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Patient Health Protection

Practical guidance on the extension of Commission Decision Annexes in the new Accession Country language

This Guidance outlines practical considerations concerning the phasing-in of Commission Decisions concerning CAPs in Croatia.

Marketing Authorisation Holders are legally obliged to provide translations of the product information in the new official language as of the date of accession. In order to facilitate the phasing-in of Commission Decisions related to the EU centralised procedure, a voluntary pre-accession checking procedure for Annex I, II, III and IV, if applicable, has been set up in cooperation with the National Competent Authorities (NCA) of the new MS. See information on our web-site under the European Union enlargement page.

This Guidance document provides further details on the inclusion of the new language and new specimens into the operational aspects of the centralised procedure. For general guidance on the handling of new applications and post-authorisation procedures and more practical aspects of the submission requirements of Annexes, please refer to the respective Pre-Submission and Post-Authorisation Guidance Documents published on the EMA Website.

Applicants/MAHs are advised to systematically discuss the best approach for their product(s) with their Product Team Leader/Project Manager, especially for Regulatory Procedures which will finalise before or around enlargement.

Provision of new language version of the Commission Decision Annexes

It is considered that 3 possibilities emerge as described below (see also tabulated summary in Appendix 1):

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CAPs with ongoing regulatory activity, with opinion before Croatia's accession date (i.e. Commission Decision expected on or after Croatia's accession date)

Commission Decisions issued as of the accession date for Croatia will legally be required to be addressed to all MSs of the EU, including Croatia. This will have direct consequences for both new applications for a centralised MA as well as for any post-authorisation application for existing CAPs. Applicants/MAHs are advised that they will be requested to provide translated annexes in all 23 official languages of the EU (+ IS/NO) for all CxMP Opinions which will be issued within 3 months prior to the accession date, so as to allow the Commission to address a Decision to all Member States as of the accession date for Croatia.

For both new and ongoing applications a post-opinion linguistic check will be conducted in cooperation with the NCA of the new MS, as part of the usual post-opinion procedures.

The following requirements will apply for the different types of applications:

1. New applications and extension applications will follow the linguistic checking procedure for human medicinal products and for veterinary medicinal products, which will now include 23 languages (+ IS/NO).

   For new product applications, applicants are required as of 3 months prior to the accession date (CHMP & CVMP) to provide translations in all languages (incl. AC language) of Annex I, II, III, and IV/127a, if applicable as provided by the QRD Product Information templates[1] , as well as Annex A, after adoption of the Opinion. The current post-opinion procedures will apply.

   After adoption of an Extension Opinion as of 3 months prior to the accession date (CHMP & CVMP), MAHs are required to provide translations in all languages (incl. AC language) of the complete set of annexes and the Annex A (if amended). A 'complete set of Annexes' includes Annex, I, II, IIIA and IIIB and IV/127a i.e. all SmPC, labelling and PL texts for all strengths and pharmaceutical forms of the product concerned, as well as Annex II and Annex IV/127a, as appropriate.

   MAHs should highlight the differences of the Extension versus the current EU authorised presentations in order to facilitate the linguistic review. MAHs should complete the list of Local Representatives for the AC in the PL in all language versions of all product presentations as part of the extension application. If such change was however not initially covered in the application, the EMA will allow that such change is introduced before finalisation of the Opinion / Decision concerned.

   MAHs should include a reference in the cover letter to the status of the voluntary pre-accession linguistic check *i.e.* date of completion/submission and procedure numbers of text versions agreed. If other changes have occurred in the AC translations of the existing presentations since the pre-accession check, such changes should also be highlighted in the relevant Annexes in this language. In addition, a reference to the latest procedure number reflected in the updated translations compared to the versions agreed during the pre-accession linguistic check must be included.

   Where such pre-accession check has not taken place, MAHs must be aware that the existing post-opinion linguistic checking procedures may not be sufficient for the new MS to review the complete product information within the available timeframes. It must therefore be envisaged that for products without pre-accession check, delays in the post-opinion transmission phase to the EC could occur pending finalisation of the translations check.

[1] Updated QRD Product Information templates including Annex I, II and III and reflecting the full list of local representatives are available on the EMA Website.

2. For **Type II variations**, for which a CxMP Opinion will be adopted as of 2 months prior to the accession date, the following requirements will apply. At submission (variations with a 30-day TT) or after adoption of a Type II Opinion (variations with a 60 or 90-day TT), MAHs are required to provide translations in all languages (incl. AC language) of the complete set of annexes.

   A 'complete set of Annexes' includes Annex, I, II, IIIA, IIIB and IV/127a i.e. all SmPC, labelling and PL texts for all strengths and pharmaceutical forms of the product concerned, as well as Annex II and Annex IV/127a as appropriate. MAHs should highlight the changes introduced during the variation procedure in order to facilitate the linguistic review.

   MAHs should complete the list of Local Representatives for the AC in the PL in all language versions as part of the variation procedure. If such change was however not initially covered in the 'scope' of the variation concerned, the EMA will allow that such change is introduced in the PL before finalisation of the Opinion / Decision concerned.

   MAHs should include a reference in the cover letter to the status of the voluntary pre-accession linguistic check *i.e.* date of completion and procedure numbers of text versions agreed. If other changes have occurred in the AC translations of the existing presentations since the pre-accession check, such changes should also be highlighted in the relevant Annexes in this language. In addition, a reference to the latest procedure number reflected in the updated translations compared to the versions agreed during the pre-accession linguistic check must be included.

   Where such pre-accession check has not taken place, MAHs must be aware that the existing post-opinion linguistic checking procedures may not be sufficient for the new MS to review the complete product information in addition to the amended text parts related to the application concerned within the available timeframes. It must, therefore, be envisaged that for products without pre-accession check, delays in the post-opinion transmission phase to the EC could occur pending finalisation of the translations check.

3. For **Type IA/IA$_{IN}$ and IB variations**, the new Variation Regulation does not provide for an updating of the Commission Decision following each Type IA/IB procedure, but rather on a yearly basis for Type IA and IB variations.

   MAHs are advised that as of one month prior to the accession date, the complete set of annexes should include the additional AC language versions for Type IA and Type IB Notifications affecting the product information (see also 'EMA Post-Authorisation Guidance'). In addition, the list of Local Representatives in the PL should be completed for the AC.

4. For **Renewals**, for which a CxMP Opinion will be adopted as of 3 months prior to the accession date, MAHs are required to provide translations in all languages (incl. AC language) of the complete set of annexes after adoption of the CxMP opinion on the renewal. A 'complete set of Annexes' includes Annex, I, II, IIIA, IIIB and IV *i.e.* all SmPC, labelling and PL texts for all strengths and pharmaceutical forms of the product concerned, as well as Annex II and IV if applicable.

   MAHs should highlight the changes introduced during the renewal procedure in order to facilitate the linguistic review.

   MAHs should complete the list of Local Representatives for the AC in the PL in all language versions as part of the renewal procedure. MAHs should include a reference in the cover letter to the status of the voluntary pre-accession linguistic check *i.e.* date of completion and procedure numbers of text versions agreed. If other changes have occurred in the AC translations of the existing presentations since the pre-accession check, such changes should also be highlighted in the relevant Annexes in this language. This includes any changes resulting from the updating of the

product information in line with the new QRD templates. In addition, a reference to the latest procedure number reflected in the updated translations compared to the versions agreed during the pre-accession linguistic check must be included.

Where such pre-accession check has not taken place, MAHs must be aware that the existing post-opinion linguistic checking procedures may not be sufficient for the new MS to review the complete product information in addition to the amended text parts related to the application concerned within the available timeframes. It must be therefore envisaged that for products without pre-accession check, delays in the post-opinion transmission phase to the EC could occur pending finalisation of the translations check.

For **Annual Re-Assessment** procedures, MAHs are advised to contact the EMA Product Team Leader/Project Manager in order to discuss the best approach for the product concerned, in view of possible other ongoing/imminent regulatory procedures where the provision of AC translations could be addressed.

5. **Transfer** procedures: at submission of transfer applications as of 2 months prior to the accession date, MAHs are required to provide translations in all languages (incl. AC language) of the complete set of annexes. A 'complete set of Annexes' includes Annex I, II, IIIA,IIIB and IV/127a *i.e.* all SmPC, labelling and PL texts for all strengths and pharmaceutical forms of the product concerned, as well as Annex II and Annex IV/127a as appropriate.

   MAHs should highlight the changes introduced during the transfer procedure.

   MAHs should complete the list of Local Representatives for the AC in the PL in all language versions as part of the transfer procedure.

   MAHs should include a reference in the cover letter to the status of the voluntary pre-accession linguistic check *i.e.* date of completion and procedure numbers of text versions agreed. If other changes have occurred in the AC translations of the existing presentations since the pre-accession check, such changes should also be highlighted in the relevant Annexes in this language. In addition, a reference to the latest procedure number reflected in the updated translations compared to the versions agreed during the pre-accession linguistic check must be included.

   Where such pre-accession check has not taken place, MAHs must be aware that delays in the transmission of the documents to the EC could occur pending finalisation of the translations check.

6. For **Arbitration / Referral** procedures, Applicants/MAHs are required as of 3 months prior to the accession date (CHMP & CVMP) to provide translations in all languages (incl. AC language) of Annex I (list of products) and Annex III (SmPC, labelling and package leaflet text) in accordance with the QRD Referral Product Information templates, after adoption of the Opinion. The current post-opinion linguistic checking procedures will apply.

7. For **PSUR** procedures where the CHMP adopts an opinion on the variation of the marketing authorisation, MAHs are required as of 3 months prior to the accession date (CHMP) to provide translations in all languages (incl. AC language) of the complete set of annexes. A 'complete set of Annexes' includes Annex, I, II, IIIA, IIIB and IV i.e. all SmPC, labelling and PL texts for all strengths and pharmaceutical forms of the product concerned, as well as Annex II and Annex IV (Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation).

CAP with ongoing/imminent regulatory activity (CxMP Opinions) after Croatia's accession date

In principle once accession occurs any further regulatory action on CAPs e.g. renewals, variations, line extensions, annual reassessments etc. are legally required to be addressed to all Member States. This implies that any final CxMP opinion after Croatia's accession date which is addressed to the Member States as well as EMA Notifications need to include relevant annexes in all Community languages. Unless such obligation is fulfilled further regulatory action on such products will be blocked / delayed.

In support of this process the MAH would be asked to supply similar elements as outlined in (i) above upon adoption of the opinion or finalisation of the procedure. These would then be processed as per the normal Decision Making Process and the product could be released on the market once the Commission Decision has been made.

CAP with no ongoing regulatory activity

It is likely that there will be MAHs who are currently marketing CAPs under a national license in the new Member State who wish to introduce the product switchover as quickly as possible in order to maintain supply continuity. Alternatively there may be MAHs who would wish to launch their product in the new Member State for the first time as soon as possible upon accession. In order to facilitate this access an Article 61(3) type Notification can be submitted to the EMA[2] . The scope of such a Notification could be "inclusion of additional local representatives of the MAH for the new MS". This would affect all language versions of the PL, including the new language.

However, a notification according to Art. 61(3) only covers labelling and/or PL. In order to allow the provision of a complete set of up-to-date product information in the new language for such a notification procedure, it has been agreed to exceptionally allow the inclusion of all SmPC, Annex II and labelling texts as part of the Notification (*see also below*). However, no changes should be introduced to the SmPC and Annex II (i.e. updating of the product information according to the latest QRD templates is not possible as part of this procedure).

In addition, MAHs should take this Notification as an opportunity to update the new language versions (which have been subject to the voluntary pre-accession linguistic check) in line with the latest EN approved text versions. This will ensure that all language versions included with the Notification will reflect the same reference EN text.

For such Notification procedure, MAHs are required to provide translations in all languages (incl. AC language) of the complete set of annexes. A 'complete set of Annexes' includes Annex, I, II, IIIA, IIIB and IV/127a *i.e.* all SmPC, labelling and PL texts for all strengths and pharmaceutical forms of the product concerned, as well as Annex II and IV/127a as appropriate. A declaration should be provided that no changes have been introduced in the SmPC, Annex II (and labelling, where appropriate).

MAHs should include in the cover letter a reference to the status of the voluntary pre-accession linguistic check *i.e.* date of completion and procedure numbers of text versions agreed. If other changes have occurred in the AC translations of the existing presentations since the pre-accession check, such changes should also be highlighted in the relevant Annexes in this language. In addition, a reference to the latest procedure number reflected in the updated translations compared to the versions agreed during the pre-accession linguistic check must be included.

Upon receipt of the above elements EMA would organise or confirm the status of the linguistic check and issue a Notification. The EMA Notification will be sent to the Commission. The changes to the

[2] Only applicable to Human medicinal products. For Veterinary products the EMA would send an appropriate notification to the Commission

Annexes introduced via the Art 61(3) notifications will be reflected in a Commission Decision in the framework of the next Regulatory procedure relating to the Marketing Authorisation concerned.

Art 61(3) Notifications may be processed within 90 days of receipt, but significantly shorter review times e.g. 60 days or 30 days could be envisaged. Where a pre-accession linguistic check has been finalised and no additional changes have been introduced, such notifications could exceptionally be submitted prior to the actual accession date, e.g. as of 2 months prior to the accession date, to allow formal EMA "sign-off" shortly after the accession date thereby removing any administrative delays to the switchover process. Where such pre-accession check has not taken place, MAHs must be aware that delays in the issuance of the EMA Notification could occur pending finalisation of the translations check.

In the **absence of any regulatory activity** within 24 months of the accession of Croatia, an Article 61(3) Notification will have to be finalised for all such products to provide these translations to the EMA. It is in the public interest to address this situation for all CAPs after the accession in view of the public information sources (EPARs/Community Register) and potential to access such products through other regulatory routes notwithstanding the legal obligation of the MAH to provide such translations as of the Accession.

Note on Generic/Hybrid/Informed Consent (IC) centrally authorised medicinal products

Marketing Authorisation Holders of reference medicinal products on which centrally authorised **Generic/Hybrid/IC** medicinal products have been based are advised on the following: considering that the product information of the reference medicinal product is generally the driver for amendments impacting on the product information of the respective generic/hybrid/IC products, MAHs of the reference products are advised to try to use the earlier slots of the process to submit their Croatian translations. The first Croatian translation received by the Agency will be the one sent to the Croatian authorities for review and will also be used as the reference text for the rest of generic/hybrid/IC products as well as for the reference one.

Once the full review of the first Croatian translation received is finalised, the EMA will proactively inform the rest of affected MAHs and will provide them with the approved text to be used as the basis of their translations. These will need to be clearly highlighted to indicate which parts of the annexes are different so that the Croatian NCA can focus on the review of those differences.

Provision of specimens for the Accession Country to the EMA

- Please note that the current policy applied for mock-ups/specimens for human medicinal products can be found on our web-site under the Mock-ups and Specimens page.

  Please note that the current policy applied for mock-ups/specimens for veterinary medicinal products can be found on our web-site under the Application guidance page.

Table 1. Overview of translation requirements for the phasing-in process of the new Accession Country language *Appendix 1*

Requirement to submit a 'complete set of Annexes' in all languages (incl. AC language)	New Application	Extension	Type II Variation	Type IA and IB	PSUR	Renewal	Art. 61(3) Notification	Transfer
Submission at time of application			√ (30-day TT) 2 months prior to the accession date	√ 1 month prior to the accession date			√	√ 2 months prior to the accession date
Submission after Opinion	√ 3 months prior to the accession date	√ 3 months prior to the accession date	√ (60/90-day TT) 2 months prior to the accession date		√ 3 months prior to the accession date when CHMP adopts an opinion on the variation of the MA	√ 3 months prior to the accession date		
Declaration that no changes have been introduced in the SmPC, Annex II (and labelling, where the notification only concerns PL)							√	
Changes due to the actual application/procedure concerned must be highlighted in the text		√	√	√	√	√	√	√
Full list of local	√	√	√	√	√	√	√	√

Requirement to submit a 'complete set of Annexes' in all languages (incl. AC language)	New Application	Extension	Type II Variation	Type IA and IB	PSUR	Renewal	Art. 61(3) Notification	Transfer
representatives must be included in the PL (where such list is provided)								
Details on status of the voluntary pre-accession check	√	√	√	√	√	√	√	√
Changes introduced in the new language since the pre-accession check must be highlighted in the text[3]	√	√	√	√	√	√	√	√

[3] *i.e.* changes from any finalised procedures which were not yet provided and checked for the AC language versions as part of the pre-accession linguistic check.