BEST PRACTICE: MANAGING BREXIT RELATED REGULATORY ACTIVITIES

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2 Revision History

When Ennov releases a new version of Ennov InSight, they issue Release Notes which explain the new features and updates. The Ennov Business Consulting Team reviews the Release Notes against each Best Practice to determine any impact to the document:

- Impact = Release notes-documented upgrade changes this Best Practice
- No Impact = Release notes-documented upgrade changes do not affect this Best Practice

When Release Notes impact Best Practice documentation, Ennov recommends that clients review the entire Release Notes for a full understanding of all changes associated with this Best Practice documentation.

Software Version	Release/ Revision Date	Summary of Change(s) (Refer to Release Notes for Full Description)
v7.3.1	28-Jun-2024	Update Best Practice for Ennov rebranding & for v7.3.1 – No Impact
v7.2	20-Jun-2023	Update Best Practice for v7.2 – No Impact
v7.1	13-Jan-2022	Update Best Practice for v7.1 – No Impact
v7.0	25-May-2021	Update Best Practice for v7.0 – Impact
v6.2 CHF2	15-Feb-2019	Update Best Practice for v6.2 CHF2 – No Impact

3 Document Purpose & Scope

Following the decision of the United Kingdom (UK) to leave the European Union (EU), there are numerous actions required to ensure that the UK is no longer responsible for regulatory activities on behalf of the EU. To be compliant with EU legislation, submissions to transfer the responsibility from the UK to an EU (EEA) country will be required. To effectively plan and track these activities in Ennov InSight, updates to existing records and the creation of new records will be required including: Applications, Events, Product Detail Sets, Sequences, and Assemblies. For each Regulatory Activity described in this document, Planning and Tracking and Publishing steps have been identified. Those organisations that are not using Ennov InSight Publisher need not carry out any of the activities related to Publishing.

4 Transfer of UK based Orphan Designation Holder for EU Centralised Products

Planning and Tracking Actions	Publisher Actions
1. Create a Transfer of Orphan Designation Event under the impacted EU Centralised Applications. Note: Where there are multiple Applications impacted, use the Global Project Plan functionality. 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Create Sequences. 4. Update Event Country Status on Submission and Approval. 5. Close Event on Approval. 6. Create References to link to Agency Correspondence.	1. Create a Transfer of Orphan Designation Event under the impacted EU Centralised Applications. 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.] An application for transfer of orphan designation has to be submitted, preferably, in advance of or at the latest in parallel with the application for transfer of the marketing authorisation, since the opinion on the orphan designation transfer has to be reached before the opinion on the marketing authorisation transfer. In order to facilitate handling of a large volume of orphan designation transfer applications from a current UK-based sponsor to a new sponsor in EEA, a combined version of each required supportive document (except product specific information) can be created covering all orphan designations affected. In such case the combined submission of transfer applications should consist of: 1. A cover letter listing all orphan designations to be transferred and confirming that supportive documents are identical, with the exception of product specific transfer forms and translations; 2. A proof of establishment of the new sponsor in the Union (EEA); 3. A letter of authorisation from the new sponsor, when applicable; 4. Separate product transfer form for each orphan designation; 5. Separate translations document for each orphan designation, when applicable.

5 Transfer of the MUMs (MUMS (Minor Use Minor Species/limited market) status for UK based Companies for EU Centralised Products

Planning and Tracking Actions	Publisher Actions
1. Create a transfer of the classification product and the MUMS/limited market classification Event under the EU Centralised Application. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Create Sequences. 4. Update Event Country Status on Submission= and Approval. 5. Close Event on Approval. 6. Create References to link to Agency Correspondence.	1. Create a transfer of the classification product and the MUMS/limited market classification Event under the EU Centralised Application 2. Create Sequence. 3. Create (Working) Assembly. For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.] To formally acknowledge the transfer, the EMA requires a letter from the original sponsor/applicant officially informing the EMA of the transfer of the classification product and the MUMS/limited market classification from the original sponsor/applicant to a sponsor/ applicant established in the Union (EEA). This letter should state the document reference number of the MUMS outcome letter confirming the MUMS classification.

6 Transfer of Qualified Person for Pharmacovigilance (QPPV) based in the UK for EU Centralised Products

Planning and Tracking Actions	Publisher Actions
1. Update QPPV details in Article 57 Database (XEVMPD). 2. Enter the new QPPV value & EV Code in Data Administration. 3. Update the QPPV, Enquiry Email, and Enquiry Phone Number fields for each impacted Registration, as applicable.	N/A
1. Create a Variation Event under the impacted EU Centralised Applications. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Create Sequences. 4. Update Event Country Status on Submission and Approval. 5. Close Event on Approval. 6. Create References to link to Agency Correspondence.	7. Create a Variation Event under the impacted EU Centralised Applications. 8. Create Sequences. 9. Create (Working) Assembly. [For SPT or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.] For veterinary medicinal products, where a DDPS is authorised as part of the marketing authorisation (or a subsequent extension procedure), a change in QPPV should be submitted via a Type IAIN variation application (classification C.I.9.a), provided that the pharmacovigilance system itself remains unchanged. In all other cases, the change in QPPV can be notified to the EMA exclusively in writing on company headed paper and sent to vet.applications@ema.europa.eu.

7 Transfer of Pharmacovigilance System Master File located in the UK for EU Centralised Products

Planning and Tracking Actions	Publisher Actions
1. Enter the new Master File Location value in Data Administration. 2. Update the MFL fields for each impacted Registration, as applicable. 3. Submit Change to Article 57 Database (XEVMPD).	N/A

8 Transferring the UK based applicant to a non-UK based applicant for an ongoing EU Centralised marketing authorisation application

Planning and Tracking Actions	Publisher Actions
1. Create an Event under the impacted EU Centralised Applications. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Sequences. 3. Update Event Country Status on Submission and Approval. 4. Close Event on Approval. 5. Update Applicant ID on the Application. 6. Create References to link to Agency Correspondence.	1. Create an Event under the impacted EU Centralised Applications. 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.] To request a change of the applicant, the following documents need to be submitted as part of responses to the Day 120 List of Questions or Day 180 List of Outstanding Issues so that by 29 March 2019 the change is implemented: 1. A letter requesting the change of applicant and signed by both the previous and the new applicant. 2. Either a confirmation (as part of the cover letter) that this marketing authorisation application does not fall under the scope of a duplicate application as per Article 82 of the Regulation (EC) No 726/2004 or the relevant authorisation from the European Commission in case the application falls under the scope of a duplicate application as described above. 3. A confirmation (as part of the cover letter) that complete and up-to-date file concerning the medicinal product or a copy of this file (including any data/documents related to the paediatric obligations, if applicable) has been made available to or has been transferred to the new applicant. 4. If applicable, a confirmation (as part of the cover letter) that the orphan designation has been transferred or request for its transfer has been made.

Planning and Tracking Actions	Publisher Actions
	5. If applicable, a confirmation (as part of the cover letter) that the minor use/minor species (MUMS)/limited market classification has been transferred or notification for its transfer has been made. 6. Updated application form and affected annexes (includes proof of establishment of the new applicant within the Union (EEA) issued in accordance with national provisions and which should be no older than 6 months). 7. Updated product information. 8. Updated mock-ups or a confirmation that that the mock-ups remain unchanged with the exception of the new name/address of the proposed MAH. 9. Updated summary of the pharmacovigilance system master file (PSMF). 10. Any other documents of the marketing authorisation dossier affected by the change of applicant, as relevant (e.g. an updated Letter of Access for an application that includes an Active Substance Master File). To facilitate the process for the change of applicant, for the confirmations to be included in the cover letter, the applicants are advised to use the standard statements in this template.

9 Registering a finished product manufacturing site in the UK as an authorised importer for EU Centralised Products

Planning and Tracking Actions	Publisher Actions
1. Create Variation Event under the impacted EU Centralised Applications to register the UK as an authorised importer within the EEA. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Create Sequences. 4. Associate Product Detail Set and update the Manufacturer as appropriate (may require Data admin updates). 5. Update Event Country Status on Submission. 6. QC PDS Details on Approval. 7. Update Event Country Status and Close Event on Approval. 8. Create References to link to Agency Correspondence. *Note: As per organisational requirements, create a UK National Import Licence Application.*	*Note: As per organisational requirements create a UK National Import Licence Application.* 1. Create Variation Event under the impacted EU Centralised Applications to register the UK as an authorised importer within the EEA. 2. Create Sequence. 3. Create (Working) Assembly. [For SPT or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.]

10 Transfer the UK based Batch Control Site to a Batch Control Site in the EAA for EU Centralised Products

Planning and Tracking Actions	Publisher Actions
1. Create Variation Event under the impacted EU Centralised Application to transfer the UK based Batch Control Site and register a Batch Control Site in the EEA. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Associate Product Detail Set and update the Manufacturer as appropriate (may require Data admin updates). 4. Create Sequences. 5. Update Event Country Status on Submission. 6. QC PDS Details on Approval. 7. Update Event Country Status and Close Event on Approval. 8. Create References to link to Agency Correspondence.	1. Create Variation Event under the impacted EU Centralised Application to transfer the UK based Batch Control Site and register a Batch Control Site in the EEA. 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.]

11 Transfer the UK based Batch Release Site to a Batch Release Site in the EAA for EU Centralised Products

Planning and Tracking Actions	Publisher Actions
1. Create Variation Event under the impacted EU Centralised Applications to transfer the Batch Release Site based in the UK. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Associate Product Detail Set and update the Manufacturer as appropriate (may require Data admin updates). 4. Create Sequences. 5. Update Event Country Status on Submission. 6. QC PDS Details on Approval. 7. Update Event Country Status and Close Event on Approval. 8. Create References to link to Agency Correspondence.	1. Create Variation Event under the impacted EU Centralised Application(s) to transfer the Batch Release Site based in the UK 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.]

12 Reviewing marketing related information in respect to the Sunset Clause

Planning and Tracking Actions	Publisher Actions
1. Navigate to Querying. 2. Open the Product Detail Set Management Tab. 3. Open the Sunset Clause Marketing Status Query. 4. In the Search Criteria screen enter as required: 5. Product Family 6. Product 7. Package Set 8. Procedure Type 9. Select Search. 10. Export Search Results to Excel.	N/A

13 Managing Updates to Local Representatives located in the UK

Planning and Tracking Actions	Publisher Actions
1. Create a new Event under the EU Centralised Application (Variation, Renewal or 61(3) Notification). 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Associate Product Detail Set and update the Label node to link to the new version of the Product Information (Patient Information Leaflet). 4. Create Sequences. 5. Update Event Country Status on Submission. 6. QC PDS Details. 7. Close Event on Approval. 8. Create References to link to Agency Correspondence.	1. Create a new Event under the EU Centralised Application (Variation, Renewal or 61(3) Notification). 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.] The corresponding amendments to labelling and package leaflet must be fully completed and implemented by the marketing authorisation holder before 30 March 2019, either as part of a regulatory procedure affecting the annexes (e.g. variation, 1. Create a new Event under the EU Centralised Application if required (Variation, Renewal or 61(3) Notification) 2. Associate Product Detail Set and update the Label node to link to the new version of the Product Information n/a renewal), or through a notification under an Article 61(3) of Directive 2001/83/EC or (for veterinary products) through a Type IAIN variation (see Variation Guideline (2013/ C 223/01), classification C.II.6.a.

14 Transferring UK Notified Bodies to an EEA Market for Medical Devices

Planning and Tracking Actions	Publisher Actions
1. Create a new Event under the EU Centralised Application (Variation, Renewal or 61(3) Notification). 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Create Sequences. 4. Update Event Country Status on Submission and Approval. 5. Create References to link to Agency Correspondence. 6. For Clients that record the Notified Body in Ennov InSight ensure it is updated accordingly.	The manufacturer has to submit a Transfer of NB request letter(submission). The new NB will re-audit and re-certify the manufacturer. 1. Create a Transfer of NB to an EEA Market for MD Event under the impacted Applications. 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.] When transferring NBs, the manufacturer should include in their file: 1. All current cycle audit reports from the previous notified body, including the report of any nonconformities and the action plan to fix any non-conformities and the EC product reports (Type examination, Design Examination); 2. All appropriate EC certificates; 3. A letter from the manufacturer effectuating the transfer; and 4. A report of any adverse events, like customer complaints and recalls, since the last audit.

15 Change of Sponsor for Clinical Trials Conducted in the EEA

Planning and Tracking Actions	Publisher Actions
1. Create a Substantial Amendment Event under the impacted Clinical Trial Applications. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Update Event Country Status on Submission and Approval. 4. Close Event on Approval. 5. Create References to link to Agency Correspondence. 6. Update the Sponsor recorded on the Clinical Trial Applications. *Note: Where there are multiple Applications impacted, use the Update Application Wizard to update the Sponsor.*	1. Create a Substantial Amendment Event under the impacted Clinical Trial Applications. 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.]

16 Change of Release Site of the Finished Product of the Investigational Medicinal Product in the EEA (manufacturer or importer)

Planning and Tracking Actions	Publisher Actions
1. Create a Substantial Amendment Event under the impacted Clinical Trial Applications. *Note: Where there are multiple Applications impacted, use the Global Project Plan functionality.* 2. Create Change and Change Details as per organisational requirements and associate the Change Details with the Events. 3. Update Event Country Status on Submission and Approval. 4. Close Event on Approval. 5. Create References to link to Agency Correspondence.	1. Create a Substantial Amendment Event under the impacted Clinical Trial Applications. 2. Create Sequence. 3. Create (Working) Assembly. [For SPT clients or enterprise licenses, please refer to the Planning and Tracking Actions for additional steps.]