the EEA is not required.

When the UK withdraws from the EU, all ongoing clinical trials with IMPs sourced from the UK will need to be imported into the EEA by a site authorised for this activity. Mandatory testing of the IMP will not be required but QP certification (by a QP at the EEA site of importation) indicating that the manufacturing standards comply with EU GMP standards will be required.

If a site in the UK is currently approved for this batch certification activity, the CT application form will need to be amended to notify the HPRA of the EEA site of batch certification. One bulk substantial amendment can be submitted which includes a line listing of all the CTs that are affected. Rather than submitting an updated application form for each product the HPRA will accept the amended section (section D.9) of the application form and apply this change to all the CTs affected. A substantial amendment fee will be required for each CT. The UK site of batch certification can remain listed on the Irish application form as long as it is clearly designated as the site for importation of IMP batches intended for the UK

7.3 Implications for Ireland as a site for clinical trials

Clinical trials are central to the development of new treatments for patients. The HPRA acknowledges the importance of ensuring that Ireland is recognised as an attractive country in which to conduct clinical trials. Ireland will continue to conduct clinical trials in line with EU legislation and within the new clinical trial regulation when it comes into force. The majority of clinical trials conducted here are multinational and international trials. The HPRA will continue to support both commercial and non-commercial sponsors in the conduct of clinical trials in Ireland.

8 PHARMACOVIGILANCE OPERATIONS

8.1 Human medicines

MAHs will need to ensure that their EU qualified person responsible for pharmacovigilance (QPPV) and their pharmacovigilance system master file (PSMF) are located within the EU/EEA. This is necessary to remain in compliance with the requirements outlined in article 104 of Directive 2001/83/EC, as amended, and in Article 7 of Commission Implementing Regulation No. 520/2012. The deputy QPPV is required to perform his/her tasks in the Union (EEA) as part of a MAH's back-up arrangements in the absence of the QPPV. There is no legal impediment to having other pharmacovigilance activities located in the UK.

Requirements for coordination of pharmacovigilance inspections undertaken by Member States, including the sharing of information on inspections planned and conducted inspections are provided for in EU legislation (Article 111 of Directive 2001/83/EC, Article 19 of Regulation No 726/2004) and associated Union procedures.

8.2 ~~Variations to marketing authorisations to change Qualified Person Responsible for Pharmacovigilance (QPPV)~~

~~Any variations required for a marketing authorisation (MA), e.g. change in location of QPPV should be completed prior to the date of the UK's departure from the EU. It is recommended that MAHs prepare and proactively screen authorisations they hold for any required changes. Variation applications should be submitted in sufficient time to ensure they are completed prior to Brexit.~~

~~Further guidance on QPPV scenarios is available in the CMD(v/h) Q&As and practical guidance documents listed at the beginning of this section.~~

8.38.2 Veterinary medicines

Article 74 of Directive 2001/82/EC states that the EU QPPV shall reside and operate in the EU/EEA. Therefore, there will be a requirement for MAHs to relocate their EU QPPV to another EU member state if it is currently located in the UK. The deputy QPPV is required to perform his/her tasks in the Union (EEA) as part of a MAH's back-up arrangements in the absence of the QPPV. There is no legal impediment to having other pharmacovigilance activities located in the UK.

The regulation of pharmacovigilance within Ireland will continue in line with EU legislation.

Any variations required for a marketing authorisation (MA), e.g. change in location of QPPV should be completed prior to the date of the UK's departure from the EU. It is recommended that MAHs prepare and proactively screen authorisations they hold for any required changes. Variation applications should be submitted in sufficient time to ensure they are completed prior to Brexit.

Further guidance on QPPV scenarios is available in the CMDv practical guidance document listed at the beginning of this section.

9 CHANGES TO IMPORT AND EXPORT REQUIREMENTS

The following advice regarding the importation, export, storage and distribution of medicines are based on the assumption that the UK will become a third country from the withdrawal date, leaving the European single market and customs union. It does not take into account however any possible future mutual recognition agreement (MRA) on good manufacturing practice (GMP) inspection between the EU and the UK. Therefore, this advice may be subject to change in the future as the negotiations on a trade deal progress.

9.1 Customs transit code

In the event that the UK remains within the common transit convention, medicines can be transported from a manufacturer in the EEA, over land through the UK (so called 'land-bridge'), to Ireland, under the Customs' transit code. Under this provision, medicines would not be

considered as exported and re-imported and, therefore, a wholesaler can receive the goods and QP certification would not be required again ~~for~~ on receipt of the product(s) in Ireland.

If your company uses the customs transit code then our understanding is that this would allow a truck to be opened in the UK, the UK stock removed and the Irish stock remain on the truck and be sent onwards to Ireland.

Similarly, Irish manufacturers can use the transit code to transport batches of medicines from Ireland across the UK to other EEA markets without the batches undergoing importation controls on re-entry into the EU/EEA.

Details on the customs procedures can be found on the [Revenue website](#) and all queries regarding it should go to Revenue directly.

9.2 Finished product coming from the UK; Importation Controls

Any Irish company that physically receives finished medicinal product from the UK (originating from a UK manufacturer or wholesaler or transiting the UK without the use of the customs transit code), will be required to hold a manufacturer's/importer's authorisation (MIA) with the activity 'Physical Importation' listed on it. Medicines coming from a third country must be first physically received at the site that holds an MIA including the activity 'Site of Physical Importation'.

In addition, the product for the Irish market would have to be QP certified again for the Irish market (this can happen at any EU site of batch release that is registered on the marketing authorisation for that product). See below section on batch testing requirements.

Where the batch release certificate checks performed by a wholesale distribution authorisation (WDA) holder may highlight a batch that potentially is non-compliant post Brexit, the HPRa would recommend that the WDA holder reverts to the relevant MAH for clarification.

~~Currently Irish legislation requires the sourcing has been updated to facilitate importation of an exempt/unlicensed medicines from a third country to be carried out under an MIA, however, legislative amendments are currently under review to amend the legislation to permit medicinal product by a wholesaler to do so with that category listed on its WDA.~~

9.3 Product testing for QP certification/release

Directives 2001/82/EC and 2001/83/EC stipulate a requirement for all batches intended for EU markets to undergo control testing in a Member State. The control tests which define the quality of the batch are those in the finished product specification. If the batch has already undergone these finished product tests in a Member State then the results from these tests, together with knowledge of the storage conditions of the batch since testing, may be taken into account by the QP when certifying the batch on importation into Ireland.

If a batch that is tested and certified in the UK before the withdrawal date, ~~or that is subject to a 'Testing Exemption' post withdrawal date,~~ is stored in the UK after ~~Brexit~~ the end of the transition period then the following would apply on each occasion that stock is imported from the UK into the EU:

- 1 Each batch of product imported from the UK ~~post-Brexit~~ must be received at a manufacturing site which is authorised as a site of physical importation – i.e. cannot be supplied direct to a wholesaler
- 2 Each batch would have to undergo certification by a QP at the manufacturing site appointed for the purpose of batch release within the product Marketing Authorisation (MA). This may or may not be the same site as ~~the batch that~~ to which the ~~product batch~~ is physically imported and certification could take place at any EU site of batch release that is registered in the marketing authorisation for that product.
- 3 The QP may take into account the results of finished product testing conducted at ~~a laboratory (EU or UK lab through the use of the above referenced 'Testing Exemption'), an earlier time point in an EU laboratory,~~ together with knowledge of the storage of the batch since testing was conducted, when dispositioning each imported batch.
- 4 The certifying QP should be in a position to confirm all necessary steps in the manufacturing and quality control (QC) of the product have been carried out in accordance with GMP and the MA and be responsible for all steps in the process carried out in a third country.
- 5 The certifying QP can rely on the quality management system (QMS) within a third country site providing that this reliance is well founded.
- 6 The site of batch release should be named in the product MA and the QP should have access to the MA.
- 7 The certifying QP must be listed on the MIA of the batch release site and complete batch certification at the named site of batch release.

~~The HPRA is open to accepting requests for exemptions for Batch Testing in line with Commission position of 25 Feb 2019 "Withdrawal of the United Kingdom and EU rules for batch testing of medicinal products". Further details on the process to apply for this exemption are available on the HPRA website.~~

9.4 Qualified person (QP) certification/release

For EU markets, all products that originate from the UK, or those imported via the UK, must be imported by a manufacturer located within the EU/EEA and certified by a Qualified Person (QP) in the EEA. If product has been QP certified in the UK and shipped to Ireland before the ~~withdrawal date~~ end of the Transition period, it can continue to be used/sold until the stock is exhausted.

The manufacturing site where the QP performing certification is located must be a named site for Batch Release in the MA. In accordance with Annex 16, the QP at this site may take into

account the confirmation by QPs at other EU site(s) further back in the manufacturing chain provided that Quality / Technical agreements are in place to reflect this situation

9.5 Process for changing the site of batch release

A company should apply to the HPRA for a manufacturer's/importer's authorisation (MIA) for batch certification/release within the Republic of Ireland. A GMP inspection will be conducted on receipt of an application. The batch certification activities must take place at the authorised address. [All necessary documentation can be found on the HPRA website](#). Queries relating to MIA applications should be directed to compliance@hpra.ie

9.6 Finished product supplied from Ireland to the UK

An Irish wholesale entity supplying the UK market will need to vary its authorisation to include the activity 'export' to continue this supply.

Irish manufacturers of medicinal products that are supplied to the UK market will need to comply with any additional requirements that may be put in place by the UK competent authorities.

9.7 Active substances

With respect to active substances for use in human medicinal products sourced from companies in the UK, an active substance distributor will also be required to register as an active substances importer. An Irish dosage form manufacturer receiving active substance from a UK source will also need to register with the HPRA as an active substance importer.

In order to import active substances manufactured in the UK, under the Falsified Medicines Directive, a written confirmation issued by the UK regulatory authority for the manufacturing site will need to be provided for each imported consignment.

With respect to active substances for use in veterinary medicinal products sourced from companies in the UK, there is no requirement for a supervisory system for active pharmaceutical ingredients and there are, therefore, no additional requirements for active substance arising from the decision of the UK to leave the EU.

10 COSMETICS

On ~~1 February 2019~~^{13 March}, the EU Commission published a ~~Q&A document to provide further information on the impact~~^{Readiness Notice, in the form} of a 'no deal' ~~Brexit on Notice to Stakeholders, regarding the Withdrawal of the UK and EU rules in the field of cosmetic products (and other products covered under the New Approach legislation).~~

This ~~Q&A follows on from the Commissions' January 2018 notice to stakeholders and November 2018 notice to stakeholders, and highlights some of the implications on labelling, representation and supply in the event of no deal.~~

~~The latest Q&A provides examples~~^{This Notice to Stakeholders outlines the legal situation applicable as of the end of the transition period, particularly advising to:}

- ~~- establish a Responsible Person (RP) in the EU and reflect this in the corresponding labelling;~~
- ~~- ensure compliance of when goods are placed on the market and in the supply chain, which includes clarification on the requirements~~^{safety assessment} in relation to ~~presentation~~^{qualifications} of the Responsible Person (RP) ~~contact details on~~^{safety assessor; and}
- ~~- take the labelling~~^{necessary steps to update the Cosmetic Product Notification Portal (CPNP).}

The ~~Q&A also reinforces the importance of updating the Cosmetic Product Notification Portal (CPNP) for products currently registered with a RP in the UK. In the event of a 'no deal' Brexit, all cosmetic products made available to the EU market as of the date of withdrawal date are required to be registered on CPNP with a RP of one of the EU-27 Member States. Information is available regarding transfer of an existing notification in CPNP to a future EU-RP in the Commission's November 2018 notice to stakeholders.~~

In the context of the UK becoming a 3rd country post Brexit, the HPRA takes this opportunity to remind Irish entities sourcing products from the UK for supply to the EU-27 to be aware that they will become an importer and potentially the RP for the product if one has not already been designated in the EU-27.

~~The notice also discusses cosmetic products placed on the EU or UK market before the end of the transition period and provides information in relation to the applicable rules in Northern Ireland after the end of the transition period.~~

The HPRA is continuing to work with the European Commission and other Member States in relation to cosmetic product issues arising from Brexit.

~~The HPRA takes this opportunity to remind Irish entities sourcing products from the UK for supply to the EU to be aware that, at the end of the transition period, they will become an~~

importer and potentially the RP for the product if one has not already been designated within the EU by written agreement.

The most up-to-date Brexit Guidance for stakeholders in relation to cosmetic products can be consulted on the Cosmetics page of our website. The HPRA encourages any responsible persons, distributors, manufacturers or retailers to take the appropriate steps in preparation for Brexit in relation to supply of compliant cosmetic products to the market. Email: cosmetics@hpra.ie

~~[EU Commission Q&A](#)~~

~~[EU Commission Notice to Stakeholders January 2018](#)~~

~~[EU Commission Notice to Stakeholders November 2018](#)~~