Brexit info meeting

5 February 2018

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Agenda

- Introduction
- Brexit from a pharmaceutical perspective
- Practical aspects
  - Variations
  - Change of RMS
  - Reference product from UK
- Q&A session
- Coffee and possibility for individual questions

Introduction
Brexit from a pharmaceutical perspective

Marie Gårdmark
Director Division of Licensing

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Brexit

- A regulatory challenge for Europe
- EMA to relocate to Amsterdam
- Business continuity plan to ensure operational continuity
- Need to re-distribute workload between agencies
- MPA prepared to take over part of UK workload
- MPA active in discussions with our ministry, HMA and EMA about the future

Brexit – how do we prepare?

- Capacity
- Financing
- Communication

Continued availability of medicines in Europe

- Art. 50 negotiations ongoing – outcome?
- Possible transition period under discussion
- In order to avoid impact on supply, prepare for worst case scenario:
- UK becomes a "third country" from 30 March 2019

Brexit from a pharmaceutical perspective

Christin Olofsson
CMDh member, senior expert Regulatory Department

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Brexit preparedness

- HMA Brexit Task Force
- EMA WG on committees' operational preparedness (human & veterinary medicines)
- HMA/EMA TF Availability of Medicines
- GMDP IWG Brexit subgroup
- CMDh & CMDv

Where to find information?

Q&As on Brexit are continuously published:

- EC https://ec.europa.eu/health/human-use_en
- EMA UK's withdrawal from the EU ('Brexit')
- CMDh http://www.hma.eu/535.html
- CMDv http://www.hma.eu/542.html

Main areas

- Industry perspective – activities currently carried out by pharmaceutical companies located in UK
- Competent authorities perspective – UK Rapporteur/RMS

Impact on activities currently based in UK

- MAH (and local representative) must be established in the EU/EEA
- Some activities must be performed in the EU/EEA, e.g. pharmacovigilance, batch release/control

Change of Rappporteur in centralised procedure

- Agreed methodology for the redistribution of work currently carried out by the UK agencies
- EMA to communicate early 2018

Change of RMS in MRP & DCP

- For the initial submission, the applicant chooses the RMS
- Similar approach for change of RMS for authorised products
- MAH to contact one of CMS for their product to act as new RMS
- UK to remain as CMS until time of Brexit when it will become a national MA in the UK
- Not possible to change RMS in an on-going procedure
- Still possible to include UK as CMS

Practical aspects – nationally authorised products (NP, MRP, DCP)

Karolina Westin
Member CMDh/v WP on Variation Regulation, Regulatory Department

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Transfer of MA, CMDh/v Q&A no.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. (NEW:) The transfer of the marketing authorisation must be fully completed and implemented by the marketing authorisation holder before 30 March 2019.

How are MA transfers and change of local representative dealt with in Sweden?

- National notification
- Information including form available on our website:
  - Innehavare av godkännande för försäljning och ombud
  - Change of MAH and Local Representative
- No separate fee
- Normally handled within 90 days

Transfer of MA – Summary of PhVig System

- In case of transfer of a MA in one or more MS the new summary of the pharmacovigilance system (human) or DDPS (veterinary) of the new MAH has to be submitted to all MS concerned via MRP variation (type IA_{IN} notification, C.I.8.a, or under category C.II.7 as applicable)
- *Exception*: A variation to submit the summary of the pharmacovigilance system will not be necessary in cases where the MA is transferred within companies belonging to the same parent company and the same PSMF will continue to be used

  (CMDh/v Q&A on variations no. 2.8)

QPPV - CMDh/v Q&A no. 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).

PSMF - CMDh/v Q&A no. 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).

Manufacturing site finished product - CMDh/v Q&A no.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).

Manufacturing site finished product - CMDh/v Q&A no.7, cont.

- 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).

Batch release site - CMDh/v Q&A no.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).

Product name in package leaflet - CMDh/v Q&A no.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.

Grouping Brexit related changes

- CMDh/v Examples for acceptable and not acceptable groupings for MRP/DCP products:
- **Acceptable groupings:**
- After a member state has triggered an Art. 50 procedure of the Treaty on European Union several changes to the finished product might be necessary, e.g. changes to MAHs, manufacturers for batch release, new summary of pharmacovigilance system (human)/pharmacovigilance system (veterinary) in case of MAH transfers or changes in the product names etc. While the transfer of the MA to a new MAH is an independent purely national application all other changes related to the consequences of this Art. 50 procedure, may be grouped in one application according to the highest variation type for the single changes.

Change of RMS

Adam Andersson
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Current situation

- Approximately 500 UK procedures in MRP/DCP where SE is CMS (400 human, 100 vet)

- SE to initially accept 100 RMS-ships

When to change?

- Transfer of RMS-ship can only be conducted when no other regulatory activity is ongoing
- It is preferable to liaise with the desired new RMS even if procedures are ongoing

- Do not wait!

How to change? (1)

- Contact the MPA via **RIC@mpa.se**

- Information on:
  - Product name and procedure number
  - ATC code
  - Current CMS
  - Ongoing procedures

- CMDh template to be published shortly

How to change? (2)

- The MPA will make a product-specific decision based on the current resource situation

- Intention to respond to all transfer requests within 30 days

Problem: Ongoing procedures

- For many products with UK as RMS, procedures are ongoing or applications submitted but not yet started

- UK prioritizes procedures where RMS transfer requests are pending

- Shortened renewal procedures: positive impact on backlog

Problem: No CMS accepts

- If all CMS in a procedure declines the RMS-ship, contact the CMDh or CMDv
- The CMDh/v will appoint a new RMS

UK reference product for generics

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UK product as ERP - CMDh/v Q&A no.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.
- 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.

MPA recommendation: If possible, avoid UK ERP for submissions already now

UK product in BE studies - CMDh/v Q&A no.11

- **Can medicinal products used in bioequivalence studies be sourced in the UK?**
- Bioequivalence studies that have been conducted with a medicinal product sourced in the UK can be used in generic/hybrid marketing authorisation applications only if the marketing authorisation for that application will be granted before 30 March 2019[3].

[3]*In exceptional cases where bioequivalence studies are intended for use in new applications which will be submitted before 30 March 2019 and if these bioequivalence studies have been already completed the applicants may consider contacting the competent authority to discuss the particular circumstances of their application in order to avoid unnecessary repetition of studies in humans or animals.*

- *Further clarification of this Q&A expected!*