# Commission notice – Application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period

(2020/C 447/05)

Since 1 February 2020, the United Kingdom has withdrawn from the European Union and has become a 'third country' ([1]). The Withdrawal Agreement ([2]) provides for a transition period ending on 31 December 2020. Until that date, Union law in its entirety applies to and in the United Kingdom ([3]). This includes the pharmaceutical acquis of the Union, in particular Directive 2001/82 ([4]), Directive 2001/83 ([5]), Commission Delegated Regulation (EU) 2016/161 ([6]) and Article 13 of Directive 2001/20 ([7]), which are of relevance for this Notice.

At the end of the transition period, Union law ceases to apply to the United Kingdom. As the Protocol on Ireland and Northern Ireland ('the IE/NI Protocol') starts to apply, some Union legislation (including the above mentioned legislation), its implementing, amending and replacing measures, however, becomes applicable to and in the United Kingdom in respect of Northern Ireland in accordance with Art 5 (4), Annex 2, point 20, of the IE/NI Protocol.

In practical terms, this means, in particular, that:

— Medicinal products (in the scope of the abovementioned legislation) placed on the market in Northern Ireland must comply with the regulatory requirements laid down in Union law (cf. Article 5 (4) of the IE/NI Protocol, read in conjunction with Annex 2 to that Protocol);

— Medicinal products must have a valid marketing authorisation in the EU or in Northern Ireland, the holder of which is located in the EU or in Northern Ireland;

— Trade in medicinal products from Great Britain to Northern Ireland or to the Union constitutes an import in the sense of applicable Union law;

— Trade in medicinal products from the Union or Northern Ireland to any other part of the United Kingdom (Great Britain) or any other third country constitutes an export in the sense of applicable Union law;

— Authorisations issued by UK authorities are, in principle, not valid under Union law, but can only be recognised in Northern Ireland if adopted in accordance with applicable Union law (cf. Article 7 (3) of the IE/NI Protocol);

— Any steps in the supply of medicines which must be carried out in the Union (e.g. batch release) in order to allow for the placing on the market of medicinal products in accordance with Union law must occur in the (geographical) scope of Union law, ie in the Union or Northern Ireland, and only actions that may be carried out in third countries may occur in Great Britain.

([1]) A third country is a country not member of the EU.

([2]) Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community (OJ L 29, 31.1.2020, p. 7) ('Withdrawal Agreement').

([3]) Subject to certain exceptions provided for in Article 127 of the Withdrawal Agreement, none of which is relevant in the context of this notice.

([4]) Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ L 311, 28.11.2001, p. 1).

([5]) Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67).

([6]) Commission Delegated Regulation (EU) 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (OJ L 32, 9.2.2016, p. 1).

([7]) Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (OJ L 121, 1.5.2001, p. 34).

The Commission and the European Medicines Agency have, since 2017, actively been disseminating all relevant information in order to draw the attention of all relevant stakeholders to the impact of the United Kingdom's withdrawal and to alert them of the need to adapt in time before the end of the transition period. The necessary changes have notably been explained in BREXIT Notices as last amended and published on 7 May 2020 for clinical trials ([8]) and on 13 March 2020 for medicinal products ([9]).

Nonetheless, some markets which have historically relied on supply of medicinal products from or through Great Britain (Cyprus, Ireland, Malta and Northern Ireland) ([10]), may still need some additional time to adapt supply chains and take account of the end of the transition period. Against that background, it is crucial that the Union's pharmaceutical acquis is implemented and enforced in a manner that both prevents shortages of medicines and ensures the high level of public health protection foreseen by Union law.

The Commission has identified the following challenges (described below) as the principal difficulties for the above-mentioned markets which are historically dependent on medicines supply from or through Great Britain in complying with the Union's pharmaceutical acquis:

1. Lack of operators holding a manufacturing authorisation necessary for imports of medicinal products from third countries;

2. Difficulties to carry out quality control testing ('batch testing');

3. Difficulties to comply with the provisions of Directive 2001/83/EC and Commission Delegated Regulation (EU) 2016/161 with respect to the placement and verification of the unique identifier.

Recognising these challenges, and taking into consideration the exceptional circumstances of the COVID-19 pandemic, the Commission takes note of the request, from both private and public stakeholders in the Union and the United Kingdom, for more time in the transition towards full compliance with the Union's pharmaceutical acquis.

## 1. **Lack of operators holding a manufacturing authorisation required for importing medicinal products from third countries**

### A. *Human and veterinary medicinal products*

According to Article 40(3) of Directive 2001/83/EC and Article 44(3) of Directive 2001/82/EC, anyone placing medicinal products from third countries on the market in accordance with Union law (in the Union or in Northern Ireland) is an importer in the sense of Union law, and must therefore hold a manufacturing authorisation issued by the Member State where the importer is established or, in the case of importers established in Northern Ireland, by the UK acting in respect of Northern Ireland in accordance with Articles 41 and 42 of Directive 2001/83/EC for human medicines and/or Articles 45 and 46 of Directive 2001/82/EC for veterinary medicines. The conditions for such a manufacturing authorisation include, inter alia, the availability of a qualified person in the Union or Northern Ireland, the inspection of the manufacturer/importer and its compliance with Good Manufacturing Practices.

According to Articles 118 of Directive 2001/83/EC and Article 84(e) of Directive 2001/82/EC, competent authorities applying the Union's pharmaceutical acquis are obliged to suspend or revoke the marketing authorisation of a medicinal product where the holder of that authorisation does not have a valid manufacturing authorisation or does not comply with one of the conditions necessary to obtain such manufacturing authorisation.

In order to allow operators in these markets historically dependent on medicines supply from Great Britain additional time to comply in full with the requirements of the Union's pharmaceutical acquis in the exceptional circumstances of a global pandemic, the competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland could apply the following practice between January 2021 and 31 December 2021.

([8]) https://ec.europa.eu/info/sites/info/files/brexit_files/info_site/clinical-trials_en.pdf

([9]) https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/notice-stakeholders-withdrawal-united-kingdom-eu-rules-medicinal-products-human-use-veterinary_en.pdf

([10]) These Member States are singled out in this Notice because of their historical dependence on the UK market for their supply of medicinal products and the fact that a large proportion of their imports of medicinal products is coming from UK.

In this case, the competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland would allow medicinal products to be imported from Great-Britain by wholesalers which are not in possession of a manufacturing authorisation as required by Article 40 of Directive 2001/83/EC and Article 44 of Directive 2001/82; and they (ii) would not suspend or revoke the marketing authorisations of those medicinal products as required by Articles 118 of Directive 2001/83 and Articles 84(e) of Directive 2001/82, provided that the following conditions are fulfilled:

— The medicinal products supplied from or through Great Britain and placed on the market in accordance with Union law (i.e. imported into the Union or Northern Ireland) have undergone quality control testing ('batch testing' ([11])) either in the Union, as provided for in Article 51(3) of Directive 2001/83/EC for human medicinal products and in Article 44 (3) of Directive 2001/82/EC for veterinary medicinal products, or in Great Britain in compliance with Article 20 (b) of Directive 2001/83/EC for human medicinal products and with Article 24b of Directive 2001/82/EC for veterinary medicinal products (see Section 2 of this Notice);

— The medicinal products supplied from or through Great Britain and placed on the market in accordance with Union law (i.e. imported into the Union or Northern Ireland) have been subject to batch release by a Qualified Person (QP) in the Union or by a QP in the UK applying equivalent quality standards to those laid down in Union law, thus ensuring an equivalent level of protection of human health;

— The operator placing medicinal products supplied from or through Great Britain on the market in accordance with Union law (in the Union or in Northern Ireland) holds a distribution authorisation issued, before the end of the transition period, in accordance with Article 77(1) of Directive 2001/83/EC for human medicinal products and/or Article 65(1)of Directive 2001/82/EC for veterinary medicinal products;

— The marketing authorisation of the medicinal product concerned has been issued by the competent authority of an EU Member State, by the Commission, or by the competent authority of the United Kingdom before the end of the transition period and in accordance with Union law;

— The medicinal products supplied from or through Great Britain are made available to the end consumer in the same market historically dependent on medicines supply from Great Britain where they are imported, and they are not made available in other EU Member States.

The competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland would in this case also report to the Commission, on a monthly basis, as regards the progress made by wholesale distributors importing medicinal products in fulfilling the conditions necessary to obtain a manufacturing authorisation laid down in Article 41 of Directive 2001/83/EC and Article 45 of Directive 2001/82/EC, including, in particular, the conclusion by those wholesale distributors of contractual relationships with qualified persons in the Union.

B. *Investigational medicinal products*

According to Article 13 of Directive 2001/20/EC, the placing on the market of investigational medicinal products from third countries in accordance with Union law also requires the importer to hold a manufacturing authorisation. After the end of the transition period, this also applies to the supply of investigational medicinal products from or through Great Britain in Cyprus, Ireland, Malta and Northern Ireland. Similarly to the requirements for manufacturing authorisations pursuant to Article 41 of Directive 2001/83 and Article 44 of Directive 2001/82, Article 13(2) of Directive 2001/20/EC also requires the holder of this manufacturing authorisation to have, permanently and continuously, at his disposal the services of at least one qualified person in the scope of application of Union law, i.e. in the Union or in Northern Ireland.

([11]) According to Article 51(1)(b) of Directive 2001/83/EC and Article 55(1)(b) of Directive 2001/82/EC, medicinal products imported into the EU have to undergo quality control testing ('batch testing') in the EU/EEA. These provisions prescribe that in the case of medicinal products coming from third countries, irrespective of whether the product has been manufactured in the Union, that each production batch has undergone in a Member State 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.

In order to allow operators in these markets historically dependent on medicines supply from Great Britain additional time to comply in full with the requirements of the Union's pharmaceutical acquis in the exceptional circumstances of a global pandemic, the competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland could apply the following practice between January 2021 and 31 December 2021 as regards investigational medicinal products.

In this case, the competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland would allow investigational medicinal products to be imported from Great-Britain by wholesalers which are not in possession of a manufacturing authorisation as required by Article 13 of Directive 2001/20/EC, provided that the following conditions are fulfilled:

— The medicinal products supplied from or through Great Britain and approved for use in accordance with Union law (i.e. imported into the EU or Northern Ireland) have undergone batch release either in the Union, as provided for in Article 13(3) of Directive 2001/20, or in Great Britain in compliance with Article 13(3) of Directive 2001/20/EC;

— The clinical trials authorisation of the medicinal product concerned has been issued by the competent authority of an EU Member State, by the Commission, or by the United Kingdom before the end of the transition period and in accordance with Union law;

— The medicinal products supplied from or through Great Britain are made available to the end consumer in the same market historically dependent on medicines supply from Great Britain where they are imported, and they are not made available in other EU Member States.

The competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland would in this case also report to the Commission, on a monthly basis, as regards progress made by operators importing investigational medicinal products in fulfilling the conditions necessary to obtain a manufacturing authorisation pursuant to Article 13 of Directive 2001/20/EC, including, in particular, the conclusion by those operators of contractual relationships with qualified persons in the Union.

2. **Batch testing of human and veterinary medicinal products**

According to Article 51(1)(b) of Directive 2001/83/EC and Article 55(1)(b) of Directive 2001/82/EC, medicinal products imported into the EU have to undergo quality control testing ('batch testing') in the EU/EEA. The requirement of a batch release site established in the Union is a fundamental pillar of the Union system of ensuring quality of medicinal products being placed on the Union market. However, with regard to the quality control testing there may be objective reasons beyond the control of the marketing authorisation holders that may have prevented the timely transfer of such testing activities to be carried out in the Union or Northern Ireland by the end of the transition period.

In these cases, Article 20(b) of Directive 2001/83/EC and 24(b) of Directive 2001/82/EC allow for importers placing medicinal products supplied from or through Great Britain on the market in Cyprus, Ireland, Malta or Northern Ireland or wholesale distributors placing such medicinal products on those markets as described under Section 1 above, to have, in justifiable cases, certain controls carried out in Great Britain. Taking into account the exceptional circumstances described in this Notice, the Commission considers that a 'justifiable case' within the meaning of Article 20(b) Directive 2001/83/EC and 24(b) of Directive 2001/82/EC occurs when the following conditions are fulfilled:

— Each batch of the medicinal product concerned is released by a qualified person (QP) on a site in the EU or by a QP on a site in the UK applying equivalent quality standards to those laid down in Union law, thus ensuring an equivalent level of protection of human or animal health, in cases falling under Section 1 above;

— The establishment designated by the third party conducting the quality control testing is supervised by a competent authority, including on-the-spot checks. Demonstrable progress towards transferring the quality control testing site to the Union or Northern Ireland is shown. Notably the batch testing site should be established within a twelve-month period after the end of the transition period, by the 31 December 2021 at the latest.

In order to make use of the derogation foreseen in Article 20(b) of Directive 2001/83/EC for human medicinal products and Article 24(b) of Directive 2001/82/EC for veterinary medicinal products, marketing authorisation holders should notify the competent authority that granted the marketing authorisation of the product concerned (Cyprus, Ireland, Malta or Northern Ireland), specifying that – and why in their view - the above criteria of a 'justifiable case' in the sense of Article 20 (b) of Directive 2001/83, and of Article 24 (b) of Directive 2001/82, are fulfilled. For medicinal products to be placed on the market in Northern Ireland, the competent authority is the MHRA. For centrally authorised products, the competent authority is EMA.

Any such notification should be submitted without undue delay and should be received as soon as possible after the end of the transition period, and in no case later than by 30 January 2021.

3. **Requirements relating to the placement of the unique identifier for medicinal products for human use**

As the IE/NI Protocol makes Directive 2001/83 applicable to and in the United Kingdom in respect of Northern Ireland in its current version, the safety features (namely the anti-tampering device and the unique identifier) laid down in Articles 54 (o) and 54a (1) of Directive 2001/83/EC also apply to medicinal products placed on the market in Northern Ireland. Without prejudice to the application of this Union legislation to and in the United Kingdom in respect of Northern Ireland, the placing on the market of medicinal products in any other part of the United Kingdom than Northern Ireland will not require the use of these safety features, like the unique identifier, foreseen in Union law.

This means that, as from 1 January 2021, packs of medicines destined for Great Britain should be separated from packs destined for Cyprus, Ireland, Malta or Northern Ireland – even where the supply route goes through Great Britain. Like for any medicinal products placed on the market in the Union, the information of the Cypriot, Irish, Maltese and Northern Irish packs needs to be uploaded in the European hub, or the repository systems of the respective territories, but not the information of the packs with a final destination in any other part of the United Kingdom than Northern Ireland (Great Britain).

As regards packs exported from the Union to any third country like the United Kingdom, Article 22 of Commission Delegated Regulation (EU) 2016/161 obliges the economic operator exporting the medicinal products to decommission any unique identifier that may have already been affixed to the pack prior to the export.

Where medicinal products are supplied, through Great Britain, to Cyprus, Ireland, Malta or Northern Ireland, it would then, in principle, be for the importer holding a manufacturing authorisation to affix a new unique identifier on the medicinal products in question when they are placed on the market (cf. Article 4 of Commission Delegated Regulation (EU) 2016/161). Nevertheless, there are currently no importers holding a manufacturing authorisation located in Cyprus, Ireland, Malta and Northern Ireland with capacity to meet the obligation to affix a new unique identifier as required by Union law as of 1 January 2021 so that compliance would be practically impossible. At the same time, allowing medicinal products without safety features on the Union market must be prevented, in order to ensure a high level of public health protection and to avoid the presence of falsified medicinal products in the Union.

The Commission therefore intends to amend Article 22 of Commission Delegated Regulation (EU) 2016/161 to address this situation.

The economic operators responsible for the export of medicinal products (placed on the market in the Union, exported to Great Britain and then imported into Cyprus, Ireland, Malta or Northern Ireland) from the Union to Great Britain would then no longer be obliged to decommission the unique identifier in accordance with Article 22 of Commission Delegated Regulation (EU) 2016/161.

Following this approach, the competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland would allow the import of medicinal products from Great Britain bearing non-decommissioned unique identifiers provided that the following conditions are fulfilled:

— the wholesale distributor or the marketing authorisation holder established in the Union and responsible for the export of the medicinal product to the United Kingdom has verified the unique identifier against the European repository or the national repository system;

— the wholesale distributor importing the product into Northern Ireland, Ireland, Cyprus or Malta has verified the unique identifier against the European repository or the national repository system;

The competent authorities of Ireland, Malta, Cyprus and the United Kingdom with respect to Northern Ireland would in this case also report to the Commission, on a monthly basis, as regards the progress made by wholesale distributors importing medicinal products in fulfilling the obligations under Directive 2001/83 and Commission Delegated Regulation (EU) 2016/161 relating to placement of the unique identifier.