



# Medicines & Healthcare products Regulatory Agency

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Head of Regulatory Affairs

[gov.uk/mhra](http://gov.uk/mhra)

26 November 2018

Dear Head of Regulatory Affairs

## **Preparations in the event of a No-Deal Brexit Preparation:**

### **Conversion of Centrally Authorised Products (CAPs) to UK Marketing Authorisations (MAs)**

We do not want or expect a no deal scenario. It is however the duty of a responsible Government to continue to prepare for a range of potential outcomes including the unlikely event of no deal.

In the unlikely event that the UK leaves the EU in a no deal scenario, the UK will need to put in place arrangements for the continued authorisation of medicinal products. This letter is to inform you of the actions we intend to take concerning CAPs and the actions we need you to take as a Marketing Authorisation Holder (MAH) of a CAP in the event of a 'no deal' scenario.

As set out in the technical notice published on the 23 August (titled 'How medicines, medical devices and clinical trials would be regulated if there's no Brexit deal'), the legislation that will come into force in this scenario will, subject to being approved by Parliament, automatically convert CAP MAs into UK MAs on 29 March 2019 (so-called 'grandfathering').

MAHs can opt-out of the grandfathering process for all or some of their CAPs by notifying the MHRA in writing by 22nd April 2019. If an MAH chooses to opt-out, after 22nd April 2019 their product(s) will no longer be licensed in the UK. This will mean they can no longer be placed on the market in the UK.

MAs for CAPs that are not currently marketed in the EU or UK can still be converted to UK MAs. For the purposes of operating the Sunset Clause, the period of three years will be restarted from the date of conversion to a UK MA.

To facilitate the grandfathering process, the MHRA will issue one or more Product Licence (PL) numbers to CAPs based on the existing UK practice for determining how many separate national licences are needed across a product range. In most cases this means that fewer UK MA numbers will be needed in comparison with the number of European Commission authorisations because all pack sizes for a presentation will be covered by a single MA number.





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The format of the UK MA is PL XXXXX/YYYY where XXXXX is the company number and YYYY is a sequential number for individual products. Where a CAP MAH already has a company number allocated by MHRA for existing national licences, that number will be used. If the CAP MAH does not have a company number allocated by MHRA then a number will need to be applied for.

There is no fee associated with the conversion from a CAP to a UK MA. In line with our existing legislation, the annual periodic fee will be payable for converted CAPs from 1 April 2019. Guidance on these fees can be found at:

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

To ensure that the grandfathering process runs smoothly, actions you are requested to take when you receive the list of products are:

1. Check the list of your currently authorised CAPs and advise us as soon as possible of any errors or omissions in that list.
2. Review the list of assigned UK MA numbers and contact us as soon as possible if you have a query in relation to the number of different UK MA numbers allocated.
3. Advise us of any CAPs that you do not want to be converted into UK MAs.
4. When the list is complete, return it to us and advise us of the UK marketing status of each of the products.

To help with our contingency planning in the unlikely event of no deal, we ask that you advise us by the end of January if you are planning to opt out and not have a UK licence for a product, ideally as part of your full return (as per points 1-4 above), or if not via a separate communication to the MHRA.

To assist with your planning, please find attached separate guidance on our proposed requirements for submitting baseline information on your product (following the MHRA's recent consultation on this matter). The specific information and further guidance on handling of any post-authorisation submissions that are pending on 29<sup>th</sup> March 2019 will be included in a follow up letter.

In the meantime, if you have any questions about this conversion process, please send them to **capconversion@mhra.gov.uk**

MHRA CAP Conversion Team



## **Guidance on Converting Centrally Authorised Products (CAPs) to UK Marketing Authorisations (MAs) – proposed requirements for submitting baseline information**

We do not want or expect a no deal scenario. It is however the duty of a responsible Government to continue to prepare for a range of potential outcomes, and in the unlikely event that the UK leaves the EU in a no deal scenario, the UK will need to put in place arrangements for the continued authorisation of medicinal products.

In addition to the letter informing you of the actions we need you to take as a Marketing Authorisation Holder (MAH) of a CAP in the event of a 'no deal' scenario, this guidance outlines our proposed requirements for submitting baseline information on your product.

We are sending you our proposed requirements at this stage, so you have as much time as possible to prepare. An explanation of how this final proposal was reached (after the recent MHRA consultation) will follow as part of the overall consultation response.

### **1. Reminder of proposed approach to grandfathering CAPs**

To ensure CAPs will continue to be authorised for use in the UK, all existing CAP MAs will automatically be converted into UK MAs and issued with a UK MA number on 29 March 2019 ("exit day").

If a CAP Marketing Authorisation Holders (MAH) does not opt-out of the automatic conversion process (as per the process set out in the letter), then in order to support the ongoing regulatory management of these converted EU MAs, the MHRA requires the submission of essential baseline data in the form of an initiating eCTD sequence and certain other related MA specific information for each converted EU MA.

### **2. Obligations of holders of converted EU MAs - Submission of the Initiating Sequence and other related information**

MAHs will have a period of one year starting on exit day to submit this data and related information in eCTD format. Until these initiating sequences are submitted and processed it will not be possible submit a variation for the converted EU MA unless there are exceptional circumstances relating to public health.

Within a period of one year starting on exit date and ending on 29 March 2020, the MHRA requires the following information to be submitted for each converted EU MA. The data submission package **must** contain:

- a. Cover letter and declaration that only approved documentation is included in the initiating sequence. The cover letter should clearly identify the submission as a "CAP Grandfathering Submission" in the title.
- b. a single eCTD initiating sequence for the converted EU MA representing the currently authorised and approved position. Where more than one dosage form or strength will be converted for the same product trade name, it is expected these will be handled as one eCTD dossier.
- c. a completed electronic application form (eAF) for each converted EU MA.



- d. a summary list of all historical regulatory activity from the date of grant of the original CAP until the data is submitted. This will include:
  - I. type of submission (e.g. initial new MAA, Variation, PSUR, Renewal, etc.)
  - II. the date of submission to the EMA
  - III. summary of submission (e.g. a short description of a variation)
  - IV. regulatory outcome (e.g. granted or not granted)
  - V. the date of the outcome
  - VI. eCTD sequence number of the submission (only for eCTD format submissions)
- e. Notification of whether the product referred to in the converted EU MA is on the UK market at the time the notification is given or, if not, whether the product has been on the UK market at any time after exit day and, if so, the date it was withdrawn from the market (for the purposes of Article 23a and Article 24 (4-6) of Directive 2001/83EC – as implemented in regulations 67 and 73 of the Human Medicines Regulations 2012), the “Sunset Clause”). This information may be included in the cover letter.
- f. The current EU procedure approved version of the Summary of Product Characteristics
- g. The current EU procedure approved versions of packaging Labels and Leaflets
  - I. the outer packaging of the medicinal product;
  - II. the immediate packaging of the medicinal product; and
  - III. the package leaflet for the medicinal product.

The Summary of Historical Regulatory Activity, and Notification of Marketing Status (sections d and e above) must be included in the Working Documents folder of the eCTD

The Cover Letter, eAF and currently approved SmPC, Packaging and Patient Information Leaflet must be included in the appropriate folders in Module 1 of the eCTD sequence

The submission must reflect only what is relevant to the product intended for the UK in order that this can be used as the start of the lifecycle for the nationally registered product(s). Inclusion of non-UK specific information could lead over time to inaccurate information held within the database and, under certain conditions, lead to difficulties with the technical validation of subsequent submissions.

The eCTD sequence must pass technical validation (details below). The MHRA will be applying an abbreviated content validation and will not be issuing a validation report, the presence of a SmPC, PIL and Packaging information are mandatory.

In constructing the initiating sequence, the MHRA expects that all information representing the currently authorised and approved position that has previously been submitted in eCTD format will be included in the initiating sequence submission. However, it is acknowledged that some information may not be available in electronic format, particularly for older products, and that it may not be possible for the initiating sequence to be entirely complete. In these circumstances, the MAH should submit what is available and the MHRA will accept a partially completed sequence, provided:

- I. all reasonable endeavours are made to include any information available in an electronic format other than eCTD format, in the appropriate eCTD structure in



accordance with eCTD technical validation criteria (placing documents in the Working Documents section of the eCTD structure should be avoided where possible and used by exception only).

- II. If the MHRA request the holder of the converted EU MA to provide any information related to the MA either before or after submission of the initiating sequence, including historical information, it must be provided without delay

### 3. Method of Submission

In the event of a no-deal scenario, the MHRA does not expect to be able to receive submissions through CESP. We are developing a new Portal to be ready by exit day, the expectation is that submissions will be made via this portal. Information on the use of this portal will be supplied in due course and in advance of exit day.

### 4. Specific information on the Preparation of the Initiating Sequence

Background information on the latest version of the eCTD standard – including EU guidance on Module 1 information – and the electronic application form can be found on the EMA e-submissions [website](#).

The MAH should construct a single, technically valid, eCTD sequence (the “Converted EU MA Initiating Sequence”) showing the current, approved information current authorised view”) of the converted EU MA(s) on the data submission date. Do not include information that has been “replaced” or “deleted” during the life cycle of the CAP MA that the converted EU MA is derived from.

The sequence should be assigned as sequence number 0000, submission type “maa” and submission unit assigned as “initial”.

Specific Points to consider:

- a. Only include UK relevant information – remove previous cover letters and application forms, remove all product information except UK specific information
- b. Remove all PSUR information, the UK will not require the PSURs to be submitted in the eCTD lifecycle
- c. Historical EU information about the PV Master File, etc. in Module 1.8. is not required. New information must be submitted as a later type IA variation.
- d. Remove all Responses to Questions in Module 1 - i.e. remove any discussion and only show the outcome in terms of the documents in the rest of Modules 1-5.
- e. The submission must include a full electronic Application Form (eAF) for each of the products in the application. The “Initial MAA” eAF should be used with the initiating sequence and only approved information should be included - any changes to the approved information must be submitted as a variation after the submission of the initiating sequence using the normal process for variations to national MAs.
- f. The Summary of Historical Regulatory Activity must begin with the original CAP MAA submission and continue up to the data submission date. This must be a list of the submission events in a table format, not the individual eCTD sequences that were



submitted for each event (noting that for some products these events will predate the eCTD). Please submit this in the same format as the Tracking Table in Module 1.0

- g. The initiating sequence must be a valid eCTD submission, built to EU Module 1 v3.0.2 and ICH v3.2.2 standards or, if these are superseded, by such standards that are applicable at the time of submission.
- h. The initiating sequence should include multiple dosage forms and strengths in a single eCTD dossier lifecycle.

## 5. Submitting the Initiating Sequence in Two Steps

The MHRA strongly prefers the submission of the initiating sequence to be a single event. However, it is recognised that some MAHs may need to submit variations to the MA before they can produce the complete initiating sequence.

In these circumstances, the MHRA will accept a two-step process where the MAH can submit a minimal initiating sequence containing at least the mandatory documents at an early point following exit day. The mandatory documents are defined in section 2(f) and 2(g). This must also be accompanied by an eAF containing at least the mandatory information (as defined in the form) and a cover letter and declaration (see section 2(a) and 2(c)). The sequence must also be technically valid (see section 4(g) above)

If MAHs take this approach, a further complete initiating sequence containing all documents electronically available and the specific other related information defined in section 2, must still be submitted within a period of one year starting on exit day. The sequence number of this submission should be sequential to the earlier minimal initiating sequence and any subsequent variations.

MAHs submitting an early minimal initiating sequence are advised to make every effort to include M3 documents. This module is frequently varied and, if the documents are not available, any subsequent variation is likely to be delayed by the need for RFIs to request missing data.

## 6. Next Steps

MAHs are encouraged to submit the initiating sequence and associated documents as soon as practicable after exit day.

For specific questions or clarification on this guidance, please contact us by email at [IPU.enquiries@mhra.gov.uk](mailto:IPU.enquiries@mhra.gov.uk)

Further guidance on handling of any post-authorisation submissions that are pending on 29<sup>th</sup> March 2019 will be issued separately.

MHRA

26<sup>th</sup> November 2018