EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Operational and Procedural preparedness update

Agenda point 4
Industry Stakeholder meeting on Brexit and operation of centralised procedure for Human and Veterinary Medicinal Products

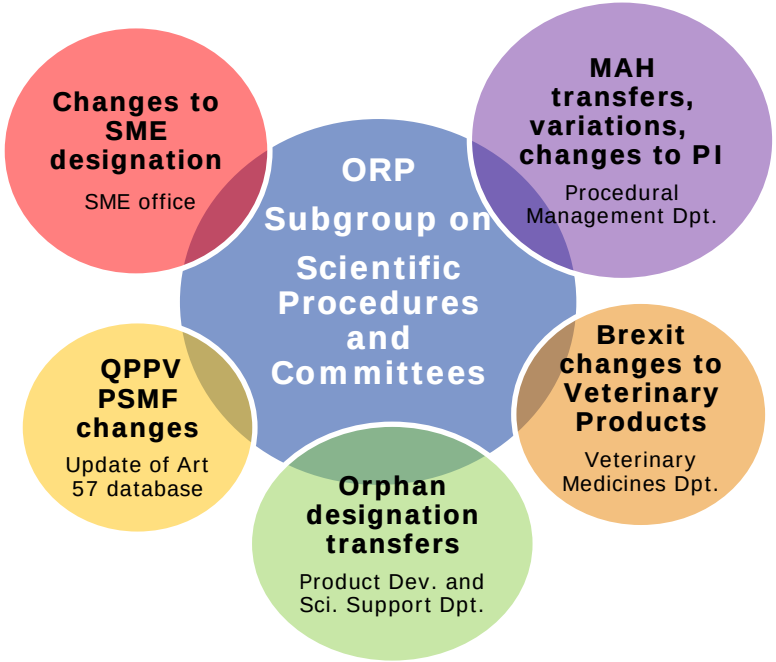
Presented on 28 January 2019 by:
Alberto Ganan Jimenez, Head of Service for Evaluation Procedures Service D
Beyhan Mustafov, Veterinary Regulatory and Organisational Support Service

Topics to be covered

- EMA tracking system of Brexit regulatory submissions
- Update of Brexit preparedness for CAPs for human use
  - MAH transfers, SMEs, transfers for Orphan designation
  - QPPV, PSMF changes
  - Manufacturing changes: Quality control testing, Batch release site, Physical importation, OMCLs
  - Co-Packaged medical devices
  - Status for SME companies
- Update of Brexit preparedness for CAPs for veterinary use

EMA tracking system of Brexit regulatory submissions

- A dedicated team at EMA is monitoring all Brexit related submissions within the different areas across the Organisation.
- The information is compared with forecasts of expected submissions based on Industry feedback from Brexit Survey responses (Jan/Mar 2018), Teleconferences with Applicants (Jul/Sep 2018) and responses to email sent to CAPs with expected upcoming submissions (Dec 2018/Jan 2019).



Update of Brexit preparedness for CAPs for Human use

Human CAPs - MAH Transfers

- There are still **26 centrally authorised products** where MAH is in the UK (**7% of Brexit MAH transfers**). Due to the short timeframe before 29 March 2019, MAHs should submit their MAHs transfers as soon as possible to ensure that a EC decision can take place before Brexit date.
- There are **12 ongoing MAAs** where the applicant is located in the UK (**80% of Brexit applicant transfers**). The need for change of applicant has been included as an "Other Concern" in D120 LoQ or D180 LoOIs. UK Applicants should be changed at the earliest opportunity to avoid any delay in CHMP opinion / EC decision.

Areas to track*	Submitted	Not submitted
MAH transfers for authorised products	365	26
Change of applicants products under MAA	3	12

Cut-off date of 18/01/2019

SMEs registered with EMA

1603 total SMEs registered with EMA*

246 *(15,3%)* UK based SMEs registered with EMA*

32 UK based SMEs have already created a EU27/EEA subsidiary due to Brexit

(***27*** qualified and ***5*** qualifications ongoing)*

Guidance for non-EEA based companies will apply after 29 March 2019

a) Establish a new legal entity in the Union (EEA) and apply for SME status directly

b) Indirectly through an Union (EEA) established SME regulatory consultancy.

* figures as of 22nd January 2019

SME Office support to Brexit related activities

- Mailings on 19th February and 30th July 2018 on guidance to UK based SMEs
- Mailing on 6 December 2018 on deadlines for SA and PA for UK based SMEs
- Individual calls (end 2018) to UK based MAHs to provide guidance and support.
- SME briefing meetings to give guidance to UK based SMEs
- Info day on 26th October 2018 with a session dedicated to Brexit
- Specific section in the SME Newsletter on Brexit related activities and guidance

SMEs based in UK and intending to continue to benefit from SME incentives are advised to contact SME office (sme@ema.europa.eu) for support and guidance.

Human CAPs - Orphan designation transfers

- There are 12 products authorised or under initial MAA with Orphan designation. Applicant should submit the OD transfer as soon as possible to ensure that an EC decision can take place before Brexit date.

Status: 1/1/18 – 15/1/19

- 319 Orphan designation (OD) transfers reviewed by EMA
- 209 OD transfers (66%) were Brexit related (either development product or CAP):
  - 159 transfers correspond to products under development
  - 50 transfers correspond to authorised CAPs

Current Status*

- 2121 EC Orphan designations
- **419** ODs with sponsor located in UK
- 88 Brexit-related OD transfers are ongoing
- 331 ODs with UK-sponsor have so far no transfer initiated
  - **of these 16 pending OD transfers there are 12 that relate to CAPs (authorised or under initial MAA)**

Cut-off date of 15/01/2019

Support to Brexit-related activities for orphan designations

- Mailing on 27 July 2018 to registered contacts for 496 orphan drug designation with UK-based sponsor, with follow-up mailing on 24 October 2018 for remaining 446 designations with UK-based sponsor
- Communication on the orphan webpage ‘Transferring an orphan designation’
- Orphan designations related to authorised orphan medicinal products (including ongoing MAA procedures) are covered by the follow-up on marketing authorisations
- **Important:** Since September 2018 all request for transfers of orphan designations need to be submitted through the IRIS system
  - Some preparatory steps are required (registration of active substance and organisation; availability of an account)
  - For further information see Transferring an orphan designation

Human CAPs - Changes to manufacturing sites

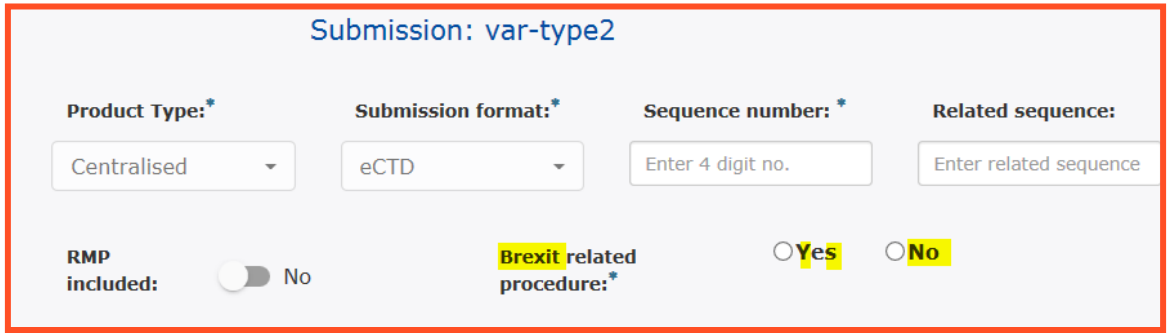
- **76% of CAPs still need to transfer manufacturing site activities** from UK to another EU/EEA Member States and have not yet submitted the variation to EMA. The transfers of these activities should be implemented by 30th March 2019.

Areas to track (UK only) *	Submitted	Not Submitted
Relocation Batch Release activities located in UK	30	79
Transfer of Batch Control activities located in UK for chemical products / biological products	9	45
Addition of physical importation	5	19
Transfer of OMCLs	0	4

*Cut-off date of 18/01/2019

Human CAPs - Changes to manufacturing sites

- Please submit all you Brexit related variations as soon as possible. This will facilitate that they are timely processed and finalised by 29th March 2019.
- Always ensure that the Brexit box is ticked when eSubmision web UI is used (.xml delivery file created) for eCTD submissions.



Human CAPs- Changes to manufacturing sites

- Changes to OMCL should be reported through the submission of a cover letter in a stand alone eCTD sequence. Please see Q17 of EMA Guidance for Brexit procedures
- MAHs should delete the manufacturing activities/sites located in UK that will become non-applicable after the UK becomes a third country (e.g. batch release, batch control for FP, physical importation of UK sites). This should take place within 2 months through the submission of a single A.7 variation (IA).

Human CAPs - QPPV / PSMF changes

- According to our records **387 human CAPs (87%)** still have the QPPV, PSMF or both located in the UK. A number of MAHs have declared that they intend to transfer the PSMF/QPPV to another EU/EEA MS by 29 March 2019.
- The changes to QPPV/ PSMF for Human CAPs should be done through the update of Art. 57 database as soon as possible. If you have done the changes, please do update Art. 57 database.

Areas to track*	Changed	Not changed
CAPS with QPPV and PSMF in UK	41	274
CAPS with PSMF in UK	10	95
CAPS with QPPV in UK	6	18
Total	57	387

Cut-off date of 18/01/2019

Human CAPs- Co-packaged with medical devices

- A mass mailing was sent to **195 MAH contact points (human only)** on 10th-11th December 2018 to request the MAH to confirm whether, for co-packaged device(s), a conformity assessment to support the CE marking was performed by a UK Notified Body and their plans in order to comply with the legal requirements.
- So far **51 CAPs** have been identified with a co-packaged medical device involving a UK Notified Body.
- MAHs are encouraged to find a new Notified Body as soon as possible for the co-packaged device(s) which have involvement with a UK Notified Body.
- Updates to the certificates should be implemented by 29th March 2019 and reported through the submission of the corresponding Type IA variation (see Question 2a EMA Brexit-related practical guidance).

Human CAPs- Update of local representatives in the Package Leaflet

- According to our records, there are still **142 human CAPs (53%)** where the UK representative also acts as local representative of other Member State(s) in the package leaflet.
- The change in package leaflet must be fully completed and implemented by the MAHs before 30th March 2019 either as part of a regulatory procedure affecting the annexes (e.g. variation, renewal), an Art. 61(3) procedure (for human products).
- If this change of local representatives takes place as part of a variation affecting the product information, please tick the Brexit box in the xml. file of the eCTD submission.

Areas to track*	Finalised	Not submitted
CAPs with UK local representatives for other MS	**125**	**142**

**Cut-off date of 18/01/2019*

Update of Brexit preparedness for CAPs for Veterinary use

Veterinary CAPs- MAH Transfers

- There is still **1 centrally authorised product** where MAH is in the UK. Due to the short timeframe before 29 March 2019, the MAH should submit the MAH transfer as soon as possible to ensure that a EC decision can take place before Brexit date.
- There are **no ongoing MAAs** where the applicant is located in UK.

Areas to track*	Submitted	Not submitted
MAH transfers for authorised products	**15**	**1**
Change of applicants products under MAA	**0**	**0**

**Cut-off date of 18/01/2019*

Veterinary CAPs- Changes to manufacturing sites

- **42% of CAPs still need to transfer manufacturing site activities** from UK to another EU/EEA Member States and have not yet submitted the variation to EMA. The transfers of these activities should be implemented by 30 March 2019.

Areas to track (UK only) *	Submitted	Not Submitted
Relocation Batch Release activities located in UK	6	8
Transfer of Batch Control activities located in UK for chemical products / immunological products	0	3
Transfer of OMCLs	5	0

*Cut-off date of 18/01/2019

Veterinary CAPs- QPPV changes

- According to our records, **7 veterinary CAPs (39%)** still have the QPPV located in the UK.
- The changes to QPPV for veterinary CAPs should be updated through a Type IA_{IN} variation or through notification to EMA (Please see Q7 of EMA Guidance for Brexit procedures)

Areas to track*	Changed*	Not changed
CAPS with QPPV in UK	**11**	**7**

**Cut-off date of 18/01/2019*

Veterinary CAPs- Update of local representatives in the Package Leaflet

- According to our records, there are still **15 veterinary CAPs (50%)** where the UK representative also acts as local representative of other Member State(s) in the package leaflet.
- The change in package leaflet must be fully completed and implemented by the MAHs before 30 March 2019, either as part of a regulatory procedure affecting the annexes (e.g. variation, renewal), or through a type IA_{IN} variation (C.II.6.a).

Areas to track*	Finalised	Not submitted
CAPs with UK local representatives for other MS	**15**	**15**

**Cut-off date of 18/01/2019*

Conclusions

Conclusions (1/2)

- EMA has been and will continue to monitor and track the submissions of required changes for **all 728 Brexit affected CAPs.**
- Currently **199 products** have completed all the necessary changes in order to comply with the legal requirements (vs. 65 products in Stakeholders meeting on 24th September 2018)
- MAHs are encouraged to submit all Brexit-related changes as soon as possible in order to facilitate the review by 29th March 2019.

Conclusions (2/2)

- MAHs are reminded of their legal obligations to inform EMA on supply issues and product withdrawals. If any potential disruption in the supply of the medicinal product is foreseen in the EU/EEA after 29th March 2019, please inform EMA as soon as possible and provide information of any measures considered to prevent any product shortages.
- Furthermore, MAHs are requested to timely inform EMA on any changes to their current plans and inform the Agency as soon as they know that the necessary changes will not be able to be done on time by emailing to EMABrexitSurveyFU@ema.europa.eu (cc Procedure manager or for veterinary medicines cc vet.applications@ema.europa.eu).

Thank you for listening

alberto.ganan@ema.europa.eu beyhan.mustafov@ema.europa.eu
European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Follow us on **@EMA_News**